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6th WORLD PARKINSON CONGRESS ABSTRACTS

Pre-Congress Courses

PCO1

Talk 1: Continuous enteral levodopa and Parkinson's
*David Standaert**
University of Alabama at Birmingham, Birmingham, AL, United States

Continuous enteral levodopa is a treatment used in advanced Parkinson disease. It is currently approved in the US as well as many countries in Europe and Asia. The technology consists of a gel which contains a carbidopa/levodopa suspension, and a pump system which delivers the gel to the intestines. The main indication for the use of carbidopa/levodopa intestinal gel infusion is to treat wearing off symptoms which develop with ordinary oral carbidopa/levodopa tablets. We will review the technology, summarize the clinical data supporting the use of this treatment, discuss scenarios in which it is likely to be beneficial, and review the complications and limitations of this approach.

PCO2

Talk 2: Apomorphine & Parkinson's
*Cecilia Peralta**
CEMIC University Hospital, Autonomous City of Buenos Aires, Buenos Aires, Argentina

Living day to day with Parkinson's disease (PD) in the advanced phase of the disease can be challenging due to motor fluctuations and dyskinesias. Apomorphine, a short-acting D1- and D2-like receptor agonist, has shown in several open label and placebo-controlled clinical trials, to provide a rapid and effective relief of unpredictable "off periods" by using intermittent apomorphine injection. Newer formulations such as continuous apomorphine infusion (CSAI) showed even higher reductions, nearly 50%, of the daily "off" time.
The use of patch pumps of small size and weight have also been applied to CSAI, requiring novel apomorphine formulations with enhanced solubility.
The TOLEDO trial, the first-randomized, placebo-controlled, double-blind, multi- center trial to assess apomorphine subcutaneous infusion in patients with PD, demonstrated that apomorphine significantly reduced "off" time compared to placebo and allowed additional reductions of oral antiparkinsonian medications.
Moreover, dyskinesia reduction appeared more pronounced in patients using CSAI, since improvements in dyskinesia usually correlate with the decrease of oral medication.
Open-label studies investigated the effects of apomorphine on non-motor symptoms, as well as the Euroinf study, which showed improvement in sleep, mood, gastro- intestinal and urinary domains, that may occur as a consequence of "off" time reduction. Additionally, apomorphine therapy seems to be less associated with impulse control disorders.
The main administration route for apomorphine has been subcutaneous. However, alternative apomorphine delivery strategies include sublingual formulation, that is easily administered. This novel formulation consists of a two-film strip that contains apomorphine, has been shown to reliably revert "off" periods in clinical trials and a reduction of 32.4% in dyskinesias.
Regarding new formulations under investigations, pulmonary delivery has the potential of very rapid entry into the systemic circulation, that is an attractive strategy to achieve rapid effect to "rescue" patients from "off" periods. An apomorphine powder formulation for delivery via an inhaler device has been developed and used, which proved well-tolerated, however, efficacy was limited.
Oral apomorphine is considered infeasible because of the almost complete first-pass hepatic metabolism of the molecule. The administration of apomorphine and its prodrug (dipalmitoyl apomorphine) via oral lipid-based formulations has recently been reported in animal models of PD.

PCO3

Talk 1: Role of anti-synuclein therapies
*Tiago Outeiro**
University Medical Center Gottingen, Göttingen, Deutschland (DEU), Germany

The aggregation of alpha-synuclein (ASYN) in Lewy bodies and Lewy neurites is the typical pathological hallmark of Parkinson's disease (PD) and other synucleinopathies. Furthermore, mutations in the gene encoding for ASYN are associated with familial and sporadic forms of PD, suggesting this protein plays a central role in the disease. Therefore, there has been great interest in targeting ASYN as a possible therapy for PD and other synucleinopathies.
In this presentation, I will present the reasoning for why ASYN might be a valid target, and some of the most promising approaches used to target ASYN. I will discuss the successes and failures, and what we might expect from ongoings efforts.

PCO4

Talk 2: Role of LRRK2 inhibitors
*Andrew West**
Duke University, Durham, NC, United States

Genetic studies have identified variants in the LRRK2 gene as important contributors to the risk of developing Parkinson's disease (PD). Biochemical and emergent biomarker studies have coalesced around LRRK2 kinase hyperactivation in disease. As LRRK2-targeting therapeutics make their way into efficacy trials to slow the progression of PD, important questions that will be disucssed include which PD patients might expect the most benefit from LRRK2 inhibition, what type of benefit might be expected, what the underlying bioloigcal mechanisms might be, and whether long term LRRK2 kinase inhibition is safe. Evidence from the last two-decades of bench research that argues in favor of targeting LRRK2 kinase activity in disease will be presented, as well as caveats and counter-indications that should be considered. This talk will then summarize findings from current PD models with respect to LRRK2 kinase activity in disease, what major knowledge gaps remain, and how observations in the clinic from the newest therapuetic trials might retro-translate back to the bench to facilitate better preditive pre-clinical research.

PCO5

Talk 3: Role of anti-inflammatory drugs
*Etienne Hirsch**
INSERM, CNRS, Sorbonne Université, Paris Brain Institute, Paris, France

Parkinson disease is a progressive and debilitating disorder which has so far eluded attempts to develop disease modifying treatment. Both epidemiological and genetic studies support a role of neuroinflammation in the pathophysiology of Parkinson disease. Post mortem studies and experimental analyses suggest the involvement of both innate as well as adaptive immunity in the degenerative process. There is also some circumstantial evidence for effects of immune therapies on the disease. Numerous epidemiological studies have used retrospective approaches to determine whether the use of anti-inflammatory drugs is associated with reduced risk of developing PD. Most of these studies have examined the commonly used non-steroidal anti-inflammatory drugs (NSAID's) but the results are still controversial. Furthermore, when anti-inflammatory therapies should be introduced, which arm of the inflammation should be targeted remains to be determine. Even more importantly, whether neuroinflammation is a primary mechanism in neurodegeneration or a secondary event triggered by another event such a protein misfolding is still unknown. All these unanswered questions will be discussed in the presentation.

PCO6

Talk 2: Imaging approaches to early diagnosis of PD
*A. Jon Stoessl**
Pacific Parkinson's Research Ctr., University of British Columbia, Vancouver, BC, Canada

In the typical outpatient setting, the diagnosis of PD is clinical and does not require neuroimaging, which is usually performed to rule out other Parkinson 'look-alike' conditions. However, the diagnosis can be challenging in early stages, and a purely clinical approach requires careful follow-up, so a high-quality structural MRI may be useful. Dopamine-based imaging with SPECT or PET can reliably differentiate between neurodegenerative parkinsonism (i.e. loss of dopamine) and health, as well as other conditions that could be mistaken for PD (e.g. essential tremor) and other non-degenerative causes of parkinsonism (e.g. medication-induced). However, dopaminergic imaging does not reliably differentiate between PD and other degenerative forms of parkinsonism such as multiple system atrophy (MSA) or progressive supranuclear palsy (PSP) and these are the usual sources of diagnostic difficulty. PET scans to assess glucose metabolism may be useful for this purpose, as the pattern of abnormality is relatively unique to each of these conditions. Increasingly, however, with the exciting possibility of treatments that might modify disease course, there is growing interest in making a diagnosis as soon as possible, even during prodromal stages (e.g. in people with a known pathogenic genetic variant, or who have a condition such as REM sleep behavior disorder, in which the risk of developing PD or a related synucleinopathy is high). In this situation, the demonstration of dopamine deficiency using imaging can provide relevant evidence of neurodegeneration even in the absence of neurological symptoms or findings on clinical examination. The utility of MRI is rapidly becoming more recognized, as advanced imaging approaches allow the quantitative measure of neuromelanin, iron or free water, all of which may be useful for early disease detection as well as monitoring disease progression. Additionally, the neurodegeneration of PD may start outside the brain and cardiac imaging may demonstrate a loss of sympathetic innervation. The role of these imaging modalities in early detection, differentiation from other clinically similar conditions and monitoring disease progression will be reviewed.

PCO7

Talk 3: Update on synuclein-based biomarkers: Current status and potential applications
*Andrew Siderowf**
University of Pennsylvania Perelman School of Medicine, Philadelphia, PA, United States

Aggregates of misfolded α-synuclein (α-syn) form the major component of Lewy Bodies and are recognized as the key pathology underlying Parkinson's disease (PD) and Dementia with Lewy Bodies (DLB). In recent years, amplification techniques, traditionally used to identify prion proteins, and suitable for detecting protein aggregates present at very low concentrations have been adapted for α-syn seeds in samples from human subjects, particularly cerebrospinal fluid (CSF). These assays have been reported under the names real-time quaking-induced conversion (RT-QuIC), protein misfolding cyclic amplification (PMCA), and most recently, the consensus name, seed amplification assay (SAA). A growing body of research has shown that α-syn SAA can identify PD and DLB patients with high sensitivity and specificity relative to age-matched healthy controls. Importantly, α-syn SAA results are almost always positive in patients with typical Lewy pathology at autopsy, but may be negative in patients with parkinsonian features, but other pathologies. Additionally, positive α-syn SAA results have been shown in patients with syndromes thought to represent prodromal PD including individuals with REM sleep behavior disorder (RBD) and idiopathic hyposmia as well as some non-manifesting carriers of genetic variants associated with PD. Because of these features, α-syn SAA is has supplanted quantitative assessment of total α-syn or phosphor-α-syn in the CSF and is rapidly becoming a crucial biomarker for PD research. Current limitations of α-syn SAA include lack of data correlating variability of quantitative α-syn SAA metrics including aggregation kinetics with clinical features and data on longitudinal changes in α-syn SAA results across the disease course. Nonetheless, the value of α-syn SAA results to stratify clinical trial participants based on underlying pathology is rapidly becoming evident to the expert community. Similarly, the use of α-syn SAA for more accurate early diagnosis is an emerging clinical indication, and prodromal screening is a potential future clinical application. Future directions include development of quantitative methods for α-syn SAA and scalable adaptation of the assay to peripheral tissue such as skin biopsy or blood.

PCO8

Talk 1: Advances in Surgical Therapy – DBS
*Vanessa Milanese Holanda**
BP - A Beneficência Portuguesa de São Paulo, Sao Paulo, SP, Brazil

Deep brain stimulation (DBS) is an established safe neurosurgical symptomatic therapy for eligible patients with advanced disease in whom medical treatment fails to provide adequate symptom control and good quality of life, or in whom dopaminergic medications induce severe side effects such as dyskinesias. DBS has a long-lasting effect on appendicular symptoms, but with progression of disease, nondopaminergic axial features become less responsive to DBS. After three decades of DBS, this procedure remains the most used and most efficient surgical treatment for some cardinal symptoms of PD. Emerging brain technologies have significantly transformed human life in recent decades and DBS innovations are

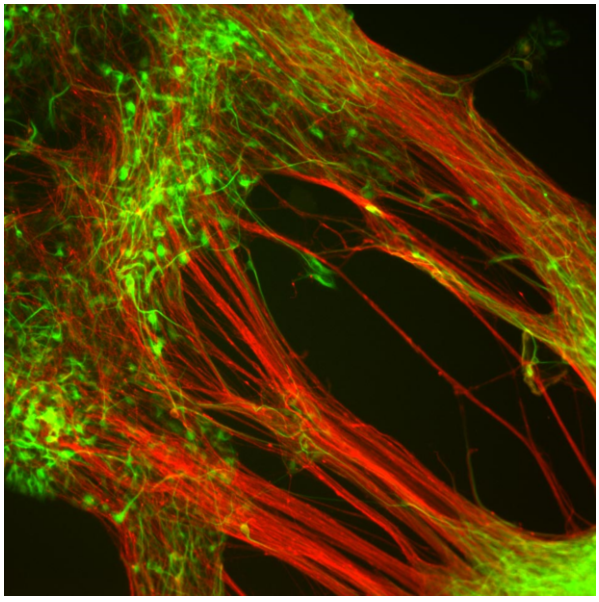
already being implemented, such as MRI-compatible DBS hardware; implantable pulse generators with rechargeable batteries and extended life up to 25 years; neuropacemakers with sensing technology allowing to record the depth electroencephalogram, especially beta activity, and adapt the stimulation accordingly, so called closed loop stimulation, with the potential to decrease side effects and battery drain; directional DBS electrodes allowing the electric current to be focused precisely on the region of interest, again to decrease side effects such as dysarthria and improve outcome; remote web-based follow-up programming and troubleshooting of the stimulation to help patients who live far away from the DBS centre; and new modes of stimulation based on judicious use of more flexible electric parameters. Furthermore, recent studies have shown that the survival of patients with DBS can be regarded as long survival with relatively little disability. Future studies are underway to evaluate the impact of technological advances such as directional lead designs and potential closed-loop stimulation paradigms.

PCO9

Talk 3: Clinical developments in dopamine cell transplantation for PD

*Agnete Kirkeby**
University of Copenhagen, Copenhagen, Denmark

Parkinson's Disease involves the loss of dopamine neurons in the Substantia Nigra, giving rise to the main dopamine-associated motoric symptoms of the disease. Previous work has shown that replacement of the lost dopamine neurons through transplantation of new neurons from human fetal ventral midbrain can, when successful, restore dopamine levels in the striatum and lead to marked clinical improvement. Several groups around the world, including our own, have now developed products of lab-grown stem cell-based dopamine neurons as a transplantation therapy for PD. The advantage of such products over fetal cell transplantation is the possibility of scaling up manufacturing of these cells to treat cohorts of patients and to also thoroughly quality control and standardize the products prior to transplantation. Here, you will hear about the preclinical data demonstrating safety and efficacy of such novel stem cell-based dopamine products as well as their current status in entering clinical trials around the world.



PCO10

Talk 2: Focused Ultrasound a window into early neurorestorative therapy for Parkinson's disease (PD)

*Raul Martinez Fernandez**
Spain

Several symptomatic treatments are available and continue to develop for Parkinson's disease (PD,). However, a major unmet need in PD research is to find disease modifying therapies.
MRI-guided focused ultrasound (MRIgFUS) has emerged as a putative symptomatic for PD earlier and also later in evolution due to its reduced invasiveness. The classic targets historically recognized for functional neurosurgery are similarly used with FUS. The end result, i.e. focal ablation, is very similar to the effect previously achieved with radiofrequency-mediated lesions by surgery. The globus pallidus pars interna (GPi) or its outflow projection to the thalamus (pallido-thalamic tract=PTT) are essentially good for treating levodopa-induced dyskinesias. The Vim of the thalamus is a primary anti-tremor target but results in tremor predominant PD are less reliable compared with essential tremor patients.
The subthalamic nucleus (STN) is the world favorite target for Deep Brain Stimulation and is perfectly organized to influence basal ganglia output and also substantia nigra pars compacta activity. We have previously demonstrated that subthalamotomy is highly efficacious and shows a good therapeutic profile in moderately advanced PD patients. The minimal invasiveness of MRgFUS, and the large clinical effect of subthalamotomy lead us to consider its application in very early stages, not only for the clinical immediate benefit in terms of motor status but also for the possibility of impacting on disease progression. On the other hand, acting primarily against disease mechanism is more desirable.
The blood-brain barrier (BBB) is a very efficient system that protects the central nervous system from bloodstream circulating molecules but also effectively restrict access to the brain to putative therapeutic molecules,. Low-intensity FUS in combination with intravenously injected microbubbles can temporarily open the BBB at specific brain targets. Thus, temporarily opening the BBB could allow delivery of drugs directly to the brain, paving the way for pathology-targeted treatments, and possibly disease-modifying therapies.

PCO11

Talk 1: Management of psychosis symptoms in Parkinson's disease

*Daniel Weintraub**
University of Pennsylvania, Ardmore, United States

Psychosis in PD (PDP) can present with misperceptions or illusions, hallucinations and delusions, and occurs with increasing frequency as the disease progresses, particularly in those with cognitive impairment. While PDP is uncommon in untreated PD patients, prospective studies report a long-term cumulative prevalence of approximately 60%. PDP is associated with both disease-related pathological changes and PD medication use. The underlying mechanisms of PDP may include hypersensitivity of mesocorticolimbic dopamine (D2/D3) receptors, serotonin-dopaminergic imbalance, cholinergic deficits, limbic and pre-frontal neurodegeneration, and connectivity changes involving attentional, thalamic and visual pathways. The hypothesized underlying neurobiological mechanisms of PDP have led to studies of atypical antipsychotics with varying serotonin:dopamine receptor-blocking properties and acetylcholinesterase inhibitors. Initial management of PDP includes ruling out delirium, infection or other reasons for PDP, and minimizing anticholinergic and other potentially contributing medications (e.g., medications with anticholinergic properties,

benzodiazepines, and other central nervous system-acting medications). After that, consideration should be given to decreasing the overall doses of PD medications starting with the medication classes thought at highest risk of inducing psychosis. If a significant decrease in PD medications cannot be undertaken (e.g., motor worsening) or is ineffective to reduce the PDP symptoms, an antipsychotic (AP) may be required. Pimavanserin is efficacious for PD but is available only in the US. Many clinicians initiate quetiapine instead. Clozapine is typically reserved for treatment-refractory patients and requires blood count monitoring. Whether APs increase risk for mortality and morbidity in PD remains an open question. Caregiver support and education at every step is critical, given the burden psychosis can place on the family. Although psychotherapy has yet to be studied as a primary intervention for PD-related psychosis, clinical experience suggests that applications of cognitive behavioral therapy (CBT) techniques, such as stimulus control, caregiver skills training, family psychoeducation, and cognitive reframing, may prove helpful. These CBT strategies may address modifiable risk factors such as healthy sleep habits, circadian rhythms, inaccurate beliefs about the meaning and cause of PD-psychosis and the medications used to treat it, as well as provide caregiver management approaches (e.g., helping the patient reframe/reality test when insight is retained vs. engaging in de-escalation techniques when insight is poor).

PCO12

Talk 2: Autonomic Symptoms: Dizziness, urinary urgency, erectile dysfunction, and constipation

*Patricio Millar Vernetti**
New York University Grossman School of Medicine, New York City, New York, United States

People with Parkinson's may be affected by non-motor symptoms, many of which may be due to autonomic dysfunction. These symptoms can be also caused or further aggravated by medications used for Parkinson's or other disorders. It's recognition and management requires a holistic and multidisciplinary approach.

PCO13

Talk 3: Cognition, depression, and anxiety

*Iracema Leroi**
School of Medicine and Global Brain Health Institute, Trinity College Dublin, Dublin, Ireland

Neuropsychiatric symptoms commonly complicate Parkinson's, including cognitive impairment, depression and anxiety. Mild cognitive impairment in Parkinson's disease (PD-MCI) occurs in approximately a quarter of people with Parkinson's, with the most common presentation being memory loss, closely followed by impaired visuospatial function, and attention/executive ability. PD-MCI is considered a harbinger of dementia in Parkinson's (PDD), with an annual conversion rate from PD-MCI to PDD of about 11%. PDD is characterised by deterioration in several cognitive domains, and significantly impacts quality of life, prognosis and care partner outcomes.
Depression and anxiety may occur in up to 40% of people with Parkinson's at any one point in time and have been described as the most distressing aspect of the condition. Apathy may be present in up to 70%. Apathy and depression are both associated with cognitive decline in Parkinson's; apathy may be a behavioural marker of the onset of PDD.
Cognitive impairment, anxiety, apathy and depression may frequently overlap and are often under-recognised in clinical settings and thus under-treated. Difficulties with diagnosis may be compounded by a lack of guidance for health professionals. This presentation will provide a background to these neuropsychiatric syndromes in Parkinson's and provide practical approaches to assessment and management, with a person-centred and pragmatic focus.

PCO14

Interprofessional Care and Parkinson's - Welcome Remarks and Introduction to the program

*Suketu Khandhar**
Kaiser Permanente, Northern California, Sacramento, CA, United States

It is well understood that those living with Parkinson's disease do better in a multidisciplinary care setting, whilst given the opportunity for self-management and empowerment. However, reality reveals this can be challenging in resource limited or underserved areas. We hope to convince the audience that sustainable multidisciplinary care is possible in all areas given passionate leadership, creativity, technology and patient engagement. We will provide examples of where such models have been successful in resource limited areas. We will begin by giving a brief overview of the rationale behind multidisciplinary and integrated care. This will be followed by 2 shared lectures outlining successful programs created in Mexico and Cameroon. We plan to challenge the audience on rethinking who the traditional members of the core care team could include. Following a brief lunch break we will take the audience on case study journey, reviewing medical management, rehabilitation management as well as cognitive/behavioral management of both a patient with young onset Parkinson's disease versus a patient with typical onset Parkinsons' disease.

PCO15

Creating something out of nothing: A case from Cameroon

*Esther Cubo**
Hospital Universitario Burgos, Burgos, Spain

Telemedicine is an effective strategy for recruiting and retaining physicians in underserved areas. Distance learning can break their professional isolation and reduce the stress related. In this regard, in 2014, a tele-education PD program was conducted in Cameroon, sponsored by the International Parkinson's Disease and Movement Disorder Society. Twenty lectures were given using synchronous video conferences throughout a year, events that connected movement disorder experts with 33 health professionals participants (52.4% women), including 16 doctors and 17 allied health professionals. Videoconferences were completed in 80% of the cases (feasibility), and attendees' participation ranged from 20% to 70% (adherence), with high satisfaction and improvement in medical knowledge (effectiveness).
Overall, this program showed a statistically significant improvement of the learning process, increased the awareness of movement disorders and connected local neurologists and other health professional with experts in the field of Movement Disorders.

PCO16

Case presentation #1 – Medical management: YOPD vs typical onset

*Nabila Dahodwala**
United States

The presentation and trajectory of Parkinson's disease varies greatly from person to person necessitating individualized care. In this program, we will use a case presentation to illustrate the similarities and differences in the medical management of Parkinson's disease in people who are younger age vs. older age in onset of Parkinson's disease. We will focus on risk factors, timing of medication, medication effects, influence of other medical diseases and age effects, among other issues.

PCO17

How has medical & surgical treatment evolved for PD?

*Vanessa Milanese Holanda**
BP - A Beneficência Portuguesa de São Paulo, Sao Paulo, SP, Brazil

The hallmark of symptomatic treatment is levodopa, which is converted to dopamine in the brain. Besides levodopa, there are many other types of medications available for the treatment of PD-related motor symptoms: anti- cholinergics, amantadine, MAOIs, COMTIs, dopamine agonists and istradefylline. A formulation of levodopa, approved by the US Food and Drug Administration (FDA) in 2018, as a 'rescue' from off periods is inhalable levodopa powder without carbidopa. Other formulations that have been found effective in smoothing out motor fluctuations include continuous intrajejunal infusion of levodopa-carbidopa intestinal gel. The efficacy of continuous infusion formulation is comparable to subthalamic nucleus (STN) deep brain stimulation (DBS) surgery though only the latter treatment led to improvement in the duration and disability of levodopa-related dyskinesias. In 2019, the FDA approved istradefylline (Nourianz), an adenosine A2 receptor antagonist, as adjunctive treatment for levodopa/carbidopa in patients with PD experiencing off episodes. Despite optimal medical therapy, many patients have a poor quality of life because of fluctuating response, troublesome dyskinesia or levodopa-unresponsive symptoms. Ablative surgical approaches such as stereotactic destruction of physiologically defined overactive brain nuclei have been largely replaced by DBS using implanted pulse generators. Unilateral focused ultrasound lesioning of the STN or thalamus (in tremor-dominant forms of PD) has been found to be beneficial in some patients, particularly if the symptoms are markedly asymmetric. Finally, spinal cord stimulation is increasingly being explored in patients with PD who are most troubled by their gait disorder. Surgical delivery of gene therapy is an emerging area of experimental therapeutics. In phase 1 study, 15 patients with moderately advanced PD underwent MRI-guided delivery of adeno-associated viral vector serotype-2 encoding the complementary DNA for the enzyme, aromatic L-amino acid decarboxylase (VY-AADC01) into the putamen. An increasing understanding of etiopathogenesis of PD has led to hypotheses about potential neuroprotective strategies that, when applied early or even in the prodromal phase, may favourably alter the progression of the disease. One of the most exciting developments of potential neuroprotective or disease-modifying therapies is the use of □-synuclein monoclonal antibodies to minimise accumulation and spread of aggregated, toxic, □-synuclein. Other antisynuclein strategies currently in development include active immunisation against synuclein, antiaggregation drugs, certain Abelson (c-Abl) kinase inhibitors, such as Nilotinib and K0706.

PCO18

What's new in research?

*Mark Cookson**
National Institute on Aging, Bethesda, Maryland, United States

Understanding what factors drive our risk of developing Parkinson's disease is a key motivator for much basic science. In this session, we will focus on the ways in which people-centered research can be used to drive insights into how Parkinson's disease evolves and progresses. A major focus of review will be on human genetics - but as we will discuss this is a complex area of investigation because the genetics of Parkinson's is complex with multiple factors having relatively stronger or relatively more modest effects on disease risk. However, there are general principles that we can extract from the complex genetics that have focussed on a small number of related pathways, of which the most informative are those where we can understand whether over- or under- activity is likely to be driving disease as this has strong implications for how we might think about new therapeutic approaches. We will extend this discussion to consider new biomarkers, again coming from donated materials from people with Parkinson's, that are changing how we can monitor disease risk and progression in relation to clinical evaluation. Finally, we will emphasize that there are very large scale efforts to broaden the basic science of Parkinson's to be much more inclusive of world wide populations, which has the potential to hugely clarify disease mechanisms by showing which are shared between groups of people.

PCO19

What new treatments are on the horizon?

*Roger Barker**
University of Cambridge, Cambridge, England, United Kingdom

In this talk i will discuss t a number of new developments in the treatment of Parkinson's. This will include work coming out of the lab highlighting possible pathways and approaches including the role of alpha synuclein and why the trial to date may have failed using antibody treatments against this target. I will also discuss the area of drug repurposing and how this is evolving and this will include a discussion on exenatide and the possibility of setting up a platform for multi arm multi stage trials in Parkinson's. I will also cover the new trials that are now starting using cell and gene tharapies as well as touch on non pharmacological approaches.

PCO20

Before we eat lunch: What about nutrition? Does it really matter?

*Silke Appel-Cresswell**
University of British Columbia, Vancouver, BC, Canada

We will review the current evidence for adhering to specific dietary patterns when living with Parkinson's. Mediterranean-type diets are associated with lower risk of developing PD, higher age of onset, slower progression and longer survival with PD. They are good candidates to improve constipation and improve the gut microbiome. In addition, Mediterranean diets have positive health benefits for a whole range of other conditions including diabetes, heart disease, cognitive function etc. Based on the MIND diet, one of the Mediterranean diets, here are recommendations for a healthy diet:
Foods to increase: green, leafy vegetables, other vegetables, nuts, berries, beans or legumes, whole grains, fish, poultry, olive oil (as main oil and in place of butter or margarine).

Foods to avoid or only consume in small quantities: fried food, processed food, sweets, pastries, pop, sweetened beverages, red meat, cheese, butter.
The ketogenic diet has so far only been studied in short-term studies, more research will be needed to make a recommendation for its use specifically in PD.
Overall, despite strong correlational evidence for benefit, interventional dietary trials in Parkinson's are lacking and are urgently needed. Despite this research gap, a healthy diet paired with other healthy lifestyle choices, e.g. exercise, is recommended as the foundation for living well with Parkinson's.
We will review the relationship of dietary protein and levodopa intake and why optimizing timing might benefit some PWP. For issues with food preparation (e.g. due to tremor), chewing, swallowing, nausea, weight loss, constipation, make sure to consult with your team including occupational therapists, speech and language pathologists, dietitians, nurses and physicians.
Enjoy your lunch!

PCO21

Behavior change: How can I make the changes "stick" in my (____) routine?
*Terry Ellis**
Boston University, Boston, MA, United States

There are many healthy behaviors that can improve the quality of life of people with Parkinson disease. Greater physical activity, regular engagement in exercise and nutritious diets are a few examples of healthy lifestyle choices that improve well-being. Though these healthy behaviors are often recommended by healthcare professionals, they are difficult to adopt and integrate into everyday life. Many people ask "how can I get started and "stick" to my routine? In this presentation, strategies to successfully facilitate behavior change will be discussed. These include strategies to either initiate and/or maintain desired healthy behaviors. Healthy behaviors can be initiated/maintained either deliberately or automatically or by using a combination of both approaches. Examples of cognitive-behavioral strategies will be provided to improve self-efficacy or confidence in the ability to succeed. In addition, habit formation will be discussed with examples of how to successfully build and strengthen habits. Suggestions that can be integrated into everyday life will be provided.

PCO22

Tips & tricks for living with Parkinson's that go beyond medication
*Darla Freeman**
Florida Center for Voice and Swallowing, Tampa, FL, United States

Parkinson's disease is a long-term condition causing changes to communication and cognition over time. These changes develop slowly and vary from person to person and can lead to social isolation. Adapting to this decline will help the person with Parkinson's to effectively communicate with others and live more independently. By using apps and compensatory strategies these disabilities can be minimized. Smartphones, apps, and online resources are becoming popular ways to assist people with Parkinson's with practice, maintenance, and supplements communication and cognitive skills. Compensatory strategies have been historically used as nontechnological tips to enhance communication and cognition. This presentation will introduce participants to applications, online resources, and compensatory strategies used to enhance diminishing communication and cognition.

PCO23

Tips & tricks for living with Parkinson's that go beyond medication
*Iracema Leroi**
School of Medicine and Global Brain Health Institute, Trinity College Dublin, Dublin, Ireland

Neuropsychiatric symptoms commonly complicate Parkinson's, including cognitive impairment, depression and anxiety. Mild cognitive impairment in Parkinson's disease (PD-MCI) occurs in approximately a quarter of people with Parkinson's, with the most common presentation being memory loss, closely followed by impaired visuospatial function, and attention/executive ability. PD-MCI is considered a harbinger of PDD, with an annual conversion rate from PD-MCI to PDD of about 11%. Dementia in PD (PDD) is characterised by deterioration in several cognitive domains, and significantly impacts quality of life, prognosis and care partner outcomes. Depression and anxiety may occur in up to 40% of people with Parkinson's at any one point in time and have been described as the most distressing aspect of the condition. Apathy may be present in up to 70%. Apathy and depression are both associated with cognitive decline in Parkinson's; apathy may be a behavioural marker of the onset of PDD.
Cognitive impairment, anxiety, apathy and depression may frequently overlap and are often under-recognised in clinical settings and thus under-treated. Difficulties with diagnosis may be compounded by a lack of guidance for health professionals. This presentation will provide some pragmatic and person-centred tips and tricks to the recognition and non-drug management of certain neuropsychiatric aspects of Parkinson's.

PCO24

Utilizing Your Care Team: Tips for communicating with your team
*Adriana Gonzalez**
University of California San Diego, San Diego, Ca, United States

In this panel discussion we will be discussing how a person with Parkinson's disease can structure their care team in order to best communicate their needs within their family and with their medical providers. From a social work perspective will discuss the importance of identifying the members of your care team and how each person can play a role in maximizing your medical care further enhancing your quality of life.

PCO25

Creativity and art: How does it impact the brain and Parkinson
Anjan Chatterjee[*,1], Miriam Bram*[*,2]*
[1] University of Pennsylvania, Philadelphia, Pennsylvania, United States
[2] World Parkinson Coalition, New York, NY, United States

Since the late 19th century, neurology has played a critical role in advancing our understanding of large-scale human behavioral systems that underpin perception, language, emotions and attention. Can neurologic conditions do the same for aesthetics? One striking observation is that brain damage can sometimes paradoxically facilitate art. I will review observations on how neurological disease changes and sometimes "improves" art

production to contextualize similar observations in Parkinson's disease (PD). Given the effects of the disease on dopamine, and dopamine's role in our reward systems, one might expect people with PD to receive less pleasure from art. I will shows that such a general effect of PD on pleasure does not occur. PD can affect judgments of beauty that are triggered by implied movement in art but not when based on other features of art. These observations speak to the resilience of patients' creativity and aesthetic appreciation in the face of changes to the brain.

PCO26

Getting the most out of the WPC 2023: Two perspectives

*Christine Jeyachandran**
Alianza Iberoamericana de Parkinson, Hurstville, NSW, Australia

Abstract - Getting the most out of the World Parkinson Congress with WPC Ambassadors Miriam Bram and Chirstine Jeyachandran
Introduction - Analogy of a dance
Program Overview
We will explain elements of the program and how you can understand which sessions are best for you and this will help you in your planning
Scientific levels
Types of talks/ events - Plenary vs Round tables etc
Exercise classes
Posters
Planning
We will share some tips to plan your day from our experiences.
- Allow time for breaks.i.e. exercise, hydration, snacks, ping pong, rest
- Connect with others
- Seek out appropriate programming ie young onset programming
- It's ok to leave a session and take a break/ meet someone in the lobby or find something else to do.
Plan B
Embrace the unexpected; be open-minded. You never know who will inspire you.
Personal Goals
Interactive discussion
3 people you want to meet
3 experiences you want to have
3 questions you want answered
Conclusion

PCO28

Advocacy & activism in Parkinson's disease: How we got here and where we need to go

*Sara Riggare**
Uppsala University, Uppsala, Sweden

This course will give an overview of the history of the field of patient advocacy and activism by presenting some important examples, both from PD and other conditions, such as HIV/AIDS and cancer. Thereafter the participants will have the option to choose to attend different sessions to hear directly from Parkinson's advocates and activists, modelling this behavior and sharing their lessons learned and tips for how to get started on one's own advocacy and activism journey. Presentations will be based on a framework presented at WPC2019 [1], that has been further developed [2]. The framework includes the following types/competences/activities/roles:
Activist – works for changes in policy and practice related to their health and healthcare needs
Mentor – shares their knowledge and experiences to teach others
Academic/Knowledge seeker - stays updated on the latest scientific articles and evidence
Patient Researcher – uses scientific methods to investigate their health issues and/or partners with established academic researchers
Self-care Expert – does what they can to learn about their health and wellbeing and works to improve it
Communicator – writes and/or speaks about their own health experiences in conferences and meetings and/or articles, blogs and social media
Hacker – addresses health issues through the use of technology
Tracker – self-monitors health issues
Healthcare Partner – creates and manages partnerships with healthcare professionals
Innovator – creates or has ideas about new solutions based on their health and healthcare needs
Entrepreneur – builds companies or organizations from their experiences with health and healthcare needs
Healthcare Coordinator – manages and coordinates multiple healthcare contacts for their health issues
REF:
[1] Duncan, T. S., & Raphael, K. (2019). Activism, awareness and roles patients play. Abstracts of the 5th World Parkinson Congress 2019.
[2] Duncan, T. S., Engström, J., Riggare, S., Hägglund, M., & Koch, S. (2022). Meeting the Burden of Self-management : Qualitative Study Investigating the Empowering Behaviors of Patients and Informal Caregivers. Journal of Participatory Medicine, 14(1). https://doi.org/10.2196/39174.

PCO29

INDIVIDUAL – Exercise & wellness

*Miriam Rafferty**
Shirley Ryan AbilityLab; Northwestern University, Chicago, Illinois, United States

People with young onset Parkinson's disease (YOPD) have unique generational challenges and opportunities when it comes to exercise and wellness. When YOPD is added to work and family roles the nonmotor symptoms of PD can make it feel even harder to balance it all. However, familiarity with technology can help support one's exercise and wellness goals.
This session will discuss the Parkinson's Foundation exercise recommendations, including: aerobic exercise; resistance training; balance, agility, and multitasking (BAM); and stretching. Research shows that exercise can improve motor and nonmotor symptoms of PD. Additionally regular exercise participation is associated with

slower declines in mobility and quality of life. However, the exercise guidelines can be overwhelming. The support of an experienced exercise professional or physical therapist can help an individual to feel accountable and motivated to exercise. They can help you uncover the best exercise routine for you, which will take into consideration your interests, abilities, goals, preferences, and access to resources (e.g., location of classes, cost, time).
Mobile health technology can help support your long-term exercise participation and wellness goals. Evidence-based mobile health applications can be used to support better exercise, sleep, nutrition, and more. You can use technology to help keep yourself accountable to your exercise or wellness goals on your own, through your social support network, or by connecting with your medical team. We will discuss how the mobile health revolution can impact your care now and in the future.

PCO30

IN RELATION – Parenting: How to talk to children
*Soania Mathur**
UnshakeableMD, Ajax, ON, Canada

Parkinson's disease not only affects the person diagnosed with this illness, but the entire family unit, including the most vulnerable, our children. Regardless of age, a diagnosis of PD in a loved one, manifested as changes in appearance and ability, may result in a certain level of fear, particularly if not acknowledged or left unexplained. That is why when the timing is right, it is important to have a conversation about Parkinson's disease.
Of course, every family is different. The age of your children and their level of understanding will guide you in terms of when, how much and what to disclose. There are however some general guidelines to consider when having this conversation including being honest in your disclosure, using words that are appropriate for their education level, focusing on hope and above all, keeping the lines of communication open.
This interactive discussion will work towards helping families learn how to approach the conversation about PD in a loved one with a focus on empowering children to gain some measure of control in a somewhat uncontrollable situation.

PCO31

Psychiatric and cognitive medication side effects in Parkinson's disease
*Daniel Weintraub**
University of Pennsylvania, Ardmore, United States

Initial treatment of clinically-significant depressive symptoms in PD typically with an antidepressant. Caution is indicated in prescribing a serotonergic antidepressant in patients also taking an MAO-B inhibitor due to possible occurrence of serotonin syndrome, although this syndrome appears uncommon. Additional antidepressant safety concerns pertain to prolonged QTc interval with some agents (e.g., citalopram), potential drug-drug interactions involving cytochrome P450 isoenzymes, and the anticholinergic properties of TCAs. For anxiety, sometimes it is necessary to use as-needed or scheduled low-dose benzodiazepine for non-motor fluctuations (NMFs) or generalized anxiety symptoms, although careful monitoring for worsening cognition, sleepiness and gait/balance is of utmost importance. Initial management of psychosis in PD includes ruling out delirium, infection or other reasons for PDP, and minimizing anticholinergic and other potentially contributing medications (e.g., medications with anticholinergic properties, benzodiazepines, and other central nervous system-acting medications). After that, consideration should be given to decreasing the overall doses of PD medications starting with the medication classes thought at highest risk of inducing psychosis. At times addition of an antipsychotic (AP) is required. Whether APs increase risk for mortality and morbidity in PD remains an open question. Impulse control disorders (ICDs) in PD include compulsive gambling, buying, sexual behaviors, and eating behaviors, and a related disorder is dopamine dysregulation syndrome (DDS; compulsive PD medication use. Dopamine agonist (DA) treatment is the strongest ICD predictor; additionally, higher-dose levodopa, amantadine and selective MAO-B inhibitor have also been associated with ICDs to a lesser extent. DDS is most associated with higher levodopa doses. Management of cognitive impairment in PD should begin with a careful review of medications, both PD and non-PD, with a particular focus on limiting or discontinuing medications with significant anticholinergic, sedating or other central nervous system-acting properties (e.g., benzodiazepines and opioid(-like) pain medications). In particular, medications with anticholinergic properties are sometimes used in PD, but are associated with long-term cognitive decline and should be avoided in older individuals with PD.

PCO32

Eat Well to Live Well with YOPD
*Richelle Flanagan**
My Moves Matter, Dublin, Dublin, Ireland

As a Dietitian who lives with young-onset Parkinson's (YOPD), I am very aware of the irony! However, my 19 years of dietetic experience led me to research the impact of diet and nutrition on Parkinson's and led me to discover that (1) diet can play a very significant role in the management of YOPD and (2) people with YOPD are not getting access to the nutrition advice they need to live well with PD. Just like exercise, what you eat and drink can improve your symptoms and may also slow progression. This will be a practical workshop where you will learn the pros and cons of different diets for YOPD; how diet affects medication and vice versa; weight management, supplements, sports nutrition considerations, sex and gender considerations, and when and how to see a Dietitian.

PCO33

MEDICAL - Medical challenges specific to YOPD
*Maria Jose Marti**
Hospital Clinic de Barcelona, barcelona, Catalonia, Spain

Young-onset Parkinson's disease (POPD) entails several phonotypic differences at the group level with late-onset PD but also unique circumstances that pose management challenges. Among the latter, both the increase in genetic predisposition and pregnancy are relevant. Younger the age of onset, the greater the risk of genetic predisposition and monogenic forms of PD due to recessive gene mutations such as Parkin or PINK1 present at an early age. Although the identification of the gene mutation can help some way in predicting evolution and response treatment, due to risk predictions for family members and the patient offspring, genetic counseling by experienced people will be mandatory. As for pregnancy, in half of women with YOPD disease symptoms deteriorate. Although data for pharmacological agents are limited, levodopa seems to be the safest option during pregnancy.

PCO34

INDIVIDUAL: Coping with PD
*Sree Sripathy**
Women's Parkinson's Project, San Jose, CA, United States

Coping with PD will be focused on each panellist's journey to PD diagnosis along with how they cope with symptoms and side effects in their daily lives. Special attention will be given to the differences experienced based on gender and implications gender may have in how people with PD are perceived.

PCO35

INDIVIDUAL: Coping with PD
*Matt Eagles**
Havas Lynx Group, Manchester, Manchester, United Kingdom

Coping with PD will be focused on each panellist's journey to PD diagnosis along with how they cope with symptoms and side effects in their daily lives. Special attention will be given to the differences experienced based on gender and implications gender may have in how people with PD are perceived.

PCO36

IN RELATION – Planning for the future & disclosure of your diagnosis
*Susan Thomas**
Healthcare Consulting, TIVERTON, Devon, United Kingdom

Parkinson's can affect anyone and although many people diagnosed with the condition are over the age of 50, those with an earlier or younger onset Parkinson's, (YOPD) will experience differing issues that will create more life challenges than older people with the condition may experience.
People with YOPD are diagnosed during the most productive years of their lives and will live longer with the disease. This presentation will outline the issues that younger people with Parkinson's (PwP), their partners and families will need to address. Concerns may arise around how, when, what and who to tell about their diagnosis alongside issues such as employment; finances, how to maintain current lifestyle, relationships and how to handle managing a young family. Anxiety, depression and cognitive disturbances can impact coping mechanisms with these psychosocial problems and will require as much attention as the motor and non-motor symptoms commonly experienced in Parkinson's. Psychosocial issues can negatively impact the emotional stability of both the PwP and family, interfering with relationships and family life.
Reliable information given in a timely way at diagnosis and throughout the course of condition as well as support from the specialist multidisciplinary team can benefit the YOPD person and their families. This presentation will suggest a check list that YOPD patients can consider to use as a resource when they are liaising with their specialist Parkinson's team.

References

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Calne SM, Lidstone SC, Kumar A Psychosocial issues in young-onset Parkinson's disease: current research and challenges Parkinsonism Relat Disord 2008;14(2):143-50. doi: 10.1016/j.parkreldis.2007.07.012. Epub 2007 Sep 21

Younger Parkinson's Alliance Podcast 'Being diagnosed with Parkinson's' available at https://www.parkinsons.org.uk/information-and-support/young-onset-parkinsons

PCO37

MEDICAL - Cognition & mental health
*Greg Pontone**
Johns Hopkins University School of Medicine, Baltimore, MD, United States

Cognitive function and mental health are major contributors to quality of life in Parkinson's disease (PD) and when impaired can have a large impact on disability and independence. Although the dopamine medications used to treat the motor symptoms of PD can affect cognitive function and mental health these issues often require a different approach to treatment. A range of medications, behavior and lifestyle changes, and allied health care providers can be important for managing these issues in order to maintain optimal functioning and quality of life in PD.

Oral Sessions

O1

Talk 1: Can the genetics of sporadic PD and DLB help in disease subtyping? What could be the therapeutic implications?
*Sonja Scholz**
National Institutes of Health, Bethesda, MD, United States

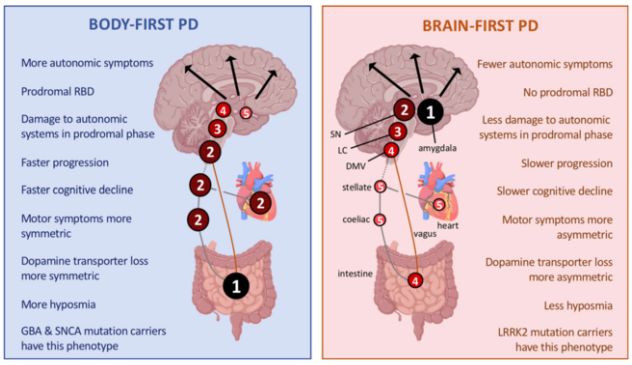
Defining the biological substrates of the clinical heterogeneity in neurological diseases is a topic of great interest. Parkinson's disease and dementia with Lewy bodies are clinically heterogeneous conditions characterized by variable combinations of motor and non-motor symptoms and complex genetic architectures. The discovery of genes contributing to disease risk and progression of these common neurodegenerative conditions has gained momentum, providing crucial insights into the underlying biological processes and opening new opportunities for the development of precision medicines. Well-characterized, longitudinal cohorts have proven to be particularly insightful for defining disease subtypes. In this presentation, I will discuss current knowledge of the clinical heterogeneity of Parkinson's disease and dementia with Lewy bodies and how genetic information can be leveraged for understanding the biological underpinnings. I will highlight the implications for translational applications, such as the development of novel diagnostic and prognostic biomarkers as well as practical aspects for clinical trial design.

O2

Talk 2: Brain-first or body-first Parkinson's disease
*Per Borghammer**
Aarhus University Hospital, Aarhus N, Denmark

Parkinson's disease (PD) is a heterogenous disorder. At the time of diagnosis, patients can show highly variable patterns of symptoms and objective neuronal dysfunction. Such subtypes of PD have varying prognoses and progression rates of the disease. Some patients develop autonomic and sleep symptoms years before

diagnosis, whereas others do not have these symptoms, when their motor symptoms begin.
The brain-first and body-first hypothesis of PD proposes that the initial formation of PD-related pathology can arise in different parts of the nervous system, and that the pathology then spreads from this initial onset site in a prion-like manner.
An onset in the nervous system of the gut leads to a body-first clinical type, in which autonomic and sleep problems appear years before parkinsonism. In contrast, if the first pathology arises in the olfactory bulb or amygdala, a brain-first type emerges. This type has very few or no prodromal symptoms before parkinsonism emerges.
This lecture presents the underlying evidence for the brain- vs-body-first hypothesis, including data from clinical patient studies, postmortem studies of patient brain tissue, and animal models.



O3

Talk 3: Different α-synuclein strains in Parkinson's disease brains
*Markus Zweckstetter**
DZNE, Göttingen, Lower Saxony, Germany

Parkinson's disease (PD) and Multiple System Atrophy (MSA) are clinically distinctive diseases that feature a common neuropathological hallmark of aggregated α-synuclein. Little is known about how differences in α-synuclein aggregate structure affect disease phenotype. To gain insight into this question, we amplified α-synuclein aggregates from PD and MSA brain extracts and analyzed the conformational properties using NMR spectroscopy and cryo-electron microscopy. We found that there was a greater structural heterogeneity among α-synuclein fibrils amplified from the PD brain compared to those from the MSA brain, possibly reflecting on the greater variability of disease phenotypes evident in PD. In addition, we show that α-synuclein fibrils amplified from MSA brain extracts are more active in oligodendroglia than α-synuclein fibrils from PD brain. Our findings raise important questions regarding the one disease-one strain hypothesis in the study of α-synucleinopathies.

O4

Talk 4: What do subtypes mean for people with Parkinson's?
*Jonny Acheson**
University Hospitals of Leicester NHS Trust, Leicester, Leicestershire, United Kingdom

What we understand about Parkinson's disease (PD) is not fixed; it is in constant evolution and as a practicing doctor and a person with PD, I find myself with a unique vantage point. I can appreciate that what we understand about PD is related to the advances in scientific and clinical knowledge however I also know that it is important to embrace what we learn from persons with disease. We hope that emerging evidence will translate into immediate greater clarity however in practice, we know that as data emerges it is usually accompanied by uncertainty and a peak of inflated expectations.
Research suggests that within the cohort of people diagnosed with PD there have emerged many sub-types with differing symptom profiles and disease courses. There remains at best, a murky consensus on definitions for 'PD subtypes,' and because subtypes can change over a lifetime, outcomes are a moving target. It is not surprising that those living with PD when faced with information on subtype are left with many more questions than answers. I will argue that we should positively embrace the uncertainty as an opportunity for education, growth and change.
I will draw on the rich architectural history of Barcelona to highlight important points and considerations about PD subtypes and I will consider implications for the future for research, education and management in the field. I will also examine the present implications for subtyping as well as the opportunities and challenges. Finally, I will advocate for a position that science and medicine when paired with a heavy dose of a patient perspective will lead us to a collaborative network which we can leverage to impact many more lives. I am fortunate to see both sides of the mountain, and my wish is that all patients reach the peak.

O5

Lecture 1: Historical Perspective of the Function and Dysfunction of the Basal Ganglia: Why it matters today
*José Obeso**
Spain

Starting with Wilson's princeps description of bilateral striatal necrosis causing the dystonia and parkinsonism characteristics of hepatolenticular degeneration (Brain 1914), the basal ganglia(BG) were considered fundamental for motor control. Indeed, Marsden (Neurology, 1982) concluded in a seminal article that "on the basis of the motor deficits observed in patients with Parkinson disease, the basal ganglia normally are responsible for: The automatic execution of learned motor plans". This notion was based in the consequences of striatal dopamine depletion observed in patients with Parkinson's disease(PD) early in evolution.
In parallel, the concept that the BG received and project from and to several cortical areas through parallel circuits involved in the control of movement, eye-movements, behavior and emotions was developed (Alexander et al, Ann. Rev.Neurosci, 1986). Simultaneously, the "direct" and "indirect" striato-pallidal projections and the pathophysiological model of the BG were described(Penney and Young, Mov Disord, 1986; DeLong, TINS, 1989) and the influence of the subthalamic nucleus(STN) in the normal and pathological states was recognized. This in turn led to the revitalization of functional neurosurgery for PD. In the ensuing years, the functional anatomy of the BG grew in complexity by realizing the role of feedback and internal loops(Obeso et al, TINS 2000) in-between different nuclei, i.e. globus pallidus pars externa-STN-globus pallidus pars interna; thalamo-striato-pallidal-thalamic projection, etc, etc, and the description of the hyperdirect cortico-STN projection(Nambu, Neurosci Res 2002).
The dopaminergic projections modulate neuronal trafficking throughout the different circuits and has a prominent role in action selection and reinforcement learning, the two basic physiological process engaging the BG. The substantia nigra pars compacta (SNpc) ventral tier innervates the striatum mostly whereas the dorsal tier innervates extra-striatal nuclei. SNpc neurons (soma) and profuse synaptic arborization exhibit a high metabolic rate and stress, leading to metabolic compromise and increased risk of cell death (Surmeier, 2011,2012).

Altogether these characteristics and particularly the net engagement in movement selection, action switching and, importantly, inhibition, are likely intimately linked to neuronal vulnerability of the SNpc in PD(Hernandez et al TINS, 2019). Furthermore, the focal motor onset clinically, and limited degeneration of ventral tier neurons and dopaminergic depletion in the posterior putamen asymmetrically, implies specific functional mechanisms triggering pathology. Indeed, we believe these are mainly driven by cortico-striatal activity and related with the large development of motor repertoire of the upper limb and cranial musculature in humans(Foffani and Obeso, 2018).

O6

Lecture 2: Why we care about the Parkinson's disease prodrome: From curious observations to therapeutic opportunities

*Eduardo Tolosa**
University of Barcelona, Barcelona, Spain

A variety of symptoms have been identify that occur before onset of classical motor symptoms in Parkinson disease (PD) in what we now call the prodromal phase of PD. Prodromal PD (PPD) symptoms include dysautonomia, pain and disturbances in smell, sleep and mood. Enrollment of PPD subjects into clinical trials aimed at delaying or preventing the progression to overt disease is one of the main goals in PD research. Such trials have disappointingly failed in the last two decades. They have been conducted in subjects with early PD when classical features of slowness combined with other features such as rigidity, tremor, and postural instability are present. Since PPD reflects less extensive disease than early manifest PD, PPD may be the optimal phase when to study neuroprotection, before damage is extensive enough to cause motor symptoms. Defining and recruiting a population of prodromal subjects that will predictably develop motor PD in a short time period (e.g., less than 4 years) will be essential for implementing such prodromal trials.
PPD studies are in progress in subjects with a single strong risk factor for developing PD (e.g., primary hyposmia, idiopathic RBD or asymptomatic genetic PD subjects) while others examine associations with PD in large population-based cohorts. Progress in these studies will not only help in the development of neuroprotective drugs but also in defining new risk factors and etiological causes and in understanding PD pathogenesis.
Mysteries abound about the prodromes of PD, such as its clinical heterogeneity, unclear progression, underlying neuropathology and absence of definitive diagnostic and progression biomarkers. Solving these issues will have enormous consequences to the PD field and should lead to effective disease prevention.

O7

Talk 1: Pathogenic conformations of alpha-synuclein

*Hilal Lashuel**
École polytechnique fédérale de Lausanne (EPFL), Lausanne, Switzerland

The accumulation of misfolded and aggregated forms of alpha-synuclein in the form of different types of intracellular inclusions, such as Lewy bodies (LBs) and Lewy neurites (LBs), is one the main pathological hallmarks of Parkinson's disease (PD) and several other neurodegenerative diseases. In vitro aggregation studies have shown that alpha-synuclein aggregation proceeds by forming soluble oligomeric forms that convert into insoluble fibrils. Mutations in alpha-synuclein or variation in the aggregation conditions led to the population of oligomers and fibrils of distinct morphological and structural properties. Recent Cryo-EM studies of alpha-synuclein fibrils isolated from postmortem brains of patients with PD, MSA, or DLB exhibit distinct biochemical and structural features, which could provide the basis for the structural classification of synucleinopathies.
In this talk, I will provide an overview of the conformational landscape of alpha-synuclein and summarize recent studies from our group where we determined and compared pathogenic properties (toxicity, seeding activity, and spreading in the brain) of various oligomeric and fibrillar forms of alpha-synuclein in primary neurons, patient-derived iPSCs, and in rodent models of pathology spreading in PD. Our work shows that while several forms of alpha-synuclein contribute to its toxicity, only specific forms of the protein are involved in seeding pathology formation or mediating cell-to-cell propagation of pathology in the brain. In addition, I will present new data demonstrating the critical role of post-translational modifications in regulating the pathogenic properties of alpha-synuclein aggregates and offer new opportunities to neutralize the seeding activity of alpha-synuclein fibrils, irrespective of differences in their structural properties. Finally, I will highlight novel conformation- and aggregate-type-independent strategies for preventing alpha-synuclein pathology formation and neutralizing the pathogenic properties of alpha-synuclein aggregates.

O8

Talk 2: Alpha-synuclein strain biology

*Anke Van der Perren**
UZ/ KU Leuven, Leuven, Belgium

Synucleinopathies, such as Parkinson's disease (PD), multiple system atrophy (MSA), and dementia with Lewy bodies (DLB), are defined by the presence of α-synuclein (αSYN) aggregates throughout the nervous system but diverge from one another with regard to their clinical and pathological phenotype. The recent generation of pure fibrillar αSYN polymorphs with noticeable differences in structural and phenotypic traits has led to the hypothesis that different αSYN strains may be in part responsible for the heterogeneous nature of synucleinopathies. To further characterize distinct αSYN strains in the human brain, and establish a structure-pathology relationship, we pursued a detailed comparison of αSYN assemblies derived from well-stratified patients with distinct synucleinopathies. We exploited the capacity of αSYN aggregates found in the brain of patients suffering from PD, MSA or DLB to seed and template monomeric human αSYN in vitro via a protein misfolding cyclic amplification assay. A careful comparison of the properties of total brain homogenates and pure in vitro amplified αSYN fibrillar assemblies upon inoculation in cells and in the rat brain demonstrates that the intrinsic structure of αSYN fibrils dictates synucleinopathies characteristics. We report that MSA strains show several similarities with PD strains, but are significantly more potent in inducing motor deficits, nigrostriatal neurodegeneration, αSYN pathology, spreading, and inflammation, reflecting the aggressive nature of this disease. In contrast, DLB strains display no or only very modest neuropathological features under our experimental conditions. Collectively, our data demonstrate a specific signature for PD, MSA, and DLB-derived strains that differs from previously described recombinant strains, with MSA strains provoking the most aggressive phenotype and more similarities with PD compared to DLB strains.

O9

Talk 3: The cellular environment in α-synuclein aggregation
*Amanda L. Woerman**
University of Massachusetts Amherst, Amherst, MA, United States

The formation of misfolded pathological protein aggregates by disease-specific proteins is a common feature of many neurodegenerative diseases, and is believed to cause neuronal dysfunction either directly or indirectly. Recent studies have strongly implicated cell-to-cell transmission of misfolded proteins through templated recruitment, or the prion mechanism, as a shared feature for the onset and progression of neurodegenerative disorders. It is also increasingly recognized that conformationally diverse strains of each disease-associated protein determine the disorder a patient develops, accounting for the observed clinical heterogeneity across subsets of neurodegenerative diseases. Notably, alpha-synuclein strains are known to cause neuropathological inclusions in specific cell types in the brain, giving rise to the hypothesis that cellular environment impacts strain formation. Using both cellular and mouse models of synucleinopathy, we tested this hypothesis, comparing replication fidelity between recombinant pre-formed fibrils (PFFs) and multiple system atrophy (MSA) patient samples. Intriguingly, we found that alpha-synuclein isolated from MSA patient samples maintains strain properties after passaging through multiple cell types, including multiple mouse models. By comparison, we observed adaptation of PFFs, suggesting the cellular environment has a stronger effect on strain selection and replication. These findings indicate that while the cellular milieu has an impact on synthetic alpha-synuclein prion strains, it may have less of an effect on disease-causing strains.

O10

Talk 1: Contributions of pesticides to human PD
*Beate Ritz**
UCLA, Los Angeles, CA, United States

Among environmental agents, pesticides have been most consistently shown to increase the risk of Parkinson's disease (PD). Pesticides are toxins that are intentionally introduced into the environment at a large scale with an intent to harm living organisms, specifically many are designed to be neurotoxic. Pesticides are important for intensive industrial scale agriculture and food production as well as vector control (malaria). Thus, it is not surprising that their use and the variety of products has grown worldwide with more than 500 active substances approved for use. This talk will first provide an overview of large studies of PD conducted in California the home of one of only two state mandated pesticide use reporting systems. For more than two decades, the California studies collected extensive residential, occupational, and lifestyle data as well as biological samples. This allowed us to gain insights into the action of pesticides associated with PD and to conduct investigations into multiple 'omics' layers to identify biologic signatures of their toxic action. Our results not only show how PD risk is affected by pesticide exposures but also how we can dissect real world exposure effects through epigenetic (methylation) and metabolomic approaches and also the gut microbiome. For example, we showed that long-term ambient organophosphate pesticide exposures interact with genetic susceptibility to increase PD risk, how these pesticides affect DNA methylation in acetylcholine receptor pathways, and how chronic low-level exposure to multiple pesticides can act on mitochondrial energy metabolism and function as recently documented in our metabolomic analyses. These real-world examples will illustrate how low-level but chronic human pesticide exposures contribute to PD onset and progression

O11

Talk 2: Chemical toxicant contribution to human PD
*Briana De Miranda**
University of Alabama at Birmingham, Birmingham, AL, United States

Even the most liberal estimates place the heritability of Parkinson's disease (PD) at around 27%, and the most prevalent PD genetic risk factors (e.g., LRRK2, GBA) show incomplete and variable penetrance, suggesting that other factors play a key role in PD development. Conversely, established evidence strongly implicates environmental factors as triggers and/or facilitators of PD, however, exogenous exposures are rarely considered in the progression, treatment, or prevention of Parkinsonism. As some of the most widespread environmental contaminants are associated with PD, such as pesticides, solvents, heavy metals, and air pollution, understanding neurodegenerative pathology caused by industrial byproducts may provide a source for modifiable influence on PD development.
To this end, the basis of this talk is to discuss how toxicant exposures increase risk for Parkinsonism, the vast array of environmental factors linked to PD risk, possible strategies to combat exogenous sources of neurotoxicity, and how we can shape policy to reduce risk of exposure. In addition, this talk will address the selective vulnerability of dopaminergic neurons in the context of environmental factors and provide evidence for how toxicants can influence disease progression and phenotype, including Lewy pathology and neuroinflammation implicated in motor and non-motor symptoms of Parkinsonism. We will consider how environmental justice may play a role in PD incidence throughout the world and examine what changes need to occur that could ultimately prevent PD for certain future populations.

O12

Talk 3: Parkinson's, a man-made disease
*Ray Dorsey**
University of Rochester - Center for Health + Technology, Rochester, NY, United States

Parkinson's is now the world's fastest growing brain disease. Its principal causes are likely certain pesticides, dry cleaning chemicals, and air pollution. All of these are preventable. In this discussion, we will explore why you have Parkinson's. We will then detail what we can all do to (1) slow the progression of the disease for those who already have it and (2) create a world where Parkinson's is increasingly rare.

O13

Talk 1: Digital monitoring of mobility – Why, where and how?
*Lynn Rochester**
Newcastle University, Newcastle Upon Tyne, Newcastle Upon Tyne, United Kingdom

Mobility is a key aspect of independence and health. It has been identified as a priority for people with Parkinson's (PwP) and one that they wish to preserve and protect. Changes in mobility include discreet measures of gait (the way we walk) as well as the amount and pattern of everyday activity. These changes are present very early, even before diagnosis; continue to evolve over time despite optimal care; and are linked to future falls risk and mobility disability. Mobility measures can also provide important insights to help identify and characterise Parkinson's, its progression and response to treatment. The way we measure mobility currently however, has

some recognised limitations. Existing approaches use more indirect methods divorced from the context in which mobility takes place. Tests typically explore the perception of changes in mobility through questionnaires or test mobility capacity using brief walking tests. In order to advance and prioritise treatments to target mobility loss we need better tools to measure it in a manner that provides a direct measure and reflects the PwP real-life experience. Digital Health Technologies (DHT) such as wearable and mobile devices allow mobility to be assessed directly and continuously as people go about their everyday activities. This offers an alternative or complimentary solution for personalised mobility assessment that allows PwP to be better informed and able to manage their own mobility issues as well providing more sensitive, precise and relevant measures for use in clinical trials to advance development of new therapies. This talk will focus on why mobility is important from the patient, research and clinical perspective and how digital health technology is transforming mobility assessment taking it from the clinic to the home. It will focus on a leading international effort to drive the necessary change led by the Mobilise-D consortium (https://www.mobilise-d.eu/) outlining the steps undertaken and the evidence to make this transformation change.

O14

Talk 2: Digital intervention
*Esther Cubo**
Hospital Universitario Burgos, Burgos, Spain

Telemedicine is particularly capable of assessing patients with Parkinson's disease (PD) and other movement disorders because much of the neurological exam findings are visual. Parts of neurological examinations can be performed during teleconsultations, providing equivalent results to in-person assessment and evaluation of candidacy for advanced PD therapies. Further, over the last decade, telemedicine has been expanded by the inclusion of Interdisciplinary healthcare systems, including specialized speech therapists, occupational therapists, physiotherapists, psychotherapists, nurses, and support groups for PD. However, further research into the implementation of multidisciplinary telemedicine services in underserved PD populations are needed in guiding decisions for patient-centered care through developed international frameworks.

O15

Talk 3: Digital evidence
*Jochen Klucken**
University of Luxembourg, Luxembourg Institute of Health, Centre Hospitalier de Luxembourg, Belval, Luxembourg

Digital Medical Devices including smartphone apps, wearable sensor-based monitoring solutions, AI-supported prediction tools are increasingly developed by engineers, data-scientists, and clinicians, jointly with Parkinson Patients. However, they usually provide better data to serve as digital biomarkers but not necessarily improve the health status of the patient or the healthcare service quality of the professional. A new type of evidence for these digital medical devices is currently being introduce in several European counties that aim to proof their clinical value for patients, professionals or both. This includes new diagnostic tools that benefit from wearable-sensor based assessments in the home-environment (digital monitoring devices), clinical-decision support concepts combing patient-reported outcome/experience measures with standardized clinical assessments, therapeutic devices focusing on gait&mobility improvement tailored to the needs individual patients. The new "evidence-based digital medicine" concept behind these regulatory assessment procedures in the European countries will be introduced in the presentation supporting reimbursement of innovative digital solutions and providing access for patients. Ultimately, this translates healthcare technology innovations to patient care, provides a new framework for evidence-based, device-aided healthcare, and connects public-private-research and development for better health of Parkinson patients.

O16

Talk 1: Using iPSC to address non-neuronal cells in PD
*Mark Cookson**
National Institute on Aging, Bethesda, Maryland, United States

Induced pluripotent stem cells (iPSC) represent an important model for understanding the effects of human genetic variation in the context of an intact endogenous genome. We have used a series of cell lines from the Parkinson's Progression Markers Initiative (PPMI) to probe how non-coding genetic variation at the LRRK2 locus on chromosome 12 affects microglial gene expression and function. The outcome of these experiments showed that cells carrying risk variants have higher LRRK2 expression and activity when IPSC are differentiated into microglia. Importantly, we found that only LRRK2 was the only gene on chromosome 12 that was differentially expressed by genotype. Furthermore, we were able to show that there are microglial-specific regions of open chromatin that allow for binding of microglia-expressed transcription factors, providing a mechanistic basis for how gene expression as a quantitative trait might manifest in a cell-type specific manner. Ongoing work include developing extensions of this work across the genome and under conditions of immune cell activation.

O17

Talk 2: Arrayed Dual CRISPRa and CRISPRo Screens for the Identification of Neurodegenerative Targets
*Adriano Aguzzi**
Institute of Neuropathology, Zürich, Switzerland

Genome-wide CRISPR phenotypic screens are clarifying many fundamental biological phenomena. Arrayed CRISPR libraries extend the screening territory to cell-nonautonomous, biochemical and morphological phenotypes. We generated two human genome-wide arrayed libraries termed T.spiezzo (gene ablation, 19,936 plasmids) and T.gonfio (gene activation and epigenetic silencing, 22,442 plasmids). Each plasmid encodes four non-overlapping single-guide RNAs (sgRNAs), each driven by a unique promoter, as well as lentiviral and transposable vector sequences. The sgRNAs tolerate most DNA polymorphisms identified in 10,000 human genomes. Deletion, activation and epigenetic silencing showed efficacy of 75-99%; lentiviral titers were ~107/ml. As a proof of concept, we performed an image-based high-content screens for modifiers of α-Syn aggregation and propagation, which identified several known and many novel downregulators and 15 upregulators of synuclein phosphorylation. We will also present the results of an arrayed genome-wide CRISPRa screen which allowed us to enumerate all modifiers of glucocerebrosidase activity using a substrate-turnover assay. In conclusion, arrayed CRISPR screens possess a remarkable potential to discover molecules relevant to neurodegenerative diseases, including pharmacologically actionable targets which may not be identifiable by large-scale human genetics.

O18

Talk 3: Using organoid culture systems to study Parkinson's disease
*Shawn Je**
Duke-NUS Medical School, Singapore, Singapore

The ability to make functional neural cells and brain-like organoids from human pluripotent stem cells (hPSCs) provides a unique opportunity to study human brain development and neural disorders. In this seminar, I will present recent findings from our laboratory - the generation of human midbrain-like organoids from hPSCs (Cho et al., Nature Communications, 2021; Jo et al., Cell Stem Cell, 2016; Kwak et al., Stem Cells, 2020) and their utilities in modeling Parkinson's disease (Jo et al., Annals of Neurology, 2021).

O19

Talk 1: Drug repurposing for PD therapies
*Lorraine Kalia**
Toronto Western Hospital, Toronto, ON, Canada

Drug development for chronic diseases such as Parkinson's disease remains an expensive and lengthy process. Currently, the estimated cost of bringing a new drug to market is $1.3 billion and the average timeframe is 13 to 15 years. Only 10% of compounds make it through the drug development pipeline to receive approval by regulatory authorities, such as Health Canada and the US Food and Drug Administration. Furthermore, just 9% of those approved in the last 10 years were for neurological disorders. Drug repurposing or drug repositioning is a strategy in which existing drugs already approved for use in humans are investigated for alternative clinical indications. In my presentation, I will examine drug repurposing as one approach to expedite the discovery and development of new therapies for Parkinson's disease. I will illustrate the concept of drug repurposing by providing examples from other diseases and from symptomatic treatments frequently used for Parkinson's disease. The focus of my presentation will be on the application of drug repurposing to the discovery of disease modifying therapies. I will review candidates that have been identified in preclinical studies and summarize drugs that have advanced to clinical trials. The potential of drug repurposing but also the challenges and limitations will be discussed. My take home message is that multiple strategies – drug repurposing being one of them – are necessary to ultimately find disease modifying therapies for Parkinson's disease.

O20

Talk 2: Development of PD drugs for genetic targets: A-synuclein, GBA, LRRK2 and beyond
*Jesse Cedarbaum**
Coeruleus Clinical Sciences LLC, Woodbridge, CT, United States

The year 2022 saw the readout of the first two clinical trials whose scientific underpinnings were based on our current concept of Parkinson's disease pathophysiology and genetics: the anti-alpha-synuclein antibodies Cinpanemab and Prasinezumab. Both trials failed to meet their primary endpoint – slowing of progression of disease severity as measured by the MDS-UPDRS, but the sponsor of the Prasinezumab trial found some signals suggesting efficacy. Another pharmaceutical company terminated its synuclein antibody program. Can we explain these trial results? What do these studies teach us for ongoing and upcoming clinical trials targeting synuclein as well as glucocerebrosidase (GBA) and LRRK2, the two most common genetic forms of PD, and other genetically linked forms of the disease? This talk will attempt to tackle these and other key questions while reviewing the landscape, progress and challenges that must be overcome in leveraging genetically-based targets in our quest to slow, halt or prevent PD progression.

O21

Talk 3: Emerging therapies targeting the immune system in PD
*Caroline Williams-Gray**
University of Cambridge/Cambridge University Hospitals NHS Trust, Cambridge, United Kingdom

There is now a wealth of evidence to support the theory that the immune system contributes to the pathogenesis of Parkinson's disease (PD). Many genetic variants linked to PD risk play a role in regulating immune responses. Epidemiological studies have demonstrated that autoimmune and inflammatory diseases are associated with increased susceptibility to PD, whilst use of immunosuppressant drugs appears to reduce PD risk. Activation of the brain's innate immune cells (the microglia) is a well-reported feature of both animal models and human PD, and the immune profile in the blood is altered with a shift towards more activated immune cells and an increase in inflammatory markers. Early clinical trials targeting immune pathways focused on microglial activation in the brain, without success. More recently targeting of the peripheral immune system has been proposed, given the emerging evidence of peripheral-central immune crosstalk: monocytes and T cells traffic into the cerebrospinal fluid (CSF) and brain in PD patients, and animal models provide evidence that these peripheral immune cells are a critical mediator of neuroinflammation and neurodegeneration. A phase 2 double-blind placebo-controlled trial repurposing the immunosuppressant drug azathioprine is currently underway, with the aim of providing proof of concept for therapies targeting peripheral immune activation in PD. The trial will evaluate whether azathioprine can slow the rate of clinical PD progression over 12 months of treatment, and whether it can reduce markers of immune activation in the CSF and neuroinflammation in the brain. (ISRCTN14616801) Future trials may take a more targeted approach to immune manipulation in PD. A small phase 1 placebo-controlled trial of sargramostim (granulocyte-macrophage colony-stimulating factor), which boosts T-regulatory cells, has provided preliminary data suggesting improvement in MDS-UPDRS motor scores over 8 weeks of treatment, and open label use of low

dose therapy for a year was well tolerated in a small number of patients. (NCT01882010) This lends support for future strategies aiming to reduce immune overactivation by altering the balance of regulatory and inflammatory T-cells in PD. Other candidates are under consideration to target innate immune activation, including Toll-like receptor blockers and inflammasome inhibitors.

O22

Talk 1: Creativity, aesthetics, the brain and Parkinson's disease
*Anjan Chatterjee**
University of Pennsylvania, Philadelphia, Pennsylvania, United States

Since the late 19th century, neurology has played a critical role in advancing our understanding of large-scale human behavioral systems that underpin perception, language, emotions and attention. Can neurologic conditions do the same for aesthetics? One striking observation is that brain damage can sometimes paradoxically facilitate art. I will review observations on how neurological disease changes and sometimes "improves" art production to contextualize similar observations in Parkinson's disease (PD). Given the effects of the disease on dopamine, and dopamine's role in our reward systems, one might expect people with PD to receive less pleasure from art. I will shows that such a general effect of PD on pleasure does not occur. PD can affect judgments of beauty that are triggered by implied movement in art but not when based on other features of art. These observations speak to the resilience of patients' creativity and aesthetic appreciation in the face of changes to the brain.

O23

Talk 2: How art can impact wellness
*Jonny Acheson**
University Hospitals of Leicester NHS Trust, Leicester, Leicestershire, United Kingdom

It is well documented that people with Parkinson's can develop or rediscover a creative side after diagnosis and art plays a part in that. The Cambridge Dictionary defines art as an activity through which people express particular ideas. This talk will explain how using art can impact wellness looking at both conventional and digital methods.
From the initial concept of a piece of artwork to the planning and actual construction of it, it is an immersive process. Styles will develop over time acknowledging that they will need to be adapted as symptoms change.
It will encourage those in the audience who have not tried art before to have a go and challenge them to start to think about what medium they could use as well as tapping in to this widely available resource to bring wellness into their community.

O24

Talk 3: How writing can support wellness
*Rebecca Gifford**
PD Avengers, Vancouver, BC, Canada

Writing can be a powerful tool in our Parkinson's resilience and self-care tool box. It offers opportunities to release emotions, take a break and breathe, clarify our thoughts and learn from our experiences. Plus, it can be a lot of fun. Rebecca will talk about what writing has offered her during her care partner journey and beyond, including as a tool for managing stress and maintaining a meaningful relationship with herself. She'll share tips for how to let go of the common insecurities and expectations that inhibit would-be writers and motivate you to free your inner storyteller.

O25

Talk 4: How dance can support wellness
*Pamela Quinn**
PD Movement Lab, New York, NY, United States

I'm going to speak about how the experience of Parkinson's as a wearable disease you can't hide makes one less concerned about what others think, which in turn has a freeing effect on the creative process. I will also talk about the the suspicion that surges of dopamine can give one a creative boost and more focusing power once one's drugs kick in. Perhaps the most interesting aspect of my talk will be the comparison of my pre-PD artistic experience with my mid-stage PD experience of making art.
As to how dance can support wellness: Moving to music gives us a much wider range of physical expression and fortitude. Music also takes us away from disease and into another realm, depending on the nature of the sound. It is transporting and can serve as a healthy escape from PD. Also, working one's body is essential to health, PD or no PD, and to offset the social isolation that comes with the disease, dance provides a social/communal antidote. Dance is joyful and can lift us out of depression. It is an effective wonder drug: inexpensive, safe and with no adverse side effects.

O26

Being a musician with Parkinsons: The high and low notes.
*Tomas Gisby**
London, United Kingdom

A point of view from a younger person with Parkinson's on the benefits and challenges of performing and creating music.
I have two different yet emotionally-intertwined interests in this topic; firstly playing instruments and music-making for personal enjoyment, and secondly working professionally in the field.
I'm keen to share my experiences in how Parkinson's has changed my involvement and relationship with music and composing, managing expectations, and keeping it fun, and discuss how it's never been easier to give music-making a go.

O27

Table 1: Aerobic exercise and PD
*Nienke de Vries**
Radboud University Medical Center (Radboudumc), Nijmegen, Netherlands

Increasing evidence indicates that aerobic exercise is beneficial in people with Parkinson's disease (PD). Besides clinical effects on for example gait and balance, a stabilizing effect on disease symptoms has been found in a few clinical studies. Moreover, exercise is among only a few available interventions for PD of which there is human and laboratory evidence of a disease-modifying potential. The mechanisms of action underlying these effects remain largely unknown to date. However, despite an enormous amount of research on exercise in PD, only a few small studies have focused on it's disease modfying potential. It also remains unclear which type and intensity of exercise is most effective. Finally, long-term adherence to (aerobic) exercise is a huge challenge.

In this roundtable session, a short overview of the current evidence on aerobic exercise will be given, based on which a discussion on all challenges related to aerobic exercise and PD will be held. Both practical issues and scientifec challenges can be discussed.

O28

Table 2: La ciencia detrás de las diferencias entre sexos
*Ariadna Laguna**
Vall d'Hebron Research Institute, Barcelona, Spain

La incidencia y prevalencia de la EP es entre 1,5 y 2 veces mayor en hombres que en mujeres. Sin embargo, hay millones de mujeres con EP en todo el mundo y no se comprenden bien las diferencias entre hombres y mujeres en la progresión natural de la enfermedad y en la contribución de los factores protectores y nocivos. Además, en general, las experiencias de las mujeres no siempre se tienen en cuenta en la gestión clínica, los estudios de investigación y los ensayos clínicos.
En los últimos años se ha empezado a reconocer las diferencias entre sexos en relación a la manifestación de los síntomas motores y no-motores de la enfermedad. Pese a ello, los estudios dirigidos a comprender las bases biológicas de esas diferencias y a adaptar el manejo de la enfermedad considerando las necesidades únicas de las mujeres siguen siendo escasos. Aunque varios hallazgos indican que los estrógenos pueden desempeñar un papel en la EP y explicar algunas diferencias sexuales, otros mecanismos como la expresión génica, la neuroinflamación, el estrés oxidativo y los factores del estilo de vida podrían estar involucrados. Por otra parte, todavía no se puede aseverar si todas esas diferencias son exclusivamente una cuestión biológica, determinadas por el sexo, o si también contribuyen aspectos socioculturales asociados al género.
La identificación precisa de las diferencias entre sexos es importante para adaptar el tratamiento, predecir los resultados y satisfacer otras necesidades individuales y sociales de las mujeres con EP. Además, es necesario hacer llegar esta información a las mujeres afectadas para mejorar su autoconocimiento y bienestar.

O29

Table 3: Parkinson's and writing to maintain wellness
*Kat Hill**
World Parkinson Coalition, Davis Phinney Foundation, Portland, OR, United States

Writing can be a powerful tool for those navigating the challenge of living with Parkinson's disease. Words can be used to create a framework to process the impact of a diagnosis and associated grief and help communicate how we present ourselves to others. Writing also builds neuroplasticity and the practice can help maintain manual dexterity.
Taking time to reflect and write about our experiences can help us create our personal narrative. There is power in making word choices to describe how our diagnosis impacts us and how we want to intentionally move into life after diagnosis.
In this round table session, participants will have the opportunity to learn the value of self-expression and importance of word choice. We will discuss ways to integrate writing into one's daily routine and how to frame a narrative to maximize wellness.
No writing experience is required, and all materials will be provided.

O30

Table 4: Subtyping in Parkinson's: What are the therapeutic implications?
*Sonja Scholz**
National Institutes of Health, Bethesda, MD, United States

Parkinson's disease is a clinically heterogeneous disease presenting with motor and non-motor symptoms. The constellation of symptoms can vary over the disease course and from patient to patient, suggesting the existence of distinct subtypes. In this presentation, I will discuss recent advances in stratifying Parkinson's disease patients and review current knowledge on clinical, pathological, and genetic subtypes. I will emphasize potential implications for developing precision medicines, such as enhanced clinical trial design and molecular diagnostics. Expanding knowledge on disease subtypes from the molecular level to the protean clinical manifestations will be key for making disease modification a reality in the field.

O31

Table 5: Independent patient research – Valuable contribution or uncontrolled data?
*Kevin McFarthing**
Independent, Oxford, United Kingdom

People with Parkinson's (PwP) know themselves better than anyone else. They have the potential to contribute to the understanding of possibilities for improvement, either through self-monitoring and subsequent change to daily protocols; or to find new ways to treat Parkinson's. PwP also experiment with supplements and other potential therapies to try and find relief from the symptoms of Parkinson's. Can this experimentation be harnessed and analysed for the benefit of other PwP?
Several attempts have been made to document and analyse these "n=1" experiments. Sara Riggare [1] and John Turner [2] are good examples of PwP who share methodologies for self-monitoring.
Attempts have been made to evaluate new potential therapies in a multiple n=1 fashion. One notable example is the establishment of Clinicrowd to test the potential of mannitol in Parkinson's [3]. The Clinicrowd website enabled PwP to share their experience with taking mannitol. Anecdotal feedback suggested improvements in symptoms with many individuals, particularly with sense of smell. However, the feedback response rate was low and potentially selected for positive observations. A subsequent small controlled trial failed to show any improvement.
Another preparation under consideration from a scientist/PwP is broccoli sprouts containing sulforaphane, an antioxidant [4]. This has been evaluated on a small-scale n=1 basis with claims of potential improvements in non-motor symptoms.
Single observations can also lead to breakthroughs in research, for example in the case of Joy Milne, "the woman who can smell Parkinson's". This has resulted in a prototype assay that has the potential to diagnose Parkinson's in a matter of minutes [5].
Multiple n=1 studies can also be conducted in controlled conditions, where several options are tested and analysed in the same individual [6].
The following questions are proposed:
1. Are symptoms best self-assessed qualitatively or using validated common methodology?
2. How can scientifically trained PwP bring potential new therapies to the notice of professional scientists?
3. Can we combine self-monitoring of disease status and progression with evaluation of new therapies to produce new opportunities? Should we?

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O32

Table 6: Understanding peripheral immune cells in the immune response in Parkinson's

*Diana Matheoud**
Université de Montréal/CRCHUM, Montréal, Quebec, Canada

Parkinson's disease (PD) is a neurodegenerative disease which is accompanied by a strong inflammation, present both in the central nervous system and the periphery. Moreover, genes PINK1 and PRKN, which are causative of familial forms of PD, are implicated in the inhibition of mitochondrial antigen presentation (MitAP), a phenomenon which acts as a potential trigger for an autoimmune response. This work's aim was to investigate the contribution of peripheral autoimmune and inflammatory processes in the etiology of PD, with a particular focus on phenomena implicating the mitochondria. Quantification of PINK1 and PRKN mRNA allowed us to determine that both genes could be inhibited by the activation – through LPS or EPEC exposition – of specific antigen-presenting cells, the monocyte-derived dendritic cells (MDDC). The expression of PRKN was also inhibited during the aging process in peripheral blood mononuclear cells. Through the investigation of T lymphocytes present in PD patients' circulation, we identified a population of T CD8+ IL-17+ (Tc17) cells which could be activated by mitochondrial antigens. Furthermore, the MDDC were identified as a major contributor to inflammation since PD patients' cells presented a specific expression profile characterized by an over-production of pro-inflammatory cytokines. This response was age-associated and corresponded with a pro-Th17 polarization of T CD4+ lymphocytes, a subtype which has been linked with autoimmune diseases. Taken together, our results support an implication of autoimmune mechanisms in the development of PD.

O33

Table 7: Treatment for PD apathy and/or fatigue: Where should we be looking?

*Kathy Dujardin**
Lille University medical center, Lille, France

Apathy and fatigue are frequent non-motor symptoms of Parkinson's disease. Apathy is usually defined as reduced motivation compared to the individual's previous level of functioning. The main manifestations are reduced interest, lack of initiative and participation in the main activities of daily life, lack of perseverance, indifference and flattening of affect, reduced engagement in social interaction. Profiles are variables since, according to individuals, the cognitive, behavioral, emotional, or social aspects may predominate. There is a frequent overlap between apathy and other non-motor symptoms of Parkinson's disease, namely fatigue. Fatigue corresponds to an abnormal and excessive lack of energy that is persistent and interferes with normal function. Despite both syndromes are highly prevalent in Parkinson's disease and are considered by many patients and caregivers as the most debilitating ones, treatment to fight them are sorely missing. Several pharmacological and non-pharmacological treatments were shown to efficiently improve Parkinson's disease-related apathy. However, the level of evidence is mostly low. Regarding the treatment of fatigue in Parkinson's disease, some interventions were shown to improve fatigue. However, most of the time, fatigue was only a secondary outcome. Currently, there is insufficient evidence to support any pharmacological or non-pharmacological treatment.
To progress and find efficient treatments, we need a better understanding of the mechanisms underlying apathy and fatigue in Parkinson's disease. The objective of this roundtable is share current knowledge regarding these mechanisms and to determine the avenues to be developed in response to patient needs. Participants are invited to share their experience regarding interventions that can improve apathy and fatigue in Parkinson's disease.

O34

Table 8: Does non-invasive brain stimulation work for PD?

*Michael Simpson**
The Hong Kong Polytechnic University, Hong Kong, Kowloon, Hong Kong

This round table will first consider what non-invasive brain stimulation is expected to achieve in the treatment of Parkinson's disease. The merits and limitations of two primary forms of non-invasive brain stimulation, transcranial magnetic and transcranial electric stimulation, will then be discussed with a view to how these approaches may be best integrated among therapeutic strategies for people with Parkinson's disease. The scope and scale of therapeutic potential and how these techniques may look moving forward will also be discussed.

O35

Table 9: The role of microglia in PD pathology

*Zhenyu Yue**
Icahn School of Medicine at Mount Sinai, New York, New York, United States

Autophagy clears protein aggregates, damaged cellular organelles, and pathogens through the lysosome. Although autophagy is highly conserved across all cell types, its activity in each cell is specifically adapted to carry out distinct physiological functions. The role of autophagy in neurons has been well-characterized, though in glial cells its function remains largely unknown. Microglia are brain-resident macrophages that survey the brain to remove injured neurons, excessive synapses, protein aggregates, and infectious agents. Current studies demonstrate that dysfunctional microglia contribute to neurodegenerative diseases. In Alzheimer's disease animal models, microglia play a critical role in regulating amyloid plaque formation and neurotoxicity. However, how microglia are involved in Parkinson's disease (PD) remains poorly understood. Propagation of aggregated α-synuclein via cell-to-cell transmission and neuroinflammation have emerged as important mechanism underlying neuropathologies in PD. Here we review converging evidence that microglial autophagy maintains α-synuclein homeostasis, regulates neuroinflammation, and confers neuroprotection in PD experimental models.

O36

Table 10: Digital and/or wearable technology for monitoring of motor and non-motor function in PD
*Christopher Hess**
University of Florida Fixel Institute for Neurological Diseases, Gainesville, FL, United States

WPC Roundtable sessions are unique sessions that allow delegates to sit down with an expert to discuss a given topic or series of topics in a very small, intimate group. Roundtable experts will give a shot overview of the predetermined topic and will then take questions from the participants. This roundtable will be focused on digital and wearable technologies in Parkinson's disease. We will discuss the current state of integration of neurotechnologies and wearable devices in Parkinson's disease care and research, and how evolving technologies will change the way that patient care is provided and research is performed in the coming decade. Seats are filled on a first-come, first served basis. Each Roundtable session can take up to 11 participants. We strongly encourage those who are interested to arrive early.

O37

Table 11: Reaching PD communities across Africa
*Omotola Thomas**
Parkinson's Africa, London, United Kingdom

Overarching goal: To engage in interactive discussions about how African Parkinson's communities can be reached, better supported, more informed, equipped with knowledge, and empowered.
Learning Objectives:
To gain better insights into how African Parkinson's communities are set up and organised;
To better understand the needs of these communities and how to best reach them;
Overview: The main emphasis of this round table will be sharing best practises for building resilient and empowered African communities. Participants can anticipate brainstorming and addressing issues like the following: What was successful? What failed to work? Do any nations on the continent, or those outside it, have empowered communities that could serve as models for others to follow.

O38

Table 12: Occupational therapists can help people with PD live their best life
*Lisa Warren**
University of Florida Health Norman Fixel Institute for Neurological Diseases, Gainesville, Florida, United States

The current medical management of Parkinson's is limited in its ability to control symptoms. Occupational therapists are uniquely positioned to bridge the gap between medication and function. OTs provide, treatment, education and recommendations to promote the health, well-being and activity participation of person's living with Parkinson's. With a skill set focused on quality of life, OTs are able to assess and address the motor and non-motor impact of Parkinson's on daily function. From initial diagnosis to end stage, occupational therapists provide goal directed therapy and education that meets the patient where they are in the disease process. Working with persons with Parkinson's and their care partners throughout motor and non-motor progression, promotes independence, safety, and an improved or stable quality of life. This round table discussion will cover the use of the occupational therapists' skill set to evaluate and address motor and non-motor symptoms that negatively impact success with activities of daily living. Looking at the patient and family through the lens of an OT, we often identify interfering aspects of Parkinson's that may not be well studied. Many have found strategies that work but lack the research to promote it. At this round table we will discuss evaluation tools, successful interventions and share little known strategies that provide a big impact to the person living with Parkinson's.

O39

Table 13: The role of the physical therapist in addressing non-motor symptoms
*Daniel Peterson**
Arizona State University, Phoenix, AZ, United States

Cognition is often impacted by PD, with particular deficits in sub-populations of PD, such as those who exhibit freezing of gait. Cognitive deficits could impact the effectiveness of physical therapy. In this interactive roundtable, we will first discuss some current research on cognitive deficits often observed in people with PD. Then, we will discuss the ways that clinicians assess cognition in their patients, as well as instances that this information should (and perhaps should not) be used to guide physical rehabilitation.

O40

Table 14: Communicating well in person and virtually
*Walter Maetzler**
Kiel University and University Hospital Schleswig-Holstein, Campus Kiel, Kiel, Germany

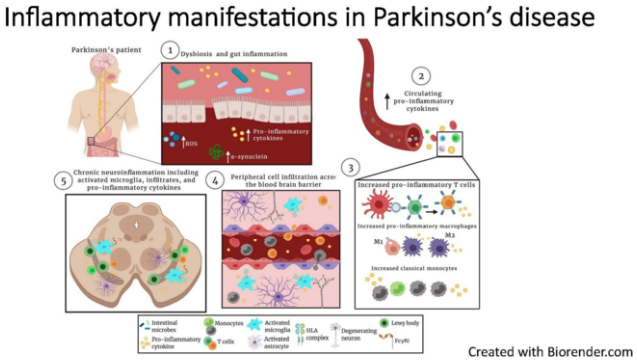
The purpose of this table is to present and discuss new communication options between people living with PD and the clinical care team or with researchers investigating aspects of PD. In an introductory presentation, new communication tools will be presented that have all the aim to increase the involvement of people living with PD in diagnostic, treatment and research decisions. These include Shared Decision Making (SDM) and Public and Patient Involvement and Engagement (PPIE). The aim of this table is to discuss the effectiveness of these tools and to give people who have little or no experience with them a basic understanding of them.

O41

Talk 1: Bringing the immune system to Parkinson's disease
*Malu Tansey**
University of Florida, Gainesville, FL, United States

Parkinson's is a multi-factorial, heterogeneous, and complex disease involving peripheral organs and the brain. Gene-by-environment interactions combine with aging to create the perfect storm for development of Parkinson's and the immune system plays a key role as the arbiter of this interplay. Clinical data and pre-clinical models of PD reveal that innate and adaptive immune dysfunction in both central and peripheral immune compartments; and recent studies from our group reveal that immunological stimulation of mouse or human peripheral blood mononuclear cells ex vivo enables detection of immune/inflammatory traits in aging cells and those with PD-relevant mutations. In addition, GI problems are common in PD and they frequently manifest decades before a clinical diagnosis. This has led to the theory that PD pathology could initiate in the intestine before advancing to the central nervous system (CNS). Chronic gut inflammation in Crohn's and ulcerative

colitis has been associated epidemiologically with increased risk for PD and the reported gut dysbiosis in pro-dromal PD could contribute to an inflammatory gut microenvironment that could trigger alpha synuclein accumulation and aggregation in enteroendocrine cells that are in contact with enteric ganglia and the latter to the vagus. We investigated the extent to which PD patients exhibit indications of intestinal inflammation in stool and identified elevated levels of specific soluble inflammatory mediators that were different between PD subjects and spouses. Follow-up studies revealed that PD subjects display low abundance of short-chain fatty acid-producing bacteria (and higher levels in men correlated with later onset of motor symptoms); in addition, low butyrate levels were associated with epigenetic changes in immune genes and correlated with depression symptoms. We have utilized various mouse models to evaluate the impact of colonic inflammation on neuron health in the brain. We discovered that the induction of damage and inflammation in the intestine sensitizes the nigrostriatal system to damage from known neurotoxins. Our findings demonstrate that use of neuroimmunological approaches to identify immune dysfunction in subjects at risk may enable the field to develop novel and more effective therapeutic approaches for immunomodulation in the peripheral blood and/or gut to delay, slow, or prevent PD development or progression.



O42

Talk 2: Peripheral immune cells in the immune response during Parkinson's disease: T-cells

*Diana Matheoud**
Université de Montréal/CRCHUM, Montréal, Quebec, Canada

Parkinson's disease (PD) is a neurodegenerative disease which is accompanied by a strong inflammation, present both in the central nervous system and the periphery. Moreover, genes PINK1 and PRKN, which are causative of familial forms of PD, are implicated in the inhibition of mitochondrial antigen presentation (MitAP), a phenomenon which acts as a potential trigger for an autoimmune response. This work's aim was to investigate the contribution of peripheral autoimmune and inflammatory processes in the etiology of PD, with a particular focus on phenomena implicating the mitochondria. Quantification of PINK1 and PRKN mRNA allowed us to determine that both genes could be inhibited by the activation – through LPS or EPEC exposition – of specific antigen-presenting cells, the monocyte-derived dendritic cells (MDDC). The expression of PRKN was also inhibited during the aging process in peripheral blood mononuclear cells. Through the investigation of T lymphocytes present in PD patients' circulation, we identified a population of T CD8+ IL-17+ (Tc17) cells which could be activated by mitochondrial antigens. Furthermore, the MDDC were identified as a major contributor to inflammation since PD patients' cells presented a specific expression profile characterized by an over-production of pro-inflammatory cytokines. This response was age-associated and corresponded with a pro-Th17 polarization of T CD4+ lymphocytes, a subtype which has been linked with autoimmune diseases. Taken together, our results support an implication of autoimmune mechanisms in the development of PD.

O43

Talk 3: Monocytes – The other peripheral immune cell in PD

*Caroline Williams-Gray**
University of Cambridge/Cambridge University Hospitals NHS Trust, Cambridge, United Kingdom

There is abundant evidence that the immune system is involved in the pathogenesis of Parkinson's disease (PD). A prominent theory which has gained much attention in recent years is that there is a specific T-lymphocyte response to proteins generated early in the course of the disease (such as aggregated alpha-synuclein and/or mitochondrial antigens) which promotes inflammation and neurotoxicity in the brain. However, activation of the non-specific 'innate' immune system also occurs in PD and represents a critical first step in the immune activation pathway. Monocytes are key cells of the innate immune system which are known to mediate the early inflammatory response to pathogens and tissue damage, and trigger subsequent activation of T-cells, leading in turn to B-cell activation. The phenotype of these innate 'early responder' cells is altered in people with PD, with an increased proportion of classical monocytes which are highly phagocytic and inflammatory, and increased expression of monocyte receptors involved in cell activation and migration. These monocyte changes vary according to clinical subtype, being most marked in those at higher risk of dementia, suggesting that variability in the innate immune response may contribute to the clinical heterogeneity of the disease. Changes in monocyte subsets have been reported not only in established PD but also prior to diagnosis in 'at risk' populations, providing support for the theory that the innate immune response contributes to disease onset. Studies of monocytes in vitro have shown that alpha-synuclein is able to activate these cells, via binding to Toll-like receptors on the cell surface, whilst bacterial toxins from the gut may also be a driver of the innate immune response in PD. The mechanisms by which monocyte activation in peripheral blood and tissues influence neuroinflammation in the brain in PD remain unclear but there is accumulating evidence of peripheral-central crosstalk, including correlation with PET markers of brain inflammation and neurodegeneration. Furthermore, animal models provide evidence that entry of monocytes into the central nervous system is critical for alpha-synuclein driven brain inflammation and neurodegeneration. Thus, targeting monocyte activation and migration may represent a useful therapeutic strategy for PD.

O44

Talk 1: Parkinson's apathy: Why do we care?

*Dawn Bowers**
University of Florida, Fixel Institute of Neurological Disorders, Gainesville, Florida, United States

Apathy is a core neuropsychiatric signature of Parkinson disease that is distinct from depression, affects between 30-70% of persons with Parkinson disease in cross-sectional studies, and worsens with disease progression. Rather than a mood disorder like depression and anxiety, apathy is a disorder of motivation that affects one's 'get up and go' across behavioral, cognitive and emotion domains. Why should we care? Apathy is linked to worsening cognition and has significant health and social consequences ranging from reduced functional independence, physical deconditioning, increased burden on caregivers, and negative implications for treatment outcomes.

This presentation will provide an update on what we know and what we do not. We will discuss risk factors for developing apathy, best tools for assessing apathy, how apathy co-occurs with other neuropsychiatric disorders like impulse control disorders, and how some treatments for depression can actually worsen apathy. We will address several great challenges in this area - ranging from paucity of empirically validated treatments for apathy to the absence of formal diagnostic criteria within the DSM-V. This presentation will highlight recent findings that certain behavioral approaches involving emotion regulation can facilitate electrophysiologic reactivity to standard emotion stimuli in persons with Parkinson disease and implications for intervention approaches. A major theme throughout this presentation will be conceptual and practical considerations facing clinicians, researchers, and families with Parkinson disease and why it matters.

O45

Talk 2: Parkinson's fatigue

*Graham "Alec" Glass**
Peak Neurology and Sleep Medicine, LLC, Anchorage, AK, United States

Fatigue and apathy can be extremely debilitating symptoms in Parkinson's Disease. These are present in up to 60% of patients across the disease course and are sometimes present before movement symptoms begin.
It is very important to distinguish these symptoms from hypersomnia (excessive daytime sleepiness), depression and anxiety that are often consistently present in PD.
Fatigue is generally defined as a lack of energy to initiate or complete and actions. Patients cannot seem to summon either the mental or physical energy to act but often aren't "sleepy" and wouldn't fall asleep if given the opportunity.
Sleepiness or drowsiness is the extreme desire to fall asleep. This is often relieved by a nap or sleep. Fatigue is typically not relieved by sleep.
Apathy on the other hand is a lost of interest in activities even when a patient does have the energy to participate in them.
Effective identification of Fatigue and Apathy often rely on the use of rating scales such as the Fatigue Severity Scale (FSS), The Parkinson's Fatigue Scale (PFS) and the Apathy Scale (AS).
Other sleep disorders including the presence of hypersomnia, Restless Legs Syndrome, Insomnia of Sleep Maintenance all must be evaluated and treated concurrently to effectively improve fatigue and/or apathy.
Depression and anxiety often travel with fatigue and apathy and should be maximally treated via both pharmacologic and non pharmacologic means to allow adequate therapy.
Ultimately, once other concomitant medical, sleep and neuropsychiatric symptoms have been addressed a number of therapies ranging from Cognitive Behavioral Therapy (CBT) to stimulant medications can be used to improve fatigue and apathy ultimately improving quality of life.

O46

Talk 3: Treatment for PD apathy and/or fatigue: Where should we be looking?

*Kathy Dujardin**
Lille University medical center, Lille, France

Apathy and fatigue are frequent non-motor symptoms of Parkinson's disease. Apathy is usually defined as reduced motivation compared to the individual's previous level of functioning. The main manifestations are reduced interest, lack of initiative and participation in the main activities of daily life, lack of perseverance, indifference and flattening of affect, reduced engagement in social interaction. Profiles are variables since, according to individuals, the cognitive, behavioral, emotional, or social aspects may predominate. There is a frequent overlap between apathy and other non-motor symptoms of Parkinson's disease, namely fatigue. Fatigue corresponds to an abnormal and excessive lack of energy that is persistent and interferes with normal function. Despite both syndromes are highly prevalent in Parkinson's disease and are considered by many patients and caregivers as the most debilitating ones, treatment to fight them are sorely missing. Several pharmacological and non-pharmacological treatments were shown to efficiently improve Parkinson's disease-related apathy. However, the level of evidence is mostly low. Regarding the treatment of fatigue in Parkinson's disease, some interventions were shown to improve fatigue. However, most of the time, fatigue was only a secondary outcome. Currently, there is insufficient evidence to support any pharmacological or non-pharmacological treatment.
To progress and find efficient treatments, we need a better understanding of the mechanisms underlying apathy and fatigue in Parkinson's disease. Current knowledge regarding the regulation of human motivated behavior, whilst incomplete, offers some avenues for the development of treatments targeting apathy. However, given the complexity of this regulation and the variability of clinical manifestations, approaches combining pharmacological treatment and other interventions have probably to be considered. Regarding fatigue, despite several hypotheses have been evoked, we currently lack insights into the mechanisms underlying this clinically heterogeneous syndrome in Parkinson's disease. A better knowledge of how the involved factors interact is thus an essential condition for the proposal of appropriate interventions.

O47

Talk 1: Exercise and physical therapy: Two sides of the same coin?

*Terry Ellis**
Boston University, Boston, MA, United States

In this presentation, the role of exercise and physical therapy for persons with Parkinson disease will be discussed. There is a growing body of evidence revealing the benefits of exercise in reducing the severity of motor symptoms, improving function and enhancing quality of life in Parkinson disease. As a result, physical therapy services and exercise are recommended as part of the standard treatment of Parkinson disease. However, many may ask "what is the difference between exercise and physical therapy?" Are both needed? Why? Under what circumstances? In this session, the distinction between exercise and physical therapy will be highlighted. The role of physical therapists will be described as it pertains to the treatment of persons with Parkinson disease. The range of treatments prescribed and delivered by physical therapists, including exercise, will be discussed. The presentation will culminate in recommendations regarding the utilization and timing of physical therapy services to optimize outcomes in Parkinson disease.

O48

Talk 2: Non-invasive brain stimulation and physiotherapy in PD

*Michael Simpson**
The Hong Kong Polytechnic University, Hong Kong, Kowloon, Hong Kong

Major challenges persist in the treatment of Parkinson's disease, not least for gait and refractory deficits resistant to conventional

pharmacotherapy. Physiotherapy is a tangible and often indispensable therapeutic option that seeks to induce lasting changes in physical capacity, to which the scale and scope of remedial effect may benefit from adjunctive non-invasive brain stimulation. Targeting pathophysiological characteristics of Parkinson's disease with transcranial magnetic and transcranial direct current stimulation has seen increased recognition over the past two decades, in part due to the potential for synergistic effects when coupled with physical therapy. Interventions targeting motor and frontal areas of the brain for gait and freezing of gait, or the cerebellum for dyskinesia, have been met with varying success. Crucially, to draw consistency from combined physiotherapy and non-invasive brain stimulation, reliable biomarkers are needed to inform stimulation protocols that optimise individualised therapeutic strategies in clinical practice.

O49

Talk 3: Action observation and motor imagery: From neurophysiology to clinical practice

*Laura Avanzino**
University of Genoa, Genoa, Italy

Motor imagery (MI) is a dynamic state during which motor actions are mentally simulated, without
actual movement. A large body of evidence suggests that imagined and executed actions recruit overlapping brain regions (i.e., premotor cortex, anterior cingulate, inferior parietal lobule, and cerebellum), although MI is thought to reflect mainly the process of movement preparation, with reduced involvement of end-stage movement execution related processes.
It is widely accepted that also the observation of actions performed by others activates in the brain the same neural structures used for the actual execution of the same actions. The neurophysiological basis of "action observation" (AO) is represented by the discovery of mirror neurons in the monkey cerebral cortex that discharge during both the execution of goal-directed actions and the observation of other individuals performing similar actions. The definition of "mirror neuron system" (MNS) comprises the cerebral areas containing mirror neurons and evidence with the use of neurophysiological techniques as transcranial magnetic stimulation and functional imaging (fMRI) suggested that a MNS is also present in the human brain. For example, during AO, the excitability of the motor cortex is enhanced, and brain areas in the frontal and parietal lobes are recruited, similarly to motor execution. The MNS is also involved in "imitation" within a circuit involving the inferior parietal lobule, the inferior frontal gyrus, and the premotor cortex.
Based on these neurophysiological premises, several studies have shown that MI and AO are effective ways to learn a new motor skill or to enhance its performance in healthy individuals, in an analogous manner to physical exercise. In rehabilitation, an adequate number of studies have been published so far that demonstrate positive effects of MI and AO training in neurological conditions with great attention in the last years to neurodegenerative diseases as Parkinson's disease (PD). In PD positive effects of AO and MI have been shown mainly on walking ability and typical motor signs of PD like freezing of gait.

O50

Talk 1: Mitochondria at the interface between neurodegeneration and inflammation

*Anne Grünewald**
Luxembourg Centre for Systems Biomedicine, University of Luxembourg, Belvaux, Luxembourg

Parkinson's disease (PD) is the fastest growing neurodegenerative disorder, lacking neuroprotective treatment options. Mitochondria have long been implicated in the pathogenesis of PD but the dimension of this involvement has been underestimated. Recent research efforts revealed that mitochondria act as information processing systems (MIPS) that regulate a multitude of cellular mechanisms well beyond energy metabolism. To explore the extent of impaired mitochondrial signaling in PD, we investigated patient-derived cellular models harboring mutations in the E3 ubiquitin ligase Parkin. Together with PINK1, Parkin mediates the clearance of dysfunctional mitochondria. In addition, the protein was suggested to control mitochondrial biogenesis via the PARIS-PGC-1α axis and to prevent mitochondrial membrane permeability by ubiquitination of the apoptotic protein BAK. In our studies, we focused on Parkin's role in preventing neuronal mtDNA dyshomeostasis, release, and glial activation at the endogenous level. Moreover, we tested the hypothesis that Parkin deficiency is also underlying PD pathogenesis in a subset of sporadic cases. Our findings suggest that Parkin co-regulates mitophagy, mitochondrial biogenesis, and mtDNA maintenance pathways, thereby protecting midbrain neurons from neuroinflammation and degeneration. With our work, we hope to pave the way for a new direction of PD therapeutics research.

O51

Talk 2: The emerging role of mitochondrial dynamics in neuroinflammation

*Kim Tieu**
Florida International University, Miami, Florida, United States

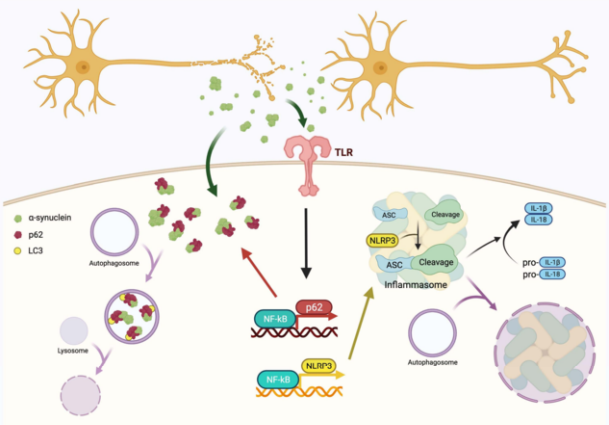
Mitochondrial dynamics involves fission, fusion and movement of mitochondria. Dynamin related protein 1 (Dpr1) is a "master regulator" of mitochondrial fission, although more recently it has also been reported to play a role in autophagy. We previously reported that Drp1 inhibition attenuated mitochondrial dysfunction, oxidative stress, impaired autophagy flux, and release of exosomes that contain neurotoxic α-synuclein. Given the important role of neuroinflammation in Parkinson's disease (PD), herein we investigated the impact of Drp1 inhibition on neuroinflammation. First, as a model of neuroinflammation, we injected Drp1+/- mice and their wild-type (WT) littermates with lipopolysaccharides (LPS), collecting the ventral midbrains (VMB) 6h later. Nanostring neuroinflammation analysis showed that LPS altered levels of many proinflammatory genes in WT mice; however, significant protection was observed in Drp1+/- littermates. The most dramatic change was lipocalin 2 (Lcn2) gene, whose gene product activates NLRP3 inflammasome. These results were validated through qPCR and Meso Scale Discovery cytokine assay. Sholl analysis demonstrated morphologically less microglial activation in Drp1+/- mice. To further investigate the role of Drp1 in microglia, we injected LPS in mice with inducible microglia-specific Drp1 deletion by crossing Drp1-LoxP with Cx3Cr1-CreERT mice, then captured individual microglia in the substantia nigra using laser microdissection, followed by qPCR analysis. Results revealed that microglia with Drp1+/- expressed less proinflammatory genes. Given that aging is a risk factor for PD, we investigated and confirmed an upregulation of LCN2 in 18-24 months old WT mice, but significantly less in Drp1+/- littermates. Lastly, we also detected increased Lcn2 in transgenic α-synuclein mice but attenuated in those crossed with Drp1+/- mice. Analogous results were found in immunofluorescent imaging of LCN2 in microglia within the midbrain of these mutant mice. Other neuropathology is being assessed. Together, our data indicate that a partial Drp1 knockout is sufficient to protect against neuroinflammation in multiple animal models. Furthermore, LCN2 - an under investigated protein in PD, may provide additional insights into PD pathogenesis.

O52

Talk 3: Neuroprotective Functions of Microglia via Autophagy Degradation in Parkinson's Disease

*Zhenyu Yue**
Icahn School of Medicine at Mount Sinai, New York, New York, United States

Microglia maintain brain homeostasis by removing neuron-derived components such as myelin and cell debris. The evidence linking microglia to neurodegenerative diseases is growing, however, the precise mechanisms remain to be clarified. Herein we report a neuroprotective role for microglia in the clearance of neuron-released α-synuclein. Neuronal α-synuclein activates microglia, which in turn engulf α-synuclein into autophagosomes for degradation via selective autophagy (termed synucleinphagy). Synucleinphagy requires the presence of microglial Toll-like receptor 4 (TLR4), which induces transcriptional upregulation of p62/SQSTM1 through the NF-κB signaling pathway. Induction of p62, an autophagy receptor, is necessary for the formation of α-synuclein/ubiquitin-associated inclusions that are degraded by autophagy. Disruption of microglial autophagy in mice expressing human α-synuclein promotes the accumulation of misfolded α-synuclein and causes midbrain dopaminergic neuron degeneration. Furthermore, autophagy-deficiency promotes senescence-associated microglia as evidenced by reduced proliferation, increased Cdkn1a/p21Cip1, dystrophic morphologies, and senescence-associated secretory phenotype (SASP). Our study thus identifies synucleinphagy of microglia, which clear α-synuclein via TLR4-NF-κB-p62 mediated selective autophagy and offers neuroprotection. Our study also demonstrates the protective role of microglial autophagy in preventing senescence.



O53

Talk 1: Digital and/or wearable technology for monitoring of motor and non-motor function in PD

*Christopher Hess**
University of Florida Fixel Institute for Neurological Diseases, Gainesville, FL, United States

We are on the cusp of an age in which novel technologies will have a dramatic impact on how we live. Advances in mobile broadband, internet communication protocols, and wearable devices will combine to create a future in which we are hyperconnected in real time, with continuous data flowing back and forth from devices in our homes and carried on our bodies. This lecture will focus on the current state of integration of neurotechnologies and wearable devices in Parkinson's disease care and research, and how evolving technologies will change the way that patient care is provided and research is performed in the coming decade.

O54

Talk 2: Should we be moving toward remote approaches to clinical trials?

*Ray Dorsey**
University of Rochester - Center for Health + Technology, Rochester, NY, United States

The COVID-19 pandemic highlighted fundamental shortcomings in our conduct of clinical research and clinical trials. Our traditional assessments of Parkinson's disease currently require in-person assessments in artificial environments (clinics) and ignore the 99.9% of the time (as noted by Dr. Sara Riggare) people with Parkinson's are outside the clinic. In addition, we routinely ask individuals with impaired driving ability, reduced mobility, and burden caregivers to come to research sites to participate in research. In this discussion, we will highlight how smartwatches, smartphones, and invisible sensors can objectively measure key features of Parkinson's disease in the real world. We will also explore how we can bring clinical trials to participants including a possible future phase 3 clinical trial that will require no office visits.

O55

Talk 1: Palliative care begins at diagnosis

*Benzi Kluger**
University of Rochester Medical Center - Neurology, Rochester, NY, United States

Palliative care (PC) is an approach to supporting patients and families affected by a serious illness that focuses on reducing suffering and improving quality of life. PC addresses the total pain of serious illness by acknowledging the whole person affected by illness, including physical symptoms, challenging emotions, spiritual wellbeing and practical matters such as planning for the future. Although many associate PC with cancer and end-of-life care, this approach is highly relevant to any serious illness, including Parkinson's, and evidence suggests that the earlier people are aware of it, the greater the benefits. In this talk we will review PC as it applies to PD and discuss ways that it can smooth your illness journey from diagnosis onwards.

O56

Talk 2: The palliative care team

*Ed Richfield**
North Bristol NHS Trust, Bristol, United Kingdom

The third talk in this session will be interlinked with the previous talks, particularly building on the powerful experiences of Larry and Rebecca Gifford, to explore how palliative approaches to care and the palliative care team, can contribute to improved, person centered care for people living with Parkinson's. Alongside the other speakers, Dr Ed Richfield will discuss the role of the palliative care physician, exploring shared decision making including where the person with Parkinson's and their caregiver may have divergent needs. We will discuss approaches to information sharing, accounting for the varied needs and experiences of people living with Parkinson's and explore the role of the multi-professional team in both delivering holistic care and targeting specific unmet needs. Finally, we consider how palliative approaches, including advance care planning (ACP), can help ensure the locus of control remains

with the person with Parkinson's and their loved ones, as they re-write their future together.

O57

Talk 3: Rewriting your future
*Rebecca Gifford**
PD Avengers, Vancouver, BC, Canada

The Parkinson's journey can be long, and the lessons begin early. In this session, Larry and Rebecca Gifford will discuss their main considerations as they work together to face Larry's Parkinson's mindfully and establish good practices early on. These include: curating and managing their care and support team, making wellness in all its forms high priority in daily life, and cultivating good communications practices in and outside of their partnership even as PD offers continuous challenges. The couple will discuss how they've empowered themselves to engage in their Parkinson's journey, find the possibilities and purpose within, and share their story as part of their own healing.

O58

Table 1: e-Health and PT
*Serene Paul**
The University of Sydney, NSW, Australia

This roundtable will discuss eHealth delivery of physiotherapy, drawing on the latest research conducted with people with Parkinson's disease and from other areas of rehabilitation where eHealth has been more widely established. The discussion will include evidence of benefits and disadvantages to eHealth delivery of physiotherapy for people with Parkinson's disease, as well as pragmatic considerations for delivery and access to eHealth-delivered physiotherapy, from both the patient and clinician perspectives.

O59

Table 2: Engaging women in clinical research
*Richelle Flanagan**
My Moves Matter, Dublin, Dublin, Ireland

Women with PD are underrepresented in research relative to the fact that 40% of people living with Parkinson's Disease (PD) are women and in some Eastern countries there prevalence is higher in women than men. Yet we do not know why. Women report differences in symptom presentation and report impacts of their hormones on their symptoms and yet there is little evidence as to why. Gender differences have been highlighted in terms of access to care and different preference for high technological reatments such as DBS. Research must also represent women with PD of different ethnicities who have even less access that white women.
All research in PD should consider the sex and gender needs and implications in order to provide better outcomes for all. High-quality, prospective, longitudinal studies looking at gender differences may ialso dentify reliable gender-sensitive biomarkers and social markers that could translate into a personalised approach for the diagnosis and management of women with PD. It is thought that barriers to women taking part in research includes the longer time to diagnosis and the lower access to neurologist care for women with PD may result in reduced referral to research studies.
Research into patient recruitment indicates that women prefer online engagement versus face-to-face visits. This may be due to women being time poor through working and/or being the main caregivers in their families, hence lacking the time to attend face-to-face visits. But little has been done to really elucidate why women are under represented. This roundtable aim to identify the barriers to women taking part in research and ways to mitigate them.

O60

Table 3: The many faces of PD – Prodromal and clinical subtypes
*Per Borghammer**
Aarhus University Hospital, Aarhus N, Denmark

Parkinson's disease (PD) is a heterogenous disorder. At the time of diagnosis, patients can show highly variable patterns of symptoms and objective neuronal dysfunction. Such subtypes of PD have varying prognoses and progression rates of the disease.
Some patients develop autonomic and sleep symptoms years before diagnosis, whereas others do not have these symptoms, when the motor symptoms appear. Some patients show fast disease-progression and increased risk of developing dementia, whereas others progress much more slowly.
The underlying causes of this heterogeneity are not fully understood, but it seems probable that genetic and environmental factors can contribute. It remains an important research aim to improve our fundamental understanding of disease heterogeneity.
Novel disease mechanisms may be uncovered, which could be specific to certain subtypes of PD. Such insights may provide a necessary foundation for the personalized treatments of the future and will allow clinical trials of disease-modifying treatments to be carried out in more homogenous subgroups of patients.

O61

Table 4: Enabling people with PD to exercise
*Natalie Allen**
The University of Sydney, Camperdown, NSW, Australia

It is well established that exercise has many benefits for people with Parkinson's disease. Exercise is like medicine; it needs to be taken frequently and reviewed regularly. This round table will discuss ways in which people with Parkinson's disease can be enabled to start and continue an exercise program over the course of their disease. We will discuss the importance of accessing a suitably qualified health professional (e.g., physiotherapist or exercise physiologist) with expertise in exercise prescription for people with Parkinson's disease. Other topics for discussion will include how to develop skills in exercise self-management, including getting motivated, setting goals, problem solving, monitoring, seeking support and knowing when to get help. Sustainable models of healthcare (e.g., the secondary prevention approach or 'dental' model) for exercise therapy and a hybrid approach (i.e., combining in-person sessions at a clinic with home-based telehealth sessions and independent exercise) will also be discussed.

O62

Table 6: How People With Parkinson's Can Participate As Consumer Advisors in PD Research Programs
*Richard Gordon**
Queensland University of Technology (QUT), Brisbane, Queensland, Australia

This Roundtable will discuss how People with Parkinson's (PwPs) can actively participate as consumers and advisors for research programs, and contribute their lived experience on projects which

aim to understand and treat PD. While most PwPs enrol as study participants in clinical trials or provide samples for research studies, there are many other ways in which people living with PD can collaborate with researchers and be more closely involved in research programs. For example, by contributing to and providing input on study designs, research directions and research funding priorities. Some examples of how PwPs are currently collaborating with research teams will be discussed in this session. For Parkinson's researchers, this session will also discuss the benefits of actively involving people living with PD at every stage of their research programs and how this can be achieved in academic settings. This roundtable session will be interactive, with opportunities for researchers and PwPs to share their experiences and ask questions.

O63

Table 7: The role of LRRK2 in gut inflammation/inflammatory bowel disease and PD

*Veerle Baekelandt**
KU Leuven, Leuven, Belgium, Belgium

Parkinson's disease (PD) is currently considered a multisystemic disorder rather than a pure brain disease. Evidence suggests that the disease can initiate in peripheral tissues and spread from the gut to the brain. Notwithstanding, the role of the gut-brain axis in that process is still unclear. In addition, the involvement of the peripheral immune system to PD pathophysiology remains elusive. Mutations in the leucine rich-repeat kinase 2 (LRRK2) gene have been widely linked with familial and sporadic PD cases. However, the actual role of LRRK2 in PD pathophysiology is far from understood. Recent studies suggest that Leucine-rich repeat kinase 2 (LRRK2) is involved in regulating both peripheral and cerebral inflammation, and may influence α-synuclein pathology at multiple levels, such as aggregation and propagation. LRRK2 has also been associated with inflammatory diseases such as inflammatory bowel disease (IBD). Large-scale population studies revealed that IBD patients have significantly elevated risk to also develop PD. On the other hand, PD patients frequently demonstrate intestinal inflammation and microbial dysbiosis.
We will review the evidence for the role of LRRK2 and the peripheral immune system in gut inflammation and gut-to-brain dissemination of α-synuclein pathology. We will discuss models and methods to test this experimentally and how this may lead to new therapeutic avenues.

O64

Table 8: Pesticides and Parkinson's

*Beate Ritz**
UCLA, Los Angeles, CA, United States

Among environmental agents, pesticides have been most consistently shown to increase the risk of Parkinson's disease (PD). Pesticides are toxins that are intentionally introduced into the environment at a large scale with an intent to harm living organisms, specifically many are designed to be neurotoxic. Pesticides are important for intensive industrial scale agriculture and food production as well as vector control (malaria). Thus, it is not surprising that their use and the variety of products has grown worldwide with more than 500 active substances approved for use. This talk will first provide an overview of large studies of PD conducted in California the home of one of only two state mandated pesticide use reporting systems. For more than two decades, the California studies collected extensive residential, occupational, and lifestyle data as well as biological samples. This allowed us to gain insights into the action of pesticides associated with PD and to conduct investigations into multiple 'omics' layers to identify biologic signatures of their toxic action. Our results not only show how PD risk is affected by pesticide exposures but also how we can dissect real world exposure effects through epigenetic (methylation) and metabolomic approaches and also the gut microbiome. For example, we showed that long-term ambient organophosphate pesticide exposures interact with genetic susceptibility to increase PD risk, how these pesticides affect DNA methylation in acetylcholine receptor pathways, and how chronic low-level exposure to multiple pesticides can act on mitochondrial energy metabolism and function as recently documented in our metabolomic analyses. These real-world examples will illustrate how low-level but chronic human pesticide exposures contribute to PD onset and progression.

O65

Table 9: Drug-repurposing: What are we really learning?

*Lorraine Kalia**
Toronto Western Hospital, Toronto, ON, Canada

Drug repurposing or drug repositioning is a strategy to expedite drug development for Parkinson's disease by investigating drugs already approved for human use for treatment of other diseases. At this roundtable, we will discuss the current state of drug repurposing for Parkinson's disease and what we are learning from preclinical and clinical studies. I will begin the group discussion by describing how drug repurposing is being applied to find disease modifying therapies including an illustrative example from my lab. Most of our conversation about drug repurposing for Parkinson's disease will be guided by questions and comments from the participants.

O66

Table 11: Clinical trials: What is the evidence for the benefit of exercise in PD?

*Erwin van Wegen**
Amsterdam University Medical Center, Amsterdam, Netherlands

Objectives for congress round table discussion on the effects of exercise in Parkinson's disease:
Discuss the different types of exercise that are most effective for people with Parkinson's disease, including aerobic exercise, resistance training, and balance and flexibility exercises.
Discuss the underlying mechanisms by which exercise may improve symptoms of Parkinson's disease, including neuroplasticity, neuroprotection, and inflammation.
Discuss the importance of individualized exercise programs that are tailored to the specific needs and abilities of people with Parkinson's disease.
Discuss the challenges and barriers to exercise for people with Parkinson's disease, and explore strategies for overcoming these barriers, such as group exercise classes, home-based exercise programs, and telehealth
Discuss the benefits of exercise for people with Parkinson's disease, including improvements in motor symptoms, balance, mood, and quality of life.
Explore the role of healthcare professionals, including physiotherapists, occupational therapists, and exercise physiologists, in promoting exercise for people with Parkinson's disease.
Discuss the latest research on exercise and Parkinson's disease, including ongoing clinical trials and future directions for research in this field.

O67

Table 10: Digital monitoring: Challenges we face and how to make it work for PD
*Lynn Rochester**
Newcastle University, Newcastle Upon Tyne, Newcastle Upon Tyne, United Kingdom

This roundtable will build on the previous session (The Digital Horizon from a Patient Perspective: Promise and Pitfalls) and link directly to the talk on Digital Monitoring of Mobility: why, where and how. It will share the learning from the largest, leading consortia effort (Mobilise-D) that is developing real-world digital tools to measure mobility continuously and accurately in the real-world with the aim of adoption in clinical care and research. The challenges to implement real-world mobility monitoring with wearable and mobile devices will be discussed from the perspective of multiple stakeholders including the person with Parkinson's, the clinician, the research community and regulatory authorities that approve digital monitoring solutions. Issues relating to demonstration of the meaningfulness of digital mobility outcomes (DMOs) derived from mobile devices; how to develop robust measures that are accurate and provide important clinical information and the barriers to their adoption in research and clinical care will be covered. What the future of mobility monitoring may look like will also be discussed. Throughout this is intended to be an exchange of information and views with the perspectives of the audience attending the roundtable being a key component to a lively discussion.

O68

Table 12: Creativity, the brain and Parkinson's disease
*Anjan Chatterjee**
University of Pennsylvania, Philadelphia, Pennsylvania, United States

This session will be a round table discussion among the speakers and a Q&A session with the audience.

O69

Table 13: Constipation in Parkinson's and how to address it
*Louise Ebenezer**
United Kingdom

What is constipation. Why people with Parkinson's experience constipation. Normal defecation. Gut dysmotility and SIBO.
How to manage constipation in Parkinson's from both non-pharmacological and pharmacological perspective. Lifestyle habits to improve constipation, including the four 'F's' in maintaining gut health.

O70

Table 14: Better communication: Let us get started
*Angela Christine Roberts**
Western University, London, ON, Canada

It has been said that conversations are central to family life. Communication challenges and family system shifts in the face of cognitive changes can negatively impact quality of life for persons with Parkinson disease, their care partners, and families. In this interactive discussion, Dr. Roberts will overview the nature of communication changes in Parkinson disease and provide practical strategies for improving family conversations and meaningful connections with others. Special emphasis will be placed on how better communication can support care goals, maintain independence, reduce caregiving burdens, and promote quality of life.

O71

Talk 2: Why should we track Parkinson's disease?
*Bas Bloem**
Radboud University Medical Center, Nijmegen, Italia, Netherlands

There are challenges in the real-time assessment of motor and non-motor features in persons with Parkinson's disease (PD). PD is the prototype of a highly variable disease, with symptoms that fluctuate both within and across different days. This is caused in part by fluctuations in response to dopaminergic medication, which occur almost invariably after several years of disease. But factors such as stress or fatigue also contribute to these fluctuations. Yet, clinical decision making remains largely based on infrequent in-person visits, which offer at best a "snapshot" of what is otherwise a complex pattern of motor improvement and worsening over the course of a day at home, with limited time to discuss the many health issues that occur in PD. Moreover, the hospital-based neurological examination is often not representative of the patient's actual functioning in daily life: it depends on the examination at the time of the visit and timing of the visit relative to medication intake. Moreover, tremor is typically worse during in-clinic examinations secondary to anxiety of the visit, while freezing is usually much less prominent. Clinical ratings can be subjective and lead to considerable inter-rater variability. Diaries offer a possible alternative, but these are susceptible to recall bias and diary fatigue, particularly in persons with cognitive decline or depression. Remote monitoring using digital solutions may well provide an answer to some of these challenges. This field has seen significant progress in the past decades. Some solutions allow for remote monitoring of PD severity, using smartwatches or other body-worn sensors, smartphones or digitally equipped smart homes. Theoretical advantages include the ability to measure individuals in a more naturalistic environment (including their own homes), to document changes quantitatively and objectively, and to offer high-frequency (even continuous) assessments, thereby offering a much more granular evaluation.

O72

Talk 1: How can imaging track PD?
*Thilo van Eimeren**
University of Cologne, Cologne, Germany

How can imaging track Parkinson's disease? The answer to this important question greatly depends on what exactly we would like to track. Experiencing first signs or symptoms of Parkinson's disease, my first question would be: is it really Parkinson's disease or could it be something else, e.g., something more benign or something more devastating. In technical terms, this would call for a 'diagnostic biomarker', an objective measure of the presence of a condition. Imaging the integrity of the dopamine system goes a long way as a diagnostic biomarker for Parkinson's disease. In this domain, molecular imaging using PET or SPECT is at the forefront, but MRI-based measures may catch up soon. Imaging can also distinguish Parkinson's disease from more aggressive, atypical forms of neurodegeneration by looking at patterns of metabolic and/or structural decline, or even directly detecting a different underlying pathology. However, I would have many other questions concerning my personal journey with Parkinson's disease. Will I be able to work and financially support my family until I retire? Will I have dementia?

When will I have to stop playing tennis? These are all questions for so-called 'prognostic biomarkers'. Imaging has great potential in anticipating clinical turning points associated with these questions. Finally, a doctor may propose a treatment to me, but concede that this treatment works nicely in some people, while others mostly have severe side effects. I would like to know in advance if I will end up in the former group or the latter. A biomarker, which can tell you this is called a 'predictive biomarker'. It predicts the response to treatment. Some imaging tools show this capability, for example predicting if deep brain stimulation will be beneficial at the individual level. Taken together, imaging tools have an established role in tracking Parkinson's disease. However, we do not yet seize the full potential of imaging to benefit people living with Parkinson's disease. Most developments are still stuck in academia and we will have to work harder to bring them into routine clinical practice.

O73

Talk 3: How can we track PD using blood and tissue-based biomarkers?

*David Standaert**
University of Alabama at Birmingham, Birmingham, AL, United States

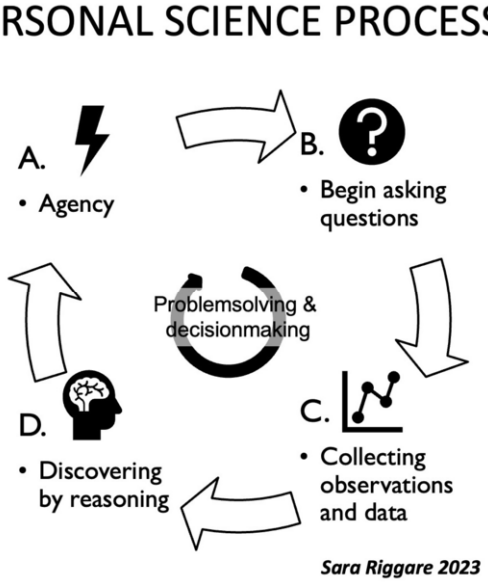
There is increasing recognition that Parkinson disease involves much more than just the brain. It is a whole-body condition that affects the blood and tissues across the body. This opens the door to the development of PD biomarkers based on analysis of blood and tissues of different kinds. This talk will explore the current understanding of the role of blood and tissue biomarkers in establishing a diagnosis of PD, tracking disease activity, and monitoring the effect of potential therapies.

O74

Talk 4: Self-tracking: To track or not to track?

*Sara Riggare**
Uppsala University, Uppsala, Sweden

For centuries, healthcare and clinical research have developed their "tracking toolbox" thereby aspiring to improve patients' health and wellbeing. Today, clinicians and scientists track Parkinson's disease (PD) e.g. using advanced imaging techniques, analyzing blood or tissue samples, or testing a patient using the Unified Parkinson's Disease Rating Scale. These procedures can be helpful by supporting (or not) a diagnosis of PD, which can assist clinicians and patients in decisions on treatment and lifestyle choices. Tracking can also be used to quantify the progression of PD for example when evaluating interventions in clinical trials, in order to help future generations of patients.
However, for a person already diagnosed with PD interested in optimizing their own wellbeing, current clinical tracking practices are not especially useful, mainly because advanced clinical tools are expensive to use and unavailable to patients. Also, the focus of conventional clinical research is often 'Is this treatment likely to work for an average patient?' It does not tell us what will actually work for an individual patient. It does not answer the question "What works for me?"
Self-tracking is a process of deliberately collecting and structuring observations about one's own life and it can be used by patients to collect data for conventional clinical group research. However, self-tracking can also be used to collect your own data and observations to answer your own questions. This process is known as 'personal science' and it can be described by the following steps:
A. Agency: Shift of perspective from passive to active
B. Begin asking questions
C. Collecting observations and data using for example digital technology or pen and paper
D. Discovering
The personal science process is iterative, focused on learning and problem solving, and can be used with or without the support of healthcare professionals. Studies have shown that personal science can help persons with PD to identify patterns in their condition and thereby better understand how different factors may impact their symptoms, as well as improve their quality of life. With more focus on personal science, living with PD can be made easier.
REF: Riggare, S. (2022). Personal science in Parkinson's disease: a patient-led research study [Radboud University]. https://repository.ubn.ru.nl/handle/2066/246940



O75

Talk 1: Changes in lipid profiles in patients with Parkinson's disease

*Nicolas Dzamko**
The University of Sydney, Camperdown, NSW, Australia

Genetic studies of patients with Parkinson's have suggested that genes involved in lipid regulating pathways may contribute to the risk of getting Parkinson's disease (PD). Lipids are important for many aspects of human biology including membrane function and cell signalling. The best-known lipid regulating PD risk gene is glucocerebrosidase, encoded by the GBA1 gene, which converts glucosylceramide to glucose and ceramide. Glucocerebrosidase is a lysosomal enzyme, important for proper lysosomal function and the degradation of unwanted proteins such alpha-synuclein. Another major PD risk gene, also implicated in lysosomal function is leucine-rich repeat kinase 2 (LRRK2). Some studies have suggested that LRRK2 can regulate the function of lysosomal glucocerebrosidase, however, whether LRRK2 risk mutations also result in changes in lipid homeostasis is unclear. To determine the extent that lipid pathways may be dysregulated in PD we conducted untargeted lipidomics using serum from two cohorts with a combined sample size of n=536. The cohorts consisted of Parkinson's patients with and without the pathogenic LRRK2 G2019S mutation, as well as sporadic Parkinson's patients and matched controls. The lipidomics approach identified approximately 1000 lipid species per person and substantial differences in serum lipid profiles were identified

between controls, Parkinson's patients and LRRK2 mutation carriers. Major dysregulated pathways included sphingolipid and glycerophospholipid metabolism, and lipid species from these classes contributed to the significant discrimination between groups. Importantly, most lipid species that differed between control and PD patients were in closely linked metabolic pathways regulated by known PD risk genes. This study supports the concept that altered lipid metabolism may contribute to PD and that further study of lipid pathways is warranted.

O76

Talk 2: Mechanisms of glycolipid-induced α-synuclein aggregation

*Joseph Mazzulli**
Northwestern University Feinberg School of Medicine, Chicago, IL, United States

Parkinson's disease (PD) is characterized by the accumulation of insoluble protein aggregates comprised mainly of fibrillar a-synuclein that accumulate in neurons and disrupt cellular function. The mechanisms that govern the conversion of a-synuclein into a pathogenic conformation are currently unknown. Genetic studies of Parkinson's disease have identified variants in proteins involved in cellular clearance pathways, including the autophagic-lysosomal system, suggesting that dysfunctional protein clearance may play a role in promoting a-syn aggregation. Lysosomal GBA1 that encodes beta-glucocerebrosidase (GCase) represents the strongest genetic risk factor for PD and dementia with Lewy bodies. Here, we present recent data on the mechanisms of a-synuclein aggregation that occur in the context of GCase dysfunction. Our data indicates that glycosphingolipid substrates directly interact with physiological a-synuclein conformers and trigger their conversion into pathogenic oligomers and fibrils. The mechanistic relationship between glycosphingolipid substrates, a-synuclein, and neurotoxicity will be discussed, as well as translational methods focused on reversing a-synuclein through promoting its clearance through lysosomes.

O77

Talk 3: Molecular mechanisms linking GCase to α-synuclein and therapeutic strategies targeting the GBA1 pathway

*Pablo Sardi**
Sanofi, Cambridge, MA, United States

Clinical, genetic and experimental evidence underlies the relevance of lysosomal dysfunction in Parkinson's disease (PD). Mutations in the lysosomal glucocerebrosidase gene (GBA1) accelerate PD progression. Multiple therapeutic approaches to modulate the glucocerebrosidase pathway are under active investigation. We will discuss these approaches and the evidence suggesting that they may also benefit a larger sporadic patient population carrying wild-type GBA1 alleles.

O78

Talk 1: Detection and classification of synuclein strains by a seed amplification assay (SAA)

*Claudio Soto**
University of Texas Health Science Center at Houston, Houston, Texas, United States

Parkinson's disease (PD) and related synucleinopathies are caused by the misfolding, aggregation and accumulation of alpha-synuclein (αSyn) deposits in the brain. One of the greatest obstacles for PD therapeutic development is the lack of early diagnosis to identify patients before substantial brain damage. Currently, there is no definitive, sensitive and predictive laboratory test to identify individuals before they show clinical symptoms. Compelling evidence suggests that misfolding and oligomerization of αSyn begins years or decades before the appearance of disease symptoms. Misfolded αSyn aggregates adopt alternative conformations in different synucleinopathies and become capable of spreading the abnormal structures in a prion-like manner through anatomically connected brain regions.
Recently, we developed a seed amplification assay (SAA), also termed PMCA or RT-QuIC, for sensitive detection of αSyn aggregates in patients affected by PD and related synucleinopathies, including dementia with Lewy bodies (DLB), multiple system atrophy (MSA) as well as a subset of Alzheimer's disease cases. This assay is based on the ability of αSyn aggregates to seed the polymerization of native αSyn employing cycles of incubation and fragmentation. To date we have screened blindly >2000 CSF samples from patients and controls from various cohorts, including PPMI and BioFIND. The results show consistently sensitivities and specificities >90% to discriminate patients from controls and have been reproduced by multiple groups independently. Furthermore, the assay can detect the marker in early prodromal cases of the disease, before any detectable brain abnormalities. Finally, αSyn-SAA can be used to discriminate distinct synucleinopathies, particularly PD and MSA. Differentiation is based on analyzing the aggregation kinetics, biochemical, biophysical and structural features of the aggregates produced in the assay. These findings indicate that αSyn aggregates present in distinct synucleinopathies corresponds to different conformational strains. Importantly, the atomic resolution structure of the aggregates amplified from MSA CSF by cryo-electron microscopy is very similar as that previously reported for the aggregates purified from MSA brain.
In conclusion, αSyn-SAA can have multiple applications for basic and translational research, including patient diagnosis, clinical trial engagement, monitoring drug efficacy, discriminating different synucleinopathies in living patients, screening of compounds for therapy, and production of αSyn aggregates for biochemical, biological and structural studies.

O79

Talk 2: Assaying misfolded synuclein in tissue biopsies for the diagnosis of PD

*Brit Mollenhauer**
University Medical Center Göttingen and Paracelsus-Elena-Klinik, Kassel, Germany, Kassel, Hesse, Germany

There is still a lack of neuroprotective strategies in α-synuclein (aSyn) associated neurodegenerative disorders [such as Parkinson's disease (PD) and Multiple System Atrophy (MSA)] due to various reasons. One of the reason is that the diagnosis is still made too late and that there is no biomarker to objectively reflect the progression of the disease that is needed for clinical trials with neuroprotective strategies as outcome measure.
Over the past years, efforts to develop progression biomarker focused on imaging strategies and biological fluids, that mostly focused on cerebrospinal fluid (CSF) in the past. Most biomarker immunoassays have so far not shown robust and clinically meaningful results. The newly developed aSyn Seed Amplification Assays (SAA) in CSF show high sensitivities and specificities for PD across various independent laboratories. In PPMI CSF samples form 1,139 participants were included and showed a sensitivity and specificity in PD and Healthy Controls (HC) of 88% and 96%. In MSA the seed dynamic can differentiate PD from MSA in some assays. Longitudinally there does not seem to be a change over

time in dilution experiments making it currently impossible to utilize this biomarker as progression biomarker. In prodromal individuals with isolated REM sleep behaviour disorder (iRBD), the signal can be detected up to 9 years before conversion to disease in the De Novo PD (DeNoPa) cohort.
In the Systemic Synuclein Sampling Study (S4) aiming to characterize aSyn in multiple biofluids and tissues within the same PD subjects (n=59) in comparison to HC (n=21). SAA was performed in CSF and with formalin-fixed and paraffin embedded submandibular gland biopsies (SMG); the sensitivity and specificity for SAA in CSF was 93% and 91% and for SMG 73% and 79%.
Therefore α-synuclein SAA in its current form in CSF can be used for stratification in clinical trials in α-synuclein aggregation disorders and also in its prodrome iRBD. Emerging evidence also shows that α-synuclein SAA may even be applied in peripheral tissue and fluids, like skin, olfactory mucosa and also saliva. Identifying subjects at risk for upcoming neuropreventive strategies need peripheral biomarker. SAA will therefore be helpful in the future, but progression biomarker are still lacking.

O80

Talk 3: Are we ready for detecting α-synuclein prone to aggregation in patients?
*Jon B. Toledo**
HMH, Houston, TX, United States

Seed amplification assays (SAAs) accurately detect misfolded α-synuclein deposition, which is the defining lesion of Parkinson's disease, dementia with Lewy bodies, and multiple system atrophy, group together as α-synucleinopathies. At their onset accuracy of clinical diagnosis is lower than in later disease stages. In clinical practice, SAAs can offer a more accurate early diagnosis and prognosis. As clinical trials seek enrollment of participants in early disease stages, biomarkers that detect the defining lesion of each neurodegenerative condition can ensure the recruitment of the targeted participants. There is another setting where SAAs could be included, although its indication needs to be determined. Like other neurodegenerative diseases, α-synucleinopathies develop for several years before the onset of motor signs and nonmotor symptoms. Also common to these diseases is the lack of confirmed disease-modifying therapies, with only symptomatic treatments as an option. The emergence of SAAs potentially detecting misfolded α-synuclein in asymptomatic disease stages poses a dilemma in the absence of disease-modifying therapies and secondary prevention strategies. In addition, the probability of a positive result will vary based on age, prodromal signs and symptoms, and genetics leading to differences in the expected number of positive tests. This presentation will review the indications, benefits, and risks of SAAs testing in these different groups.

O81

Talk 1: Building resilience and capacity to live well with Parkinson's
*Shanthipriya Siva**
Saarfoundation, Chennai, Tamilnadu, India

Adversity brings out an important character in u resilience
Ways to Meet Adversity with Resiliency
1. Give it Time. Even the most resilient people need time to adjust to the new reality when a major life event occurs. ...don't be harsh on yourself
2. Change the Way You Look at Things. ...
3. Seek positivity in Negative
4. Be Grateful for the Experience. ...
5. Be active and engaged
6. incremental thinking-set realistic goals and work towards it
7. Don't Make Self-care kOptional. ...
8. Don't Take Yourself Too Seriously.
Resilience is the process and outcome of successfully adapting to difficult or challenging life experiences, especially through mental, emotional, and behavioral flexibility and adjustment to external and internal demands.

O82

Talk 2: Pre-habilitation: Preventing complications
*Ryan Duncan**
Washington University in St. Louis - School of Medicine - Program in Physical Therapy, St. Louis, Missouri, United States

The progressive nature of Parkinson disease (PD) increases the chances of experiencing complications associated with the disease. Common PD-related complications include motor and non-motor problems. Motor complications include gait difficulty, balance problems, falls, and fall-related injuries. Non-motor complications include cognitive impairment, depression, and pain. Rehabilitation and exercise are often effective in managing complications. However, too often there is a reactive approach to managing complications in PD. This is a problem because waiting to participate in rehabilitation and exercise until after complications are present poses significant difficulties for patients, caregivers, and rehabilitation providers. In this presentation, we will discuss the role of rehabilitation and exercise in managing and, ideally, preventing these complications. We will emphasize the need for a pro-active approach, or pre-habilitation, aimed at implementing effective rehabilitation and exercise strategies designed to delay or prevent the onset of these complications in people with PD.

O83

Talk 3: Optimising care provided in hospital for people with Parkinson's
*Richard Genever**
Chesterfield Royal Hospital NHS Foundation Trust, Chesterfield, United Kingdom

People living with Parkinson's may become hospitalized. Usually the admission is for another reason, but may have impact on how they live with the condition.
In this session I will describe 5 scenarios and an approach to support people living with Parkinson's in each of them.
1) Reduced mobility in someone known to be living with Parkinson's
2) Suspected Parkinson's in a hospital patient.
3) Confusion or psychosis in a hospitalized person with Parkinson's
4) Supporting a person with Parkinson's when a Nothing by Mouth decision has been made.
5) People with Parkinson's undergoing surgery.

O84

Talk 1: The multiple facets of locus coeruleus involvement in neurodegeneration
*Cristina Miguelez**
University of the Basque Country, Leioa, Bizkaia, Spain

Loss of neurons in the substantia nigra pars compacta has been historically considered the main hallmark of Parkinson's disease (PD), leading to lack of dopamine, dysfunction through the basal ganglia circuitry and the appearance of the cardinal motor features.

The onset of PD may, however, begin several years before the motor manifestation when highly prevalent non-motor alterations appear, including hyposmia, depression, anxiety, pain, sleep disorders or cognitive impairment. At present, PD is considered a multisystemic disease with diverse motor and non-motor symptomatology that severely affects other nuclei and neurotransmission systems prior to the degeneration of nigral neurons. The locus coeruleus (LC) harbours neuromelanin containing noradrenergic neurons and is among the brain stem areas first affected and displaying Lewy bodies in the brain. This tiny nucleus has been considered a homogeneous structure for the last 50 years, but recent methodological advances have allowed us to discover that the LC is composed of different neuron clusters with very distinct functions. Some LC cells are able to co-release dopamine and noradrenaline, as happens in the prefrontal cortex or the hippocampus. In PD, LC dysfunction is associated with the aforementioned prodromal non-motor symptoms, and monitoring LC dysfunction could therefore provide valuable information about early degeneration. In addition, detection of noradrenergic deterioration will contribute in predicting the progression of the disease, as the LC exerts a key influence on the homeostasis of dopaminergic networks. In preclinical studies, damaging the LC in parkinsonian animals leads to more pronounced loss of dopaminergic neurons and motor deficits, while conversely, boosting noradrenergic synthesis ameliorates dopaminergic degeneration. Although the exact mechanism is still unknown, experimental and clinical studies have suggested that the central noradrenergic system exerts inhibitory control on neuroinflammation, activating anti-inflammatory and neuroprotective cellular pathways. In this talk I will discuss the importance of the LC in the early detection and progression of PD, and introduce some of our related scientific findings.

O85

Talk 3: Role of the pedunculopontine nucleus in the pathophysiology of PD

*Juan Mena-Segovia**
Rutgers University, Newark, New Jersey, United States

The pedunculopontine nucleus (PPN) is a midbrain structure involved in distinct aspects of motor initiation and motor execution. The PPN provides a dense innervation to dopamine neurons of the substantia nigra composed by a heterogeneous mix of afferents including cholinergic, glutamatergic and GABAergic axonal fibers. Experimental manipulation of each of these circuits produces different responses in dopamine neurons and different effects on motor behavior, highlighting the complexity of PPN function for gating movement. The PPN has been traditionally considered as an interface between the basal ganglia and lower motor circuits, with multiple bidirectional connections involving all of the basal ganglia nuclei, the thalamus and the spinal cord, among others. Early histopathological evidence of degeneration of PPN cholinergic neurons in PD supported its role in the pathophysiology of the disease. Recent advances in the characterization of the anatomical and functional properties of PPN neurons have revealed selective motor and cognitive functions for PPN neurons that are associated to their molecular and/or connectivity profiles. In my talk, I will summarize the most recent evidence of the multifarious motor functions encoded by PPN neurons. Furthermore, I will show evidence that PPN neurons modulate cognitive functions that precede action initiation. Finally, I will discuss how the aberrant activity of each PPN subgroup in PD or its animal models will have different behavioral consequences and how understanding this heterogeneity could lead to identifying distinct clinical manifestations associated with PPN dysfunction.

O86

Talk 3: Targeting the vaso-intestinal peptidergic system to decrease anxiety in Parkinson's disease

*François Georges**
University of Bordeaux-CNRS-UMR-5293, Bordeaux, France

The degeneration of dopamine neurons of the substantia nigra pars compacta is well known in motor symptoms of Parkinson's disease (PD). However, other dopaminergic populations degenerate and give rise to non-motor symptoms such as anxiety which has a high prevalence in PD patients and strongly affect quality of life. One of these structures, the dorsal raphe nucleus (DRN), has been identified as a potential structure involved in anxiety and depression in PD. Indeed, the dopaminergic neurons of the DRN degenerate in PD and a part of them co-releases the vaso-intestinal peptide (VIP) onto two anxiety hubs of the brain: the oval nucleus of the bed nucleus of the stria terminalis (ovBNST) and the central nucleus of the amygdala (CeA). In this study, using innovative neurotechniques we anatomically and functionally characterize this sub-population of DRN dopaminergic neurons co-experessing VIP in physiological condition. Besides the absence of studies on the role of VIP in the ovBNST and CeA, the degeneration of this pathway could be a potential cause of the high prevalence of anxiety in PD.

O87

Talk 1: Preclinical vs prodromal PD – How can we define them?

*Lana Chahine**
University of Pittsburgh, Pittsburgh, PA, United States

The pathology leading to Parkinson's disease (PD) begins years before the disease is diagnosed.
In early stages, the underlying pathological changes may be detectable with disease-specific biomarkers, but remain clinically silent—that is, without any detectable signs or symptoms. This is the preclinical phase of PD. As the underlying pathology progresses, symptoms and signs emerge. This is the prodromal phase of PD; in this phase, symptoms and signs are present but are mild or do not otherwise encompass the full syndrome that currently constitutes diagnostic criteria for PD. Some symptoms of the PD prodrome, such as changes in olfaction, mood, or autonomic function, are common but nonspecific, also occurring in individuals who will not go on to develop PD. Other prodromal features, such as REM sleep behavior disorder, have high specificity but are less common.
In this session, the preclinical and prodromal stages of PD will be defined. Biomarker evidence of the preclinical phase will be discussed, including dopaminergic imaging and measures of pathologic alpha-synuclein. The distinction between the preclinical phase of PD and the phase during which an individual is at-risk but remains free of evidence of disease will be explained. Challenges related to defining clinical onset will be discussed. The prodromal PD syndrome will be reviewed, and multimodal assessment to maximize specificity in identifying prodromal PD will be introduced. The potential of sensitive biomarkers and quantitative measures of motor and non-motor function to define and redefine the stages will be highlighted.

O88

Talk 2: Screening for PD risk – Are we ready for population-based approaches?
*Alistair Noyce**
Queen Mary University of London, London, United Kingdom

There are differing strategies to identify individuals at risk of or in the earliest phases of Parkinson's disease, who may benefit most from disease-modifying clinical trials. Strategies include identifying individuals that carry a single disease-causing gene mutation, a combination of genetic risk factors, individuals with a single strong clinical risk factor (such as REM sleep behaviour disorder or idiopathic anosmia), or individuals identified through algorithms such as the MDS criteria for prodromal Parkinson's and the PREDICT-PD algorithm.

In this second talk of the session, I will briefly recapitulate concepts from the first talk. I will move on to discuss screening as a concept in preventive medicine and reflect on the requirements that screening programs must meet. I will cover the different potential options for screening, with an emphasis on population-based approaches. I will reflect on how far algorithms can take us in terms of stratification and what additional proximity markers and/or biomarkers maybe needed. I will consider some of the ethical arguments for and against screening, as well as the implications of risk disclosure to individuals.

O89

Talk 3: Disease-modification trials in prodromal PD – Hopes and barriers
*Michele Hu**
Oxford University, Nuffield Department of Clinical Neurosciences, Oxford, Oxfordshire, United Kingdom

The numbers of people living with Parkinson's globally are projected to double from 2015 to 2040, and we are already seeing effects of this worldwide expansion for which we are ill prepared. So far, a total of nineteen phase 3 intervention trials focusing on patients with manifest Parkinson's and motoric symptoms, have all failed to demonstrate significant changes in disease progression. In the search for a cure and effective disease modification, focus is now shifting to studying Parkinson's at its earlier stages. My talk focuses on the challenges and opportunities of future trials in isolated RBD (iRBD), a prodromal form of Parkinson's and related alpha-synuclein disorders. Individuals with sleep-study diagnosed iRBD provide the opportunity to intervene at an earlier disease phase, when higher densities of salvageable brain neurons remain without the confounding effects of symptomatic therapies (ie levodopa) that are frequently seen in manifest Parkinson's. Planned delivery of the first ever placebo-controlled trial of iRBD participants recruited across Australia and the UK will be discussed. My vision is to help researchers improve iRBD participant access to clinical trials, providing outcome measures that are sensitive to change, cost effective and quick to administer in clinic and at home. The delivery of effective disease modifying therapies for iRBD will also provide key mechanistic insights into how best to slow down trajectories for other forms of prodromal Parkinson's and manifest Parkinson's disease.

O90

Talk 1: Swallowing and Parkinson's
*Yael Manor**
Tel Aviv Sourasky Medical Center, Tel Aviv, Israel, Israel

Swallowing disorders (dysphagia) is a common complication (up to 100%) in patients with Parkinson's disease and it is documented in all phases of swallowing. The severity of dysphagia is not necessarily related to the overall severity of the disease. Parkinsonian patients are "silent aspirators" with decreased cough reflexes, reduced clinical signs and lack of awareness. Aspiration is seen in more than half of the PD patients and aspiration pneumonia is one of the major causes of death. Early detection of the swallowing dysfunction will allow early intervention and aid to maintain patients' quality of life (QOL).
There are three procedures for evaluation of patients with swallowing disorders: (1) the bed side evaluation that is performed by the speech language pathologist (SLP) at the clinic or at the patient's room. (2) The videofluoroscopy swallowing study (VFSS) and (3) the Fiberoptic Endoscopic Evaluation of Swallowing (FEES). The VFSS and the FEES are instrumental evaluations and are considered to be the gold standard procedures in swallowing evaluation. The goal of the swallowing evaluation is to examine the oral and pharyngeal phases of swallowing and to assess not only whether the patient is aspirating, but also the reason for aspiration, so appropriate treatment can be initiated.
Once the specific problem has been defined, the swallowing therapist, can design an appropriate intervention program to manage the swallowing disturbances. Several treatments options for dysphagia are currently available specifically targeting swallowing function. The main goals are to reduce morbidity and mortality associated with pulmonary infections and malnutrition and to maintain a satisfactory QOL. Swallowing therapy, generally delivered by SLPs, with a multidisciplinary team including a dietician, ENT, gastroenterologist, psychologist and neurologist aims to improve the safety and efficiency of swallowing by means of compensatory and rehabilitative strategies. Neurostimulation techniques have been proposed for dysphagia treatment in adjunct to conventional swallowing therapy. Patients' cooperation, ability to follow directions and understanding of the importance of the therapy techniques are crucial skills for successful intervention.

O91

Talk 2: Best options for nutrition in Parkinson's
*Silke Appel-Cresswell**
University of British Columbia, Vancouver, BC, Canada

In talk 2 "Best options for nutrition in Parkinson's" we will review the current evidence for adhering to specific dietary patterns when living with Parkinson's. Mediterranean-type diets are associated with lower risk of developing PD, higher age of onset, slower progression and longer survival with PD. They are good candidates to improve constipation and improve the gut microbiome. In addition, Mediterranean diets have positive health benefits for a whole range of other conditions including diabetes, heart disease, cognitive function etc. Based on the MIND diet, one of the Mediterranean diets, here are recommendations for a healthy diet:
Foods to increase: Green, leafy vegetables, Other vegetables, Nuts, Berries, Beans or legumes, Whole grains, Fish, Poultry, Olive oil (as main oil and in place of butter or margarine), Drink sufficient fluids!
Foods to avoid or only consume in small quantities: Fried food, Processed food, Sweets, pastries, Pop, sweetened beverages, Red meat, Cheese, butter.

The ketogenic diet has so far only been studied in short-term studies, more research will be needed to make a recommendation for its use specifically in PD.
Overall, despite strong correlational evidence for benefit, interventional dietary trials in Parkinson's are lacking and are urgently needed. Despite this research gap, a healthy diet paired with other healthy lifestyle choices, e.g. exercise, is recommended as the foundation for living well with Parkinson's.

O92

Talk 3: Constipation in Parkinson's and how to address it
*Louise Ebenezer**
United Kingdom

What is constipation. Why people with Parkinson's experience constipation. Normal defecation. Gut dysmotility and SIBO.
How to manage constipation in Parkinson's from both non-pharmacological and pharmacological perspective. Lifestyle habits to improve constipation, including the four 'F's' in maintaining gut health.

O93

Table 1: Tips for building a Parkinson's movement
*Larry Gifford**
PD Avengers, Vancouver, Canada

In 2020, I found myself suddenly in a position to radically change the focus of my life's purpose. Being the leader of a Parkinson's movement was never on my bucket list. Just three years from diagnosis, I had cultivated a small network of like-minded individuals who were frustrated by the inaction in solving PD, the closed and often duplicated research projects, competition instead of collaboration between organizations and woeful lack of action as it pertains to ending Parkinson's. The path of a movement is never a straight line, there are twists and turns along the road to success. In this roundtable, I'll answer your questions and share the highs lows of our first years, the frustrations, pain points, successes and what I would do if I were starting PD Avengers today.

O94

Table 3: What are the most promising cell transplantation approaches for PD?
*Jun Takahashi**
Center for iPS Cell Research and Application, Kyoto University, Kyoto, Japan

Human induced pluripotent stem cells (iPSCs) can provide a promising source of midbrain dopaminergic (DA) neurons for cell replacement therapy for Parkinson's disease (PD). Towards the clinical application of iPSCs, we have developed a method for 1) scalable DA neuron induction on human laminin fragments and 2) sorting DA progenitor cells using a floor plate marker, CORIN. The grafted CORIN+ cells survived well and functioned as midbrain DA neurons in the 6-OHDA-lesioned rats and showed a minimal risk of tumor formation. In addition, we performed a preclinical study using primate PD models. Regarding efficacy, human iPSC-derived DA progenitor cells survived and functioned as midbrain DA neurons in MPTP-treated monkeys. Regarding safety, cells sorted by CORIN did not form any tumors in the brains for at least two years. Moreover, we found that MRI and PET imaging was useful in monitoring the survival, expansion, and function of the grafted cells as well as the immune response by the host brain. Based on these results, we started a clinical trial to treat PD patients at Kyoto University Hospital in Kyoto, Japan, in 2018. The trial evaluates the safety and efficacy of transplanting human iPS cell-derived DA progenitors into PD patients' putamen. Using a stereotaxic surgical technique, we implant approximately 5 or 10 million cells into the bilateral putamen of the patients. The target is seven patients, and we will observe each of them for two years. The trial is now ongoing without any severe adverse events.

O95

Table 4: Dopamine dorsal raphe dysfunction causes anxiety and depression in a progressive mouse model of Parkinson's disease
*Rosario Villalba**
Instituto Cajal, Consejo Superior de Investigaciones Científicas, CSIC, Madrid, Spain

Parkinson's disease (PD) is the most prevalent motor neurodegenerative disease, affecting up to 7 million of people in the world. Reflecting the progressive character of the disease, PD symptoms appear in a longitudinal temporal pattern along the neuropathological burden. Preceding motor impairment, most of PD patients suffers anxiety/depression, the most common and disabling emotional comorbidities. Although the anatomical and molecular bases are not well stablished, some studies point that the dorsal raphe nucleus is affected at early parkinsonian stages, overlapping with the appearance of the emotional symptoms. Besides the serotonergic, the dorsal raphe nucleus is composed by different neuronal populations, among others, the dopaminergic neurons. This population, due to its connectivity with limbic structures and the regulation of the serotonergic tone, encodes emotional valence such as arousal, social interaction and pain regulation, all of them processes that, strikingly, are disrupted in a high percentage of parkinsonian patients at prodromal stages.
To determine the implication of the dorsal raphe dopamine neurons in anxiety and depression comorbidity in PD, we have used a progressive mouse model of PD that specifically accumulates human alpha-synuclein in TH-positive neurons. We studied the appearance of emotional sings in combination with histological, electrophysiological, functional and molecular approaches to link dysfunctional dopaminergic neurons in the DRN with the onset of anxiety and depression.
Our results demonstrate that the onset of emotional signs overlaps with dopaminergic dysfunction in the dorsal raphe nucleus, that impairs dopaminergic signalling over their target areas and reduce serotonergic activity. These results causally link, for the first time, dorsal raphe dopamine dysfunction with parkinsonian anxiety and depression. Funded by Spanish Ministries of Science and Innovation (PID2019-111693RB-I00) and UE (H2020-SC1-BHC-2018-2020, grant agreement n° 848002) and by NextGeneration EU/PRTR (MICIN/CSIC/PTI+ NeuroAging).

O96

Table 5: The importance of early detection, evaluation, and treatment of speech and voice disorders for the newly diagnosed
*Darla Freeman**
Florida Center for Voice and Swallowing, Tampa, FL, United States

Research indicates 89 percent of persons with Parkinson's will have a communication disorder over the course of the disease. Challenges with speech and voice may include difficulty with vocal projection and imprecise articulation. Activities such as talking on the phone, being understood during conversation, and conversing at

work can be impacted by a decline in communication and lead to social isolation. These symptoms may not manifest during the initial stages of the disease nonetheless understanding these changes is beneficial for early detection and maintaining quality of life throughout the continuum of the disease. As part of the medical care team Speech-Language Pathologists (SLP) provide evaluations to obtain baseline data and treat communication disorders across all stages of the disorder. Through the lens of an SLP, this round table discussion is aimed at describing early signs and symptoms of communication disorders to assist in making informed decisions regarding the identification, evaluation, and treatment of communication challenges during the early stages of the disease.

O97

Table 6: Environmental risk factors and Parkinson's

*Briana De Miranda**
University of Alabama at Birmingham, Birmingham, AL, United States

This roundtable discussion will be centered on toxicant exposures that influence risk for Parkinson's disease, such as pesticides, heavy metals, chlorinated solvents, air pollution, and particulate matter. We will discuss how the environment influences all disease and contributes to all forms of Parkinson's, including those attributed to genetics. Additionally, we will address how exposure might shape the phenotype of neurologic disease (e.g., motor and cognitive symptoms) and if there are realistic expectations to limit exposure or offset environmental damage to biological systems, and if we can accurately model this in the research lab. Discussions on risk factors from occupational sources are welcome, including military service, industrial, and agricultural work.

O98

Table 7: Can PD Drugs be designed for specific genetic targets: How close are we?

*Jesse Cedarbaum**
Coeruleus Clinical Sciences LLC, Woodbridge, CT, United States

Aside from the "Big Three" – Synuclein, LRRK2 and Glucocerebrosidase (GBA), many genes have been associated with PD risk and progression. Experimental therapeutics targeting each of these genes are in clinical trials, and more are on the way. Is targeting the protein products of PD associated genes a promising therapeutic avenue? Or should we be targeting other factors – proteins or processes that modify the effect of specific genes, or even immunological mechanisms that help the body fend off and repair the damage caused by the true underlying cause of PD?

O99

Table 8: All this talk about data: How do we ensure it is secure?

*Jochen Klucken**
University of Luxembourg, Luxembourg Institute of Health, Centre Hospitalier de Luxembourg, Belval, Luxembourg

Whenever we hear about digitalization of healthcare or technical innovations including sensor-derived data, or artificial intelligence supporting the patient and the clinical decision of the healthcare professionals we get scared about potential data misuse. Even though, we use a lot of data-driven applications such as online-shops, chat messengers, social media platform, email-software, etc. every day without worrying too much about data security, in healthcare this is discussed as a hot and controversial topic. One reason for this could be, that we are not having experiences with the benefit of data usage - therefore, we will discuss in the round-table discussion the different aspects of data availability for research and care, as well as the benefit that can be generated by data usage. In fact, data security and protection against misuse will be less of the problem in the future, that the actual consented usage of data and its transparency. Ethical discussion and consideration is needed to define how to make data safe, useful, and maintain privacy and patient-awareness.

O100

Table 11: Freezing of gait in Parkinson's: What do we really know?

*Elisa Pelosin**
University of Genova, Genova, Italy

Freezing is defined as ''brief, episodic absence or marked reduction of forward progression of the feet despite the intention to walk' (Giladi and Nieuwboer 2008; Nutt et al. 2011).
With disease progression, the prevalence and the severity of FoG symptoms increase leading to a progressive loss of the independence of the daily life activities thus affecting patients' quality of life. In addition to this, FOG is one of the most common causes of falls in PD, contributing to high fall rates ranging from 35% to 90%. (Perez-Lloret, 2014; Latt, 2009; Allen, 2013).
To date, freezing pathophysiology is unclear because of its phenomenological complexity involving motor, cognitive, and emotional aspects of behavior (Togo,2023)
FOG is surprisingly difficult to assess in daily clinical practice. However, this is explained by several factors. First, it is an episodic phenomenon (Snijders, 2008), its observation may require the use of triggering tricks (Hereman, 2013). Second, freezing episodes are dramatically reduced when patients shift from an automatic control of gait to a more goal-directed one (Hallett, 2008; Redgrave, 2015). Third, patients are typically in the "on" dopaminergic state when they visit the clinician, while FOG is more common (and severe) in the "off" state. These difficulties in assessing FOG are problematic given that optimal management depends on valid and reliable assessment (Nonnekes, 2015).
Recent systematic reviews (Cosentino, 2020; Gilat 2021) showed promising findings on the potential benefits of some physiotherapy interventions, such as action observation, treadmill combined with cueing, behavioral strategies, and prolonged homebased exercise trainings. However, to design treatments that fit the best for PD patients who are troubled by regular freezing, FOG-specific or FOG-related exercises should be the first-line interventions to be applied.
Gaps remain to be filled to further optimize the multidisciplinary management needed for this common and disabling symptom in PD.

O101

Table 12: DBS and Parkinson's

*Genko Oyama**
Juntendo University Faculty of Medicine, Tokyo, Japan

Deep brain stimulation (DBS) is a powerful treatment option for PwPs struggling to maintain their fluctuating motor symptoms. The technology for DBS has been advanced. Particularly, directional lead and sensing and adaptive technologies much improved the fine tune of DBS settings, which may result in an improvement in the quality of life of PwPs. However, there are pros and cons, and not all people are eligible for this treatment. In this round table discussion, we will discuss these points.

O102

Table 13: The role of genetics in the pathophysiology of PD

*John Hardy**
University College London, London, United Kingdom

The major pathology of Parkinson's disease is the Lewy body. Electron microscopical examination of Lewy bodies reveals them to be membrane bound inclusions, probably derived from lysosomes. Inside these structures are packed membranes and mitochondria. Synuclein is a highly expressed membrane associated protein which coats membranes consistent then, with the histological staining of Lewy bodies with synuclein. These data are consistent with the genetic analysis of both simply genetic Parkinson's disease and the sporadic disease. These analyses have identified synuclein and lysosomal genes as well as genes involved in the elimination of damaged mitochondria (mitophagy) as causative for the disorder. In my talk I will discuss these pathways and discuss how failures in lysosomal pathways could lead to synuclein deposition and how and why failures in mitophagy could lead to selective dopaminergic neuronal loss. Genetic analysis is, therefore, pointing to age related failures to protein degradative pathways as the underlying cause of Parkinson's disease. These findings suggest that treating the disease may be achievable either by decreasing the demands on these pathways (such as by reducing synuclein expression or reducing mitochondrial damage) or by potentiating lysosome clearance pathways.

O103

Table 14: Steps to build a more patient-centered approach to care

*Neil Archibald**
South Tees Hospitals NHS Foundation Trust, Middlesbrough, United Kingdom

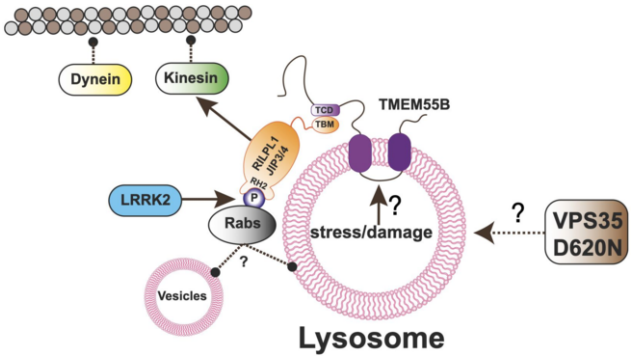
Patient-centered care is often quoted as the aim of medical services but seems less clear how this is achieved or the benefits that this brings. In this session, we take a look at different models of care in Parkinson's and how they might be developed to improve patient and carer engagement and outcomes. I will be drawing from my experience as an NHS Parkinson's consultant and the son of a Parkinson's patient. I am not a clinical academic so expect this session to be based on the ups and downs of working in a busy Parkinson's service in the UK. We will discuss where the service started, how it has developed over the last 10 years and where it might be headed in the next 10.

O104

Talk 1: VPS35 and LRRK2

*Dario Alessi**
MRC Protein Phosphorylation and Ubiquitylation Unit, Dundee, United Kingdom

Autosomal dominant mutations that activate the Leucine Rich Repeat Protein Kinase-2 (LRRK2), are associated with familial Parkinson's disease. Recent work indicates that hyperactivation of LRRK2 results in lysosomal stress and dysfunction which is potentially linked to Parkinson's. LRRK2 encodes a multidomain protein and phosphorylates a group of Rab GTPases including Rab8A and Rab10 at a conserved Ser/Thr residue located at the centre of the effector binding switch II motif. LRRK2 phosphorylated Rab8A and Rab10 then interact with a group of scaffolding proteins containing an RH2 domain including RILPL1 (RILP-like protein 1). I will provide an update of where we are with understanding how LRRK2 is activated by binding to various Rab proteins and by the D620N mutation in the VPS35 retromer component. I will describe recent work that provides new molecular insight into how the LRRK2 phosphorylated Rab proteins recruit and interact with a new set of effectors on the lysosome and how this might be regulated by lysosomal dysfunction/stress. If time permits I will also describe work that we have done to characterize the specificity of the PPM1H phosphatase that specifically dephosphorylates Rab proteins.



O105

Talk 2: LRRK2 and SNCA
*Laura Volpicelli-Daley**
University of Alabama at Birmingham, Birmingham, AL, United States

Both α-synuclein and leucine rich repeat kinase 2 (LRRK2) play major roles in Parkinson's disease (PD). Dominantly inherited mutations in SNCA and LRRK2 and cause Parkinson's disease. Genome wide association studies consistently show that polymorphisms in both genes increase PD risk. Lewy pathology composed of fibrillar α-synuclein is a characteristic of PD. Increased kinase activity of mutant LRRK2 is the mostly likely cause of PD susceptibility. Several studies show that neuronal expression of mutant LRRK2, particularly the most common G2019S-LRRK2, increases α-synuclein aggregation. However, α-synuclein is not a direct substrate for LRRK2. What are the potential mechanisms by which LRRK2 facilitates α-synuclein inclusion formation? Mutant LRRK2 inhibits chaperone mediated autophagy of α-synuclein leading to higher expression levels, thus facilitating aggregation. In addition, LRRK2 kinase activity plays a role in presynaptic targeting of α-synuclein. Neuronal expression of G2019S-LRRK2 reduces the membrane association of α-synuclein, and cytosolic α-synuclein more readily forms abnormal aggregates. G2019S-LRRK2 also causes dissociation of normal α-synuclein multimers into monomeric α-synuclein that more readily aggregates. LRRK2 phosphorylates Rab GTPases such as Rab3a and Rab10 which are found at the presynaptic terminal. Abnormal LRRK2 kinase induced hyperphosphorylation of Rab3, and Rab10 could alter effectors involved in presynaptic α-synuclein function. Finally, the effect of mutant LRRK2 on activity of excitatory neuron activity could influence the spread of Lewy pathology throughout the brain.
It is important to note that 65% of individuals with G2019S-LRRK2 show Lewy pathology, whereas only 35% of individuals with other LRRK2 mutations do. Recent evidence suggests that the presence of Lewy pathology may increase the risk of cognitive decline and psychiatric symptoms in the context of mutant LRRK2. Indeed, it is possible that Lewy pathology causes cognitive symptoms rather than causing loss of dopamine neurons associated motor symptoms. Regardless, these findings highlight the existence of PD subtypes and the need for personalized therapeutic strategies to target the underlying disease mechanisms.

O106

Talk 3: LRRK2 and GBA
*Matthew LaVoie**
University of Florida, Gainesville, FL, United States

Autosomal recessive mutations in the GBA1 gene encoding glucocerebrosidase cause the lysosomal storage disorder Gaucher's disease. Heterozygous carriers of most GBA1 mutations have dramatically increased Parkinson's disease (PD) risk, but the mechanisms and cells affected remain unknown. Emerging data suggest both cell autonomous and non-cell autonomous mechanisms in the etiology of PD, and glucocerebrosidase expression is relatively enriched in astrocytes. However, the impact of its mutation in these cells has not yet been addressed. Therefore, we have evaluated the impact of GBA1 mutation on both neuron and astrocyte function, as well as a consideration of how LRRK2 biology intersects with GBA1-dependent pathology. Our results add to the growing evidence for trafficking defects playing an important role in the etiology of PD and how independent pathologic pathways may intersect.

O107

Talk 1 :The role of genetics in the pathophysiology of PD
*John Hardy**
University College London, London, United Kingdom

The major pathology of Parkinson's disease is the Lewy body. Electron microscopical examination of Lewy bodies reveals them to be membrane bound inclusions, probably derived from lysosomes. Inside these structures are packed membranes and mitochondria. Synuclein is a highly expressed membrane associated protein which coats membranes consistent then, with the histological staining of Lewy bodies with synuclein. These data are consistent with the genetic analysis of both simply genetic Parkinson's disease and the sporadic disease. These analyses have identified synuclein and lysosomal genes as well as genes involved in the elimination of damaged mitochondria (mitophagy) as causative for the disorder. In my talk I will discuss these pathways and discuss how failures in lysosomal pathways could lead to synuclein deposition and how and why failures in mitophagy could lead to selective dopaminergic neuronal loss. Genetic analysis is, therefore, pointing to age related failures to protein degradative pathways as the underlying cause of Parkinson's disease. These findings suggest that treating the disease may be achievable either by decreasing the demands on these pathways (such as by reducing synuclein expression or reducing mitochondrial damage) or by potentiating lysosome clearance pathways.

O108

Talk 2: Genetic testing in PD – What is currently possible? What is useful? Where are the challenges, and what is the future?
*Christine Klein**
University of Luebeck, Lübeck, Germany

A monogenic cause or strong genetic factor predisposing to Parkinson's disease (PD) can be detected in ~15% of all patients and can unequivocally establish a diagnosis of (genetic) PD. Confirmed forms of monogenic PD resembling idiopathic PD clinically include four dominantly (SNCA-PD, LRRK2-PD, VPS35-PD, and CHCHD2-PD) and three recessively inherited forms (PRKN-PD, PINK1-PD, DJ1-PD). Detailed genotype and phenotype information on these conditions is available at https://www.mdsgene.org. Pathogenic variants in GBA are the

strongest known genetic risk factor for PD and are sometimes viewed as acting in a dominant fashion with highly reduced penetrance. Genetic testing is currently the only possible means to identify unaffected carriers of pathogenic variants in PD genes who are at (high) risk of developing PD in the future.
There are no established international guidelines for clinical diagnostic testing for PD; however, most available recommendations agree that a genetic test may be considered in patients with early-onset PD, a positive family history, or individuals with a specific ethnic background where specific pathogenic variants are common due to a founder effect (for example, the p.G2019S variant in LRRK2 in patients of Ashkenazi Jewish or North African Berber descent).
Availability and type of genetic testing vary widely internationally and range from full coverage through the health care system to no reimbursement at all. Likewise, there is a broad spectrum of different means of genetic testing including hot-spot or singe-gene sequencing, gene panels, exomes, and genomes, with panel sequencing currently being the most widespread approach in clinical diagnostics. Of further note, clinically relevant genetic testing results can be obtained in a research context (where they are sometimes limited to the custom content of arrays otherwise designed for genome-wide association studies) or within the framework of direct-to-consumer genetic testing. Challenges arise from variable technical quality - especially when it comes to calling pathogenic variants in GBA -, the occurrence of variants of unknown significance, the overall scarcity of genetic counseling opportunities, and economic constraints. A future perspective may be gene-targeted treatments for specific forms of monogenic PD, the first clinical trials for which are currently underway requiring the identification and stratification of suitable study participants.

O109

Talk 3: How does genetic information impact clinical trial designs?
*Roy Alcalay**
Tel Aviv Sourasky Medical Center, TEL AVIV, Israel

The field of Parkinson's disease (PD) genetics has tremendously advanced since the first discovery of PD-causing mutations in the synuclein (SNCA) gene in 1997. Over the course of the following decade multiple additional genes linked to PD were discovered. Mutations in these genes are very rare and are present in several families with a strong family history of PD or in people with very early onset of PD. In 2004, the link between mutations in the genes GBA and LRRK2 and PD was discovered. Mutations in these genes are much more common and combined are present in about 10% of all people with PD. This discovery opens a window of opportunity for novel treatments for PD. The underlying hypothesis is that intervention on the biological pathway of these genes may help slow down or even prevent PD in carriers of these mutations. Additionally, such interventions may possibly slow down or prevent PD even in people with PD without mutations in whom these biological pathways are altered.
Multiple researchers in academia and pharmaceutical companies develop interventions targeting the biological pathways GBA or LRRK2. Most proposed interventions aim to increase the activity of the protein encoded by GBA, called glucocerebrosidase or reduce the activity of the of the protein encoded by LRRK2. The most advanced study of an international phase-2 was concluded in 2022, but failed to show a positive effect.
The recruitment to precision medicine clinical trials in PD is challenging. By clinical trial design, participants must know their genetic status prior to receiving an intervention. Therefore, such interventions can be tested only with a team effort, including those with PD who receive their genetic results and enroll into precision medicine studies. To achieve this goal, there is an international effort to make genetic data accessible for people with PD and their clinicians, including the PD GENEration study (primarily in North America and the Dominican Republic) and the ROPAD study (primarily in Europe and Israel).
The overall goal of these clinical trials is to tailor PD treatment in different individuals based on their own genetics aiming to reverse the pathological process that led to PD.

O110

Talk 1: Advances in research, science and treatment: autonomic dysfunction
*Patricio Millar Vernetti**
New York University Grossman School of Medicine, New York City, New York, United States

Advances in research related to autonomic dysfunction in Parkinson's can lead to a better understanding of symptoms that may present throughout the life of a person with Parkinson's, how can they affect their life, and provide insight into how to better manage them and prevent complications.

O111

Talk 2: Depression and apathy
*Iracema Leroi**
School of Medicine and Global Brain Health Institute, Trinity College Dublin, Dublin, Ireland

In Parkinson's, mental health symptoms such as apathy and depression are common and may impact significantly on quality of life, motor function and prognosis in people living with Parkinson's. People with Parkinson's often report depression as the most distressing aspect of their condition. At any given time, up to 40% of people with Parkinson's will have significant symptoms of depression and/or anxiety. Apathy may be present in up to 70%. Apathy and depression are both associated with cognitive decline in Parkinson's; apathy may be a behavioural marker of the onset of dementia in Parkinson's. Moreover, the impact of apathy and depression in Parkinson's can negatively impact care partner outcomes.
Apathy and depression may frequently overlap and are also often under-recognised in clinical settings and thus under-treated. Difficulties with diagnosis may be compounded by a lack of guidance for health professionals. This presentation will provide a background to these neuropsychiatric syndromes in Parkinson's and provide practical approaches to assessment and management, with a person-centred and pragmatic focus.

O112

Talk 3: Fatigue and sleep
*Graham "Alec" Glass**
Peak Neurology and Sleep Medicine, LLC, Anchorage, AK, United States

Fatigue and unrefreshing sleep are common and debilitating symptoms in Parkinson's Disease. These are present in up to 60% of patients across the disease course and are sometimes present before movement symptoms begin.
Fatigue is generally defined as a lack of energy to initiate or complete and actions. Patients cannot seem to summon either the mental or physical energy to act but often aren't "sleepy" and wouldn't fall asleep if given the opportunity.

Sleepiness or drowsiness is the extreme desire to fall asleep. This is often relieved by a nap or sleep. Fatigue is typically not relieved by sleep.
Although insomnia of sleep initiation is present in PD, sleep maintenance is the most common type of insomnia seen in PD patients and is the most frequent overall sleep compliant. The fragmentation of sleep associated, can result in worsened motor and cognitive function.
Effective identification of fatigue and other sleep disorders in PD relies on clinical history as well as on the use of rating scales such as the Fatigue Severity Scale (FSS), The Parkinson's Fatigue Scale (PFS), Parkinson's Disease Sleep Scale (PDSS) and Epworth Sleepiness Scale (ESS).
Depression and anxiety often travel with fatigue and poor quality sleep and should be maximally treated via both pharmacologic and non pharmacologic means to allow adequate therapy of sleep disorders.
Ultimately, once other concomitant medical and neuropsychiatric symptoms have been addressed a number of therapies ranging from Cognitive Behavioral Therapy (CBT) to pharmacologic therapies can be used to improve fatigue and insomnia in PD ultimately improving quality of life.

O113

Debate side 1 - Lewy bodies; much more than alpha-synuclein aggregates

*Wilma Van de Berg**
AmsterdamUMC, Vrije University Amsterdam, Amsterdam, Netherlands

Parkinson's disease (PD) is neuropathologically characterized by Lewy bodies and Lewy neurites in the predilected regions in the brain and dopaminergic cell loss. The misfolded protein alpha-synuclein (aSyn), is considered to be one of the main components of Lewy bodies. Noteworthy, the aSyn pathology in brain tissue exhibit diverse morphological, structural and molecular compositions across brain regions and patients. Unfortunately, there is currently no experimental model that can mimic the Lewy body formation and maturation in the human brain. So high-resolution imaging and biochemical studies of postmortem human brain tissue samples of well-characterized donors are important to unravel the cellular mechanisms driving the onset and progression of the disease.
It is still a matter of debate if aggregated aSyn is the cause of PD, or if this is merely a common downstream neuropathological phenomena. Recent microscopy studies showed that the majority of neuronal aSyn aggregates in the postmortem human brain are composed of accumulated vesicles, cytoskeletal proteins and cellular organelles and membrane fragments. Based on these results, one could argue that impaired vesicle trafficking and lipid metabolism are the main drivers of the disease. In brain tissues and biofluids of PD patients, changes in spingolipids, phospholipids and cholesterol have been reported. On a subcellular level, these changes may lead to impairment of autophagy pathways, including chaperone-mediated autophagy, the main aSyn degradation pathway. Importantly, genetic and postmortem studies have provided a wealth of evidence for disturbed mitochondrial function, autophagy, neuroinflammation and malfunction of the adaptive immune response, which could all act upstream of aSyn aggregation. As such, the Lewy body formation might be the result of a highly-ordered cellular program to encapsulate damaged proteins and lipids.

O114

Debate side 2 – Lewy bodies: A major driver of neurodegeneration

*Hilal Lashuel**
École polytechnique fédérale de Lausanne (EPFL), Lausanne, Switzerland

It has been more than 100 years since Lewy bodies (LBs) were first discovered in the brain of Parkinson's disease patients and more than 20 years since alpha-synuclein (α-syn) aggregates were identified as one of the main components of LBs. However, several fundamental questions regarding how LBs are formed, their composition, and whether they protect against or cause neurodegeneration in Parkinson's disease (PD) and other synucleinopathies remain unanswered. Recent application of advanced electron microscopy, mass spectrometry and imaging technologies in combination with access to novel antibodies has enabled major advances towards deconstructing the complexity of LBs and alpha-synuclein pathology in the brain and reverse engineering LB formation in neurons and rodent models. These studies show that the process of LB formation involves a complex interplay between α-syn fibrillization, posttranslational modifications, and interactions between α-syn aggregates and proteins, lipids, and membranous organelles. Furthermore, they provide strong evidence linking the process of LB formation, rather than merely α-syn fibril formation, as one of the major drivers of neurodegeneration through disruption of cellular functions and proteostasis, and inducing mitochondria damage and deficits, and synaptic dysfunctions.
Relying on recent insights into the 1) clinical heterogeneity of PD; 2) the biochemical and ultrastructural properties of LBs in the brain; 3) the heterogeneity of alpha-synuclein pathology and co-occurrence of other co-pathologies in PD and aging brains, I will present working models and hypotheses that could explain the relationship, or lack of, between alpha-synuclein pathology, and neurodegeneration in sporadic and some genetic forms of PD.
I will then present evidence that 1) supports important roles for the processes of alpha-synuclein misfolding, aggregation, and LB formation in the development and progression of sporadic and some genetic forms of PD; 2) shows how these processes could contribute to neuronal dysfunction and degeneration through a combination of both loss and gain of toxic mechanisms; and 3) demonstrate that targeting the native state of alpha-synuclein and/or alpha-synuclein pathology formation and spreading represents a viable strategy for developing disease-modifying therapies to treat PD. I will close by emphasizing the need for combination therapies that account for the pathological and clinical heterogeneity of PD and other synucleinopathies.

O115

Talk 1: What are the most promising cell transplantation approaches for PD?

*Jun Takahashi**
Center for iPS Cell Research and Application, Kyoto University, Kyoto, Japan

Human induced pluripotent stem cells (iPSCs) can provide a promising source of midbrain dopaminergic (DA) neurons for cell replacement therapy for Parkinson's disease (PD). Towards the clinical application of iPSCs, we have developed a method for 1) scalable DA neuron induction on human laminin fragments and 2) sorting DA progenitor cells using a floor plate marker, CORIN. The grafted CORIN+ cells survived well and functioned as midbrain DA neurons in the 6-OHDA-lesioned rats and showed a minimal risk of tumor formation. In addition, we performed a preclinical study using primate PD models. Regarding efficacy, human iPSC-derived DA

progenitor cells survived and functioned as midbrain DA neurons in MPTP-treated monkeys. Regarding safety, cells sorted by CORIN did not form any tumors in the brains for at least two years. Moreover, we found that MRI and PET imaging was useful in monitoring the survival, expansion, and function of the grafted cells as well as the immune response by the host brain. Based on these results, we started a clinical trial to treat PD patients at Kyoto University Hospital in Kyoto, Japan, in 2018. The trial evaluates the safety and efficacy of transplanting human iPS cell-derived DA progenitors into PD patients' putamen. Using a stereotaxic surgical technique, we implant approximately 5 or 10 million cells into the bilateral putamen of the patients. The target is seven patients, and we will observe each of them for two years. The trial is now ongoing without any severe adverse events.

O116

Talk 2: What are the gene therapy and growth factor approaches for PD?

*Krystof Bankiewicz**
AskBio, Columbus, OH, United States

At present there is a significant unmet need for clinically available treatments for Parkinson's disease (PD) patients to stably restore balance to dopaminergic network function in a long-term fashion. Growth factors hold considerable promise for disease modification in neurodegenerative disorders such as PD.
Although multiple clinical trials with growth factors have now been performed in PD patients the results have been mixed. It has been rationalized that improving administration with MRI-monitored convection enhanced delivery (CED) might overcome the limitation of insufficient putaminal coverage to achieve clinical improvements in motor function.
Two growth factors, glial cell line derived neurotrophic factor (GDNF) and neurturin (NRTN), have garnered significant attention in the novel in vivo gene therapy field. However, only AAV2 GDNF (AB-1005) is currently active in gene therapy trials for PD. A Phase 1b study utilizing MRI-guided bilateral putaminal CED delivery of AAV2 GDNF has just completed enrollment (NCT04167540).
In this Phase 1b study AAV2 GDNF has so far demonstrated an encouraging safety profile where the neurosurgical procedure was well tolerated, and all 11 participants have completed 9 or more months of clinical follow-up. Putaminal coverage was >60%. No serious adverse events (SAEs) were associated with AAV2 GDNF. Reported adverse events (AEs) primarily occurred peri-operatively or were related to underlying PD.
Participants in the Mild Cohort (<5 years since clinical diagnosis of PD and MDS-UPDRS III OFF score ≤32; n=6) demonstrated stable MDS-UPDRS Part II and Part III OFF and ON scores at 6 and 12 months from baseline.
Participants in the Moderate Cohort (≥4 years since clinical diagnosis of PD and MDS-UPDRS III OFF score 33–60; n=4) demonstrated improvements on MDS-UPDRS Part II (–5.0 ± 3.5 pt) and Part III OFF (–18.8 ± 5.4 pt) at 12 months.
Although the placebo effect limits interpretation of small open-label studies such as this, these preliminary findings suggest potential stabilization in the Mild Cohort and possible early improvements in the Moderate Cohort. Further longitudinal evaluation and a controlled study is planned to confirm these initial findings.

O117

Talk 1: Exercise for life

*Miriam Rafferty**
Shirley Ryan AbilityLab; Northwestern University, Chicago, Illinois, United States

Best care for people with Parkinson's disease (PD) includes encouragement of exercise. The question is no longer whether to exercise. The question is which exercise? Other challenges include how to stay motivated to exercise as the disease changes. While neurologists can encourage and provide exercise education, individuals with PD must perform that exercise on their own and/or with the help of community exercise professionals, physical therapists, and a social support network. The purpose of this session is to provide insight into considerations for prescribing exercise to maintain motivation and adherence over time.
Parkinson's specific exercise guidelines have been developed by the Parkinson's Foundation in collaboration with the American College of Sports Medicine. Exercise is also recommended as a part of physical therapy guidelines from around the world. The Parkinson's Foundation guidelines include 150 minutes per week of moderate-vigorous intensity aerobic exercise; 2-3 days per week of strengthening; 2-3 days per week of balance, agility and multi-tasking exercises; and 2-3 days per week of stretching. The American Physical Therapy Association makes strong recommendations for including aerobic, strengthening, and balance training into physical therapy care due to a high level of evidence, with flexibility included as a part of warm-up and cool-down activities. European and Canadian physical therapy guidelines recommend that neurologists consider referring people with PD to physical therapy early after their diagnosis for individually tailored exercise prescription.
In their entirety, these exercise guidelines can be overwhelming. Applying the guidelines in a comprehensive, but manageable, weekly program can take the skill of an experienced exercise professional or physical therapist. The support of a professional can also help an individual to feel accountable and motivated to exercise. They can also help you adapt your routine as your disease changes. Finding the best exercise plan for you should take into account your interests, abilities, goals, preferences, and access to resources (e.g., location of classes, cost). At the end of this presentation, you should feel more confident moving forward with your best exercise plan, with the understanding that you probably don't have a full-time job to exercise!

O118

Talk 2: Enabling people with PD to exercise

*Natalie Allen**
The University of Sydney, Camperdown, NSW, Australia

It is well established that exercise has many benefits for people with Parkinson's disease (PD). Current evidence-based guidelines, such as the Parkinson's Foundation's Parkinson's Exercise Recommendations and the American Physical Therapy Association's Physical Therapy Guidelines guide exercise prescription. However, translating exercise guidelines into effective, feasible, modifiable and sustainable programs that meet the person with PD's needs can be challenging. This presentation will focus on methods of enabling people with PD to start exercising and continue exercising over the course of the disease. Prescribed exercise needs to meet the individuals' goals; account for symptoms and preferences; and adapt to changing needs over time. Health professionals with training in exercise prescription for people with PD (e.g., physiotherapists and exercise physiologists) are trained to prescribe and monitor effective exercise programs. They are also

trained to enable the development of skills in exercise self-management, including knowledge about the benefits of exercise, goal setting, problem solving, monitoring (e.g., using a step counter) and accessing social support and exercise opportunities in the local community. Learning skills in how to manage an exercise program can help people with PD to increase their motivation and exercise self-efficacy, monitor their progress and 40ecognize when to seek professional help. Long-term exercise prescription with modifications as needed over time can be achieved sustainably through implementing a secondary prevention model of care, where the person with PD is referred to an appropriate exercise professional as soon as possible after diagnosis. They can attend exercise check-up sessions every 6 to 12 months, with short bursts of more intensive exercise therapy as required. In between, the person with PD continues with their exercise program in the community. Adopting a hybrid approach is one way to implement this secondary prevention model. A hybrid approach combines in-person sessions at a clinic with home-based telehealth sessions and independent exercise. Exercise that is prescribed, monitored and progressed using this approach is effective, feasible, acceptable and sustainable. It is never too early or too late to start exercising but maintaining exercise habits in the long term is the key to optimal mobility and well-being.

O119

Talk 3: Exercise delivery in an online world

*Josefa Domingos**
Radbound University, Lisbon, Portugal

Emerging care models for Parkinson's disease (PD) are using technology to deliver hybrid approaches to care, where in-person and online sessions can complement each other. The use of technology is an obvious solution to facilitate access to care and reduce the burden of transportation, costs, and demands on care partners. Yet, we still need to overcome several barriers, including limited evidence, insurance models, and technology asymmetries, before it reaches true efficacy, safety, and implementation.
Particularly in delivering exercise online, there are concerns regarding safely integrating exercises commonly used during in-person settings. Is it possible to monitor safety appropriately when viewing participants in little boxes?
Safe, evidence-based practices must be a priority for care in all settings, including online. Without robust evidence, professionals may favor unnecessary procedures and foster unrealistic expectations in people with PD, particularly those with less favorable profiles, placing individuals at risk of falls, injury, or frustration.
But what shall we do while we wait for the evidence?
The Covid pandemic pushed us to experiment with disruptive care models, and now we must be prepared to refine them. We know that online programs led by professionals with PD-specific expertise can better foster safety, just as they do for in-person programs. These professionals can better select which exercises to apply to individuals at risk and adapt to their changing needs. We also know that adherence and ongoing motivation are major challenges. While we must be careful about safety, we also want to be careful not to underestimate the person's capacity and compromise benefits, motivation, and adherence.
In this session, we will share examples of achieving these two objectives.
Ultimately, exercises that challenge balance might be more appropriately applied in person for better results and fewer risks. While exercises with strong aerobic components that require less supervision, such as dance and boxing, already have preliminary evidence supporting safety in online formats. Yet, several questions should fuel future research: Are we aiming to replace in-person sessions or complement them? Should we focus on creating new exercises that build upon technology instead of reproducing in-person activities? And how can online exercise replicate social connections and interactions better?

O120

Table 2: Women and Parkinson's disease: Unmet needs

*Soania Mathur**
UnshakeableMD, Ajax, ON, Canada

Parkinson's disease is often thought to primarily affect a specific demographic, that is, older white men. This stereotype is reflected in the long-standing illustration of the stooped elderly man that dominates medical media. But this disease knows no gender boundaries and as PD is the fastest-growing and second-largest neurological condition worldwide, it is vital that we have a clear approach towards all those affected including women.
The medical literature and anecdotal reports from the community reveal a lack of insightful, comprehensive information about how Parkinson's affects women and optimal management of this disease in this population. We know that symptoms, both motor and nonmotor can be different. Women have more tremor, more levodopa-induced dyskinesias, restless leg syndrome and experience an increase in certain nonmotor symptoms such as mood and sleep disturbances, anxiety and depression, fatigue, apathy and pain. We also know of the variability in the clinical symptoms and effectiveness of medication throughout a woman's menstrual cycle as well as lifetime hormonal status. Women also face different psychosocial issues; the most important being poorer quality of life at diagnosis, negative self-image, fear of not being heard and less social support.
How best do we manage the unique presentation and variability of this disease in women?
How do we approach optimizing quality of life for women living with PD in all stages of their life? How can we increase participation of women in clinical trials so that we can learn the necessary information to address these issues?
Join the discussion to address unmet needs and how to optimize quality of life for women living with the challenge of Parkinson's disease.

O121

Table 3: Swallowing and Parkinson's

*Yael Manor**
Tel Aviv Sourasky Medical Center, Tel Aviv, Israel, Israel

Dysphagia affects the most cardinal aspect of human functions, the ability to eat and drink. The discomfort, nutritional problems, malnutrition and dehydration, weight loss, difficulties in handling oral medication and the high incidence of aspiration pneumonia as a cause of death attest to the clinical importance of this problem. It is well recognized that dysphagia is associated with reduction in the quality of life (QOL) of patients with Parkinson's disease (PD). Early assessment of swallowing disturbances and adequate treatment of dysphagia in patients with PD might not only prevent aspiration but may also increase the level of safety while eating and decrease the fear of choking.
At the round table we will discuss some of the common signs and symptoms of swallowing disturbances in PD, such as:

- Difficulty to control food or saliva in the mouth
- Difficulty to initiate the swallowing reflex
- Coughing before, during or after a swallow
- Frequent coughing towards the end or immediately after a meal
- Chocking before, during or after a swallow

- Recurrent pneumonia
- Weight loss when no other reason can be defined
- Gurgly voice quality – wet voice quality after swallowing
- Increase in saliva in the pharynx after a swallow, toward the end of the meal or after a meal
- Food gets stuck in the throat

Another point that will be discussed is when and how to get early swallowing screening and/or evaluation so early intervention can be initiated. Finally, the swallowing intervention program approaches will be described. It will be clarified that the most important aspect of management is the accurate diagnosis of the neuromotor or anatomic problem affecting swallowing. Once the specific problem has been defined, the swallowing therapist can design an appropriate intervention programme to manage the swallowing disturbance both in terms of nutrition and of rehabilitation of swallowing patterns. The importance of the patients' understanding of their pathological swallowing pattern will be stressed.

O122

Table 4: Mobility challenges in PD: Causes and connections

*Kaylena Ehgoetz Martens**
University of Waterloo, Waterloo, ON, Canada

Several mobility problems are associated with Parkinson's disease (PD) that include gait and balance impairments. Freezing of gait (FOG) is a severe gait disturbance that is commonly experienced by people living with Parkinson's disease, and has a significant impact on falls, independence and quality of life. Freezing of gait can be defined as a sudden inability to move the feet forward despite the intention to walk. It is complex, yet debilitating, and remains difficult to treat due in large part to its heterogeneous nature. Freezing of gait can vary in presentation ranging from severe shuffling to trembling to complete akinesia. It can also vary in responsiveness to medication, as well as there are a variety of contextual triggers which provoke FOG. The highly variable nature of this phenomenon makes it challenging to study in both clinical and research settings, and as a result, our understanding of its mechanistic causes remain incomplete. While culminating evidence suggests that freezing is multi-faceted and influenced by a variety of impairments across cognitive, motor and affective domains, further research is needed to characterize and understand the heterogeneity related to FOG in order to develop novel and effective therapeutic interventions.

O123

Table 5: (Spanish) Mitos y barreras en torno a la participación en la investigación / Myths and barriers around participating in research

*Ignacio Mata**
Cleveland Clinic/Case Western Reserve University, Cleveland, OH, United States

Los seres humanos llevamos miles de años utilizando metodologías científicas (investigación) para comprender mejor la naturaleza, las enfermedades, etc. En esta mesa redonda presentaremos lo que es un estudio de investigación y cómo los científicos los utilizan para responder a preguntas específicas y comprender mejor la enfermedad de Parkinson. También explicaremos la diferencia entre los que comparan los efectos de una determinada intervención (intervencionistas), como los ensayos clínicos, y los que se limitan a observar y recoger datos en un grupo de individuos (observacionales). A continuación, discutiremos algunas de las barreras que tienen los científicos para reclutar participantes en diferentes estudios de investigación, y desmentiremos algunos mitos y conceptos erróneos que tienen muchos individuos y que pueden impedir su participación en la investigación.
También ofreceremos ejemplos y formas de identificar estudios de investigación de confianza.
El objetivo de este debate es proporcionar todos los conocimientos y las herramientas para sentirse cómodo al participar en una investigación.

O124

Table 6: Familial PD: Tips for treating a family vs a single patient

*Leonidas Stefanis**
NKUA and BRFAA, Athens, Attiki, Greece

Familial PD in practical terms refers mostly to PD cases presenting across multiple generations, in families with autosomal dominant inheritance. Relatively benign forms exist, such as in the context of LRRK2 mutations; penetrance is modest, and the overall family burden, although significant, is not devastating, given that the age of onset is quite similar to idiopathic PD, many times beyond retirement age, and the course rather slow. Contrast this with cases with autosomal dominant PD due to mutations in the SNCA gene encoding for alpha-synuclein. Although there is variability in disease manifestation between carriers of different SNCA mutations, carriers of the most commonly identified p.A53T SNCA mutation and their families face an uphill battle. The disease invariably hits every generation, and afflicted subjects usually become incapacitated at a productive age, as the mean age of onset is 45 years of age and the disease course, regarding both motor and non-motor aspects, often quite rapid. It is clear that the family environment is critical in the management of the single patient, who has often witnessed the harrowing aspects of the disease in close relatives, usually his or her parents. The treating neurologist and his team have to take into account the family history and the repercussions it may have on the expectations of the single patient and his or her family. It is essential that an atmosphere of hope and support is offered, as it has to be conveyed that a) there is a host of medical and non-medical interventions that are now available that may not have been available to the patient's parents, b) the disease course even amongst patients with the same SNCA mutation, is variable, and c) there is hope for new disease-modifying treatments, especially since aberrant alpha-synuclein, the undeniable cause of the disease in such families, is the target of intense therapeutic development. Similar encouragement needs to be conveyed to the whole family, including caregivers, together with the urge to participate in non-interventional and interventional clinical studies, which are sorely needed in this group of subjects with rare genetic synucleinopathies.

O125

Table 7: Parkinson's Apathy: Why do we care?

*Dawn Bowers**
University of Florida, Fixel Institute of Neurological Disorders, Gainesville, Florida, United States

Evidence over the past two decades points to apathy being a core neuropsychiatric signature of Parkinson disease. This roundtable will provide an update on what we know and what we do not know about apathy, including best practices for improving apathy in persons with PD. We know that apathy is distinct from depression, affects between 30-70% of persons with PD, can occur early and progressively worsen with disease progression. Rather than a mood disorder, apathy is a disorder of motivation that affects one's get up and go in terms of behavior, thinking, and emotions. Why should we care? Apathy can have potent health and interpersonal

consequences, ranging from physical deconditioning, increased burden on caregivers, and negative effects on treatment outcomes. We will discuss risk factors for developing apathy, and how some treatments for depression can worsen apathy. This will be highly interactive roundtable where participants share their tips and their best advice. As part of the roundtable, we will highlight a behavioral intervention for improving apathy, including the Parkinson Active Living Program (PAL, Butterfield) that we use at the University of Florida.

O126

Table 8: Action observation and motor imagery: From neurophysiology to clinical practice

*Laura Avanzino**
University of Genoa, Genoa, Italy

Motor imagery (MI) is a dynamic state during which motor actions are mentally simulated, without
actual movement. A large body of evidence suggests that imagined and executed actions recruit overlapping brain regions (i.e., premotor cortex, anterior cingulate, inferior parietal lobule, and cerebellum), although MI is thought to reflect mainly the process of movement preparation, with reduced involvement of end-stage movement execution related processes.
It is widely accepted that also the observation of actions performed by others activates in the brain the same neural structures used for the actual execution of the same actions. The neurophysiological basis of “action observation” (AO) is represented by the discovery of mirror neurons in the monkey cerebral cortex that discharge during both the execution of goal-directed actions and the observation of other individuals performing similar actions. The definition of “mirror neuron system” (MNS) comprises the cerebral areas containing mirror neurons and evidence with the use of neurophysiological techniques as Transcranial magnetic stimulation and functional imaging (fMRI) suggested that a MNS is also present in the human brain. For example, during AO, the excitability of the motor cortex is enhanced, and brain areas in the frontal and parietal lobes are recruited, similarly to motor execution. The MNS is also involved in “imitation” within a circuit involving the inferior parietal lobule, the inferior frontal gyrus, and the premotor cortex.
Based on these neurophysiological premises, several studies have shown that MI and AO are effective ways to learn a new motor skill or to enhance its performance in healthy individuals, in an analogous manner to physical exercise. In rehabilitation, an adequate number of studies have been published so far that demonstrate positive effects of MI and AO training in neurological conditions with great attention in the last years to neurodegenerative diseases as Parkinson’s disease (PD). In PD positive effects of AO and MI have been shown mainly on walking ability and typical motor signs of PD like freezing of gait.

O127

Table 9: Every person with PD needs a palliative care team

*Ed Richfield**
North Bristol NHS Trust, Bristol, United Kingdom

This round table discussion offers the opportunity to explore the role of the palliative care team and palliative approaches to care and the way in which they may positively influence the lived experience of people living with Parkinson’s. Using practical examples, we will explore how palliative care approaches may be applicable from the time of diagnosis and throughout the course of the condition, what this means for the way in which palliative care can be accessed and how things could change to improve accessibility. Palliative care services incorporate a range of professionals with complementary skill sets, we will discuss how these can be utilized to provide both holistic approaches to care and focused expert help for specific unmet needs. People with Parkinson’s, their caregivers and family may have different needs at any given time, we seek to explore how a service can recognize and respond to this effectively. Finally, we will discuss the way in which health setting influences the nature of palliative care services for people with Parkinson’s and how an understanding of this can help us improve access, in order to address unmet care needs.

O128

Table 10: Biological brain changes observed following exercise in Parkinson’s: What do they tell us?

*Mark Hirsch**
Carolinas Rehabilitation, Charlotte, NC, United States

The aim of this round-table is to dialogue about possible barriers and future opportunities to develop and implement a patient-centric inclusive research agenda on biological brain changes observed with exercise in Parkinson disease. We must accelerate our work efforts together to move the field forward in what we refer to as “radical collaboration”. World-wide there is a growing interest in the neurosciences and in the science of exercise and neuroplasticity in Parkinson disease. For years, it was believed that exercise was a waste of time or that intense exercise was to be avoided as it was thought to worsen Parkinson disease by, for example, increasing the amount of underlying muscle tone. Traditionally, individuals living with Parkinson’s disease are engaged by the biomedical community in research to advance knowledge as “subjects” or “objects” of research and rarely as “equal partners”, “colleagues” or ”collaborators”. Recently, participatory approaches to research and clinical care such as patient-centric care, personalized medicine, participatory medicine, participatory healthcare, patient-scientists, and shared decision-making processes have slowly begun to emerge in the field of Parkinson disease. However, differences in the goals and perceived value of biomedical research on exercise, perceived hierarchical inequities in the medical doctor/patient research system, and terminology used by the biomedical community to disenfranchise people living with Parkinson disease and their care-partners (a.k.a. “the stakeholders”) may influence the progress of a participatory process. Participatory research and clinical care is a lot more complex than ever imagined. In addition, we need to bring these insights to those who will use the results, including the incorporation of new results on exercise and neuroplasticity into the training of clinicians.

O129

Table 11: Assaying misfolded synuclein in fluid and tissue biopsies for the diagnosis of PD

*Brit Mollenhauer**
University Medical Center Göttingen and Paracelsus-Elena-Klinik, Kassel, Germany, Kassel, Hesse, Germany

There is still a lack of neuroprotective strategies in α-synuclein (aSyn) associated neurodegenerative disorders [such as Parkinson’s disease (PD) and Multiple System Atrophy (MSA)] due to various reasons. One of the reason is that the diagnosis is still made too late and that there is no biomarker to objectively reflect the progression of the disease that is needed for clinical trials with neuroprotective strategies as outcome measure.
Over the past years, efforts to develop progression biomarker focused on imaging strategies and biological fluids, that mostly focused on cerebrospinal fluid (CSF) in the past. Most biomarker

immunoassays have so far not shown robust and clinically meaningful results. The newly developed aSyn Seed Amplification Assays (SAA) in CSF show high sensitivities and specificities for PD across various independent laboratories. In PPMI CSF samples form 1,139 participants were included and showed a sensitivity and specificity in PD and Healthy Controls (HC) of 88% and 96%. In MSA the seed dynamic can differentiate PD from MSA in some assays. Longitudinally there does not seem to be a change over time in dilution experiments making it currently impossible to utilize this biomarker as progression biomarker. In prodromal individuals with isolated REM sleep behaviour disorder (iRBD), the signal can be detected up to 9 years before conversion to disease in the De Novo PD (DeNoPa) cohort.
In the Systemic Synuclein Sampling Study (S4) aiming to characterize aSyn in multiple biofluids and tissues within the same PD subjects (n=59) in comparison to HC (n=21). SAA was performed in CSF and with formalin-fixed and paraffin embedded submandibular gland biopsies (SMG); the sensitivity and specificity for SAA in CSF was 93% and 91% and for SMG 73% and 79%.
Therefore α-synuclein SAA in its current form in CSF can be used for stratification in clinical trials in α-synuclein aggregation disorders and also in its prodrome iRBD. Emerging evidence also shows that α-synuclein SAA may even be applied in peripheral tissue and fluids, like skin, olfactory mucosa and also saliva. Identifying subjects at risk for upcoming neuropreventive strategies need peripheral biomarker. SAA will therefore be helpful in the future, but progression biomarker are still lacking.

O130

Table 12: Pre-habilitation: Preventing complications
*Ryan Duncan**
Washington University in St. Louis - School of Medicine - Program in Physical Therapy, St. Louis, Missouri, United States

The progressive nature of Parkinson disease (PD) increases the chances of experiencing complications associated with the disease. Common PD-related complications include motor and non-motor problems. Motor complications include gait difficulty, balance problems, falls, and fall-related injuries. Non-motor complications include cognitive impairment, depression, and pain. Rehabilitation and exercise are often effective in managing complications. However, too often there is a reactive approach to managing complications in PD. This is a problem because waiting to participate in rehabilitation and exercise until after complications are present poses significant difficulties for patients, caregivers, and rehabilitation providers. In this presentation, we will discuss the role of rehabilitation and exercise in managing and, ideally, preventing these complications. We will emphasize the need for a pro-active approach, or pre-habilitation, aimed at implementing effective rehabilitation and exercise strategies designed to delay or prevent the onset of these complications in people with PD.

O131

Table 13: Optimizing care provided in hospital for people with Parkinson's
*Richard Genever**
Chesterfield Royal Hospital NHS Foundation Trust, Chesterfield, United Kingdom

This round table discussion supports the earlier presentation on 'Optimizing care provided in hospital for people with Parkinson's'.
The aim is to expand on the themes identified in the earlier session and to discuss ways to identify potential hazards before they happen and to put supportive measures in place.
There will be the opportunity to discuss approaches to clinical scenarios.

O132

Table 14: What are the major advances in basic research in PD?
*Tiago Outeiro**
University Medical Center Gottingen, Göttingen, Deutschland (DEU), Germany

Parkinson's disease (PD) was described more than 200 years ago. The most effective therapies for PD have been developed around 60 years ago and, unfortunately, we have only witnessed incremental improvements in the treatment of PD. Although our knowledge of the molecular mechanisms involved in PD has evolved significantly in the past 30 years, it is widely accepted we face gaps and challenges in the detailed understanding of the molecular etiology of PD. In this session, I will discuss the major advances in the PD field and how they promise to open novel possibilities for therapeutic intervention.

O133

Talk 1: Prevalence of co-pathologies in Parkinson's disease
*Lauren Walker**
Newcastle University, Newcastle upon Tyne, United Kingdom

The hallmark protein aggregation deposited in the brain of people with Parkinson's disease is alpha-synuclein, however pathology associated with other neurodegenerative diseases can also be found in the brain which can affect the prognosis and trajectory of the disease course. Microscopic examination of the brain enables us to examine the prevalence of additional protein deposits. The most common co-pathologies are those seen in people with Alzheimer's disease (AD) (i.e. hyperphosphorylated tau and amyloid β (Aβ)), however other common co-pathologies include white matter lesions, TDP-43 inclusions, and argyrophilic grains. I will discuss the prevalence of common pathologies across the Parkinson's disease spectrum, the vulnerability of particular brain regions, and how this may affect the clinical progression.

O134

Talk 2: The role of alpha-synuclein and co-pathology on cognitive and non-motor symptoms
*Georgina Aldridge**
University of Iowa, Iowa City, Iowa, United States

Aggregated alpha-synuclein is found in Lewy Body Dementias (LBD), Parkinson's disease (PD), and around half of patients with Alzheimer's dementia (AD). Similarly, aggregation of proteins associated with AD (beta-amyloid, tau) and frontotemporal dementia (TDP-43), are often also found in patients with Lewy Body Dementias. Intriguingly, mixed pathology is more common than "pure" pathology, making it essential to understand how different protein aggregates contribute to symptoms and progression.
There is strong evidence supporting an association between alpha-synuclein, dopaminergic cell loss, and motor symptoms. By contrast, the role of alpha-synuclein and other protein-aggregate co-pathologies in non-motor symptoms remains unclear. Non-motor symptoms range from loss of smell to dream enactment to light-headedness with standing. Of the numerous symptoms described in LBD, arguably some of the least well understood include neuropsychiatric symptoms such as depression, hallucinations,

psychosis, anxiety and cognitive fluctuations (spontaneous changes in arousal and attention).
Our group uses deep-phenotyping of autopsy cases to generate hypotheses for how co-pathologies in specific brain regions contribute to complex non-motor symptoms. Pathological deep-phenotyping includes evaluation of beta-amyloid, alpha-synuclein, TDP-43 and tau aggregates at multiple target brain regions, including the brainstem. For example, despite lacking amyloid pathology, we have found co-morbid alpha-synuclein, phospho-tau and TDP-43 pathology, including in the locus coeruleus of a patient that had severe cognitive fluctuations and hallucinations. Our preliminary studies also show frequent tau co-pathology (with alpha-synuclein) in the dorsal raphe of LBD patients. When possible, pathology is then combined with detailed information on non-motor symptoms such as anxiety, depression and psychosis.
Finally, our team uses viral overexpression and fibril-spread models in mouse to evaluate the effects of isolated pathology in potential target regions. For example, the presence of alpha-synuclein outside of the brainstem is a defining feature of LBD, but the effect of isolated alpha-synuclein in cortical cells is not well understood. We have found that locally overexpressed alpha-synuclein in prefrontal cortex causes increased survival of dendritic spines. Using a similar strategy, our team is currently investigating the effect of local overexpression and aggregation of alpha-synuclein and tau in brainstem regions such as dorsal raphe and locus coeruleus.

O135

Talk 3: Contributions of co-pathologies in activating the immune response in PD
*Ashley Harms**
University of Alabama at Birmingham, Department of Neurology, Birmingham, AL, United States

Co-pathologies are a core feature of Parkinson Disease (PD). Along with Lewy body formation due to a-synuclein (a-syn) inclusions, ß-amyloid (Aβ) and tau aggregates are also implicated in the pathological progression of PD. Aβ plaques and phosphorylated-tau fibers are present in the brain of over 50% of PD cases. Studies have also shown that these three pathologies synergistically interact and may promote the aggregation of each other. Innate and adaptive immune responses in the brain, marked by infiltration of peripheral immune cells, gliosis, and the increase in pro-inflammatory cytokines in the brain, are prominent in PD and have also been associated with Aβ and tau pathology. However, animal models of these single pathologies do not fully recapitulate the immune response that is seen to be such an important component of human disease. To test the hypothesis that Aβ, tau and a-syn co-pathologies converge to drive pathology and neuroinflammation, a key component of PD, we developed a novel co-pathology model in mice and non human primates. This model incorporates a-syn, Aβ, and Tau in interconnected brain regions more accurately modeling human disease. With this clinically relevant model of PD, we aim to further explore and understand mechanisms of how these co-pathologies enhance pathology, neuroinflammation, and neurodegeneration in PD.

O136

Talk 4: Co-pathologies and Parkinson's: What it all means to those living with PD?
*Soania Mathur**
UnshakeableMD, Ajax, ON, Canada

While certain proteinopathies or pathologic processes are associated with specific neurodegenerative diseases, and form disease-specific aggregates, different pathologies can coexist in various neurologic diagnoses. Much research is being done to determine the effect of co-pathologies, and understand what cascade of events and interactions may result in the manifestations of disease resulting perhaps in differing phenotypes. But what does this research mean to patients? How does understanding the impact of co-pathologies potentially change our understanding of Parkinson's disease? Will this research change clinical management of this disease? What should the patient community know? This talk will discuss the relevance of this science in lives oof patients with PD.

O137

Talk 1: Body-first and brain-first PD animal models mimic human PD subtypes
*Nathalie Van Den Berge**
Aarhus University, Aarhus N, Danmark, Denmark

In Parkinson's disease (PD), α-synuclein (α-syn) pathology can propagate along the brain-body axis affecting multiple organs. Patients display highly heterogeneous early disease phases, limiting accurate and early diagnosis. Increasing data suggests disease heterogeneity can be explained by variable disease initiation sites (body or brain) or by variable morphology of the dominant α-syn strain. Importantly, the cellular environment is known to impact strain characteristics. We hypothesize, for the first time, that both (1) disease initiation site and (2) α-syn strain morphology are interdependent determinants of the clinical and histopathological profile of PD subtypes.
Here, we aim to model body- or brain-first PD by injecting aggregated α-syn in the gut or amygdala of 14-month old wild-type rats, respectively. Characterization of both models is performed using immunostainings against α-syn pathology, [18F]PE2I (DaT) PET scans, ex vivo [123I]MIBG (cardiac) and [18F]FEOBV (enteric) tracer readouts and symptom scoring. Second, we aim to explore subtype-specific α-syn pathology in brain and several peripheral tissues. Characterization of α-syn strain differences is performed using several conformation-specific luminescent conjugated oligothiophenes (LCO).
Our body-first model mimics human body-first PD with symmetric α-syn pathology in the brain, ultimately leading to bilateral dopaminergic neurodegeneration (Fig. 1). Additionally, we observe cardiac and enteric denervation, and α-syn pathology in peripheral tissues. Our brain-first model appears to mimic brain-first human PD, with predominant unilateral pathology that evolves into predominant unilateral neurodegeneration. In the brain-first rodents, we did not observe cardiac denervation, similar to human brain-first PD. Our preliminary LCO-data indicate that (1) α-syn strains are region- and organ-specific, (2) α-syn strains are associated to disease initiation site, (3) the mix of observed α-syn strains is more variable in the brain-first compared to the body-first subtype.
Our two complementary animal models are the first direct attempt to recapitulate human PD subtypes, with a comprehensive approach including several PD features (old age, peripheral pathology etc.). This study provides compelling mechanistic insight into why PD is an asymmetric disorder in some patients, and symmetric in others. And early stratification, based on imaging biomarkers and detection of subtype-specific pathology in tissue biopsies, has potential applications in clinical trials and personalized treatment.

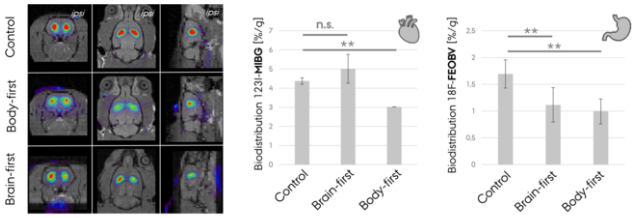


Figure 1. Imaging-based phenotyping of brain-first and body-first PD rodent model. Left: [18F]PE2I (DaT) PET scans were performed at 8-9 months in brain-first rodents, and at 5.5-6.5 months in gut-first rodents, as well as control rats. Brain-first rodents show predominantly unilateral decrease, whereas body-first show bilateral, symmetric decrease compared to controls. Right: ex vivo tracer experiment with [123I]MIBG shows 36% cardiac denervation in body-first rodents but no reduction in brain-first rodents. Ex vivo tracer experiment with [18F]FEOBV shows 35% and 42% enteric denervation in brain-first and body-first rodents, respectively (preliminary data).

O138

Talk 2: Bidirectionality: Gut-to-brain and brain-to-gut propagation of synucleinopathy

*Ayse Ulusoy**
German Center for Neurodegenerative Diseases, Bonn, NRW, Germany

The vagus nerve serves as a crucial pathway for communication between the brain and body. Its neuronal activity controls the function of various peripheral tissues and organs. Dysfunction or damage to the vagus nerve can result in a range of symptoms and conditions, including digestive problems, a common non-motor symptom of Parkinson's disease. In Parkinson's disease, alpha-synuclein accumulates not only in the brain but also in the gut. Interestingly, the pathology also is present in the vagus nerve. This suggests that the nerve may be involved in the development of Parkinson's disease by transferring alpha-synuclein pathology from the gut to the brain or vice versa. To investigate the role of the vagus nerve in transferring alpha-synuclein, we developed animal models of alpha-synuclein spreading using viral vectors to enhance alpha-synuclein expression in the vagal nuclei or the midbrain. Our studies have shown that alpha-synuclein can spread through the vagus nerve in a stereotypical pattern, reaching more frontal brain regions. Experiments also showed that this spreading involves transfer of alpha-synuclein from one neuron to another. Interestingly, this interneuronal spread of alpha-synuclein was bi-directional. We demonstrated that the vagus nerve, not only is involved in the caudo-rostral spreading, but also can take up alpha-synuclein from more frontal brain regions (i.e., midbrain) and transfer the protein to the stomach wall through preganglionic vagal projections. Given that the vagal nuclei are exposed to the external environment, they may be more susceptible to oxidative stress and accumulation of ROS. To test this hypothesis, we treated mice with paraquat, a ROS-generating agent, and observed that increased oxidative stress led to the formation of oxidatively modified forms of alpha-synuclein and enhanced spreading of the protein to more frontal brain regions. In addition, we used chemogenetic tools to increase neuronal activity in the vagal nuclei and found that this also led to increased oxidative stress, formation of oxidatively modified forms of alpha-synuclein, and enhanced spreading. Overall, our data suggest that the vagus nerve is a critical pathway for alpha-synuclein pathology spread and that increased oxidative stress, oxidatively modified forms of alpha-synuclein, and neuronal activity play significant roles in promoting the pathology and its spreading.

O139

Talk 3: The potential contributions of the gut microbiota to alpha-synuclein pathology in the gut and brain

*Timothy Sampson**
Emory University, School of Medicine, Atlanta, GA, United States

Persons with Parkinson's disease (PD) display significantly altered gut microbiome composition. Changes in the gut microbiome have been shown to alter pathological outcomes in PD mouse models, however, the mechanisms and specific bacterial taxa involved remain poorly understood. As the gut microbiome is intimately associated with metabolic and immunologic processes, we are working to understand whether PD-associated bacteria are capable of modifying accumulation of alpha-synuclein in the intestinal tract. Here, we have used gnotobiotic, humanized-synuclein mice, associated with distinct microbes, to dissect single organism contributions to intestinal pathology. Measurement of both synuclein accumulation and inflammatory responses allows us to identify organisms with the capacity to alter disease processes. We highlight the ability of individual microbial taxa to uniquely shape PD-relevant pathology and neuroinflammatory states. By pinpointing the specific effects of PD-associated microbes on intestinal and neuro-inflammation and synuclein accumulation, we hope to identify bacteria that may contribute to disease severity, progression, or etiology.

O140

Talk 1: Biological brain changes observed following exercise in Parkinson's: What do they tell us?

*Mark Hirsch**
Carolinas Rehabilitation, Charlotte, NC, United States

While it is now widely accepted that encouraging adoption of a healthy lifestyle (including promotion of physiotherapy, exercise and community-based physical activity) is a key nonpharmacologic treatment strategy to improve quality of life for individuals at all stages of Parkinson disease, the evidence of exercise-induced neuroplasticity in human PD is still in its early infancy. In this presentation I will discuss a emerging published evidence (last 10-15 years) on possible exercise-induced cortiocostriatal neuroplasticity in human Parkinson disease. Exercise-induced mechanisms in human PD CNS to be discussed will include treadmill-training-induced increase in maximal excitability of the corticomotor system (Fisher, 2008), increase in dopamine D2 receptor density within the dorsal striatum (Fisher, 2013), improvement in bilateral posterior putamen binding after ultra-marathon (Daviet, 2014), balance-training-induced changes in gray matter volume in basal ganglia circuitry (Sehm, 2014), exercise-induced increase in dopamine release in caudate and ventral striatal activation (Sacheli 2019), striatal dopamine transporter availability after physical activity or virtual rehabilitation (Shih, 2019; Toldo 2021), changes in connectivity (including connectivity of the putamen with the sensorymotor cortex) with higher-intensity bicycle exercise (van der Kolk, 2019; Segura, 2020; Johansson, 2022), and exercise-induced increase in brain-derived neurotrophic factor (Frazzitta, 2014; Zoladz, 2014; Marusiak, 2015; Angelucci, 2016; Sajatovic, 2017; Azevedo, 2022). Although the evidence of exercise-induced neuroplasticity in human PD is still scarce, this evidence will be presented in a participatory manner that is hoped to advance discoveries through hypothesis-driven collaborative research, in which people with Parkinson's disease are engaged in research as "partners" or "collaborators", rather than as "subjects" or "objects" of the research – a system we refer to as radical collaborative "participatory health care". It is hoped the presentation will generate conversations, new hypotheses and research

questions (with significant input to the intellectual content from the audience) to further elucidate the meaning of biological brain changes observed following exercise in Parkinson disease.

O141

Talk 2: Clinical trials: What is the evidence for the benefit of exercise in PD?
*Erwin van Wegen**
Amsterdam University Medical Center, Amsterdam, Netherlands

By now, exercise is considered effective in improving motor symptoms in Parkinson's disease (PD). Whether therapeutic exercise is able to delay or stop disease progression or definitively improve non-motor consequences of PD is still a matter of debate. In this presentation we highlight some key studies and give an overview of evidence based information yielded from randomized controlled trials regarding benefits exercise and PD symptoms. We will review the methodology used in the RCTs, the results of the trials, and the implications of the findings. Specifically, we will explore how exercise has been shown to improve motor and non-motor function and quality of life in Parkinson patients. The lecture will conclude with a discussion of the implications of the findings for the development of best practices for treating Parkinson disease, transitioning to the third lecture in this series.

O142

Talk 3: How can we design better exercise trials in PD?
*Daniel Corcos**
Northwestern University, River Forest, Illinois, United States

It is axiomatic that exercise is medicine. This presentation will focus 12 issues and questions that should help the design of future exercise trials. First, it is crucial to involve people with PD in the front end of the design of some types of research studies – participatory action research in which people with PD are true partners. Second, we need to rethink control groups and consider testing findings directly against clinically important differences. Third, we need to distinguish studies that are designed to take advantage of neuroplasticity and potentially target disease modification from those which are designed for symptom reduction. We need to develop agreed upon paradigms for disease modification studies. Fourth, we need to understand the acute effects of exercise as well and the chronic effects of exercise and how best to take medication in the context of exercise. Fifth, we need to determine the minimal exercise prescription that delivers positive results. Sixth, what are the mechanisms exercise affects and does this inform the optimal time spent in exercising. Seventh, how can we increase the sustainability and durability of exercise interventions? Will people do what exercise trials suggest once the support and external motivation for taking part in the study are removed? What strategies can be developed to improve adherence to the exercise prescription? Trials of the future should explicitly test for sustainability and have long term follow-up time periods. Eighth, what are the best outcomes to assess and what are the best exercise interventions for different outcomes? Ninth, what is the best exercise progression to help people as the disease progresses? Tenth, can we generalize results from one exercise modality to another? Eleventh, what is the impact of chronotropic insufficiency on exercise capacity? Ten percent or more of people with PD cannot achieve age predicted maximal heart rate. Does this affect how their signs and symptoms respond to exercise? Twelfth, how can we increase the diversity of people recruited to exercise studies in PD?

O143

Talk 1: Aging well with Parkinson
*Alison Yarnall**
Newcastle University, Newcastle upon Tyne, United Kingdom

Age is the biggest risk factor for developing Parkinson's disease, and age also influences progression. People who develop Parkinson's later in life may experience different symptoms from those with a younger onset. The prevalence of Parkinson's disease and thus the associated non-motor symptoms will increase in future years due to secular trends in the age-structure of populations, both UK and worldwide. Rising age in the general population often equates to an increase in co-morbidities and associated polypharmacy. Other important age-associated conditions include sarcopenia, the progressive loss of muscle mass and strength, and osteoporosis, where reduction in bone mineral density and bone mass may be seen.
This talk will therefore cover some conditions and overlap in conditions that may occur in older adults with Parkinson's. Differences between young onset Parkinson's and how ageing-associated diseases that can affect mobility and movement will be reported. How to age well in Parkinson's including multidisciplinary, personalised care will be covered. A clinical perspective on identification, management and treatment of specific age-associated features will be highlighted.

O144

Talk 2: Cognitive impairment and dementia
*Greg Pontone**
Johns Hopkins University School of Medicine, Baltimore, MD, United States

Parkinson's disease (PD) often progresses to include cognitive impairment. The cognitive impairment associated with PD can range from mild (e.g., limited to one or two types of cognitive function without much impact on day to day function) to severe (e.g., global impairment with an inability to function independently). This talk will review how to identify cognitive changes associated with PD compared to other disease processes and normal aging. Brain changes associated with cognitive impairment in PD will be described to facilitate an understanding of the goals and limitations of currently available treatments. Finally, we will explain the best-evidence lifestyle choices and strategies to limit the impact of cognitive changes on daily function and quality of life in people living with PD.

O145

Talk 1: Mitochondrial abnormalities underlying PD – What's on the horizon?
*Edward A. Fon**
Montreal Neurological Institute, McGill University, Montreal, Quebec, Canada

Parkinson's disease (PD) is a common, devastating neurodegenerative disorder that affects over 8 million people worldwide and the numbers will only grow as the population ages. PD involves the death of dopamine neurons in the midbrain as well as other cells in the brain, which leads to devastating motor, non-motor and functional impairment. Although treatment is available, its effectiveness diminishes over the long term. Both environmental and genetic studies strongly implicate mitochondrial dysfunction in PD. My laboratory has a longstanding interest in understanding the role of mitochondria in PD and in understanding how PINK1 and

Parkin, two recessive PD genes, function in a common pathway regulating mitochondrial quality-control. Despite the many advances in our understanding of Parkin and PINK1 function, much work remains in order to decipher their precise role in mitochondrial biology and disease. In this workshop talk, we will discuss how PINK1/Parkin regulate mitochondrial autophagy (mitophagy) and how other PD genes affect mitochondria. We will also discuss the structural basis of parkin/PINK1 activation by mitochondrial damage and how Parkin variants found in the population and in patients with PD can help rationalize the function of Parkin in mitochondrial quality control and better guide the design of future therapies.

O146

Talk 2: Lysosomal abnormalities underlying PD – From bench to bedside

*Roy Alcalay**
Tel Aviv Sourasky Medical Center, TEL AVIV, Israel

The underlying mechanism of Parkinson's disease (PD) is still unknown. Much of our knowledge of potential causes of PD is derived from neuropathological studies (autopsies) and from genetic data. In most PD autopsies, there are aggregates of the protein alpha synuclein (a-syn) in Lewy bodies. Indeed, genetic studies also point to a-syn as an important contributor to PD pathogenesis, given that mutations in the gene SNCA that encodes a-syn are associated with PD.
A-syn is degraded in the lysosome, the recycling bin of the cells. In 2004, the link between a lysosomal enzyme glucocerebrosidase (GBA1) and PD was discovered. In fact, variants in GBA1 are amongst the most common genetic risk factors of PD, and homozygous mutations in the gene cause a lysosomal storage disorder, Gaucher disease. Ever since the link between GBA1 and PD was discovered, research on the role of the lysosome in PD has gained traction. Mutations in additional lysosomal storage disorder genes have since been associated with PD (e.g. ASAH1, GALC, SMPD1). In addition, the link between PD and the LRRK2 gene, which is a common cause of dominantly inherited PD may be explained by its role in the lysosome or the endolysosomal pathway. Therefore, the lysosome has become a drug target for novel intervention to slow down or prevent PD. The underlying hypothesis of targeting the lysosome is that the degradation of a-syn is impaired in PD because of lysosomal dysfunction and that improving the capability of the lysosome to recycle a-syn would slow down the pathological process of a-syn aggregation. There are multiple potential drug targets in the lysosome. Intuitive drug targets in the lysosome are enzymes that have been genetically linked to PD, specifically GBA and LRRK2. Other potential drug targets include lysosomal channels, such as the TRP channel subfamily (TRPML1), which its activation may help enhance a-syn degradation. In summary, genetic data point to the lysosome and the endolysosomal pathway as key players in the pathogenesis of PD. We are hopeful that this insight will lead to novel interventions that may slow down or prevent PD.

O147

Talk 3: Mitochondria-lysosome contact site dynamics in disease

*Yvette Wong**
Northwestern University Feinberg School of Medicine, Chicago, IL, United States

Mitochondria and lysosomes are key organelles for regulating neuronal function and homeostasis, and have both been genetically and functionally implicated in the pathogenesis of Parkinson's disease. We have found that these two organelles directly interact with one another at inter-organelle membrane contact sites known as mitochondria-lysosome contacts, allowing for their bidirectional crosstalk. These contact sites allow for mitochondrial regulation of lysosomal network dynamics, and conversely for lysosomal regulation of mitochondrial dynamics networks including mitochondrial fission events and inter-mitochondrial untethering events. Using advanced high spatial and temporal resolution live microscopy, we have further shown that mitochondria-lysosome contact dynamics and function are further misregulated in multiple neurodegenerative diseases, including genetic models of Parkinson's disease, which contribute to downstream defects in mitochondrial and lysosomal networks. Together, these studies highlight a major role for mitochondria-lysosome contact sites in contributing to the etiology of neurological disorders including Parkinson's disease.

O148

Talk 1: Infection and risk of Parkinson's disease

*Elena Kozina**
Thomas Jefferson University, Philadelphia, PA, United States

A growing body of evidence from both clinical and preclinical studies suggests that Parkinson's disease (PD) arises from a multifactorial etiology that includes exposures to pesticides, herbicides, and infectious agents that interact with an underlying genetic predisposition. Given that these environmental agents first enter the body (versus brain), it is critical to examine the role of peripheral immune signaling as a contributor to the development of PD. In relation to viral infections, neurotropic viruses (H5N1, West Nile and WEEV) have the ability to infect cells in the CNS regions affected in PD. However, most viral infections do not appear to have this ability including H1N1, RSV and SARS-CoV-2. In addition to viruses, bacterial infections have also been shown to act as peripheral triggers of neuron loss in the susceptible individuals. Recent preclinical studies from our lab showed that the pandemic 2009 H1N1 and 2019 SARS-CoV-2 (alpha variant) viruses induce a significant and persistent DA cell loss and neuroinflammatory response in the SN of mice carrying the G2019S LRRK2 mutation with no phenotype observed in the infected wt controls. We have also demonstrated that the peripheral immune dysfunction, induced by viral and bacterial infections, in LRRK2-mediated PD may have been the initiating site of signals, and thus the cause, of the CNS related pathologies. Using chimeric mouse models, we found that the replacement of peripheral T- and B-cells carrying LRRK2 mutations with wt cells diminished LPS-mediated neuroinflammation which resulted in the absence of the DA neuron loss in the, still, genetically mutant brain. Conversely, the presence of LRRK2 mutations in lymphocytes alone (all cells in the brain are wt) is sufficient to induce LPS-mediated neuronal loss. Remarkably, we observed that LPS-induced DA cell loss was not associated with the recruitment of peripheral immune cells into the brain's parenchyma suggesting that circulating factors from the dysregulated immune cells were responsible for the immune activation and neuron loss in the brain. Overall, our studies indicate that the PD-associated DA neuron death can be regulated by underlying immune signaling solely arising from the activated peripheral immune system, which may provide new targets for therapeutic intervention.

O149

Talk 2: Infections and associated medical complications on neuropsychological function in Parkinson's disease
*Catherine Price**
University of Florida, Gainesville, FL, United States

This session will review cognitive and brain-behavioral profiles of Parkinson's disease (PD), and how viral infections (e.g., SARS-CoV-2) with and without associated complications may alter the trajectory of PD cognitive function over time. We will begin by summarizing the known neuropsychological domains of change with Parkinson's disease, and then present biological system pathways of change with common viral diseases as well as SARS-CoV-2. This will lead to a discussion on the role of viral-induced inflammation on brain-behavior systems and associated cognitive systems. The session will additionally summarize complications of viral infections that can also alter the neuropsychology of PD (including sepsis, medical interventions requiring anesthesia, and delirium). At the end of the talk, audience members will be able to: 1) explain how systemic infections can exacerbate cognitive and behavioral problems in Parkinson's disease; 2) elaborate on the impact of community-wide infections on PD; and 3) lise additional complications of viral infections and how they may alter the neuropsychological trajectory of PD.

O150

Talk 3: COVID-19 and Parkinson's disease
*Alfonso Fasano**
Toronto Western Hospital - UHN, Toronto, Ontario, Canada

The rapidity with which coronavirus disease 2019 (COVID-19) has swept across the globe has favored the proliferation of studies which lack scientific rigor and the literature on Parkinson's disease (PD) has not been immune. As a result, studies focusing on the relationship between severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), COVID-19 and PD have provided conflicting results.
This lecture will answer 6 questions based on the available evidence: 1) Are PD patients at higher risk for contracting COVID-19 and are there specific contributing factors to that risk? 2) How does COVID-19 affect PD symptoms? 3) How does COVID-19 present in PD patients? 4) What are the outcomes in PD patients who contract COVID-19? 5) What is the impact of COVID-19 on PD care? 6) Does COVID-19 increase the risk of developing PD?
It does not appear that PD is a specific risk factor for COVID-19. On the other hand, there is increasing evidence for the many direct and indirect negative effects of this pandemic on the motor and non-motor symptoms of PD. Although many PD patients present with typical COVID-19 symptoms, some present atypically with isolated worsening of parkinsonian symptoms, requiring increased anti-PD therapy and having worse outcomes. Mortality data on PD patients with COVID-19 has been quite inconclusive (ranging from 5.2% to 100%) but newer data are now available. Single cases of acute hypokinetic-rigid syndrome have been described but no other convincing data has been reported. The critical analysis of these cases seems to suggest that in some cases a true parkinsonism wasn't present (e.g. in case of encephalitis with reversible akinetic mutism), in other cases parkinsonism wasn't typical (e.g. it lacked levodopa-responsiveness) and resulted from vascular lesions. The majority of these 'new-onset' PD cases were subclinical PD with a faster progression after the infection.
In conclusion, while there's no convincing reason to be overly worried, a coordinated effort is required to assimilate data and answer these questions in larger PD cohorts.

O151

Talk 1: Better communication: Let us get started
*Angela Christine Roberts**
Western University, London, ON, Canada

It has been said that conversations are central to family life. Communication challenges and family system shifts in the face of cognitive changes can negatively impact quality of life for persons with Parkinson disease, their care partners, and families. Dr. Roberts will overview the nature of communication changes in Parkinson disease and their impact on family systems and care. Special emphasis will be placed on how better communication can support care goals, maintain independence, reduce caregiving burdens, and promote quality of life.

O152

Talk 2: A patient-centered approach to care
*Neil Archibald**
South Tees Hospitals NHS Foundation Trust, Middlesbrough, United Kingdom

Patient-centered care is often quoted as the aim of medical services but seems less clear how this is achieved or the benefits that this brings. In this session, we take a look at different models of care in Parkinson's and how they might be developed to improve patient and carer engagement and outcomes. I will be drawing from my experience as an NHS Parkinson's consultant and the son of a Parkinson's patient. I am not a clinical academic so expect this session to be based on the ups and downs of working in a busy Parkinson's service in the UK. We will discuss where the service started, how it has developed over the last 10 years and where it might be headed in the next 10.

O153

Talk 3: Communicating within the scientific and research systems

*Walter Maetzler**
Kiel University and University Hospital Schleswig-Holstein, Campus Kiel, Kiel, Germany

Many people living with PD are interested in improving the understanding and treatment options for the disease by participating in research projects. The successes of this commitment, together with scientists and people working in therapy development, can be seen in the large number of excellent publications on the understanding of PD and in the therapy options for the disease that have advanced in recent decades. They are remarkable. This talk will deal with essential aspects that seem to me to be necessary for further successful scientific development in PD: It will inform about the designs of studies for a better understanding of PD and clinical trials that are common today, and touch on new developments on the scientific horizon. Then the latest developments in Patient and Public Involvement and Engagement (PPIE) in scientific projects will be presented. This is a relatively new concept based on the belief that involvement of patients in any scientific project from the outset delivers benefits in the design and conduction of relevant research. Tools for effective implementation of PPIE will be demonstrated with the help of practical examples.

O154

Table 1: Freezing, falling and postural decline: What can be done?

*Anat Mirelman**
Israel

The purpose of the roundtable is to discuss issues that heavily impact patient's daily living and quality of life namely freezing of gait, falls and postural instability. The prevalence rates of freezing of gait (FOG) in Parkinson's disease (PD) vary widely, ranging from 14.0 to 55.1%, while postural instability and falls are even more common among patients with moderate to advance PD. Prospective studies show that between 45% and 68% of people with PD will fall each year, with a large proportion (50–86%) falling recurrently, representing a significant cause of disability and loss of independence. Information on the causes of these phenomena's will be provided while the discussion will focus on available treatments and effective strategies for prevention. The roundtable will be interactive, welcoming input from participants.

O155

Table 3: The role of breathing exercises in managing Parkinson's

*Michelle Troche**
Teachers College, Columbia University, New York, NY, United States

Swallowing and cough are life sustaining functions which are overlaid on the respiratory system and that often become impaired with Parkinson's disease. There is research to support several approaches to rehabilitating/improving swallowing and cough function in people with PD. Most of these, involve 'exercising' our breathing muscles or modifying the way we breathe to improve the effectiveness and safety of swallowing and cough. Some examples include: respiratory-swallow training, expiratory muscle strength training, and cough skill training. We will briefly discus the research to support these treatment approaches and will discuss how they can be integrated into daily practice to improve health and quality of life.

O156

Table 4: Subcutaneous L-dopa infusion vs other device-aided therapies – Who shall have what?

*Per Odin**
Lund University, Lund, Skane, Sweden

Advanced Parkinson therapy has so far included subcutaneous treatment with apomorphine with portable pumps, intestinal infusion of Levodopa-carbidopa gel and Deep Brain stimulation. The individual choice between these therapies has been based on indications and contraindications for the therapies, effects of the therapies against motor and non-motor symptoms, side effects and complications, as well as preferences of the patient and the caregiver. During 2023 a further option will reach the market in many countries - subcutaneous infusion of L-dopa with portable pumps. Results from the clinical studies performed have recently been published and demonstrate effects, side effects and complications of this therapeutic option, thus also its advantages and disadvantages relative the other forms of advanced therapy. During this round table session we will shortly summarize the results of clinical studies with subcutaneous L-dopa infusion and discuss how this treatment shall be positioned in the advanced treatment selection process.

O157

Table 5: Alpha-synuclein strain competition

*Amanda Woerman**
University of Massachusetts Amherst, Amehrst, MA, United States

In a subset of patients with Lewy body disease, the presence of glial inclusions as a co-pathology is largely ignored. However, in some of these patients, this represents the presence of both Lewy body disease and multiple system atrophy, a related but distinct neurodegenerative disease. My lab is interested in understanding how the presence of two pathogenic alpha-synuclein strains, or diseases, in the same patient modify or alter the clinical presentation of disease. We are also interested in understanding what this means for patients when successful therapeutics are identified. To address these questions, we are currently investigating the role of alpha-synuclein strain competition in an animal model of synucleinopathy.

O158

Table 6: Speak your truth

*Miet De Letter**
Ghent University, Ghent, Belgium

This round table highlights 9 truths and/or misconceptions related to communication in Parkinson's disease. Using a series of statements, the session interactively seeks evidence-based answers to questions about speech and language changes and effects of medical and speech therapies on speech and language in individuals with Parkinson's disease. After this session the participant will have acquired knowledge about 1.the diversity in speech profiles in Parkinson's disease and parkinsonism syndromes, 2. the interaction between speech perception and production in persons with Parkinson's disease, 3. the effects of

Parkinson's disease on auditory function, 4. the impact of deep brain stimulation and levodopa on speech and language, 5. the diversity in speech therapy strategies 6. how therapy effects can be transferred to daily communicative situations 7. the difference in the pragmatic language use of parkinson's disease patients in their daily communication with professional caregivers versus family, 8. the interaction of cognition, motor skills and communication in Parkinson's disease and 9. the added value of interprofessional collaboration in speech therapy rehabilitation.
This round table will stress the importance of speech therapy within an interprofessional context. This lecture fits perfectly with the lecture 'Speak your truth' or the session 'take a deep breath' in which the importance of breathing training for communication and consequently for quality of life will be discussed.

O159

Table 7: Prodromal Parkinson's: Ready for clinical trials?
*Lana Chahine**
University of Pittsburgh, Pittsburgh, PA, United States

Because the biological changes leading to Parkinson's disease (PD) begins years before the disease is diagnosed, it is a prime candidate for early detection and intervention. The PD prodrome—the period of time when there is underlying pathology that has not yet fully manifested—is marked by several symptoms, signs, and biomarker changes. With increasingly precise methods with which to identify individuals who are at risk for developing PD comes the opportunity to conduct clinical trials to test interventions to prevent or delay progression in this group. In this roundtable session, key questions related to preparing for clinical trials in prodromal populations will be discussed: Who? What? How? and When? Who will constitute the samples in the first clinical trials; what profile of prodromal features and biomarkers will define the inclusion criteria? What interventions should be tested? How, with what outcome measures, will we measure the effect of the intervention? When will the data and infrastructure be ready for the first trials to prevent or delay progression in individuals at-risk for PD?

O160

Table 8: Screening for PD risk – Are we ready for population-based approaches?
*Alistair Noyce**
Queen Mary University of London, London, United Kingdom

There are differing strategies to identify individuals at risk of or in the earliest phases of Parkinson's disease, who may benefit most from disease-modifying clinical trials. Strategies include identifying individuals that carry a single disease-causing gene mutation, a combination of genetic risk factors, individuals with a single strong clinical risk factor (such as REM sleep behaviour disorder or idiopathic anosmia), or individuals identified through algorithms such as the MDS criteria for prodromal Parkinson's and the PREDICT-PD algorithm.
In this second talk of the session, I will briefly recapitulate concepts from the first talk. I will move on to discuss screening as a concept in preventive medicine and reflect on the requirements that screening programs must meet. I will cover the different potential options for screening, with an emphasis on population-based approaches. I will reflect on how far algorithms can take us in terms of stratification and what additional proximity markers and/or biomarkers maybe needed. I will consider some of the ethical arguments for and against screening, as well as the implications of risk disclosure to individuals.

O161

Table 9: LRRK2 and Parkinson's
*Matthew LaVoie**
University of Florida, Gainesville, FL, United States

Contemporary questions in the LRRK2 field surround what are the similarities and differences in the biochemical features of the various pathogenic mutations? In what cell types mutant LRRK2 fosters disease? Do changes in WT LRRK2 kinase activity have a role in sporadic disease? Certainly there are other topics welcomed. We hope to foster a lively discussion!

O162

Table 10: The state of genetics in Parkinson's
*Andrew Singleton**
NIH, Bethesda, MD, United States

There has been considerable progress in our understanding of the genetic basis of Parkinson's disease. This roundtable will center on discussing why genetics is critical for understanding and treating disease, how far we have come, and where the field is going. The participants will take part in a discussion that will include these topics in addition to issues such as penetrance, complex genetic risk, the importance of diversity in genetic investigation, and the now- and next- generation methods that are being applied.

O163

Table 11: Genetic testing in PD – What is currently possible?
*Christine Klein**
University of Luebeck, Lübeck, Germany

A monogenic cause or strong genetic factor predisposing to Parkinson's disease (PD) can be detected in ~15% of all patients and can unequivocally establish a diagnosis of (genetic) PD. Confirmed forms of monogenic PD resembling idiopathic PD clinically include four dominantly (SNCA-PD, LRRK2-PD, VPS35-PD, and CHCHD2-PD) and three recessively inherited forms (PRKN-PD, PINK1-PD, DJ1-PD). Detailed genotype and phenotype information on these conditions is available at https://www.mdsgene.org. Pathogenic variants in GBA are the strongest known genetic risk factor for PD and are sometimes viewed as acting in a dominant fashion with highly reduced penetrance. Genetic testing is currently the only possible means to identify unaffected carriers of pathogenic variants in PD genes who are at (high) risk of developing PD in the future.
There are no established international guidelines for clinical diagnostic testing for PD; however, most available recommendations agree that a genetic test may be considered in patients with early-onset PD, a positive family history, or individuals with a specific ethnic background where specific pathogenic variants are common due to a founder effect (for example, the p.G2019S variant in LRRK2 in patients of Ashkenazi Jewish or North African Berber descent).
Availability and type of genetic testing vary widely internationally and range from full coverage through the health care system to no reimbursement at all. Likewise, there is a broad spectrum of different means of genetic testing including hot-spot or singe-gene sequencing, gene panels, exomes, and genomes, with panel sequencing currently being the most widespread approach in clinical diagnostics. Of further note, clinically relevant genetic testing results can be obtained in a research context (where they are sometimes limited to the custom content of arrays otherwise designed for genome-wide association studies) or within the framework of direct-

to-consumer genetic testing. Challenges arise from variable technical quality - especially when it comes to calling pathogenic variants in GBA -, the occurrence of variants of unknown significance, the overall scarcity of genetic counseling opportunities, and economic constraints. A future perspective may be gene-targeted treatments for specific forms of monogenic PD, the first clinical trials for which are currently underway requiring the identification and stratification of suitable study participants.

O164

Table 12: Dysautonomia: What is it and how is it related to Parkinson's?
*Patricio Millar Vernetti**
New York University Grossman School of Medicine, New York City, New York, United States

The autonomic nervous system (ANS) is a part of the nervous system that automatically manages functions we cannot control voluntarily such as sweating, digestion, blood pressure, and micturition. Different functions of the ANS may be affected at different times during the course of Parkinson's, from pre-motor to more advanced stages.

O165

Table 13: Depression, apathy & PD: What do we know and what can we do about these symptoms?
*Iracema Leroi**
School of Medicine and Global Brain Health Institute, Trinity College Dublin, Dublin, Ireland

In Parkinson's, mental health symptoms such as apathy and depression are common and may impact significantly on quality of life, motor function and prognosis in people living with Parkinson's. People with Parkinson's often report depression as the most distressing aspect of their condition. At any given time, up to 40% of people with Parkinson's will have significant symptoms of depression and/or anxiety. Apathy may be present in up to 70%. Apathy and depression are both associated with cognitive decline in Parkinson's; apathy may be a behavioural marker of the onset of dementia in Parkinson's. Moreover, the impact of apathy and depression in Parkinson's can negatively impact care partner outcomes.
Apathy and depression may frequently overlap and are also often under-recognised in clinical settings and thus under-treated. Difficulties with diagnosis may be compounded by a lack of guidance for health professionals. This presentation will provide a background to these neuropsychiatric syndromes in Parkinson's and provide practical approaches to assessment and management, with a person-centred and pragmatic focus.

O166

Table 14: Synaptic function of alpha-synuclein
*Dragomir Milovanovic**
Laboratory of Molecular Neuroscience, German Center for Neurodegenerative Diseases (DZNE), Berlin, Berlin, Germany

Synucleinopathies encompass a family of neurodegenerative diseases, among which the most notable is Parkinson's Disease. The hallmark of these disorders is the misfolding and aggregation of alpha-synuclein, one of the central proteins for the regulation of neurotransmission. Neuronal communication depends on the tightly regulated spatial and temporal release of the messenger molecules known as neurotransmitters. Neurotransmitters are packed into synaptic vesicles (SVs). Functionally, alpha-synuclein is a presynaptic protein responsible for the SV cycle and neurotransmitter release. In pathology, alpha-synuclein forms insoluble fibrils that can mature into intracellular inclusions able to capture numerous cytosolic proteins and intracellular organelles. At this roundtable, we will discuss several emerging roles of alpha-synuclein function at synaptic boutons, such as its ability to modulate the condensates of SVs. Namely, hundreds of SVs form biomolecular condensates through the interaction with synapsins, the highly abundant family of synaptic phosphoproteins and alpha-synuclein. In our discussion, I will focus on the importance of the local protein concentration, protein binding to membrane, and protein-protein interactions of alpha-synuclein, and how the failure of these roles leads to the onset of cellular pathology present in Parkinson's Disease.

O167

Talk 1: Synaptic function of alpha-synuclein
*Dragomir Milovanovic**
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O168

Talk 2: The role of α-synuclein in the nucleus
*Vivek Unni**
United States

Although pathologic aggregation of the protein α-synuclein (α-syn) is tightly associated with Parkinson's Disease (PD), Multiple System Atrophy and Dementia with Lewy Bodies, we still do not have a clear understanding of what role this protein plays in disease pathogenesis. Multiple different biochemical and cellular pathways can be regulated by α-syn and have been implicated in neurodegeneration, but the most well-established normal function for α-syn is in the regulation of neurotransmitter release from vesicles in the presynaptic nerve terminal. In addition to this synaptic localization and function, it was noticed from its discovery that α-syn is also present in the cell nucleus (the name synuclein being a contraction of "synapse" and "nucleus"). Although its synaptic function has been extensively studied, much less is known

about possible functions within the nucleus. Even whether its localization there is real or not has been a matter of controversy at times. Recent work from multiple labs has now documented its presence within the nucleus using a variety of approaches, strongly suggesting a real nuclear localization and function in this cellular subcompartment. Multiple normal and abnormal functions for α-syn within the cell nucleus are being studied, including direct DNA binding, induction of DNA strand breaks, regulation of histones, helicases, transcription, mRNA processing and stability, and DNA repair. In addition, α-syn has recently been added to the list of nuclear proteins that can undergo liquid-liquid phase separation (LLPS) under certain circumstances. LLPS is thought to be important for creating specific microdomains within a cell to limit biochemical reactions to specific points in time and space without the need of biological membranes and is potentially critical for many nuclear and non-nuclear processes. Dysregulation of LLPS is also hypothesized to play roles in protein aggregation associated with many neurodegenerative diseases. I will present an overview of this emerging field of nuclear α-syn biology and propose how it could contribute to neurodegeneration in PD and related disorders.

O169

Talk 3: The role of the synuclein in the mitochondria
*Gabriele Kaminski**
University of Cambridge, Cambridge, United Kingdom

The relationship between α-synuclein and Parkinson's disease (PD) has been extensively studied, particularly regarding its potential impact on mitochondrial function. While the link between PD and mitochondrial dysfunction is well-established, the specific role of α-synuclein in this process is still not fully understood. Research has suggested that α-synuclein may play a role in regulating neuronal mitochondrial dynamics, including processes such as fusion-fission, transport, and clearance. However, it is currently unclear if α-synuclein is a primary cause or a result of mitochondrial dysfunction. In my talk, I will provide an overview of the structural, biophysical, and biochemical properties of α-synuclein and how they may influence relevant mitochondrial processes. Additionally, I will discuss the current state of research on the topic, highlighting areas that need further investigation.

O170

Talk 1: Evolution of phenotypic PD subtypes during the premotor and motor stage
*Connie Marras**
University Health Network, University of Toronto, Toronto, ON, Canada

This presentation will describe the heterogeneity of PD from the clinical/ symptom perspective in the premotor and motor stages, and the evolution of symptoms along the course of the disease. The evidence for PD subtypes explaining this heterogeneity will be examined. Previously described PD subtyping systems will be described and contrasted. Four uses of subtyping will be explored, including predicting evolution of symptoms and outcomes, understanding pathophysiology, clinical trial design and guiding treatment decisions. For each of these the state of the field will be examined and the steps described to move the field forward toward precision medicine in PD will be proposed.

O171

Talk 2: Evolution of genetic PD subtypes during the premotor and motor stage
*Susanne Schneider**
Germany

Various genetic subtypes of PD have been delineated. Recognizing their characteristics may be crucial for the development of precision medicine. Indeed, the genetic forms vary with regards to their mode of inheritance, penetrance, the clinical presentation (including the mean age at onset, key symptoms and the clinical course, i.e. disease progression) and treatment response. Similarly, differences in PD pathology (e.g. a-synuclein burden) and imaging patterns have been recognized. Further complicating, even for the same gene different variants may be associated with heterogeneous presentations. To provide an overview, the evolution of genetic PD subtypes during the premotor and motor stage will be reviewed in this talk.

O172

Talk 3: Tailored treatment and prevention of different PD subtypes
*Alberto Espay**
University of Cincinnati, Cincinnati, Ohio, United States

The living cognitive dissonance in the field of Parkinson's disease is that while we recognize that no two patients are alike, we also accept that a common biomarker in most of those affected must be sufficiently relevant as a "target of therapy" to slow disease progression in everyone. This clinicopathologic model of Parkinson's disease has been convergent: Lewy pathology (and any secondary metabolic, inflammatory, apoptotic, or proteolytic dysfunction such aggregated proteins are reported to engender) is presumed to drive both symptoms and neuronal loss in all patients affected. In other fields of medicine, Precision Medicine has required shifting from lumping to splitting. Disease-modifying treatments have succeeded first in a very small subset of patients, whose molecular/biological abnormalities were corrected with targeted molecular/biological interventions. In laying the foundation for a Precision Medicine future in the approach to Parkinson's, the matching between the biological type of patient and the mechanism of the putative neuroprotective intervention cannot be considered equivalent to any other trial-improvement strategy. A "perfect trial" (e.g., better designs, more sensitive endpoints, earlier patient populations) cannot overcome a fundamental mismatch between the main molecular mechanism of the intervention tested (e.g., specific mitochondrial enhancement) and the main molecular pathophysiology of the population targeted (e.g., specific mitochondrial dysfunction). Only after treatments are demonstrated to be effective in the disease state can they be used to prevent such types of disease in those with the same molecular/biological risk. To this end, future biomarker development programs should aim toward identifying biomarkers of divergence, that is, present in some but absent in most –to distinguish one subtype of Parkinson's disease or prodrome with specific therapeutic relevance from all others, regardless of the clinical manifestations. From such a clinically agnostic study of aging, patients with well-defined molecular subtypes may be enrolled into N-of-1 or adaptive clinical trials. This is an expensive and labor-intensive but transformational effort that will require a cultural change and substantial investment and synergy from foundations, industry, and governments.

O173

Talk 1: Mobility challenges in PD: Causes and connections
*Kaylena Ehgoetz Martens**
University of Waterloo, Waterloo, ON, Canada

Several mobility problems are associated with Parkinson's disease (PD) that include gait and balance impairments. Freezing of gait (FOG) is a severe gait disturbance that is commonly experienced by people living with Parkinson's disease, and has a significant impact on falls, independence and quality of life. Freezing of gait can be defined as a sudden inability to move the feet forward despite the intention to walk. It is complex, yet debilitating, and remains difficult to treat due in large part to its heterogeneous nature. Freezing of gait can vary in presentation ranging from severe shuffling to trembling to complete akinesia. It can also vary in responsiveness to medication, as well as there are a variety of contextual triggers which provoke FOG. The highly variable nature of this phenomenon makes it challenging to study in both clinical and research settings, and as a result, our understanding of its mechanistic causes remain incomplete. While culminating evidence suggests that freezing is multi-faceted and influenced by a variety of impairments across cognitive, motor and affective domains, further research is needed to characterize and understand the heterogeneity related to FOG in order to develop novel and effective therapeutic interventions.

O174

Talk 2: Freezing: Assessment, early detection and rehabilitation options
*Nicholas D'Cruz**
KU Leuven, Leuven, Belgium

Freezing of gait (FOG) is a complex and disabling mobility impairment in Parkinson's disease (PD). Due to its paroxysmal nature, FOG contributes to about 60% of falls in people with PD. Besides its direct impact on mobility, FOG also impacts non-mobility-related aspects of quality of life. Interventions that aim to reduce FOG severity or delay its onset are therefore of critical importance.
Part of the complexity of FOG is that its onset signifies a milestone where multiple brain systems become involved in the disease expression. As such, restoring mobility after this point becomes more challenging, with several studies showing that motor (re)learning potential is lower in freezers as compared to non-freezers. Therefore, to improve the impact of therapy on FOG, early detection of risk and delivery of intervention is required. In this presentation, we will look at the known clinical and imaging risk factors for developing FOG, and discuss their utility for screening FOG risk.
Another aspect of complexity is that the presence of FOG is difficult to assess, and this impacts the ability to correctly detect its onset. For example, in an ongoing multicenter study, almost 30% of the participants who were self-described non-freezers showed FOG during a sensitive FOG-provoking task. Challenges in assessing the severity of FOG also impact the ability to accurately measure treatment effects. To address this, much recent work aims to improve the objective measurement of FOG in the lab and at home, both under supervision, and using unsupervised methods. We will discuss these advances and their usability in research as well as in clinical scenarios.
Finally, we will briefly cover the latest rehabilitation strategies for FOG, and present the best evidence-based therapeutic framework to tackle FOG at different stages of the disease.

O175

Talk 3: Treatments for gross mobility challenges: Medication, technology and rehabilitation
*Alfonso Fasano**
Toronto Western Hospital - UHN, Toronto, Ontario, Canada

Axial motor signs—including gait impairment, postural instability and postural abnormalities—are common and debilitating symptoms in people with Parkinson disease (PD). Falls in particular are a major determinant of poor quality of life, immobilization, and reduced life expectancy. Dopamine replacement therapy provides variable effects but in advanced stages the effect is, at best, partial. Likewise, deep brain stimulation (DBS) of the subthalamic nucleus or globus pallidus internus is an established treatment for 'appendicular' motor signs (limb tremor, bradykinesia and rigidity). However, the effects of DBS on axial signs are much more variable.
We will discuss the effect of L-dopa and non-dopaminergic drugs as well as the successes and failures of DBS in managing axial motor signs. We will also address the possible merits of new DBS targets — including the pedunculopontine nucleus area and substantia nigra pars reticulata — to specifically alleviate axial symptoms as well as new neuromodulation techniques such as spinal cord stimulation.
Regular exercise and rehabilitation remain the most important – and safest – strategies to alleviate these problems. However, the identification of individual factors and how to implement these treatments from a practical standpoint needs a reappraisal, also depending on the specific healthcare systems. Two novel aspects will be discussed in this regard: compensatory strategies and split-belt treadmill training (SBTM). As for the former, compensation may inspire strategy that best matches the needs and preferences of the subjects suffering from axial problems. As for the latter, several studies have shown that the irregularity of inter-limb coordination and defective amplitude generation leading to sequence effect might be coupled and result from the same maladaptive motor behavior, eventually resulting in freezing of gait. Thus, SBTM can be an effective tool to improve parkinsonian gait, especially if combined with other treatments.

O176

Talk 1: Global approaches to functional characterization of GWAS data and causal variation: From association to function
*Danielle Posthuma**
Netherlands

Genome-wide association studies (GWAS) have successfully identified many novel loci for neuropsychiatric traits. At the same time the results of GWAS showed that these traits are highly polygenic, mostly influenced by large numbers of weakly associated variants. Interpreting such polygenic results is challenging. Recent large-scale initiatives, provide fine-scaled atlases of functional genetic elements at cellular level. This novel information can be used to interpret results from GWAS studies and facilitate biological understanding of complex traits. In this session, I will discuss our work on GWAS for Alzheimer disease and how we can use external bioinformatic resources to interpret our findings. I will discuss previous and ongoing work as part of the Psychiatric Genomics Consortium - Alzheimer's working group.

O177

Talk 2: Promoter-enhancer interactome and the risk for PD/disease

*Gerhard (Gerry) Coetzee**
Van Andel Institute, Grand Rapids, MI, United States

More than 90% of GWAS signals for Parkinson's Disease (PD) reside in non-coding DNA, mostly in enhancers. Traditionally risk loci were annotated by the nearest gene on linear DNA, although such genes are sometimes not the target gene imposing risk. Genome-wide maps of risk enhancers are available for many cell types and can be used to better understand risk. They are for example, PMID33106633 (Montine lab), PMID: 33828297 (Lander lab), PMID: 34774128 & PMID: 35840754 (Ren lab). Mechanistic insight is lacking, however, as to exactly how the one allele imposes risk vs. the other protection. Therefore, detailed biochemical analyses are needed, which for example may include differential transcription factor involvement. A poster-child example where this is lacking is at rs356182. It has a meta p-value for PD risk = 3.9x10-154, a meta odds ratio = 1.32, and with the G-risk allelic frequency in Caucasians = 37%. This risk SNP resides in an enhancer some 89kb telomeric of the transcription start site of SNCA, the gene that encodes alpha-synuclein(α-syn). Thus, SNCA has for a long time been assumed to be the target gene of this risk enhancer mainly since mutations of SNCA lead to familial PD and since α-syn is present in Lewy body inclusions. However, this is not the whole story. My lab has accumulated evidence, using genomic editing approaches, that this assumption is incomplete and that the risk enhancer in fact impinge on the expression of hundreds of genes across the genome that are associated with biological mechanisms not typically ascribed to α-syn. Additionally, we describe a functional role for SNCA as a regulator of cell cycle in developing neurons. These results serve as a prime example of the necessity and application of functional analyses of risk-SNPs, beyond simply assigning variants exclusively to the nearest gene.

O178

Talk 3: Building genomic predictive models through machine learning (ML) algorithms

*Mike Nalls**
United States

This talk covers applications of supervised and unsupervised learning as applied to Parkinson's Disease to attempt to better facilitate precision medicine. This will include early detection and sub typing as well as interesting unexpected dividends from these analyses like potential biomarkers with he overall goal being to treat the right patients at the right time.

O179

Talk 1: Deep brain stimulation for Parkinson's – Personalized targeting

*Vanessa Milanese Holanda**
BP - A Beneficência Portuguesa de São Paulo, Sao Paulo, SP, Brazil

Developments in deep brain stimulation (DBS) continue to rapidly emerge. Proper selection of surgical candidates is considered critical not only for successful DBS, but also to prevent complications by adequately planning surgical procedures. DBS interdisciplinary team approach provided important information on risk for hospitalization and improvement in quality of life following DBS surgery. Unilateral globus pallidus internus (GPi) or subthalamic nucleus (STN) DBS, rather than bilateral DBS, could be a modifiable risk factor for preventing cognitive decline associated with DBS therapy for PD. Studies of DBS targeting the posterior subthalamic area have shown an excellent effect on both Parkinsonian and essential tremor. The nucleus basalis of Meynert (NBM) is the main source of cholinergic innervation of the cortex and undergoes atrophy in patients with PD dementia. Low-frequency DBS to stimulate that nucleus may be beneficial to slow down the cognitive decline. Future studies should prospectively contrast unilateral and bilateral DBS with best medical therapy to develop more personalized therapies to optimize motor and non-motor function in patients with PD and could also study the brain networks involved in verbal fluency decline associated with DBS.

O180

Talk 2: Stereotactic lesioning for Parkinson's disease: New uses, new approaches

*Binit Shah**
University of Virginia, Charlottesville, Virginia, United States

MRI-guided focused ultrasound is a novel modality that has been approved for thermoablative treatment in Parkinson disease and essential tremor. There is also growing potential for neuromodulation and selective blood-brain barrier disruption with low intensity focused ultrasound. This talk with present the basis for thermoablative treatments for movement disorders as well as current safety, efficacy, and durability data. Additionally, future applications of low-intensity focused ultrasound in movement disorders therapeutics will be discussed.

O181

Talk 3: Emerging neuromodulatory and neurotechnology-based approaches for PD

*Jill Ostrem**
University of California San Francisco, San Francisco, CA, United States

Deep brain stimulation (DBS) therapy is a well-established treatment of PD motor fluctuations, bradykinesia, rigidity, tremor, and dyskinesia and allows for reduction in medications. The DBS system includes a brain lead(s) with multiple electrodes, an extension wire(s) tunneled under the skin, and a neurostimulator(s) placed in the subclavicular region. The DBS leads are implanted into the subthalamic nucleus (STN) or globus pallidus interna (GPi) nuclei using stereotactic neurosurgical techniques and intraoperative physiological confirmation or real-time interventional magnetic resonance imaging. Clinicians adjust stimulation parameters (amplitude, pulse width, rate), choosing the most appropriate DBS electrode(s) maximizing therapeutic benefits and minimizing adverse effects. DBS implantation is generally safe, with serious surgical complications being relatively uncommon.
Recently, major DBS technology advances have occurred. We now have smaller rechargeable and MRI compatible neurostimulators. Targeting specific nuclei/tracts has become more precise with high-resolution imaging/tractography/functional MRI and structural connectomes. DBS can now deliver directional current and shape electrical activity to parts of the target nuclei/tracts, improving targeting and preventing unwanted side effects. Some modern systems allow volume of tissue activation visualization tools that lay over patient specific MRI anatomy. DBS systems now offer a broader range of stimulation parameters, and some offer remote programming using a physician tablet over the internet. Wearable data is being introduced to the workflow to optimize programming. One commercial system can deliver stimulation, record, and store

data (local field potentials) from the electrode. Oscillatory activity in target nuclei in specific frequency bands has been found to correlate with severity of bradykinesia and rigidity (beta band power). These and other discovers are leading to adaptive or closed loop DBS approaches where DBS stimulation varies depending on relevant brain "control" signals.
Despite the growing interest in DBS, there are barriers to widespread adoption. Patient fear of brain surgery, reluctance of clinicians to refer patients, shortage of personnel trained in DBS programming, and limited access to expert centers likely all contribute. Future PD DBS will likely see an even more personalized approach, targeting milder patients, exploring possible disease modification strategies, and hopefully reaching more patients in the world who can benefit from this powerful therapy.

O182

Talk 1: Harnessing your breath to improve swallowing and cough function
*Michelle Troche**
Teachers College, Columbia University, New York, NY, United States

Swallowing and cough are life sustaining functions which are overlaid on the respiratory system and that often become impaired with Parkinson's disease. There is research to support several approaches to rehabilitating/improving swallowing and cough function in people with PD. Most of these, involve 'exercising' our breathing muscles or modifying the way we breathe to improve the effectiveness and safety of swallowing and cough. Some examples include: respiratory-swallow training, expiratory muscle strength training, and cough skill training. In this presentation we will briefly discus the research to support these treatment approaches and will discuss how they can be integrated into daily practice to improve health and quality of life.

O183

Talk 2: Speak your truth
*Miet De Letter**
Ghent University, Ghent, Belgium

This talk focusses on the importance of early recognition of communication disabilities in people with Parkinson's Disease aiming to prevent communicative difficulties in the early stages of Parkinson's Disease and improve quality of speech in the advanced stages. Evidence based practice of speech therapy approaches will be highlighted and discussed with a focus on transfer to everyday speech conversations.
Since daily communication is considered as a continuum of motor speech processing, language, paraverbal, nonverbal and metalinguistic behavior, it is important to spend enough time and energy to their common basis, more specifically a stable body posture and an adequate speech breathing. While body posture and speech breathing have an influence on voice, articulation, prosodic characteristics and intelligibility, cognitive functions have an influence on pragmatic language use. In this context, I will demonstrate how communication in persons with Parkinson's Disease can be hampered by pragmatic difficulties in terms of turn-taking organization and action formation. Since pragmatic disabilities seem to reduce fluency and increase dependence on the conversation partner, awareness of pragmatic aspects during speech therapy is strongly recommended.
In conclusion, speech breathing and pragmatic functions will be stressed as important determinants of daily quality of communication and as important functions to focus on in prevention and rehabilitation of communication disorders.

O184

Table 1: Cognitive impairment and dementia
*Greg Pontone**
Johns Hopkins University School of Medicine, Baltimore, MD, United States

Open forum discussion of how cognitive impairment impacts daily functioning in Parkinson's. The types of cognitive impairment--which cognitive domains are most often involved--and the risk for progression to dementia will be reviewed. Clinical screening and methods for assessing cognition in Parkinson's will be introduced with a focus on scales most appropriate for clinical settings.

O185

Table 2: Disease modification trials in prodromal PD – Hopes and barriers
*Michele Hu**
Oxford University, Nuffield Department of Clinical Neurosciences, Oxford, Oxfordshire, United Kingdom

The numbers of people living with Parkinson's globally are projected to double from 2015 to 2040, and we are already seeing effects of this worldwide expansion for which we are ill prepared. So far, a total of nineteen phase 3 intervention trials focusing on patients with manifest Parkinson's and motoric symptoms, have all failed to demonstrate significant changes in disease progression. In the search for a cure and effective disease modification, focus is now shifting to studying Parkinson's at its earlier stages. My talk focuses on isolated RBD (iRBD), a prodromal form of Parkinson's and related alpha-synuclein disorders. Individuals with sleep-study diagnosed iRBD provide the opportunity to intervene at an earlier disease phase, when higher densities of salvageable brain neurons remain without the confounding effects of symptomatic therapies (ie levodopa) that are frequently seen in manifest Parkinson's. Planned delivery of the first ever placebo-controlled trial of iRBD participants recruited across Australia and the UK will be discussed. My vision is to help researchers improve iRBD participant access to clinical trials, providing outcome measures that are sensitive to change, cost effective and quick to administer in clinic and at home. The delivery of effective disease modifying therapies for iRBD will also provide key mechanistic insights into how best to slow down trajectories for other forms of prodromal Parkinson's and manifest Parkinson's disease.

O186

Table 4: What are the gene therapy and growth factor approaches for PD?
*Krystof Bankiewicz**
AskBio, Columbus, OH, United States

At present there is a significant unmet need for clinically available treatments for Parkinson's disease (PD) patients to stably restore balance to dopaminergic network function in a long-term fashion. Growth factors hold considerable promise for disease modification in neurodegenerative disorders such as PD.
Although multiple clinical trials with growth factors have now been performed in PD patients the results have been mixed. It has been rationalized that improving administration with MRI-monitored convection enhanced delivery (CED) might overcome the limitation

of insufficient putaminal coverage to achieve clinical improvements in motor function.
Two growth factors, glial cell line derived neurotrophic factor (GDNF) and neurturin (NRTN), have garnered significant attention in the novel in vivo gene therapy field. However, only AAV2 GDNF (AB-1005) is currently active in gene therapy trials for PD. A Phase 1b study utilizing MRI-guided bilateral putaminal CED delivery of AAV2 GDNF has just completed enrollment (NCT04167540).
In this Phase 1b study AAV2 GDNF has so far demonstrated an encouraging safety profile where the neurosurgical procedure was well tolerated, and all 11 participants have completed 9 or more months of clinical follow-up. Putaminal coverage was >60%. No serious adverse events (SAEs) were associated with AAV2 GDNF. Reported adverse events (AEs) primarily occurred peri-operatively or were related to underlying PD.
Participants in the Mild Cohort (<5 years since clinical diagnosis of PD and MDS-UPDRS III OFF score ≤32; n=6) demonstrated stable MDS-UPDRS Part II and Part III OFF and ON scores at 6 and 12 months from baseline.
Participants in the Moderate Cohort (≥4 years since clinical diagnosis of PD and MDS-UPDRS III OFF score 33–60; n=4) demonstrated improvements on MDS-UPDRS Part II (–5.0 ± 3.5 pt) and Part III OFF (–18.8 ± 5.4 pt) at 12 months.
Although the placebo effect limits interpretation of small open-label studies such as this, these preliminary findings suggest potential stabilization in the Mild Cohort and possible early improvements in the Moderate Cohort. Further longitudinal evaluation and a controlled study is planned to confirm these initial findings.

O187

Table 5: Exercise for life
*Miriam Rafferty**
Shirley Ryan AbilityLab; Northwestern University, Chicago, Illinois, United States

Best care for people with Parkinson's disease (PD) includes encouragement of exercise participation. The question is no longer whether to exercise. The question is which exercises to do? Exercise participation should include some aerobic, strengthening, balance, and stretching activities. However, the dose of these exercise activities can vary from person-to-person based on their experience, abilities, needs, and preferences. We can also discuss the ever-present concern of how to stay motivated to exercise as the disease changes. This roundtable will provide insight into considerations for prescribing exercise to maintain motivation and adherence. Discussion may include ways that people with Parkinson's, their support systems, and healthcare providers can participate in, support, or prescribe, guideline-concordant exercise routines.

O188

Table 6: Myths and barriers around participating in research
*Ignacio Mata**
Cleveland Clinic/Case Western Reserve University, Cleveland, OH, United States

Humans have been using scientific methodologies (research) to better understand nature, diseases, etc for thousands of years. In this roundtable we will introduce what a research study is and how scientist use them to answer specific questions and better understand Parkinson's Disease. We will also explain the difference between those that compare the effects of a certain intervention (interventional), like clinical trials, and those that just observe and collect data in a group of individuals (observational). We will then discuss some of the barriers that scientist have to recruit participants in different research studies, and we will debunk some myths and misconceptions that many individuals have which may prevent their participation in research.
We will also provide examples and ways to identify trusted research studies.
The goal of this discussion is to provide all the knowledge and tools to feel comfortable about participating in research.

O189

Table 7: Discussing the need and impact of diversity in scientific research
*Dayne Beccano-Kelly**
UK Dementia Research Institute / Cardiff University, Cardiff, United Kingdom

The topic of diversity in the workplace, as an area of research and in society as a whole is not a new one, despite its current hot-button status. However, despite increased attention on the subject, the value of a diverse workplace in STEM fields is not universally 56ecognized. In many countries diversity in the scientific workforce is low. The impact of this within academia is multifaceted: implicit biases are reinforced; imbalances are perpetuated. Moreover, effects spill over into impacts on the research being conducted, and scientific rigour suffers. With less representation, there is a reduced drive to investigate aspects of Parkinson's that affect diverse groups differently.
From what work has been performed, differences in presentation, onset and progression of Parkinson's appears different in different groups. Despite the importance of this information, a stigma is also associated with research into differences between our differences. Here we would like to discuss these points, the benefit in addressing them, and the impact on all aspects of the Parkinson's community. We will talk about the initiatives in place and the foundations being put in place. We believe an open discussion about diversity is what is needed to achieve the best possible research, care and knowledge required to beat Parkinson's and improve science.

O190

Table 8: Prevalence of co-pathologies in Parkinson's disease
*Lauren Walker**
Newcastle University, Newcastle upon Tyne, United Kingdom

The hallmark protein aggregation deposited in the brain of people with Parkinson's disease is alpha-synuclein, however pathology associated with other neurodegenerative diseases can also be found in the brain which can affect the prognosis and trajectory of the disease course. Microscopic examination of the brain enables us to examine the prevalence of additional protein deposits. The most common co-pathologies are those seen in people with Alzheimer's disease (AD) (i.e. hyperphosphorylated tau and amyloid β (Aβ)), however other common co-pathologies include white matter lesions, TDP-43 inclusions, and argyrophilic grains. I will discuss the prevalence of common pathologies across the Parkinson's disease spectrum, the vulnerability of particular brain regions, and how this may affect the clinical progression.

O191

Table 9: Consequences of co-pathologies on the clinical presentation and progression of Parkinson's disease

*Georgina Aldridge**
University of Iowa, Iowa City, Iowa, United States

This will be a table discussion on the consequences of co-pathologies on the clinical presentation and progression of Parkinson's disease. Protein co-pathologies include amyloid and tau, usually found in Alzheimer's disease, as well as TDP-43, usually found in frontotemporal dementia. Co-pathologies have often been ignored and even excluded from studies, hindering our understanding. At this table we can discuss the current knowledge regarding how we can use case studies and animal models to understand the roll of these common co-morbid pathologies, and future questions you feel need to be addressed.

O192

Table 10: The mechanism of protein aggregation: What it all means for Parkinson's

*Celine Galvagnion**
University of Copenhagen, Copenhagen, Denmark

In this round table, we will discuss the relevance of the mechanistic studies of the formation of alpha-synuclein amyloid structures / co-structures, including the recently discovered phenomenon of liquid-liquid phase separation and the high degree of polymorphism of alpha-synuclein fibrils, to understand the molecular determinants responsible for the early events of alpha synuclein aggregation and neuronal toxicity and the formation of Lewy Bodies.
Parkinson's Disease is characterized by the presence of protein-lipid inclusions called Lewy Bodies, whose main constituent is alpha-synuclein This protein is intrinsically disordered and has been found to self-assemble and co-assemble with lipid molecules into a range of structures including different types of oligomers, nano-discs, proto-fibrils and mature fibrils of different morphology and structure, that differ in their toxicity to neurons. The mechanistic events leading to the formation of these structures and the polymorphism of alpha-synuclein fibrils highly depend on the solution conditions (e.g. pH, presence of salts, lipids, crowding agents …). Indeed, alpha-synuclein can undergo, in the presence of crowding agents, liquid-liquid phase separation, a process by which monomeric proteins are sequestered in a small droplet potentially leading to the initiation of amyloid fibril formation. The physiological relevance of such a phenomenon could also be discussed.
Moreover, we will discuss the connection of the different polymorphs of alpha-synuclein fibrils formed in vitro, with those derived from patients' postmortem brain samples. The recently resolved structures of alpha-synuclein fibrils extracted from patients suggest that fibrillar polymorphism is not only observed in vitro, but could be a disease-defining feature which may provide a rationale for the high heterogeneity of Parkinson's Disease phenotypes, and between different synucleinopathies.

O193

Table 11: How can we design better exercise trials in PD?

*Daniel Corcos**
Northwestern University, River Forest, Illinois, United States

The round table will focus on 12 issues and questions I presented in my talk plus any other exercise and participatory topics participants would like to discuss. The twelve topics of my presentation are as follows. First, it is crucial to involve people with PD in the front end of the design of some types of research studies – participatory action research in which people with PD are true partners. Second, we need to rethink control groups and consider testing findings directly against clinically important differences. Third, we need to distinguish studies that are designed to take advantage of neuroplasticity and potentially target disease modification from those which are designed for symptom reduction. We need to develop agreed upon paradigms for disease modification studies. Fourth, we need to understand the acute effects of exercise as well and the chronic effects of exercise and how best to take medication in the context of exercise. Fifth, we need to determine the minimal exercise prescription that delivers positive results. Sixth, what are the mechanisms exercise affects and does this inform the optimal time spent in exercising. Seventh, how can we increase the sustainability and durability of exercise interventions? Will people do what exercise trials suggest once the support and external motivation for taking part in the study are removed? What strategies can be developed to improve adherence to the exercise prescription? Trials of the future should explicitly test for sustainability and have long term follow-up time periods. Eighth, what are the best outcomes to assess and what are the best exercise interventions for different outcomes? Ninth, what is the best exercise progression to help people as the disease progresses? Tenth, can we generalize results from one exercise modality to another? Eleventh, what is the impact of chronotropic insufficiency on exercise capacity? Ten percent or more of people with PD cannot achieve age predicted maximal heart rate. Does this affect how their signs and symptoms respond to exercise? Twelfth, how can we increase the diversity of people recruited to exercise studies in PD?

O194

Table 12: Mitochondrial abnormalities underlying PD – From bench to bedside

*Edward A. Fon**
Montreal Neurological Institute, McGill University, Montreal, Quebec, Canada

Parkinson's disease (PD) is a common, devastating neurodegenerative disorder that affects over 8 million people worldwide and the numbers will only grow as the population ages. PD involves the death of dopamine neurons in the midbrain as well as other cells in the brain, which leads to devastating motor, non-motor and functional impairment. Although treatment is available, its effectiveness diminishes over the long term. Both environmental and genetic studies strongly implicate mitochondrial dysfunction in PD. My laboratory has a longstanding interest in understanding the role of mitochondria in PD and in understanding how PINK1 and Parkin, two recessive PD genes, function in a common pathway regulating mitochondrial quality-control. Despite the many advances in our understanding of Parkin and PINK1 function, much work remains in order to decipher their precise role in mitochondrial biology and disease. In this roundtable session, we will discuss how PINK1/Parkin regulate mitochondrial autophagy (mitophagy) and how other PD genes affect mitochondria. We will also discuss the structural basis of parkin/PINK1 activation by mitochondrial damage and how Parkin variants found in the population and in patients with PD can help rationalize the function of Parkin in mitochondrial quality control and better guide the design of future therapies.

O195

Table 13: Infectious agents as a trigger for Parkinson's
*Elena Kozina**
Thomas Jefferson University, Philadelphia, PA, United States

A growing body of evidence from both clinical and preclinical studies suggests that Parkinson's disease (PD) arises from a multifactorial etiology that includes exposures to pesticides, herbicides, and infectious agents that interact with an underlying genetic predisposition. Given that these environmental agents first enter the body (versus brain), it is critical to examine the role of peripheral immune signaling as a contributor to the development of PD. In relation to viral infections, neurotropic viruses (H5N1, West Nile and WEEV) have the ability to infect cells in the CNS regions affected in PD. However, most viral infections do not appear to have this ability including H1N1, RSV and SARS-CoV-2. In addition to viruses, bacterial infections have also been shown to act as peripheral triggers of neuron loss in the susceptible individuals. Recent preclinical studies from our lab showed that the pandemic 2009 H1N1 and 2019 SARS-CoV-2 (alpha variant) viruses induce a significant and persistent DA cell loss and neuroinflammatory response in the SN of mice carrying the G2019S PD-associated LRRK2 mutation with no phenotype observed in the infected wt controls. We have also demonstrated that the peripheral immune dysfunction, induced by viral and bacterial infections, in LRRK2-mediated PD may have been the initiating site of signals, and thus the cause, of the CNS related pathologies. Using chimeric mouse models, we found that the replacement of peripheral T- and B-cells carrying LRRK2 mutations with wt cells significantly diminished LPS-mediated neuroinflammation which resulted in the absence of the DA neuron loss in the, still, genetically mutant brain. Conversely, the presence of LRRK2 mutations in lymphocytes alone (all cells in the brain are wt) is sufficient to induce LPS-mediated neuronal loss. Remarkably, we observed that LPS-induced DA cell loss was not associated with the recruitment of peripheral immune cells into the brain's parenchyma suggesting that circulating factors from the dysregulated immune cells were responsible for the immune activation and neuron loss in the brain. Overall, our studies indicate that the PD-associated DA neuron death can be regulated by underlying immune signaling solely arising from the activated peripheral immune system, which may provide new targets for therapeutic intervention.

O196

Table 14: (Español) Apatía y fatiga en enfermedad de Parkinson
*Mayela Rodriguez-Violante**
Instituto Nacional de Neurologia y Neurocirugia, Ciudad de Mexico, Mexico City, Mexico

Characterizing the clinical phenotype of the entire non-motor profile of Parkinson's Disease (PD) is challenging. Non-motor symptoms have been widely acknowledged to hold a vital part in the clinical spectrum of PD (Rota, 2022).
Apathy is a prevalent, multidimensional neuropsychiatric condition in PD. Prevalence of fatigue is as high as 50% in PD, and PD patients (PwP) attending the 2013 World Parkinson Congress voted fatigue as the leading symptom in need of further research (Eglit, 2020; Siciliano, 2018; Kluger, 2016).
Apathy and fatigue are two key non-motor symptoms of PD. Their identification is mainly hindered by the lack of a consensus on these subjective symptoms. Although often underrecognized, they significantly contribute to PwPs and their caregivers' Quality of life (QoL) (Lazcano-Ocampo, 2020).
Several non-motor symptoms appear to be associated with fatigue (Siciliano, 2018). Additionally, anxiety, depression, excessive daytime sleepiness, apathy, and impairment in activities of daily living related to motor symptoms were independently associated with worse health-related QoL (Kuhlman, 2019). PwP with more severe motor symptoms, cognitive impairment, depression, anxiety, RBD, excessive daytime sleep, fatigue, low education level, long disease course, poor QoL, and lower DA dosage are more prone to apathy (Luo, 2022).
Pharmacological and nonpharmacological strategies targeting apathy and fatigue may improve QoL in PwP (Siciliano, 2018). Further research and understanding are needed for discovering biomarkers of certain NMS, including apathy and fatigue. More work is needed to gather a robust evidence base for guiding the treatment of these troubling NMS, which exert a significant impact on QoL for PwP and their caregivers (LeWitt, 2020).
Moreover, there have been numerous reports of newly emerging or acutely deteriorating non-motor symptoms in PwP who had been infected by the Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2), while some of these symptoms, like fatigue, pain, depression, anxiety, and cognitive impairment, have also been identified as part of the long-COVID syndrome due to their persistent nature (Rota, 2022). Taking this into consideration, research on non-motor symptoms is necessary to develop an integrated care approach for PwP and their caregivers.

Poster Presentations

BASIC SCIENCE: Etiology, genetics, epidemiology, and toxicants

P01.01

SARS-CoV-2 and the brain: implications for Parkinson's disease
Eduardo A. Albornoz[*,1], Julio Aguado[2], Alberto Amarilla[3], Daniel Watterson[3], Ernst J. Wolvetang[2], Trent M. Woodruff[1]*
[1] School of Biomedical Sciences, Faculty of Medicine, University of Queensland, Brisbane, QLD, Australia
[2] Australian Institute for Biotechnology and Nanotechnology, University of Queensland, Brisbane, QLD, Australia
[3] School of Chemistry and Molecular Biosciences, University of Queensland, Brisbane, QLD, Australia

Although coronavirus disease-2019 (COVID-19) is primarily a respiratory disease, there is increasing recognition that SARS-CoV-2 infection is associated with brain complications, including severe neurological manifestations and long-term post-infection effects (Long COVID). These complications may include a potential direct or secondary impact on neurodegenerative diseases such as Parkinson's Disease (PD). We recently reported that SARS-CoV-2 infection and its spike protein can promote NRLP3 inflammasome activation in human microglia, activating the same inflammatory response in the brain that is exhibited in PD. We identified that SARS-CoV-2 spike glycoprotein played an important role not only in activating the NLRP3 inflammasome but also in priming the pathway allowing for heightened activation by alpha-synuclein. Strikingly, SARS-CoV-2 and spike protein-mediated microglial inflammasome activation was significantly enhanced in the presence of alpha-synuclein fibrils and was entirely ablated by NLRP3-inhibition. To further explore links between COVID-19 and PD, in this study, we tested the impact of SARS-CoV-2 in altering dopaminergic neuron survival in vivo. We demonstrate that acute SARS-CoV-2 infection

in mice, leads to a loss of midbrain neurons, as measured by a significant reduction in tyrosine hydroxylase immunolabeling. We next utilized human-derived brain organoids (BOs) to explore the effects of SARS-CoV-2 infection on human brain tissue. As the presence of senescent cells is known to contribute to organismal aging and neurodegeneration, we hypothesized that part of the neurotoxic environment following COVID-19 could be reinforced by SARS-CoV-2-induced cellular senescence in the brain. To test this, we infected human BOs with multiple SARS-CoV-2 variants and screened for the presence of cellular senescence markers (p16, p21), DNA double-strand break accumulation, the abundance of cells exhibiting senescence-associated beta-galactosidase activity and used transcriptomics to evaluate the senescence-associated secretory phenotype (SASP). We detected significantly heightened levels of these parameters in SARS-CoV-2-infected organoid regions, compared to uninfected organoids, with pharmacological intervention using senolytics remarkably attenuating these aging phenotypes. Thus, we show for the first time that SARS-CoV-2 can trigger cellular senescence and dopaminergic degeneration in the brain, supporting the concept that viral-mediated chronic inflammation could contribute to PD, and highlighting an avenue for novel therapeutic approaches.

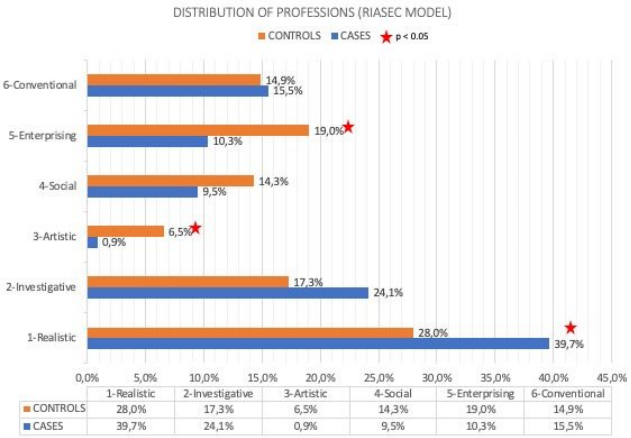
P01.02

PROPARK study: Is there an association between PROfessional occupation and PARKinson's disease?

Elena Natera Villalba[1], Victoria Ros Castelló[1], Arantxa Sánchez Sánchez[1], Ana Gómez López[1], Paula Pérez Torre[1], Carlos Estévez Fraga[2], Isabel Pareés Moreno[1], Juan Carlos Martínez Castrillo[1], Araceli Alonso-Canovas[,3]*

[1] Hospital Universitario Ramón y Cajal, Madrid, Spain
[2] Neurodegenerative Disorders Unit. University College London-Queen Square Institute of Neurology, London, United Kingdom
[3] Neurology Department. Hospital Universitario Ramón y Cajal, Madrid, Spain

Background: A potential association between Parkinson's disease (PD) and occupation has been previously explored, yielding conflicting results. Professional environmental exposures or a negative work life impact might influence the dopaminergic degeneration leading to PD. On the other hand, a study found that professions involving creative skills were significantly less represented in PD, suggesting a prodromal, preclinical dopaminergic denervation could influence creativity and subsequently professional choices.
Methods: Case-control study in a Movement Disorders Unit and General Neurology Clinic. Cases were persons with a clinical diagnosis of PD (PwP). Controls were persons with neurological diseases, excluding atypical parkinsonisms, essential tremor, and dementia, to avoid clinical overlap. Professional categories were registered according to the RIASEC model (R-ealistic: agriculture, livestock, basic works; I-nvestigative: science and Health; A-rtistic: culture, art; S-ocial: teaching, journalism; E-nterprising: bussiness, salesmen; C-onventional: administration and finance).
Results: A total of 400 patients (232 PwP, 168 controls) were included. PwP were significantly older (71.6+9.6 vs. 65.3+12.2 years, p<0.001) and more frequently male (58.2% vs. 41.8%, p<0.001). Dystonia (42), hemifacial spasm (29), stroke/TIA (19) and migraine (17) were the most frequent diagnoses among controls.
The most prevalent groups of professions among PwP were R-ealistic (39.7% vs. 27.9%), and I-nvestigative (24.1% vs. 17.3%), with a higher frequency vs. controls (p=0.0003).
We observed an increased frequency of R-ealistic professions in PwP (40% vs. 28%, p:0.015475), while creative professions (A-rtistic) (1% vs. 7%, p: .001551) and E-nterprising professions (10% vs. 19% p:0.013294) were significantly more common among controls (Figure 1). These differences remained significant after multivariate logistic regression (OR 0.52, 95% CI 0.31-0.86, p=0.0062) There was a trend towards more frequent S-ocial professions among controls (14% vs 10%) and more frequent I-nvestigative professions among PwP (24% vs 17%).
Conclusions: In line with the previous study, PwP reported a distinct professional profile, with a higher frequency of R-ealistic, and less frequent A-rtistic and E-nterprising professions. Our study suggests that higher levels of routine and less creative professions might be more appealing for subjects who subsequently develop PD and influence their professional choices. Work-related environmental exposures, along with other work life related changes, cannot be ruled out and might also influence this association.



	1-Realistic	2-Investigative	3-Artistic	4-Social	5-Enterprising	6-Conventional
CONTROLS	28,0%	17,3%	6,5%	14,3%	19,0%	14,9%
CASES	39,7%	24,1%	0,9%	9,5%	10,3%	15,5%

P01.03

Pathogenic or likely pathogenic GRN variants are present in ~0.2% of patients with Parkinsonism

Christian Ganoza[,1], Ruslan Al-Ali[1], Ana Westenberger[2], Tatjana Usnich[2], Jörg Rennecke[1], Volha Skrahina[1], Ilona Csoti[3], Christine Klein[2], Arndt Rolfs[1], Peter Bauer[1], Christian Beetz[1]*

[1] Centogene GmbH, Rostock, Germany
[2] Lübeck University, Lübeck, Germany
[3] Gertrudis Klinik Biskirchen, Biskirchen, Germany

A clinical diagnosis of Parkinson's disease (PD) relies on the presence of parkinsonism. Parkinsonism, however, may also be one of the early manifestations of frontotemporal dementia (FTD). Heterozygous mutations in the GRN gene are the second most frequent cause of monogenic FTD. The present study aimed at determining the frequency of GRN-FTD among patients that are clinically diagnosed with PD.
The Rostock parkinson's disease study (ROPAD) genetically analyses patients with a clinical diagnosis of PD, applying a dedicated multi-gene panel. GRN is one of the 'ROPAD research genes', i.e., genes that are not covered by the standard ROPAD genetic diagnostic report. We mined ROPAD genetic data for variants in GRN and classified all observed variants according to the recommendations of the American College Of Medical Genetics (ACMG criteria). Numerous features were compared between patients with pathogenic or likely pathogenic GRN variants, and patients from the rest of the ROPAD cohort.
Among ~12k ROPAD participants, we identified N=24 individuals (~0.2% of all), who were heterozygous for any of a total of N=15 distinct pathogenic or likely pathogenic variant in GRN. Most of the many available clinical and sociodemographic data were similar in GRN-positives vs. GRN-negatives from the ROPAD cohort. GRN-

positives, however, had significantly higher scores for the UPDRS-relevant parameters 'facial expression', 'freezing of gait' and 'finger tapping'.
A significant fraction of patients with a clinical diagnosis of PD does actually suffer from GRN-FTD. Pertinent candidate patients may be flagged by certain clinical parameters.

P01.04

Cytochromes P450 are new potential players in Parkinson's disease

Rita Bernhardt[*,1], Philip Hartz[1], Tobias Fehlmann[2], Gudrun Wagenpfeil[3], Marcus Unger[4]*
[1] Institut für Biochemie, Fachbereich Biologie, Universität des Saarlandes, Naturwissenschaftlich-Technische Fakultät, Campus B2.2, D-66123 Saarbrücken, Germany
[2] Institut für Klinische Bioinformatik, Universität des Saarlandes, Campus E2.1, D-66123 Saarbrücken, Germany
[3] Institut für Medizinische Biometrie, Epidemiologie und Medizinische Informatik, Universität des Saarlandes, Kirrberger Strasse, D-66421 Homburg, Germany
[4] Klinik für Neurologie, SHG Kliniken Sonnenberg, 66119 Saarbrücken, Germany

Cytochromes P450 (P450s) are involved in different reactions in the human body and SNPs (single nucleotide polymorphisms) in CYP2D6 and CYP2E1 have been associated with the susceptibility of Parkinson's disease (PD). Our aim was to evaluate the role of all 57 human P450s and their redox partners for the etiology and pathophysiology of PD and to identify this way novel potential players for PD. The PPMI (Parkinson's Progression Markers Initiative) database was used to extract the gene sequences for these proteins to analyze the association of SNPs with the occurrence of PD. Using statistical analyses, we identified SNPs which were significantly over-represented in patients with a genetic predisposition for PD (GPD patients) or in idiopathic PD (IPD patients) compared to HC (healthy controls). Three main groups of P450s have been found to display a significant over-representation (OR>5) of SNPs in PD: xenobiotic-metabolizing P450s, P450s participating in the metabolism of eicosanoids and P450s catalyzing the degradation of cholesterol supporting the role of toxic compounds, inflammation as well as cholesterol metabolism in the pathogenesis of PD. Also, the redox partners of P450 show SNPs with OR>5 in PD patients. Taken together, we show that SNPs in 26 out of 57 P450s are at least 5-fold over-represented in PD patients suggesting these P450s as new potential players in the pathogenesis of PD. For the first time exceptionally high OR values (up to 12.9 in selected P450s) were found. This points to an important function of P450s in the pathogenesis of PD and will lead to a deeper insight into the origin and development of PD. It can be applied to identify new biomarkers and it will pave the way to develop novel strategies for a causative treatment of this disease.
The work was supported by a research grant from the "Dr. Rolf M. Schwiete Stiftung" Mannheim/Germany. The work was made possible by accession to the PPMI database.

P01.05

Indentification of suspected familial monogenic cases of Parkinson's disease in the Australian Parkinson's genetics study

Svetlana Bivol[*,1], Nicholas G. Martin[2], Kishore R. Kumar[3], Miguel E. Renteria[2]*
[1] QIMR Berghofer Medical Research Institute, Molendinar, QLD, Australia
[2] QIMR Berghofer Medical Research Institute, Brisbane, QLD, Australia
[3] Concord Repatriation Hospital, Sydney, NSW, Australia

Background: While the exact causes of PD are still not fully understood, a growing body of evidence suggests that genetics plays a significant role in its development, with both monogenic and polygenic forms existing. Monogenic forms, accounting for around 5-10% of PD cases, are characterised by distinct clinical features and may require a different approach to treatment and management compared to idiopathic PD.
Objective: The Australian Parkinson's Genetics Study (APGS) is a nationwide effort to unravel the genetic underpinnings of PD, and our goal is to identify and characterise suspected monogenic cases of PD. To this end, we are screening the APGS database for participants with an early age of onset and/or a familial history of PD, and will recontact them to determine their eligibility for whole-genome sequencing and receive a genetic diagnosis and genetic counselling.
Preliminary Results: As of December 2022, our database includes 6,302 participants, out of which 879 (13.9%) reported symptoms onset before the age of 50, 1593 (25.3%) had a familial history of PD and 265 (4.2%) had both an early age at onset and a familial history. These participants are on average 58 years old, 56% are males and 91% are of European ancestry.
Next Steps: At the congress, we will present descriptive statistics of sociodemographic, clinical, lifestyle and environmental variables for the group of suspected monogenic PD cases and will reach out to them to gauge their interest in undergoing the genetic counselling process and receiving their results.

P01.06

Larger intracranial and subcortical brain volumes influence a higher Parkinson's disease risk

Zuriel Ceja[*,1], Santiago Diaz-Torres[2], Luis M. García-Marín[2], Miguel E. Rentería[2]*
[1] QIMR Berghofer Medical Research Institute, uruapan, Michoacán, Mexico
[2] QIMR Berghofer Medical Research Institute, Brisbane, Queensland, Australia

Parkinson's disease (PD) is a late-onset and genetically complex neurodegenerative disorder. While previous studies have identified genetic variants and group differences in brain morphometry associated with PD, a better understanding of the genetic and molecular pathways underpinning these associations is necessary to elucidate the etiology of PD and pinpoint potential therapeutic and intervention targets. In the present study, we sought to identify potential causal genetic effects between PD and neuroimaging phenotypes. We observed a positive significant genetic correlation between PD and intracranial volume and the volumes of the brainstem, pallidum, putamen, ventral diencephalon, nucleus accumbens, caudate nucleus, brainstem, and thalamus at a whole-genome level. In addition, Mendelian randomisation investigations suggest that a larger volume of the putamen, ventral diencephalon, pallidum, caudate, and brainstem could influence the development of PD independently of the potential causal genetic effects of intracranial volume. Overall, our findings suggest that genetic variants influencing larger intracranial and subcortical brain volumes, possibly during earlier stages of life, influence the risk of developing PD later in life.

P01.07

Contribution of whole exome sequencing in Parkinson's disease: A review of WES in 929 patients by Guillaume Cogan, France

Guillaume Cogan, Alexis Brice, Thomas Courtin*
Paris Brain Institute, Paris, France

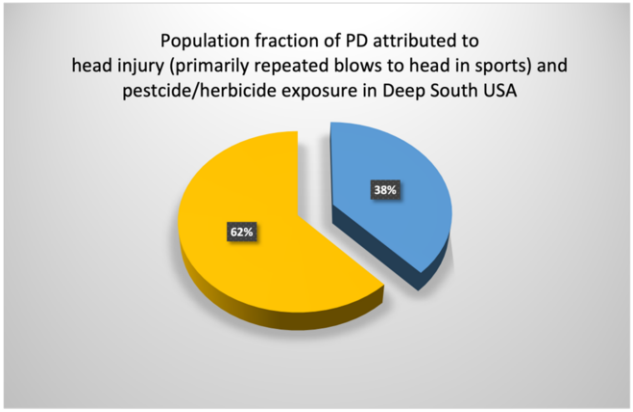
Parkinson's disease (PD) is the second most frequent neurodegenerative disorder after Alzheimer's disease, affecting more than 1% among people older than 60 years old. Although the etiology is mostly unknown, an early onset, a familial form and an atypical presentation might evoke a monogenic etiology. To date, more than a dozen causative genes have been identified and validated but many additional genetic diseases can present with parkinsonism and various additional clinical features. We performed whole exome sequencing (WES) in 929 patients with early-onset and/or a positive family history who had previously been excluded from known PD genes. 736 were isolated cases and 193 familial cases from 68 families. Among these 68 families, 43 were compatible with autosomal dominant, 22 with autosomal recessive transmission and inheritance mode was unknown for 4 patients. Male/Female sex ratio was 1.48 and average age at onset 39,6 years old (range 3 to 87 years). Using this approach, we identified 9 patients with likely pathogenic or pathogenic variants (1%), according to the American College of Medical Genetics (ACMG) criteria (class 4 and 5 variants) in ADCY5, ATP7B, DNAJC12, MAPT, PPP2R5D, PNPLA6, POLG and SPR. All these results were confirmed by either clinical, biological and/or radiological data (i.e. the patient with MAPT variant had typical frontotemporal dementia, whereas the patient with biallelic ATP7B variants presented the classical cerebral MRI alterations of Wilson's disease). These results allow to provide a new diagnostic to these patients, sometimes with a possible treatment (i.e. ADCY5-related patients are improved by caffein uptake and Wilson's disease treated by a copper chelator or an inhibitor of its absorption). In addition, 44 patients (5%) carried variants of unknown significance (VUS) in other genes possibly associated with parkinsonism. Finally, although slightly increasing the diagnostic performance, many patients remain without a genetic diagnosis after WES despite a strong enrichment of potentially genetic cases in our series. Further studies with whole genome sequencing including long-read sequencing are needed to further decipher the genetic architecture of Parkinson's disease.

P01.08

Population fraction of Parkinson's disease attributed to avoidable risk factors: A case-control study in the Deep South United States

*Gwendolyn Cohen, David Standaert, Haydeh Payami**
The University of Alabama at Birmingham, Birmingham, Alabama, United States

Background: Parkinson's disease is the fastest growing neurologic disease globally. The pandemic-like spreading is a looming catastrophe unless a prevention is found. PD is multifactorial. The genetic components may be difficult to escape, but environmental risk factors are not. The main risk factors for PD are family history of PD (combination of shared environment and genotype at 90 susceptibility loci), head trauma, and exposure to pesticides/herbicides including agent orange. We addressed three voids in knowledge. Are these risk factors independent? Are they all operative in any given population or do one or few risk factors predominate in a population-specific manner? What is the population attributable fraction for each risk factor (PAF: fraction of PD that would be eliminated if the risk factor is removed)?
Methods: We enrolled 808 PD cases and 415 neurologically healthy controls at the University of Alabama at Birmingham in the Deep South of United States. We collected multidimensional data via medical records and self-reported history, tested to determine which risk factors associate with PD in this population, assessed their interdependence, and calculated PAF.
Results: All risk factors are at play in this population, and their effects are independent. In the order of odds ratio (OR): exposure to agent orange (OR=7.7, P=6E-4), repeated blows to head in contact sports (OR=4.3, P=2E-6), pesticides/herbicides exposure (OR=2.8, P=2E-9), family history of PD (OR=2.8, P=1E-11), and concussion or head injury requiring medical care (OR=2.1, P=5E-5). The PAF estimates in order of impact were pesticides/herbicides exposure 21% [14.6-27.2], family history 21% [15.4-26.7], repeated blows to head 10% [5.1-15.4], head injury requiring medical care or concussion 10% [4.9-15.9], and agent orange 4% [-0.7-8.8]. Considering the modifiable risk factors together, PAF was 28% [21.2-34.6] for repeated blows to head and pesticide/herbicide exposure, and 38% [30.8-45.6] for head injury, repeated blows, pesticides/herbicides and agent orange.
Conclusion: 1/3 of PD cases in the Deep South are attributed to exposure to herbicides/pesticides and participating in violent contact sports.



P01.10

Retinal ganglion cell integrity measurements as biomarkers of Parkinson's disease risk in young adults

Santiago Diaz Torres*[,1], Samantha Lee[2], David A Mackey[2], Stuart MacGregor[3], Puya Gharahkhani[3], Miguel E Renteria[3]
[1] The University of Queensland / Queensland Institute of Medical Research, Brisbane, QLD, Australia
[2] Centre for Ophthalmology and Visual Science (incorporating the Lions Eye Institute), The University of Western Australia, Perth, WA, Australia
[3] QIMR Berghofer Medical Research Institute, Brisbane, QLD, Australia

Optical coherence tomography (OCT) is a non-invasive eye imaging technique that measures the thickness of retinal layers, including the retinal nerve fiber layer (RNFL) and the ganglion cell-inner plexiform layer (GCIPL), which are measures of the integrity of the retinal ganglion cells. Previous studies have shown that individuals with Parkinson's disease (PD) have reduced RNFL and GCIPL thicknesses as measured by OCT. Our study aimed to investigate whether genetic predisposition to PD is associated with these OCT measures in a population-based sample.
Western Australian young adults (aged 20 at baseline and 28 at follow-up) underwent OCT imaging (n~600). Their RNFL, GCIPL

and overall retinal thicknesses were recorded, as well as their longitudinal changes between ages 20 and 28 years old. Participants were genome-wide genotyped using the Illumina platform and imputed using the TOPMed reference panel, their genotypes were used to estimate individual polygenic risk scores (PRS) for Parkinson's disease based on genome-wide summary data from the largest PD genome-wide association study available to date. A linear regression model was used to assess whether PD PRS was associated with changes in thickness at a younger age. Each eye was considered as an independent measurement and measures were adjusted for axial length.
Significant associations ($P<0.05$) were observed between PD PRS and OCT measures. A higher PRS was associated with a thinner Peripapillary RNFL in young adults and an overall thinner retina at 20 years and 28 years. The PRS of PD was also associated with longitudinal changes in retinal thickness from age 20 to 28 years old.
Our results suggest that retinal morphometric measurements of the retinal ganglion cells and their longitudinal change in young adults are influenced by genetic susceptibility to PD. Thus, their utility as potential PD risk biomarkers warrants further exploration. Further research is needed to understand the underlying mechanisms behind the relationship between PD and measures of the retinal ganglion cell integrity.

P01.11

Dry cleaning chemicals and a possible cluster of Parkinson's disease

Maryam Zafar[1], Meghan Pawlik[1], Samantha Lettenberger[1], Madeleine Coffey[1], Aayush Sarkar[1], Peggy Auinger[1], Caroline Tanner[2], Samuel Goldman[3], Briana De Miranda[4], Karl Kieburtz[5], Heidi Schwarz[6], Melanie Braun[6], Richard Barbano[6], Jamie Adams[5], Daniel Kinel[1], Ray Dorsey[,5]*
[1] Center for Health + Technology, University of Rochester, Rochester, NY, United States
[2] Department of Neurology, Weill Institute for Neurosciences, University of California-San Francisco, San Francisco, CA, United States
[3] San Francisco VA Health Care System, San Francisco, CA, United States
[4] Center for Neurodegeneration and Experimental Therapeutics, Department of Neurology, University of Alabama at Birmingham, Birmingham, AL, United States
[5] Center for Health + Technology, Department of Neurology, University of Rochester, Rochester, NY, United States
[6] Department of Neurology, University of Rochester, Rochester, NY, United States

Objective: To examine the health outcomes of a cohort potentially exposed to dry cleaning chemicals.
Background: Trichloroethylene (TCE) is a ubiquitous chemical that has been used to decaffeinate coffee, degrease engines, and dry clean clothes. Chemicals like TCE can pollute groundwater and evaporate, entering buildings. TCE, a known carcinogen, is associated with a 500% increased risk of Parkinson's disease (PD), but few studies have examined potentially exposed cohorts.
Methods: We examined a cohort of attorneys who worked adjacent to a dry-cleaning site contaminated with TCE and other chemicals. We evaluated the cohort by surveys, clinical assessments, or both, and invited an additional group of attorneys without known exposure to TCE to complete clinical assessments, including the investigator-administered Gelb diagnostic criteria and the MDS-UPDRS. We reviewed medical records of deceased or incapacitated attorneys.
Results: Of 82 potentially exposed attorneys, we evaluated 75 (91.4%) by either surveys (Phase I, n=65), clinical assessments (Phase II, n=46) or medical records reviews (Phase II, n=12), or both. Across both phases, 15 were deceased (mean age at death 74.5 (9.7) years, 1 female) and 60 were living (mean age 73.0 (15.5) years, 8 female). 75 presumably unexposed, control attorneys (mean age 64.9 (10.3) years, 26 female) also participated.
Of the potentially exposed participants, 4 (5.3%) had PD and 1 (1.3%) had multiple systems atrophy. Among the potentially exposed who completed clinical assessments, 9 (19.6%) had "possible" PD per the Gelb criteria. Fourteen (18.7%) of the potentially exposed had a TCE-related cancer (liver, kidney, non-Hodgkin's lymphoma, prostate, multiple myeloma). Of the 75 control attorneys, 1 (1.3%) had PD, 14 (18.6%) had possible PD, and 4 (5.3%) had a TCE-related cancer.
MDS-UPDRS motor scores of participants who completed a clinical evaluation were 9.5 (8.1) for the potentially exposed and 7.7 (7.6) for control examinations administered in-person, and 4.9 (6.3) and 3.2 (3.2) for remote examinations of the potentially exposed and controls, respectively.
Conclusion: The high prevalence of PD and cancers in this cohort is concerning. More detailed evaluations, now and in the future, are necessary to help characterize the role of TCE in the rise of PD globally.

P01.12

Do Parkinson's susceptibility risk factors also influence age of onset?

Amali S. Fernando, Santiago Díaz-Torres, Nicholas G. Martin, Miguel E. Renteria*
QIMR Berghofer Medical Research Institute, Brisbane, QLD, Australia

Background: Parkinson's disease (PD) is a complex neurodegenerative disorder with a multifactorial etiology, including both genetic and environmental factors. Some established risk factors, such as family history, smoking, coffee consumption, exposure to pesticides, and head trauma, have been identified as contributing to an individual's susceptibility to PD. However, the association between these risk factors and the age of onset of PD symptoms remains poorly understood.
Methods: We used data from the Australian Parkinson's Genetics Study pilot, comprising 1308 PD cases with available information on risk factors and age of onset of symptoms. We employed a linear model to examine the association between potential risk factors and age of onset of PD. Additionally, we used linear mixed-effects models to analyze the interaction between these risk factors and an individual's family history of PD. To account for multiple testing, we applied a Bonferroni correction (0.05/number of risk factors) in our analysis.
Results: We observed significant statistical associations between age of onset and several risk factors, including BMI, soda consumption, high caffeinated tea intake, high alcohol and smoking habits, exposure to pesticides and herbicides, incidents of head trauma, incidents of brain infection, and family history. We also found that having relatives diagnosed with PD increases the risk of an earlier onset of the disease. Notably, the effects on the age of onset did not change when adjusted for the interaction between PD family history.
Conclusion: Our study suggests that some of the known PD susceptibility risk factors are also associated with PD age of onset differences among individuals. These findings could help inform the development of more accurate early screening methods and personalized interventions for people at risk of developing PD.

P01.13

Shared molecular pathways underlie the relationship between Parkinson's disease and chronic pain

Luis Garcia Marin, Freddy Chafota, Miguel Renteria*
QIMR Berghofer Medical Research Institute, Herston, QLD, Australia

Parkinson's disease (PD) is characterized by both motor and non-motor symptoms. Chronic pain, which is defined as pain lasting for more than three months, is a common non-motor symptom of PD. Between 40-80% of people with PD experience chronic pain, particularly musculoskeletal pain, but also neuropathic, dystonic, and central pain. Despite their high comorbidity, the relationship between PD and chronic pain has not been interrogated on a genetic level. Therefore, the molecular mechanisms that underlie this association remain widely unknown. To shed light on this issue, we leveraged genome-wide association studies (GWAS) summary data to identify genomic segments that are involved in the development of both PD and chronic pain. We used the GWAS-pairwise and MAGMA methods to explore the biological pathways and genes in the identified genomic segments of interest. Gene enrichment analysis of these segments revealed links to the NF-κB pathway, which is involved in the regulation of inflammatory mediators during inflammation and is expressed in microglia, neurons, and astrocytes. We also observed overlap in pathways related to the regulation and trafficking of synaptic vesicle proteins, which play a key role in synaptic transmission, as well as pantothenic acid regulation and the pathway in which acetyl coenzyme A is converted to butyric acid. This supports the hypothesis that physiological levels of short-chain fatty acids in the intestine may help suppress inflammation. In addition, we found significant overlap in pathways related to mitochondrial metabolism and platelet activation. Overall, our study provides evidence of shared molecular pathways involved in the development of both PD and chronic pain. These findings may lead to the identification of novel targets for the development of interventions to manage pain-related symptoms or slow disease progression in PD.

P01.15

Towards a molecular definition of human midbrain dopaminergic neuron subtypes at the single cell level

Ka Wai Lee[1], Kimberly Siletti[1], Emelie Braun[1], Miri Danan-Gotthold[1], Rebecca Hodge[1], Alejandro Mossi Albiach[1], Lars E. Borm[1], Elin Vinsland[1], Lijuan Hu[1], Peter Lönnerberg[1], Trygve Bakken[2], Song-Lin Ding[2], Xiaofei Li[1], Xiaoling He[3], Žaneta Andrusivová[4], Michael Clark[2], Tamara Casper[2], Nick Dee[2], Jessica Gloe[2], C. Dirk Keene[5], Julie Nyhus[2], Herman Tung[2], Anna Marie Yanny[2], Joakim Lundeberg[4], Roger A. Barker[3], Erik Sundström[1], Ed S. Lein[2], Sten Linnarsson[1], Ernest Arenas[1]*
[1] Karolinska Institute, Stockholm, Sweden
[2] Allen Institute for Brain Science, Seattle, Washington, United States
[3] University of Cambridge, Cambridge, United Kingdom
[4] KTH Royal Institute of Technology, Stockholm, Sweden
[5] University of Washington, Seattle, Washington, United States

Current cell-based strategies for disease modeling, drug development and cell replacement therapy for Parkinson's disease (PD) rely on the generation and use of authentic human midbrain dopaminergic (mDA) neurons from either pluripotent stem cells or through direct reprogramming of somatic cells. However, our definition of adult or embryonic mDA neuron subtypes and our knowledge of the molecular mechanisms leading to their generation are very limited, hampering further progress in this field.

In a previous study, we examined the development of the human midbrain by single-cell RNA-sequencing (scRNA-seq) and defined the presence of multiple lineages and cell types, including 3 subtypes of mDA neurons (La Manno et al., 2016). More recently, Kamath et al (2022) examined the adult human substantia nigra by scRNA-seq in postmortem samples and identified 10 different subtypes of mDA neurons, including a primate-specific subtype and a subtype predominantly affected in PD.
In this study, we performed a detailed analysis of mDA neurons in vivo, in both embryonic and adult tissues, at single-cell resolution. Our results unravel a greater diversity of prenatal mDA neurons, and a higher complexity of adult mDA neuron subtypes than previously reported. By understanding the heterogeneity of mDA neurons in development and adult stages, as well as the developmental cascades leading to their generation, a more precise roadmap for the generation specific mDA neuron subtypes relevant for PD modeling or cell replacement therapy is now available. In addition, our results provide essential standards to allow researchers assessing the purity and quality of mDA neuron cell preparations for medical or biomedical applications.

P01.16

Parkinson's disease is associated with large-scale microbial dysbiosis which may promote disease progression

Avril Metcalfe-Roach[1], Mihai Cirstea[1], Adam Yu[1], Hena Ramay[2], Davide Martino[2], Laura Sycuro[2], Silke Appel-Cresswell[1], B. Brett Finlay[1]*
[1] University of British Columbia, Vancouver, BC, Canada
[2] University of Calgary, Calgary, AB, Canada

Background: Parkinson's disease (PD) is reproducibly associated with changes to the gut microbiome, including reduced short-chain fatty acid-producing bacteria and altered carbohydrate metabolism. We previously used 16S sequencing to show that certain disease-associated taxa correlate with the abundance of toxic proteolytic metabolites, though the significance of microbial changes with respect to disease etiology remains unclear. In the current study, we utilize metagenomic sequencing to characterize taxonomic and functional changes to the PD microbiome and to explore their relation to metabolites and disease progression.
Methods: 300 participants (197 PD, 103 controls) attended ≤5 yearly study visits in order to track the progression of motor and nonmotor symptoms, including depression and fatigue. Stool (n=300) and blood serum (n=125) were collected at baseline and processed for metagenomics and metabolomics, respectively.
Results: PD-derived stool samples had reduced microbial connectivity and nine differentially-abundant species compared to controls. Hexuronate degradation-related pathways were depleted, which was driven by Faecalibacterium prausnitzii, and other pathways correlated strongly with proteolytic metabolites. Other functional changes suggest gut environment alterations which may drive certain dysbioses and impede gut barrier function. Blautia obeum and Blautia wexlerae trended with faster and slower disease progression, respectively.
Conclusion: The Parkinsonian microbiome is significantly altered at the community and species level, with potential implications for disease progression. Dysbiosis of the gut environment as seen in PD may influence the abundance and phenotype of resident bacteria, potentially impacting the efficacy and safety of probiotic therapeutics.

P01.17

β-adrenoreceptor drugs and incidence of Parkinson's disease in women from the French E3N cohort study

Thi Thu Ha Nguyen[*,1], Agnès Fournier[1], Émeline Courtois[2], Fanny Artaud[1], Sylvie Escolano[2], Pascale Tubert-Bitter[2], Isabelle Degaey[1], Emmanuel Roze[3], Ismaïl Ahmed[2], Anne C.M. Thiébaut[2], Alexis Elbaz[1]*

[1] Université Paris-Saclay, UVSQ, Univ. Paris-Sud, INSERM U1018, Team « Exposome, heredity, cancer and health », CESP, 94807, Villejuif, France, Villejuif, France

[2] Université Paris-Saclay, UVSQ, Univ. Paris-Sud, INSERM U1018, Team « High-dimensional biostatistics for drug safety and genomics », CESP, 94807, Villejuif, France, Villejuif, France

[3] Sorbonne Université, AP-HP, Hôpital Pitié-Salpêtrière, Département de Neurologie, Paris, France; INSERM U1127, CNRS 7225, Institut du Cerveau, Paris, France, Paris, France

Given the increasing prevalence of Parkinson's disease (PD), there is an urgent need to identify therapies to slow its progression and delay, or even prevent, its onset. Repurposing available drugs indicated for other diseases represents a promising strategy. Some previous studies suggested that β2-adrenoreceptor agonists (β2AA) mainly indicated for asthma were associated with reduced PD incidence, but the evidence is so far conflicting.

The aim of our project was to examine the association between β2AA use and PD incidence in a large cohort of French women followed over 15y. We also examined β-adrenoceptor blockers (β-blockers, primarily indicated for cardiovascular diseases). We used data from the E3N cohort study of French women followed since 1990. Our analyses are based on women (mean age=63y) alive and free of PD on 01/01/2004 (when drug claims databases became available) and followed until 31/12/2018. Incident PD patients were ascertained using multiple sources and validated by experts. We compared PD incidence in women who initiated either β2AA or β-blockers (>1 prescription, ever users) during the follow-up and in other women (never users). Given the prodromal PD phase, drug exposure was assessed up to 5y prior to PD diagnosis to reduce the risk of reverse causation. Analyses were adjusted for numerous confounders, in particular drugs indications to reduce the risk of indication bias.

For β2AA, 579 of 81,890 women developed PD and 15,169 started using β2AA. Compared to never users, PD incidence was significantly reduced by ~35% in ever users in analyses with a 5y-lag. Regarding β-blockers, 552 PD cases and 13,081 ever users were identified among 75,896 women. In analyses without a lag, PD incidence was increased by ~35% in ever users of β-blockers compared to never users but this association was no longer significant in analyses with a 5y-lag.

Our findings are in agreement with the hypothesis that β2AA may have a beneficial role in PD that needs to be confirmed in clinical trials. Alternatively, the association between β-blockers and PD is likely due to reverse causation because β-blockers may be used to treat tremor in the years before PD diagnosis.

P01.19

Update on PD GUT metagenome

Haydeh Payami[*,1], Gwendolyn Cohen[1], Stewart Factor[2], Eric Molho[3], Timothy Sampson[2], David Standaert[1], Zachary Wallen[1], Cyrus Zabetian[4]*

[1] University of Alabama at Birmingham, Birmingham, AL, United States

[2] Emory University, Atlanta, GA, United States

[3] Albany Medical College, Albany, New York, United States

[4] University of Washington, Seattle, WA, United States

Background: Some PD cases may start in the gut and spread to the brain. In a recent study of gut metagenome, we reported a newly enrolled large dataset with 490 persons with PD (PwP) and 234 neurologically healthy controls (NHC), analyzed using deep shotgun sequencing (ref.1). We found widespread dysbiosis causing imbalances in carbohydrates and SCFA metabolism, synthesis and degradation of neuroactive molecules, overproduction of neurotoxicants, depletion of neuroprotective molecules, and overabundance of opportunistic pathogens. Here, we present another independent dataset with equally large sample size (526 PwP, 316 NHC) and high-resolution deep shotgun sequences. First, we replicate the findings of dataset 1 in dataset 2, then embark on analysis of two datasets combined.

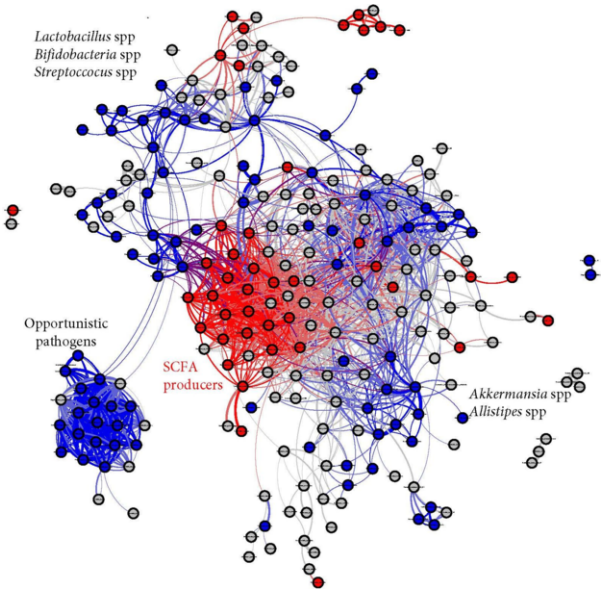
Methods: Study was conducted using standard methods from start to end by a single team of investigators (NGRC). Subjects were enrolled at four sites in the U.S. during 2014-2020. DNA was extracted from stool and deep-sequenced (50M reads/sample). Sequences were processed using bioBakery and analyzed using MaAsLin2, ANCOM-BC, and SparCC (see ref.1 for details as methods are kept consistent).

Results: Based on dataset 1, we reported 84 species as being elevated or depleted in PD (ref.1). In dataset 2, 80% of PD-associated species replicated with statistical significance, 6% trended, 14% did not replicate. Network of polymicrobial clusters, including SCFA producers, probiotic Lactobacillus and Bifidobacterium species, and opportunistic pathogens were replicated. Intra-genus heterogeneity was replicated. Imbalances in microbial pathways and genes that result in overabundance of LPS, LPP and TMA, and depletion of SCFA, dopamine, glutamate, and nicotinamide were also replicated. Increase in E. coli, its immunogens and curli were not replicated. We have only begun the combined analysis. It is readily clear that doubling the N reduces the noise considerably, streamlines and brings more clarity to the structure and correlation of polymicrobial networks. The added information content, going from N~700 in ref.1 to N~1500 subjects in pooled data, is substantial.

Conclusion: We will present results of two unprecedentedly large and high-resolution datasets side-by-side, which will demonstrate extent and the drivers of dysbiosis, reproducibility, and information content of gut metagenome for PD research, treatment, and prevention.

Ref.

[1] Nat Commun. 2022 Nov15. PMID:36376318.



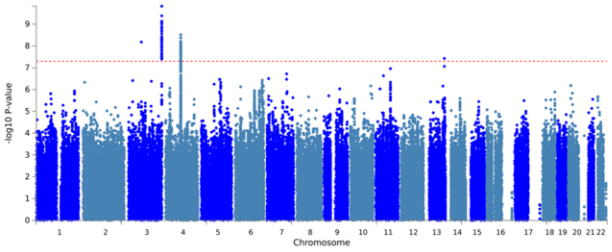
P01.20

Genome wide association studies using SNP1 reveals new associated genes with Parkinson Disease in a Latino Cohort

Thiago Peixoto Leal[1], Miguel Inca-Martinez[1], Emily Mason[1], Douglas Loesch[2], Andrea RVR Horimoto[3], Elif Sarihan[1], Mario Cornejo-Olivas[4], Luis Torres[5], Pilar Mazzetti[4], Carlos Cosentino[5], Elison Sarapura-Castro[4], Andrea Rivera-Valdivia[4], Angel C. Medina[6], Elena Dieguez[7], Victor Raggio[8], Andres Lescano[8], Vitor Tumas[9], Vanderci Borges[10], Henrique B. Ferraz[10], Carlos R. Rieder[11], Artur Schumacher-Schuh[12], Bruno L. Santos-Lobato[13], Carlos Velez-Pardo[14], Marlene Jimenez-Del-Rio[14], Francisco Lopera[14], Sonia Moreno[14], Pedro Chana-Cuevas[15], William Fernandez[16], Gonzalo Arboleda[16], Humberto Arboleda[16], Carlos E. Arboleda-Bustos[16], Dora Yearout[3], Cyrus P. Zabetian[3], Timothy A. Thornton[3], Timothy D. O'Connor[17], Ignacio F. Mata[1], the Latin American Research Consortium on the Genetics of Parkinson's Disease (LARGE-PD)[1]*

[1] Cleveland Clinic, Cleveland, Ohio, United States
[2] University of Maryland, Baltimore, Maryland, United States
[3] University of Washington, Seattle, Washington, United States
[4] Instituto Nacional de Ciencias Neurologicas, Lima, Peru
[5] Universidad Peruana Cayetano Heredia, Lima, Peru
[6] Universidad Nacional del Altiplano, Puno, Peru
[7] Universidad de la República, Universidad de la República, Uruguay
[8] Universidad de la República, Montevideo, Uruguay
[9] Universidade de São Paulo, Ribeirão Preto, Brazil
[10] Universidade Federal de São Paulo, São Paulo, Brazil
[11] Universidade Federal de Ciências da Saúde de Porto Alegre, Porto Alegre, Brazil
[12] Universidade Federal do Rio Grande do Sul, Porto Alegre, Brazil
[13] Universidade Federal do Pará, Belém, Brazil
[14] Universidad de Antioquia (UdeA), Medellín, Colombia
[15] Universidad de Santiago de Chile, Santiago, Chile
[16] Universidad Nacional de Colombia, Bogotá, Colombia
[17] University of Maryland School of Medicine, Baltimore, United States

Objective: Our objective was using SNP1, a tool that performs a Genome Wide Association Study (GWAS) including Local Ancestry (LA) information, in Parkinson Disease (PD) using data from Latin American Research consortium on the Genetics of PD. LA is the inference of genetic ancestry of a particular chromosomal region of an individual.
Background: GWAS have identified several loci in associated with PD, but these studies were performed, for the most part, in European and Asian populations, leading to a limited understanding of the genetic component in other populations. We recently performed the first PD GWAS [1] in Latin American cohort, but the methods employed did not use LA, which could lead to a loss of statistical power due to the genetic heterogeneity.
Methods: We performed genetic quality control (QC), inferred the relatedness between the individuals and those at greater than second degree were removed. We inferred the LA in the remaining samples using RFMix and African, European and Native-American samples from 1000 Genomes as reference [2]. We also imputed the QC data using TOPMed imputation server and variants with quality score (r^2) < 0.8 were removed. We performed the GWAS analysis using the SNP1 implemented on admix-kit [3] (Figure 1).
Results: We identified four risk loci: The rs73841264 is inside ROBO2 gene, that encodes a protein that perform axon guidance functions to regulate brain wiring broadly throughout the nervous system, which includes midbrain dopamine neurons, and it is also involved in other functions on the neurons [4]. The rs78820950 is near the NRROS gene and it was observed in Loesch et al. 2021 with suggestive p-value. The rs28647362 is inside the SNCA gene. The rs951706337 is near the FAM155A gene.
Conclusion: The inclusion of LA boosted the results from our previous GWAS and allowed us find three new genes associated with PD (ROBO2, NRROS and FAM155A) and reinforced association with the SNCA gene. These results highlights the importance to properly deal with these evolutionary forces when dealing with admixed populations such as Latin Americans.
[1] PMID: 34227697
[2] PMID: 36055201
[3] PMID: 34824480
[4] PMID: 28394253



P01.21

Differences in cytochrome P450s genes between genetically predisposed Parkinson's disease individuals with and without disease signs

Polina Petkova-Kirova[*1], Stephan Baas[2], Gudrun Wagenpfeil[3], Marcus Unger[2], Rita Bernhardt[1]*

[1] Institut für Biochemie, Fachbereich Biologie, Universität des Saarlandes, Saarbrücken, Germany
[2] Klinik für Neurologie, SHG Kliniken Sonnenberg, Saarbrücken, Germany
[3] Institut für Medizinische Biometrie, Epidemiologie und Medizinische Informatik, Universität des Saarlandes, Homburg, Germany

While the majority of Parkinson's disease cases are of idiopathic origin, about 5-10% are familial and linked to mutations in genes like LRRK2, SNCA, PRKN and others. Interestingly, not all genetically predisposed individuals develop the disease and the question arises as to where the difference lies. Cytochromes P450 (CYPs) are involved in the biotransformation of toxic compounds and in many physiological processes. In previous research, by using the PPMI (Parkinson's Progression Markers Initiative) database and statistical analysis, we were able to show that single nucleotide polymorphisms (SNPs) in human CYPs and their three redox partners (cytochrome P450 reductase (POR), adrenodoxin reductase (AdR) and adrenodoxin (Adx)) are associated with the expression of PD in idiopathic and genetically predisposed patients. We demonstrated that SNPs in 26 out of the 57 human CYPs and in 2 out of their 3 redox partners are related to PD with odd ratios (OR) values >5. In the present research, using the same approach, we evaluated the differences in the SNPs of the 57 CYPs, POR, AdR and Adx between individuals, who are genetically predisposed and develop PD (GPD patients) and those, who are genetically predisposed, but do not develop the disease (GUN patients). We found that 50 out of 57 CYPs and 2 redox partners out of 3 have SNPs being different between GUN and GPD patients with 11 CYPs having SNPs with OR ratios above 5. Interestingly, CYPs involved in drug and xenobiotic metabolism are not found among the latter, suggesting that the conversion of toxic compounds does not play a very significant role in differentiating between GPD and GUN patients, although it does when comparing GPD patients and healthy controls. In contrast, SNPs in CYPs involved in fatty acid, eicosanoid, sterol and vitamin metabolism show OR values >5,

pointing to a more prominent role of intrinsic physiological processes in the expression of the disease.
This work was supported by a research grant from the “Dr. Rolf M. Schwiete Stiftung” Mannheim/Germany. The work was made possible by accession to the PPMI database.

P01.22

High-throughput proteomics in the study of Parkinson’s disease progression

Raquel Real[*,1], Laura Winchester[2], Alejandro Martinez-Carrasco[1], Michael A Lawton[3], Yoav Ben-Shlomo[3], John Hardy[1], Alejo Nevado-Holgado[2], Donald G Grosset[4], Huw R Morris[1]*
[1] University College London, London, United Kingdom
[2] University of Oxford, Oxford, United Kingdom
[3] University of Bristol, Bristol, United Kingdom
[4] University of Glasgow, Glasgow, United Kingdom

Background: Parkinson’s disease (PD) presents with a constellation of motor and non-motor symptoms, but disease severity and progression are heterogeneous. The factors that contribute to disease heterogeneity are still incompletely understood. High-throughput proteomic studies have the potential to identify proteins relevant for disease progression.
Objectives: We aimed to identify a proteomic signature associated with progression to dementia in PD.
Methods: Using an aptamer-based assay (SomaScan® assay, v4.0), we measured the baseline levels of more than 4,000 serum proteins in PD cases from the UK-based longitudinal Tracking Parkinson’s cohort. After standard quality control steps, 3,381 aptamers and 748 samples were available for analysis. We performed linear regression to explore if genetic variants of interest (such as in APOE and GBA) were associated with differential serum protein expression. Gene enrichment analysis was carried out using Metascape. We also performed survival analysis using a Cox proportional hazard model adjusted for sex, age and disease duration at baseline. The endpoints were defined as dementia or all-cause mortality, and false discovery rate (FDR)-corrected P-values <0.05 were considered significant.
Results: 748 PD patients with a mean age at onset of 67.3 +- 8.8 were analysed. Mean disease duration to study baseline was 1.3 +- 0.9 years. Nine percent of the PD cases developed dementia and 5.9% died during follow-up. Nineteen proteins were differentially expressed in carriers of the APOE e4 allele compared to non-carriers, with enrichment of proteins involved in the regulation of intracellular transport, lipid 66ennsylvania and endocytosis. The survival analysis using dementia as the endpoint identified five proteins upregulated in PD dementia, including UNC13A. Using mortality as the endpoint, the survival analysis identified several proteins differentially expressed, including an enrichment in proteins associated with the regulation of insulin-like growth factor transport and uptake.
Discussion: Preliminary results have identified UNC13A as being associated with progression to dementia in PD. This protein plays a role in neurotransmitter release at excitatory synapses and has been identified as a risk factor for both ALS and fronto-temporal dementia, suggesting common mechanisms between neurodegenerative disorders.

P01.25

Parkinson Disease in women: How does sex affect motor and non-motor symptoms?

Francisca Ruiz Gonzalez[*,1], Silvia Enriquez Calzada[2], Daniela Samaniego Toro[2], Helena Xicoy[2], Sara Belmonte[3], Miquel Vila[2,4], Jorge Hernandez-Vara[3], Ariadna Laguna[2,5]*
[1] Fundacion de Gen, Santa Cruz de Tenerife, Gran Canaria, Spain
[2] Neurodegenerative Diseases Research Group, Vall Hebron Research Institute (VHIR)- Network Center for Biomedical Research in Neurodegenerative Diseases (CIBERNED), Barcelona, Catalonya, Spain
[3] Neurology department, Movement Disorders Unit, Vall Hebron University Hospital, Barcelona, Spain
[4] + Aligning Science Across Parkinson’s (ASAP) Collaborative Research Network, Chevy Chase, MD, USA + Institut de Neurociències (Inc), Universitat Autònoma de Barcelona (UAB), Barcelona, Spain. + Department of Biochemistry and Molecular Biology, Autonomous University of Barcelona, Barcelona, Spain + Catalan Institution for Research and Advanced Studies (ICREA), Barcelona, Spain
[5] + Aligning Science Across Parkinson’s (ASAP) Collaborative Research Network, Chevy Chase, MD, USA + Institut de Neurociències (Inc), Universitat Autònoma de Barcelona (UAB), Barcelona, Spain

Background and Objective: Parkinson’s disease (PD) is a neurodegenerative disorder causing a variety of motor and non-motor symptoms, 66ennsylva 1,4 times more frequently in men. Differences between men and women in the natural progression of the disease and in the contribution of protective and deleterious factors are not well understood. Overall, women experiences are not always considered in clinical management, research studies and clinical trials. We aimed to collect women health experiences in order to assess the impact of female sex in PD symptoms.
Methods: We designed an online questionnaire considering the four phases of women’s reproductive and 66ennsylvani periods to explore the association between female sex and PD severity of motor and non-motor symptoms.
Results: A total of 290 surveys were included. The mean age at diagnosis was 49,5 years old (±11.5; range 18-75). At the time of answering the survey, 64 (22%) women were in the reproductive phase of their lifes, 50 (17,2%) in the perimenopause, 42 (14,5%) in the menopause, and 134 (46,2%) in the post menopause. The presence of digestive, swallowing and urinary problems correlated with the phase of life. Around half of the participants (n=144) reported fluctuations of symptoms, mainly motor, irrespective of their life phase. A 69% (44) of women diagnosed during reproductive age reported observing changes in their symptoms and response to medication during their menstrual cycle, particularly during the week of menstruation. On the other hand, 63% (31) of the menopause participants reported no changes in syntomatology, and 77% (10) of those receiving hormonal replacement therapy reported no symptom improvements.
Conclusions: The results obtained in this descriptive study broaden our knowledge of sex differences in PD and highlight the importance of understanding changes in symptoms during the menstrual and menopause cycles, contributing to build new lines of investigation to improve patients life quality.

P01.26

Persistent microgliosis and neurodegenerative processes in a SARS-CoV-2-model

Cara Schreiber[*,1], Christopher Käufer[2], Anna-Sophia Hartke[2], Ivo Wiesweg[2], Stephanie Stanelle-Bertram[3], Sebastian Beck[3], Nancy Mounogou Kouassi[3], Berfin Schaumburg[3], Gülsah Gabriel[3], Franziska Richter[1]*

[1] Department of Pharmacology, Toxicology and Pharmacy, University of Veterinary Medicine Hannover; Center for Systems Neuroscience, Hannover, Germany

[2] Department of Pharmacology, Toxicology and Pharmacy, University of Veterinary Medicine Hannover, Hannover, Germany

[3] Leibniz Institute for Experimental Virology, Hamburg, Germany

(1) **Introduction:** COVID-19 leads to neurological symptoms in up to 76% of the patients. Persisting symptoms far beyond recovery are common in many patients and point towards a progression of neurological impairment. Neuroinflammation post viral infection is a potential risk factor for the development of neurodegenerative diseases such as Parkinson's Disease (PD) and Alzheimer's Disease (AD).

(2) **Aims:** We examined the impact of COVID-19 on neuroinflammatory and neurodegenerative processes in hamster brains during and post SARS-CoV-2 infection. Hamsters showed mild to moderate symptoms, representing the clinical symptoms of most human patients. Our aim was to investigate whether a SARS-CoV-2 infection could lead to processes associated with neurodegenerative diseases such as PD or AD. First results were recently published (Käufer et al. 2022). Here we present further follow up analysis.

(3) **Methods:** 8 to 10 weeks old hamsters were intranasally infected with 10^5 PFU SARS-CoV-2 solved in PBS (mock-infected: only PBS) under BSL-3 conditions. The animals were euthanized 3, 6, 14 and 21 days post infection. Afterwards, brain sections were analyzed via immunohistochemistry.

(4) **Results:** Although, we found no viral proteins in the brain parenchyma, there was persisting microgliosis after viral clearance. This finding is of special interest due to the fact, that viral infections and progressive neuroinflammation are risk factors for PD and AD. Histological evaluation indicated alterations of the neuronal homeostasis, which are associated with neurodegenerative diseases.

(5) **Conclusions:** The results indicate that a SARS-CoV-2 infection is a potential risk factor for neurodegenerative diseases such as AD and PD.

P01.27

What causes Parkinson's Disease?

*Jennifer Thornton**
Shy Family, Lincoln, CA, United States

Parkinson's disease and Lewy body Disease can now be diagnosed by a simple skin biopsy that is 95% to 99% accurate. For years, our family has found that the cause of our loved ones skin issues were the cause of his diagnosis. Through research, meeting with dozens of doctors and personal experience we have found that a mite caused his skin issues. Mites cause spinal injury, reduced gut motility, lack of smell, and sleep issues. Little is studied about acariasis in the human body where mites have been reported to attack the urinary, otic, pulmonary, intestinal, oral (anaphylaxis), and vaginal systems. Mites also cause bullous arthropod bite reactions sometimes identified as senile hemangiomas on people who are sensitive individuals with hypersensitivity immune reaction to insect saliva. Symptoms show up twenty years prior to diagnosis. Most cases of Parkinson are not hereditary. Brain cells start dying off due to abnormal alpha-synuclein causing the clumping in Nerve cells resulting in the symptoms of Parkinson's Disease. A team of researchers at the University of Texas at Arlington have found hard evidence of horizontal DNA transfer, which is the swapping of genetic material between non-mating species – between some parasites and their vertebrate hosts. We believe that a research study could prove our theory that alpha-synuclein is turning abnormal after a bite from a mite.

P01.28

The DRD4 gene polymorphism is associated with the severity of impulse control disorder using dopamine agonists in Parkinson's disease

Viviana Torres Ballesteros[*,1], Mario Ezquerra[2], Jesica Perez[2], Ruben Fernandez-Santiago[2], Manel Fernandez[2], Francesc Valldeoriola[1]*

[1] Parkinson's Disease and Movement Disorders Unit-Neurology Service, Hospital Clinic, Barcelona, Cataluña, Spain

[2] Lab of Parkinson disease and other Neurodegenerative Movement Disorders: Clinical and Experimental Research, Institut d'Investigacions Biomèdiques August Pi I Sunyer (IDIBAPS), Barcelona, Spain

Background: Using dopamine agonists (DA) has been recognized as the major risk factor for impulse control disorder (ICD). However, not all patients using DA develop ICD, or it appears in a broad spectrum of severity which can suggest an environmental or genetic predisposition.

Several neurotransmitter genes have been linked to ICD susceptibility, and in the dopaminergic system the DRD4 gene is a studied candidate, characterized by a variable number of tandem repeats (VNTR) varying from 2 to 11 repeats. Individuals carrying at least one allele of 7-repeat or more (7R+) demonstrate an increased risk for compulsive and addictive behaviors, neuropsychiatric diseases, personality traits as novelty-seeking, financial risk, and binge eating or gambling after dopaminergic stimulation.

We aimed to evaluate the association between the DRD4 VNTR and the appearance of ICD in PD patients using DA.

Methods: We studied 241 PD patients using DA. 145 men (63.9%) and 87 women (36.1%). We defined development of an ICD as a positive score on the Questionnaire for Impulsive-Compulsive Disorders in Parkinson's Disease. We considered a severe ICD consequence as the occurrence of family or work dysfunctions, hypersexuality that affects the couple and their environment, prostitution, weight gain greater than 5 kg, and financial insolvency. DNA was extracted from peripheral blood. The DRD4 48-bp VNTR was characterized by a PCR amplification procedure.

Results: ICD was reported in 104 patients (43.15%), 29 women (12.03%), and 75 men (31.12%). The most frequent type of ICD was hypersexuality (17.01%). DRD4 7R+ was reported in 29 (12.03%) patients with ICD. Kaplan-Meier analysis showed sex and age of PD onset was related with ICD appearance (figure). Cox analysis adjusting for age at PD onset, sex, and LEDD revealed no effect of DRD4 polymorphism (P=0149) on ICD appearance but was significant in relation with severe consequences of ICD. HR 1.875. Longrank test P: <0.018.

Conclusion: PD patients using DA and carrying DRD4 7R+ present severe ICD consequences. Our results support the genetic susceptibility of ICD and may allow to consider a clinical – genetic therapeutic approach, avoiding the use of dopamine agonists in subpopulations at genetic risk of ICD.

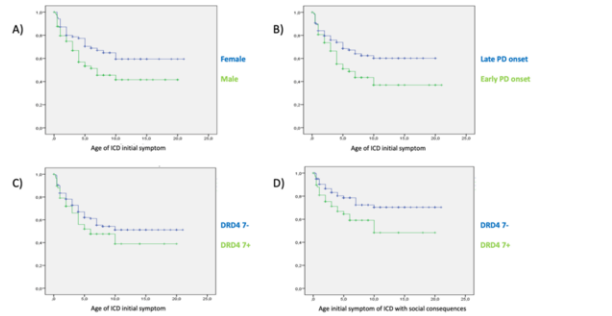


Figure. Kaplan-Meier curve of cumulative incidence of PD patients treated with DA until impulse control disorder (ICD) appearance or censoring date, taking into account **A)** sex (P value=0.009), **B)** age at PD onset (P value=0.005) and DRD4 VNTR 48 bp polymorphism, **C)**. Cox analysis adjusting for age at PD onset, sex, and LEDD revealed no effect of DRD4 polymorphism (P=0149) on ICD appearance, **D)** but was significant when specifically analyzed ICD with serious social consequences P value=0.01. N= 241 treated PD patients. Age at PD onset was defined dichotomizing sample according the median cutoff (early ≤53 years, late > 53 years). DRD4 was dichotomized based on presence or absence of any allele of risk 7 repeats of higher (7- or 7+).

P01.29

Nuclear functions of alpha-synuclein in DNA double-strand break repair

Moriah Arnold[1], Dorthe Payne-Larsen[2], Pamela Cassidy[1], Stephan Witt[3], Vivek Unni[,1]*
[1] Oregon Health & Science University, Portland, Oregon, United States
[2] Danish Cancer Society Research Center, Copenhagen, Denmark
[3] Louisiana State University Health Shreveport, Shreveport, Louisiana, United States

Pathologic aggregation of the protein α-synuclein (α-syn) is tightly associated with several neurodegenerative diseases for which there are no disease-modifying therapies, including Parkinson's Disease (PD), Multiple System Atrophy and Dementia with Lewy Bodies. Although different biochemical and cellular pathways related to α-syn biology have been implicated in neurodegeneration, we still lack a clear understanding of how abnormalities associated with this protein cause neuronal dysfunction and cell death in PD and related diseases. Recently published studies from our lab have unexpectedly suggested a role for α-syn within the cell nucleus in DNA binding and repair. We have documented a functional role for α-syn in the repair of nuclear DNA double-strand breaks (DSBs) via the non-homologous end-joining (NHEJ) pathway and that this function might be compromised in Lewy Body-containing neurons. Our more recent data suggest α-syn could be important specifically in the nucleolar subcompartment of the nucleus for DSB repair. Using the human SK-Mel28 cell line, our data suggest that α-syn and the marker of DSB repair, γH2AX, are both preferentially enriched within the nucleolus and the colocalization between these two proteins is significantly greater in the nucleolus compared to the nucleoplasm. Knocking out α-syn significantly increases γH2AX levels within the nucleolus, and these levels are attenuated when α-syn is transgenically reintroduced into the knockout background. Within the nucleolus, αSyn significantly colocalizes with nucleophosmin and treacle, two proteins important for DSB repair of ribosomal DNA (rDNA). Inducing rDNA DSBs using the endonuclease I-PpoI significantly increases nucleolar γH2AX, α-syn and α-syn's colocalization with other proteins important for DSB repair. Lastly, knocking out α-syn significantly increases γH2AX levels after I-PpoI induction. These results suggest that α-syn may play an underappreciated role in the nucleolus, allowing cells to more faithfully repair DSBs within rDNA, thereby supporting cell survival in the presence of genotoxic stress.

P01.30

Non-motor symptoms of Parkinson's disease in Mexico: Case series

Xavier Vilchis, Jose Eduardo Solórzano Quiroz, Jose Antonio Fernandez, Alejandro Medardo Gonzalez*
Hospital Juarez de Mexico, Mexico City, State Mexico, Mexico

Abstract: Parkinson's disease (PD) is a chronic, progressive, disabling disorder characterized by the death of dopaminergic neurons in the substantia nigra pars compacta with alpha synuclein deposits with extrapyramidal (motor) signs that are necessary for diagnosis, however, there are inconspicuous non-motor symptoms (NMS) that are a key component of the disease and quality of life (Politis M et al Movement Disorders. 2010 14;25(11):1646-51).
Objective: To describe the MNS of patients with PD treated at the Hospital Juárez de México.
Methods: Retrospective, descriptive, cross-sectional study. Thirty-four patients who met inclusion, exclusion or elimination criteria in the period 2021-2022 were studied, using a 22-question questionnaire in search of MNS variables. Data were analyzed with IBM SPSS 25 for measures of central tendency for quantitative and qualitative variables.
Results: The demographic analysis showed a predominance of male gender (71%) with mean age 68 years (±10.7). The clinical study showed that the time of evolution was 6 years (±4.1), the scale to assess functionality was the Hoehn-Yahr scale where most patients (44%) were independent of the family (II) and only 3% had severe disability (V). NMS were present in the whole sample, since 60% had at least 10 symptoms, which in order of frequency were nocturia(55%), constipation(52%), unexplained pain(52%), sexual dysfunction(53%), insomnia(47%), depression(44%), anxiety (41%), vivid dreams(32%), salivation(32%), REM sleep disorders(29%), restless legs(26%), falls(23%), urinary urgency(20%), diaphoresis(17%), hallucinations(14%), apathy(11%), unexplained weight loss(11%), diaugesia/dyssomias (8%), dysphagia(8%) and fecal incontinence(5%).
Conclusions: Intentional search for NMS in PD is essential for care as only the minority do not present them and implies a continuous deterioration of quality of life that needs a multidisciplinary approach.

P01.31

Genetic findings of the Rostock International Parkinson's Disease (ROPAD) Study

Ana Westenberger[,1], Volha Skrahina[2], Tatiana Usnich[3], Christian Beetz[2], Eva-Juliane Vollstedt[4], Jefri J. Paul[2], Filipa Curado[2], Snezana Skobalj[5], Hanaa Gaber[2], Maria Olmedillas[2], Xenia Bogdanovic[2], Björn-Hergen Laabs[6], Najim Ameziane[2], Nathalie Schell[4], Krishna K. Kandaswamy[2], Inke König[6], Alexander Balck[4], Henrike Hanssen[4], Max Borsche[4], Ilona Csoti[7], Katja Lohmann[4], Meike Kasten[4], Norbert Brüggemann[4], Arndt Rolfs[2], Christine Klein[4], Peter Bauer[2]*
[1] Institute of Neurogenetics, University of Lübeck, Luebeck, Schleswig-Holstein, Germany
[2] Centogene GmbH, Rostock, Germany
[3] University of Lübeck, Lübeck, Germany
[4] Institute of Neurogenetics, University of Lübeck, Lübeck, Germany
[5] Cenogene GmbH, Rostock, Germany
[6] Institute of Medical Biometry and Statistics, University of Lübeck, Lübeck, Germany
[7] Parkinson-Center, Gertrudisklinik Biskirchen, Leun, Germany

The Rostock Parkinson's Disease (ROPAD) study is the largest and most comprehensive genetic screening study of monogenic Parkinson's disease (PD) to date. The study aimed to investigate

the frequency and spectrum of PD genetic causes in 51 genes that have an established or possible relevance to PD in a multiethnic cohort of 12,580 PD patients. The participants were not preselected for specific age at onset (AAO), family history, or inheritance pattern. The molecular diagnostic yield was 15%, with 1,871 patients receiving a genetic diagnosis of PD primarily based on GBA1 risk variants (10.4%), or pathogenic/likely pathogenic variants in LRRK2 (2.7%) or PRKN (0.9%). The remaining patients received a genetic PD diagnosis due to SNCA (0.2%), GCH1 (0.2%), and PINK1 (0.1%) variants or variants in one of 10 other genes (0.1%). Furthermore, dual genetic diagnoses (patients with variants in two PD-related genes) were made in ~0.3% of ROPAD participants. The 1,871 genetically diagnosed patients had a male-to-female ratio of ~1.4, median AAO of 55 years (36.7% had an AAO of ≤50 years), and positive family history in ~36% of cases. Compared to the cohort of patients who did not receive a genetic PD diagnosis, the male-to-female ratio and AAO were significantly lower and positive family history was significantly more frequent in the genetically diagnosed participants. Interestingly, 3.4% of patients carried a single heterozygous pathogenic/likely pathogenic variant in autosomal-recessive (AR) PD-related genes. Their median AAO was significantly lower than in patients who had no relevant variants in PD genes and significantly higher than in patients who received a genetic diagnosis of PD, supporting a distinct contribution of monoallelic variants in AR PD-related genes to PD heritability. About 0.6% of the ROPAD study participants had positive genetic testing findings in genes related to dystonia/dyskinesia or dementia. In addition to providing the most comprehensive and relevant insight into the frequency and spectrum of PD genetic causes to date, the ROPAD study, for the first time, allows for data-based, differential genetic counseling in different constellations of AAO and family history, leading pre- and post-test counseling to the next level of specificity and informing patient prioritization and stratification for clinical trials.

P01.32

Elevated trimethylamine (TMA) from the gut microbiota drives synuclein pathology and immune activation in Parkinson's disease

Zizheng Xian[*,1], Nanthini Jayabalan[1], Katherin Roper[1], Helen Woodhouse[1], John O'Sullivan[1], Robert Adam[1], Anumantha Kanthasamy[1], Gene Tyson[2], Richard Gordon[2]*
[1] University of Queensland, Brisbane, Queensland, Australia
[2] Queensland University of Technology, Brisbane, Queensland, Australia

Gastrointestinal (GI) dysfunction and increased GI permeability is a common feature of early-stage Parkinson's disease (PD). A growing body of evidence suggests that increased gut permeability and inflammatory seen in PD patients could be the consequence of gut microbiome dysbiosis. However, mechanisms and pathways that substantiate a causal relationship between the gut and the brain in PD onset and progression, are yet to be defined. Trimethylamine (TMA), a brain-permeable metabolite of bacterial-origin bears a positive association with the rate of PD progression. TMA is rapidly oxidized to Trimethylamine N-oxide (TMAO), which has been shown to disrupt the blood-brain barrier and systemic inflammation. In this study, we measured and compared levels of TMAO and its metabolites in both circulation (blood) and clearance (urine) in a cohort of healthy (n=44) and PD (n=46) individuals. We also performed the high-resolution shotgun metagenomics studies to assess GI-tract microbiome composition and functional pathway activation during PD. Our result indicated a significant elevation of pro-inflammatory TMAO levels in PD patients in both blood and urine. Surprisingly, we also uncovered elevated levels of neurotoxic Formaldehyde (FA), a downstream catabolite of TMA, in PD patients compared to healthy controls. Our high-resolution functional metagenomics studies demonstrate for the first time that TMA-generating bacteria, as well as bacterial enzymatic pathways responsible for its generation to be increased in PD patients. This included elevated Clostridium species Our mechanistic studies also revealed that circulating TMAO can accelerate synuclein aggregation and immune activation in microglia and PBMCs. We also uncovered a trend towards loss of beneficial bacteria which produce anti-inflammatory metabolites, such as butyrate, in PD patients. Taken together, our results provide novel mechanistic insights into how gut dysbiosis and altered microbial metabolism can drive disease progression in PD. If confirmed, these results would provide the therapeutic rationale for targeting microbial dysbiosis and GI dysfunction for disease modification in PD.

BASIC SCIENCE: Cell death, neuroprotection and trophic factors

P02.01

Apoptosis-related markers from peripheral blood mononuclear cells as potential biomarkers of Parkinson's disease

Mária Brodňanová[*,1], Michal Cibulka[1], Milan Grofik[2], Natália Huňarová[3], Andrea Ižarik Verešpejová[3], Egon Kurča[2], Martin Kolísek[1]*
[1] Biomedical Centre Martin, Jessenius Faculty of Medicine in Martin, Comenius University Bratislava, Martin, Slovakia
[2] Clinic of Neurology, Jessenius Faculty of Medicine and University Hospital in Martin, Comenius University Bratislava, Martin, Slovakia
[3] Department of Medical Biochemistry, Jessenius Faculty of Medicine in Martin, Comenius University Bratislava, Martin, Slovakia

Aim: The purpose of this study is to elucidate the involvement of apoptosis-related markers from peripheral blood mononuclear cells (PBMC) in the onset and development of Parkinson's disease (PD) and to decide on their suitability as biomarkers of the disease progression.
Background: PD is accompanied by the apoptosis process of both neuronal cells in specific regions of the brain and peripheral blood cells. Moreover, it has been speculated that markers of activated apoptosis of lymphocytes from PD patients could be associated with the severity and the duration of the disease and are significantly associated with the loss of dopaminergic 69ennsyl. PBMC from PD patients could possess typical neuropathological signs, might directly participate in pathological cascade leading to PD symptoms.
Subjects & Methods: 30 H-Y scale ½ PD patients (7/23 F/M ratio, mean age 64,7 ± 10,2), 30 H-Y scale ¾ patients with idiopathic PD (10/20 F/M ratio, mean age 63,9 ± 11,2) from the Center for Diagnostic and Therapy of Extrapyramidal Diseases at UHM and 59 gender and age matched control probands (17/42 F/M ratio, mean age 64,3 ± 10,5) were enrolled in our study. Isolated viable PBMC from peripheral venous blood were used to analyse the expression profile of 35 apoptosis-related proteins using proteome profiler Human Apoptosis Array Kit (R&D). Subsequently, the most eminent apoptosis-related markers were quantified by western blot analysis with specific antibodies.
Results: Cell lysates isolated from PBMC of PD patients and matched controls were investigated for the presence and relative level of specific apoptosis-related proteins. Based on the results of the proteome analysis, we decided to quantify nine of the most prominent apoptosis-related markers by utilizing Western blot analysis and to compare the expression profiles between groups. Among others, the initiator Caspase-8 and Caspase-9 and executioner Caspase-3 and Caspase-7 in both their total and active

forms. Results of quantification of these potentially clinically relevant will be presented at the conference. PBMC apoptosis-related proteins may serve as clinically relevant markers carrying predictive value in respect to the progression and severity of PD.
Acknowledgement: This study was supported by grant APVV-19-0222 to MK.

P02.02

The repositioning of pomalidomide as a novel disease-modifying drug: Evidence from the alpha synuclein based rodent model of Parkinson's disease
Anna R Carta*[,1], Maria Francesca Palmas[1], Michela Etzi[1], Augusta Pisanu[2], Chiara Burgaletto[3], Maria Antonietta Casu[4], Alfonso De Simone[5], Giuseppina Cantarella[3], Nigel Greig[6]
[1] Department of Biomedical Sciences, University of Cagliari, Cagliari, Italy
[2] National Research Council, Institute of Neuroscience, Cagliari, Italy
[3] Department of Biomedical and Biotechnological Sciences, University of Catania, Catania, Italy
[4] National Research Council, Institute of Translational Pharmacology, Cagliari, Italy
[5] Department of Pharmacy, University of Naples "Federico II", Naple, Italy
[6] Drug Design & Development Section, Translational Gerontology Branch, Intramural Research Program, National Institute on Aging, National Institutes of Health, Baltimore, MD, United States

The drug repositioning is currently a valuable strategy in the quest for disease modifying drugs in Parkinson's disease, due to the high cost and low success rate of new drug development. Based on the recognized dysregulation of the immune response in PD, which is characterized by chronic CNS infiltration of peripheral immunocytes and neuroinflammation bringing about neuronal damage, we tested the disease-modifying properties of the immunomodulatory imide drug (ImiD) pomalidomide. We used a translational rat model of PD based on the intranigral bilateral infusion of toxic oligomers of human α-synuclein (H-αSynOs), which largely reproduces cardinal neuropathological and symptomatic features of the first stage of disease progression including motor and non motor symptoms, dopaminergic degeneration, alpha-synuclein aggregates and neuroinflammation in critical brain areas. Pomalidomide was chronically administered for two-months (20 mg/kg; i.p. three times/week) and symptomatic as well as neuropathological parameters were measured thereafter.
The intranigral infusion of H-αSynOs induced an impairment in motor performance that was fully rescued by pomalidomide, as assessed via a battery of motor tests modelling different aspects of the disease, including the beam traversal test, the gait test and the vermicelli test. Moreover, H-αSynOs-infused rats displayed a 40–45% cell loss within the substantia nigra (SN), as measured by stereological counting of TH+ and Nissl-stained neurons, that was largely abolished by pomalidomide. The inflammatory response to H-αSynOs infusion and the pomalidomide treatment was evaluated both in CNS and peripherally. A reactive microgliosis was present in the SN three months after H-αSynOs infusion, with cells displaying a pro-inflammatory profile and TNF-α overproduction. Importantly, the pomalidomide treatment profoundly affected the phenotype of reactive microglia, which displayed an anti-inflammatory profile, with decreased TNF-α production and an increase of the anti-inflammatory cytokine IL-10. Moreover, the H-αSynOs infusion induced a dysregulation of serum cytokine content, with elevated levels inflammatory cytokines and chemokines, that was largely restored by pomalidomide.
We provide comprehensive evidence that pomalidomide mitigates PD symptoms via neuroprotective activity in a neuropathological model of PD, and support the clinical testing of this drug for repositioning as a novel disease-modifying strategy in PD.

P02.03

Identification of new neuroprotective molecules
Joanna Fombonne[*,1], Kristina Radkova[2], Erika Cosset[2], Merja Voutilainen[3], Catherine Guix[2], Mart Saarma[3], Patrick Mehlen[2]*
[1] CRCL – UMR5286/INSERM1052, Lyon, France
[2] Cancer Research Center of Lyon – INSERM1052/UMR5286, Lyon, France
[3] University of Helsinki, Helsinki, Finland

Objectives: One of the major therapeutic challenges in Parkinson's disease is to slow down or stop dopaminergic neurons degeneration. To this end, we identified neuroprotective molecules acting as survival cue through a particular class of receptors, called dependence receptor. Indeed, these receptors are promising target since they induce cell survival in the presence of their corresponding ligand/survival molecule whereas they trigger cell death in their absence. Given that such dependence receptors are expressed by dopaminergic neurons, we tested the survival effect, and larger, the neuroprotective role of different ligands. We also search for mimetics of these neuroprotective molecules for therapeutic aims.
Methods: The protective effect of the molecules was assessed in vitro and in vivo. Primary cell cultures and differentiated iPS cells into dopaminergic neurons has been used upon rotenone or 6-hydroxydopamine (6OHDA) stress. As in vivo model, we used 6-OHDA injured rat which mimics the progressive neurodegeneration that occurs during Parkinson's disease.
Results: We identified a promising neuroprotective molecule able to rescue specifically dopaminergic neurons from rotenone and 6-OHDA-induced cell death and to improve the 6-OHDA injured rat phenotype. More importantly, we are currently developing a mimetic of this molecule which could lead to clinical applications.

P02.04

Male sex bias in Parkinson's disease is linked to an accelerated age-dependent neuromelanin accumulation
Camille Guillard Sirieix[*,1], Jordi Romero-Giménez[2], Thais Cuadros[1], Annabelle Parent[1], Ariadna Laguna[3], Miquel Vila[4]*
[1] Vall d'Hebron Research Institute (VHIR)-Center for Networked Biomedical Research on Neurodegenerative Diseases (CIBERNED), Barcelona, Spain; Aligning Science Across Parkinson's (ASAP) Collaborative Research Network, Chevy Chase, MD 20815, USA, Barcelona, Spain
[2] Vall d'Hebron Research Institute (VHIR)-Center for Networked Biomedical Research on Neurodegenerative Diseases (CIBERNED), Barcelona, Spain
[3] Vall d'Hebron Research Institute (VHIR)-Center for Networked Biomedical Research on Neurodegenerative Diseases (CIBERNED), Barcelona, Spain; Aligning Science Across Parkinson's (ASAP) Collaborative Research Network, Chevy Chase, MD 20815, USA; Autonomous University of Barcelona, Cerdanyola del Vallès, Barcelona, Spain, Barcelona, Spain
[4] Vall d'Hebron Research Institute (VHIR)-Center for Networked Biomedical Research on Neurodegenerative Diseases (CIBERNED), Barcelona, Spain; Aligning Science Across Parkinson's (ASAP) Collaborative Research Network, Chevy Chase, MD 20815, USA; Autonomous University of Barcelona, Cerdanyola del Vallès, Barcelona, Spain; Catalan Institution for Research and Advanced Studies (ICREA), Barcelona, Spain

Background: Men have a higher incidence and prevalence of Parkinson's disease (PD), earlier disease onset, more severe motor

symptoms, and more frequent cognitive decline compared to women. However, most PD studies do not consider the influence of sex, thus the molecular mechanisms underlying sex differences in PD remain largely unknown. Estrogens modulate dopaminergic pathways and improve PD symptoms in both men and women. Estrogens are also able to modulate melanin production in the skin and we have reported that age-dependent intracellular neuromelanin (NM) accumulation above a pathogenic threshold triggers PD pathology in rats overexpressing melanin-producing enzyme tyrosinase (TYR).
Objectives: We assessed whether differences in nigral NM production/accumulation could underlie the differential effect of sex on PD.
Methods: First, using postmortem human brain tissue, we compared intracellular NM levels in the substantia nigra (SN) of both controls and PD patients, separating men from women. We then assessed the effect of sex on NM-linked pathology in AAV-TYR-injected rats, either male or female, nigrally injected with AAV-TYR.
Results: We found that intracellular NM levels within nigral dopaminergic neurons of healthy human controls are significantly higher in men than in women, with men reaching earlier the pathogenic threshold of NM accumulation even in the absence of PD.
We also observed that AAV-TYR-injected male rats exhibit an earlier and greater accumulation of NM compared to female animals, reaching earlier the pathogenic threshold of intracellular NM accumulation.
Remarkably, ovariectomized (OVX) female rats injected with AAV-TYR accumulated NM more rapidly than non-OVX females and reached pathological NM levels similar to their male counterparts.
Conclusions: Our results suggest that an increased/accelerated accumulation of NM in men across life may underlie their higher risk to develop PD, compared to women.

P02.05

SARS-CoV-2 induces dopaminergic neuron loss in midbrain organoids

Javier Jarazo[*1], Eveline Santos da Silva[2], Enrico Glaab[3], Danielle Perez Bercoff[2], Jens Schwamborn[1]*
[1] OrganoTherapeutics, Esch-sur-Alzette, Luxembourg
[2] HIV Clinical and Translational Research Group, Luxembourg Institute of Health, Esch-sur-Alzette, Luxembourg
[3] Biomedical Data Science, Luxembourg Centre for Systems Biomedicine, University of Luxembourg, Esch-sur-Alzette, Luxembourg

Objectives: COVID-19 presents numerous symptoms mostly associated with the respiratory tract. However, recent evidence showed that the SARS-CoV-2 virus affects the nervous system. We evaluated the effect of the infection in midbrain organoids to determine if cells and pathways related to the onset of Parkinson's disease (PD) are affected.
Methods: The effect of the virus after short- and long-term cultures (4 days, and 1 month) post-infection was analyzed. Features measured included the degree of dopaminergic differentiation (TH), neurite fragmentation, and the level of activated astrocytes (GFAP and S100beta). Bulk RNAseq was performed to determine the effects of the infection on gene expression.
Results: After infection with SARS-CoV-2, the levels of dopaminergic neurons were significantly reduced in both short and long-term culture. Moreover, neurite fragmentation of TH positive neurons in infected organoids significantly increased respective to controls in long-term cultures. Within the same infected organoid TH/SARS-CoV-2 double positive neurons presented an altered morphology and high degree of neurite fragmentation compared to uninfected TH positive neurons. Activation of astrocytes was significantly reduced after infection in the short-term culture. While the levels of S100beta recovered over time, they still remained lower in infected organoids. In both short- and long-term culture, SARS-CoV-2 colocalized more with certain types of cells showing a marked preference for GFAP positive and TH positive cells when normalized to their respective abundance in the organoid. Gene expression analysis revealed a disruption in gene pathways related to vesicle transport, endosomal and autophagy pathways following infection with SARS-CoV-2.
Conclusions: Infection of midbrain organoids with Sars-Cov-2 induced a clear neurodegenerative process of TH positive neurons, while affecting main pathways known to be affected in PD patients.
Reference: This work will be presented as well in the ADPD 2023 Alzheimer's & Parkinson's Diseases Conference, 28/3-1/4/2023.

P02.06

The neuroprotective effect of NLX-112 in MPTP-treated mice is mediated through upregulation of astrocytic GDNF

William H. Powell[1], Lucy E. Annett[1], Ronan Y. Depoortère[2], Adrian Newman-Tancredi[3], Mahmoud M. Iravani[1]*
[1] University of Hertfordshire, Hatfield, United Kingdom
[2] Neurolixis, Castres, Tarn, France
[3] Neurolixis, Castres, France

Introduction: Preventing dopaminergic (DA) neuronal death is key to halting the progression of Parkinson's Disease (PD). There is evidence for serotonin 5-HT1A agonists having neuroprotective effects on DA 71ennsyl, and NLX-112 is a potent and selective 5-HT1A agonist currently undergoing clinical development for L-DOPA-induced dyskinesia in PD. Therefore, we examined the neuroprotective potential of NLX-112 in a MPTP mouse model of PD.
Method: C57BL mice (n=8-10/group) were treated i.p. once daily for 15 days as follows: Group 1 (G1): 1 ml/kg saline; G2: 1 mg/kg NLX-112; G3: 5 days saline followed by 5 days MPTP (total 120 mg/kg) and 5 days saline subsequently; G4: 15 days of NLX-112 plus MPTP on days 5-10. Two weeks following last treatments, striatal and substantia nigra (SN) sections were prepared to detect changes in DA neurons & DA nerve terminals, astrocytes, and inflammation-associated microglia by immunohistochemical detection of tyrosine-hydroxylase (TH), glial fibrillary associated protein (GFAP) and ionized calcium-binding adapter molecule 1 (Iba1), respectively. Glial-derived neurotrophic factor (GDNF) was also assessed in nigral and striatal sections because it was previously shown to be upregulated in astrocytes following an inflammatory insult.
Results: In G3, MPTP caused a loss of TH+ve DA neurons in the SN (-29%) and of TH+ve fibre density in the striatum (-55%) compared to G1 and G2. In G4 NLX-112 attenuated the MPTP-induced DA neuron and nerve terminal loss (-5% and -28% respectively). In the striatum, MPTP (G3) massively increased GFAP-immunoreactivity (ir), and this was reduced by NLX-112 (G4). In G1,G2 and G3, some astrocytes co-expressed GDNF and there were no differences between the 3 groups. However, in G4, striatal GFAP-GDNF colocalization was increased by 333% in the striatum and by 173% in the SN. In the SN, MPTP increased Iba1+ve microglia by 117% (G3) compared to G1 and G2. In G4, MPTP-induced increase in nigral microglia was completely abolished by NLX-112.
Conclusion: Overall, the present study shows that NLX-112 exhibits neuroprotective properties in MPTP-treated mice. In this model, NLX-112's protective effects are likely mediated through reversal of MPTP-induced inflammation as shown by inhibition of microgliosis and by upregulation of the neurotrophic factor, GDNF, in astrocytes.

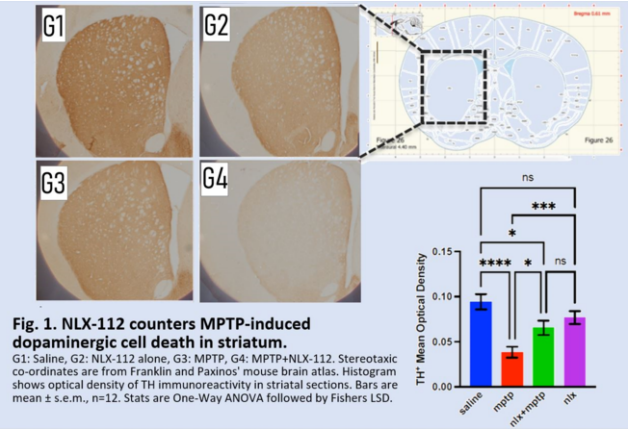


Fig. 1. NLX-112 counters MPTP-induced dopaminergic cell death in striatum.
G1: Saline, G2: NLX-112 alone, G3: MPTP, G4: MPTP+NLX-112. Stereotaxic co-ordinates are from Franklin and Paxinos' mouse brain atlas. Histogram shows optical density of TH immunoreactivity in striatal sections. Bars are mean ± s.e.m., n=12. Stats are One-Way ANOVA followed by Fishers LSD.

P02.07

Function and neuroprotective potential of Flcn knockout in Parkinson's disease

Julia Obergasteiger[*,1], Owen Fergusen[1], Cyril Bolduc[1], Anthony Bilodeau[1], Thomas Durcan[2], Flavie Lavoie-Cardinal[1], Emmanouil Metzakopian[3], Martin Levesque[1]*
[1] Cervo Brain Research Center, Universite Laval, Quebec, QC, Canada
[2] McGill University, Montreal, QC, Canada
[3] UK Dementia Research Institute at University of Cambridge, Cambridge, United Kingdom

Parkinson's disease (PD) is the second most common neurodegenerative disorder, characterized by various motor and non-motor symptoms in patients. One of the main hallmarks of the disease is the loss of dopaminergic (DA) neurons in the substantia nigra pars compacta (SNc). No cure is available for PD and current treatments only alleviate the symptoms of the disease. Therefore, there is an unmet need to provide new therapeutic targets. We performed a CRISPR-based, genome-wide screen to identify new target genes rescuing the degeneration of DA neurons. We identified several new targets and one of them is the Flcn gene. Flcn is implicated in the mTOR pathway, able to regulate autophagy and interacts with several Rab GTPases involved in endocytic trafficking. Furthermore, Flcn was shown to regulate mitochondrial biogenesis. Importantly, when DA neurons are exposed to oxidative stress, Flcn knockout (KO) increases their viability in vitro. To understand the physiological role of Flcn in DA neurons and validate its neuroprotective effect, we knocked out Flcn in mouse dopamine neurons of the SNc. To model PD, we used AAV-mediated expression of human alpha-synuclein (aSyn) in the SNc. After 16 weeks we performed locomotor assessment and histological analysis of the brain. Flcn KO in SNc dopamine neurons ameliorates the motor deficits induced by aSyn overexpression and it rescues the loss of dopaminergic neurons in the midbrain and their terminals in the striatum. Most importantly, Flcn KO also reduces the levels of phosphorylated aSyn in the SNc. In parallel, we use iPSC-derived DA neurons as a model of human PD in vitro, specifically iPSCs derived from a patient with the triplication of the SNCA gene (3xSNCA), coding for aSyn, and its isogenic control. 3xSNCA neurons display mitochondrial deficits that are rescued with Flcn KO. Specifically, Flcn KO reduces reactive oxygen species and it is also modulating the autophagy-lysosome pathway, specifically the number of lysosomes. In this study, we used an unbiased screening method to identify a new neuroprotective target for PD. Following target validation, we will identify drugs capable of modulating Flcn expression and test their efficacy to modify disease onset and/or progression.

P02.08

Therapeutic role of MicroRNA 34a in Parkinson's disease via inhibiting expression of colony-stimulating factor 1 and subsequent anti-neuroinflammation and neuroprotection

*Ming Yew, Ping Heng Tan**
Department of Anesthesiology, Chi Mei Medical Center, Tainan, Taiwan

In terms of neurodegenerative diseases, Parkinson's disease (PD) is one of the most widespread. Currently, however, treatments are only available to alleviate symptoms. A new therapeutic target is urgently needed. In recent years, novel molecule of colony stimulating factor 1 (CSF1) (macrophage colony stimulating factor, MCSF) in microglia were found to play important role in the activation of microglia and induction of neuroinflammation. CSF1 receptor (CSF1R) are target genes of microRNA 34a (mir 34a). PD neuroinflammation is supposedly inhibited by mir 34a through inhibition of CSF1R expression. Mir 34a was found to be effective in improving neuronal damage in our study. This treatment can significantly suppress the upregulation of proinflammatory cytokines associated with interferon-gamma stimulation, including inducible nitric oxide synthase (iNOS), cyclooxygenase-2 (COX-2), and nuclear factor kappa-light-chain-enhancer of activated B cells (NF-B). M2-type microglial markers, such as arginase-1 and Ym-1, were increased in BV2 murine microglial cells by the treatment. SH-SY5Y cells treated with Mir 34a also showed a significant increase in brain-derived neurotrophic factor (BDNF) and 72ennsylv-cAMP response element-binding protein (p-CREB). As well, we evaluated the effects of mir 34a on zebrafish PD models. By decreasing endoplasmic reticulum (ER) stress biomarkers, mir 34a was effective in reversing 6-OHDA-induced locomotor deficits and improving tyrosine hydroxylase (TH). Results suggest that mir 34a might have an antineuroinflammation and antiapoptotic effect on PD.

P02.09

SERCA as a preclinical disease modifying drug target against α-synuclein aggregate dependent dysfunctions

Zagorka Vitic*[,1], Lasse Reimer[2], Nelson Ferreira[2], Claus E. Olesen[3], William Dalby Brown[4], Jakob Ulstrup[3], Gergo Kovacs[2], Marina Lopez Incera[2], Lara Perucho[2], Cristine Betzer[2], Sara A. Ferreira[2], Nanna Møller Jensen[2], Hjalte Gram[2], Marina Romero-Ramos[2], Poul Henning Jensen[2]
[1] Aarhus University, Aarhus, Denmark
[2] Department of Biomedicine, Aarhus University, 8000 Aarhus C, Denmark & DANDRITE, Danish Research Institute of Translational Neuroscience, 8000 Aarhus C, Denmark, Aarhus, Denmark
[3] Department of Biomedicine, Aarhus University, 8000 Aarhus C, Denmark, Aarhus, Denmark
[4] WDB Consulting, Copenhagen, Denmark, Copenhagen, Denmark

The aggregation of the α-synuclein in inclusions called Lewy bodies and neurites is a pathological signature of Parkinson's disease (PD). Another pathogenetic characteristic of the disease is an imbalance of Ca2+ homeostasis. In healthy neurons, resting Ca2+ levels are to a large degree regulated by the SERCA pump, which transports Ca2+ from the cytosol to the endoplasmic reticulum (ER). Using different cell models, we have shown that α-synuclein binds to and activates the SERCA pump, and described a clear connection between early-stage α-synuclein aggregates and reduced cytosolic Ca2+ levels. This early phenomenon is followed by drastically

increased cytosolic Ca2+ levels, that eventually leads to neuronal cell death. Treatment with the specific SERCA inhibitor, cyclopiazonic acid (CPA), normalizes the initial reduction of cytosolic Ca2+, protects the cells against α-synuclein-aggregate stress and improves viability both in in vitro and a Caenorhabditis elegans model.
To validate SERCA as a preclinical drug target, we administered CPA in drinking water in two mouse PD models. A first model based on intramuscular injection of preformed fibrillar (PFF) α-synuclein in the h-A53T-α-syn transgenic M83 line, which induces CNS pathology and rapid onset of the motor impairment phenotype. CPA treatment in this model delayed the age-of-onset of motor symptoms (clasping behavior and rotarod performance) and prolonged survival compared to non-treated animals. Immunohistochemistry showed a reduction in Phospho-Ser129 and aggregated α-synuclein species and reduced MHCII expression in the brain. Currently, we are analyzing the impact of CPA treatment on a second PD model in which we stereotaxically inject PFF α-synuclein in the striatum of wild-type mice.
In conclusion, our results demonstrate that pharmacological SERCA inhibition protects against the inter-neuronal spreading of templated α-syn pathology, signifying that involved downstream processes may be important therapeutic targets for treatment of α-synucleinopathies

BASIC SCIENCE: Protein misfolding and handling

P03.01

Copper supplementation rescues impaired motor phenotype in a novel mouse model of SOD1 proteinopathy

Amr Abdeen[*,1], Benjamin Rowlands[1], Connor Karozis[1], Veronica Cottam[1], Joel Siciliano[1], Fabian Kreilaus[1], Richard Harwood[2], Julia Forkgen[1], Sarah Rosolen[1], Sara Nikseresht[3], Benjamin G. Trist[1], Kai Kysenius[3], Michael Gotsbacher[4], David Bishop[5], Rachel Codd[4], Peter J. Crouch[3], Kay L. Double[1]*
[1] Brain and Mind Centre and School of Medical Sciences (Neuroscience), Faculty of Medicine and Health, The University of Sydney, Sydney, NSW, Australia
[2] Sydney Microscopy and Microanalysis, The University of Sydney, Sydney, NSW, Australia
[3] Department of Biochemistry and Pharmacology, Faculty of Medicine, Dentistry and Health Sciences, The University of Melbourne, Melbourne, Victoria, Australia
[4] School of Medical Sciences (Molecular and Cellular Biomedicine), Faculty of Medicine and Health, The University of Sydney, Sydney, NSW, Australia
[5] Hyphenated Mass Spectrometry Laboratory, Faculty of Science, University of Technology, Sydney, NSW, Australia

Misfolding and abnormal deposition of the cuproenzyme superoxide dismutase 1 (SOD1) is a pathological feature of the Parkinson's disease substantia nigra pars compacta (SNc) where its accumulation is associated with decreased regional copper levels. We posited that SOD1 proteinopathy contributes to dopamine neuron loss, and thus developed a novel murine model (hSOD1WT/Ctr1+/-) which combines high levels of wildtype human SOD1 and brain copper deficiency to test this hypothesis. Immunofluorescent dual-labelling of misfolded SOD1 and tyrosine hydroxylase (TH) demonstrated a marked increase in aggregated SOD1 protein in TH+-dopamine neurons within the SNc hSOD1WT/Ctr1+/- mice compared with control mice. Three-dimensional reconstruction of these images demonstrates that the preponderance of SOD1 aggregates is outside TH+-neuron cell bodies, suggesting the accumulation of SOD1 in neuronal processes and glia, or their release into the extracellular space. Quantitative stereology revealed that the density of TH+-dopamine neurons in the SNc was significantly reduced in hSOD1WT/Ctr1+/- mice compared with all mouse strains ($p < 0.05$). These data support our hypothesis that wildtype SOD1 is prone to misfolding in a cellular environment of copper deficiency and that resultant SOD1 proteinopathy is associated with SNc dopamine neuron death in an age-related manner. Behavioural assessment of our mouse model at 5-months demonstrated impaired grip strength ($p < 0.001$) and balance beam performance ($p < 0.001$). Copper supplementation using the blood-brain barrier permeable copper delivery agent CuATSM (15 mg/kg daily for 3 months) resulted in a 3.4-fold increase in midbrain copper levels in five-month-old hSOD1WT/Ctr1+/- mice. CuATSM treatment did not modify grip strength in hSOD1WT/Ctr1+/- mice but dramatically improved balance beam performance (reduced number of paw slips, $p < 0.001$; reduced latency, $p < 0.05$). Our findings have implications for Parkinson's disease and ALS where aggregated wild-type SOD1 is a pathological feature, and support ongoing clinical trials of CuATSM treatment in Parkinson's disease and ALS patients (ClinicalTrials.gov Identifier: NCT03204929; NCT02870634).

P03.02

Lysosomal function and its role in oligodendrocytes in Synucleinopathies

Denise Balta[*,1], Ida Pirkl[2], Kristina Battis[2], Philipp Arnold[3], Jürgen Winkler[2], Friederike Zunke[2]*
[1] University Hospital Erlangen, Erlangen, Germany
[2] University Hospital, Erlangen, Bavaria, Germany
[3] Institut of Functional and Clinical Anatomy, Erlangen, Bavaria, Germany

Parkinson's disease (PD) and Multiple System Atrophy (MSA) belong to a subgroup of neurodegenerative disorders, also termed Synucleinopathies. The characteristic hallmark of these progressive diseases is intracellular inclusions rich in alpha-Synuclein (a-Syn) within neurons and glial cells. Mechanisms of a-Syn clearance are of great interest within many investigations. Lysosomes have been shown to play a major role in a-Syn degradation, especially the proteases cathepsin B, D, and L. Their dysfunction triggers a-Syn accumulation in neurons. However, their contribution to a-Syn pathology in glial cells is still elusive. Therefore, we aim to characterize lysosomal enzyme function in 1) an immortalized oligodendroglia cell line (CG4) with and without stable a-Syn overexpression, and 2) oligodendrocytes derived from human induced pluripotent stem cells (hiPSCs). We have examined the function of aforementioned cathepsins on protein and mRNA expression levels and investigated their cellular distribution by immunofluorescence stainings in GC4 cells. Furthermore, lysosomal enzyme activity of the immortalized oligodendroglial cells were determined and compared. As a next step, we aim to investigate lysosomal enzyme function, processing, and influence of pathological a-Syn on the lysosomal system in hiPSCs.
Our data indicate a general upregulation of the RNA expression level for cathepsin B, D, and L in a differentiated control and a-Syn overexpressing CG4 cell model. Interestingly, the a-Syn overexpressing line shows the highest enzyme activity of cathepsin D and B compared to the control after differentiation. This finding also correlates to the mature and active forms of aforementioned cathepsins observed by immunodetection. It seems that a-Syn overexpression, at least in this cell model, leads to the upregulation of the specific cathepsins, which are involved in its degradation. A possible explanation for this could be an adaptive mechanism of the

overexpressing cells, to cope with the persistently high expressed a-Syn levels.
Taken together, our data contributes to improved knowledge about the lysosomal function in oligodendrocytes in health and under pathological conditions, and might contribute to future therapeutic approaches in neurodegenerative diseases.

P03.03

Proteomic analysis of Parkinson's patient midbrain neurons reveals a sub-proteome of metastable proteins that are susceptible to aggregation
Nandkishore Belur, Joseph Mazzulli*
Northwestern University, Chicago, Illinois, United States

One of the hallmark features of neurodegenerative disease pathology is the accumulation of specific aggregation-prone proteins. Alpha-synuclein (a-syn) protein aggregates have been well documented as major component of neuropathology in Dementia with Lewy bodies (DLB) and Parkinson's disease (PD) brains. In addition, genetic analyses have implicated the autophagic-lysosomal pathway (ALP) to be dysregulated, which may promote the accumulation of a-syn and other metastable, aggregation-prone proteins in DLB and PD. The accumulation of a-syn alone is also sufficient to induce lysosomal dysfunction, by inhibiting lysosomal biogenesis or cargo delivery into lysosomal compartments. Because cellular clearance is affected in a general way in PD, we hypothesized that multiple proteins beyond a-syn might aggregate in patient neurons. Furthermore, the global changes that occur in proteome solubility in PD are not well defined. To this end, we analyzed lysosomal function, a-synuclein accumulation, and neurite degeneration in human induced pluripotent stem cell (iPSc)- derived mid-brain neurons from a PD patient harboring A53T mutation and its isogenic control. We performed a comprehensive unbiased quantitative proteomic study to characterize the composition of insoluble proteome in these cultures. Our data indicates that a specific subset of proteins undergo a solubility shift that is partly dictated by basic physiochemical properties of amino acid residues and structural features. Our studies indicate that multiple proteins beyond a-syn aggregate in PD patient cultures, and future functional studies on these metastable proteins may help to shed light on the pathophysiology of DLB/PD. This study may also help identify novel therapeutic targets to help restore proteostasis imbalance caused by a-syn-induced solubility changes in the proteome.

P03.04

Assessment of phosphorylated α-synuclein deposits in the skin and GI tract in prodromal Parkinson's disease
Martin Ingelsson[1], Paul de Roos[2], Vincenzo Donadio[3], Alex Incensi[3], Anish Behere[1], Rocco Liguori[3], Joakim Bergström[1], Lars Lannfelt[1], Per Hellström[4], Dag Nyholm[2]*
[1] Department of Public Health and Caring Sciences, Geriatrics, Uppsala University, Uppsala, Sweden
[2] Department of Medical Sciences, Neurology, Uppsala University, Uppsala, Sweden
[3] IRCCS Istituto delle Scienze Neurologiche di Bologna, UOC Clinica Neurologica, Bologna, Italy
[4] Department of Medical Sciences, Gastroenterology/Hepatology, Uppsala University, Uppsala, Sweden

Alpha-synuclein (α-syn) forms Lewy bodies and Lewy neurites in the Parkinson's disease (PD) brain, but patients often also display abnormally phosphorylated α-syn deposits (p-syn) in skin and gastrointestinal (GI) mucosa. In this study, we have analyzed the presence of p-syn in skin and GI biopsies from subjects with prodromal PD. For comparison, we included patients with already diagnosed PD and healthy control individuals.
We included 31 subjects (10 PD, 16 prodromal PD and 5 healthy controls). Proximal (neck) and distal (lower leg) skin sites, as well as gastric/duodenal and colonic/sigmoideal mucosa, were targeted with several biopsies from each region. Tissues were processed to generate ten µm sections that were analyzed with immunofluorescence against p-syn.
Nine of the ten PD cases were found to be p-syn positive in at least one skin biopsy (eight in lower leg, three in neck and two at both locations). Also nine out of ten patients were positive in at least one GI biopsy (seven gastric/duodenal, seven colonic/sigmoideal and five at both locations). Eight of the ten cases were positive in both at least one skin and GI site, whereas only one was positive at all the investigated sites. For the prodromal PD subjects, six were p-syn positive in at least one skin biopsy (five in lower leg, four in neck and three at both locations). Moreover, two prodromal subjects displayed presence of p-syn in gastric/duodenal samples, whereas none of them were detected as positive in colon/sigmoideum. Two of the prodromal subjects were positive in both at least one skin and GI site. None of the controls showed any p-syn reactivity in neither the skin nor the GI tract.
Our data suggest that deposition of p-syn in peripheral tissues may occur already at a prodromal stage in some PD patients. In such individuals, especially distal skin sites may be affected. Thus, our findings lend support to the hypothesis that in a subset of PD patients the disease can originate in the peripheral nervous system.

P03.05

Discovery of new E3 ligases for alpha-synuclein clearance
Nur Kocaturk, Zhiyuan Li, Ian Ganley, Gopal P. Sapkota*
University of Dundee, MRC Protein Phosphorylation & Ubiquitylation Unit, Dundee, United Kingdom

Parkinson's disease (PD) is one of the most common motor-related neurodegenerative diseases and thus far they are untreatable. Genetic alterations in SNCA gene have been shown to be linked to PD and accumulation of aberrant fibrillary forms of alpha-synuclein constituting major part of Lewy bodies that are key hallmark of PD. Accumulation of fibrillary forms of alpha-synuclein is suggested to be contributed to neuronal cell death. Therefore, removal of pathogenic forms of alpha-synuclein offers a therapeutic potential. Cells have two major systems for removal of proteins: autophagy and ubiquitin-proteasome system. Both systems utilize polyubiquitylation as a degradation signal, which are conjugated to the target proteins by the E3 ubiquitin ligases and removed by deubiquitylating enzymes (DUBs) reversibly. In this study, we performed a siRNA-based high-throughput screen to identify E3s and DUBs that regulate alpha-synuclein turnover. The detection of alpha-synuclein in cell extracts was done by a sensitive ELISA assay. From the screen, several E3s previously unlinked to PD pathogenesis or alpha-synuclein turnover were found to significantly alter the abundance of endogenous alpha-synuclein levels in cells. We discovered that one of our key hits directly modifies alpha-synuclein with ubiquitin on several lysine residues. Knockdown and knockout tests further validated key regulatory role of the E3 on alpha-synuclein stability. We are now also validating whether other E3 ligases also target alpha-synuclein in a similar manner. Uncovering the roles of these will potentially allow opportunities for a better understanding of the PD pathogenesis and new therapeutic developments against PD.
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P03.06

Super-resolution microscopy informs on the molecular architecture of alpha-synuclein inclusions in model systems and in the human brain

Diana Lazaro[*1], Patrick Weish[2], Luís Palmares*[*2], Patrícia Santos[2], Christine Stadelmann[3], Virginia M-Y. Lee[4], John Q. Trojanowski[4], Günter U. Höglinger[5], Silvio O. Rizzoli[6]*
[1] University of Pennsylvania, Philadelphia, United States
[2] Department of Experimental Neurodegeneration, Center for Biostructural Imaging of Neurodegeneration, University Medical Center Göttingen, Göttingen, Germany
[3] Institute of Neuropathology, University Medical Center, Göttingen, Germany
[4] Department of Pathology and Laboratory Medicine, Institute on Aging and Center for Neurodegenerative Disease Research, University of Pennsylvania School of Medicine, Philadelphia, United States
[5] Department of Neurology Medizinische Hochschule Hannover, Hannover, Germany
[6] Department of Neuro- and Sensory Physiology, University Medical Center Göttingen, Excellence Cluster Multiscale Bioimaging, Göttingen, Germany

Lewy bodies (LBs) and Lewy neurites are pathological hallmarks of Parkinson's disease and other progressive neurodegenerative disorders known as Lewy body diseases (LBD). These proteinaceous depositions are immunopositive for alpha-synuclein (aSyn) and several other proteins, as neurofilament components. The structural organization and composition of aSyn inclusions is still unclear and needs to be addressed in greater detail, as this may open novel avenues for our understanding the disease-relevant pathological events.
In this study, we investigated the molecular architecture of aSyn, both in cell models and in human brain tissue, using state-of-art super resolution X10 Expansion microscopy (ExM). This approach physically expands specimens embedded into a swellable gel, preserving their biological information. Then, the specimen can be analyzed using standard epifluorescence microscopes, thereby obtaining nanoscale information.
The combination of different cell models, and human brain tissue enabled us to distinguish different types aSyn assemblies (e.g. ring shape or tubular structures), and a conserved pattern of aSyn inclusions surrounded/encaged by intermediate filament proteins. Overall, X10 ExM enabled us to gain insight into the architecture and biology of aSyn inclusions, and constitutes a powerful tool in the quest to understanding underlying disease mechanisms in synucleinopathies.

P03.07

Lysosomal lipid alterations caused by glucocerebrosidase deficiency promote lysosomal dysfunction, chaperone mediated- autophagy deficiency, and alpha-synuclein pathology

Marta Martinez-Vicente[1], Eddie Pradas-Gracia[*1], Alba Navarro-Romero[1], Irene Fernandez-Gonzalez[1], Marta Montpeyo[1], Jordi Riera[1], Mercedes Arrue-Gonzalo[1], Clara Carnicer-Caceres[2], Laura Castillo-Ribelles[2], Jose Antonio Arranz-Amos[2]*
[1] Vall d'Hebron Institut de Recerca (VHIR), Barcelona, Spain
[2] Hospital University Vall d'Hebron, Barcelona, Spain

Objective: The first genetic risk factor for developing PD is the presence of mutations in the GBA gene that encodes the lysosomal enzyme glucocerebrosidase (Gcase). An inverse relationship between the loss of Gcase activity and the accumulation of alpha-synuclein has been demonstrated in different PD models and samples from PD patients carrying GBA mutations. The objective of this study was to generate and characterize a new in vitro neuronal model of Parkinson's diseases associated to GBA that allowed us to investigate the link between the loss of Gcase and alpha-synuclein pathology.
Methods: We have generated a set of differentiated and stable human dopaminergic cell lines that express the two most prevalent GBA mutations, i.e. N370S and L444P, as well as GBA knock out as an in vitro disease modeling system. We performed a deep analysis of the consequences triggered by the presence of mutant GBA and the loss of the Gcase activity in the ER, mitochondria but especially focusing in the lysosomal compartment.
Results: A variety of events triggered by the initial loss of Gcase activity lead to intralysosomal accumulation of sphingolipids and cholesterol, lysosomal dysfunction, and impairment of chaperone-mediated autophagy (CMA), along with other events previously described in PD-GBA models. These pathogenic mechanisms contribute, directly and indirectly, to an increase in the accumulation and aggregation of alpha-synuclein.
Conclusions: We describe a new molecular mechanism to understand how the initial loss of Gcase activity can lead to general lysosomal dysfunction and to alterations in lysosomal lipid composition that impair CMA activity and promote abnormal accumulation of alpha-synuclein.

P03.09

Aged periventricular microglia contribute to CSF-borne aggregated αSyn spreading

Salomé Sirerol-Piquer[*1], Ana Pérez-Villalba[2], Pere Duart-Abadia[1], Laura Blasco-Chamarro[1], Pau Carrillo-Barberà[1], Ulises Gomez-Pinedo[3], Victoria Navarro[4], Benjamin Dehay[5], Javier Vitorica[4], Azucena Pérez-Cañamás[1], Francisco Pérez-Sánchez[1], Miquel Vila[6], Isabel Fariñas[1]*
[1] BIOTECMED, Universidad de Valencia., Valencia, Spain
[2] UCV, Valencia, Spain
[3] Hospital Clínico San Carlos, Madrid, Spain
[4] Instituto de Biomedicina de Sevilla (Ibis). Universidad de Sevilla, Sevilla, Spain
[5] Université de Bordeaux, Institut des Maladies Neurodégénératives, France, France
[6] Vall d'Hebron Instituto de Investigación (VHIR), Barcelona, Spain

Microglia represent a specialized population of macrophage-like cells in the central nervous system (CNS) considered immune sentinels, constantly scanning and surveying the environment through their ramified processes. Microglial phagocytosis is important for the clearance of pathogens and abnormal proteins from the CNS and provides the first host defence. However, aging has a detrimental impact on microglial morphology (reduced ramification and fragmented processes) and function. Compelling evidence suggests that these age-related changes might have an impact in the progression of neurodegenerative disorders.
Parkinson's disease (PD), one of the most age-associated neurodegenerative disorders, is characterized by the misfolding and aggregation of alpha-synuclein (αSyn) in intraneuronal inclusions. Interestingly, increasing evidence supports the idea that misfolded forms of αSyn can be released from neurons and propagate from cell to cell, and throughout the brain, inducing the abnormal misfolding of native forms of the αSyn protein in healthy neurons, suggesting a prion-like pathological progression.
Here we show that mouse periventricular microglia survey the cerebrospinal fluid (CSF) and are highly efficient in the clearance of toxic aggregated forms of αSyn delivered into the lateral ventricle CSF. With age, functional impairment in this capacity results in the abnormal aggregation of endogenous αSyn in both microglia and neurons. Our data suggest that periventricular microglia avoid the

spreading of aggregated αSyn from the CSF in young animals whereas dysfunctional aged contribute to progression of the pathology.

P03.10

Impaired autophagic-lysosomal fusion in Parkinson's patient midbrain neurons occurs through ykt6 and is rescued by farnesyltransferase inhibition

Caleb Pitcairn[*,1], *Naomi Murata*[1], *Annie Zalon*[1], *Iva Stojkovska*[2], *Joseph Mazzulli*[1]
[1] Northwestern University, Chicago, Illinois, United States
[2] German Center for Neurodegenerative Disease (DZNE), Munich, Germany

Macroautophagy is a catabolic process that coordinates with lysosomes to degrade aggregation-prone proteins and damaged organelles. Loss of macroautophagy preferentially affects neuron viability and is associated with age-related neurodegeneration. We previously found that a-synuclein (a-syn) inhibits lysosomal function by blocking ykt6, a farnesyl-regulated SNARE protein that is essential for hydrolase trafficking in midbrain neurons. Using Parkinson's disease (PD) patient iPSC-derived midbrain cultures, we find that chronic, endogenous accumulation of a-syn directly inhibits autophagosome-lysosome fusion by impairing ykt6-SNAP-29 complexes. In wild-type cultures, ykt6 depletion caused a near-complete block of autophagic flux, highlighting its critical role for autophagy in human iPSC-derived neurons. In PD, macroautophagy impairment was associated with increased farnesyltransferase (Ftase) activity, and Ftase inhibitors restored macroautophagic flux through promoting active forms of ykt6 in human cultures and mice. Our findings indicate that ykt6 mediates cellular clearance by coordinating autophagic-lysosomal fusion and hydrolase trafficking, and that macroautophagy impairment in PD can be rescued by Ftase inhibitors.

P03.11

SUMO system changes in PD and SUMOylation inhibitor promotion of autophagy subtypes as a novel therapy

Matthew K. Boag[1], *Shamini Vijayakumaran*[1], *Jacob Clark*[2], *Angus Roberts*[1], *Ruth E. Carmichael*[2], *Kevin A. Wilkinson*[2], *Stephen Wood*[3], *George D. Mellick*[3], *Jeremy M. Henley*[2], *Dean L. Pountney*[*,1]
[1] School of Pharmacy and Medical Sciences, Griffith University, Southport, QLD, Australia
[2] School of Biochemistry, University of Bristol, Bristol, United Kingdom
[3] Griffith Institute for Drug Discovery, Griffith University, Nathan, QLD, Australia

Evidence is mounting for links between Parkinson's disease (PD) and the Small Ubiquitin-like Modifier (SUMO) system. SUMO is a ubiquitin homologue that, like ubiquitin, is conjugated to and deconjugated from substrate proteins by a system of enzymes thereby modifying the structure and function of the SUMO-conjugated proteins in a wide range of cellular systems. The coordinated action of E1 (activating; SAE1/SAE2), E2 (conjugating; Ubc9) and the E3 (ligating; e.g. PIAS3) enzymes attaches SUMO via its C-terminal glycine to specific substrate lysine residues. SUMOylation is a reversible process achieved via the actions of a family of SUMO-specific deSUMOylation enzymes known as SENPs, the main regulators of this pathway. SUMO conjugates have been found in pathological protein inclusion bodies in PD and other neurodegenerative diseases. SUMO pathway components were investigated in cell cultures derived from olfactory epithelium biopsies from PD patients (n=8) and age-matched controls (n=8). Western analysis and immunofluorescence showed changes in several SUMO-1 conjugates in PD compared to normal controls. Western analysis also revealed that total levels of the deSUMOylase isoenzyme, SENP3, which has been linked to the induction of mitophagy upon iron chelation, were significantly increased in PD compared to normal controls. SENP3 expression was also increased in PD compared to normal human brain tissue from substantia nigra (n=17) and striatum (n=21) and in a neuroblastoma cell model. There were no significant differences in the76xpressionn of other SUMO pathway enzymes (Ubc9 and SAE2). In previous studies, inhibiting SUMOylation in primary rat neurons and SH-SY5Y cells was found to induce autophagy-dependent clearance of alpha-synuclein aggregates (aggrephagy). Iron is also enriched in PD brain tissue in both glial cells and neurons and in the current study, immunofluorescence and Western analysis revealed that inhibiting SUMOylation in an SH-SY5Y model also resulted in clearance of accumulated ferritin, the major cellular iron storage protein, due to ferritinophagy. The autophagy gene master regulator, TFEB, which is inhibited by SUMOylation, interacts with both autophagy subtypes. The SUMO system, which may be altered in PD, could therefore provide novel targets for the therapeutic activation of autophagy pathway subtypes mediating the removal of both pathological protein aggregates and iron.

P03.12

Combination of fluorescence lifetime and anisotropy imaging microscopy to measure intracellular microenvironment as early diagnosis of neurodegenerative diseases

Soheila Sabouri[*,1], *Hamid Soleimaninejad*[2], *Yuning Hong*[1]
[1] La Trobe University, Melbourne, VIC, Australia
[2] intelligent imaging innovations (3i), Melbourne, VIC, Australia

Proteostasis imbalance is the hallmark of neurodegenerations, however, there is still no efficient, direct method to monitor unfolded and aggregated protein states as a result of proteostasis imbalance in live cells [1]. This research aims to measure and quantify cellular proteostasis efficiency and local microenvironment alterations by applying our fluorescence-based strategy and methodology. In the first project, we have synthesized a peptide-conjugated thiol-reactive probe to detect free-cysteine exposed unfolded proteins to achieve this goal. This fluorescent dye strongly emits when it reacts with unfolded proteins while it weakly fluoresces with folded proteins and small molecule biothiols, such as GSH (glutathione) [2]. We further applied our fluorogenic probe to measure proteostasis impairments in cells under stress conditions. By using flow cytometry, confocal, and fluorescence lifetime imaging microscopy, we can visualize and quantify intracellular protein unfolding and aggregation with the assist of the probe. In the second project, we designed and synthesized a mitochondrial targeting fluorescent probe for measuring the microenvironment in mitochondria under different conditions. This probe exhibited high fluorescence emission and longer lifetime in viscous media. In vitro experiments confirmed that this probe is only sensitive to viscosity, but not to H2O2, pH, ion strength and polarity. We validated our probe in inflammation, autophagy, and mitophagy model cells induced by drugs in both cancerous and non-cancerous cells. By using flow cytometry, confocal microscopy and advanced microscopic techniques like fluorescence lifetime and anisotropy imaging microscopy, we obtained detailed information to map mitochondria viscosity in cells under stress conditions [3]. Overall, our probes and methodology may open a new window to a detailed understanding of proteostasis and mitochondria functions in neurodegenerations and other diseases.

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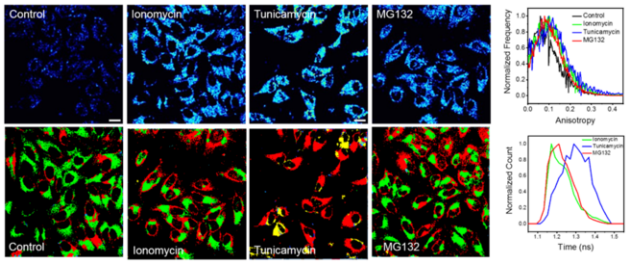


P03.14

Directed evolution of the human molecular chaperone DNAJB1 towards the alpha-synuclein protein

Come Stellio[*,1], Marie-Pierre Castanié-Cornet[2], Axel Mogk[3], Bernd Bukau[4], Pierre Genevaux[1]*
[1] CNRS, Toulouse, France
[2] Université Paul Sabatier Toulouse III, Toulouse, France
[3] Center for Molecular Biology of Heidelberg University (ZMBH), Heidelberg, Germany
[4] Center for Molecular Biology of Heidelberg University-German Cancer Research Center, Heidelberg, Germany

Parkinson's disease is a neurodegenerative disease in which the aggregation of the alpha-synuclein (α-syn) protein is involved. Molecular chaperones are a class of proteins that helps other proteins to fold without being a part of their final structure. One of them, DNAJB1 has been previously identified as a potential modulator of α-syn aggregation (Gao et al, 2015; Wentink et al, 2020). In this work, we used a bacterial tool that allowed to quickly select variants of the DNAJB1 chaperones that are supposed to interact better with the α-syn protein. Thanks to this in vivo assay, we were able to identified single point mutations in the DNAJB1 chaperone. Next, we performed in-vitro assays to fully characterize our DNAJB1 variants and asses their capacity to modulate the aggregation, and their cooperation with their partners. Our results show that no variants lost their general functions, and all of them have a bit improved their reactions towards the monomeric form of α-syn. This study could be used to create therapeutic agents that would be mimicking the comportment of our variants.

P03.15

Interplay of α-synuclein aggregation and mitochondrial function in PD

Carmen Venegas[*,1], Patrycja Mulica[2], Thais Arns[2], Dimitrios Kyriakis[2], Sylvie Delcambre[2], Sandro L Pereira[2], Paul MA Antony[2], Rejko Krüger[2], Alexander Skupin[2], Anne Grünewald[2]*
[1] University of Luxembourg, Belvaux, Luxembourg
[2] Luxembourg Centre for Systems Biomedicine, University of Luxembourg, Belvaux, Luxembourg

Parkinson's disease (PD) is the fastest growing neurodegenerative disorder. In PD, the demise of dopaminergic neurons in the substantia nigra pars compacta coincides with a widespread accumulation of α-synuclein (α-syn) in so-called Lewy bodies.

Although many mechanisms are proposed to trigger PD, mitochondrial dysfunction has emerged as key pathological feature of PD. Analyses in human postmortem brain tissue and (iPSC-derived) cellular models provided strong evidence for the disruption of mitochondrial dynamics, bioenergetic deficits, increased ROS, and an accumulation of somatic mutations in the mitochondrial genome. Furthermore, it has been demonstrated that a-syn is able to induce mitochondrial dysfunction.
In light of these findings, the objective of the current study was to evaluate the impact of α-syn on mitochondrial homeostasis in iPSC-derived midbrain neurons.
We differentiated iPSCs from healthy controls, sporadic and α-syn-mutant (A53T and SNCA triplication) PD patients into neurons to evaluate how the accumulation of α-syn drives mitochondrial dysfunction. We performed (single-cell) RNA-sequencing, high-content imaging and digital PCR analyses at three different time points of differentiation to assess a-syn accumulation and to perform deep-mitochondrial and neuronal phenotyping.
RNA sequencing analysis revealed differences in the neuronal expression profile between controls and PD patients at the different time points 14, 30 and 45 days. We could observe higher α-syn expression in all the PD lines compared with the controls and that this difference increases over time. In addition, the longitudinal analysis highlighted altered neuronal development as well as synaptic function.
Our data indicate that α-syn accumulation occur in iPSCs midbrain neurons triggering neuronal dysfunction. As a next step, we will analyze how α-syn exerts its toxicity and address the functional relationship between α-syn and mitochondria. This is essential to develop novel targeted PD therapeutics.

P03.16

Uncovering secretory mechanisms underlying the spreading of alpha-synuclein

Aurore Filaquier[1], Marie-Laure Parmentier[1], Julien Villeneuve[*,2]*
[1] CNRS Institute of Functional Genomics (IGF), Montpellier, France
[2] CNRS UMR 5203, Montpellier, France

Emerging evidence indicates that unconventional protein secretion (UPS), a process poorly characterized, is critical for the dissemination of alpha-synuclein (alpha-SNC), a toxic aggregate-prone protein that cause Parkinson's disease. Hence to uncover mechanisms underlying this process is of fundamental importance.
Toward this objective, we developed new assays to monitor specifically and accurately αSNC secretion. We then used these assays for targeted approaches allowing us to identified secretory lysosomes and factors associated to lysosomal storage disorders as essential for alpha-SNC UPS. Their characterization will be pursued and we will investigate how lysosomes acquired secretory properties.
We will also use an adaptation of our platform for pooled CRISPR screen to highlight factors at every step of alpha-SNC transport. The use of iPSC-derived neurons and lines expressing distinct alpha-SNC variants should allow us to reveal key players for the UPS of toxic aggregate-prone variants.
Finally, we will validate identified mechanisms in drosophila and zebrafish models that have proven their usefulness and complementarity in studying misfolded protein spreading and modelling most relevant features of neurodegenerative diseases.
At the crossroad of critical challenges, our project will make important advances into basic mechanisms that will then be exploited for biomedical applications.

BASIC SCIENCE: Mitochondria, oxidative stress, and pathogens

P04.01

Characterizing immune alterations in a rat model of Parkinson's disease through single-cell RNA sequencing

Sara A. Ferreira[*,1], Ankita Singh[1], Johanne Lauritsen[1], Ida H. Klæstrup[1], Tulieca Jeyaseelan[1], Sara K. Nissen[1], Poul H. Jensen[1], Jørgen Kjems[2], Lin Lin[3], Marina Romero-Ramos[1]*
[1] DANDRITE & Department of Biomedicine, Aarhus University, Denmark, Aarhus, Denmark
[2] Interdisciplinary Nanoscience Center (iNano), Aarhus University, Denmark, Aarhus, Denmark
[3] Department of Biomedicine, Aarhus University, Denmark, Aarhus, Denmark

Immune changes in the brain and periphery in Parkinson's disease (PD) patients have been documented, but how the central and peripheral immune systems impact disease progression is yet unknown. Alpha-synuclein (α-syn) pathological aggregates are the main component of Lewy bodies, the pathological hallmark of PD. Misfolded α-syn can act as a pro-inflammagen and initiate an inflammatory response on both peripheral and central myeloid cells, ultimately inducing both innate and adaptive immune responses. However, our current comprehension of the different immune cell types involved in the disease progression remains elusive. We aim to identify and describe new immune subtypes involved in the α-syn-induced inflammation in the brain and periphery using state-of-the-art techniques such as Single-cell RNA sequencing (scRNAseq). To do so, we have injected murine α-syn pre-formed fibrils (PFF), monomeric α-syn or PBS into the striatum of male and female rats and performed scRNAseq on total brain cells 2- and 6-months post-injection. In parallel, blood and spleens were collected for evaluation of peripheral immune alterations. Bioinformatic analysis and validation are currently ongoing. Preliminary data show that the α-syn PFF-injected animals had an expansion of the responsive microglia, together with a macrophage and T-cell response. The immune events were sex-specific. In addition, the injection of monomeric α-syn resulted in long-lasting immune changes that differed from the PFF α-syn but also from the PBS control group. Immunohistochemical analysis has revealed enhanced phosphorylated α-syn pathology in PFF-injected animals after 2 months, resulting in significant dopaminergic neurodegeneration after 6 months. With the ongoing analysis, we expect to uncover disease-related immune changes in the brain critical for disease progression that might also explain the sex dimorphism seen in PD.

P04.02

Monocyte mitochondrial function in Parkinson's disease

*Fatima Afaar**
The University of Sydney, Sydney, New South Wales, Australia

Parkinson's Disease (PD) is the most common neurodegenerative movement disorder and one of the world's fastest-growing neurological disease. Within Australia alone 37 new cases of PD are diagnosed daily. The clinical course for many patients with PD is long and slow, often occurring over decades. There are currently no treatments that can slow or stop PD, resulting in a progressively incapacitating disorder that culminates in considerable disability. A lack of simple blood-based biomarkers to diagnose and track the progression of PD is a main contributor to the current lack of treatments. Mitochondrial dysfunction and increased oxidative stress have presented as having significant roles in the progression of PD. The objective of this study was to establish a flow cytometry assay to assess mitochondrial and reactive oxygen species (ROS) levels in Healthy Controls and PD Patients monocytes using flow cytometry, to determine if these measures may comprise PD biomarkers. A second objective was to determine if putative small molecule PD therapies targeting genetic PD targets (LRRK2 and GBA) could ameliorate mitochondrial dysfunction in PD patient monocytes. The study constituted a total of 50 subjects; 25 healthy controls and 25 PD patients that were age and sex matched. No difference in mitochondrial or ROS levels was seen between control and PD patient monocytes, and thus the effectiveness of PD drugs to ameliorate mitochondrial dysfunction could not be concluded. However, a positive correlation was present between PD patients ROS levels and the MDS-UPDRS-III scale, which is an assessment of motor symptoms severity in PD. These results suggest that monocyte superoxide levels may comprise a biomarker for PD progression.

P04.03

Alpha-synuclein alters the neuronal lipidome and regulates phosphatidylserine synthesis at the Mitochondria-Associated ER Membranes (MAM) in patient-derived neurons modeling Parkinson's disease

Peter Barbuti[*,1], Cristina Guardia-Laguarta[1], Taekyung Yun[1], Gérald Cruciani[2], François Massart[2], Bruno Santos[2], Simone Larson[2], Claire Dording[2], Nobutaka Hattori[3], Estela Area-Gomez[4], Rejko Krüger[2], Serge Przedborski[1]*
[1] Columbia University, New York, NY, United States
[2] Luxembourg Centre for Systems Biomedicine (LCSB), Belval, Luxembourg
[3] Juntendo University, Tokyo, Japan
[4] Centro de Investigaciones Biológicas Margarita Salas – CSIC, Madrid, Spain

Significant challenges facing Parkinson's disease (PD) today include identifying at-risk individuals in the prodromal stage of disease, and the lack of useful biomarkers indicating disease progression and treatment efficacy. Excess of the neuronal protein alpha-synuclein (αSyn) is associated with PD, yet αSyn itself has proven to be an unreliable biomarker, moreover the functional role of physiological αSyn remains incompletely understood. Analysis of serum from PD patients including familial PD cases harboring p.A53T mutations in the αSyn-encoding gene SNCA has identified several lipid species as predictors of PD phenotypes. To elucidate the origin of those changes we processed iPS-derived midbrain dopaminergic neurons (mDANs) expressing the same pathogenic p.A53T αSyn mutation by lipidomic profiling using ultra-performance liquid chromatography/tandem mass spectrometry (UPLC-MS/MS). To determine if all pathogenic αSyn variants shared a common lipid disease signature we further processed patient-derived, iPS-derived mDANs carrying the pathogenic p.A30P αSyn mutation and a SNCA gene-locus duplication, validating 11 congruent lipid biomarkers.
Since many of the proteins required for lipid metabolism, including αSyn are found at the mitochondria-associated ER membranes (MAM), we hypothesized that altered endogenous levels of physiological or pathogenic αSyn would modify this transient, biochemically active, lipid raft-like domain. We report that non-physiological αSyn alters ER-Mitochondrial communication and a functional role of physiological αSyn is to drive the de novo synthesis of phosphatidylserine (PtdSer) – a tightly regulated phospholipid exclusively synthesized at the MAM. We find that pathological neurons have a greater abundance of PtdSer and have altered levels of fatty acid saturation within the same lipid class. To provide further mechanistic understanding we performed subcellular fractionation experiments to enrich for the MAM, finding that

physiological αSyn dosage regulates PtdSer synthesis by feedback-control regulation of PtdSer synthase 2 (PSS2).
Our results reveal αSyn-driven changes in MAM activity alter the neuronal lipidome. The consequences of an altered lipidome, including too much PtdSer, is not well understood. Yet, as PtdSer is the key "eat-me" signaling factor for immune cells to perform non-cell autonomous cell death. This suggests a potential interplay between αSyn driven lipid alterations and neuroinflammation that may, in-part underlie PD pathogenicity.

P04.04

Impact of chronic stress in Parkinson's disease pathogenesis: Role of microglial glucocorticoid receptors in the regulation of innate immunity-associated supramolecular organizing centres (SMOCs)

Pierre Besnault[*1], Sharmilee Antoine[1], Sheela Vyas[2], Stephane Hunot[1]*
[1] Paris Brain Institute, Paris, France
[2] Institute of Biology Paris Seine, Paris, France

Chronic stress (CS), a phenomenon encountered in daily living, has emerged as a potential environmental factor involved in the emergence and progression of PD. While CS is known to be a major risk factor of depression, the latter is also recognised as a clinical risk factor of PD. Environmental stress induces complex and adaptive biological responses supported by the physiological stress system i.e., the Hypothalamic-Pituitary Adrenal (HPA) axis. Stress-induced blood release of glucocorticoids (GCs) by the HPA axis activates glucocorticoid receptors (GRs) which among other aspects play a central role in immune and neuronal functions. However, chronic stress (CS) over protracted period can result in a deregulation of the HPA axis and disrupted GR functions eventually compromising the immune system. Our main objective is to highlight the role of chronic stress in the development and progression of PD, and to document the underlying cellular and molecular mechanisms. In microglial cells, the brain tissue macrophages, Supramolecular Organizing Centres (SMOCs), considered as innate immune signaling organelles, can generate a wide range of effector responses involved in inflammatory processes evoked by pathological aggregated proteins such as PD-associated alpha-synuclein (aSyn). Therefore, we hypothesized that chronic stress-induced GR impairment in microglial cells could exacerbate harmful inflammatory reactions through an overactivation of SMOC-dependant pathways. Our data indicate that 1/ chronic unpredictable mild stress (CUMS), a model of daily living stress resulting in anxiety- and depressive-like behaviour in mice, leads to decreased microglial GR expression associated with increased microglial activation and loss of dopaminergic neurons in a synucleinopathic mouse model of PD. 2/ Microglial-specific GR deletion by gene targeting results in aggravated neuropathology in PD-like mice. 3/ Microglial GR negatively modulates the myddosome pathway, a Toll-like Receptor (TLR)-dependent SMOC engaged in inflammatory response evoked by aggregated aSyn. 4/ Microglial GR-dependent control of myddosome function may involve transcriptional regulation of negative feedback factors of this SMOC. Overall, our data provide mechanistic insights into stress-related changes in brain immune cells and call for caution in using GR-based drugs for therapeutic intervention which may prove inefficient in patients with compromised GR function.

P04.05

Stratifying people with sporadic Parkinson's disease by pathological mechanism in patient-derived fibroblasts

Toby Burgess[*1], Thomas Payne[2], Stephen Bradley[2], Sarah Roscoe[2], Oliver Bandmann[2], Heather Mortiboys[2]*
[1] Sheffield Institute for Translational Neuroscience, sheffield, South Yorkshire, United Kingdom
[2] SITRAN, sheffield, United Kingdom

Objectives: To stratify a new cohort of Sporadic Parkinson's disease (sPD) patients into small, homogeneous subgroups defined by specific mitochondrial and lysosomal dysfunction.
Background: sPD is widely recognised as a heterogeneous disorder, both clinically and mechanistically. Several dysfunctional mechanisms have been identified, including mitochondrial and lysosomal dysfunction. However, clinical trials select participants without considering mechanism heterogeneity and continually fail to reach efficacy outcomes.
Methodology: We investigated mitochondrial and lysosomal dysfunction, two key mechanisms of sPD and promising targets for therapeutics. Imaging and biochemical assays assessed mitochondrial and lysosomal health parameters in fibroblasts from a new cohort consisting of 35 sPD patients and 24 healthy individuals. The sPD population was then stratified by assessing patterns of dysfunction across these parameters. Validation of these subgroups is currently being undertaken in the patient fibroblasts and induced Dopaminergic Neurons.
Statistical Analysis Approach: The results for each parameter were transformed to z-scores in proportion to the entire control population. Composite z-scores across triplicate repeats were calculated, using the sum of the Pearson correlation coefficients between all components, and was repeated for both media conditions to provide a single z-score for each parameter per cell line. Population differences were then interrogated using the T-test and F-test of equality of variance.
Results: We confirmed that the sPD population was significantly heterogeneous in 88% of mitochondrial and lysosomal parameters. Stratification of this cohort by distinct patterns of dysfunction identified four unique subgroups, defined by mitochondrial dysfunction, lysosomal dysfunction or both. The top 3 patients in each subgroup were selected for validation and mechanism studies, which discovered a significant reduction in maximal respiration in the pure mitochondrial dysfunction subgroup.
Conclusion: This study suggests that it is possible to stratify cohorts of sPD patients providing a possible model for clinical trial recruitment in order to aid the effectiveness, and therefore approval, of new therapeutics and support an approach to personalised treatment plans.

P04.06

Parkin deficiency impairs mtDNA dynamics and propagates inflammation

Sandro Lino Cardoso Pereira[*,1], Kobi Wasner[1], Semra Smajic[1], Jenny Ghelfi[1], Sylvie Delcambre[1], Cesar A. Prada-Medina[2], Evelyn Knappe[3], Giuseppe Arena[1], Patrycja Mulica[1], Gideon Agyeah[1], Aleksandar Rakovic[3], Ibrahim Boussaad[1], Katja Badanjak[1], Jochen Ohnmacht[1], Jean-Jacques Gérardy[4], Masashi Takanashi[5], Joanne Trinh[3], Michel Mittelbronn[1], Nobutaka Hattori[5], Christine Klein[3], Paul Antony[1], Philip Seibler[3], Malte Spielmann[2], Anne Grünewald[1]*

[1] Luxembourg Centre for Systems Biomedicine, University of Luxembourg, Esch-sur-Alzette, Luxembourg
[2] Max Plank Institute for Molecular Genetics, Berlin, Germany
[3] Institute of Neurogenetics, University of Lübeck, Lübeck, Germany
[4] National Center of Pathology, Laboratoire National de Santé, Dudelange, Luxembourg
[5] Department of Neurology, Juntendo University, Tokyo, Japan

Parkin is an E3 ubiquitin ligase which when mutated may cause autosomal recessive Parkinson's disease (PD). Along with PINK1, Parkin is notably known to act in the clearance of dysfunctional mitochondria, a process called mitophagy. Nevertheless, accumulating evidence attribute diverse regulatory functions to Parkin beyond mitophagy. These, include roles in processes such as mitochondrial biogenesis and mitochondrial membrane permeability, which might drive mitochondrial DNA (mtDNA) release and thereby elicit neuroinflammation. However, direct investigation of such mechanisms in patient-derived neurons and their implication to PD is inexistent.
In this study, we sought to explore Parkin's role in averting neuronal mtDNA dyshomeostasis, its release and in the activation of downstream inflammatory processes.
Induced pluripotent stem cells (iPSC) of PRKN mutation carriers and healthy controls were used to generate midbrain neurons. A deep analysis of mitochondrial genome maintenance and biogenesis was performed by applying live-cell imaging and proteomic, mtDNA integrity, and gene expression analyses. We further studied immune response activation in postmortem brains using single-nuclei RNA sequencing and by evaluating interleukin expression in neuron-microglia co-cultures.
Mitochondrial biogenesis was impaired in PRKN-mutant neurons causing mtDNA dyshomeostasis. These deficits were linked to decreased NAD+/NADH ratios which resulted in the dysregulation of SIRT1, a major controller of mitochondrial biogenesis and clearance. Furthermore, Parkin-deficient cells significantly increased mtDNA release into the cytosol. This phenotype was reproduced by cobalt-elicited chemical hypoxia in WT neurons, which also lowered NAD+/NADH ratios and replicated all the other reported effects caused by Parkin deficiency. MtDNA dyshomeostasis was also observed in the postmortem midbrain from a PRKN -mutation carrier, which presented a higher proportion of microglia overexpressing proinflammatory cytokines. Concordantly, increased IL-6 expression was observed in neuron-microglia co-cultures generated from Parkin-deficient iPSCs when exposed to mtDNA/LPS.
Our findings highlight the regulatory role of Parkin in mitochondrial biogenesis and mtDNA maintenance pathways, thereby exerting protective roles against neuroinflammation and degeneration.

P04.07

Gut-brain axis: Could ureases from gut bacteria play a role in the development of neurodegenerative diseases?

Matheus V.C. Grahl[1], Brenda S. Andrade[2], Ana Paula A. Perin[3], Gilda A. Neves[3], Cristian Follmer[4], Kelvin S. Hohl[5], Augusto F. Uberti[1], Celia R Carlini[6]*

[1] Laboratory of Neurotoxins, Brain Institute, and Graduate Program in Medicine and Health Sciences, Pontifical Catholic University of Rio Grande do Sul, Porto Alegre, RS, Brazil
[2] Laboratory of Molecular Pharmacology, Institute of Biomedical Sciences, Health Sciences Center, Federal University of Rio de Janeiro, Rio de Janeiro, RJ, Brazil
[3] Laboratory of Molecular Biology of Pathogens, Center of Biotechnology, Graduate Program in Cellular and Molecular Biology, Federal University of Rio Grande do Sul, Porto Alegre, RS, Brazil
[4] Laboratory of Biological Chemistry of Neurodegenerative Disorders, Institute of Chemistry, Department of Physical-Chemistry, Federal University of Rio de Janeiro, Rio de Janeiro, RJ, Brazil
[5] Graduate Program in Biological Sciences: Biochemistry, Federal University of Rio Grande do Sul, Porto Alegre, RS, Brazil
[6] Federal University of Rio Grande do Sul, Porto Alegre, RS, Brazil

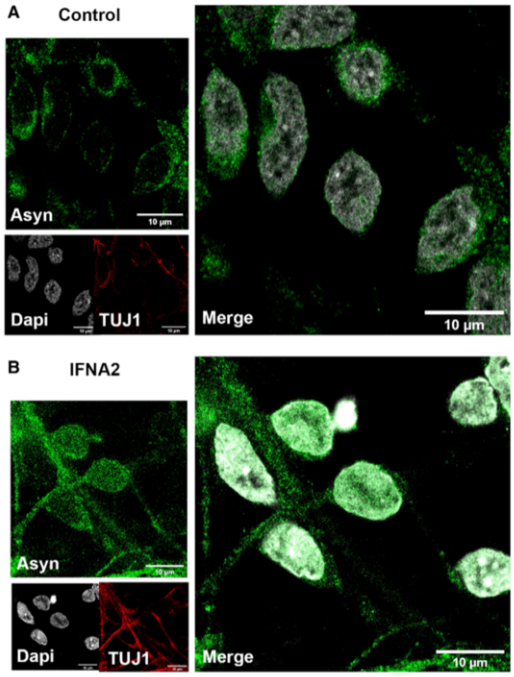
Although some genetic causes of Parkinson's Disease (PD) are recognized, most of the cases are sporadic with unknown pathogenesis. Intestinal dysbiosis seems to play a role in neurodegenerative pathologies. PD patients have an altered gut microbiota, with prevalence of Enterobacteriaceae, among which is Proteus mirabilis. It has been reported that mice treated orally with P. mirabilis developed motor deficits, loss of dopaminergic neurons in the substantia nigra, had increased levels of pro-inflammatory markers and deposits of α-synuclein in the colon and the brain, pointing to a role of this bacterium in PD pathogenesis.
As many human bacterial pathogens, P. mirabilis is a great producer of urease, an enzyme that catalyzes the hydrolysis of urea producing carbon dioxide and ammonia. Besides the toxicity of the released ammonia, ureases from different sources also cause biological effects that are independent of the enzyme's activity. Here we investigated a possible role of P. mirabilis urease (PMU) and its B subunit (PmUreβ) in the development of PD. For in vivo studies, the purified proteins were given to mice ip (20 mg/kg) daily during 1 week and 8 and 16 days after the last injection, behavioral tests were performed. Brain homogenates were subjected to immunochemical assays. Analyzes of TNF-α and IL-1β expression were performed in cultured cells (SH-SY5Y, HEK 293, BV-2, Caco-2). Cellular permeability assay with Dextran-FITC was carried out in HEK 293 monolayers. In vitro fluorescence studies were made to follow the kinetics of α-synuclein fibrillation. Our results indicated that PMU induced an increase in pro-inflammatory cytokines in cultured cells and altered permeability in HEK293 monolayers. Animals treated ip with PmUreβ showed anxiety-like symptoms while mice treated with PMU had depressive-like behavior. No motor deficits were observed. Brain homogenates of treated animals had a decreased content of α-synuclein, and increased levels of caspase-9 and of tyrosine hydroxylase, indicating with a reduction in dopaminergic neurons. In vitro, α-synuclein interacted with PMU, but not PmUreβ, with alterations in the fibrillation kinetics. We concluded that, under the conditions tested, PMU has pro-inflammatory effects in cultured cells and given ip to mice, PMU induces neuroinflammation and behavioral changes that are relevant to PD pathogenesis.

P04.08

Investigating the role of alpha-synuclein in neuronal innate immunity and its role in the interferon response pathway

Andrew Chai[*,1], Tilo Kunath[1], Matthieu Vermeren[1], Brendan Monogue[2], David Beckham[2]*
[1] University of Edinburgh, Edinburgh, Midlothian, United Kingdom
[2] UC Denver, Denver, United States

Alpha synuclein (αSyn), and the oligomeric and fibrillar conformations it adopts, is a major pathological molecular driver of dementia with Lewy bodies (DLB), Parkinson's disease (PD), and other synucleinopathies. However, αSyn's physiological role is not fully undefined, leading to a poor understanding of how its normal function is related to its pathophysiological disease mechanisms.
Recent evidence suggests αSyn has innate immune roles in protecting neurons from neurotrophic viruses, with mouse in vivo models showing increased susceptibility and morbidity to viral infection when αSyn is knocked-out. However, no functional studies in human disease models have investigated the innate immune role of αSyn in the CNS.
We investigated αSyn transcription, protein expression, and protein localisation, in human pluripotent stem cell (hPSC)-derived cortical neurons and neuroblastoma SH-SY5Y cells stimulated with viral mimics of infection and innate immune activators, such as Poly (I:C) and Type-I interferons.
We showed that Type-I interferon (IFN) stimulation in hPSC-derived cortical neurons showed significantly modulated extracellular αSyn secretion into conditioned media. We also showed that Type-I IFN stimulation in cortical neurons increased nuclear localisation of αSyn in a subset of neurons, which may elude to a dynamic change in subcellular localisation of αSyn when under acute interferon treatment.
Changes in αSyn protein levels and subcellular localisation due to innate immune stimulation may provide mechanistic understanding into αSyn's unique role in CNS innate immunity. Furthermore, changes in αSyn structure, conformation, and localisation due to innate immune stimulation may reveal links between infection and αSyn-mediated neurodegenerative diseases such as DLB and PD.



P04.09

Phosphoproteome profile variability in peripheral blood mononuclear cells of Parkinson's disease patients: A pilot study

Michal Cibulka[*,1], Mária Brodňanová[2], Milan Grofik[3], Andrea Ižarik Verešpejová[4], Natália Huňarová[4], Egon Kurča[3], Martin Kolísek[2]*
[1] Jessenius Faculty of Medicine in Martin, Comenius University Bratislava, Martin, Slovakia
[2] Biomedical Centre Martin, Jessenius Faculty of Medicine in Martin, Comenius University Bratislava, Martin, Slovakia
[3] Clinic of Neurology, Jessenius Faculty of Medicine and University Hospital in Martin, Comenius University Bratislava, Martin, Slovakia
[4] Department of Medical Biochemistry, Jessenius Faculty of Medicine in Martin, Comenius University Bratislava, Martin, Slovakia

Aim of the study: The primary goal of the presented study was to elucidate possible alterations of the activated kinases' profile in peripheral blood mononuclear cells (PBMC) of Parkinson's disease patients.
Background: Parkinson's disease (PD) is one of the most frequent neurodegenerative disorders, with the highest prevalence during senescence. Numerous pathological mechanisms, including oxidative stress, chronic deficiency of nutrients, perturbations of mitochondrial homeostasis or altered mechanisms of proteasome, are linked to the onset and progression of PD. However, the exact interplay between molecular pathological mechanisms remains elusive. Cellular signalome constitute intricate regulatory network responsible for temporal and spatial harmonization of molecular processes, thus cellular integrity and homeostasis. There is a limited amount of information regarding signalome dysregulation during the PD progression.
Materials and methods: 30 H-Y scale 1/2, 30 H-Y scale 3/4 PD patients and 60 sex- and age- matched controls were enrolled for the study. Molecular hallmarks of neurodegenerative pathologies have been shown to project into molecular physiology of PBMCs. PBMCs were isolated from peripheral venous blood by centrifugation of blood stacked on Histopaque-1077®. Isolated cells were subsequently lysed and panel of 43 phosphorylated kinases was analysed with Proteome Profiler Human Phospho-Kinase Array Kit (R&D), representing a robust targeted proteomic analysis.
Results: We identified kinases Src (phosphorylated on Tyrosine 419) and Yes (phosphorylated on Tyrosine 426) as candidate kinases, putatively dysregulated in PBMC of our cohort of PD patients. As these kinases are thus potentially clinically relevant, we quantify signals of Src and Yes kinases by Western blot. These results will be presented on WPC 2023. Src kinase belongs to a family of kinases that regulate signal transduction by diverse cell surface receptors and is involved in such fundamental cellular processes as cell growth, differentiation, migration and survival. Yes kinase is a proto-oncogene non-receptor tyrosine kinase, belonging to a Src kinase family. It is involved in cell growth and survival, cell-cell adhesion and cytoskeleton remodelling. The Src kinase family has been shown to be involved in neurodegeneration and is speculated to be a potential therapeutic target.
Funding: This study was supported by grant APVV-19-0222 to MK.

P04.10

Reduction of age-dependent neuromelanin accumulation by cerium oxide as a potential therapy for Parkinson's disease

Joana Margalida Cladera Sastre*[,1], Thais Cuadros[1], Marta Gonzalez-Sepulveda[1], Lena Montaña[2], Victor Puntes[3], Miquel Vila[4]
[1] Neurodegenerative Diseases Research Group, Vall d'Hebron Research Institute (VHIR)-Center for Networked Biomedical Research on Neurodegenerative Diseases (CIBERNED). Aligning Science Across Parkinson's (ASAP) Collaborative Research Network, Chevy Chase., Barcelona, Spain
[2] Design and Pharmacokinetics of Nanoparticles Group, Vall Hebron Research Institute (VHIR), Barcelona, Spain
[3] Design and Pharmacokinetics of Nanoparticles Group, Vall Hebron Research Institute (VHIR). Catalan Institution for Research and Advanced Studies (ICREA). Institut català de Nanociència i Nanotecnologia (ICN2), CSIC, The Barcelona Institute of Science and Technology (BIST). Networking Research Centre for Bioengineering, Biomaterials, and Nanomedicine (CIBER-BNN)., Barcelona, Spain
[4] Neurodegenerative Diseases Research Group, Vall d'Hebron Research Institute (VHIR)-Center for Networked Biomedical Research on Neurodegenerative Diseases (CIBERNED). Aligning Science Across Parkinson's (ASAP) Collaborative Research Network, Chevy Chase. Institut de Neurociències (INc-UAB), Autonomous University of Barcelona. Department of Biochemistry and Molecular Biology, Autonomous University of Barcelona. Catalan Institution for Research and Advanced Studies (ICREA)., Barcelona, Spain

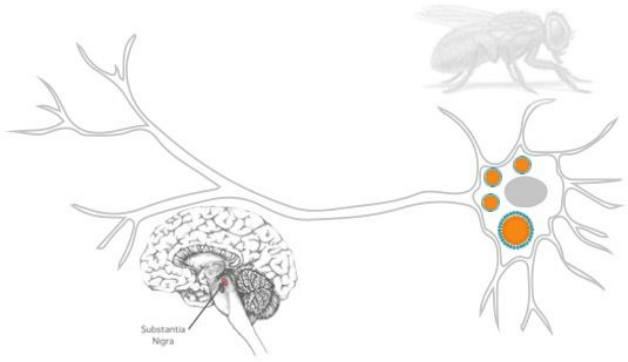
In Parkinson's disease (PD) there is a preferential degeneration of neurons that contain the pigment neuromelanin, especially dopamine (DA)-producing neurons of the substantia nigra pars compacta and norepinephrine (NE)-producing neurons of the locus coeruleus. Neuromelanin is an oxidative byproduct of DA and NE metabolism that progressively accumulates with age. It is formed, at least partially, by oxidation of excess cytosolic tyrosine, L-DOPA or DA into [o-]quinones, which derives into eumelanin or pheomelanin melanic components via the formation of aminochrome or 5-S-cysteinyl-dopamine/dopa precursors, respectively. In contrast to humans, neuromelanin does not appear spontaneously in most animal species, including rodents, and PD is an exclusively human condition. Using humanized neuromelanin-producing rodents, we recently found that neuromelanin can trigger PD pathology when accumulated above a specific pathogenic threshold.
Here we assessed whether neuromelanin production can be therapeutically reduced by decreasing catechol oxidation. This study was performed in vitro using SH-SY5Y human neuroblastoma cells genetically modified to produce neuromelanin by inducible expression of melanin-producing enzyme tyrosinase (i.e. TR5TY6 cells). Differentiated TR5TY6 cells were treated with different doses/regimens of various antioxidant compounds, including cerium oxide (CeO2) nanoparticles, cysteamine, N-acetylcysteamine (NAC) and edaravone, and then processed for the quantification of neuromelanin production and cell viability. From all these treatments, cerium oxide was able to significantly reduce intracellular neuromelanin levels and to prevent neuromelanin-linked cell death. We are now assessing the potential therapeutic effects of cerium oxide in vivo using our recently developed humanized neuromelanin-producing parkinsonian rats.
Our results suggest that age-dependent neuromelanin production can be therapeutically modulated by targeting catechol oxidation, thereby opening a new potential therapeutic path for PD and, in a broader sense, brain aging.

P04.11

Consequences of neuronal abnormal fat storage in human cellular and Drosophila Parkinson's disease models

Nathalie Davoust[*,1], Victor Girard[1], Florence Jollivet[1], Marie-Helène Canron[2], Marion Celle[1], Jean-Noël Arsac[3], Thierry Baron[3], Benjamin Dehay[2], Ronald Kühnlein[4], Bertrand Mollereau[1]*
[1] Laboratory of Biology and Modeling of the Cell (LBMC), ENS de Lyon, Lyon, France
[2] Neurodegenerative Disease Institute, University of Bordeaux, Bordeaux, France
[3] Anses, University of Lyon, Lyon, France
[4] Institute of Molecular Biosciences, University of Graz, Graz, Austria

Parkinson's disease (PD) is a neurodegenerative disease characterized by the neurotoxic aggregation of the alpha-synuclein (αSyn) protein. Genetic association studies reveal risk factors for PD linked to lipid metabolism, and abnormal fat storage in lipid droplets (LDs) has been reported in cellular models of the disease. However, the function of such accumulation in neurons or glial cells remains unknown. To understand the relationship between αSyn pathological conversion and the accumulation of LDs, we used the powerful genetic Drosophila (fruit fly) model of PD and human neuronal cell lines. We found that LD-coating proteins and αSyn co-localize at the surface of LDs in neuronal cells and Drosophila photoreceptor neurons. We then observed using a biochemical approach that the process of αSyn aggregation was enhanced in the presence of LDs. We thus propose that the association of αSyn with LDs could contribute to αSyn aggregation. We are currently investigating the mechanisms regulating LD turnover and the progression of the pathology in PD cellular and Drosophila models and in post-mortem brain section of PD patients.



P04.12

Peripheral and central immune changes in early PD: Baseline analysis of the AZA-PD trial cohort

Julia Greenland[*,1], Jonathan Holbrook[2], Caroline Williams-Gray[2]*
[1] Department of Clinical Neuroscience, University of Cambridge, Cambridge, Cambridgeshire, United Kingdom
[2] University of Cambridge, Cambridge, United Kingdom

Given the substantial evidence implicating the immune system in both the development and progression of Parkinson's disease (PD), we are conducting a clinical trial repurposing azathioprine, an immunosuppressant drug, with the aim of slowing down the progression of the disease and establishing proof of concept for immunosuppression as a disease modifying strategy in PD. AZA-PD is a randomised placebo-controlled, double-blind phase II trial in patients with early PD, within three years of diagnosis and with no

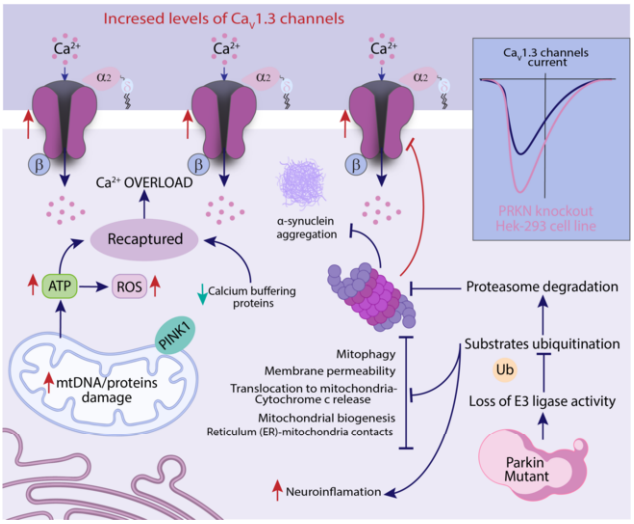
immune or inflammatory comorbidities. Participants are taking azathioprine/placebo for one year, with clinical assessments every 6 months and a primary outcome of the change in gait/axial subscore of the MDS-UPDRS in the OFF state after 12 months of treatment, a measure which has been shown to be the most sensitive component of the MDS-UPDRS III to disease progression. In addition, we are collecting mechanistic outcome measures evaluating activation of the immune system before and after treatment, using [11C]PK11195 PET neuroimaging, cytokine analysis and immunophenotyping of immune cells in the blood and cerebrospinal fluid (CSF).
The trial opened in April 2021 and recruitment was completed in July 2022, with 67 participants randomised to treatment, meeting our target sample size. The last trial visit is scheduled for February 2024.
Blood immunophenotyping data from the AZA-PD baseline visit (pre-treatment) is being compared to data from 30 age-matched controls with no immune/inflammatory comorbidities who have undergone immunophenotyping using the same panel of markers. We are characterising key populations of cells including subsets of CD4+ and CD8+T lymphocytes, B lymphocytes, monocytes and natural killer cells using flow cytometry. In addition, we have collected CSF from a subset of35 trial participants and 9 controls and performed a complimentary immunophenotyping panel, enabling us to assess infiltration of peripheral immune cells into the CSF.
Analysis of this baseline immunophenotyping data is ongoing and will be presented in full at the WPC. Preliminary results indicate an activated immune profile in the PD group. In particular, the data show a significantly lower proportion of T regulatory cells in PD, which have a vital role in maintaining immune tolerance and limiting chronic inflammation.

P04.13

The ubiquitin E3 ligase Parkin regulates CaV1.3 channel functional expression with a prospective role in Parkinson's disease pathogenesis

Lizbeth Grimaldo[*1], Alejandro Sandoval[2], Paz Duran[3], Liliana Gómez-Flores-Ramos*[*4], Ricardo Félix[5]*
[1] The National Institute of Public Health of Mexico (INSP), Cuernavaca, Morelos, Mexico
[2] School of Medicine FES Iztacala, National Autonomous University of Mexico (UNAM)., Tlanepantla, State of Mexico, Mexico
[3] Department of Molecular Pathobiology, College of Dentistry, New York University., New York, New York, United States
[4] Conacyt, Population Health Research Center, National Institute of Public Health., Cuernavaca, Morelos, Mexico
[5] Department of Cell Biology, Centre for Research and Advanced Studies of the National Polytechnic Institute (Cinvestav-IPN), Mexico City, Mexico

L-type calcium channels, comprised of four isoforms (CaV1.1-1.4), are one of the most important and studied types of calcium channels. The CaV1.3 isoform is mainly located in postsynaptic regions of adult substantia nigra dopaminergic neurons, contributing to their pacemaker activity. Extensive epidemiological studies demonstrated a neurological association between CaV1.3 dysregulated expression or activity and Parkinson's disease (PD) since dysregulated calcium homeostasis is an important PD stressor. Interestingly, increased levels of CaV1.3 in the post-mortem brains of early-stage PD patients have been observed. Also, a recent report showed that increased levels of short and long CaV1.3 isoforms were sustained despite neuron loss in an MPTP mouse model. Moreover, ubiquitination and proteasome degradation have been associated as critical mechanisms that control trafficking, localization, and abundance of voltage-gated calcium channels. Previously, we showed that Parkin, an E3 ligase enzyme of the ubiquitin-proteasome system (UPS), interacts with neuronal CaV2.2 channels promoting their ubiquitin-mediated degradation. Genome-wide association studies have identified pathogenic genetic variants of PRKN, increasing the risk of developing familial and sporadic PD. Most of the Parkin mutations are large rearrangements that disrupt its ligase activity. In a recent study, isogenic PRKN null iPSC-derived DA neurons exhibited elevated apoptosis process, abnormal neurite morphology, high rotenone susceptibility, elevated levels of T-type calcium channels, and altered calcium homeostasis. This study aimed to gain insight into how Parkin regulates the CaV1.3 channel expression levels by the UPS system. Immunoprecipitation assays showed the interaction between Parkin and the CaV1.3 channels expressed in HEK-293 cells and neural tissues. Parkin overexpression reduced surface and total CaV1.3 levels and decreased current density. Consistent with this, patch-clamp recordings in the presence of an inhibitor of the UPS, MG132, prevented the effects of Parkin. Also, Parkin overexpression reduced the half-life of the pore-forming CaV1.3α1 protein. Finally, electrophysiological recordings in a PRKN knockout HEK-293 cell line generated by CRISPR/Cas9 indicated an increased current density. Our results suggest that in physiological conditions, Parkin promotes the proteasomal degradation of CaV1.3 and that alterations in this mechanism might be relevant to PD's pathophysiology.



P04.14

Bruton's Tyrosine Kinase (BTK) is a druggable therapeutic target for neuroprotection in Parkinson's disease

Nanthini Jayabalan[*1], Natalia Birch[1], Natalie Groves[1], Katerina Hanton[1], Sara Jose[1], Robert Adam[2], John O'Sullivan[2], Nellwyn Hagan[3], Dimitry Offengeim[3], Richard Gordon[1]*
[1] University of Queensland, Herston, QLD, Australia
[2] Department of Neurology, Royal Brisbane and Women's Hospital, Brisbane, Queensland, Australia
[3] Precision Neurology and Neuroinflammation Cluster, Sanofi Genzyme, Cambridge, Massachusetts, United States

Parkinson's disease (PD) is a progressive, neurodegenerative disorder of aging that is characterised by accumulation of α-synuclein aggregates, persistent neuroinflammation and loss of dopaminergic neuron. The etiology of PD is mostly unknown, but it likely involves both environmental and genetic factors. Neuroinflammation can be observed early in the disease process

and is still strongly evident in post-mortem analyses of PD patient brains. Persistent immune activation has thus been closely linked to disease progression based on accumulating evidence from clinical studies and experimental models. Inhibition of the NLRP3 inflammasome has recently been shown to prevent α-synuclein pathology and dopaminergic neurodegeneration. The aim of the study was to examine if Bruton's Tyrosine Kinase (BTK), a key driver of the NLRP3 inflammasome activation, is activated in experimental PD and determine if the inhibition of this kinase leads to improved PD outcomes. Herein, we demonstrate that BTK is highly upregulated in the nigrostriatal system of human PD patients. We demonstrate that BTK is activated by pathological synuclein and triggers NLRP3 inflammasome activation in microglia. BTK is also activated in the nigrostriatal system of experimental PD models at the same timepoints as NLRP3 activation. Interestingly, we have also shown that pharmacological inhibition of BTK ameliorates markers of neurotoxic astrocytes in PD experimental models. Additionally, daily oral dosing with BTK inhibitors effectively reduces NLRP3 inflammasome activation markers and neuropathology in pre-clinical models of PD and improves dopaminergic neuron survival. Together, our results identify BTK as novel therapeutic target for neuroprotection in PD for disease modification.

P04.15

β-Glucocerebrosidase-1 (GBA1) signalling in immune cells inhibits inflammasome activation in Parkinson's disease

Nanthini Jayabalan[*,1], Madison Young[1], Katerina Hanton[1], Kerry Roper[1], Sara Jose[1], Robert Adam[2], John O'sullivan[2], Peter Lansbury[3], Richard Gordon[1]*
[1] University of Queensland, Herston, QLD, Australia
[2] Department of Neurology, Royal Brisbane and Women's Hospital, Brisbane, Queensland, Australia
[3] Bial Biotech, Cambridge, MA, United States

disease modification. However, the specific positive and negative regulators of immune activation which are dysregulated in PD remain poorly defined. Glucocerebrosidase 1 (GBA1), the gene encoding the lysosomal enzyme glucoslyceramidase (GCase), has been identified as the most important genetic risk factor contributing to the development of PD. Our current understanding of the functional role of GCase in PD has been informed primarily through studies in neurons. In this study, we aimed to investigate the relationship between inflammasome activation and GCase dysfunction in immune cells in PD. In this study, we uncovered that microglia expressed high levels of GBA mRNA and protein compared to astrocytes or dopaminergic neuronal cells. Therefore, we hypothesised that lysosomal GCase could be a potential regulator of inflammasome activation triggered by lysosomal rupture or mitochondrial dysfunction. We uncovered that NLRP3 inflammasome activation with α-synuclein induced a marked loss of GCase protein expression and enzymatic activity in primary microglial cells. Additionally, the progressive loss of GCase activity and expression correlated with inflammasome activation and IL1β release in microglia exposed to synuclein aggregates. Using the small molecule GCase activator LTI-291 (BIA 28-6156), we found that pharmacological activation of GCase could effectively suppress inflammasome activation markers triggered by synuclein aggregates. Most importantly, once-daily oral dosing with LTI-291 prevented neuroinflammation and neuropathology linked to PD in the nigrostriatal system. Together, our studies identify GBA activation as a novel therapeutic target for neuroprotection in PD, providing a new therapeutic paradigm by which to target chronic NLRP3 activation in PD and ameliorate chronic immune activation and neuropathology in PD.

P04.16

The influence of vagus-mediated immune modulation in the progression of Parkinson's disease and its hypothesized subtypes

Ida Klaestrup[*,1], Sara K. Nissen[2], Louise E. Warming[2], Sara A. Ferreira[2], Johanne Lauritsen[2], Hjalte Gram[2], Poul H. Jensen[2], Nathalie Van Den Berge[3], Marina Romero-Ramos[2]*
[1] Aarhus University, Biomedicine, Aarhus, Denmark
[2] DANDRITE & Department of Biomedicine, Aarhus University, Aarhus, Denmark
[3] Nuclear Medicine and PET Centre, Aarhus University Hospital & Department of Clinical Medicine, Aarhus University, Aarhus, Denmark

In Parkinson's Disease (PD) intraneuronal aggregated alpha-synuclein (ASYN), induces neuronal dysfunction and death, affecting predominantly substantia nigra, but also other neurons in the central and peripheral nervous system (CNS & PNS). In parallel to neurodegeneration, central and peripheral immune changes occur in PD, an inflammatory process where ASYN plays a central role that will influence neuronal health. Borghammer's team recently proposed two PD subtypes based on the initiation site of ASYN pathology: 1) a body-first subtype that starts in the gut and enters the brainstem bilaterally via the vagus nerve (VN); these patients show a faster PD progression than 2) the brain-first subtype of milder progression. Brain-first PD is proposed to spread unilaterally from the forebrain toward the lower brainstem and finally the periphery. In both subtypes, the VN is affected albeit at different time points. The VN exerts an anti-inflammatory modulation (inflammatory reflex), that might be disrupted by ASYN pathology promoting inflammation and contributing to the faster progression in the body-first subtype. To investigate this, we have mimicked aspects of the body-first PD subtype in a rat by injecting preformed fibrils (PFF) of mouse ASYN into the gut. We are analyzing data generated from peripheral and brain immune cells using flow cytometry and immunohistochemistry, plasma cytokine levels, and ASYN pathology in PNS and CNS. Our preliminary data suggest an increase of MHCII+ cells in the brain of the PFF-ASYN injected animals vs. the PBS control after 14 weeks, suggesting an early immune response in CNS.

P04.17

Microvascular changes and blood-brain barrier alterations in a progressive mouse model of synucleinopathy

Kristina Lau, Lisa Porschen, Franziska Richter, Birthe Gericke*
University of Veterinary Medicine Hannover, Department of Pharmacology, Toxicology and Pharmacy, Hannover, Germany

Dysfunction of blood-brain barrier (BBB) is suggested to play a critical role in the pathological mechanisms and progression of Parkinson's disease (PD). PD-related pathology such as alpha-synuclein (aSyn) accumulation and inflammatory processes potentially affect the integrity of the BBB early in disease progression, which in turn may alter the crosstalk of the central and peripheral immune response. Importantly, BBB dysfunction could also affect drug response in PD. Therefore, there is urgent need to resolve the underlying molecular mechanisms of BBB dysfunction in PD.
Here we analyzed microvascular changes on a cellular and molecular level during disease progression in a mouse model with overexpression of human aSyn (Thy1-aSyn, line 61, Chesselet, Richter et al. 2012 Neurotherapeutics). This model replicates characteristic motor and non-motor symptoms of PD, aSyn pathology and dopamine loss. Male Thy1-aSyn and wild-type age-matched controls were used at two different ages reflecting different

stages of disease progression. Brain capillaries from cortex and striatum were isolated and protein extracts subjected to Western blotting for analysis of BBB function-associated proteins.
We observed altered levels of transporter proteins and endothelial cell adhesion molecules in Thy1-aSyn mice, indicative of endothelial activation due to inflammatory processes. Furthermore, high expression levels of metalloproteinases and brain region specific changes in tight junction proteins were found in brain capillaries of Thy1-aSyn mice compared to wild-type. Importantly, several of these changes were specific to brain region and progression stage. Interestingly, confocal laser scanning microscopy revealed accumulation of human aSyn in brain capillaries isolated from Thy1-aSyn mice. To further characterize the integrity of the BBB, brain sections were immunohistochemically stained for lectin (for vessels) and aquaporin-4 (AQP4, for astrocyte end feet) expression. Quantification showed a brain-region specific decreased vessel and AQP4 density in Thy1-aSyn mice in the absence of overt leakage from blood to brain parenchyma.
Our data reveals intricate alterations in key proteins of BBB function together with histological evidence for altered structure of the brain vasculature. Further studies are required to understand how these alterations contribute to PD pathogenesis and progression, and to reveal novel therapeutic targets.

P04.18

An 80% improvement in UPDRS was followed by no progression in the last seven years in one Parkinson's patient. Here are the five lifestyle changes made, and how they might work

Patrick Bradshaw[1], William M Curtis[,2], Jeffrey Bohnen[3], William Seeds[4]*
[1] Department of Biomedical Sciences, Quillen College of Medicine, East Tennessee State University, Johnson City, TN, United States
[2] Department of Biomedical Sciences, Quillen College of Medicine, East Tennessee State University, Johnson City, TN 37614, USA, Bowie, MD, United States
[3] University of Michigan, Ann Arbor, MI, United States
[4] Seeds Scientific Performance Research, Spire Institute, Geneva, OH, United States

Mitochondrial quality control (MCQ), proteostasis, lipostasis, neurotransmitter synthesis, and antioxidant protection are all deficient in Parkinson's disease neurons. Together these deficiencies likely lie upstream of alpha-synuclein accumulation, neuroinflammation, and neuronal cell death. Therefore, these deficiencies are high value targets for treatment to delay onset and treat symptoms. Cells can potentially remedy these deficiencies when an individual initiates a regimen of intermittent fasting, exercise, and dietary modifications. These lifestyle choices can be performed at times of the day to entrain circadian rhythms and enhance metabolism. Key steps of the metabolic enhancement likely include 1) feed forward upregulation of NAD production through interactions of SIRT1 and BMAL1, 2) enhanced NADPH synthesis by the cytoplasmic isocitrate dehydrogenase pathway, which could restore monoamine neurotransmitter synthesis and power antioxidant defense, 3) restoration of [ATP]/[ADP] in neurons and neural epigenetic modification by the increased levels (R)-3-hydroxybutyrate, 4) upregulated plasmalogen synthesis in peroxisomes, 5) increased synthesis of cardiolipin and enhanced mitochondrial biogenesis, and 6) Interactions of superoxide, NO, H2O2, DJ-1, NADPH, and other actors to enhance the selective mitophagy of defective organelles through a process that we named the superoxide sentinel hypothesis of MCQ. We present the clinical case of a subject who was diagnosed with PD 20 years ago and who has followed the lifestyle and dietary changes for over seven years with the result that the UPDRS initially improved by 80% and has not changed significantly in seven years. We propose methods for evaluating the efficacy of disease modification that uses forecast modeling and machine learning techniques adapted from techniques used by a leading global financial institution, which resulted in a two-hundred-fold improvement in the accuracy of their forecasts. The circadian-based therapy described here has the potential to be a game changer for PD patients that could make moderate lifestyle changes.

P04.19

Immunoproteasome PSMB8 subunit increased in in Parkinson's disease

Hyeoi-Il Ma[,1], Huu Dat Nguyen[2], Linh Nhat Nguyen[2], In Hee Kwak[3], Young Eun Kim[3]*
[1] Hallym University Sacred Heart Hospital, Anyang, Kyunggi-Do, South Korea
[2] Hallym Neurological Institute, Hallym University, Anyang, South Korea
[3] Dept. of Neurology, Hallym University Sacred Heart Hospital, Anyang, South Korea

Background: Immunoproteasome, a part of ubiquitin–proteasome system, is involved in protein degradation and immune response. However, the relationship between immunoproteasome and Parkinson's disease (PD) was not evaluated clearly. We hypothesized that the shift of immunoproteasome attributes to PD due to its role in immune system and protein homeostasis.
Objective: To determine whether immunoproteasome in peripheral blood mononuclear cells is expressed differently between patients with PD and healthy controls (HCs) and to test its value as a biomarker of PD.
Methods: Blood samples were collected from 19 HCs and 40 patients with PD of comparable ages. Peripheral blood mononuclear cells were isolated and used to measure the mRNA levels of three catalytic subunits of immunoproteasome, namely, PSMB8, PSMB9, and PSMB10. Then, protein levels of immunoproteasome were confirmed by Western blot. Besides, the expression of immunoproteasome subunits in central nervous systems was indicated through postmortem slides.
Results: PSMB8 mRNA in PD group significantly increased compared to HCs. The ratio of PSMB10 and PSMB8 (PSMB10/8) best reflected difference between the PD and HCs($p = 0.002$). It can discriminate all PD, mild PD and drug-naive PD from HCs. We found correlation between the PSMB10/8 ratio with the UPDRS total and Part III score. In addition, the immunoproteasome upregulated in protein level in PBMCs of patients with Parkinson's disease. Besides, postmortem study showed that immunoproteasome PSMB8 level expressed abundantly in PD brain compared to HCs.
Conclusion: The expression of PSMB8 increased in PD, and the PSMB10/8 ratio can differentiate Parkinson's disease from HCs.

P04.20

Immune signaling through the gut-brain axis in a Drosophila model of PD

Alfonso Martin-Peña, Joshua Lopez-Sccarim, Beatriz Gomes, Malu Gámez Tansey*
University of Florida, Gainesville, FL, United States

The triggering factors of disease progression and the mechanisms of molecular spreading have remained elusive for most neurodegenerative disorders (ND). In many cases, the lack of understanding of the earliest pathophysiological process at the molecular level constitutes the main barrier to development of effective therapies that can prevent, halt or slow this process to

modify disease course. We posit that brain-body communication from the gastrointestinal (GI) tract to the central nervous system via vagus nerve neurotransmission has a pivotal role in transducing signals from the gut microenvironment (GME) to the brain. In fact, peripheral symptoms, particularly in the gastrointestinal system, can arise decades before the onset of the classic motor symptoms in ND. We have developed an integrated system to investigate the function of humoral pathways and analyze physiological alterations before and after symptoms onset. We have found that expression of human alpha-synuclein (hSNCA) in the epithelial cells of the fly gastrointestinal tract trigger sleep disturbances (a PD hallmark) and motor deficits. Interestingly, sleep deprivation in animal models induces accumulation of reactive oxygen species (ROS) dominantly within the gut epithelia. All these gastrointestinal insults trigger the production and release of proinflammatory cytokines. In this regard, abdominal injection of rhTNF in flies leads to increased day-time sleep, as well as expression of anti-microbial peptides. These features offer an ideal model to investigate the interaction between sleep, hSNCA, ROS and proinflammatory molecules, and how neuroinflammatory signals from these peripheral processes trigger impairments in brain function.
To test whether corrupted and pathogenic proteins expressed in the gut will spread to the brain, we employed the Gal4/UAS system in Drosophila and expressed WT hSNCA in gut epithelium cells. We then monitored behavior in aging flies expressing hSNCA and analyzed their locomotor activity along with several sleep parameters. Simultaneously, we investigated the neuroinflammatory response through the three main immune pathways in Drosophila (TNF/Toll/IMD).
We observed that flies selectively expressing hSNCA in enterocytes exhibited significant impairment in their daily activity pattern that specifically affected their behavior during the diurnal phase but not during the nocturnal period. Interestingly, these flies also showed increased daytime sleepiness without changes to their nocturnal sleep patterns.

P04.21

The intranigral infusion of alpha synuclein oligomers induces a cognitive decline underpinned by altered neuronal firing and neuroinflammation in cognition-related areas

Maria Francesca Palmas[*1], Michela Etzi[1], Claudia Sagheddu[1], Maria Francesca Manchinu[2], Michele Santoni[1], Chiara Camoglio[1], Giuliana Fusco[3], Alfonso De Simone[4], Paola Fadda[1], Marco Pistis[1], Nicola Simola[1], Ezio Carboni[1], Augusta Pisanu[5], Anna Rosa Carta[1]*
[1] University of Cagliari - Department of Biomedical Sciences, Monserrato, Italy
[2] Istituto Di Ricerca Genetica e Biomedica Del Consiglio Nazionale Delle Ricerche, Monserrato, Italy
[3] University of Cambridge - Centre for Misfolding Diseases, Department of Chemistry, Cambridge, United Kingdom
[4] University of Naples "Federico II" - Department of Pharmacy, Naples, Italy
[5] National Research Council - Institute of Neuroscience, Cagliari, Italy

Cognitive dysfunction is a main non-motor symptom of Parkinson's disease (PD), whose pathological correlate remains elusive, mainly for the lack of a valid preclinical neuropathological model. Clinical studies have reported the presence of inflammatory markers in the brain of parkinsonian patients with cognitive decline, pointing at neuroinflammation as a contributing pathological factor.
We investigated this issue in the translational rat model of PD based on the intranigral bilateral infusion of pre-formed human alpha synuclein oligomers (H-αSynOs) within the substantia nigra pars compacta (SNpc), which largely reproduces cardinal neuropathological and symptomatic features of the first stage of disease progression. H-αSynOs-infused rats displayed a mild cognitive decline in the two-trial recognition task in a Y maze and the novel object recognition (NOR) test performed three months after oligomer infusion. This cognitive impairment was associated with an altered inflammatory response in the anterior cingulate cortex (ACC) and in discrete subfields of the dorsal hippocampus. Indeed, we found increased number of microglial cells expressing large amount of the proinflammatory cytokine TNF-α as compared to vehicle-infused rats, supporting a role of neuroinflammation in this symptomatic aspect. Moreover, the ACC of H-αSynOs infused rats displayed an altered electrophysiological activity in vivo, and a decreased expression of the neuron-specific immediate early gene (IEG) Npas4 (Neuronal PAS domain protein 4) and the AMPA receptor subunit GluR1. Diffused deposits of phospho-alpha synuclein (p-αSyn) and Lewy neurite-like aggregates were found in the SNpc, striatum and subthalamic nucleus, suggesting the spreading of toxic protein within anatomically interconnected areas. All together, we present a neuropathological rat model of PD that recapitulates cognitive symptoms of PD, which adds to the classical motor aspects previously described. H-αSynOs infusion induces a neuroinflammatory environment in distant cognitive relevant regions, and an altered neuronal activity that may account for the cognitive deficits.

P04.22

Elucidating the link between mitochondrial stress responses and cellular senescence using human induced pluripotent stem cell-derived neurons and glia

Maria Jose Perez Jimenez[*1], Mariella Bosch[2], Stefanie Kalb[2], Hariam Raji[2], Michela Deleidi[2]*
[1] DZNE, Tubingen, Baden-Wurttemberg, Germany
[2] German Center for Neurodegenerative Diseases (DZNE), Tubingen, Germany

Protein aggregation and mitochondrial dysfunction are hallmarks of aging and neurodegenerative diseases, and strategies aimed at these pathological pathways may aid in the prevention of neuronal loss. The mitochondrial unfolded response (UPRmt) is a conserved mechanism that promotes mitochondrial protein quality control and organelle function under stress conditions by upregulating a variety of chaperones and proteases. However, research in C.elegans suggests that UPRmt may be detrimental for dopaminergic neurons and it exacerbates alpha-synuclein pathology. However, the actual role of UPRmt in Parkinson's disease and other neurodegenerative disorders remains unclear. The lack of relevant model systems has hampered the investigation of the mechanisms underlying human UPRmt and its differential role in glial and neuronal cells in health and disease.
To overcome this limitation and to investigate the cell-type-specific role of mitochondrial stress responses in brain health and disease, we developed human induced pluripotent stem cell (iPSC)-derived models of UPRmt. Combining imaging, functional, and RNA-sequencing investigations in iPSC-derived neurons, astrocytes, and microglia, we found that pharmacological activation of UPRmt leads to the upregulation of genes linked to cytosolic protein quality control, mitochondrial metabolism, and neurodegenerative disease pathways. Additionally, our results show an early and prominent activation of UPRmt in iPSC-derived astrocytes and microglia compared to iPSC-derived neurons. Interestingly, our findings suggest that UPRmt activation in glial cells induces a dysregulation of the inflammatory response and a senescence-like phenotype that could contribute to neurodegeneration. We are currently employing single cell-RNA sequencing in human iPSC-derived tricultures to

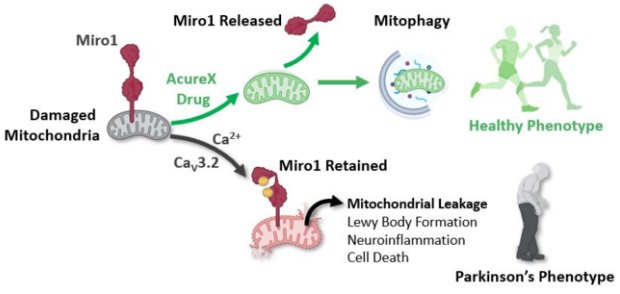
dissect the molecular mechanisms underlying such cell-type-specific mitochondrial stress responses and the impact of cell-cell interactions on senescence and immune pathways.

P04.23

The CaV3.2 T-type calcium channel is a novel target dysregulating miro1-dpendent mitophagy and driving Parkinson's disease pathology

Sean Pintchovski, Chung-Han Hsieh, Atossa Shaltouki, Eric Beattie, Ashley Gonzalez, Bill Shrader*
AcureX Therapeutics, San Carlos, California, United States

Mitophagy defects represent a major underlying pathology driving neurodegenerative conditions like Parkinson's disease (PD). The mitochondrial protein Miro1 has recently emerged as a key gatekeeper regulating the initiation of mitophagy, whereby Miro1 must be released from mitochondria for mitophagy to proceed. Critically, a failure to remove Miro1 has been found in sporadic PD (sPD) human brain tissues, in brain tissue of the well-established AAV-A53T mouse model of PD, and in PD subject iPSC-derived dopaminergic neurons carrying either the A53T SNCA, G2019S LRRK2, or N370S GBA genetic risk factors. These findings demonstrate that Miro1 retention and impaired mitophagy are key hallmarks and drivers of PD pathology.
AcureX utilized a combination of pharmacological, genetic, and physiological approaches to elucidate that the CaV3.2 isoform of the T-type voltage-gated calcium channel is a novel target that uniquely prevents the release of Miro1 from mitochondria, thereby inhibiting mitophagy and causing neuronal cell death. The critical role of CaV3.2 in PD pathology is further supported by (1) genetic association of a CaV3.2 mutation with PD risk, (2) CaV3.2 gain-of-function activity that increases mitochondrial calcium levels, and (3) selective upregulation of CaV3.2 (compared to the two other T-type channel isoforms, CaV3.1 and CaV3.3) in PD subject iPSCs and iPSC-derived dopaminergic neurons.
Based on AcureX's foundational discoveries linking CaV3.2 to Miro1 retention and neuronal degeneration in PD, we are developing first-in-class CaV3.2 selective inhibitors as novel disease-modifying therapies for the treatment of PD. These selective CaV3.2 inhibitors will be optimized to rescue Miro1-dependent mitophagy and neuronal viability to help significantly slow or potentially halt the progression of PD and substantially improve the quality of patients' lives.



P04.24

High levels of cell-Free mitochondrial DNA deletions in cerebrospinal fluid from patients with idiopathic, but not LRRK2, Parkinson's disease

Margalida Puigròs[1], Anna Calderon[1], Alexandra Pérez-Soriano[2], Cristina de Dios[1], Manel Fernández[3], Anna Colell[1], Maria-José Martí[2], Eduard Tolosa[2], Ramon Trullas[1]*
[1] Neurobiology Unit-IIBB-CSIC / IDIBAPS / CIBERNED, Barcelona, Catalunya, Spain
[2] Neurology Service, Parkinson's disease and Movement Disorders Unit, Institut Clínic de Neurociències, Hospital Clínic de Barcelona, University of Barcelona / IDIBAPS / CIBERNED, Barcelona, Catalunya, Spain
[3] Neurology Service, Parkinson's disease and Movement Disorders Unit, Institut Clínic de Neurociències, Hospital Clínic de Barcelona, University of Barcelona / IDIBAPS, Barcelona, Catalunya, Spain

The etiology of the majority of cases of Parkinson's disease (PD) is still unknown and classified as idiopathic (iPD). Pathogenic mutations in single nuclear genes, such as LRRK2, cause genetic forms of PD in a fraction of total disease cases. Remarkably, mitochondrial dysfunction underlies both idiopathic and genetic forms of PD.
The mitochondrial DNA genome (mtDNA) is a key regulator of mitochondrial function. Deletions of the human mtDNA genome accumulate during normal aging. The most frequent mtDNA deletion, known as "common deletion", causes mitochondrial dysfunction when the number of mtDNA copies with this deletion exceeds a certain threshold. Several studies have reported increased levels of mtDNA deletions in PD. Nonetheless, whether the accumulation of mtDNA deletions is somatic or depends on cell type remains unresolved.
The content of circulating cell-free mtDNA (cf-mtDNA) in the cerebrospinal fluid (CSF) distinguishes idiopathic from LRRK2-related PD, suggesting that a different type of mitochondrial dysfunction underlies neurodegeneration in these two forms of the disease. We examined the presence of deletions in cf-mtDNA by simultaneously quantifying different regions of the mtDNA molecule with a novel multiplex digital PCR assay, which allows absolute quantification of mtDNA molecules containing deletions.
Using this method, we found that cf-mtDNA in CSF from patients with iPD exhibits a high proportion of deletions compared with LRRK2 mutation carriers with or without PD. Furthermore, we found that the CSF content of cf-mtDNA differentiates idiopathic from LRRK2 PD, confirming previous data. These results provide further support to the hypothesis that the mechanisms causing mtDNA dysfunction differ between idiopathic and genetic PD.
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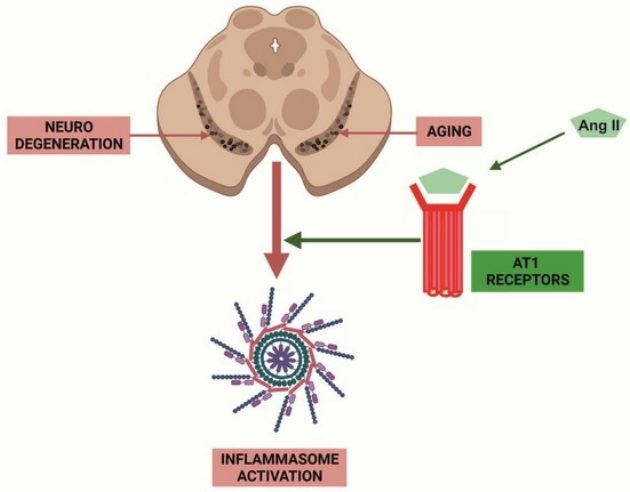
P04.25

Blocking the angiotensin type-1 receptor reduces NLRP3 inflammasome upregulation in the substantia nigra of aging and PD animal models

Aloia Quijano Ocampo, Carmen Díaz Ruíz, Andrea López López, Begoña Villar Cheda, Ana Muñoz Patiño, Ana Isabel Rodríguez Pérez, José Luis Labandeira García*
Universidade de Santiago de Compostela-CiMUS, Santiago de Compostela, A Coruña, Spain

The pro-oxidative and pro-inflammatory axis of the tissue renin-angiotensin system (RAS) has been shown to be involved in

changes observed in aging and age-related diseases, such as Parkinson's disease (PD).
In this work, we studied the effect of NLRP3 inflammasome activation in aging and early stages of dopaminergic degeneration in PD models. Furthermore, we studied whether the brain RAS, through the pro-oxidative and pro-inflammatory axis angiotensin II (AngII)/AngII receptor type 1 (AT1R), mediates inflammasome activation.
Substantia nigra (SN) of aged rodents and 6-hydroxydopamine (6-OHDA) PD models showed increased mRNA expression of inflammasome-related components (NLRP3, pro-IL1B and pro-IL18) and increase in protein levels of the cytokines IL1B and IL18, which were inhibited by the AT1R antagonist candesartan.
The role of the AngII/AT1R axis in inflammasome activation was confirmed in the SN of rats injected intraventricularly with AngII, and in primary mesencephalic cultures treated with 6-OHDA, which was also blocked by candesartan.
Moreover, observations in the SN of young and aged AT1R and AT2R knockout mice confirmed the involvement of AT1R in nigral inflammasome activation.
Altogether, we have shown a major role of the AngII/AT1 axis on NLRP3 inflammasome upregulation induced by aging and dopaminergic degeneration in substantia nigra (SN), possibly related to a decrease in dopamine levels.



P04.26

Non-cell autonomous effects of neuromelanin on Parkinson's disease pathogenesis

Gerard Roch, Maria Sellés, Joan Compte, Marta Gonzalez-Sepulveda, David Ramos-Vicente, Thais Cuadros, Joana M Cladera-Sastre, Annabelle Parent, Ariadna Laguna, Jordi Bové, Miquel Vila*
Institut de Recerca Vall d'Hebron, Barcelona, Spain

Objectives: Activation of both innate and adaptive immune responses occurs in Parkinson's disease (PD) postmortem brains. PD-linked inflammatory changes are highly localized within neuromelanin (NM)-containing areas, in which extracellular NM released from dying neurons is surrounded by or in contact with activated microglia and cytotoxic T lymphocytes. However, whether NM-linked immune response contributes to the neurodegenerative process remains unknown, partly because in contrast to humans NM is absent in common experimental animals such as rodents. Here we will characterize the relationship between NM-linked immune response and PD-like pathology using novel NM-producing PD rodent models based on the constitutive or viral vector-mediated overexpression of melanin-producing enzyme tyrosinase (TYR).
Methods: We first characterized histologically the NM-linked immune response, both innate and adaptive, in human postmortem PD brains and in NM-producing TYR-overexpressing animals, the latter at different time-points post-TYR expression. To determine the potential contribution of NM-linked immune response to PD-like pathology, we next injected AAV-TYR into the substantia nigra of genetically-modified MHC-II KO mice, which lack the capacity of MHCII-mediated antigen presentation, or T-cell deficient athymic nude rats.
Results: In both human PD brains and NM-producing rodents, AI-based quantifications of the inflammatory/immune response confirmed increases in microglial/macrophage activation (Iba1/CD68), astrocytic response (GFAP) and T-cell infiltration (mostly CD8) in close association with extracellular NM debris released from dying neurons. In TYR-expressing rodents, both innate and adaptive immune responses occurred at very early stages of the neurodegenerative process, even preceding overt neurodegeneration in this model. We are now assessing whether modulation of the immune response in NM-producing MHC-II KO mice and athymic nude rats influence NM-linked Lewy pathology and/or nigrostriatal degeneration in these animals.
Conclusions: Activation of innate and adaptive immune responses by extracellular NM occurs at very early stages of the neurodegenerative process and may thus contribute to PD pathology and progression.

P04.27

Viscosity sensitive AIE probes: Solid fluorescent tools for mapping mitochondria viscosity in proteostasis disordered in neurodegenerative cells

Soheila Sabouri[1], Hamid Soleimani Nejad[2], Tze Cin Owyong[3], Yuning Hong[1]*
[1] La Trobe University, Melbourne, VIC, Australia
[2] intelligent imaging innovation (3i), Melbourne, VIC, Australia
[3] University of Melbourne, Melbourne, VIC, Australia

Mitochondrial viscosity sensing is one of the most efficient ways to reflect cellular health conditions. Mitochondria micro-viscosity changes is closely correlated with abnormal intracellular bioprocesses and severe diseases. Viscosity sensitive mitochondria targeting probe may provide a valuable opportunity to measure mitochondrial micro-viscosity changes within the living cell, which is beneficial for studying and understanding subcellular processes precisely. In this work, we developed the Aggregation-Induced Emission (AIE), mitochondria targeting fluorescence probe which could be used to monitor mitochondria micro-environment changes. First, we validated the viscosity response in vitro, we applied our designed probe to measure the change of mitochondria viscosity in cells experiencing autophagy, mitophagy, and inflammation. Modern microscopic techniques, such as fluorescence lifetime imaging microscopy and fluorescence anisotropy imaging microscopy visualized mitochondrial viscosity alterations to better understand mitochondria stress response mechanisms and gain more precise information from mitochondrial micro-viscosity. Finally, we also mapped mitochondria micro-environment changes in proteostasis-disordered cells. Our obtained results showed substantial efficacy in intracellular viscosity mapping and is hopefully applied for clinical applications such as neurodegenerative disease diagnosis and therapy control.

P04.28

Acetylation of intestinal proteins: A potential mediator of systemic inflammation in Parkinson's disease

Verena Schmitt[*,1], Ippei Miyagawa[2], Birthe Gericke[3], Martin Regensburger[1], Franz Marxreiter[1], Franziska Richter[1], Mario M. Zaiss[2], Jürgen Winkler[1], Wei Xiang[1]*
[1] University Hospital Erlangen, Department of Molecular Neurology, Erlangen, Germany
[2] University Hospital Erlangen, Department of Internal Medicine, Erlangen, Germany
[3] University of Veterinary Medicine, Department of Pharmacology, Toxicology and Pharmacy, Hannover, Germany

Sporadic Parkinson's disease (sPD) is linked to prodromal gastrointestinal (GI) symptoms, accompanied by immune alterations in the both brain and gut, including autoimmune features. Notably, autoantibodies against protein acetylation (PA) have been associated with autoimmune diseases like rheumatoid arthritis. Although the triggers for PA are still uncovered, involvement of GI processes is assumed.
Objectives: We hypothesize that intestinal PA leads to the formation of anti-acetylated protein antibodies (AAPAs), which may be associated with sPD. Thus, we explored PA in the gut and AAPA in the serum of patients with sPD.
Methods: Using immunodot blot, we determined PA levels in fecal samples from 20 sPD and 19 healthy individuals as well as in intestinal contents obtained from transgenic PD mice and non-transgenic controls. Moreover, we determined serum AAPA levels in 12 PD and 14 healthy individuals using an enzyme-linked immunosorbent assay. To understand the potential transport mechanism of acetylated proteins along the gut-brain axis, we assessed PA in isolated extracellular vesicles (EVs) from human feces via Western blot.
Results: We detected increased PA levels in small intestine-derived intestinal contents in PD mice compared to controls. Interestingly, PA levels decreased in intestinal contents collected from the caecum, colon, or feces of PD mice. Consistently, fecal PA levels in PD patients were significantly lower than those in healthy controls. Furthermore, acetylated proteins were enriched in EVs isolated from human fecal samples. Serum analysis revealed that up to 58% PD patients show a high AAPA level.
Conclusion: We demonstrate the presence of PA in the GI content of PD mice and in the feces of patients. In our animal cohort, the small intestine appears to be the primary intestinal region, where PA occurs. Moreover, AAPA production in a considerable part of PD patients implies the involvement of the PA-to-AAPA cascade in systemic inflammation associated with a fraction of PD cases. Identification of intestinal PA in EVs suggests the involvement of EVs in transport of acetylated proteins from the gut for triggering AAPA production. Our results provide the basis for further analysis of PA in larger cohorts of sPD patients.

P04.29

PINK1-PD neurons display altered tyrosine hydroxylase phosphorylation

Karan Sharma[*,1], Katharina Zittlau[2], Boris Macek[2], Julia Fitzgerald[2]*
[1] Hertie Institute for Clinical Brain Research, Department of Neurodegeneration, University of Tübingen, Tübingen, Germany
[2] University of Tübingen, Tübingen, Germany

Loss of mitochondrial quality and death of dopaminergic neurons in the substantia nigra are key hallmarks of PINK1-Parkinson's Disease (PD). PINK1 is a Ser/Thr kinase that is highly regulated at the mitochondria and is known to phosphorylate several outer mitochondrial membrane proteins thereby mediating PINK1-Parkin mitophagy after mitochondrial depolarization and/or mitochondrial stress. We performed a phospho-proteomic screen with crude mitochondria enriched from PINK1 wildtype (WT) and knockout (KO) human iPSC-derived dopaminergic neurons and found an enzyme - Tyrosine Hydroxylase (TH) to be less phosphorylated at Ser19 in the absence of PINK1. TH is a crucial enzyme known to be involved in the rate-limiting step of dopamine biosynthesis. To validate our findings, we used immunofluorescence imaging and immunoblotting to visualize localization and quantify phosphorylated TH Ser19 respectively and confirmed that TH is less phosphorylated in PINK1 KO and PINK1 Q126P neurons compared to their WT isogenic controls. The PINK1 Q126P mutation was found in several PD patients and has been shown to affect the stability of PINK1. We also observed a higher nuclear localization of phosphorylated TH Ser19 in PINK1 KO and Q126P mutation neurons. However, the overall protein level of total TH is not significantly affected. We postulate that PINK1 could be directly or indirectly involved in the phosphorylation of TH at Ser19. This reduction of TH Ser19 phosphorylation is known to affect TH activity and may lead to a decreased production of dopamine and other catecholamines. Here, we identify a novel observation in PINK1-PD neurons that could be relevant for the early events in disease etiology.

P04.30

Systemic inflammation activates coagulation and immune cell infiltration pathways in brains with propagating α-synuclein fibril aggregates

Anne-Line S. Laursen[*,1], Mikkel V. Olesen[1], Jonas Folke[1], Tomasz Brudek[1], Florence Sotty[2], Kate L. Lambertsen[3], Karina Fog[2], Louise T. Dalgaard[4], Susana Aznar[1]*
[1] Centre for Neuroscience & Stereology, Bispebjerg and Frederiksberg Hospital, Copenhagen University Hospital, Copenhagen NV, Denmark
[2] Lundbeck A/S, Valby, Denmark
[3] Department of Neurobiology, Institute of Molecular Medicine, University of Southern Denmark, Odense C, Denmark
[4] Department of Natural Science and Environment, Roskilde University, Roskilde, Denmark

Aim: Pathological brain aggregates of α-synuclein (α-syn) characterizes a group of diseases defined as synucleinopathies. Recent studies implicate inflammation as one of the central pathogenic mechanisms but how it is linked to α-syn pathology is still unknown. In the present study, we aimed to address this by inducing a mild, systemic inflammation in a pre-formed fibril (PFF)-induced mouse model of α-syn pathology.
Methods: Three weeks after intra-striatal injections of human α-syn PFFs, mice were subjected for 3 weeks to repeated intraperitoneal injections of low concentrations (1 mg/ml) of lipopolysaccharide (LPS), a component of gram-negative bacteria.
Results: Histological analysis confirmed brain propagation of α-syn aggregation in PFF-injected mice independent of LPS-injections. No motor dysfunction was observed at this stage as measured in the pole test. Spleen immune cell profiling and multiplex cytokine analysis confirmed LPS-induced changes in populations of T- and B-cells, monocytes, and neutrophils, and increased brain TNF-α, IL-β, IL-10 and KC/GRO levels. LC-MS/MS analysis in the forebrain area and subsequent downstream ReactomeGSA pathway analysis revealed that PFF-injections induced alterations in mitochondrial metabolism and synaptic signaling, and Western Blotting additionally showed elevated β-fibrinogen levels in the forebrain. Systemic inflammation induced by LPS resulted in an overrepresentation of pathway related to fibrin clotting, integrin signaling and B cell receptor signaling in the PFF-injected mice.
Conclusions: In conclusion, energy homeostasis, synaptic signaling and BBB permeability seems to be altered at early stages

of α-syn pathology, and interestingly, a systemic inflammatory insult shifts the brain proteome without apparently affecting α-syn pathology load.

P04.31

Investigating the mechanisms by which progranulin deficits contribute to Parkinson's disease pathology

Oihane Uriarte Huarte, Jake S. Boles, Rebecca L. Wallings, Noelle K. Neighbarger, Cassandra L. Cole, Malú Gámez Tansey*
University of Florida College of Medicine, Gainesville, Florida, United States

Parkinson's disease (PD) is a complex multifactorial disease with no cure available. Even though PD has been studied for more than 200 years, its etiology remains unknown; thus, discovering new mechanisms that prevent neuronal loss is of great interest to the field. Even though alpha-synuclein aggregation has been considered the primary pathological mechanism responsible for neuronal death, the hypothesis that other mechanisms such as inflammation or lysosomal dysfunctions also contribute to neuronal loss is gaining attention. In this context, progranulin (PGRN), a secreted glycoprotein whose reduced expression is linked to several neurodegenerative diseases such as FTD or AD, has been recently linked with PD, where low PGRN levels in the plasma of PD patients correlate with PD progression and severity. PGRN is expressed in neurons, brain-resident microglia, and peripheral immune cells. Although its specific function is still unclear, it has been linked with lysosomal functions and immune system regulation. Hence, we hypothesize that PGRN deficits contribute to PD pathology by exacerbating the inflammatory response in the periphery and the brain and contributing to alpha-synuclein aggregation due to a disruption in the lysosomal pathway. To test our hypothesis, we will combine in vitro and in vivo mouse models and complement our findings with single-cell approaches to identify specific neurodegenerative mechanisms at the cell-specific level. Our data indicate that myeloid PGRN-deficient immune cells react differently to several immunological challenges, including IFN-γ, LPS, or alpha-synuclein. Compared with WT, PGRN KO pMACs express less Tnf in response to IFN-γ but express more Tnf in the presence of human PFFs. PGRN KO pMACs display altered GBA index, MHCII, and MV109, which might be responsible for the observed differences in the immunological response of PGRN-deficient myeloid cells. We expect this study will shed light on the understanding of novel mechanisms contributing to PD-associated pathology and will pave the way to develop new neuroprotective therapeutic strategies.

P04.32

Mitochondrial DNA copy number inferred from whole genome sequencing data is lower in individuals with Parkinson's disease

Longfei Wang, Liam Fearnly, Haloom Rafehi, Jiru Han3, Melanie Bahlo*
The Walter and Eliza Hall Institute of Medical Research (WEHI), Parkville, VIC, Australia

Mitochondrial dysfunction is known to be associated with Parkinson's disease (PD). Mitochondrial DNA copy number (mtDNA-CN) is an easily measurable and accessible proxy for mitochondrial function. mtDNA-CN estimated from whole-genome sequencing (WGS) data has been determined to be more accurate when compared to traditional qPCR techniques and estimates derived from microarray data (Longchamps et al. 2020). However, the accuracy of the existing methods is affected by GC nucleotide bias. With the rapid increase in availability of WGS data, more accurate and efficient methods are required. We have developed a new mtDNA-CN estimator with GC bias adjustment and strict sequencing quality controls, which can be applied to large-scale WGS data. We applied the proposed method to the Parkinson's Progression Markers Initiative (PPMI) dataset, which includes 1,809 individuals with WGS data from whole blood samples. We performed association tests between the mtDNA-CN and PD diagnosis, known mutations, motor and non-motor symptoms using linear regression models adjusted with age and sex. We found that blood-derived mtDNA-CN is lower in individuals with PD (p-value < 2e-16, effect size = -0.189), which has been previously demonstrated using the qPCR method (Pyle et al. 2016). We also found lower mtDNA-CN in people with prodromal non-motor PD (p-value = 1.25e-08, effect size = -0.349). The association tests with PD symptoms show that mtDNA-CN is significantly associated with motor experiences assessed by MSD-UPDRS II (p-value = 6.48e-14, effect size = -0.009) and MSD-UPDRS III (p-value = 6.88e-14, effect size = -0.005) and non-motor symptoms, including cognitive impairment score from the Montreal Cognitive Assessment (MoCA, p-value= 2.15e-06, effect size = 0.012), REM sleep behaviour disorder assessment using the Stiasny Kolster score (p-value = 0.00016, effect size = -0.012), the Epworth Sleepiness Scale (p-value = 7.16e-08, effect size = -0.014), and the University of Pennsylvania Smell Identification Test (UPSIT) score (p-value < 2e-16, effect size = 0.011). Our findings suggest that mtDNA-CN derived from blood may be a potential biomarker for PD.

P04.33

Uncovering the interaction between gut microbial factors and GBA1 mutations in the pathogenesis of Parkinson's disease

Christin Weissleder, Insa Hirschberg, Michela Deleidi*
German Center for Neurodegenerative Diseases (DZNE) and Center of Neurology, Hertie Institute for Clinical Brain Research, University of Tübingen, 72076, Tübingen, Germany, Tübingen, Baden-Württemberg, Germany

In vitro, in vivo, and clinical data indicate that microbial alterations are associated with inflammation and α-synuclein aggregation in the gut that could ultimately be propagated to the brain via the enteric nervous system. To date, the exact role of microbial factors in the initiation of Parkinson's disease (PD) remains controversial. Interestingly, a few studies show that short-chain fatty acids (SCFAs) exacerbate gut inflammation in mouse colitis models. In this study, we aim at dissecting the role of microbial factors and potential interaction with glucocerebrosidase (GBA1)- related genetic risk to impact inflammation and promote α-synuclein pathology. To this end, we employed induced pluripotent stem cell-derived macrophages and microglia from unaffected controls and GBA PD cases (L444P, E326K) to characterise the effects of different microbial factors (LPS, SCFAs: acetate, propionate, butyrate). Our data show that butyrate, but not acetate or propionate, enhances the secretion of cytokines and chemokines in both control microglia (TNFα, IL1β, IL6) and macrophages (CCL4, CXCL1, CXCL8). Whole-cell lysate proteomic analysis of butyrate-treated control macrophages and microglia uncovered significant changes in pathways associated with interferon type I response and lipid storage. Secretion of inflammatory cytokines and chemokines in response to LPS was reduced in microglia (TNFα, IL6, IL1ß, IL4, IL23) and macrophages (TNFα, IL6, CCL3, CCL5, CCL20, CXCL1) with both GBA1 mutations compared to isogenic controls. Macrophages and microglia also displayed a significantly lower phagocytic capacity compared to isogenic controls, indicating a less active phenotype of immune cells with GBA1 mutations. These results suggest that butyrate as well as GBA1 mutations alter key functions of peripheral and brain-resident immune cells. Given the

known link between glucocerebrosidase and α-synuclein, ongoing work is addressing the interaction between genetic vulnerability and SCFAs on neuro-immune interactions and PD pathology using intestinal and midbrain organoids.

P04.34

Validation of clinical stage NLRP3 inflammasome inhibitor RRx-001 for disease modification in Parkinson's disease

Madeleine Yule[*,1], Natalia Birch[1], Katerina Hanton[1], Nanthini Jayabalan[1], Rob Adams[2], John O'Sullivan[2], Brian Oronsky[3], Tony Reid[3], Richard Gordon[1]*
[1] UQ, Brisbane, QLD, Australia
[2] Royal Brisbane Hospital, Brisbane, QLD, Australia
[3] EpicentRx, San Diego, CA, United States

The global Incidence of Parkinson's disease is increasing, highlighting the urgent need to develop effective treatment options which could halt disease progression. Unresolving inflammation is an important pathological feature of Parkinson's disease which is linked to progression of the disease. Converging lines of evidence from multiple studies and research groups has shown that the NLRP3 inflammasome activation is the primary driver of the progressive dopaminergic neuron loss which occurs in people with Parkinson's disease. RRx-001 is a phase 3 chemoprotective small molecule drug which is a covalent NLRP3 inhibitor that is brain permeable. This study aims to investigate the effectiveness of RRx-001 therapy to reduce neuroinflammation and neuropathology induced by NLRP3 inflammasome activation in models of Parkinson's disease. We confirmed a significant reduction in inflammasome activation and inflammatory markers in murine and human immune cells relevant to Parkinson's disease. Further, RRx-001 prevented mitochondrial dysfunction and fragmentation in dopaminergic neurons treated with neurotoxicant. Using an in vivo model of Parkinson's, we found that daily administration of RRx-001 reduced neuroinflammation and rescued the neuropathology in the nigrostriatal system. We also found that RRx-001 increased protective NRF2 gene expression in the brain with once daily dosing. Together, our data demonstrates that RRx-001 can mitigate NLRP3 inflammasome activation in immune cells and the brain, and is neuroprotective. Our results indicate that RRx-001 is a novel, disease-modifying therapeutic for neuroprotection in Parkinson's disease.

P04.35

Understanding the mechanisms of a-syn spreading and degradation: Role of tunneling nanotubes and lysosomes

*Chiara Zurzolo**
Institut Pasteur, Paris, France

The accumulation of α-synuclein aggregates in specific brain regions is a hallmark of synucleinopathies including Parkinson's disease. α-Synuclein aggregates propagate in a "prion-like" manner and can be transferred inside lysosomes to recipient cells through tunneling nanotubes (TNTs), which are actin-based, thin cellular protrusions connecting remote cells. However, how lysosomes contribute in the spreading of α-synuclein aggregates is unknown. By using super-resolution and electron microscopy, we find that α-synuclein fibrils affect the morphology of lysosomes and impair their function in neuronal cells. In addition, we demonstrate that α-synuclein fibrils induce peripheral redistribution of lysosomes, likely mediated by TFEB, increasing the efficiency of α-synuclein fibrils' transfer to neighboring cells. We also show that lysosomal membrane permeabilization allows the seeding of soluble α-synuclein in cells that have taken up α-synuclein fibrils from the culture medium and, more importantly, in healthy cells in co-culture following lysosome-mediated transfer of the fibrils. Moreover, we demonstrate that seeding occurs mainly at lysosomes in both donor and acceptor cells after uptake of α-synuclein fibrils from the medium and following their transfer. Finally, by using a heterotypic co-culture system, we determine the origin and nature of the lysosomes transferred between cells and we show that donor cells bearing α-synuclein fibrils transfer damaged lysosomes to acceptor cells, while also receiving healthy lysosomes from them. These findings thus contribute to the elucidation of the mechanism by which α-synuclein fibrils spread through TNTs, while also revealing the crucial role of lysosomes. We propose that lysosomes damaged by α-synuclein fibrils become a hub for seeding new aggregates and function as a Trojan horse facilitating the propagation of misfolding and the dissemination of aggregates through TNTs.
We are currently addressing both the role of different glial cells, namely astrocytes and neuroglia, and of the inflammatory processes in the spreading and degradation of α-Synuclein in primary cells.

BASIC SCIENCE: Pathology

P05.01

Novel antibodies against oligomeric alpha synuclein

Johanne Aarup Lauritsen[*,1], Janni Nielsen[2], Sanne Simone Kaalund[3], Susana Aznar[3], Daniel Otzen[2], Marina Romero-Ramos[1]*
[1] Danish Research Institute of Translational Neuroscience (DANDRITE), Nordic EMBL Partnership for Molecular Medicine, & Department of Biomedicine, Aarhus University, Aarhus, Denmark
[2] Department of Molecular Biology and Genetics & Interdisciplinary Nanoscience Center (iNano), Aarhus University, Denmark, Aarhus, Denmark
[3] Center for Neuroscience and Stereology, Bispebjerg and Frederiksberg Hospital, Denmark, Copenhagen, Denmark

Aggregation of alpha-synuclein (a-syn) is common in synucleinopathies, including Parkinson's disease (PD), multiple system atrophy (MSA), and dementia with Lewy bodies (DLB). However, the cell type affected, and the neuronal death observed differ across these diseases. It is proposed that different a-syn strains may contribute to such disparities. The current tools to study a-syn pathology show overlapping pathology among the diseases, limiting a "correct" diagnosis. In addition, current antibodies (Abs) do not recognize the so-called oligomeric forms of a-syn, thus hindering the study of pre-LB pathology. We aim to identify novel a-syn-specific Abs, that enable better recognition and distinction of progressive a-syn pathology across brain regions and diseases. 29 monoclonal Abs were obtained after immunization of mice with different oligomers of human a-syn and tested with ELISA for affinity towards monomeric and oligomeric a-syn. Those with the highest selective affinity for oligomeric a-syn were selected for histology. Immunohistochemistry (IHC) was performed on rodent PD models overexpressing human a-syn. Commercial Abs were used for comparison and co-stainings, and based on their degree of co-localization five Abs were selected for further analysis. These were used for IHC in post-mortem brain tissue from patients with different synucleinopathies, for the detection of a-syn pathology. In parallel, pre-absorption with monomeric a-syn prior to IHC on rodent brains was used to better determine the preferential affinity of a-syn species. Our preliminary data show that all Abs can recognize human and rodent a-syn albeit to a different extent. Co-immunofluorescence showed that the Abs detected pathology seen by the commercial Abs, but also additional ones not observed with those. Pre-absorption with monomeric a-syn resulted in changes in

the quantity of a-syn pathology, either an increase or decrease depending on the Abs' monomeric/oligomeric affinity. Furthermore, the Abs were able to find pathology in post-mortem human brain tissue from both PD, DLB, and MSA patients.

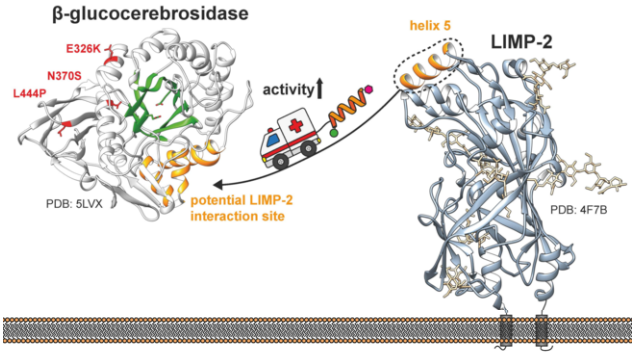
P05.03

Activating beta-glucocerebrosidase by exploiting its transporter LIMP-2

Jan Philipp Dobert[*,1], Simon Bub[2], Rebecca Mächtel[3], Alice Drobny[3], Dovile Januliene[4], Arne Möller[4], Philipp Arnold[5], Friederike Zunke[3]*

[1] University Hospital Erlangen, Department of Molecular Neurology, Erlangen, Germany
[2] Institute of Anatomy, Functional and Clinical Anatomy, Friedrich-Alexander-University Erlangen-Nürnberg (FAU), Erlangen, Germany
[3] Department of Molecular Neurology, University Hospital Erlangen, Erlangen, Germany
[4] Department of Structural Biology, Osnabrück University, Osnabrück, Germany
[5] Institute of Anatomy, Functional and Clinical Anatomy, Friedrich-Alexander-University Erlangen-Nürnberg (FAU), Erlangen, Germany

Mutations in the GBA1 gene are the cause of the lysosomal storage disorder Gaucher disease and are among the highest genetic risk factors for the development of the neurodegenerative disorder Parkinson disease (PD). GBA1 encodes the lysosomal enzyme beta-glucocerebrosidase (GCase), which orchestrates degradation of glucosylceramide (GluCer) in the lysosome. Recent studies have shown that GluCer accelerates alpha-synuclein aggregation and that loss of GCase activity along with lysosomal dysfunction is a hallmark in the PD brain. In turn, restoring GCase activity has been shown to alleviate alpha-synuclein aggregation and pathology in cell and mouse models, manifesting modulation of GCase as a promising novel treatment approach for PD. Ongoing research and clinical trials are aiming to identify GCase activating compounds for clinical application.
In this study, we investigated the interaction of the lysosomal membrane protein and GCase transporter LIMP-2 with wild type (wt) GCase and the most prominent disease-associated disease variants: p.E326K, p.N370S and p.L444P. Our data reveals that LIMP-2 not only mediates transport of GCase to the lysosome, but functions as an allosteric activator of the enzyme. Overexpression of LIMP-2 boosted lysosomal transport of GCase and rescued activity of the E326K variant in HEK293T cells. Further, in vitro activity of purified GCase wt and E326K was increased in presence of a recombinant LIMP-2 ectodomain.
Through biochemical studies and preliminary structural analyses, we then identified a single helix in the LIMP-2 ectodomain that proved to be sufficient for binding and activation of GCase in vitro. Based on this helix, we designed a custom lysosome-targeted peptide that was able to restore lysosomal GCase activity in primary human fibroblasts of PD patients harboring GBA E326K mutations. These findings expose the LIMP-2 protein as well as its GCase interaction site as potential therapeutic targets to rescue GCase activity in PD.



P05.04

Quantification of neurons in the rodent dorsal motor nucleus of the vagus using unbiased stereology

Eugenia Harbachova, Pietro La Vitola, Angela Rollar, Helia Aboutalebi, Ayse Ulusoy, Donato A. Di Monte*
DZNE, Bonn, Germany

Neurons in the dorsal motor nucleus of the vagus nerve (DMV) project long axons that innervate a variety of peripheral tissues/organs (e.g., heart, lung, digestive tract) and, by doing so, regulate their functions. In Parkinson's disease, DMV neurons are affected by neurodegenerative processes and represent early targets of alpha-synuclein pathology. An increasing number of in vivo studies is focusing on the pathophysiology of DMV neurons and, as part of these investigations, a precise and reproducible assessment of the integrity of DMV tissue and counting of DMV neurons is critical. This assessment faces significant challenges, however, particularly when carried out using image analysis techniques. For example, the DMV is very compact and small in size. Furthermore, during pathophysiological processes, assessment of DMV neurons using their phenotypic markers (e.g., choline acetyltransferase, ChAT) may be significantly impaired by downregulation of these markers. Finally, the entire DMV as well as its neurons may undergo volume reductions that would affect outlining of the nucleus, neuronal detection and counting. The purpose of this study was to develop and validate an unbiased stereological counting approach using the optical fractionator method for the quantification of DMV neurons in mice and rats. Initial analyses were performed in a set of 10 mice and 9 rats. 35-µm thick coronal sections of the brainstem were sampled. Every fifth section was stained with cresyl violet, DMV was delineated based on anatomical/morphological criteria and analyzed using the Stereoinvestigator software. Stereological counts of Nissl-positive DMV neurons revealed a total of 3375 ± 49 and 3894,72 ± 86 cells per side in mice and rats, respectively. A separate set of analyses was carried out in DMV sections that were stained with anti-ChAT. Data showed that the number of ChAT-positive DMV neurons was approximately 5% lower than the total count of Nissl-stained cells. Finally, in validation experiments, we were able to detect time- and dose-dependent losses of DMV neurons induced by alpha-synuclein overexpression. Data demonstrated feasibility, accuracy and reproducibility of DMV stereological counting that allowed us to detect even a 5% decrease in neuronal number.

P05.05

Blood markers predictive of molecular changes in the brain and clinical outcome in Parkinson's disease

Krithi Irmady[*,1], Caryn Hale[1], Rizwana Qadri[1], Sitsandziwe Simelane[1], John Fak[1], Thomas Carroll[1], Serge Przedborski[2], Robert Darnell[3]*
[1] Rockefeller University, NEW YORK, New York, United States
[2] Columbia University, NEW YORK, New York, United States
[3] Rockefeller University/Howard Hughes Medical Institute, New York, New York, United States

The molecular basis of clinical heterogeneity in Parkinson's disease remains poorly understood. Moreover, the ability to use blood markers that reflect changes in the brain to predict the heterogeneous outcomes of PD including disease progression and development of cognitive and motor complications, would be of enormous clinical value. We undertook deep RNA sequencing from the caudate and putamen of postmortem PD (n=35) and control (n=40) striatum, and compared molecular profiles with clinical features and samples obtained from antemortem peripheral blood from an independent cohort. Cognitive and motor complications of PD were associated with molecular changes in the caudate and putamen respectively. Later and earlier-onset PD were molecularly distinct, and disease duration was associated with distinct changes in caudate and putamen. Remarkably, molecular signatures in the brain associated with PD and its heterogeneous clinical features were also evident in antemortem peripheral blood and correlated with disease severity. In summary, these results identify molecular mechanisms that underlie clinical features of PD and their detection in PD patients' blood offers potential prognostic value.

P05.07

Heterozygous GBA N370S mutation does not uniformly reduce GCase activity or cause lysosomal dysfunction in iPSC-derived neurons

Adahir Labrador-Garrido, Katherine Moruzi, Siying Zhong, Shikara Keshiya, Glenda Halliday, Nicolas Dzamko*
University of Sydney, Sydney, NSW, Australia

GBA1 encodes the lysosomal enzyme glucocerebrosidase (GCase), a key part of the lysosomal/autophagy system that is associated with the clearance of alpha-Synuclein (aSyn) in Parkinson's disease (PD) neurons. Heterozygous mutations in GBA1 are a significant risk factor for PD. More than 300 pathogenic variants have been identified, with the most common mutation being the N370S point mutation. The majority of GBA1 mutations are hypothesized to cause a loss of GCase activity, which in turn would lead to impairments in the lysosomal/autophagy system and accumulation of aSyn. However, studies investigating the relationship between GCase and aSyn pathology are largely inferential and results can vary based on specific GBA1 mutations. In this project we have determined the relationship between aSyn, GCase and lysosomal/autophagy using induced pluripotent stem cell (iPSC) derived neurons with the common pathogenic GBA1 N370S mutation. Cell lines from controls and GBA N370S mutation carriers (n=4 per group) were successfully differentiated into mature neurons and GCase activity, aSyn pathology and markers of lysosomal/autophagy measured at baseline and following treatment with aSyn pre-formed fibrils. The GBA1 N370S mutation did not uniformly reduce GCase activity in neurons compared to controls, and the mutation had no significant effect on aSyn accumulation or lysosomal/autophagy in 3 out of 4 lines tested either at baseline or when pathology was initiated with aSyn fibrils. Only one cell line showed significant differences in GCase activity, aSyn pathology and Lysosomal/autophagy and demonstrated a mild response after treatment with GCase modulating drug treatment. We conclude that the GBA1 N370S mutation is a very mild mutation and does not uniformly impact GCase activity in differentiated neurons. These results may be important when thinking about stratification of patients for clinical trials of drugs aimed at enhancing GCase activity.

P05.08

Ultrasensitive determination of Ecto-GPR37 in plasma as a potential biomarker for Parkinson's disease

Marc López Cano*[,1], Josep Argerich[2], Per Svenningsson[3], Francisco Ciruela[2]
[1] Idibell, L'Hospitalet de Llobregat, Spain
[2] Universitat de Barcelona, Barcelona, Spain
[3] Karolinska Institute, Stockholm, Sweden

Parkinson's disease (PD) is the second most common type of neurodegenerative disorder, with hallmarks of Lewy body formation, neuronal death, and synaptic loss in the substantia nigra. Although potential diagnostic and prognostic biomarkers have been widely evaluated (i.e., α-synuclein species), no conclusive data have been obtained. Consequently, there is an urge to describe specific and reliable biomarkers of PD.
GPR37, also known as parkin associated endothelin-like (Pael) receptor, is an orphan G protein-coupled receptor (GPCR) that has been implicated in important physiological mechanisms and in the neuropathology of PD. Interestingly, GPR37 undergoes constitutive metalloprotease (MP)-mediated cleavage and shedding of the ectodomain [1]. Therefore, the N-terminal GPR37 ectodomain (i.e., ecto-GPR37) is constitutively released by cells into the extracellular environment. It has been hypothesized that the shedding of ecto-GPR37 may be altered in PD as receptor expression and MP levels increase. Consequently, ecto-GPR37 levels in patients with PD have been determined in cerebrospinal fluid (CSF) [2], an accessible source of brain-derived proteins and metabolites, reflecting molecular changes that occur in the central nervous system.
However, CSF obtention may be uncomfortable for patients and carries certain medical risks, as it is obtained by epidural puncture. In that sense, blood-based (i.e., plasma) neurodegeneration biomarkers of neurodegeneration have obvious advantages over CSF biomarkers. The collection of blood is inexpensive, less invasive, and a more feasible measure for use in the general population, especially if serial collection is needed. To this end, based on QuanterixTM single molecule array technology (SiMoA®), we engineered and optimized an ultrasensitive digital enzyme-linked immunosorbent assay (ELISA) to quantify ecto-GPR37 in plasma from both neurological controls and subjects with PD.
This project was founded by The Michael J. Fox Foundation (MJFF-001051)

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P05.09

Neuropathological alterations in subjects initially diagnosed by polysomnography with isolated REM sleep behavior disorder

Gerard Mayà, Alex Iranzo, Carles Gaig, Joan Santamaria, Mònica Serradelll, Laura Molina-Porcel, Ellen Gelpi, Iban Aldecoa*
Hospital Clínic de Barcelona, Barcelona, Spain, Spain

Background: REM sleep behavior disorder is a parasomnia caused by the dysfunction of the subcoeruleus nuclei and the n. magnocellularis and related circuits. More than 90% of isolated REM behavior disorder (IRBD) patients at 15 years of diagnosis are at risk of developing Parkinson's disease (PD, 45%), dementia with Lewy bodies (DLB, 45%) or multiple system atrophy (MSA, 10%). Neuropathological studies of firstly diagnosed IRBD are scarce.
Methods: Eighteen patients with IRBD diagnosed by polysomnography were followed up until death and participated in the Brain Donation Program (2005–2020). Standard neuropathological evaluation and semiquantitative assessment of pathological alpha-synuclein (AS) deposits and the degree of gliosis and neuronal loss in specific brain areas, including those related to REM sleep behavior disorder, were performed.
Results: 94% of participants were male, with a mean age (+/- SD) of 71 ± 6 years at IRBD diagnostic PSG and of 80 ± 6 years at death. Clinical antemortem diagnosis was DLB (n=10), PD (n=5) and IRBD (n=3). All patients had an underlying synucleinopathy, 17 of the Lewy body type (LBD) and one patient had a MSA. All had frequent brainstem alpha-synuclein pathology and 94% had moderate neuronal loss in the locus coeruleus/subcoeruleus complex. A caudo-rostral gradient of alpha-synuclein pathology from midbrain over limbic and neocortical areas was observed in IRBD patients that progressed to PD or DLB. All patients had some degree of co-pathology: 12 Alzheimer's disease neuropathological change (ADNC), of which 6 had intermediate/high severity (all in neocortical AS stages), 11 age-related tau astrogliopathy, 4 argyrophilic grain disease, 3 progressive supranuclear palsy and 3 limbic predominant age-related TDP-43 encephalopathy.
Conclusions: IRBD results from an underlying synucleinopathy with prominent brainstem involvement that may progress to DLB, PD or MSA. The gradient of pathology and neuroanatomical distribution is more in line with a "body-first" progression hypothesis of LBD. Among age-related co-pathologies, ADNC is particularly frequent in the neocortical LBD stages and likely modulates the clinical phenotype, especially dementia.

P05.10

Post-mortem quantification of cortical glia cells in patients with Parkinson's Disease

*Mikkel Vestergaard Olesen**
Center for Neuroscience and Stereology, Bispebjerg University Hospital, Copenhagen, Denmark

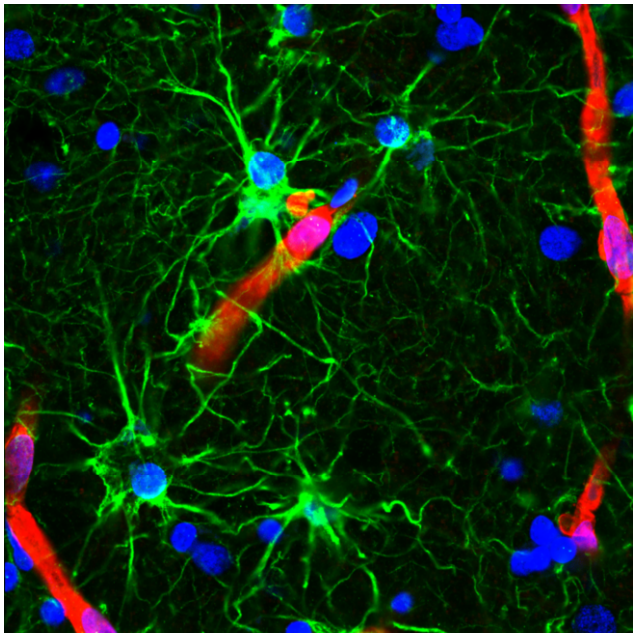
Background: Parkinson's disease (PD) is a debilitating neurodegenerative disorder, characterized by motor and non-motor symptoms, and increasing evidence suggest that several neocortical areas are involved in both disease characteristics. Previous studies have yielded insights into the pathological processes of the cerebral cortex with data showing microglia activation and altered concentrations of proinflammatory cytokines in frontal and temporal areas, among other changes. This suggests that cortical neuroinflammation may play a critical role in the progression of PD. The impact of PD on the number of neocortical cells, including brain immune cells, is sparsely studied and no previous studies have examined for potential quantitative changes in the glial cell population. Therefore, the present study aimed to quantify the total number of neocortical neurons- and glial cell sub-types in PD patients compared to control subjects.
Materials and Methods: We used the stereological method, the optical disector, to estimate the total number of neocortical neurons, oligodendrocytes, astrocytes and microglia in frontal-, temporal-, parietal and occipital cortices in postmortem brain tissue from 10 PD patients and 12 age- and gender-matched control subjects.
Results: In the entire neocortex and its associated subdivisions, there were no significant differences in any cell numbers between PD patients and control subjects, except a significant decrease of 35% in the total number of oligodendrocytes in the frontal cortex of patients with PD.
Conclusion: The results of the present study demonstrate no changes in the number of microglia and astrocytes which argues against severe neuroinflammation in the cortex. Our finding of similar neuron numbers in PD- and control brains agree with previous stereological data and suggests that PD primarily affects subcortical neurons. Finally, the loss of oligodendrocytes in frontal cortex might be associated to impairment of white matter tracts and future studies are warranted to clarify the functional relevance of oligodendrocyte loss in PD.

P05.11

Post-mortem analysis of Parkinson's disease brains after long-term deep brain stimulation of the subthalamic nucleus

Jonathan Munro[1], Francis Desmeules[1], Sylvine Cottin[1], Angela Noecker[2], Marie-Ève Tremblay[1], Peter V. Gould[1], Stephan Saikali[1], Mélanie Langlois[1], Cameron C. McIntyre[2], Michel Prud'homme[1], Léo Cantin[1], Martin Parent[,1]*
[1] Université Laval, Quebec City, Quebec, Canada
[2] Duke, Durham, NC, United States

Deep brain stimulation (DBS) of the subthalamic nucleus (STN) is an effective surgical treatment for Parkinson's disease (PD), alleviating motor symptoms and restoring patients' quality of life. Research into the long-term effects of DBS on the human brain is lacking. This study aims to investigate the neuroanatomical and neurochemical alterations induced by chronic stimulations of the STN, and to correlate these changes with clinical outcomes and estimated electrical current delivered in the brain parenchyma. Brains of PD patients who had received more than 9 years of DBS treatment in the STN were used. For each brain, 3D graphical representations of the basal ganglia and DBS electrodes were produced to determine the electrical current propagation throughout the tissue using patient-specific DBS computational modelling (StimVision2). Immunofluorescence and confocal microscopy were used to determine the immunoreactivity of various proteins. Quantification and morphological analyses of different cell types and blood vessels were performed. Along the electrode path, a 300-500 µm-width GFAP positive fibrillary gliosis was observed, with elevated expression of the growth factor GDNF. Near active contacts, astrocytes showed higher number of varicose processes that were in close apposition to GLUT1+ blood vessels. The number of Iba1+ microglia as well as the CD68 phagocytic marker was reduced and there were increased levels of VEGF and Claudin5 on GLUT1+ blood vessels, suggesting angiogenesis and increased blood brain barrier integrity. A detailed morphological analysis of microglia indicates that they were more active in the stimulated area of the STN. Overall, our post-mortem analysis indicates significant changes induced by long-term DBS of the STN involving glial cells and blood-brain barrier.



P05.12

Single molecule array assay for phosphorylated alpha-synuclein detection in cerebrospinal fluid

Camilla Pedersen, Guido Alves, Jodi Maple-Grødem, Johannes Lange*
Stavanger University Hospital; University of Stavanger, Stavanger, Norway

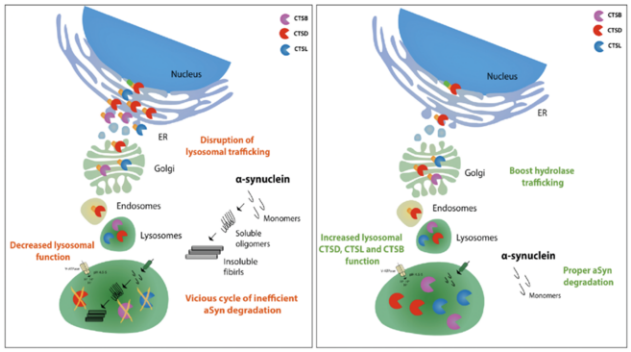
Background: Currently, the diagnosis of Parkinson's disease (PD) is a challenge given the range and severity of symptoms that patients may experience. Thus, there is a great need for biomarkers that can help in the diagnosis of PD. The majority of α-syn in Lewy bodies of PD patients is phosphorylated at serine 129 (pS129-α-syn). Further, pS129-α-syn is associated with α-syn toxicity and altered function in PD. Therefore, pS129-α-syn is a potential biomarker for PD. To assess pS129-α-syn, ultrasensitive methods are needed. The aim of this project is to develop and validate a single molecule array (SIMOA) assay to detect pS129-α-syn in cerebrospinal fluid (CSF).
Methods: Our in-house SIMOA assay uses commercially available antibodies. Different combinations of pS129-α-syn and α-syn antibody pairs were screened for sensitivity, specificity and dynamic range on the Mesoscale Discovery platform, and promising combinations were further tested on the SIMOA platform. Reagent preparation, initial testing of antibody pairs on the SIMOA, and optimization were carried out according to the manufacturer's protocols and recommendations.
Results: The new SIMOA assay is able to reliably quantify pS129-α-syn in CSF samples, using small volumes of sample. Validation included parallelism, dilution linearity, spike recovery, and precision.
Conclusion: SIMOA assays offer superior performance in terms of sensitivity, reproducibility, and elimination of matrix effects. Our in-house SIMOA assay for pS129-α-syn is well-suited for pS129-α-syn analysis in CSF samples.

P05.14

Reciprocal effects of alpha-synuclein aggregation and lysosomal homeostasis in synucleinopathy models

Alice Drobny[1], Fanni Boros[1], Caleb Pitcairn[2], Joseph Mazzulli[2], Friederike Zunke[,3]*
[1] Department of Molecular Neurology, University Hospital Erlangen, Friedrich-Alexander University Erlangen-Nürnberg (FAU), Erlangen, Germany
[2] The Ken and Ruth Davee Department of Neurology, Northwestern University Feinberg School of Medicine, Chicago, United States
[3] University Hospital Erlangen/ Friedrich-Alexander-University (FAU), Erlangen, Germany

Background: Lysosomal dysfunction has been implicated in a number of neurodegenerative diseases such as Parkinson's disease (PD). Various molecular, clinical and genetic studies emphasize a central role of lysosomal pathways and proteins contributing to the pathogenesis of PD. Within PD pathology the synaptic protein alpha-synuclein (aSyn) converts from a soluble monomer to insoluble amyloid fibrils. The aim of our study is to unravel the effect of aSyn aggregates on lysosomal turnover, particularly focusing on lysosomal homeostasis and cathepsins. Since these enzymes have been shown to be directly involved in the lysosomal degradation of aSyn, impairment of their enzymatic capacity has extensive consequences.
Methodology: In our study, we applied state-of-the-art technology of patient-derived induced pluripotent stem cells (iPSCs) and mouse brain samples to examine the effect of intracellular, pathological aSyn conformers on cell homeostasis and lysosomal function on dopaminergic neurons by biochemical analyses.
Results: In patient-derived dopaminergic neurons and mouse models with aSyn aggregation, we show that lysosomal trafficking of cathepsins is impaired, resulting in reduced proteolytic activity of cathepsins in the lysosome. Additionally, we rescued cathepsin function by utilizing a farnesyltransferase inhibitor (FTI), which boosts hydrolase transport via the activation of the SNARE-protein ykt6.
Conclusions: Our findings demonstrate a strong interplay between aSyn aggregation pathways and function of lysosomal cathepsins. It appears that aSyn directly interferes with enzymatic activity of cathepsins which might lead to a vicious cycle of impaired alpha-synuclein degradation. Moreover, our data highlights lysosomal proteases as therapeutic target for PD.



BASIC SCIENCE: Animal and cellular models of Parkinson's disease and Parkinsonisms

P06.03

The assessment of VILIP-1 in crosstalk with FAM19A3 as an early biological biomarker in LPS-induced inflammatory model of Parkinson's disease in rats

Mai M. Anwar[*,1], Mohamed H. Fathi*[2]
[1] Department of Biochemistry, National Organization for Drug Control and Research (NODCAR)/Egyptian Drug Authority (EDA)., Cairo, Egypt
[2] Department of Nucleic Acid & Protein structure, Center of Genomics, Proteomics and Bioinformatics, Agricultural Genetic Engineering Research Institute (AGERI)., Cairo, Egypt

Background: There is an urgent growing need to identify novel blood-based and cerebrospinal fluid (CSF) biomarkers that can detect Parkinson's disease (PD) pathology during its early stages. Visinin-like protein 1 (VILIP-1) is a type of neuronal calcium-sensor protein that is suggested to be increased in the blood, CSF, and brain in accordance with PD progression. FAM19A3 is a member of cluster TAFA genes found to be highly expressed as a drawback of neurodegeneration. Multiple risk factors may contribute to the progression of Parkinson's disease (PD) including neuroinflammation and immune dysfunction. It is suggested that exaggerated VILIP-1 and FAM19A3 release in the cerebrospinal fluid (CSF) and brain tissue may promote dopaminergic neuron damage by inducing neuroinflammation leading to PD. These biomarkers in addition to being detected in the blood can also reflect the degree of brain damage acting as an early biological and therapeutic index for PD. **Aim:** The current study aims to investigate whether the estimation of serum, CSF, and brain VILIP-1 and FAM19A3 levels may be considered an efficient and reliable biomarker for PD. **Methods:** A single dose of lipopolysaccharides (LPS) was injected into the right substantia nigra pars compacta (SNpc). The experimental design included male rats divided into a control normal group, a short-term LPS-induced PD group (30 days), and a long-term LPS-induced PD group (60 days). Rotarod behavior test was conducted to assess brain lesions severity and motor dysfunction. VILIP-1, FAM19A3, α-Syncline, and inflammatory factors were detected in the serum, CSF, and brain tissue to demonstrate PD pathological damage. **Results:** Increased expression of VILIP-1 and FAM19A3 were observed in the serum and CSF in correlation with PD progression in the brain tissue associated with elevated levels of inflammatory cytokines. **Conclusion:** The present study supports the efficiency of using VILIP-1 and FAM19A3 as an indicator for the degree of dopaminergic neuron damage acting as an early biomarker for PD.

P06.06

Establishment of a 3D iPSC-based neurovascular model to investigate Parkinson's disease pathophysiology

Valentina Baruffi[*,1], Veronica Testa[1], Meritxell Pons Espinal[1], Livia Piatti[2], François Korbmacher[2], Ivonne Richaud[3], Alicia Garrido[4], Eduardo Tolosa[4], Angel Raya[5], Maria Bernabéu Aznar[2], Antonella Consiglio[6]*
[1] Department of Pathology and Experimental Therapeutics, Bellvitge University Hospital-IDIBELL / Institute of Biomedicine (IBUB) of the University of Barcelona (UB)., Barcelona, Spain
[2] European Molecular Biology Laboratory (EMBL) Barcelona, Barcelona, Spain., Barcelona, Spain
[3] Regenerative Medicine Program, Bellvitge Biomedical Research Institute (IDIBELL), and Program for Clinical Translation of Regenerative Medicine in Catalonia (P-CMRC), Hospital Duran i Reynals, Hospitalet de Llobregat, 08908 Barcelona, Spain / Centre for Networked Biomedical Research on Bioengineering, Biomaterials and Nanomedicine (CIBER-BBN), Madrid, Spain., Barcelona, Spain
[4] Department of Neurology, Hospital Clínic de Barcelona, Institut d'Investigacions Biomèdiques August Pi i Sunyer (IDIBAPS), University of Barcelona (UB), 08036 Barcelona, Spain., Barcelona, Spain
[5] Regenerative Medicine Program, Bellvitge Biomedical Research Institute (IDIBELL), and Program for Clinical Translation of Regenerative Medicine in Catalonia (P-CMRC), Hospital Duran i Reynals, Hospitalet de Llobregat, 08908 Barcelona, Spain. / Centre for Networked Biomedical Research on Bioengineering, Biomaterials and Nanomedicine (CIBER-BBN), Madrid, Spain. / Institució Catalana de Recerca i Estudis Avançats (ICREA), Barcelona, Spain., Barcelona, Spain
[6] Department of Pathology and Experimental Therapeutics, Bellvitge University Hospital-IDIBELL, 08908 Hospitalet de Llobregat, Spain; Institute of Biomedicine (IBUB) of the University of Barcelona (UB), Barcelona, Spain. / Department of Molecular and Translational Medicine, University of Brescia, Brescia BS, Italy., Barcelona, Spain

Parkinson's disease (PD) is characterized by a progressive loss of dopaminergic neurons in the substantia nigra of the brain, as well as persistent inflammation not only in the brain but also in the periphery. Abnormal accumulation and aggregation of alpha-synuclein in the form of Lewy bodies and Lewy neurites represent another neuropathologic hallmark of PD. In order to investigate the role of the adaptive immune system in disease pathogenesis here, we use PD patient-specific iPSCs to build a new microfluidic 3D neurovascular (NVU) model to recapitulate both the brain and blood compartments separated by a layer of endothelial cells (ECs). With this model, we will evaluate whether astrocyte secretion of alpha-synuclein and other cytokines promotes blood-brain barrier (BBB) dysfunction and neuronal degeneration. Preliminary data demonstrated the ability of dopaminergic neurons to develop a healthy neural network when embedded within collagen in a 3D microenvironment. Moreover, after establishing the 3D brain NVU model containing iPSC-derived control astrocytes, we found that they establish contact with ECs through their end-feet. Ongoing experiments are performed to evaluate changes in vessel permeability and the impact of the interactions between PD astrocytes and PD ECs on dopamine neurons. By perfusing lymphocytes through the microvessels, we are now in the process to quantify transmigration to the brain-like compartment and test their role in neurodegeneration. So far, we have been able to observe that PD T lymphocytes induce cell death when co-cultured with dopaminergic neurons derived from PD patients, but not when cultured with those derived from the respective isogenic control.
Future experiments will determine i) whether astrocytes-related inflammation may cause BBB dysfunction increasing T lymphocytes infiltration and amplifying the development of neuroinflammation in PD; and ii) if the innate immune system (microglia) might prevent or exacerbate the effect of the adaptive immune system on neuronal degeneration.
Thus, this project will establish a novel 3D neurovascular model to improve our understanding on PD and guide the development of future therapies.

P06.07

NMR-based metabolomic analysis of gut-brain interactions in Parkinson's disease modeled in Drosophila

Marylène Bertrand[1], Xiaojing Yue[2], Céline Landon[1], Serge Birman[,2]*
[1] Molecular Aspects of Life Team, Biomolecular NMR Group, Centre for Molecular Biophysics, CNRS, Orléans, France
[2] Genes Circuits Rhythms and Neuropathology, Brain Plasticity Unit, CNRS, ESPCI Paris, PSL University, Paris, France

The gut-brain axis is a major pathway that appears to be involved in the initiation and propagation of neuronal abnormalities. Our work focuses on two proteins, α-synuclein and LRRK2, which are known to play a central role in the disease and which are present and altered in the brain and gut of Parkinson's patients. Using Drosophila models, we are analysing by NMR spectroscopy the metabolic changes induced by the expression of pathogenic human mutant forms of these proteins in the brain and intestine, at an early and advanced stage (10 and 30 days of adult life, respectively), in order to highlight the reciprocal influences of these two organs during the course of the disease. This research could thus provide a better understanding of the interactions between the microbiota, the gut and the brain in Parkinson's disease, including the relationship between gut inflammation and neuronal death. It could also identify early biomarker metabolites that would be common to pathologies induced by mutated α-synuclein and LRRK2, potentially allowing the disease to be detected at an early stage. The initial results and current progress of our study will be presented.

P06.08

Exacerbation of alpha-synuclein pathology by B-lymphocyte depletion.

*Tomasz Brudek**
Bispebjerg-Frederiksberg Hospital, Copenhagen NV, Please Select, Denmark

Multiple System Atrophy (MSA) is characterized by aggregation and deposition of misfolded alpha-synuclein (αSyn) causing a disruption of brain cell networks followed by failure of cellular defenses. These pathological aggregates act as self-antigens, and our findings point towards a failure in the immune clearance mechanisms in MSA. Naturally occurring autoantibodies (NAbs) are crucial for phagocytosis and inhibition of pathological protein aggregation. We have accumulated data showing a decline in the binding of NAbs to αSyn in MSA, suggesting that αSyn aggregates may not be fully recognized and cleared by the immune system.
Our main hypothesis is that αSyn aggregation is normally inhibited by anti-αSyn NAbs in a process called immune clearance. Thus, based on our results obtained from MSA patients, we hypothesize that B cell depleted transgenic MSA mice are more prone to αSyn-aggregation and show increased αSyn brain pathology in comparison to their non-depleted wild-type (WT) littermates. Thus, the aim was to test this hypothesis by inducing a B lymphocyte depletion by employing monocyte-mediated antibody-dependent cellular cytotoxicity and therefore immune decline in a preclinical αSyn transgene model of MSA.
Eight weeks old MSA mice (a transgenic model expressing full αSyn140 (GenBank: BC108275.1) under the murine myelin basic protein promoter in C57BL/6N mice) and their WT littermates were treated every 3 weeks for 6 months with sterile and endotoxin-free anti-CD20 (MB20-11, 300 µg/mouse) or isotype-matched control mAbs injected i.v. through lateral tail veins. Eventually, the mice were euthanized, spleens, brains, and blood sera were saved for further analyses.
Using Flow Cytometry, we successfully validated the depletion of the B lymphocytes by anti-CD20 antibodies. Behavioral tests, pole and gait topography, showed no significant differences between the anti-CD20 and the isotype treatments in both WT and MSA mice.
By Western Blotting, we evaluated the levels of murine and human αSyn as well as phosphorylated αSyn (p-αSyn). We found significantly increased levels of murine αSyn in WT mice treated with CD20 antibodies vs. isotype treatment. There were no differences in the levels of human αSyn and p-αSyn.
Our results validate our hypothesis that humoral immune responses are important factors in αSyn clarence mechanisms.

P06.09

G2019S LRRK2 exacerbates inflammation and neurodegeneration in models of PD and colitis

Diego Cabezudo, George Tsafaras, Eva Van Acker, Chris Van den Haute, Veerle Baekelandt*
KU Leuven – Research Group for Neurobiology and Gene Therapy, Leuven, Belgium

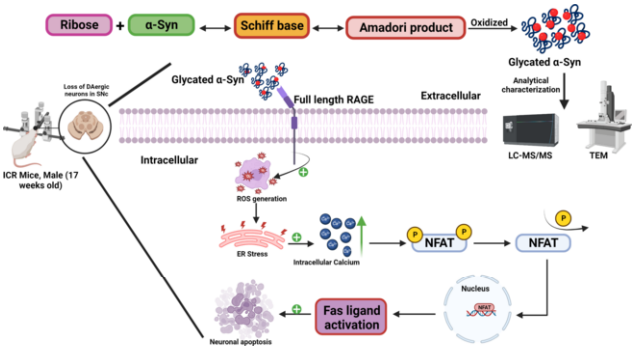
Mutations in the Leucine-rich repeat kinase 2 (LRRK2) are the most common genetic cause of PD. The exact role of LRRK2 in PD pathogenesis remains unclear, but a great body of evidence links this protein with the immune system. Using knock-in mice carrying the most common LRRK2 mutation (G2019S), we modelled PD by inducing the overexpression of α-synuclein in the substantia nigra using recombinant adeno-associated vectors (rAAV). The presence of the LRRK2 mutation increased the degeneration of the dopaminergic neurons leading to a more severe phenotype. A-synuclein overexpression induced a higher level of neuroinflammation in the G2019S mice as well as lysosomal dysfunction in the substantia nigra. Additionally, we studied the effect of G2019S-LRRK2 in a model of gut inflammation using dextran sodium sulphate (DSS). Mutant LRRK2 increased the gut inflammation after DSS administration, leading to a more severe phenotype in the knock-in mice. Bone marrow transplantation of WT cells into G2019S mice fully rescued from the exacerbated response to DSS, proving the key role of LRRK2 in the immune response. Furthermore, pharmacological inhibition of LRRK2 reduced the colitis phenotype and inflammation. Finally, we combined experimental colitis with rAAV α-synuclein overexpression in the substantia nigra and found that gut inflammation aggravated the PD-related motor deficits and neurodegeneration in G2019S mice. Taken together, our results link LRRK2 with the immune response in the brain and in the gut and provide evidence that peripheral inflammation can impact the brain's homeostasis and contribute to neurodegeneration in PD.

P06.10

Glycated alpha-synuclein modulates the novel receptor for advanced glycation endproducts signaling pathway: A detailed molecular mechanism and it exacerbates on early onset of Parkinson's disease-like phenotypes

Sayan Chatterjee[*,1], *Harsh Thakkar*[2], *Amit Khairnar*[3], *Ravi Shah*[4]
[1] National Institute of Pharmaceutical Education and Research-Ahmedabad (NIPER-A), An Institute of National Importance, Dept. of Pharmaceuticals, Ministry of Chemicals and Fertilizer, Govt. of India, Uttarpara, West Bengal, India
[2] National Institute of Pharmaceutical Education and Research-Ahmedabad (NIPER-A), An Institute of National Importance, Dept. of Pharmaceuticals, Ministry of Chemicals and Fertilizer, Govt. of India, Ahmedabad, Gujarat, India
[3] International Clinical Research Centre, St. Anne's University Hospital, Brno, Brno, Czech Republic
[4] National Institute of Pharmaceutical Education and Research-Ahmedabad (NIPER-A), An Institute of National Importance, Dept. of Pharmaceuticals, Ministry of Chemicals and Fertilizer, Govt. of India, Gandhinagar, Gujarat, India

Background: Intracytoplasmic inclusion of Lewy bodies, primarily containing alpha-synuclein (α-Syn), is a pathological hallmark for Parkinson's disease (PD). While the glycation with methylglyoxal (MGO) results in α-Syn misfolded and aggregation has been studied, the effects of glycated α-Syn and how it affects the α-Syn aggregation at the early onset of PD have not been investigated.
Aim: To elucidate, the molecular mechanism underlying glycated α-Syn mediated dopaminergic neurodegeneration (DAergic) in the substantia nigra (SN) via the RAGE/Calcineurin/NFAT/Fas-Ligand signaling pathway.
Methodology/Principle finding: Through rDNA technology, we first purified and characterized recombinant human α-Syn (rh α-Syn). We established that glycation (an unavoidable age-associated post-translational modification) with d-ribose and characterized it by LC-MS/MS, transmission electron microscopy (TEM), MALDI TOF-MS and atomic force microscopy (AFM) analysis. Furthermore, post-translational toxicity of α-Syn was investigated in wild-type ICR mice by intranigral injection of a single dosage of glycated α-Syn (2μg/μl). Behavioral assessments were done every week. To check glycated α-Syn induced neurodegeneration, age-dependent sensitivity of DAergic neurons, and contribution in RAGE/Calcineurin/NFAT/Fas-Ligand signaling cascade, immunohistochemical analysis were performed at different time points (28, and 56-day post-surgery).
Results: After rh α-Syn was successfully purified, we found the mass increment (2kDa) of glycated α-Syn by using MALDI TOF-MS. This was supported by the use of TEM and AFM to find alterations in the internal structure of this protein. At 56-days post-surgery, immunofluorescence labeling revealed an upregulation of RAGE resulting in significant ($p<0.001$) loss of TH+ neurons in SNc. Iba1 and GFAP expression were elevated in order to activate the inflammatory cascade caused by RAGE. Additionally, we found that glycated α-Syn increased malondialdehyde (MDA) levels resulting in ROS production, which may have contributed to the upregulation of Calcineurin/NFAT/Fas-Ligand. Overall, our findings showed that glycated α-Syn induced apoptosis and age-dependent sensitivity of DAergic neurons to degeneration by activating caspase 8 and 3.
Conclusions: We uncovered that d-ribose-derived glycation played a significant role in the exacerbation or anticipation of early onset of PD-like symptoms, indicating that anti-glycation or anti-diabetic agents may be effective in treating Parkinson's disease.

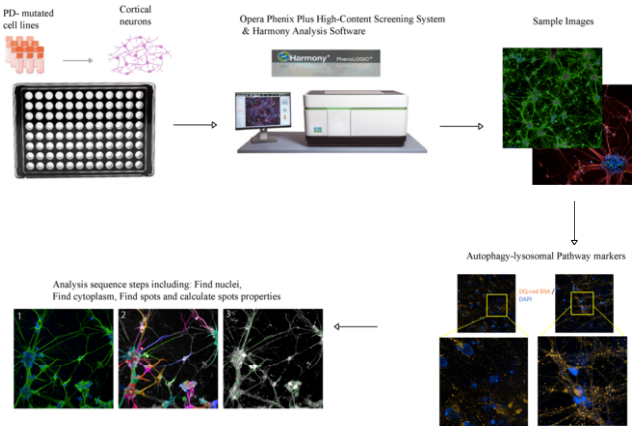


P06.11

A high-content analysis pipeline for quantifying the autophagy-lysosomal pathway in IPSC-derived cortical neurons carrying Parkinson's disease associated mutations

Jessica Chedid[*,1], *Adahir-Labrador Garrido*[1], *Gautam Wali*[1], *Dad Abubonsarah*[2], *Lachlan Thomson*[2], *Carolyn Sue*[1], *Deniz Kirik*[3], *Clare Parish*[2], *Glenda Halliday*[1], *Nicolas Dzamko*[1]
[1] University of Sydney, Sydney, NSW, Australia
[2] The Florey Institute, Melbourne, VIC, Australia
[3] Lund University, Lund, Switzerland

Parkinson's disease (PD) associated mutations in the genes LRRK2, PRKN and SNCA can manifest different variants of PD both clinically and pathologically. However, several studies also point to a common role of these mutations in the regulation and subsequent dysfunction of the autophagy-lysosomal pathway (ALP). The effect of mutations in these genes on the ALP has rarely been directly compared. We developed a high-content analysis pipeline using image cytometry to assess ALP in cortical neurons differentiated from induced pluripotent stem cells (iPSCs) from controls and from PD patients carrying mutations in LRRK2, PRKN and SNCA (n=3 per group). MAP2 positive cortical neurons expressing markers of different cortical layers (TBR1, CTIP2 or BRN2) were successfully differentiated from iPSCs. Live imaging and fixing/staining were performed to measure multiple readouts of ALP (P62, LC3, lysotracker, Mitotracker and DQ-red BSA). Imaging and analysis were performed using the Opera Phenix System and Harmony software respectively and an automated analysis pipeline was developed to measure ALP readouts in at least 1500 cells per condition across the 12 cell lines. Data to date indicate dysfunctional lysosomal degradation in the LRRK2 mutated cell lines as measured by an increase in the number, size and intensity of DQ red-BSA (lysosomal substrate) accompanied by an increase in phospho-α-synuclein expression, an expression that appears to be localised to the neurites of the cells rather than the cell bodies. Ongoing validation of this work may offer a new robust, unbiased, time-effective, and highly customizable method to decipher the enigmatic role of the ALP in genetic and sporadic forms of PD.



P06.12

Delineating neurodegenerative interactions of VPS35 and LRRK2 in rodent models of Parkinson's disease

Xi Chen, Lindsey Cunningham, Nathan Levine, An Phu Tran Nguyen, Darren Moore*
Van Andel Institute, Grand Rapids, Michigan, United States

Mutations in the VPS35 gene encoding a core component of the retromer complex have emerged as a cause of late-onset, autosomal dominant Parkinson's disease (PD). At present, the mechanism(s) by which familial VPS35 mutations precipitate neurodegeneration in PD are poorly understood and the extent to which mutant VPS35 interacts with other PD-linked gene products in rodent models is uncertain. VPS35 and the retromer have so far been functionally connected to the PD-linked proteins, α-synuclein, parkin, and LRRK2. Mutations in the LRRK2 gene are the most common cause of autosomal dominant PD and have been shown to increase LRRK2 kinase activity. Emerging evidence suggests that VPS35 mutations may operate upstream or in parallel to LRRK2 where they either directly or indirectly induce kinase activation that potentially mediates neurodegeneration. However, the consequences of increased LRRK2 kinase activity in D620N VPS35 rodent models have not been formally evaluated. We previously developed a PD animal model based upon the AAV-mediated overexpression of human D620N VPS35 in the nigrostriatal pathway of adult rats that induces dopaminergic neurodegeneration and axonal damage. Our ongoing studies seek to evaluate the impact of VPS35 overexpression on LRRK2 kinase activity in the brains of commonly utilized rat genetic backgrounds. Furthermore, we are utilizing LRRK2-deficient models to define the contribution of LRRK2 to mechanisms associated with mutant VPS35-induced neurotoxicity. To explore the pathological significance of LRRK2 kinase activation, we assessed the impact of LRRK2 deletion in mice on the pronounced dopaminergic neuronal loss induced by the AAV-mediated D620N VPS35 overexpression. Surprisingly, we find that LRRK2 deletion fails to provide neuroprotection against mutant VPS35, and potentially worsens neurodegeneration, suggesting that LRRK2 does not operate downstream to mediate the pathogenic effects of mutant VPS35. Oppositely, we find no evidence that human G2019S LRRK2 increases vulnerability to D620N VPS35 overexpression, and instead we find this genetic combination to be significantly protective. It is ambiguous how G2019S LRRK2 mediates this protective effect, but these data suggest a regulatory mechanism between VPS35 and LRRK2 potentially at the level of modulating lysosomal stress. Collectively, our studies will establish whether LRRK2 kinase activity serves a useful therapeutic target in VPS35-linked PD.

P06.13

Selective manipulation of parvalbumin-expressing neurons in the substantia nigra pars reticulata restores motor behaviors in experimental parkinsonism

Lorena Delgado Zabalza*[,1], Nicolas Mallet[1], Maurice Garret[2], Christelle Glangetas[1], Cristina Miguelez Palomo[3], Jérôme Baufreton[1]
[1] Univ. Bordeaux, CNRS, IMN, UMR 5293, F-33000 Bordeaux, France, Bordeaux, France
[2] Univ. Bordeaux, CNRS, INCIA, UMR 5287, F-33000 Bordeaux, France, Bordeaux, France
[3] University of the Basque Country (UPV/EHU). 48940 Leioa, Spain, Leioa, Spain

The substantia nigra pars reticulata (SNr) is the main output structure of the murine basal ganglia (BG), a subcortical network controlling the execution of motor programs but also cognitive and associative learning functions. The activity of this network is primarily impacted following the loss of midbrain dopaminergic neurons in Parkinson's disease (PD). Recent molecular and anatomical studies have revealed a cellular heterogeneity in the SNr associated with distinct behavioural functions. However, cell-type specific contributions to PD-related motor dysfunctions have not been elucidated yet. In this study, we investigated the functional properties of parvalbumin-expressing SNr neurons (SNr-PV+). We demonstrated that SNr-PV+ neurons have a dorso-lateral distribution in the SNr and possess specific electrophysiological properties compared to SNr neurons not expressing the PV. In a mouse model of PD, we found that only SNr-PV+ neurons intrinsic excitability is reduced ex vivo due to a downregulation of NALCN background channels. Nevertheless, SNr-PV+ neurons display a bursty pattern activity in anaesthetized Parkinsonian mice in vivo which is driven by pathological glutamatergic inputs. Indeed, pharmacological blockade of these glumatergic inputs was able to reduce this bursting activity and increase their time in pause. These results suggest that the hypoexcitability of SN-PV+ neurons shown ex vivo in parkinsonian states renders these neurons more sensitive to glutamatergic inputs. Finally, we demonstrated that chemogenetic inhibition of SNr-PV+ neurons is sufficient to alleviate motor impairments in Parkinsonian mice. Overall, our findings establish a cell-type specific dysfunction in the Parkinsonian state in the main output nucleus of the BG and provide a new cellular therapeutic target to alleviate motor symptoms in PD.

P06.14

Characterizing patterns of neural activity in midbrain organoids as a model for studying Parkinson's disease

Ghislaine Deyab[,1], Nguyen-Vi Mohamed[2], Rhalena Thomas[1], Jiarui Ao[1], Xue Er Ding[1], Julien Sirois[1], Carol X-Q Chen[1], Lenore Beitel[1], Thomas Durcan[1], Edward Fon[1]*
[1] McGill University, Montreal, QC, Canada
[2] MEDTEQ+, Montreal, Canada

Human derived midbrain organoids (hMOs) are a promising tool that can be used to study Parkinson's disease (PD) on a patient specific level by capturing the genetic background of patients. Yet, much is unknown about how accurately hMOs recapitulate the human brain in health and disease. In this study, we aim to determine whether hMOs can capture changes in neural activity associated with PD. We have generated hMOs using induced pluripotent stem cells derived from PD patients and their CRISPR corrected controls and recorded their network activity using a Micro-Electrode Array (MEA). Using custom Python scripts, we then compared these patterns of activity between mutant and control (CTL) hMOs. In organoids derived from patients carrying a synuclein triplication mutation, we

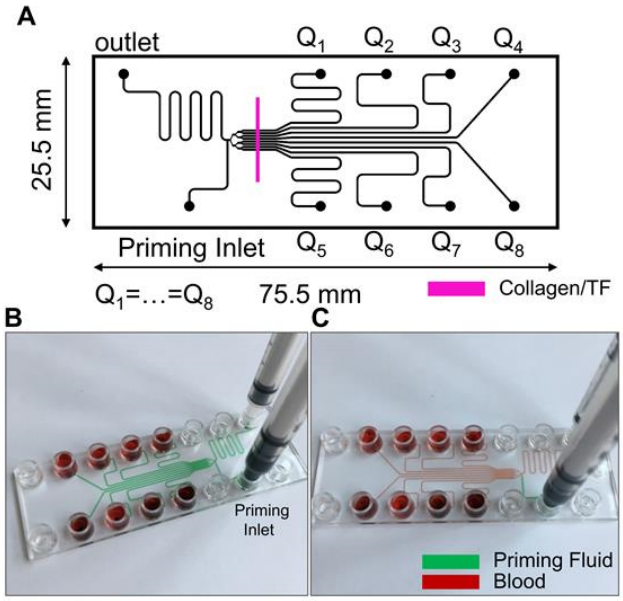
see a decrease in overall activity across the organoid compared to their isogenic CTLs. However, mutant hMOs showed an increase in the strength of single neuron and population wide bursts. This suggests that the organization of neural activity is shifted towards strong bursting activity, which is complementary to neural activity described in mouse models of PD and may reflect compensatory mechanisms as a response to cell death. To test if this change in activity was due to a decrease in dopamine transmission, we treated hMOs with exogenous L-Dopa and recorded their activity before and after treatment. Here, we saw a decrease in the number of bursts and population bursts in mutant hMOs but not CTLs. This suggests that observed changes in mutant hMOs may be due to decreased dopamine transmission. In contrast hMOs harboring A53T mutations show little to no activity compared to their isogenic CTLs. A live-dead assay was performed on dissociated organoids through Fluorescence-Activated Cell Sorting (FACS) to determine the ratio of live to dead cells. At 50 days old the number of live cells was similar in A53T and CTL hMOs. However, starting at 100 days old, the number of live cells in A53T hMOs dramatically decreased (~17% live cells) compared to CTLs (~80% live cells). If shown to be reproducible, this study will help validate the reliability of using organoids as a model to study PD in a patient specific manner.

P06.15

Point of care microfluidic testing of platelets and coagulation using whole blood under hemodynamic conditions

*Scott Diamond**
University of Pennsylvania, Philadelphia, PA, United States

Background: Patients with Parkinson's Disease (PD), either during clinical care or clinical trial participation, often have their blood subjected to analysis. Compared to spinal fluid, whole blood is far easier to obtain. With respect to PD, platelets are a rich source of □-synuclein, parkin, amyloid-□, dopamine, glutamate, and serotonin and have been implicated in neuroinflammatory processes. Additionally, rapid blood testing may assist in bleeding risk, thrombosis, or cardiovascular risk assessment.
Method: Microfluidics are devices that allow the control of microliter streams of biologics, cells, and reagents under controlled conditions of flow, thus stream-lining analytical protocol. Such devices have found use in recreating stem cell differentiation pathways, blood brain barrier, and vasculature structures. For blood analysis, an 8-channel device was designed as an injection-molded single-use disposable chip to expose whole blood flow for 8 controlled clotting events on a micropatterned surface of fibrillar collagen and lipidated tissue factor (TF). Such devices have proven useful to study platelet thromboxane, prostacyclin, P2Y1, P2Y12, P2X1, GPVI, PAR-1, PAR-4, nitric oxide signaling, phosphatidylserine exposure as well as thrombin and fibrin generation.
Results: For whole blood clotting at venous wall shear rate of 200 s-1, the intrachip CV for platelet and fibrin deposition was 10% and the interdonor CV was 30% for platelet and 22% for fibrin deposition (across 10 healthy donors). The devices can also be used to provide a quantitative signal of direct oral anticoagulants (DOACs). Using fibrin generation in whole blood clots revealed IC50's of 120 nM for rivaroxaban and apixaban, and 60 nM for dabigatran. The ease of use and versatility of the 8-channel device offers the opportunity for the PD research community to explore platelet and coagulation biology in large patient cohorts, ex vivo pharmacological testing, and high dimensional platelet phenotyping.



P06.16

Non-invasive monitoring of midbrain dopaminergic progenitor cell differentiation

Nicola Drummond[*1], Daniel Tikhomirov[2], David McNay[2], Yixi Chen[2], Maurice Canham[2], Mio Iwasaki[3], Mariah Lelos[4], Asuka Morizane[5], Tilo Kunath[2]*
[1] The University of Edinburgh, Edinburgh, United Kingdom
[2] Centre for Regenerative Medicine, The University of Edinburgh, Edinburgh, United Kingdom
[3] Centre for iPS Cell Research and Application, Kyoto University, Kyoto, Japan
[4] Cardiff University, Cardiff, United Kingdom
[5] Kobe City Medical Center, Kobe, Japan

Midbrain dopaminergic (mDA) neuron loss causes the motor symptoms associated with Parkinson's. These mDA progenitor cells can be differentiated from pluripotent stem cells (PSCs). However, the protocol for production of mDA progenitors is very sensitive to slight perturbations and requires fine adjustments for different cell lines. Methods to non-invasively monitor the production of these progenitors will be beneficial, but currently do not exist. For cell replacement therapy this will reduce batch failure rates and thereby reduce the production cost as well as improve the reliability of the cell product. For disease modelling this will allow consistent production of robust and reliable mDA neurons.
One method to non-invasively monitor mDA differentiation is to analyse the conditioned medium. PSCs and mDA cells have unique secretomes that dynamically change during the differentiation process. Candidate-secreted biomarkers in the literature, in-house transcriptomic data, and unbiased proteomic analysis of conditioned medium were used to identify a library of putative mDA biomarkers. The levels of each protein in conditioned medium was measured by ELISA over a time-course. This has allowed us to identify a number of novel secreted biomarkers that positively and negatively correlate with efficient differentiation of mDA progenitor cells. We have multiplexed a number of the biomarkers on the Luminex system and we can detect a number of these markers simultaneously in the same sample. Several of the novel secreted biomarkers, including Trefoil Factor 3, can predict the efficiency of mDA progenitor cell production as early as seven days into the differentiation process.

We have identified a number of novel biomarkers of mDA neurons that are predictive of cultures that are on the correct trajectory to produce highly enriched cultures of mDA progenitors.

P06.18

DNAJC12 deficiency in Parkisonism

*Jesse Fox**
University of British Columbia, Vancouver, British Columbia, Canada

Biallelic mutations in DNAJC12 were recently discovered as a cause of early/juvenile-onset parkinsonism. The DNAJC family proteins function as molecular co-chaperones with highly conserved J-domains which aid in the folding of nascent proteins, refolding misfolded or aggregate-prone proteins, targeting cytotoxic proteins for degradation, or mediating translocation across intracellular membranes. Importantly, there are five known DNAJC proteins expressed in the human brain which have been implicated in PD (DNAJC5, DNAJC6, DNAJC12, DNAJC13, & DNAJC26). More specifically, studies have determined a role of these co-chaperones in regulating cellular quality control, preventing cytotoxic protein aggregation and maintaining homeostatic dopamine neuronal function.
In this research, we characterize a novel DNAJC12 knock-out mouse line and use in vitro models to elucidate DNAJC12 function in neurons. DNAJC12 has been implicated in dopamine homeostasis which is central to the etiology of PD. We confirm a positive interaction between DNAJC12 and tyrosine hydroxylase (TH), the rate-limiting enzyme in dopamine synthesis, and use our model systems to further characterize DNAJC12's role in regulating TH activity and dopamine production. We further assess mitochondrial bioenergetics and explore overlapping phenotypic spectrums of DNAJC12-deficiency with GCH1-deficiency, the rate-limiting enzyme in tetrahydrobiopterin (BH4) synthesis which is a co-factor for aromatic amino acid hydroxylates, including TH.

P06.19

DNAJC13 p.N855S in Parkinson's disease

*Jesse Fox**
University of British Columbia, Vancouver, British Columbia, Canada

Parkinson's disease (PD) is a common neurodegenerative disorder for which genetic studies have discovered multiple causative genetic mutations to highlight convergent cellular pathways. In 2014 DNAJC13 p.N855S was linked to autosomal dominant late-onset PD in Canadian Mennonite families. In 2016 that assignment was challenged by the publication of TMEM230 p.R141L in the largest pedigree. Here we provide an analysis of the functional consequences in vivo of DNAJC13 p.N855S mutation in a knock-in mouse model.
Disease segregation shows comparable evidence for TMEM230 and DNAJC13 linkage, depending on the affected phenotypes specified. DNAJC13p.N855S has a greater lifetime penetrance, the protein is highly conserved within and across species, and substitutions at this position are rare. In primary cultures, DKI neurons show excessive endosomal tubulation consistent with loss-of-function studies. Heterozygous DNAJC13 p.N855S KI (DKI) mice exhibit behavioral phenotypes (including open field locomotion, grip strength and balance/coordination) at different ages compared to WT littermates, as well as differences in expression of synaptic vesicular proteins and membrane transporters (α-synuclein, VAMP2, VGluT1 and DAT) by immunofluorescence confocal imaging and/or protein biochemistry. To further test our model, we inject in the striatum unilaterally with pre-formed alpha-synuclein fibrils or control in heterozygous DKI mice and WT littermates to assess neurodegeneration of dopamine neurons in the Substantia nigra, animal behaviour and locomotion, neurotransmitter levels ex vivo and presence of pathology.

P06.20

Utilising preclinical murine models to investigate sleep and circadian system dysfunction in Parkinson's disease

Nicholas Garner[*,1], Pu Reum Kim[1], Marco Weiergraeber[2], Richard Gordon[3], Katerina Hanton[3], Henrik Oster[4], Oliver Rawashdeh[1]*
[1] School of Biomedical Sciences, Faculty of Medicine, University of Queensland, Brisbane, Australia
[2] Experimental Neuropsychopharmacology, Federal Institute for Drugs and Medical Devices, Kurt-Georg-Kiesinger-Allee, Bonn, Germany
[3] UQ Centre for Clinical Research, Faculty of Medicine, The University of Queensland, Brisbane, Australia
[4] Institute of Neurobiology, Marie-Curie-Straße, Lübeck, Germany

Sleep dysfunction and circadian disturbances are among the earliest non-motor features of Parkinson's disease, preceding motor manifestations by up to 15 years. Parkinson's is characterized by a degeneration of dopaminergic neurons of the nigrostriatal and mesolimbic systems and the occurrence of Lewy bodies containing pathological alpha-synuclein (α-syn). So far, the contribution of each pathological presentation to the non-motor symptoms experienced remains unclear. We aimed to help elucidate this by modelling and assessing the contribution of each pathology at a prodromal stage to alterations in sleep and circadian functions. To test how dopaminergic neurodegeneration confined to the nigrostriatal pathway, or fibril-related alterations in neuronal processes may alter circadian rhythms of physiology and behavior, we utilized well-established preclinical models of each hallmark of the disease. Mice were unilaterally injected with either the neurotoxin 6-hydroxydopamine (OHDA) to cause targeted dopaminergic neurodegeneration or with preformed fibrils of human α-syn (PFF). Next, video-EEG through wireless radiotelemetry was performed under numerous experimental paradigms designed to observe and challenge sleep and circadian function. We assessed the regulation of sleep timing, the rate of adaptation to changes in geophysical time, and the circadian free-running period of activity cycles under constant darkness. We also investigated sleep propensity using the maintenance of wakefulness test and sleep homeostasis by assessing sleep rebound and recovery after sleep deprivation. We found that each pathological hallmark of Parkinson's uniquely contributes to sleep and circadian function alterations. In addition, we have characterized a baseline for these PD mouse models, which are a promising tool in investigating treatments that may elevate symptoms of sleep and circadian disruption for future studies. With the results of our study, we aim to provide the broader community with a greater understanding of the contributions of each pathology of sleep dysfunction and circadian disturbances.

P06.21

Impact of α-Synuclein inclusions on glutamatergic synapses in the amygdala in a PFF mouse model of PD

Nolwazi Gcwensa, Dreson L Russell, Khaliah Long, Charlotte F Brzozowski, Laura Volpicelli-Daley*
University of Alabama at Birmingham, Birmingham, Alabama, United States

Objective: Parkinson's disease is a neurodegenerative disorder characterized by α-synuclein inclusions termed Lewy Pathology.

Lewy pathology in the amygdala of PD patients is robust and at least 80% of PD sufferers experience non-motor symptoms such as apathy, hallucinations, anxiety, and depression potentially caused by α-synuclein inclusions causing dysfunction in the amygdala. However, the mechanisms by which inclusions could cause defects within the amygdala have not been well-studied. Synucleinopathy has been demonstrated to reduce dendritic spine density in mouse primary hippocampal neurons, and in mouse models of synucleinopathy. Microglial activation and synapse pruning have recently been shown to play a role in synapse degeneration in neurodegenerative disease. We hypothesise that α-synuclein inclusions induce microglial activation resulting in degeneration of synapses of affected neurons in the amygdala.
Methods: 3-or 4-month-old mice are injected intrastriatally with fibrils to induce inclusion formation in the basolateral amygdala (BLA) or monomer or PBS negative controls. Thereafter, brains are harvested 6 and 12 post injection. Structured Illumination Microscopy (SIM) is used to resolve synapses and 3D surfaces of synaptic puncta are rendered using Imaris software to measure the volume of synaptic compartments. Additionally, changes to the activation state of microglia and changes in the engulfment of synaptic material by activated microglia in response to inclusions are measured.
Results: We showed significant reduction in the density of vGLUT1+ puncta in the lateral amygdala of mice 6 weeks after PFF injection compared to controls. Additionally, we showed a significant increase in density of IBA1+ microglia and a significant reduction in projections per IBA1+ microglia indicating microgliosis in PFF injected mice. Rendered 3D surfaces of IBA1+ microglia and vGlut1+ puncta showed a significant increase in presynaptic material engulfed by microglia and an increase in trafficking of engulfed material into microglial lysosomes in PFF injected mice.
Conclusion: Our preliminary data show potential loss of synapses in the amygdala of mice with pre-formed fibril (PFF)-induced α-synuclein inclusions compared to control mice. Additionally, we observe robust microgliosis at early time points following initiation of α-synuclein formation. Thus, we conclude an association between activated microglia and changes in vGLUT1+ puncta in the amygdala as a feature of α-synuclein pathophysiology.

P06.22

Modeling PRKN/PARK2-associated Parkinson's disease
Christopher J. Griffey[*,1], Alf H. Lystad[2], Anne Simonsen[2], Robert E. Burke[1], Ai Yamamoto[1]*
[1] Department of Neurology, Columbia University, New York, NY, United States
[2] Department of Molecular Medicine, University of Oslo, Oslo, Norway

Parkinson's disease (PD) is characterized by the selective degeneration of midbrain dopaminergic neurons. Genetic studies have revealed causative and risk loci associated with a proportion of PD cases, such as PRKN/PARK2, encoding parkin and when mutated causes a rare familial form of autosomal recessive PD. Cell-based studies have linked parkin to mitochondrial turnover by autophagy, or mitophagy, but to date, manipulating this gene in rodents has not robustly recapitulated core features of PD. This has called into question how reliably we can model genetic forms of PD to what degree we can capture cell type-specific vulnerabilities in PD and other neurodegenerative diseases in nonhuman mammalian systems.
Here, we find that global, inducible deletion of Prkn/Park2 (parkin iKO) in the adult mouse leads to age-dependent motor impairments that are responsive to levodopa treatment. We report that these behavioral defects are associated with pathological changes in nigrostriatal dopaminergic neurons and striatal gliosis. We also show metabolomic alterations in the parkin iKO brain that precede degenerative changes, and present a new, in vivo mitophagy reporter system to investigate the relationship of parkin's described role in mitochondrial homeostasis to the observed phenotypes. These results provide critical insight into parkin's contribution to mitophagy and dopaminergic neuron stability in the mammalian brain.

P06.23

Involvement of serotonergic descending pathways on pain in a mouse model of parkinsonism
Zoé Grivet[*,1], Franck Aby[2], Rabia Bouali-Benazzouz[1], Frédéric Naudet[1], Aude Verboven[1], Abdelhamid Benazzouz[#,1], Pascal Fossat[#,3]*
[1] Université de Bordeaux, Institut des Maladies Neurodégénératives - CNRS UMR5293, Bordeaux, France
[2] Université de Bordeaux, Institut des Maladies Neurodégénératives - CNRS UMR5293 & SATT AST, Bordeaux, France
[3] Université de Bordeaux, Institut des Maladies Neurodégénératives - CNRS UMR5293. [#]equal contribution, Bordeaux, France

Parkinson disease (PD) is characterized by the degeneration of a certain category of neurons: the dopaminergic neurons. The loss induces the apparition of the well-known motor symptoms but also to non-motor symptoms. The main non-motor symptom is chronic pain, which affects highly the quality of life of 60 to 80% of the patients. However, the mechanisms leading to this symptom are not defined yet as we do not clearly know how the disease affect the circuit of pain.
The spinal cord corresponds to a key area in the pain circuits as it is the first relay of the nociceptive information. It receives the nociceptive signal from the periphery of the body and then sends it to the higher cerebral area where the pain will be created. This corresponds to the ascending pathway and it is highly modulated by the descending pathways. These pathways are projecting from the brain to the spinal cord. Their role is to modulate the ascending information in order to limit the pain sensation.
Our hypothesis is that in Parkinson disease the descending pathway and more particularly the serotonergic one is losing its analgesic role, which would explain the hypersensitivity observed in patients.
To test this, we are using a mouse model of Parkinsonism and genetic tools, which artificially help us to modulate the activity of the descending pathway. This allows us to define the role of the descending pathway and how it can be affected by the depletion of the dopaminergic neurons.
Until know, we showed that the loss of dopamine neurons makes the 5-HT descending pathway switching from an analgesic role to a proalgesic one as we could see that in pathological conditions, the activation of the pathway does not induce anymore a decrease of pain but an increase of it.
Now raise the question of the mechanisms leading to this switch in order to develop potential therapeutic targets to treat the chronic pain in parkinsonian patients.

P06.25

Fluorescence lifetime imaging and immunohistochemical analysis of neuropathological changes related to Parkinson's disease in murine duodenal tissues

Jana Harsanyiova[*,1], Alzbeta Kralova Trancikova[2], Martin Kolisek[1]*
[1] Comenius University in Bratislava, Jessenius Faculty of Medicine in Martin, Biomedical Centre Martin, Martin, Slovakia
[2] Comenius University in Bratislava, Jessenius Faculty of Medicine in Martin, Biomedical Centre Martin; Slovak Academy of Sciences, Institute of Neuroimmunology, Martin, Slovakia

Parkinson's disease (PD) is a progressive neurodegenerative disease where the incidence increases significantly with age. The disease is characterized by the degeneration of dopaminergic neurons and the formation of Lewy bodies and Lewy neurites in the central nervous system (CNS). The PD onset is thought to be localized to peripheral organs (e.g., gastrointestinal tissues or the olfactory bulb) several years before CNS pathology. Therefore, identifying the neuropathological changes associated with PD before the involvement of the CNS could become a promising tool for the early diagnosis of the disease. In our study, we focused on the early detection of the pathologically aggregated proteins associated with PD in different layers of mouse gastrointestinal tissues by using two advanced microscopic methods.
Pathology associated with PD in a murine model was induced by oral administration of neurotoxin rotenone, and duodenal tissues were collected after 0, 4, 6, 8, 10, and 12 weeks of rotenone application. Whole-mount tissues were stained with Thioflavin S (ThS) or specific antibodies and analyzed using a combination of two innovative methods: fluorescence lifetime imaging analysis (FLIM) and confocal/multiphoton microscopy to detect pathological aggregates of synuclein in mucosal, submucosal, and muscle layers.
Using FLIM analysis, we detected a gradual increase of ThS fluorescence in duodenal samples after 4 weeks of rotenone administration, depending on the length of the rotenone application. After 8 weeks of rotenone treatment, immunohistochemical staining of whole-mount tissues revealed the presence of pathological synuclein-positive aggregates.
Our experiments revealed the suitability of the used innovative microscopic methods for complex whole-mount samples. Based on our results, FLIM technique appears to be adequately sensitive to detect early and gradual changes related to pathological synuclein aggregation in a mouse model of the Parkinson's disease.
Acknowledgement: This work was supported by the Slovak Research and Development Agency APVV-20-0331 and VEGA 1/0371/21.

P06.26

Focused ultrasound as a novel therapeutic for depression in Parkinson's disease

Rachael Herlihy, Francisco Alicandri, Hudy Berger, Huda Rehman, Yifan Kao, Kainat Akhtar, Emily Mahoney-Rafferty, Angela Tawfik, Rachel Skumurski, Damian Shin*
Albany Medical College, Albany, New York, United States

While motor disturbances are the most common symptoms of Parkinson's disease (PD), depression appears in 40% of people with PD as a non-motor symptom that increases functional disability, exacerbates motor dysfunction, and reduces quality of life. Among these patients, only 50% respond to antidepressants and alternative therapeutics are needed. Vagus nerve stimulation (VNS) improves treatment-resistant depression in the general population, but this antidepressant effect has not been demonstrated in the PD population. To fill this gap, we apply focused ultrasound (FUS) to a peripheral ganglion, which mimics VNS but is targeted downstream of the vagus nerve non-invasively, and assess changes in depressive-like behavior in an animal model of PD. We hypothesize that FUS to a peripheral ganglion improves depressive-like behavior in PD rats. If validated, our study is significant in revealing that FUS neuromodulation, akin to non-invasive VNS, is efficacious for depression in PD. Here, male Sprague Dawley rats are made parkinsonian ('PD') from craniotomy surgery and unilateral injection of 6-hydroxydopamine (6-OHDA) into the medial forebrain bundle. Forepaw akinesia is evaluated with the limb-use asymmetry test, and depressive-like behavior is assessed with the sucrose preference test (SPT) and forced swim test (FST). After, brain slices are immuno-stained with tyrosine hydroxylase (TH) to visualize and quantify dopaminergic cell and axon degeneration in the substantia nigra pars compacta and striatum, respectively. We found that PD rats not only exhibited forelimb akinesia and >90% loss of TH immunostaining ipsilateral to the lesioned side, but also demonstrated depressive-like behavior, which was improved by FUS in the SPT. Data regarding PD rats and efficacy with FUS in the FST remains to be seen. In conclusion, non-invasive FUS to a peripheral ganglion improved depressive-like behavior in PD rats. Further research will shed light on the plausible clinical utility of FUS as a novel therapeutic for depression in PD patients.

P06.27

Reduction in alpha-synuclein levels after antisense oligonucleotides treatment in patient derived midbrain organoids

Javier Jarazo[*,1], Isabel Rosety[1], Mario Richter[2], Jan Stoehr[3], Michael Schulz[2], Peter Reinhardt[2], Jens Schwamborn[1]*
[1] OrganoTherapeutics, Esch-sur-Alzette, Luxembourg
[2] AbbVie Deutschland GmbH & Co KG, Ludwigshafen am Rhein, Germany
[3] AbbVie Cambridge Research Center, Cambridge, United States

Objectives: Accumulation of aggregated alpha-synuclein is one of the hallmarks in the pathogenesis of most Parkinson's disease (PD) cases, thus it is an interesting target for new therapeutics. In this study we determined if antisense oligonucleotides (ASOs) can reduce the levels of alpha-synuclein, as well as their impact in differentiation efficiency in midbrain organoids.
Methods: Midbrain organoids derived from control and patient carrying a triplication in the alpha-synuclein gene were used for assessing the effect of Gapmer ASOs directed against alpha-synuclein. A series of regimens and concentrations were used: a 12-, 25- or 50-day treatment until the organoids reached a differentiation of 50 days; and the concentrations selected were 0.01nM, 0.033nM, and 0.1nM, with an untreated condition as control.
Results: No major toxicity was detected after treatment with the ASOs, since the proportion of pyknotic nuclei was lower than 5% across regimens and concentrations. Treatment with ASOs produced a significant reduction in the levels of total and phosphorylated alpha-synuclein in a regimen and dose dependent manner. The S129 phosphorylated form of alpha-synuclein was also reduced in a similar way as alpha-synuclein but to a lesser extent. Reduction in the levels of alpha-synuclein was detected in both lines, and with immunofluorescence and western blot analysis. The shortest regimen produced a significant increase of dopaminergic neurons in the patient specific midbrain organoids, but only a tendency to be increased was observed with the other treatment conditions.
Conclusions: The clear reduction in the levels of alpha-synuclein after treatment with ASOs in the context of a patient model that recapitulates all the key features of PD in vitro, indicates that ASOs are an interesting treatment candidate to further develop.

Reference: This work will be presented as well in the ADPD 2023 Alzheimer's & Parkinson's Diseases Conference, 28/3-1/4/2023.

P06.28

Cell autonomous role of leucine-rich repeat kinase in dopaminergic neuron survival

Jongkyun Kang, Guodong Huang, Long Ma, Youren Tong, Phoenix Chen, Jie Shen*
Harvard Medical School/Brigham and Women's Hospital, Boston, MA, United States

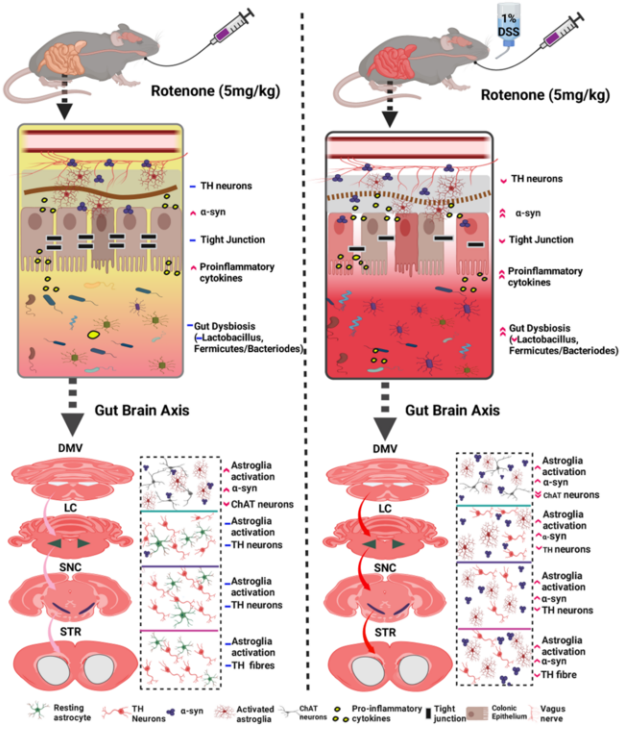
Mutations in LRRK2 are the most common genetic cause of Parkinson's disease (PD). Previous studies showed that germline deletions of LRRK2 and its homologue LRRK1 results in age-dependent loss of dopaminergic neurons in the substantia nigra pars compacta (SNpc), but the earlier mortality and lower body weight of LRRK double knockout (DKO) mice raised the possibility that the observed dopaminergic neurodegeneration may be cell extrinsic. In this study, we investigate whether LRRK is required for dopaminergic neuron survival in a cell autonomous manner through the generation of dopaminergic neuron-specific LRRK conditional DKO (cDKO) mice. We found that LRRK cDKO mice of both sexes exhibit normal body weight and mortality but nevertheless develop significant decreases of dopaminergic neurons at the ages of 20 and 24 months. In contrast to the reduction of dopaminergic neurons in LRRK DKO mice at 15 months of age, the number of dopaminergic neurons in LRRK cDKO mice at this age is unaffected. Furthermore, DA neurodegeneration is accompanied with increases of apoptosis and elevated microgliosis in the SNpc of LRRK cDKO mice. Surprisingly, quantitative electron microscopy analysis showed similar number and area of electron-dense vacuoles in SNpc neurons of LRRK cDKO and control mice at 25 months of age, compared to age-dependent, dramatic increases of electron-dense vacuoles in surviving SNpc neurons of LRRK DKO mice. These results demonstrate an essential, cell autonomous role of LRRK in dopaminergic neuron survival and suggest a cell non-autonomous contribution of LRRK to the integrity of dopaminergic neurons.

P06.29

Experimental colitis accelerates intragastric rotenone-induced alpha-synuclein pathology and its progression from the gut to the brain

Nishant Sharma[1], Monika Sharma[2], Disha Thakkar[3], Hemant Kumar[4], Sona Smetanova[5], Lucie Buresova[5], Petr Andrla[5], Amit Khairnar*[,6]
[1] Department of Pharmacology and Toxicology, National Institute of Pharmaceutical Education and Research, Ahmedabad, Ahmedabad, Gujarat, India
[2] Department of Pharmacology and Toxicology, National Institute of Pharmaceutical Education and Research, Ahmedabad (NIPER-A)., Gandhinagar, Gujarat, India
[3] National Institute of Pharmaceutical Education and Research, Ahmedabad (NIPER-A)., Gandhinagar, Gujarat, India
[4] Department of Pharmacology and Toxicology, National Institute of Pharmaceutical Education and Research, Ahmedabad (NIPER-A), Gandhinagar, Gujarat, India
[5] RECETOX, Faculty of Science, Masaryk University, Brno, Czech Republic, Brno, South Moravia, Czech Republic
[6] Department of Pharmacology and Toxicology, National Institute of Pharmaceutical Education and Research, Ahmedabad (NIPER-A), Fakultni Nemocnice U Sv Anny, International Clinical Research Center, Brno, Czech Republic, Brno, South Moravia, Czech Republic

Background: The involvement of GI inflammation and local exposure to neurotoxins in the gut provides the most detailed explanation of Parkinson's disease (PD) etiopathogenesis via aberrant accumulation and spreading of alpha-synuclein (α-syn) aggregates from the gut to the brain.
Objectives: This study sought to determine whether people with colitis have increased vulnerability in the presence or absence of environmental toxins to developing PD pathology.
Methods: To induce colitis, 10 months old C57BL/6 mice were pre-exposed to 3 cycles of 7 days of 1% (w/v) DSS administration in drinking water. After colitis induction, animals received a low dose of intragastric rotenone for the next 8 weeks, followed by testing for Parkinsonian behavior and GI phenotypes of inflammation. At the end of the 17th week, colon, brain stem, and midbrain tissue were isolated and analyzed for α-syn, inflammatory markers, and dopaminergic neuronal loss. Fecal microbial composition was assessed by 16S rRNA sequencing analysis.
Results: We found that rotenone alone exposure for 8 weeks did not affect colitis severity and colonic tight junction (TJ) protein expression (ZO-1, Occludin, and Claudin-1). On the contrary, we found that chronic rotenone administration in the presence of pre-existing colitis increased proinflammatory mediators, altered gut microbiota composition, and reduced TJ's protein expression. This damage was also accompanied by impairment of GI functions, and poor behavioral performances suggested to result in aberrant rotenone-induced α-syn pathology in the colon. Results showed that α-syn pathology specific to the mice administered with rotenone post-colitis produced signs of dopaminergic dysfunction along the nigrostriatal path, including the dorsal motor nucleus of the vagus and locus coeruleus.
Conclusions: These findings indicate that long-term rotenone exposure in conjunction with early inflammatory intestinal milieu exacerbates the progression of α-syn pathology and aggravates neurodegeneration in the intragastric mouse PD model.
Keywords: Parkinson's disease; Gut inflammation; Inflammatory bowel disease; Alpha-synuclein progression; Gut-brain axis.



P06.30

Human α-synuclein-holding familial Parkinson's disease-linked Ala-53 to Thr mutation causes sleep and circadian dysfunction in transgenic mice

Pureum Kim[*,1], Nicholas Garner[1], Henrik Oster[2], Oliver Rawashdeh[1]*
[1] The University of Queensland, Brisbane, QLD, Australia
[2] University of Lübeck, Lübeck, Germany

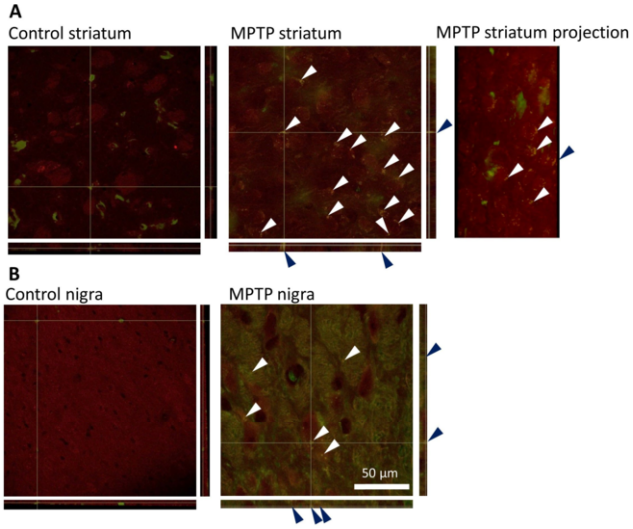
Sleep dysfunction and circadian disturbances are among the earliest non-motor features of PD, preceding motor manifestations by many years. PD is characterised by the occurrence of Lewy bodies containing phosphorylated alpha-synuclein (α-synP). By modelling the accumulation of pathological α-synP, a hallmark of the disease, we aimed to investigate the impact of pathological human Ser129-phosphorylated α-synuclein (α-synP) accumulation in the brain of mice on sleep homeostasis and circadian function.
We used the preclinical M83 transgenic mouse model, which expresses the A53T mutated form of human α-syn protein, which can cause PD in humans. EEG/EMG radiotelemetry data and video surveillance were acquired under different experimental conditions and at different stages of disease progression. To test whether the accumulation of pathological α-synP in the brain modifies the biological clock and/or downstream clock-regulated physiology and behavior, we assessed the response of the circadian system to entrainment signals and its role in the organism's adaptation to changes in environmental timing. To assess sleep quality and sleep homeostasis, we used polysomnography, the gold standard for measuring sleep, by assessing electroencephalography (EEG), electromyography, body temperature and video recordings under different experimental conditions.
We found that the accumulation of pathological α-synP alters the sleep/wake profile, brain activity, sleep quality and significantly impacts centrally regulated circadian rhythms. Furthermore, M83 mice progressively develop changes in their responsiveness to environmental resetting cues (e.g., light) necessary to maintain the alignment of the sleep/wake cycle to geophysical time and to adapt to environmental changes, such as temporal shifts in day/night cycles.
Our findings suggest that the circadian clock and clock-regulated pathways controlling overt rhythms of behavior and physiology, including sleep, are progressively altered by pathological brain α-synP with age. The M83 transgenic model is a valuable tool to investigate the pathogenesis of human α-synucleinopathy during the prodromal stages of PD and for screening and developing disease-modifying therapies.

P06.32

Sub-acute MPTP treatment increases α-synuclein levels and its aggregation in mice

Lucía Lage Pita, Ana Isabel Rodríguez Pérez, José Luis Labandeira García, Antonio Domínguez Meijide*
University of Santiago de Compostela-CIMUS, Santiago de Compostela, A Coruña, Spain

The main hallmarks of Parkinson's disease (PD) are a defined staged neuroinflammatory progression and the presence of protein aggregates termed Lewy bodies. One of the characteristics of these aggregates, is the presence of misfolded forms of α-synuclein. There has been some controversy regarding the MPTP parkinsonian mouse model as a model for α-synuclein aggregation as it has been reported that acute and chronic MPTP mice do not manifest α-synuclein aggregates; more recently, several groups have observed the presence of α-synuclein aggregates in MPTP-treated mice. In the present work, we have studied the formation of α-synuclein aggregates in neurons, astrocytes, and microglial cells in a 5-day sub-acute MPTP parkinsonian mouse model comparing with control mice to help clarify this controversy. We used staining with Thioflavin S (ThS), a fluorescent dye that binds to fibrillar amyloid structures, combined with immunocytochemistry for α-synuclein, TH, GFAP and IBA-1 and we observed, using confocal microscopy, that MPTP-treated mice manifest the presence of α-synuclein, which increased with aggregation stimulation. Besides, we used this model to assess changes in these aggregates by fluorescent microscopy analysis in these groups quantifying the area for each antibody-ir and for ThS binding by measuring the area of the particle. We observed that, in both substantia nigra (SN) and striatum, there is a significant increase in the expression of α-synuclein and in ThS staining after sub-acute treatment with MPTP in comparison with the controls and the same results were observed when we individually analyzed the aforementioned cell types. In addition, we observed decrease in the number of neurons and an increase in the number of microglial cells in both areas. These results confirm that, under our experimental conditions, treatment with MPTP leads to the formation of aggregates in mouse brain that is combined with a significant increase in α-synuclein expression. Thus, the present results suggest that sub-acute MPTP treatment increases the number of α-synuclein aggregates in mouse brain.



P06.33

Anatomo-radiological correlations in a Parkinson's disease animal model

Chirine Katrib[*,1], Hector Hladky[1], Régis Bordet[1], David Devos[1], Charlotte Laloux*[*,2], Nacim Betrouni[1]*
[1] UMR-S1172, Lille Neuroscience and Cognition, Lille, France
[2] UMR-S1172, LilNCog, Lille Neuroscience and cognition, Lille, France

Advanced methods in neuroimaging analysis are providing new insights into the mechanisms underlying Parkinson's Disease (PD). They have shown predictive abilities in detecting early changes in the brain, and correlating them with different disease related symptoms. By using preclinical models of the disease, this work aims to decipher the tissular signatures of these imaging changes by establishing correlation with histological findings.
Rats receive a double bilateral intranigral injection of the AAV alpha-synuclein, then undergo several behavioral tests to evaluate motor and cognitive functions over a 4-month period. Three MRI acquisitions are held at 2-,10- and 18-weeks post-injection, including a whole-brain T2w and T2*w. Histological studies are led

to evaluate dopaminergic degeneration, iron accumulation and alpha synuclein deposits in the brain.
This PD model shows a moderate and progressive dopaminergic neurodegeneration, with 30% loss of TH+ neurons in the nigrostriatal pathway at 4-months post-injection. It also exhibits diffuse synucleinopathy in the brain. Behavioral tests reveal deficits in sensori-motricity, attention and visuo-spatial learning. Whole-brain VBM analysis show hypointense signals between MRI sessions 2 and 3, in the nigrostriatal pathway, the hippocampus, the fimbria, as well as the limbic, insular, and prefrontal cortex. Indeed, these regions are directly related to the motor and executive functions impaired.
Spatial and functional correlations between imaging analysis and behavioral & histological profiles of established PD animal models, has the potential to explain the changes observed in imaging on a cellular and molecular level, and to help better understand the physiopathology of the disease. These imaging markers correlated to tissue markers, could be studied in a clinical context as a tool for early diagnosis and/or a means of monitoring the evolution of the pathology or the effectiveness of therapeutic strategies.
Acknowledgements: We thank France Parkinson's association for funding the project and Lille University and Inserm for PhD student funding. We thank all members of the Lille In vivo imaging and function platform (UMS2014 US41 Lille Biology and Health platforms), the BioImaging Center Lille (BICeL), Lille Animal Facilities, and the Degenerative and vascular cognitive disorders Team, UMR1172 LilNCog Center, for their work and support.

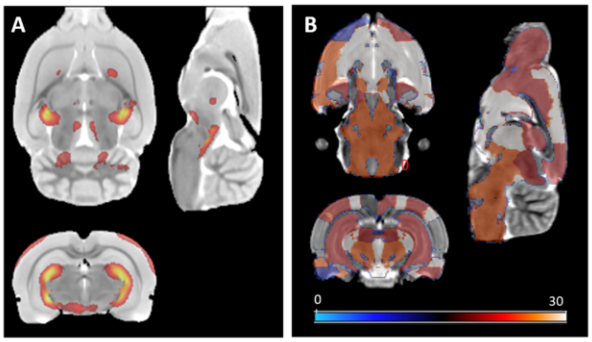


Figure: 3D representations of voxel base morphometry signal changes (A) and alpha-synuclein spreading (B) in the brain of AAV-mediated alpha-synuclein overexpression rat model, 18 weeks after surgery

P06.34

Characterization of retinal structure and function in the tau knockout mouse model of Parkinson's disease
Pei Ying Lee[*,1], Yolanda Tan[1], Vickie Wong[1], Da Zhao[1], Katie Tran[1], David Finkelstein[2], Bang Bui[1], Christine Nguyen[1]*
[1] The University of Melbourne, Parkville, VIC, Australia
[2] Florey Institute of Neuroscience and Mental Health, Parkville, VIC, Australia

Aim: Recent evidence suggests that visual disturbances precede motor symptoms in Parkinson's disease (PD). The eye being an outpouching of the brain, provides an easily accessible window through which PD neural changes can be probed. Characterizing retinal changes in PD could be used as biomarkers to support diagnosis and to monitor PD during clinical trials. Tau is reduced in human idiopathic PD, this tau knockout mouse model has behavioural, neurodegenerative and biochemical similarities with the human condition. This study aims to characterize retinal structure and function using the tau knockout mouse model at stages equivalent to prodromal and late PD.

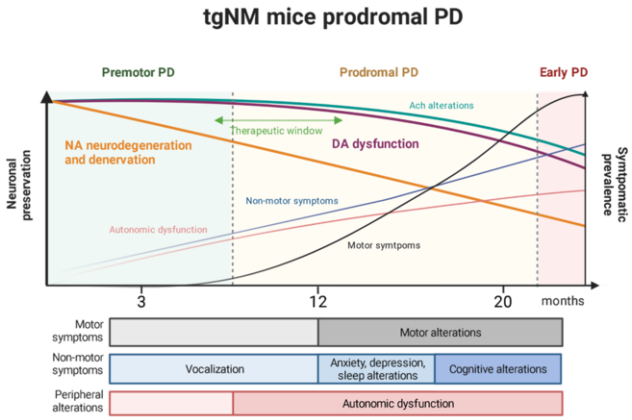
Methods: Retinal structure and function were assessed using optical coherence tomography (OCT) and electroretinography (ERG), respectively. The OCT provides thickness measures of retinal layers. The ERG provides an index of the health of the major cell classes in the retina. Two ages were examined: (1) 7-8 months old (prodromal; wild-type n = 10, tau knockout n = 11); and (2) 17-18 months old (late; wild-type n = 12, tau knockout n = 12). A two-way ANOVA, with a post hoc Sidak's multiple comparison, was conducted to compare the effects of age and genotype.
Results: Tau knockout mice showed significant differences in all retinal layer thicknesses compared to age-matched wild-type mice. Notably, there was a significant interaction effect in outer nuclear layer thickness ($p = 0.02$), where 8-month-old tau knockout mice showed the greatest thinning (49.9 ± 1.4 µm vs. wild-type 60.9 ± 1.6 µm, $p < 0.01$). There was also significant reduction in interneuron function in tau knockout mice compared to wild-type mice (bipolar cell function, $p = 0.01$; amacrine cell function $p < 0.01$).
Conclusions: The tau knockout mouse model of PD manifested retinal structural and functional deficits as early as 8 months of age. These measures may serve as biomarkers for understanding tau-related changes in the eye of people living with PD.

P06.35

Modulation of the gut microbiota modifies Parkinson's disease-like pathology in transgenic neuromelanin-producing mice
Marina Lorente Picon[*,1], Núria Peñuelas[1], Marta Gonzalez-Sepulveda[1], Marc Velilla[2], Gisela Besa[3], Annabelle Parent[1], Josep A. Villena[4], Miquel Vila[5], Ariadna Laguna[6]*
[1] (1)Vall d'Hebron Research Institute (VHIR), Barcelona, Spain; (2) Center for Networked Biomedical Research on Neurodegenerative Diseases (CIBERNED), Madrid, Spain, Barcelona, Spain
[2] (1)Vall d'Hebron Research Institute (VHIR), Barcelona, Spain; (3) CIBERDEM, CIBER on Diabetes and Associated Metabolic Diseases, Instituto de Salud Carlos III, Madrid, Spain, Barcelona, Spain
[3] (1) Vall d'Hebron Research Institute (VHIR), Barcelona, Spain, Barcelona, Spain
[4] (1)Vall d'Hebron Research Institute (VHIR), Barcelona, Spain; (3) CIBERDEM, CIBER on Diabetes and Associated Metabolic Diseases, Instituto de Salud Carlos III, Madrid, Spain; (4)Universitat Autònoma de Barcelona, Barcelona, Spain, Barcelona, Spain
[5] (1)Vall d'Hebron Research Institute (VHIR), Barcelona, Spain; (2) Center for Networked Biomedical Research on Neurodegenerative Diseases (CIBERNED), Madrid, Spain; (4)Universitat Autònoma de Barcelona, Barcelona, Spain; (5)Catalan Institution for Research and Advanced Studies (ICREA), Barcelona, Spain., Barcelona, Spain
[6] (1)Vall d'Hebron Research Institute (VHIR), Barcelona, Spain; (2) Center for Networked Biomedical Research on Neurodegenerative Diseases (CIBERNED), Madrid, Spain; (4)Universitat Autònoma de Barcelona, Barcelona, Spain;, Barcelona, Spain

Accumulating evidence indicate that alterations in the gastrointestinal (GI) function and the gut microbiota represent a risk factor for Parkinson's disease (PD). Changes in the gut-brain axis can affect both the enteric and central nervous systems, which might have implications in understanding disease pathophysiology and for the development of disease modifying therapeutic strategies.
To clarify how the gut-brain axis is involved in disease pathogenesis and/or in modulating the manifestation of PD symptoms, we used a new transgenic neuromelanin-producing mouse model (tgNM) that mimics the age-dependent accumulation and brain-wide distribution of neuromelanin occurring in humans.
These animals exhibit gastrointestinal dysfunction (i.e. altered fecal output, gut permeability) in the prodromal phase before the

appearance of dopaminergic dysfunction. These functional alterations correlated with an altered composition of the fecal microbiome and metabolome, as well as increased fecal and intestinal inflammation markers. Next, we assessed if modulation of the gut microbiota could affect the manifestation of both motor and non-motor symptoms in tgNM mice. First, we fed the animals with a high fat diet (HFD) and evaluated the worsening of the peripheral and brain pathology observed in tgNM mice. Second, we performed fecal microbiota transplants (FMT) from young wild-type mice and assessed their potential neuroprotective and beneficial effects.
Our results indicate that modelling human brain pigmentation in mice is sufficient to induce prodromal gastrointestinal dysfunction and that the newly generated neuromelanin-producing mouse model represents a valuable tool to test disease-modifying strategies for PD based on the modulation of the gut-brain axis.
Figure 1: Schematic diagram summarizing the appearance of pathological features and the manifestation of motor and non-motor alterations in tgNM mice as a new model of prodromal Parkinson's disease.



P06.36

IPSC-derived human midbrain-striatal assembloid for Parkinson's disease modeling
Beatriz Elena Lucumí Villegas[*,1], Julia Obergasteiger[1], Valerie Clavet-Fournier[2], Flavie Lavoie Cardinal[1], Samer Hussein[3], Martin Lévesque[1]*
[1] CERVO Brain Research Center, Department of psychiatry and neurosciences, Université Laval, QUÉBEC, QUÉBEC, Canada
[2] CERVO Brain Research Center, QUÉBEC, QUÉBEC, Canada
[3] Centre de recherche du CHU de Québec, Department of molecular biology, medical biochemistry and pathology, Université Laval, QUÉBEC, QUÉBEC, Canada

Parkinson's disease (PD) is a neurodegenerative disease characterized by the accumulation of misfolded alpha-synuclein (aSyn) and death of dopaminergic neurons forming the nigrostriatal pathway. Despite intensive research, the exact pathophysiological mechanisms of PD are still unknown, in part due to the lack of a disease model that can accurately reproduce biological processes at the cellular and organotypic level. Existing models either lack a human background or fail to reproduce complex neuronal connectivity. Assembloids, which are 3D structures generated from human stem cells are composed of region-specific organoids that can mimic complex neuronal connections. This project aims to develop an in vitro model of PD consisting of a midbrain-striatal assembloid that recapitulates the circuitry and connections of the nigrostriatal pathway as well as key features of the synucleinopathy. To this end, midbrain dopaminergic (MO) and striatal GABAergic organoids (SO) were developed using human induced pluripotent stem cells carrying PD-related mutations or their isogenic controls. Identity of MO and SO was confirmed by midbrain dopamine (TH, LMX1A, FOXA2) and striatal GABA-neuron markers (DARPP32, GAD67, BCL11B). Fluorescently labeled organoids were fused at DIV 50 to visualize the development of projections to the opposite organoid. The "nigrostriatal" connectivity assessment was also performed in 3D, combining assembloid clearing (iDisco) and a light-sheet imaging system. Our results revealed a time-dependent increase in axonal arborization from the midbrain to the striatal side. High-resolution STED microscopy was employed to analyze synaptic connections (Bassoon, PSD95), showing that a proportion of dopaminergic axons form synaptic contacts with striatal neurons, while some dopaminergic axonal boutons appear to lack postsynaptic counterparts. In agreement with previous studies indicating that a large proportion of dopaminergic boutons use volume transmission. We are now functionally assessing the assembloids by using an opsin-mediated stimulation in the MO and by imaging a dopamine sensor in the SO. We also evaluate the impact of PD mutations on nigrostriatal connectivity and temporal development of synucleinopathies, where the pathology is modeled using preformed aSyn fibrils. Summarizing, we have created a human neuronal model to study the mechanisms of neurodegeneration involved in PD, which can be used to develop and test new treatments for PD.

P06.37

Characterization of a seeding-based model of REM-sleep behavioral disorder in mice
Hansoo Yoo[1], Russell Luke[2], Brittany Dugan[2], Jimmy Fraigne[2], Jonah Lourie[3], Jefferson Steltz[3], Yuling Liang[3], Lauren Torres[3], John Peever[2], Kelvin Luk[,3]*
[1] Yonsei University, Seoul, South Korea
[2] University of Toronto, Toronto, Canada
[3] University of Pennsylvania, Philadelphia, PA, United States

REM sleep behavior disorder (RBD) is established as a highly predictive symptom of future alpha-synucleinopathy, including Parkinson's disease (PD). Although the disease mechanisms of RBD remain speculative, a long-standing but largely untested hypothesis is that RBD is caused by aSyn-mediated degeneration of subcoeruleal (SLD) neurons that regulate REM sleep atonia. This complex could also serve as a portal for the early spread of Lewy pathology to higher brain regions. Development of a robust animal model that incorporates synucleinopathy and recapitulates RBD would offer a unique opportunity to study a prodromal phase of PD. We demonstrate here that injection of aSyn preformed fibrils (PFF) into the SLD seeds aSyn aggregation that subsequently propagates through its connectome and induces an RBD-like phenotype. We also determine the molecular identity of SLD neurons susceptible to aSyn pathology in both mouse and human and characterize unique gene expression changes in this region following the onset of synucleinopathy.

P06.38

Using patient-derived hiPSC microglia to characterize LRRK2 signaling in Parkinson's disease
Emma MacDougall, Eric Deneault, Sophie Luo, Edward Fon*
McGill University, Montreal, Quebec, Canada

Autosomal dominant mutations in the gene encoding dual function GTPase and serine/threonine kinase, leucine rich repeat kinase 2 (LRRK2), are the most common genetic cause of Parkinson's disease (PD). All LRRK2 pathogenic mutations, including the most

common G2019S mutation increase kinase activity in vivo. Although the exact function of LRRK2 is unknown; there is evidence that it plays a role in immune function, including high expression in immune cells such as microglia. Additionally, LRRK2 is known to phosphorylate a subset of Ras analogue in brain (Rab) small GTPases. However, the role of LRRK2 signaling in microglia and how it may contribute to PD pathogenesis remains elusive. This work aims to investigate LRRK2 signalling in microglial cells by using RNA sequencing to evaluate transcriptomic changes associated with loss of or hyperactivation of LRRK2 kinase. A collection of human induced pluripotent stem cell (hiPSC) lines, including a LRRK2 G2019S patient line, an isogenic control with correction of the G2019S mutation in the patient background, a wildtype (WT) control line, and a LRRK2 knockout (KO) line have been generated and differentiated into hiPSC-derived microglia-like cells (iMGLs). The identity of the iMGLs has been validated by assessment of microglial markers by flow cytometry, IF, and qPCR. Expression of LRRK2 and phosphorylation of its canonical Rab targets has been confirmed in iMGLs by western blotting. Stimulation of iMGLs with inflammatory agents has been shown to increase LRRK2 expression levels, and thus phosphorylation of LRRK2-target Rabs. Of the inflammatory stimuli tested, treatment of iMGs with interferon-gamma was found to elicit the greatest increase in LRRK2 expression and downstream Rab phosphorylation. Whole transcriptome RNA sequencing analysis was performed on unstimulated and interferon-gamma treated iMGLs. Analysis of differentially expressed genes (DEGs) is ongoing. Identifying DEGs between LRRK2 KO, WT and G2019S iMGLs will shed light on cellular pathways affected by LRRK2 activity in microglial cells, and the involvement of LRRK2 in determining the state of microglia along the continuum from resting to reactive. Ultimately this work will lead to a better understanding of the pathogenesis underlying, and the role of inflammation and microglia in, LRRK2-associated and sporadic PD.

P06.39

Heterozygosity of the GBA1 L444P mutation impairs hippocampal-dependent memory tasks, synapse biology, and lysosomal function

Casey Mahoney-Crane, Sumedha Bobba, Eli Berry, Laura Volpicelli-Daley*
The University of Alabama at Birmingham, Birmingham, Alabama, United States

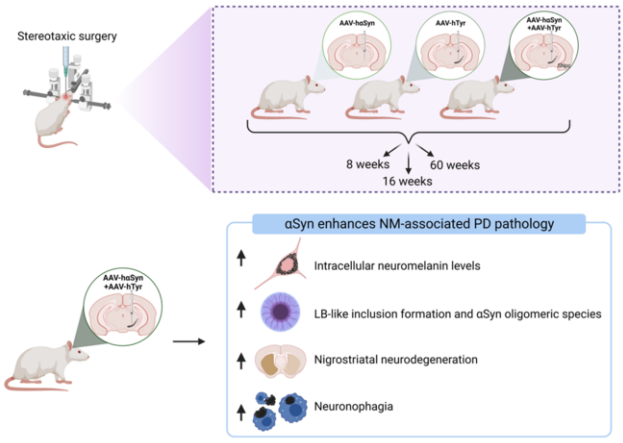
The most common genetic risk factor of Parkinson's disease is heterozygous mutations in the GBA1 gene which encodes for the lysosomal enzyme, glucocerebrosidase (GCase). Mutant GCase is associated with an accumulation of α-synuclein (α-syn) termed Lewy pathology, which pathologically characterizes PD. Clinically, heterozygosity of the GBA1 L444P mutation (GBA1+/L444P) leads to a 5.6-fold increased risk of cognitive impairments, including dementia. Another lysosomal enzyme, Cathepsin B (CatB), aids in α-syn cleavage and may play a role in α-syn pathology development. In this study, we used GBA1+/L444P knock-in mice of both sexes and their wildtype littermates (GBA1+/+) as controls, to determine the effects of this severe GBA1 mutation on lysosomal function and synapse biology. By three-months of age, hippocampal expression of the presynaptic excitatory marker, vGLUT1, is reduced by~36%, while the inhibitory counterpart, vGAT, is increased by ~31% compared to GBA1+/+ mice. This may contribute to spatial memory deficits observed by 9-months of age through the Y maze and Barnes maze behavioral tasks. These mice additionally exhibit hippocampal lysosomal dysfunction as early as three-months through the reduction of GCase activity and CatB protein expression. Collectively, lysosomal dysfunction and alterations in synapse biology may contribute to the increased spatial memory deficits observed in mice expression the GBA1L444P mutation. Elucidating the molecular mechanism behind cognitive impairs will likely aid in the development of novel therapies that can slow the progression of Parkinson's disease and other α-synucleinopathies.

P06.40

Crosstalk between alpha-synuclein and neuromelanin exacerbates Parkinson's disease pathology in melanized tyrosinase-expressing rodents

Alba Nicolau-Vera, Thais Cuadros, Joana M Cladera-Sastre, Jordi Romero-Giménez, Annabelle Parent, Ariadna Laguna, Miquel Vila*
Vall d'Hebron Research Institute (VHIR)-Center for Networked Biomedical Research on Neurodegenerative Diseases (CIBERNED), Barcelona, Spain

Parkinson's disease (PD) is characterized by a preferential loss of neurons containing the pigment neuromelanin (NM), especially dopaminergic neurons of the substantia nigra (SN), and the presence in affected neurons of alpha-synuclein (αSyn)-containing insoluble cytoplasmic aggregates termed Lewy bodies (LB). While αSyn aggregation is considered a central pathogenic event in PD, the mechanisms and significance of LB formation remain unknown. It has been reported that αSyn redistributes to the lipid component of NM at early PD stages and is entrapped within NM granules extracted from PD, but not control, brains. The increased concentration of neuronal αSyn and NM pigment in SN neurons may predispose these neurons to LB formation and cell death. However, it has not yet been possible to experimentally assess in vivo a potential pathological interaction between αSyn and NM because, in contrast to humans, NM is absent in common experimental animals such as rodents.
We have recently developed the first rodent model of human-like NM production based on the viral vector-mediated nigral expression of melanin-producing enzyme tyrosinase (AAV-TYR). This has revealed that NM can trigger PD pathology when accumulated above a specific pathogenic threshold. Here we aim to assess the potential interaction between αSyn and NM by combining αSyn overexpression with TYR-induced NM production in rodents.
AAV-mediated nigral expression of human αSyn in melanized TYRr-expressing rats resulted in an increase of intracellular NM levels, a more sustained LB-like inclusion formation, an exacerbated presence of αSyn oligomeric species and an enhanced nigrostriatal degeneration and neuronophagia.
Overall, our results indicate that increased levels of αSyn, as it occurs in PD patients, may accelerate age-dependent NM accumulation and enhance NM-linked PD pathology. Elucidating a potential crosstalk between αSyn and NM might thus be crucial for understanding PD etiopathogenesis and for the development of novel disease-modifying therapeutic strategies.



P06.41

Healthy human iPSC-derived astrocytes rescue the degenerative phenotype of p.A53T-αSyn iPSC-derived neurons generated from Parkinson's disease patients

Olympia Apokotou[1], Christina Paschou[2], Anastasios Kollias[2], Era Taoufik[2], Rebecca Matsas[2], Florentia Papastefanaki[3]*
[1] Human Embryonic and Induced Pluripotent Stem Cell Unit, Hellenic Pasteur Institute, Athens, Greece
[2] Laboratory of Cellular and Molecular Neurobiology-Stem Cells, Hellenic Pasteur Institute, Athens, Greece
[3] Human Embryonic and Induced Pluripotent Stem Cell Unit, Hellenic Pasteur Institute, Laboratory of Cellular and Molecular Neurobiology-Stem Cells, Hellenic Pasteur Institute, Athens, Greece

Astrocytes, the most abundant cells in human brain play critical roles in maintaining neuronal health while they may also exert neuroprotective or neurotoxic effects upon disease. However, their involvement in Parkinson's disease (PD) pathogenesis remains largely unexplored, especially when compared with the intensive research on neuron-intrinsic dysfunction. PD is characterized by progressive loss of midbrain dopaminergic neurons whilst the histopathological disease hallmark is the presence of intracellular protein inclusions termed Lewy bodies. Only 5-10% of cases have been linked with mutations in specific genes, such as the SNCA gene encoding for α-synuclein (αSyn). The best-characterized mutation is pA53T-αSyn (G209A in SNCA), causing a familial form of PD with early onset and severe phenotype. While the disease mechanisms remain unresolved, cell reprogramming provides a unique human setting for the identification and interpretation of PD phenotypes. We have previously established an induced pluripotent stem cell (iPSC)-based neuronal model of PD from patients harboring the p.A53T-αSyn mutation, which exhibits disease-associated phenotypes, including intraneuronal protein aggregates, axonal pathology, and reduced synaptic connectivity. To investigate the contribution of astrocytes in PD, here we generated ventral midbrain-patterned astrocytes from p.A53T-αSyn patient iPSCs and healthy controls. p.A53T-αSyn astrocytes displayed phospho-Ser129-aSyn deposits and intense cytoplasmic vacuolization. In a co-culture setup of p.A53T-αSyn or control neurons on either p.A53T-αSyn or control astrocytes at all possible combinations, we examined their reciprocal interplay. We observed compromised neuronal viability of both control and p.A53T-αSyn neurons when co-cultured with p.A53T-αSyn astrocytes. Moreover, the degenerative phenotype of mutant neurons was exacerbated in co-culture with mutant astrocytes, presenting prominent intraneuronal accumulation of protein aggregates and other typical PD histopathological hallmarks including Lewy body-like formations, Lewy neurites, and retraction bulbs. Interestingly, these phenotypes were reversed when p.A53T-αSyn neurons were cultured on control astrocytes. Our data support a critical role of mutant astrocytes in the neurodegeneration process and a remarkable ability of healthy astrocytes in rescuing neurodegeneration of mutant neurons.
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P06.42

A novel autoimmune alpha-synuclein-induced model of Parkinson's disease

Rebekah Parkinson[1], Jessica Petitt[1], Alexandre Rcom-H'cheo-Forgues[1], Rebecca Buckland[1], Christopher Parish[1], Anne Bruestle[1], Nathalie Dehorter[2]*
[1] Australian National University, Canberra, ACT, Australia
[2] Australian National University and University of Queensland, Canberra, ACT, Australia

There is increasing evidence that Parkinson's disease (PD) is an autoimmune disorder. Studies have found elevated blood immune cell counts in patients and revealed that alpha-synuclein could act as an antigenic epitope, driving both innate and adaptive immunity. However, the mechanistic role of the immune system in contributing to PD pathogenesis remains a question that researchers have been unable to address due to limitations with current animal models. To resolve this, we established the first immune-induced mouse model of PD whereby alpha-synuclein-induced immune activation triggers dopaminergic cell loss and motor deficits.
This model consists of a single peripheral injection of alpha-synuclein protein in adjuvants in wildtype mice, which triggers immunity, identified by raised blood cell counts, such as monocytes, lymphocytes, and neutrophils. These mice display significant behavioural and neurological alterations compared to control conditions (i.e., non-injected mice, sham, and mice lacking adaptive immunity, Rag1tm1Mom). To more specifically discern the trigger of these symptoms, we injected an alpha-synuclein peptide (α-syn61-75EQVTNVGGAVVTGVT) known to elicit an antigenic response to CD4+ T cells in Parkinson's patients. These mice also developed deficits in locomotion and gait kinematics. This was supported with neurological changes in the substantia nigra, including significant decrease of dopaminergic cell density, greater colocalization of MJFR-14-6-4-2+ alpha-synuclein aggregates and increase in pro-inflammatory cells, such as microglia and astrocytes. Further changes were observed within the nigro-striatal pathway, including decreased dopamine within the striatum, and increased alpha-synuclein aggregation in the locus coeruleus. On-going investigations involve characterising the pathophysiological cellular and molecular deficits in dopaminergic and striatal neurons.
Overall, this study uncovers a causal link between immune cells and alpha-synuclein in driving PD pathogenesis. As the first murine immunological model of PD, it provides the basis for exploring preventive and therapeutic interventions such as immunotherapies and inflammasome inhibitor drugs.

P06.43

Modelling human brain-wide pigmentation induces Parkinson-like pathology and transcriptomic alterations in vivo

Ariadna Laguna[1], Nuria Peñuelas[,2], Marta Gonzalez-Sepulveda[3], Alba Nicolau[3], Sébastien Arthaud[4], Camille Guillard-Sirieix[3], Marina Lorente-Picón[3], Joan Compte[3], Helena Xicoy[5], Lluís Miquel-Rio[6], Jiong Liu[4], Annabelle Parent[3], Thais Cuadros[3], Jordi Romero-Giménez[5], Gemma Pujol[5], Eliana Markidi[5], Lydia Giménez-Llort[7], Patrice Fort[4], Analia Bortolozzi[6], Iria Carballo-Carbajal[5], Miquel Vila[8]*

[1] 1Neurodegenerative Diseases Research Group, Vall d'Hebron Research Institute (VHIR)-Network Center for Biomedical Research in Neurodegenerative Diseases (CIBERNED), Barcelona, Spain2Aligning Science Across Parkinson's (ASAP) Collaborative Research Network, Chevy Chase, MD, USA 3Institut de Neurociències (INc-UAB), Autonomous University of Barcelona, Barcelona, Spain, Barcelona, Spain

[2] Vall d'Hebron Research Institute, Barcelona, Spain

[3] 1Neurodegenerative Diseases Research Group, Vall d'Hebron Research Institute (VHIR)-Network Center for Biomedical Research in Neurodegenerative Diseases (CIBERNED), Barcelona, Spain 2Aligning Science Across Parkinson's (ASAP) Collaborative Research Network, Chevy Chase, MD, USA, Barcelona, Spain

[4] Université Claude Bernard Lyon 1, CNRS, INSERM, Centre de Recherche en Neurosciences de Lyon CRNL U1028 UMR5292, SLEEP, F-69500, Bron, France, Bron, France

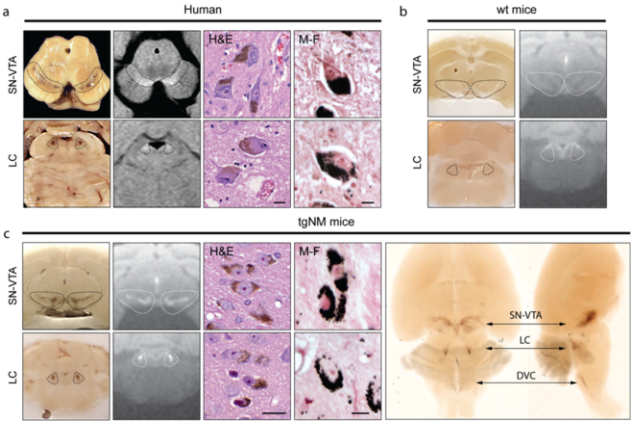
[5] Neurodegenerative Diseases Research Group, Vall d'Hebron Research Institute (VHIR)-Network Center for Biomedical Research in Neurodegenerative Diseases (CIBERNED), Barcelona, Spain, Barcelona, Spain

[6] Department of Neuroscience and Experimental Therapeutics, IIBB–CSIC, August Pi i Sunyer Biomedical Research Institute (IDIBAPS)-Center for Networked Biomedical Research on Mental Health (CIBERSAM), Barcelona, Spain, Barcelona, Spain

[7] Institut de Neurociències (INc-UAB), Autonomous University of Barcelona, Barcelona, Spain, Barcelona, Spain

[8] 1Neurodegenerative Diseases Research Group, Vall d'Hebron Research Institute (VHIR)-Network Center for Biomedical Research in Neurodegenerative Diseases (CIBERNED), Barcelona, Spain 2Aligning Science Across Parkinson's (ASAP) Collaborative Research Network, Chevy Chase, MD, USA 3Institut de Neurociències (INc-UAB), Autonomous University of Barcelona, Barcelona, Spain6Department of Biochemistry and Molecular Biology, Autonomous University of Barcelona, Barcelona, Spain 7Catalan Institution for Research and Advanced Studies (ICREA), Barcelona, Spain, Barcelona, Spain

Parkinson's disease (PD) is characterized by a preferential degeneration of neuromelanin(NM)-containing neurons, especially neurons from substantia nigra pars compacta (SNpc) and locus coeruleus (LC). NM pigmentation in the human brain is also present, at varying degrees, in most catecholaminergic neuronal groups. We have previously shown that intracellular NM levels in SNpc may set a threshold for the initiation of PD in a rodent model based on the unilateral viral-vector mediated nigral overexpression of melanin-producing enzyme tyrosinase. Here, we generated a new transgenic NM-producing mouse model (tgNM) based on the tyrosine hydroxylase (TH)-specific overexpression of human tyrosinase, mimicking the bilateral distribution of pigmentation within the whole human brain (i.e. cathecholaminergic groups A1-A14). In parallel to NM intracellular buildup, tgNM mice exhibit major early/prodromal PD features, including degeneration of LC preceding SNpc dysfunction, motor and non-motor behavioral alterations, synuclein-positive inclusions and neuroinflammation. Genome-wide transcriptomic analysis of NM-containing regions, including SNpc, ventral tegmental area and LC, revealed alterations in PD-related biological pathways that correlate with previously published human PD postmortem studies. Interestingly, GPNMB gene, which has been recently identified as a genetic risk factor for PD, was found upregulated in all pigmented areas. We are now modulating GPNMB levels in the context of NM-accumulating PD models to understand its role in NM-induced PD pathology. Overall, our results show that modelling brain-wide human NM accumulation in mice leads to age-dependent noradrenergic neurodegeneration, dopaminergic dysfunction, motor and non-motor deficits, and PD-associated neuropathological features and molecular alterations.



P06.44

Interneuronal transfer and brain spreading of synaptic proteins: specific effects of synuclein proteins

Rita Pinto-Costa, Michael Klinkenberg, Michael Helwig, Angela Rollar, Raffaella Rusconi, Donato A Di Monte, Ayse Ulusoy*
DZNE, Bonn, North Rhine-Westphalia, Germany

Neuron-to-neuron transfer of pathogenic alpha-synuclein species is a mechanism of likely relevance to Parkinson's disease development. Experimentally, interneuronal alpha-synuclein spreading from the low brainstem toward higher brain regions can be achieved by targeted overexpression of alpha-synuclein in the dorsal medulla oblongata (dMO); this overexpression is triggered by an injection of adeno-associated viral vectors (AAVs) delivering human alpha-synuclein DNA into the mouse vagus nerve. The purpose of this study was to investigate the specificity of overexpression-induced alpha-synuclein spreading; in particular, experiments were designed to determine whether other synaptic proteins, when overexpressed in the dMO, were also capable of advancing caudo-rostrally, reaching pontine, midbrain and forebrain areas. Three proteins were tested, and experiments/analyses were carried out in mice that received a vagal injection of AAVs encoding for VAMP2, SNAP25 or beta-synuclein. Data showed no evidence of interneuronal protein transfer in animals injected with VAMP2- or SNAP25-AAVs. In contrast, overexpression of beta-synuclein was followed by its detection within dystrophic axons in brain regions rostral to the dMO. Another important difference found in mice treated with VAMP2- and SNAP25- vs. beta-synuclein-AAVs was that only overexpression of beta-synuclein was associated with significant protein aggregation in the dMO. Taken together, these findings indicate that protein overexpression and synaptic localization are not necessarily linked to interneuronal protein transfer and brain spreading. Data support the notion that unique structural/functional properties of alpha- and beta-synuclein underlie their interneuronal mobility and that this mobility could be mediated, at least in part, by the propensity of alpha- and beta-synuclein to form intraneuronal aggregates.

P06.45

Immunosuppressive tocilizumab prevents astrocyte-induced neurotoxicity in hiPSC-LRRK2 PD by targeting receptor IL-6

Meritxell Pons Espinal[*,1], *Lucas Blasco-Agell*[1], *Valentina Baruffi*[1], *Irene Fernandez-Carasa*[1], *Pol Andrés-Benito*[2], *Angelique di Domenico*[3], *Yvonne Richaud*[4], *Laura Marruecos*[5], *Lluis Espinosa*[5], *Alicia Garrido*[6], *Eduardo Tolosa*[6], *Michael J. Edel*[7], *Manel Juan Otero*[8], *José Luis Mosquera*[9], *Isidre Ferrer*[2], *Angel Raya*[10], *Antonella Consiglio*[11]

[1] Department of Pathology and Experimental Therapeutics, Bellvitge University Hospital-IDIBELL / Institute of Biomedicine (IBUB) of the University of Barcelona (UB), Hospitalet de Llobregat, Spain
[2] Neuropathology, Bellvitge Biomedical Research Institute (IDIBELL) / Network Research Center of Neurodegenerative Diseases (CIBERNED), Hospitalet de Llobregat, Spain
[3] Department of Pathology and Experimental Therapeutics, Bellvitge University Hospital-IDIBELL / Institute for Neurodegenerative Diseases, University California San Francisco, Hospitalet de Llobregat, Spain
[4] Regenerative Medicine Program, Bellvitge Biomedical Research Institute (IDIBELL), and Program for Clinical Translation of Regenerative Medicine in Catalonia (P-CMRC) / Centre for Networked Biomedical Research on Bioengineering, Biomaterials and Nanomedicine (CIBER-BBN), Hospitalet de Llobregat, Spain
[5] Institut Municipal d'Investigacions Mèdiques, Institut Hospital del Mar d'Investigacions Mèdiques, Parc de Recerca Biomèdica de Barcelona, Barcelona, Spain
[6] Centre for Networked Biomedical Research on Neurodegenerative Diseases (CIBERNED) / Department of Neurology, Hospital Clínic de Barcelona, Institut d'Investigacions Biomèdiques August Pi i Sunyer (IDIBAPS), University of Barcelona (UB), Barcelona, Spain
[7] Autonomous University of Barcelona, Faculty of Medicine, Unit of Anatomy and Embryology / University of Western Australia, Faculty of Medicine, Discipline of Medical Sciences and Genetics, School of Biomedical Sciences, Bellaterra, Spain
[8] Immunology Department–CDB, Hospital Clinic de Barcelona, Institut d'Investigacions Biomèdiques August Pi i Sunyer (IDIBAPS), University of Barcelona (UB), Barcelona, Spain
[9] Bioinformatics Unit, Institut d'Investigació Biomèdica de Bellvitge – IDIBELL, Hospitalet de Llobregat, Spain
[10] Regenerative Medicine Program, Bellvitge Biomedical Research Institute (IDIBELL), and Program for Clinical Translation of Regenerative Medicine in Catalonia (P-CMRC) / Centre for Networked Biomedical Research on Bioengineering, Biomaterials and Nanomedicine (CIBER-BBN) / Institució Catalana de Recerca i Estudis Avançats (ICREA), Hospitalet de Llobregat, Spain
[11] Department of Pathology and Experimental Therapeutics, Bellvitge University Hospital-IDIBELL / Institute of Biomedicine (IBUB) of the University of Barcelona (UB) / Neuropathology, Bellvitge Biomedical Research Institute (IDIBELL) / Department of Molecular and Translational Medicine, University of Brescia, Hospitalet de Llobregat, Spain

Parkinson's disease (PD) is a multiorgan disorder, characterized by chronic inflammation, both in the brain and in the periphery, in addition to neuronal degeneration. We have previously shown that iPSC-technology can be used to recapitulate PD-relevant disease-associated phenotypes and provided direct evidence that α-synuclein transferred from astrocytes exerts non-cell-autonomous neuronal dysfunction on dopaminergic neurons in Parkinson's disease (PD). Here, applying our hiPSC-based model, we describe, for the first time, that PD astrocytes present a unique pro-inflammatory cytokine profile and transcriptional inflammatory related pathways, with increased IL-6 secretion that directly and negatively impacted on neuronal survival. Mechanistically, we show that neuronal cell death is mediated by IL-6 signaling via IL-6 receptor expressed in human PD neurons, leading to downstream activation of STAT3. Importantly, astrocyte-induced cell death in PD disease midbrain neurons could be prevented by blocking IL6R-mediated signaling using the FDA-approved antibody, tocilizumab. Moreover, postmortem tissue brain analysis of early-stage PD patients revealed increased numbers of dopamine neurons over-expressing IL-6R and of reactive astrocytes over-expressing IL-6, compared to healthy brains.
Thus, our findings provide new insights into the potential role of astrocyte-mediated inflammatory signaling in PD neuropathology and highlight potential way for new therapies based on IL-6 immunomodulation for preventing PD pathogenesis.

P06.47

Nuclear α-Synuclein detection and α-Synuclein-histones interactions

Angela Rollar[*,1], *Shirley S. L. Lee*[2], *Ayse Ulusoy*[2], *Donato A. Di Monte*[2]

[1] Deutsches Zentrum für Neurodegenerative Erkrankungen (DZNE), Bonn, Germany
[2] DZNE, Bonn, Germany

Pathological accumulation of alpha-synuclein (αSyn)-containing inclusions is a hallmark of Parkinson's disease (PD). αSyn is a synaptic protein and, under normal conditions, is predominantly detected in brain specimens from humans and experimental animals in the form of immunoreactive punctae corresponding to synaptic boutons. Evidence from both humans and animal models also indicates that accumulation of αSyn outside neuronal terminals can occur as a consequence of pathological processes and, under these circumstances, specific protein immunoreactivity may be present with neuronal perikarya as well as within neuronal nuclei. Here, our aim was to develop and validate a novel technique to detect nuclear αSyn localization and to study αSyn-histone interactions. For this study, experiments and analyses were carried out in the substantia nigra pars compacta of rats in which αSyn overexpression was triggered by a unilateral intraparenchymal injection of adeno-associated viral vectors (AAVs) delivering human αSyn DNA. Neither cytosolic nor nuclear αSyn was detected in non-injected control animals. Quite in contrast, cytosolic αSyn accumulation in the substantia nigra ipsilateral to the AAV injection was associated with intranuclear protein localization. The latter was specifically detected using a proximity ligation assay (PLA). For this assay, samples were incubated first with a pair of primary antibodies and then with secondary antibodies conjugated with PLA oligonucleotide probes; the two primary antibodies were anti–human αSyn and anti-histone H3. A parallel set of analyses were aimed at assessing the possibility that post-translationally modified forms of αSyn were also present within nuclei of the overexpressing neurons. Samples processed for PLA were incubated, for example, with anti-histone H3 and with an antibody recognizing aggregated but not monomeric αSyn. Results of these analyses revealed clear PLA signals, supporting the notion that, once it enters nuclei, αSyn undergoes self-assembly processes. As indicated by earlier in vitro studies, intranuclear protein aggregation could be promoted by αSyn-histone interactions. In summary, our results underscore the importance of investigations into mechanisms and consequences of nuclear αSyn transfer; future studies will be facilitated by the availability of sensitive and accurate detection methodologies, such as the one described in this study.

P06.48

Exploring the role of the lysosomal lipid flippase ATP10B in the nigrostriatal dopaminergic pathway of rats

Maria Sanchiz-Calvo[*1], Eduard Bentea[1], Christopher Cawthorne[2], Mirte De Ceuninck[1], Teresa Torre-Muruzabal[1], Chris Van den Haute[1], Peter Vangheluwe[3], Veerle Baekelandt[1]*

[1] Laboratory of Neurobiology and Gene Therapy, KU Leuven, Leuven, Belgium
[2] Molecular Small Animal Imaging Center (MoSAIC), KU Leuven, Leuven, Belgium
[3] Laboratory of Cellular Transport Systems, KU Leuven, Leuven, Belgium

Objectives: ATP10B is a lysosomal P-type transport ATPase recently associated with early-onset Parkinson's disease. Compound heterozygous mutations of ATP10B were found in a Belgian cohort of patients with early-onset Parkinson's disease and dementia with Lewy bodies, which decrease the ATPase activity of the protein. Interestingly, decreased ATP10B mRNA levels have been observed in the substantia nigra of patients with sporadic Parkinson's disease as well. We demonstrated that ATP10B is a transmembrane lysosomal flippase responsible for the translocation of glucosylceramide and phosphatidylcholine from the inner to the outer lysosomal membrane in cellular systems, although its role in vivo remains poorly understood (Marin, S. et al. Acta Neuropath, 2020). In the current study, we aimed to explore the role of ATP10B in vivo by downregulating its expression in neurons of the substantia nigra of rats.
Methods: AAV2/7 vectors encoding 2 different shRNAs (miR5 and miR7) targeting distinct regions of rat ATP10B under a neuronal promoter were unilaterally injected in the substantia nigra pars compacta of adult female Wistar rats. A vector with a scrambled sequence was used as control. Longitudinal behavioral evaluation was performed during 12 months using tests for spontaneous locomotion (open-field), motor coordination and balance (rotarod), catalepsy (bar test), and motor asymmetry (cylinder, elevated body swing). In addition, we assessed longitudinal in vivo striatal dopamine transporter binding using 18F-FE-PE2I PET imaging.
Results: ATP10B downregulation in nigral neurons led to a time-dependent decrease in striatal dopamine transporter binding in vivo. Behavioral phenotyping revealed significant motor deficits indicative of decreased unilateral dopaminergic neurotransmission, including decreased spontaneous locomotion and rearing, impaired motor coordination and balance, catalepsy, and motor asymmetry. Similar findings were observed for the two shRNAs. Preliminary data from a pilot experiment revealed increased expression of pathologically Ser129-phosphorylated-α-synuclein together with decreased striatal dopaminergic innervation.
Conclusion: Our findings highlight an important role of ATP10B in the nigrostriatal dopaminergic pathway, and show parkinsonian deficits in rats with decreased nigral expression of ATP10B. Ongoing histological and biochemical characterization including changes in α-synuclein, lipid metabolism and the lysosomal system will provide a better understanding of the model.

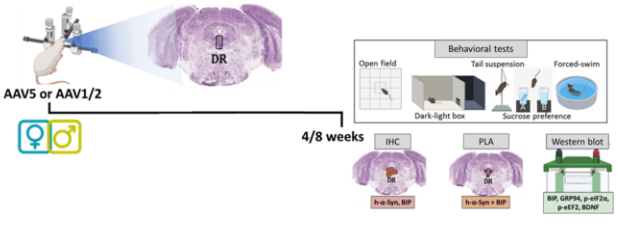
P06.49

Ketamine as a modulator of endoplasmic reticulum stress in a cross-sex mouse model of Parkinson's disease with depressive phenotype

Unai Sarriés-Serrano[1], Lluis Miquel-Rio[2], Verónica Paz[2], Jose Javier Meana[3], Analia Bortolozzi[*2]*

[1] Institute of Biomedical Research of Barcelona (IIBB), Spanish National Research Council (CSIC); August Pi i Sunyer Biomedical Research Institute (IDIBAPS); Biomedical Research Networking Center for Mental Health (CIBERSAM), ISCIII; Department of Pharmacology, University of the Basque Country, Barcelona, Spain
[2] Institute of Biomedical Research of Barcelona (IIBB), Spanish National Research Council (CSIC); August Pi i Sunyer Biomedical Research Institute (IDIBAPS); Biomedical Research Networking Center for Mental Health (CIBERSAM), ISCIII, Barcelona, Spain
[3] Biomedical Research Networking Center for Mental Health (CIBERSAM), ISCIII; Department of Pharmacology, University of the Basque Country; Biocruces Bizkaia Health Research Institute, Leioa, Spain

Introduction: Anxiety and depression are the most prevalent non-motor neuropsychiatric disorders in Parkinson's disease (PD) patients (40-50%), with higher incidence in women than in men. Neuropathological studies have demonstrated the presence of Lewy bodies, α-synuclein (α-Syn) positive staining, in raphe serotonin (5-HT) neurons in early stages of PD, accompanied in some cases by neuronal loss, and morphological changes of 5-HT fibers, linked to neuropsychiatric symptoms. We hypothesize that α-Syn accumulation in 5-HT system induces endoplasmic reticulum (ER) stress, leading to neuroplasticity changes in brain circuits controlling emotional functions.
Methods: Administration of recombinant AAV vector serotype 5 (AAV5) or AAV1/2 to overexpress wild-type or A53T mutated h-α-Syn in raphe 5-HT neurons of male or female mice. Four- and eight-weeks post-AAV infusion, behavioural phenotype was examined. H-α-Syn and BIP proteins were detected by immunohistochemistry and proximity ligation assay (PLA). Unfolded protein response (UPR) pathway markers (BIP, GRP94, p-eIF2α, and p-eEF2) and BDNF were assessed by Western-blot. Single doses of ketamine or citalopram (10 mg/kg, i.p.) were administered and behaviour and UPR markers were assessed. Statistical analysis was performed by t-test or one-way ANOVA.
Results: We detected by PLA h-α-Syn and BIP protein interactions in raphe 5-HT neurons of AAV5 female and male mice. AAV5 male mice showed depressive-like phenotype in tail suspension and forced swim tests, and reduced raphe BDNF levels. In parallel, significant increases in BIP, GRP94, p-eIF2α and p-eEF2 proteins were detected in raphe nuclei, suggesting activation of PERK pathway. These results were replicated after mutant h-α-Syn overexpression in raphe 5-HT neurons. Opposite to males, AAV5 female mice showed anxiety-like phenotype in dark-light box test and anhedonia in sucrose preference test, with no differences in tail suspension and forced swim tests. Furthermore, no PERK pathway activation was observed in AAV5 females, at least 4 weeks later. Ketamine or citalopram reversed depressive-like phenotype, suggesting AAV-α-Syn mouse model in 5-HT neurons is appropriate to assess depressive disorder in PD.
Conclusions: Overall, h-α-Syn overexpression in 5-HT neurons affects in a sex-dependent manner PERK proteostasis, inducing different depressive/anxious behavioural profiles. Modulation of ER stress and PERK pathway by ketamine offers a potential therapeutic strategy for neuropsychiatric symptoms in PD.



P06.51

Unveiling the impact of glial autophagic dysfunction in the initiation and progression of Parkinson's disease

Aurora Scrivo[*,1], Veronica Testa[1], Valentina Baruffi[1], Merixtell Pons Espinals[1], Irene Fernandez Carasa[1], Eduardo Tolosa[2], Angel Raya[3], Antonella Consiglio[4]*

[1] Department of Pathology and Experimental Therapeutics, Bellvitge University Hospital-IDIBELL / Institute of Biomedicine (IBUB) of the University of Barcelona (UB), Hospitalet de Llobregat, Spain

[2] Department of Neurology, Hospital Clínic de Barcelona, Institut d'Investigacions Biomèdiques August Pi i Sunyer (IDIBAPS), University of Barcelona (UB), Barcelona, Spain

[3] Stem Cell Potency Lab, Regenerative Medicine Program, Bellvitge Biomedical Research Institute (IDIBELL), Hospital Duran i Reynals/ Center for Networked Biomedical Research on Bioengineering, Biomaterials and Nanomedicine (CIBER-BBN)/ Institució Catalana de Recerca i Estudis Avançats (ICREA), Hospitalet de Llobregat, Spain

[4] Department of Pathology and Experimental Therapeutics, Bellvitge University Hospital-IDIBELL, 08908 Hospitalet de Llobregat, Spain; Institute of Biomedicine (IBUB) of the University of Barcelona (UB)/ Department of Molecular and Translational Medicine, University of Brescia, Hospitalet de Llobregat, Spain

Parkinson's disease (PD), is the second most common neurodegenerative disorder worldwide. Characterized by distinct motor and cognitive impairments, PD severely debilitates patients's lives. Unfortunately, by the time symptoms are detected, more than 50% of neurons have already been lost, highlighting the lack and urgent need of reliable preclinical/prodromal biomarkers of the disease. For this purpose, researchers have focused their efforts for decades on finding detectable mechanisms altered in neurons, but the study on non-neuronal (glial) cells has received relativelyy little attention. Using a combination of molecular, cellular, and imaging approaches, within this project, we aim to test the hypothesis that impaired mechanistic regulation, and specifically lysosomal protein degradation, in glial cells underlies miscommunication between brain cells. More specifically, we hypothesize that these alterations lead to the modification of proteins released in extracellular vesicles (EVs), which in turn impair neuronal functionality and survival. In order to efficiently translate our data to the clinic, we used a model of human iPSC-derived astrocytes or microglia, and asses the level of diverse autophagic pathways in PD compared to healthy individuals (WT). Interestingly, at an early stage of differentiation, PD microglial cells already display lower autophagic activity than WT. This phenotype appears to be associated with a decrease in lysosomal biogenesis. We are now in the process of characterizing specific EV features associated with this phenotype that may differ in PD-derived glial cells. Attractively, EVs can be detected in patients biofluids such as cerebrospinal fluid (CSF) and protein content measured. Thus, by characterizing EVs composition in PD-derived glial cells, we hope to generate a map of possible PD biomarkers and reveal the factors involved in the onset of the disease, opening new avenues for the prevention of PD.

P06.54

Investigating the role of astrocytes and microglia in driving neurodegeneration in Parkinson's disease using an hiPSC-based in vitro model

Veronica Testa[*,1], Valentina Baruffi[2], Meritxell Pons Espinal[2], Franz Arnold Ake[3], Marieke Alzeer[2], Irene Fernandez Carasa[2], Yvonne Richaud-Patin[4], Eduardo Tolosa[5], Angel Raya[6], Mireya Plass[3], Antonella Consiglio[7]*

[1] Department of Pathology and Experimental Therapeutics, Bellvitge University Hospital-IDIBELL / Institute of Biomedicine (IBUB) of the University of Barcelona (UB), L'Hospitalet de Llobregat, Spain

[2] Department of Pathology and Experimental Therapeutics, Bellvitge University Hospital-IDIBELL / Institute of Biomedicine (IBUB) of the University of Barcelona (UB), Barcelona, Spain

[3] Gene Regulation of Cell Identity Lab, Program for Clinical Translation of Regenerative Medicine in Catalonia (P-CMRC), Hospital Duran i Reynals, Barcelona, Spain

[4] Stem Cell Potency Lab, Regenerative Medicine Program, Bellvitge Biomedical Research Institute (IDIBELL), Hospital Duran i Reynals / Center for Networked Biomedical Research on Bioengineering, Biomaterials and Nanomedicine (CIBER-BBN), Barcelona, Spain

[5] Department of Neurology, Hospital Clínic de Barcelona, Institut d'Investigacions Biomèdiques August Pi i Sunyer (IDIBAPS), University of Barcelona (UB), Barcelona, Spain

[6] Stem Cell Potency Lab, Regenerative Medicine Program, Bellvitge Biomedical Research Institute (IDIBELL), Hospital Duran i Reynals / Center for Networked Biomedical Research on Bioengineering, Biomaterials and Nanomedicine (CIBER-BBN) / Institució Catalana de Recerca i Estudis Avançats (ICREA), Barcelona, Spain

[7] Department of Pathology and Experimental Therapeutics, Bellvitge University Hospital-IDIBELL / Institute of Biomedicine (IBUB) of the University of Barcelona (UB) / Department of Molecular and Translational Medicine, University of Brescia (Brescia, Italy), Barcelona, Spain

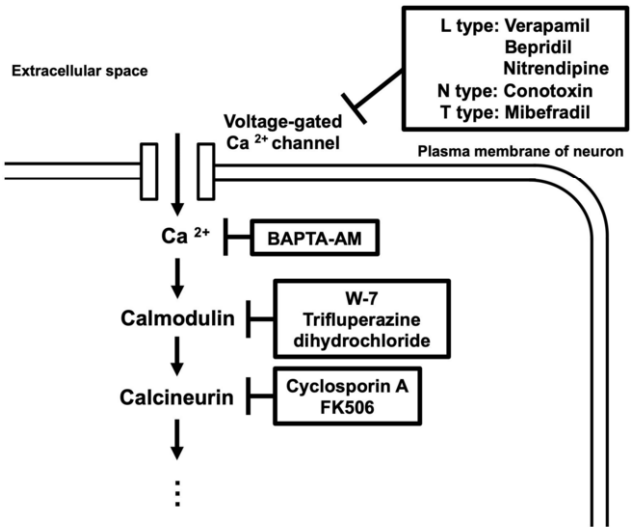
Parkinson's disease (PD) is a common, chronic, incurable neurodegenerative disease associated with a selective loss of dopamine-producing neurons in the midbrain, responsible for controlling body movements, together with the presence of misfolded α-synuclein deposits within neurons. Although the majority of PD cases are of unknown cause, approximately 5% have been shown to have a genetic basis, including mutations in the LRRK2 gene, which are found in the largest number of familial PD patients. Associated with neurodegeneration, several neuroinflammatory signs have been also described in PD. Here, we hypothesized that alterations in LRRK2 gene may contribute to innate immune dysregulations that may possibly play a role on neurodegeneration in PD. Using a combination of induced pluripotent stem cell (hiPSC)-based disease modeling and CRISPR/Cas9-mediated genome edition, here we successfully developed a novel hiPSC-derived triple culture, in which LRRK2 PD-derived astrocytes and microglia (hMG), or their respective isogenic controls, were co-cultured with healthy dopaminergic neurons (DAn). The results suggest that, by our late timepoint, LRRK2 PD-derived astrocytes are the main driver of DAn death. However, the suffering of DAn can be exacerbated by the concomitant presence of LRRK2 PD-derived hMG, suggesting the existence of a crosstalk between these two cell types. By exploiting the scRNAseq technique, we hope to reveal the dysregulated pathways in the transcriptome of each of the cell types under all conditions and timepoints, to identify the early mechanisms by which these two glial cell types contribute to neurodegeneration. Thus, these studies may have a significant impact on unravelling novel LRRK2-related pathways involved in the non-cell autonomous mechanisms of PD, possibly helping to find new early markers of pathology and new targets for treatments.

P06.55

Ca2+–calmodulin–calcineurin signaling modulates α-synuclein transmission

Jun Ueda, Norihito Uemura, Tomoyuki Ishimoto, Tomoyuki Taguchi, Masanori Sawamura, Etsuro Nakanishi, Masashi Ikuno, Shuichi Matsuzawa, Hodaka Yamakado, Ryosuke Takahashi*
Kyoto University Graduate School of Medicine, Kyoto, Japan

Objective: Parkinson's disease is one of the most common neurodegenerative diseases. The presence of Lewy bodies, which are composed of misfolded and fibrillized α-synuclein, is a pathological feature of Parkinson's disease. There is growing evidence that the interneuronal propagation of misfolded α-synuclein underlies the progression of Parkinson's disease. Previous research has shown that the neuronal uptake of fibrillized α-synuclein is activity-dependent; however, the detailed mechanisms underlying activity-dependent α-synuclein transmission in Parkinson's disease remain unclear. The objective of this study is to examine whether α-synuclein transmission is affected by Ca2+–calmodulin–calcineurin signaling in cultured cells and mouse models of Parkinson's disease. **Methods**: Mouse primary hippocampal neurons were used to examine the effects of the modulation of Ca2+–calmodulin–calcineurin signaling on the neuronal uptake of α-synuclein preformed fibrils. The effects of modulating Ca2+–calmodulin–calcineurin signaling on the development of α-synuclein pathology were examined using a mouse model injected with α-synuclein preformed fibrils. **Results:** Modulation of Ca2+–calmodulin–calcineurin signaling by inhibiting voltage-gated Ca2+ channels, calmodulin, and calcineurin blocked the neuronal uptake of α-synuclein preformed fibrils via macropinocytosis. The inhibition of L-type, N-type, and T-type voltage-gated Ca2+ channels reduced the neuronal uptake of α-synuclein preformed fibrils, whereas the inhibition of P/Q-type and R-type voltage-gated Ca2+ channels did not. We summarized the drugs used in our experiments and their mechanisms of action in Figure 1. In wild-type mice inoculated with α-synuclein preformed fibrils, we found that inhibiting calcineurin ameliorated the development of α-synuclein pathology. **Conclusion:** Our data suggest that Ca2+–calmodulin–calcineurin signaling modulates α-synuclein transmission and has a potential as a therapeutic target for Parkinson's disease.



P06.57

Age-related elevations in type-I interferon signalling control brain-gut transmission in the α-synuclein pre-formed fibril model of Parkinson's disease

Harrison Waters, Shuyan Chen, Peter Crack, Juliet Taylor*
The University of Melbourne, Parkville, Victoria, Australia

Emerging evidence suggests that α-synuclein, a major component of Lewy bodies, may be responsible for spreading pathological processes in Parkinson's disease (PD). Furthermore, it is hypothesised that α-synuclein may be able to spread from the brain to the enteric nervous system (ENS), to cause subsequent GI dysfunction. This study therefore investigated the contribution of the type-I IFNs to the progression of pathology from the brain to the gut in the alpha-synuclein (αSyn) pre-formed fibril (PFF) mouse model of PD. αSyn PFFs (8□g) were stereotaxically injected into the right dorsal striatum of wildtype (C57/BL6) and IFNAR1-/- mice at 8-12 weeks (young) or 46-50 weeks (aged) of age (n=5-8). The neuroinflammatory response in the brain, gut, and plasma was determined by qPCR, western blot analysis, ELISA, and immunohistochemistry at 6-months, post injection. Changes in gait were assessed by DigiGait analysis. The results depict an αSyn-induced pro-inflammatory response that was exacerbated at 6-months, with aged wildtype mice displaying an elevated type-I IFN response (IRF7 and STING expression), and increased IL-1β and TNF-α expression. This response was attenuated in age-matched IFNAR1-/- mice and was supported by improvements in gait (stride length and stance/swing) compared to alpha-synuclein injected wildtype mice. An elevated peripheral immune response was also identified with increased TNF-α plasma levels detected by ELISA in αSyn-injected aged wildtype mice. An analysis of gut tissue confirmed a transmission of pathology with mRNA levels of TNF-α, IL-1β, IRF3, IRF7, and STING all significantly upregulated in the duodenum of αSyn-injected aged wildtype mice. Furthermore, western blot analysis confirmed an increase in p-αSyn levels in the duodenum of αSyn-injected aged wildtype mice (but not IFNAR1-/- mice) compared to sham mice. Significantly, these gut responses were attenuated in young mice that had received intra-striatal injections of αSyn PFFs. Our findings confirm a key role for the type-I IFNs in regulating the age-related neuroinflammatory response influencing αSyn pathology in both the brain and gut. They further support a role for the gut-brain axis in driving the pathology in PD and implicate the type-I IFNs as a putative therapeutic target to slow this progression.

P06.58

TLR2 mediated α-synuclein pathology development and the contribution of astrocytes in a midbrain model of Parkinson's disease

Fiona Weiss, Glenda Halliday, Nicolas Dzamko*
School of Medical Sciences, Faculty of Medicine and Health and the Brain and Mind Centre, University of Sydney, Sydney, NSW, Australia

Parkinson's disease (PD) is characterised by the pathological deposition of aggregated α-synuclein (α-syn) in neurons and glial cells in the CNS, as well as the loss of dopaminergic (DA) neurons of the substantia nigra of the midbrain. The abnormal accumulation of α-syn is thought to contribute to DA neuronal death and thus underlie the development of clinical symptoms. In addition, innate immune pathogen receptor toll-like receptor 2 (TLR2) is increased in the PD brain and its activation contributes to α-syn pathology propagation in neurons through autophagy inhibition. Recent

evidence suggests astrocytic involvement in PD pathogenesis, but the role of astrocytes remains unclear. Here, induced pluripotent stem cells from idiopathic PD patients were differentiated into a midbrain model involving neurons, including DA neurons and astrocytes, enabling investigation into DA neuronal health and the contribution of astrocytes and neighbouring neurons. In this model, the activation of TLR2 inhibited the autophagy lysosomal pathway, and potentiated α-syn pathology seeded by pre-formed fibrils in neurons and astrocytes. This resulted in a significant, selective decrease in DA neurons. Astrocytes also showed impaired autophagy and reduced ability to clear accumulated α-syn. Impaired autophagy in astrocytes was associated with an increase in SerpinG1, an A1 neurotoxic protein, indicating a shift to a reactive astrocyte phenotype. Taken together, these results suggest the dysfunction of astrocytes could reduce their ability to provide supportive functions to DA neurons in the PD brain and contribute to DA neuronal loss.

P06.60

Modelling of axonal degeneration in Parkinson's disease using hiPSC-derived midbrain dopaminergic neurons carrying SNCA gene duplication

Wei Xiang[*,1], Yanni Schneider[1], Aron Koller[1], Marie Andert[1], Lukas Seebauer[1], Katharina Pieger[2], Johannes Schlachetzki[3], Johann Helmut Brandstätter[2], Jürgen Winkler[1]*
[1] Department of Molecular Neurology, University Hospital, FAU University Erlangen-Nürnberg, 91058 Erlangen, Bavaria, Germany
[2] Department of Biology, Animal Physiology, FAU Universität Erlangen-Nürnberg, Erlangen, Bavaria, Germany
[3] Department of Cellular and Molecular Medicine, University of California, San Diego, CA, United States

Parkinson's disease (PD) is the most common neurodegenerative movement disorder, clinically characterized by motor symptoms. The motor dysfunction is primarily attributed to the loss of midbrain dopaminergic neurons (mDAns). Extensive studies have provided evidence supporting the pathological relevance of abnormal aggregation of α-synuclein (aSyn) in mDAn degeneration. The causal connection of aSyn to PD is also substantiated by genetic findings that point mutations and multiplications of the aSyn gene (SNCA) are linked to monogenic PD. There is mounting evidence that axonal degeneration precedes the loss of the respective neurons. Due to a correlation between aSyn level and its aggregation propensity, we hypothesize that increased aSyn levels promote its aggregation, thereby compromising axonal integrity. Hence, we investigated mDAns derived from human-induced pluripotent stem cells (hiPSCs) generated from PD patients carrying a SNCA duplication (SNCADupl). To elucidate specific effects of aSyn dose response, we compared SNCADupl mDAns with those differentiated from hiPSC lines of healthy donors and from an isogenic hiPSC line with corrected SNCA dosage (SNCACorr). The SNCACorr line was generated using CRISPR/Cas9 gene editing in a hiPSC SNCADupl line. By comparing with control and SNCACorr mDAns, we confirmed an elevated aSyn expression in SNCADupl mDAns, accompanied by enhanced aSyn aggregation. Moreover, SNCADupl mDAns exhibited remarkably changes in neuritogenesis, characterized by increased primary neurites, however, with reduced neurite outgrowth. Using an aSyn antibody, which preferentially binds to distinct aggregated aSyn species, we observed an accumulation of aggregated aSyn along the neurites of SNCADupl mDAns. To explore furthermore the mechanism underlying the neuritic alterations observed in SNCADupl mDAns, we studied the interplay between aggregated aSyn and microtubule organization. We detected a preferential interaction of aggregated aSyn with β-tubulin isoforms, like β-tubulin-III. Coincidently, biochemical cell fractionation revealed an increase of insoluble βtubulin-III, co-distributed with aggregated aSyn. Collectively, our data from the study on SNCADupl mDAns suggest an interference of aSyn aggregation with the microtubule network contributing to neurite dysfunction and ultimately leading to neuronal loss. Our study further demonstrates the suitability of hiPSC-derived SNCADupl mDAns in modelling axonal degeneration and dysfunction for future studies.

P06.61

A novel mouse model to investigate the formation of oligodendroglial α-synuclein aggregates in multiple system atrophy (MSA)

Hodaka Yamakado[*,1], Tomoyuki Ishimoto[1], Miki Oono[1], Takashi Ayaki[1], Katsuya Nishida[2], Itaru Funakawa[2], Seiji Kaji[1], Takakuni Maki[1], Shu-ichi Matsuzawa[1], Ryosuke Takahashi[1]*
[1] Kyoto University, Kyoto, Kyoto, Japan
[2] Hyogo-Chuo National Hospital, Sanda, Japan

The common pathological hallmark of Parkinson's disease (PD), dementia with Lewy bodies (DLB) and multiple system atrophy (MSA) is the presence of alpha synuclein (αsyn) aggregates. In MSA these aggregates are observed mainly in oligodendrocytes (OLG) and called glial cytoplasmic inclusions (GCIs), but how αsyn preferentially accumulates in OLGs has remained a mystery. We previously reported that in mice inoculated with αsyn preformed fibrils (PFFs), αsyn accumulated in OLGs long after the αsyn aggregate formation in neurons, suggestive of their neuronal origin. However, a detailed spatial and temporal analysis of αsyn aggregate formation in OLGs was technically difficult due to the background neuronal aggregates. The aim of this study was to create a mouse model that enables the sensitive and specific detection of αsyn aggregates in OLGs and the analysis of their preferential accumulation in OLGs. We generated transgenic mice that express human αsyn-green fluorescent protein (GFP) fusion proteins in OLGs under the control of the 2', 3'-cyclic nucleotide 3'-phosphodiesterase (CNP) promoter (CNP-SNCAGFP Tg mice). When inoculated with αsyn PFFs, these mice exhibited distinct GFP-positive aggregates in the processes of OLGs as early as 1 month post-inoculation, and their number and size increased overtime in a centripetal manner, suggesting that αsyn aggregates may be initially formed in the processes of OLGs in MSA. Furthermore, when these mice were inoculated with brain homogenate (BH), more aggregates were produced with MSA BH than those with DLB BH, and the difference was greater in OLGs than in neurons. In conclusion, CNP-SNCAGFP Tg mice are useful for monitoring the development of αsyn aggregates in OLGs and investigating the formation of GCIs in MSA.

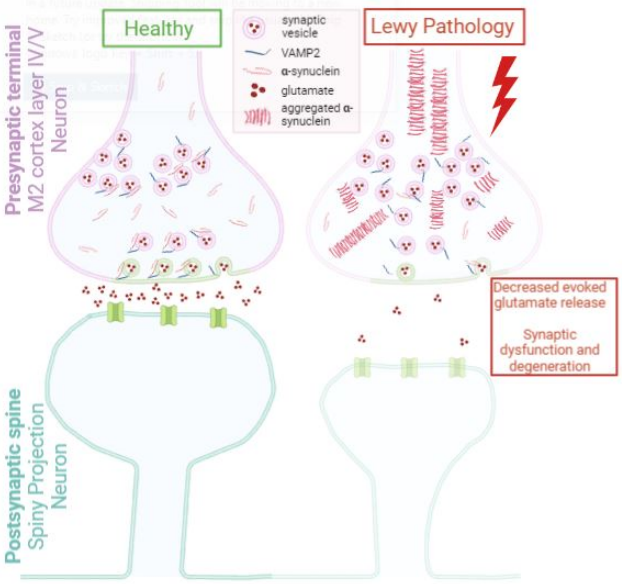
BASIC SCIENCE: Brain physiology and circuitry

P07.01

Impact of α-synuclein pathology on corticostriatal synapses in Parkinson's disease

Charlotte Brzozowski[*,1], Harshita Challa[1], Douglas Nabert[2], Preston Wagner[2], Nolwazi Gcwensa[1], Laura Volpicelli-Daley[1], Mark Moehle[2]*
[1] Department of Neurology, Center for Neurodegeneration and Experimental Therapeutics, University of Alabama at Birmingham, Birmingham, AL, United States
[2] Department of Pharmacology and Therapeutics and Center for Translational Research in Neurodegeneration, University of Florida, Gainesville, FL, United States

Objective: Proteinaceous inclusions composed of α-synuclein are pathological hallmarks of Parkinson's disease (PD). α-Synuclein pathology is abundant in the pre-supplementary motor area (preSMA) in humans - homologous to the secondary motor cortex (M2) in mice - which is also the only known cortical area to show overt neuron loss in PD. M2 projections to the striatum play a role in executive function, one of the most common cognitive domains affected in PD. Templated formation of α-synuclein inclusions has recently been shown to disrupt cortical projections and impair corticostriatal plasticity. Here, we endeavor to understand how M2-striatal connections are impaired by the corruption of presynaptic α-synuclein into pathological aggregates, which may contribute to PD-related executive dysfunction.
Methods: We performed whole-cell patch clamp recordings from spiny projection neurons (SPNs) in C57Bl6/J mice 6 weeks after striatal α-synuclein pre-formed fibrils (PFFs) inoculations. Another group of mice was injected with PFFs into the M2. Using optogenetic approaches, we co-expressed the infrared-shifted channelrhodopsin Chrimson-R in the M2 to record light-elicited M2-projection specific evoked glutamate release onto SPNs. Lastly, we utilized Expansion Microscopy (ExM) to assess for abnormalities in synaptic morphology and synapse loss of corticostriatal synapses in the presence of α-synuclein pathology.
Results: We show impaired evoked corticostriatal glutamate release onto SPNs in striatal PFF injected animals compared to controls. Additionally, we found changes to the intrinsic properties and excitability of SPNs. M2 projection-specific pathology experiments show reduced evoked glutamate release onto SPNs and a significant increase in paired-pulse ratio, suggesting presynaptic dysfunction of M2 projections. Using ExM superresolution imaging, we show a decrease of corticostriatal glutamatergic synapses in mice with α-synuclein inclusions and a paradoxical enlargement of inclusion-positive glutamatergic terminals in the dorsomedial striatum.
Conclusion: Our combined efforts in physiology and high resolution imaging point to a critical dysfunction of corticostriatal synapses in neurons harboring α-synuclein inclusions. The findings from M2-specific injections suggest this region may be more susceptible to α-synuclein pathology-mediated changes than other cortical regions. Our data is unraveling how aggregated α-synuclein disturbs corticostriatal synaptic function and future studies will assess how this contributes to the symptoms of PD.



P07.02

Cortical compensatory mechanisms for adaptive split-belt walking in people with Parkinson's disease

Femke Hulzinga[*,1], Paulo Pelicioni[2], Nicholas D'Cruz[1], Veerle de Rond[1], Pieter Ginis[1], Moran Gilat[1], Alice Nieuwboer[1]*
[1] KU Leuven, Heverlee (Leuven), Vlaams-Brabant, Belgium
[2] University of New South Wales, Sydney, NSW, Australia

Background and aim: Adapting gait while navigating the environment is challenging for people with Parkinson's disease (PwPD), leading to poor mobility and falls. The neural mechanisms underlying gait adaptation in PwPD are still unclear. Previous research using functional near-infrared spectroscopy (fNIRS) to investigate cortical activity during gait focused on the prefrontal cortex and did not address gait adaptation. A split-belt (SB) treadmill allows studying gait adaptation as it induces gait asymmetry by imposing a different speed on each leg separately. Therefore, this study investigated cortical activity associated with SB-walking compared to tied-belt (TB) walking in four cortical areas using fNIRS in PwPD and older adults (OA).
Methods: Forty-two PwPD and 42 OA performed seven trials of TB-walking and SB-walking, where one leg was reduced 50% in speed. Cortical activity was captured with fNIRS as oxygenated (HbO) and deoxygenated hemoglobin in the prefrontal cortex (PFC), supplementary motor area (SMA), premotor cortex (PMC) and posterior parietal cortex (PPC). Gait adaptation outcomes were mean step length asymmetry and variability. Preliminary analysis also included correlation analyses between HbO concentrations during SB-adaptation and cognition, balance and PD-related clinical outcomes.
Results: PwPD showed higher PMC (HbO p=0.006) and PPC (HbO p=0.002) activity compared to OA regardless of condition. No condition or group effect was present for PFC, and SMA activity. There were no group differences in step length asymmetry and variability during SB-walking. Correlation analysis showed that higher PMC and PPC activation were associated with poor set-shifting (Trail-Making-Test part B, r=0.317, p=0.041) and balance performance (MiniBEST, r=0.333, p=0.031) in OA but not in PwPD. No significant correlations were observed between these outcomes or other PD-specific ones and PMC or PPC activity.

Conclusions: This preliminary analysis showed that PwPD increased PMC and PPC activity unrelated to gait adaptation. Interestingly, this increased cortical activity was not driven by performance differences compared to controls, implying pathology-specific compensation. OA showed associations between increased cortical activity and impaired set-shifting and balance, pointing to compensatory cortical reserve not present in PwPD. Future analysis needs to unpick how cortical activity changes impact on the adaptive changes within each group over time.

P07.03

Overexpression of human α-synuclein in serotonin neurons drives brain functional disconnection in a PD-like mouse model with depressive phenotype

Lluis Miquel-Rio[1], Maria Torres-López[2], Verónica Paz[1], Carme Casal[3], Emma Muñoz-Moreno[4], Xavier López-Gil[4], Analia Bortolozzi*[,1]
1 Institute of Biomedical Research of Barcelona (IIBB), Spanish National Research Council (CSIC); August Pi i Sunyer Biomedical Research Institute (IDIBAPS); Mental Health Networking Biomedical Research Centre (CIBERSAM), ISCIII, Barcelona, Spain
2 Institute of Biomedical Research of Barcelona (IIBB), Spanish National Research Council (CSIC); August Pi i Sunyer Biomedical Research Institute (IDIBAPS), Barcelona, Spain
3 Institute of Biomedical Research of Barcelona (IIBB), Spanish National Research Council (CSIC), Barcelona, Spain
4 Magnetic Resonance Imaging Core Facility, August Pi i Sunyer Biomedical Research Institute (IDIBAPS), Barcelona, Spain, Barcelona, Spain

Introduction: Anxiety and depression are the most prevalent neuropsychiatric disorders in Parkinson's disease (PD) and significantly contribute to a loss of quality of life. While deficits in the dopaminergic system are implicated in both motor and non-motor manifestations, neuropathological and neurochemical alterations in the serotonergic (5-HT) system, which regulates mood and emotional states, occur during the premotor phase of PD and contribute to a wide range of non-motor symptoms. Additionally, aggregates of α-synuclein (α-Syn) were identified in raphe nuclei in the early stages of the disease. However, the relationship between α-Syn pathology and structural and functional changes occurring in the brain is not well understood. Our aim was to study whether synaptic plasticity and functional connectivity are affected by α-Syn accumulation in the efferent brain regions from 5-HT raphe nuclei in the early stages of a depression/PD-like mouse model.
Methods: A new mouse model of α-synucleinopathy in the 5-HT system based on AAV5-induced overexpression of wild-type human-α-synuclein (h-α-Syn) in 5-HT neurons of raphe nuclei was used. Male mice were assessed 4 and 8 weeks later. Cytoskeletal motor components (MAP2), synaptic vesicle associated proteins (SV2A), and synaptophysin were examined by confocal microscopy. Brain functional connectivity was analyzed using the resting state (rsfMRI) by BOLD and ICA signals. Cellular activity was measured by Egr-1 mRNA expression in several interconnected brain areas.
Results: AAV5-induced accumulation of human α-Syn in the 5-HT neurons of raphe nuclei leads to progressive presynaptic pathology in interconnected brain regions, characterized by downregulation of MAP-2 protein in different 5-HT-innervated cortices (e.g. prelimbic, infralimbic, cingulate and motor cortices), caudate-putamen, and different subfields of hippocampus as well as an upregulation of SV2A and synaptophysin proteins in cingulate and motor cortices, and caudate-putamen.
In parallel, abnormalities in neuronal activity were found in cortical and subcortical brain areas, assessed by Egr-1 mRNA expression. Specific regional differences in resting-state functional activity changes occur in caudate-putamen and hippocampus eight weeks post-injection, prior to neurodegeneration.
Conclusions: This study provides preliminary evidence for altered synaptic and fMRI markers linked to α-Syn pathology in emotional brain circuits and has translational importance for identifying PD patients at risk for depression.

P07.04

Advancing adaptive subthalamic deep brain stimulation for gait disturbances and freezing of gait in Parkinson's disease

Marie-Laure Welter[1], Brian Lau[2], Ludovic Saint-Bauzel[3], Carine Karachi[2], Mathieu Yeche[1], Sinan Haliyo[3], Alexandre Guerre[3], He Shenghong[4], Huiling Tan[,4]*
[1] Paris Brain Institute, Paris, France
[2] Brain Institute, Paris, France
[3] ISIR, Paris, France
[4] Oxford University, Oxford, United Kingdom

In Parkinson's disease (PD), gait disorders with the freezing of gait (FoG) phenomenon, gradually worsen with time, affecting more than half of all patients. Associated with an increased risk of falls, injuries and mortality, it poses a major burden to patients and their families. FoG and falls are poorly improved by dopaminergic drug treatments or deep brain stimulation (DBS) of the subthalamic nucleus (STN). Up to now, the treatment of FoG is still difficult because of a complex physiopathology, with an interaction between motor and cognitive-emotional functions that remains poorly understood. Another problem is that walking disorders are treated as permanently and identical during a day, with continuous treatments that are poorly adapted to their episodic character, and dependent on the environment in which the subject walks. An increased synchronization of STN neuronal activity in the beta band (8-35 Hz) has been identified as linked to the severity of akinesia, and used successfully to trigger the so-called "closed loop" DBS to treat it. In this proposal, we aim to better understand the neural basis of FoG in PD to predict the occurrence of these transient FoG episodes. In particular, we will investigate how cortical and subcortical neural oscillations will lead to abnormal muscle activities associated with FoG. For this purpose, we will record cortical and STN neuronal activity in PD patients while walking in various conditions of gait by using virtual reality tools and developing gait models. In addition, we also hypothesize that an adaptative STN DBS based on the STN activity or gait cycle phases could relief or prevent FoG. Therefore, we will evaluate the effectiveness of a novel biomimetic pattern of STN DBS in promoting resistance to FoG and explore other stimulation patterns to disrupt pathological brain oscillations and muscle activities leading to FoG. This research program will pave the way for early detection of episodic gait disturbances that could be used to control switching between DBS stimulation patterns that are most appropriate for minimizing risk of falling.

BASIC SCIENCE: Dopamine, receptors, and other neurotransmitters

P08.02

The mGluR5-A2AR-D2R heteromeric complex: Considerations for Parkinson's disease treatment

Francisco Ciruela[*,1], Wilber Romero-Fernández[2], Jaume Taura[1], Rene Crans[1], Marc López-Cano[1], Ramón Fores-Pons[3], Manuel Narváez[4], Jens Carlsson[2], Kjell Fuxe[3], Dasiel Borroto-Escuela[4]*
[1] Universitat de Barcelona, L'hospitalet de Llobregat, Spain
[2] Uppsala Univesity, Uppsala, Sweden
[3] Karolinska Institutet, Stockholm, Sweden
[4] Universidad de Málaga, Málaga, Spain

The adenosine A2A receptor (A2AR), dopamine D2 receptor (D2R) and metabotropic glutamate receptor type 5 (mGluR5) form mGluR5-A2AR-D2R heteroreceptor complexes in living cells and in rat striatal neurons. We showed that the A2AR protomer plays a key role within this heteroreceptor complex [1], thus providing key allosteric receptor-receptor interactions that allows fine-tuning modulation of the D2R function. Our in cellulo experiments demonstrated that co-expression of A2AR promoted mGluR5-D2R heteromer formation, and mGluR5 agonist-mediated inhibition of D2R-Gi/o protein activation. Interestingly, when the mGluR5-A2AR-D2R heteroreceptor complexes were evaluated in vivo, we showed that the expression of the A2AR in the mouse dorsal striatum was necessary for the D2R and mGluR5 to form complexes visualized by proximity ligation assay. Subsequently, the effects of the mGluR5 negative allosteric modulator raseglurant (1 mg/kg) was studied on locomotor activity in mice. A significant increase in locomotor activity was observed in wild-type mice after raseglurant treatment, as previously described. Importantly, this enhancement of locomotion was not observed in A2AR or D2R knockout mice. In fact, failure to see enhancement in raseglurant-mediated locomotion in the absence of A2AR may reflect the importance of this receptor in the functionality of the mGluR5-A2AR-D2R heteroreceptor. Finally, while raseglurant reduced haloperidol-induced catalepsy in wild-type mice, in A2AR-/- mice its action was dramatically reduced, supporting a functional role for mGluR5 and A2AR in enhancing D2R blockade that results in catalepsy. In conclusion, in the wild-type mouse, mGluR5 activity enhances inhibition of D2R signaling through a positive allosteric modulation of A2AR function, thus resulting in weak dopaminergic signalling. However, in the A2AR-/- mouse, mGluR5-mediated positive allosteric modulation of A2AR disappears and D2R is released from both mGluR5- and A2AR-mediated transinhibition, thus resulting in increased dopaminergic signalling.

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P08.03

Spatio-temporal dynamic of DA in the execution of goal-directed movements in rats

Sophie Gauthier, Ana Dorison, Manon Leclerc, Alison McDonald, Nicolas Mallet*
Institute of Neurodegenerative Diseases, Bordeaux, France

The ability to produce movements adapted to our environment is crucial in our daily lives. Years of research to understand this function, which is crucial to our survival, have placed dopamine (DA) as key in motor selection and execution processes. Indeed, beyond its role in the reward circuit, this neuromodulator is known to be central in motor control. This capital function is well-illustrated in Parkinson's disease (PD), where the death of dopaminergic neurons induces severe motor symptoms, such as difficulties in initiating movements (akinesia), and their slowness (bradykinesia). Importantly, the neurophysiological mechanisms underlying motor execution are not fully elucidated. Thus, this study aimed at determining the temporal contribution of DA in these processes. First, we developed a "reach-and-grasp" motor task, in which rats perform a goal-directed skilled movement to press a lever in order to obtain an expected outcome (40 uL of sucrose 5%). Then, we studied the effect of a lack of DA on dexterous movement execution. We mimicked neuronal death observed in PD via the injection of 6-OHDA in the STR. This aimed at characterizing the temporal and spatial dynamic of motor symptoms development. Our results demonstrate the necessity of DA in short time scale (in range of minutes) in the DLS and question the necessity of fast-scale DA dynamics to control online motor execution. In contrast, DA transmission at a slower time scale seems to be important for the reinforcement and the maintenance of the striatal neuronal activity that is necessary for optimal motor execution. Importantly, correlated to the extent of the lesion, we observed in the following days of the chronic depletion a functional recovery during which motor deficits were alleviated. Thus, our results illustrate the resilience capacity of the DLS to the lack of DA. We are currently investigating compensatory mechanisms via calcium imaging in D1-cre and A2A-cre rats. This characterization could bring innovative ideas to develop new therapeutic strategies for PD.

P08.04

Physiological functions of aldehyde dehydrogenase 1A1-positive midbrain dopaminergic neuron

Md Ahsan Habib[*,1], Lupeng Wang[2], Lisa Chang[2], Lixin Sun[2], Huaibin Cai[2]*
[1] National Institutes of Health, Bethesda, Maryland, United States
[2] National Institute on Aging, Bethesda, Maryland, United States

Both motor and non-motor functions are affected in Parkinson's Disease (PD), which is associated with loss of midbrain dopaminergic neurons, particularly the aldehyde dehydrogenase 1A1-positive (ALDH1A1+) dopaminergic neuron subtype. The current study sought to characterize the physiological functions of ALDH1A1+ dopaminergic neuron subtype in a mouse model of PD with various behavioral tests. To understand the function of ALDH1A1+ dopaminergic neuron subtype in the midbrain, we selectively ablated the ALDH1A1+ dopaminergic neurons in substantia nigra compacta (SNc) and ventral tegmental area (VTA) respectively in the Aldh1a1-P2A-CreERT2 knock-in mouse line. In contrast to our previous findings that ALDH1A1+ SNc subpopulation is critical for rotarod motor skill acquisition and high-speed voluntary locomotion, VTA ALDH1A1+-ablation did not significantly alter parameters of voluntary movements and motor-skill learning acquisition. These indicate that only the SNc, but not the VTA, ALDH1A1+ dopaminergic neuron subtype regulates skill learning

acquisition and the vigor of the movements. Besides motor functions, genetic ablation of ALDH1A1+ SNc, but not VTA, dopaminergic neuron subtype shows significant working memory deficit using Y-maze spontaneous alternation test. On the other hand, in a classic fear conditioning task, ablation of VTA ALDH1A1+ dopaminergic neurons displayed significantly elevated retention for fear memory, but SNc ALDH1A1+ ablation did not significantly alter responses in the task. In addition, to further tested their involvement in instrumental conditioning, we used a nose-poke based food pellet retrieval operant task. We observed that while VTA-ALDH1A1+-ablation group did not lag in learning, they showed significantly reduced motivation for obtaining food reward when the task required high-effort actions. Both SNc and VTA ALDH1A1+ subtypes do not display obvious alteration of anxiety-like responses in the open field, elevated plus maze and light dark box test. Our comprehensive findings compare and characterize physiological functions of major dopaminergic neuron subtypes in the midbrain, revealing their distinctive roles in motor and non-motor functions.

P08.05

PD antibodies without side effects: Dr. Mehmet Oz, probably the most famous medical doctor of our time, has said, "The next big frontier in medicine is energy medicine."

*Jeffrey Harsh**
American Trail Foundation, Oakley, Kansas, United States

Alpha-Synclein has been implicated in the path physiology of Parkinson's disease (PD) and Lewy body dementia (DLB). Mutations A30P and A3T are associated with PD while mutation E46K has been linked to DLB. These mutated α-synucleins form fibrils more rapidly than the wild-type protein in aqueous solution1. A-Synucleins are the major components of Lewy bodies and Lewy neurites in both diseases2. I have combined the antibody frequencies of both a-synucleins and Lewy bodies. Together, these limited tests have revealed that Anti-LRRK2, (Alpha-Syclein antibody) when combined with the oligomers antibodies, became much more effective then by themselves. We create true steller frequencies then generating anti-alpha-Synuclein antibody's void of actual pathogens!
However our method of doing so differs from the rest of the pack. We are using a German made Tesla Technology, and create a frequency of the anti-body so the immune system can have a target. Unlike Vaccines, we never use any of the actual molecules of lab anti- body's proteins; genes relating to Parkinson are given to humans or animals. That equals no side effects.
Our approach is a breakthrough. We will use because you do not have to stay in the hospital for two hours getting your antibody.
Just take a deep breath of the nasal fine spray pump two or three times a day!
PD causes and effects are multifaceted. But our efficacy in testing and historical research has led us to believe one of the major causes of PD is mercury poisoning. We believe mercury causes the alpha synuclein to misfold causing toxic clumps. (You know the rest of the story). Also 24dD and 245T Hubersides, attack the autonomic novice system of humans to scramble info or generate autonomic dysregulation. It does the same to plants. Their roots burst and the plant dies. Jeffrey Harsh has a Doctoral Degree in Naturopathic Medicine from a University in the British West Indies. He is an accepted member of Mensa. (ID number 1124319)

P08.06

70 years of historical brain life cell therapy for PD, and thank God it is not created from aborted human fetus!

*Jeffrey Harsh**
American Trail Foundation, Oakley, Kansas, United States

70 years of historical brain life cell therapy for PD, and thank God it is not created from Aborted human fetus! By Jeffrey J. Harsh PHD
When I was on the board of directors of the National Health Federation, the President was a great elegant lady named Maureen Solomon. She started a clinic in Tijuana, Mexico, that imported different live cells from Germany Six months later I saw and felt the results of a younger body and I have been using them ever since. As the cells in the different organs in our body age, they divide and die by autolysis. Each time this atrophy happens, the new replacement cells lose information and that equals ageing. Reprogramming the DNA with young unadulterated cells, causally reverses aging. By using cells from neonatal unborn animals. Not from aborted human baby cells!
Available for the past 70 years in Europe, porcine Embryonic Organo Supplementation (EOS) is now available in the form of embryonic cellular preparations, making it possible, and affordable, to receive the incredible benefits of EOS without traveling to expensive European Clinics.
Cell Life USA's EOS uses similar principals as those used in cell therapy, however, instead of extracting whole intact cells, EOS starts with the selection of specific organ tissue from an organic porcine embryo and through proprietary technology, it is processed into a bio-available form of a nutritional supplement.
Many years of experience have demonstrated that porcine are the best donor animals for humans because they are vital, hardy animals and immunologically, their bodies are the closest match to the human body. they only fit into the receptor sites of the target organ and begin to support the function of that specific target organ.
Cell Life USA's EOS preparations are derived from specific embryonic organ cell tissues and are ideally suited to support anti-aging and health maintenance. They are for oral use only and can often perform little miracles in supporting body structure and body function.
For years now I have been using Live Cell therapy. Many believe I look 15 to 20 years younger then i am; and the same with my daughter.

P08.07

Functional assessment of dopaminergic neurons derived from human lineage-restricted undifferentiated stem cells in a rat Parkinsonian model

Muyesier Maimaitili[1], Muwan Chen[1], Fabia Febbraro[2], Ekin Ücüncü[1], Johanne Lauritsen[1], Ida Hyllen Klæstrup[1], Rachel Kelly[,1], Marina Romero-Ramos[1], Mark Denham[1]*
[1] Danish Research Institute of Translational Neuroscience (DANDRITE), Nordic EMBL Partnership for Molecular Medicine, Aarhus University; Department of Biomedicine, Aarhus University, Aarhus, Denmark
[2] Department of Biomedicine, Aarhus University; Department of Clinical Medicine, Aarhus University, Aarhus, Denmark

Current differentiation methods can generate mesencephalic dopamine (mesDA) neurons from human pluripotent stem cells (hPSCs) after long-term in vitro culturing. However, when mesDA progenitors are transplanted in vivo, dopamine neurons are a small component of the surviving graft [1,2,3]. To address this limitation, we knocked out four genes in hPSCs (Gbx2, Cdx1/2/4) that are critical for the specification of non-dopaminergic lineages, to create a new type of stem cell which we named lineage-restricted

undifferentiated stem cells, or more specifically, 4X cells [4]. We tested these cells in a rat Parkinsonian model after incubation under hindbrain differentiation conditions.
Nude rats were given a 6-OHDA-induced medial forebrain bundle lesion and four weeks later 250,000 cells (H9 or 4X) differentiated to 16 DIV were transplanted into the striata. A third group of rats were lesioned but did not undergo transplantation (6-OHDA group). The amphetamine-induced rotational test and cylinder test were used to assess behaviour throughout the study, where the rats were sacrificed 19 weeks post-transplant for histological analyses.
Before transplantation, all groups exhibited similar behavioural impairment in the rotation and cylinder tests, confirming there was a significant loss of dopamine in the striatum. However, by 8 weeks post-transplantation, rats that received 4X cells showed a complete correction of amphetamine-induced ipsilateral rotation, whereas H9 rats only showed recovery at 18 weeks, and not to the same extent. Spontaneous motor behaviour in the cylinder test was also improved in 4X rats by 18 weeks post-transplantation, as they used their contralateral paw significantly more than prior to transplantation. Contrastingly, H9 rats almost never used their contralateral forelimb throughout the entire study.
Postmortem quantification of graft-derived TH-positive cells showed that there were significantly more TH-positive cells per graft in 4X-transplanted rats than in H9-transplanted rats. Furthermore, the estimated TH-positive graft volume was over 5 times larger in the 4X rats than the H9 rats.
Overall, our 4X cells are a promising new therapy for Parkinson's disease, as they produced a robust population of mesDA neurons and rapid behavioural recovery in vivo.
[1] Kim et al., 2021.
[2] Nolbrant et al., 2017.
[3] Piao et al., 2021.
[4] Maimaitili et al., 2021.

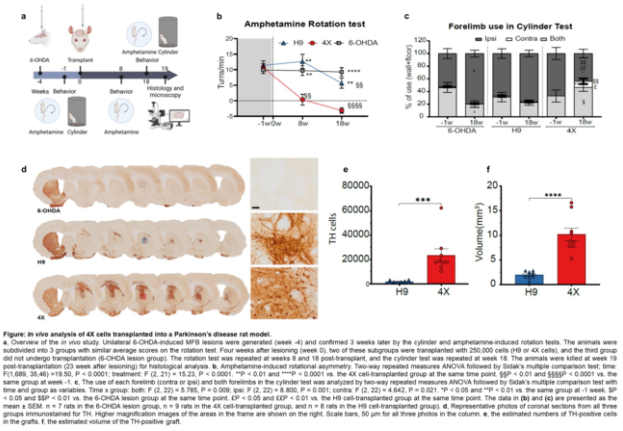


Figure: *In vivo* analysis of 4X cells transplanted into a Parkinson's disease rat model.
a, Overview of the *in vivo* study. Unilateral 6-OHDA-induced MFB lesions were generated (week -4) and confirmed 3 weeks later by the cylinder and amphetamine-induced rotation tests. The animals were subdivided into 3 groups with similar average scores on the rotation test. Four weeks after lesioning (week 0), two of these subgroups were transplanted with 250,000 cells (H9 or 4X cells), and the third group did not undergo transplantation (6-OHDA lesion group). The rotation test was repeated at weeks 8 and 18 post-transplant, and the cylinder test was repeated at week 18. The animals were killed at week 19 post-transplantation (23 week after lesioning) for histological analysis. **b**, Amphetamine-induced rotational asymmetry. Two-way repeated measures ANOVA followed by Sidak's multiple comparison test; time: $F(1.689, 35.46) = 19.50$, $P < 0.0001$; treatment: $F(2, 21) = 15.23$, $P < 0.0001$. $^{**}P < 0.01$ and $^{****}P < 0.0001$ vs. the 4X cell-transplanted group at the same time point. $^{§§}P < 0.01$ and $^{§§§§}P < 0.0001$ vs. the same group at week -1. **c**, The use of each forelimb (contra or ipsi) and both forelimbs in the cylinder test was analyzed by two-way repeated measures ANOVA followed by Sidak's multiple comparison test with time and group as variables. Time x group: both: $F(2, 22) = 5.785$, $P = 0.009$; ipsi: $F(2, 22) = 8.800$, $P = 0.001$; contra: $F(2, 22) = 4.642$, $P = 0.021$. $^{a}P < 0.05$ and $^{aa}P < 0.01$ vs. the same group at -1 week. $^{$}P < 0.05$ and $^{$$}P < 0.01$ vs. the 6-OHDA lesion group at the same time point. $^{£}P < 0.05$ and $^{££}P < 0.01$ vs. the H9 cell-transplanted group at the same time point. The data in (**b**) and (**c**) are presented as the mean ± SEM. n = 7 rats in the 6-OHDA lesion group, n = 9 rats in the 4X cell-transplanted group, and n = 8 rats in the H9 cell-transplanted group). **d**, Representative photos of coronal sections from all three groups immunostained for TH. Higher magnification images of the areas in the frame are shown on the right. Scale bars, 50 µm for all three photos in the column. **e**, the estimated numbers of TH-positive cells in the grafts. **f**, the estimated volume of the TH-positive graft.

P08.09

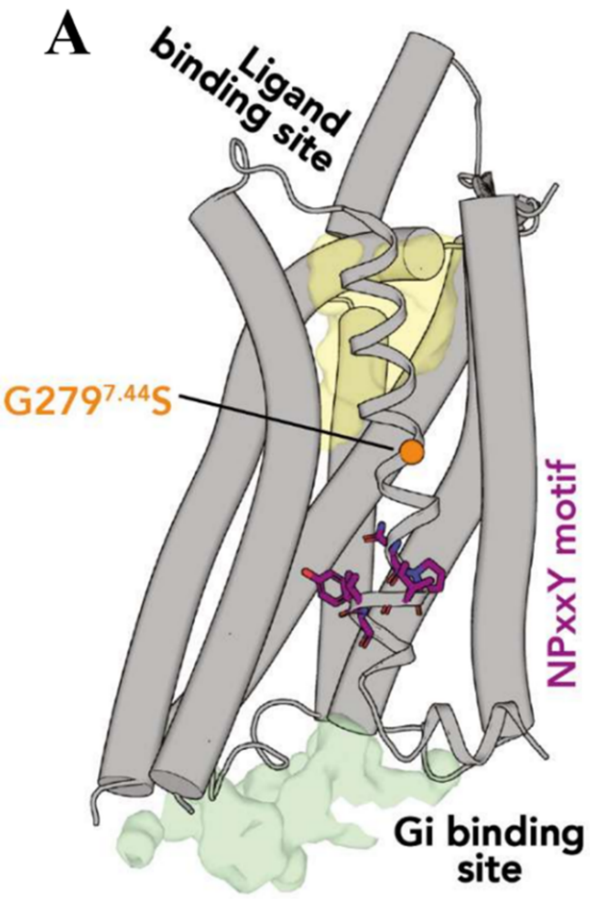
Calcium-sensor linkage of N-methyl-D-aspartate receptors to the MAP kinase pathway is blockade by α-synuclein in cortical and hippocampal neurons and microglia
Gemma Navarro Brugal, Irene Reyes, Jaume Lillo, Iu Raïch, Rafael Rivas-Santisteban, Joan Biel Rebassa, Rafael Franco*
University of Barcelona, Barcelona, Spain

N-methyl-D-aspartate receptors (NMDAR) respond to glutamate to allow the influx of calcium ions. Upon interaction of the ion with calcium-binding proteins, these undergo conformational changes that are important for both neurotransmission and neural cell function and fate. However, our knowledge about the connection between NMDAR function and signaling via calcium-binding-proteins is still scarce. Using a heterologous expression system, we demonstrate that NMDAR may interact with the EF-hand calcium binding proteins calmodulin, calneuron-1 and NCS1 but not with caldendrin. Calmodulin in microglia, and calmodulin and NCS1 in neurons, are necessary for NMDA-induced MAP kinase pathway activation. In fact, NMDAR were present in primary cultures of cortical and hippocampal neurons and microglia. Remarkably, signaling to the MAP kinase pathway was blunted by α-synuclein aggregates that are involved in the progression of Parkinson disease. Calcium sensors were not protective suggesting that these proteins do not mediate a negative feedback regulation but potentiate NMDAR-mediated signaling events. The results show that calcium sensors are important for NMDAR function both in neurons and microglia and that the expression of receptor-calcium sensor complexes, specially those involving NCS1 are altered in neural cells from Parkinson disease.

P08.10

Adora1 mutation linked to early-onset Parkinson's disease alters adenosine A1-A2A receptor heteromers formation and function
Laura Isabel Sarasola*[,1], Clàudia Llinas del Torrent[2], Victor Fernandez-Dueñas[1], Sergi Ferré[3], Leonardo Pardo[2], Francisco Ciruela[1]
[1] University of Barcelona, L'Hospitalet de Llobregat, Spain
[2] Universitat Autonoma de barcelona, Bellaterra, Spain
[3] National Institute of Health, Baltimore, MD, United States

Adenosine is an endogenous autacoid purine nucleoside involved in several physiological functions. In the brain, it modulates neurotransmission through inhibitory adenosine A1 receptors (A1Rs) and stimulatory A2A receptors (A2ARs). These G protein-coupled ARs are involved in motor function and related to neurodegenerative diseases such as Parkinson's disease (PD). In line with this, a recent study associated a new autosomal recessive mutation (G279S) within the A1R gene to the development of early onset PD. Here, we aimed at investigating the impact of this mutation on receptors' structure and function. Our results revealed that the G279S A1R mutation does not alter receptor's ligand binding, constitutive activity or coupling to transducer proteins (i.e., Gαi and Gαq) in transfected cells. However, G279S mutation reduced A1R-A2AR heteromer formation and abolished the heteromer-dependent ligand-independent modulation that A1R exerts over the constitutive and agonist-induced activation of the A2AR. Interestingly, computational studies supported that the G279S A1R mutation could have a negative effect on the heterodimer interface stability. Overall, our results indicate that G279S mutation does not modify A1R canonical signalling, whereas it reduces the ability of A1R to act as a negative allosteric modulator of A2AR function.



BASIC SCIENCE: Neuropharmacology

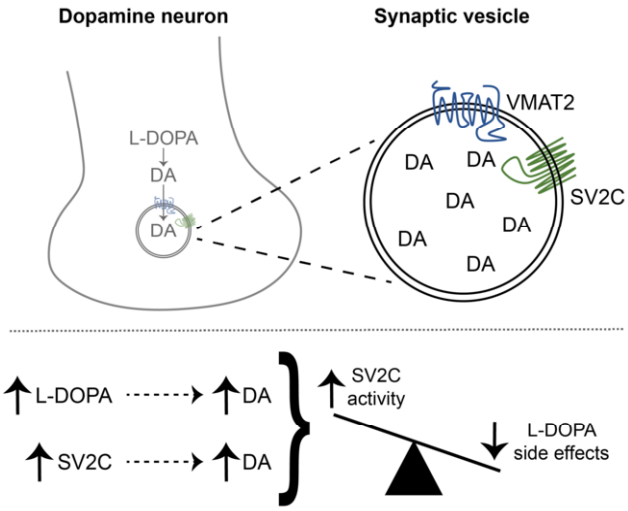
P09.01

Therapeutic targeting of synaptic vesicle glycoprotein 2C (SV2C) in Parkinson's disease

Meghan Bucher, Joshua Bradner, Gary Miller*
Columbia University Irving Medical Center, New York, New York, United States

Dopamine mishandling has been a recognized feature of Parkinson's disease (PD) since the 1960s when decreased dopamine was observed in post-mortem brain tissue from PD patients and it was discovered that L-DOPA supplementation rescued motor deficits. L-DOPA is the first-line therapeutic for managing motor symptoms in PD patients; however, its use results in adverse side effects and its efficacy decreases over time. Furthermore, while dopamine mishandling was originally thought of as a pathologic hallmark of PD, later studies showed a pathogenic role due to cytosolic dopamine participating in neurotoxic reactions. To maintain neuronal health and proper dopamine transmission, the cytosolic pool of dopamine is regulated through vesicular sequestration by vesicular monoamine transporter 2 (VMAT2) and our work has demonstrated it is retained in the vesicle by synaptic vesicle glycoprotein 2C (SV2C). Mutations in the coding region of SLC18A2, the gene for VMAT2, are rare but severe, resulting in infantile parkinsonism. In addition, gain of function mutations in the promoter region of SLC18A2 have been associated with decreased risk of PD, suggesting that enhanced activity confers protection. Recently, a SNP in SV2C associated with PD was identified and replicated by GWAS, substantiating previous work that identified SV2C as a modifier of: 1) nicotine's protective effect against developing PD, 2) GBA-associated PD, and 3) differential responses of PD patients to the therapeutic L-DOPA. Taken together, these data indicate that the vesicular handling of dopamine is a viable therapeutic target for PD and may provide the dual benefit of: 1) improving motor symptoms by regulating vesicular dopamine dynamics, either alone or by improving L-DOPA efficacy, and 2) conferring neuroprotection by minimizing the neurotoxic cytosolic pool of dopamine. Thus, we hypothesize that therapeutically targeting SV2C may modify disease progression and improve efficacy of symptomatic interventions. There is precedent for therapeutically targeting SV2 proteins demonstrated by the efficacy of the SV2A modulator Levetiracetam for epilepsy. Here, we present initial results from an in vitro plate-reader based assay utilizing a fluorescent dopamine analogue (FFN206) used to screen a range of VMAT2- and SV2C-modifying compounds including Tetrabenazine, Reserpine, Chloroquine, Bupropion, Levetiracetam, and Padsevonil.

Hypothesis: Increased SV2C activity will enhance the therapeutic profile of L-DOPA to alleviate motor symptoms in PD patients.



P09.02

Golexanolone, a GABAA receptor-modulating steroid antagonist, improves fatigue, anxiety, depression, and some cognitive and motor alterations in a rat model of Parkinson's disease

Paula Izquierdo-Altarejos[1], Yaiza M Arenas[2], Mar Martínez-García[2], Gergana Mincheva[2], Magnus Doverskog[3], Thomas P Blackburn[3], Lars Öhman[3], Marta Llansola[2], Vicente Felipo[2]*
[1] Principe Felipe Research Centre (CIPF), Valencia, Spain
[2] Centro de Investigación Príncipe Felipe, Valencia, Spain
[3] Umecrine Cognition AB, Solna, Sweden

Parkinson's disease (PD) affects more than 6 million people worldwide, and will affect more in coming decades. There are no drugs available for PD that alter progression of disease. Current symptomatic treatments provide limited relief and have side effects.

Enhanced GABAergic neurotransmission contributes to PD pathogenesis and to some motor and non-motor symptoms. In animal models, GABA levels are increased in substantia nigra pars compacta, leading to reduced expression of tyrosine hydroxylase (TH) in neurons which contributes to the behavioural deficits. TH expression may be restored by blocking GABAA receptors, supporting that enhanced GABAA receptors activation mediates reduced TH expression and some behavioural deficits. Patients and animal models with PD may also show cognitive impairment, fatigue, anxiety, and depression.
We hypothesized that golexanolone, a well-tolerated GABAA receptor-modulating steroid antagonist in clinical development, that reduces GABAA receptors activation and neuroinflammation, may improve some motor and non-motor deficits in a rat model of PD.
We used the unilateral 6-OHDA rat model. Rats positive in the apomorphine-induced rotation test were included, together with sham-operated controls. Golexanolone treatment (50 mg/Kg, daily, intragastric) started four weeks after surgery.
Rats with PD showed increased fatigue in the treadmill test and anxiety in the open field test. Golexanolone reversed the increase in fatigue and in anxiety.
In the sucrose preference test, rats with PD showed anhedonia, a symptom of depression, which was also reversed by golexanolone.
Motor coordination was impaired in 6-OHDA-treated rats in the motorater and rotarod tests. Golexanolone reversed the impairment in motor coordination in the motorater, but not in the rotarod test.
Alterations in locomotor gait were analysed in the CatWalk. 6-OHDA-treated rats showed increased initial dual stance and reduced swing. These alterations were reversed by golexanolone.
6-OHDA-treated rats show impaired short-term memory in the Y maze, which was improved by golexanolone.
These results show that golexanolone treatment may be useful to improve a variety of the symptoms that severely affect the patients quality of life: anxiety and depression, fatigue, some aspects of motor coordination and of locomotor gait, and some aspects of cognitive function. These beneficial effects would be due to reduction of GABAergic neurotransmission and neuroinflammation.

P09.03

Validating a novel therapeutic approach co-targeting immune activation and dopaminergic neuron loss in Parkinson's disease

Aishwarya Johnson[*,1], Sara Jose[2], Hariharan Saminathan[3], Richard Gordon[4]*
[1] QUT, Queensland, Australia
[2] UQ, Brisbane, Australia
[3] UAEU, Al Ain, United Arab Emirates
[4] QUT, Brisbane, Australia

Parkinson's disease (PD) is a progressive neurodegenerative disorder characterized by selective loss of dopaminergic neurons in the ventral mid-brain. This degeneration of dopaminergic neurons triggers irreversible and debilitating motor and non-motor deficits. Currently, only symptom management is available for PD, with no means to slow or stop disease progression. Therefore, there is an urgent unmet need to develop new and more effective treatments for disease modification. As PD is a complex disease with multiple mechanisms driving disease pathogenesis, we hypothesized that targeting multiple mechanisms such as inflammation, mitochondrial dysfunction and oxidative stress could be more effective compared to current approaches which target a single pathological pathway. In this study, we identified a novel therapeutic approach to modulate the Fyn Kinase pathway that is expressed in immune cells that drive inflammation and in dopaminergic neurons which degenerate in Parkinson's disease. We uncovered for the first time that one of the tyrosine phosphatases - PTEN (Phosphatase and Tensin homolog deleted on chromosome 10) a lipid and protein tyrosine phosphatase functions as a switch to activate Fyn and drive chronic inflammation in PD and dopaminergic death through mitochondrial dysfunction. This study further validates PTEN as a very early stress sensor in response to oxidative stress and neurodegenerative toxicants in models of PD. Pharmacological inhibition of PTEN functions as an effective "off-switch" for the pathological Fyn kinase pathway and reduces both inflammation in activated microglia, as well as neuronal loss in neurotoxicant-induced death of dopaminergic neurons. Our results suggest that PTEN could be a disease-modifying pharmacological target that could be targeted to block multiple pathological mechanisms in PD including inflammation, neuronal death and mitochondrial dysfunction. Future studies will evaluate if this approach can also target synuclein pathology in preclinical models of PD.

P09.05

Identification of new RXR-Nr4a (Nur) nuclear receptor complex selective compounds for Parkinson's disease

David Cotnoir-White[1], Catherine Levesque[1], Maxime Tremblay[1], Anne Marinier[1], Sylvie Mader[1], Daniel Levesque[*,2]*
[1] University of Montreal, Montreal, Canada
[2] University of Montreal, Faculty of pharmacy, Montreal, Quebec, Canada

Retinoid X receptors (RXRs) play a role as master regulators due to their capacity to form heterodimers with several other nuclear receptors, contributing to important aspects of biology and to an array of pathological conditions. For instance, it has been shown that RXR-Nr4a (including Nurr1 and Nur77) signaling is deregulated during Parkinson's disease and its treatment. While RXR drugs, also called "rexinoids" have been developed to modulate activity of RXR-containing dimers, their lack of selectivity strongly limits their use for specific therapeutic approaches. We describe here a new high throughput screening (HTS) approach to identify novel rexinoids selective for RXR-Nurr1/Nur77 heterodimers, which represent interesting targets for Parkinson's disease. The initial screens were conducted by measuring coactivator recruitment to the RXR-Nurr1/Nur77 dimers in Protein Complementation - Bioluminescence Resonance Energy Transfer assays (PCA-BRET). This approach identified new chemical entities with rexinoid activity. Selectivity of compounds against undesirable off-targets was tested in robust assays. This was achieved by developing new gene reporter assays, in which the DNA binding domain of the RXR partner (retinoic acid receptor, vitamin D receptor, thyroid hormone receptor) was mutated to recognize a glucocorticoid response motif (DBDmut). Structure-activity relationship (SAR) analysis led to improvements in potency for the primary target and increased selectivity against undesired off-targets. To confirm the validity of our approach, we ran an additional screen against the RXR-Nurr1(DBDmut) heterodimer using the newly developed a glucocorticoid/retinoid (½GRE-½DR5)x3 hybrid reporter assay. Interestingly, this approach identified the same hits that were selected from the PCA-BRET assay to undergo SAR. Preliminary data support good pharmacokinetic parameters of optimized hits (PK and BBB passage). These results indicate that the platform we developed can be used to identify new heterodimer selective rexinoids. This work was supported by IRICoR, a Canadian center of excellence in commercialization and research specialized in drug discovery and the Weston Brain Institute of Canada.

P09.06

Epigenetic deregulation in striatal neurons during impulse control disorders related to dopamine agonists in Parkinson's disease: towards the identification of therapeutic target

Louise-Laure Mariani[*,1], Jean-Antoine Girault[2], Denis Herve[2], Olga Corti[3], Jean-Christophe Corvol[3]*
[1] Paris Brain Institute Sorbonne University, Paris, France
[2] Inserm, Paris, France
[3] Paris Brain Institute, Paris, France

Impulse Control Disorders (ICDs) are frequent and severe behavioral complications of Parkinson's Disease (PD). Their cumulative incidence is 46% at 5 years, and can increase in certain genetic forms of PD. The main ICDs are pathological gambling, binge eating, compulsive shopping and hypersexuality. Despite the possible negative consequences, the behaviors are repeated without control, defining those behaviors as impulsive and compulsive, which impact negatively life and social-occupational functioning of PD patients and their caregivers. Pathophysiology of ICD is still imperfectly understood.
In cells, there are stable « epigenetic » marks modifiying the way DNA is used and genes are expressed, without modifying their sequence. In the brain of PD patients, these epigenetics marks are modified during the treatments of PD. All the PD patients treated by dopaminergic medications do not develop ICDs but it is not known which epigenetic and gene expression modifications are linked to the occurrence of ICD in patients.
Some validated rodent models generate strong and frequent ICDs. They allow to study in an integrated approach these behaviors et their underlying biological abnormalities and molecular mecanisms.
Our study, through an innovative approach combining animal models and Next-generation sequencing, explores the epigenetic and gene expression (transcription and methylation), in specific brain regions, in specific subpopulation of neurons, to identify new pathophysiological and therapeutic targets.

P09.07

A model to test novel therapeutic interventions for Parkinson's disease: The Thy1-aSyn ("line 61") mice

Franziska Richter Assencio, Christopher Kaeufer, Birthe Gericke, Malte Feja*
University of Veterinary Medicine Hannover and Center of Systems Neuroscience, Hannover, Germany

Development of disease-modifying interventions for Parkinson's disease (PD) is hampered by a lack of translation from pre-clinical to clinical trials. One strategy for improvement is to increase predictive validity of pre-clinical studies by using extensively characterized animal models with a comprehensive set of validated pharmacodynamic readouts. Mice over-expressing full-length, human, wild-type alpha-synuclein under the Thy-1 promoter (Thy1-aSyn line 61) reproduce key features of sporadic PD, such as progressive loss of striatal dopamine, alpha-synuclein pathology, deficits in motor and non-motor functions and elevation of inflammatory markers (Chesselet, Richter et al. 2012 Neurotherapeutics; Chesselet & Richter 2011 Lancet Neurology). Extensive work with this model by multiple laboratories over the past decade increased knowledge on pathomechanisms of alpha-synuclein pathology and down-stream pathways. Interestingly, while postnatal transgene expression is widespread in central and peripheral neurons, the extent and progression of downstream pathology differs between brain regions, thereby replicating the characteristic selective vulnerability of neurodegenerative diseases. In depth characterization of these readouts in conjunction with behavioral deficits has led to more informative endpoints for pre-clinical trials. Each intervention tested in Thy1-aSyn line 61 enhances knowledge on how molecular targets, pathology and functional behavioral readouts are interconnected, thereby further optimizing the platform. Here we present latest discoveries on effects of drugs or exercise using Thy1-aSyn line 61 including discussion on potential predictive validity.

P09.08

Uncovering the interaction between the cannabinoid CB1 receptor and the angiotensin AT2 receptor. Overexpression of AT2-CB1 receptor heteromers in the striatum of 6-hydroxydopamine hemilesioned rats.

Rafael Rivas-Santisteban[*,1], Jaume Lillo[2], Iu Raïch[2], Ana Muñoz[3], Alejandro Lillo[2], Ana I. Rodríguez-Pérez[3], José L. Labandeira-Garcia[3], Gemma Navarro[2], Rafael Franco[2]*
[1] Universitat de Barcelona, Barcelona, Spain
[2] UB, Barcelona, Spain
[3] USC, Santiago de Compostela, Spain

The potential of cannabinoid and angiotensin receptors as targets in the therapy of Parkinson's disease (PD) is of great interest. The endocannabinoids, which are neuromodulators that act through the CB1 and CB2 cannabinoid receptors, and the renin angiotensin-system, which is relevant for regulation of the correct functioning of several brain circuits, have been identified as potential targets. Resonance energy transfer assays in a heterologous system showed that the CB1 receptor (CB1R) can directly interact with the angiotensin AT2 receptor (AT2R). Coactivation of the two receptors results in increased Gi-signaling. The AT2-CB1 receptor heteromer imprint consists of a blockade of AT2R-mediated signaling by rimonabant, a CB1R antagonist. The expression of the heteromer has also been found in primary striatal neurons, as confirmed by in situ proximity ligation assays. In addition, increased expression of the AT2-CB1 receptor heteromeric complexes was detected in the striatum of a rodent PD model consisting of rats hemilesioned using 6-hydroxydopamine. Expression of the heteromer was upregulated in the striatum of lesioned animals and, also, of lesioned animals that upon levodopa treatment became dyskinetic. However, there was no upregulation in the striatum of lesioned rats that did not become dyskinetic upon chronic levodopa treatment. These results suggest that therapeutic developments focused on the CB1R should consider that this receptor can interact with the AT2R, which in the CNS is involved in mechanisms related to addictive behaviors and to neurodegenerative and neuroinflammatory diseases. Therefore, the AT2-CB1 receptor heteromer could be a promising new target to combat Parkinson's disease.

P09.09

Clemizole hydrochloride reduces alpha-synuclein toxicity in Parkinson's disease models: A behavioural and mechanistic study

Bhupesh Vaidya, Pankaj Gupta, Joydev K. Laha, Ipsita Roy, Shyam Sunder Sharma*
National Instiiute of Pharmaceutical Education and Research (NIPER), SAS Nagar, Mohali, Punjab, India

Transient receptor potential canonical 5 (TRPC5) channels are one of the members of the Transient receptor potential family which are activated in response to elevated oxidative stress. These channels are widely expressed in the brain areas such as the striatum and midbrain. We have previously shown that the upregulation of these channels in these brain areas plays a major role in the pathophysiology of neurodegenerative disorders such as Parkinson's disease. In the present study, we investigated the

effects of alpha-synuclein toxicity on TRPC5 channels expression with emphasis on mitochondrial dysfunctions, oxidative stress and apoptosis. Alpha-synuclein pre-formed fibrils were bilaterally infused into the striatum of Sprague-Dawley rats as well as administered to the SH-SY5Y cells. Then the effect of clemizole hydrochloride treatment, a potent TRPC5 channel inhibitor on behavioural, molecular and biochemical parameters were evaluated both in vitro as well as in vivo. Exogenous treatment with alpha synuclein pre-formed fibrils increased TRPC5 levels, along with reduced tyrosine-hydroxylase expression in the striatum and midbrain. Moreover, it produced mitochondrial dysfunctions, which were confirmed using expression studies for Peroxisome proliferator-activated receptor-gamma coactivator-1 alpha and transcription factor-A, mitochondrial. In the SH-SY5Y cells treated with alpha-synuclein preformed fibrils we did not observe any changes in overall cell viability but mitochondrial health of the cells was compromised. We also observed elevated ROS levels using H2DCFDA and mitosox dyes. However, co-treatment with clemizole reversed these changes and accorded overall protection from alpha-synuclein toxicity. Finally, we also demonstrated the ability of clemizole hydrochloride to reduce TRPC5 expression and restore tyrosine hydroxylase expression following alpha synuclein treatment. Taken together, our results provide novel insights into potential of clemizole hydrochloride and other TRPC5 modulators to protect from alpha synuclein toxicity in neurodegerative disorders such as Parkinson's disease.

BASIC SCIENCE: Electrophysiology and functional imaging, optogenetics

P10.02

Alpha-synuclein-induced nigrostriatal degeneration and pramipexole treatment lead to compulsive behaviours and abnormal frontostriatal plasticity

Mélina Decourt, Eric Balado, Maureen Francheteau, Anaïs Balbous-Gauthier, Pierre-Olivier Fernagut, Marianne Benoit-Marand*
Laboratoire de Neurosciences Expérimentales et Cliniques, Université de Poitiers, INSERM U1084, Poitiers, France

Objective: Clinical studies have demonstrated that pramipexole (PPX) treatment of Parkinson's disease (PD) induces non-motor side effects (impulse control disorders, ICD) affecting up to 30% of patients. The pathophysiology of ICD is still poorly known, but it was shown that the orbitofrontal cortex (OFC) and the striatum are key structures. In this context, we have investigated the effects of PPX in a PD rat model during a signal attenuation task and on frontostriatal plasticity.
Methods: Nigrostriatal degeneration was induced by viral-mediated overexpression of human mutated alpha-synuclein in the substantia nigra of rats and PPX treatment was realized during 20 days. Post-training signal attenuation task was performed to assess compulsivity behaviour, before and after surgery, and during PPX treatment. Frontostriatal plasticity was assessed using anesthetized in vivo electrophysiology recordings after high frequency stimulation (HFS). The post-mortem analysis (proteins and RNA detections) are in progress.
Results: The results of signal attenuation task combined with previous studies suggest that the pattern of dopaminergic degeneration is crucial to induce compulsive behaviour. Moreover, electrophysiological recordings demonstrated that whereas HFS of the OFC induced a long-term potentiation of striatal responses to further OFC stimulations, nigrostriatal lesion, PPX treatment and the combination of both led to a long-term depression of striatal responses following HFS stimulation of OFC.
These experimental data complete the knowledge of ICD physiopathology suggesting a crucial involvement of dopaminergic denervation pattern and of PPX treatment to develop compulsive behaviours. Moreover, we highlight a dysfunction of frontostriatal pathways induced by nigrostriatal degeneration and PPX treatment.

P10.03

Parkinsonian beta oscillations in the cortico-basal ganglia network during movement: Beyond the frequency range

*Marc Deffains**
Institute of Neurodegenerative Diseases – CNRS UMR 5293, Bordeaux, France

In Parkinson's disease, the slowness of movement (bradykinesia) and paucity or absence of movement (akinesia) are accompanied by abnormal synchronous oscillations of activity within a neuronal network including subcortical structures (the basal ganglia), the thalamus and the cerebral cortex. These abnormal oscillations reflect rhythmic electrical activity in different populations of neurons in the network and may interfere with the normal functioning of the network, especially during the execution of a movement. However, the anti/hypokinetic role of these neuronal oscillations is only partially consistent with the available data. Moreover, characterization of oscillations goes beyond their frequency and other oscillation features, such as wave pattern and coherence/phase relationship between the different nodes of the neuronal network, may be specifically linked to hypo-kinetic motor disturbances observed in parkinsonian patients. In this project, we propose to study the importance of the synchronization of oscillatory neuronal activities between the different nodes of the network – rather than their frequency – in the emergence/materialization of these motor symptoms. To do so, we will simultaneously record neural activity in the different nodes of the network during movement in monkeys before and after induction of parkinsonism. Ultimately, our results will allow us to propose new biomarkers and new therapeutic targets which will then be tested in the parkinsonian monkeys to develop innovative therapeutic strategies aiming at restoring normal movement.

P10.04

LRRK2 G2019S mutation causes hyperexcitability of iPSC-derived cortical neurons

Shiva Nag Kompella, Dayne Becanno-Kelly*
DRI, Cardiff University, Cardiff, United Kingdom

The underlying molecular changes that precede late-stage neuronal loss in Parkinson's are yet to be unravelled. With growing evidence of the importance of neuronal dysfunction preceding degeneration, we focus on understanding the temporality of PD. Previous studies have shown increased glutaminergic activity in LRRK2 G2019S knock-in mouse cortical neurons. We analysed the electrophysiological properties of LRRK2 G2019S mutant iPSC-derived cortical neurons and isogenic control lines longitudinally using the whole-cell patch clamp technique to further assess these changes.
Our preliminary data demonstrate a measurable increase in the excitability of LRRK2 G2019S mutant neurons versus isogenic wild-type controls. LRRK2 G2019S neurons exhibited an increase in both frequency and amplitude of spontaneous excitatory post-synaptic currents (sEPSCs) at 68-69 days in vitro (DIV). Intriguingly this difference was transient and lost upon further maturation (101 – 103 DIV). In addition to sEPSCs, spontaneous action potential

(sAP) firing was observed in 62% of G2019S cortical neurons (n = 5/8) while no sAPs' were seen in control neurons (n=6). This increased spontaneous activity of G2019S neurons was also confirmed using FLIPR assay wherein oscillating calcium transients were observed compared to controls. Our interrogation led us to the hypothesis that these changes could be linked to the greater percentage of cells expressing sodium currents in G2019S neurons (n = 4/6) compared to its isogenic controls (n = ¼). Interestingly, G2019S neurons also exhibited lower resting membrane potential (RMP). Neurons expressing sodium currents generated stable trains of action potentials upon induction in both wild-type and G2019S at 68-69 DIV. However, upon maturation to 101 – 103 DIV, G2019S mutation exhibited a decreased spike amplitude induced by 125epolarizing pulse. Whilst preliminary, our data indicate an early hyperexcitable phenotype of LRRK2 G2019S mutant iPSC-derived cortical neurons perhaps related to a change in maturation rate.

P10.05

Globus pallidus contribution to motor behaviour in normal and Parkinson's disease states: Optogenetic studies in murine models

Abdel-Mouttalib Ouagazzal[*,1], Sonia Di Bisceglie Caballero[2], Aurelia Ces[3], Martine Liberg[2], Frederic Ambroggi[3], Marianne Amalric[3]*
[1] Cognitive Neuroscience Laboratory (UMR7291), Marseille, France
[2] AMU, LNC (UMR7291), Marseille, France
[3] CNRS, LNC (UMR7291), Marseille, France

The degeneration of nigrostriatal dopaminergic neurons in Parkinson's disease (PD) triggers a range of functional compensatory changes in basal ganglia (BG) circuits that lead to development of motor symptoms. Excessive inhibition of globus pallidus externa (Gpe) by striatal GABAergic neurons is considered a central mechanism contributing to the expression of motor symptoms because of its widespread projections to all BG nuclei and to the thalamus and the cortex. While electrophysiological investigations in animal models of PD provide support for this view, behavioral studies assessing beneficial effects of global Gpe stimulations in the context of dopamine (DA) depletion are scarce and the reported results are controversial. Here, we used an optogenetic approach and the standard unilateral 6-hydroxydopamine (6-OHDA) nigrostriatal dopamine (DA) lesion model of PD to assess beneficial effects of Gpe stimulation on motor deficits in mice. The behavioral effects of optogenetic inhibition of Gpe were also studied in normal mice under the same testing conditions to verify whether reduced Gpe activity reproduces the typical motor deficits of DA lesion. To modulate GPe activity, the excitatory opsin, ChR2(H134R), and the inhibitory opsin, iC++, were expressed in Gpe neurons under the control of the human synapsin-1 promoter using an adeno-associated virus vector. Global unilateral Gpe activation restores a range of motor deficits (ipsilateral circling behavior, forelimb use akinesia, locomotor hypoactivity and bradykinesia) in hemi-parkinsonian mice at optical stimulation parameters ineffective in non-lesioned controls. Unilateral photoinhibition of Gpe in normal mice did not impair locomotor behavior indicating that merely reducing Gpe activity is not sufficient to mimick motor deficits induced by a DA lesion. Bilateral Gpe photoinhibition had no effect on spontaneous locomotor activity but reduced exploration directed towards salient spatial cues (illuminated nose-poke modules), suggesting that recruitment of Gpe may vary depending on the motor behavior involved. Collectively, these findings shed a new light on the functional role of Gpe and suggest that complex structural and functional compensatory remodeling of Gpe efferent neurons may contribute to motor deficits of PD.

P10.06

Analysis of Parkinson`s neuronal disease using microelectrode recording and simulation data with subthalamic-nucleus deep brain stimulation

Venkateshwarla Rama Raju[*,1], Lavanya Neerati[2]*
[1] CMR College of Engineering & Technology, jawaharlal Nehru Tehnological University, Hyderabad, Telangana, India
[2] Osmania University, Hyderabad, Telangana, India

To label the system performance using computational simulation and statistical models which can assist to detect the ideal parameters of deep brain stimulation (DBS) for Parkinson`s diseased conditions (patients), to apply relating the functional-analysis to test the expected-mechanisms for computing the ripples (oscillations) during nuclei interaction, and finally to subjugate oscillations through high frequency stimulations with DBS.

Parkinson disease (PD) is a complex neurodegenerative disorder, categorized with hallmark motoric-feature manifestations, i.e., signs and symptoms. It is connected by pathological, oscillatory-neuronal-activity within parallelly connected basal-ganglion (BG) motor circuitry. DBS is successively applied to somatically deflective or refractile (refractive) PD. But choice of stimulus parameters is depending on skilled evaluation of Parkinson`s, ensuing in a long-lasting prolonged fine-tuning passé or retro also a sub optimum well-chosen (high-quality) superior parameter. Hence, the study reconnoiters third and fourth-order control theory-based systems models of oscillatory activity in BG.

Describing functional analysis are applied to test plausible and probable mechanisms for generating oscillations while networking nucleus followed by exploring the clampdown, i.e., suppressing ripples thru high-frequency-stimulations (HfS). The hypothetical consequences (outcomes) to suppress ripples activity gained by applying fourth order, also previous models, are enhanced to fit prognostically acquired local-field-potentials (LFPs) data attained (Fig 1) as PD patients thru implanted pulse generators (IPGs) microelectrode recording (MER) via STN-DBS. Close agreement between power of ripples computed for an array of stimulus-amplitudes is detected RMS:0-69-0.99 (Fig`s 2-4, and Tables 1,2).

Findings of our proposed study shows that the behavioral performance of the system plus suppression of pathological-neuronal ripples through the DBS are significantly labeled by macroscopic-models presented. Plus, a third-order model is good enough to prototype the quantifiable model data clinically with no extra intricacy.

Improving the system behavioral performance by applying computational-simulation and statistical-modelling can assist in the similarity of best induced stimuli parameters for Parkinson constraints in incontrovertible-settings. Our prototype can be deciphered to clinical tool to help in setting DBS parameters, could be plausibly adjusted to signify distinct patient's pathological-state by means of a biomarker (LFP) of Parkinson's.

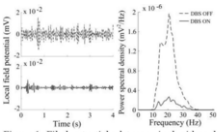


Figure 1. Filed potentials data acquired with embedded macro electrodes as of subthalamic-nuclei of PD subject demonstrated prior to 130 Hz stimuli at a current of 1.5volts plus 60μs pulse-width. Spectral-density was estimated with Welch's technique, is built on complete field potentials with MER recording for the given stimulus—settings.

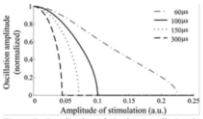


Figure 2. Amplitudes-of-ripples (oscillations) which are normalized-values in 4th-order network-series model (condensed) of neuronal-synchrony as a function of strength (amplitude)-of-applied stimuli, stated in a certain arbitrary or random-unit (a.u./or r.u.). 4 dissimilar stimulus-pulse-widths are open. h_1 is selected to be 0.1 for all cases and in every case (▼).

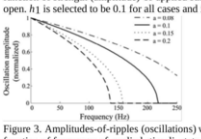


Figure 3. Amplitudes-of-ripples (oscillations) which are normalized-values in 4th-order network-series model (condensed) of neuronal-synchrony as a function of frequency-of-applied stimuli, stated in a certain arbitrary or random-unit (a.u./or r.u.). 4dissimilar stimulus-pulse-widths are open. h_1 is selected to be 0.1 for all cases and in every case (▼).

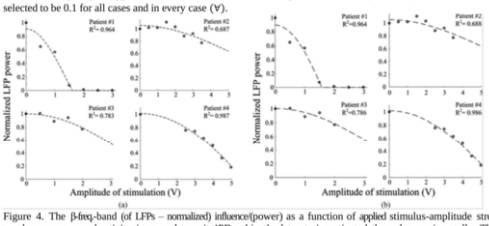


Figure 4. The β-freq-band (of LFPs – normalized) influence(power) as a function of applied stimulus-amplitude strength for hypothetical-models of synchronous neuronal-activity, improved to suit 4PD subject's datasets investigated through experimentally. The data is exposed (·) laterally through theoretic-fit to the model-prototype adjusted for that specific Parkinson (PD-patient) as the stimulus-strength is bigger. Stimulus-frequency is set at 130Hz, plus pulse-width set at 60μs, except for patient PDP-S$_{25}$ where a pulse-width of 90μs was executed. The RMS (R^2) value computed for every-fit is incorporated. (a) 3rd-order model-type of synchronous neuronal-activity. (b) 4th-order network-series model (abridged) of synchronal/synchronic or (synchronous) neuronal-activity.

P10.07

Impact of alpha-synuclein overexpression on electrophysiological properties of the locus coeruleus neurons

Jone Razquin[*1], Laura De las Heras-García[1], José Angel Ruiz-Ortega[1], Lorena Delgado[2], Jérôme Baufreton[2], Gloria González-Aseguinolaza[3], Harkaitz Bengoetxea[4], Cristina Miguélez[1]*

[1] Faculty of Medicine and Nursing, University of the Basque Country (UPV/EHU), Dept. of Pharmacology, Leioa, Spain, Leioa, Bizkaia, Spain

[2] CNRS UMR 5293, Institut des Maladies Neurodégénératives, Bordeaux, France, Bordeaux, France

[3] CIMA, Navarra Institute for Health Research, Gene Therapy and Regulation of Gene Expression Program, Pamplona, Spain, Pamplona, Navarra, Spain

[4] University of the Basque Country, Neuroscience, Leioa, Spain, Leioa, Bizkaia, Spain

Parkinson's disease (PD) is a neurodegenerative process characterized by the presence of Lewy bodies, affection of many neurotransmitter systems and manifestation of motor and nonmotor symptoms. Notably, half of PD patients are diagnosed with dementia within ten years of being diagnosed with PD, though cognitive decline can appear before or years after clinical PD diagnosis. Interestingly, the locus coeruleus (LC) that contains the highest density of noradrenergic neurons in the brain, is among the brain stem areas first displaying Lewy bodies in the disease, and is associated with cognitive decline, among other non-motor symptoms. Despite its small size, it projects to almost all brain areas and exerts a key influence on the homeostasis of dopaminergic networks. Recent evidence indicates that the noradrenergic neurons of the LC display notable diversity, including distinct clusters that project to the hippocampus, which is a key nucleus in cognitive processing. Our aim is to study if overexpressing alpha-synuclein triggers LC neuron dysfunction. To do so, we used an animal model of prodromic PD by overexpressing alpha-synuclein in the LC using viral-vectors. We performed additional stereotaxic injection of retrobeads in the CA1 layer of the hippocampus and two weeks after we studied the intrinsic properties of those LC neurons that project to CA1 using patch clamp recordings. Already in the control group we observed that this cluster of neurons shows different maximal firing rate and properties of the action potential compared to other LC neurons. Alpha-synuclein overexpression also had an impact in those characteristics. Due to the importance of LC degeneration in early stages of PD, monitoring LC dysfunction could provide valuable information about early phases and cognitive decline in PD patients

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P10.08

A spectrotemporal analysis of local field potentials in the subthalamic nucleus during language processing

Patrick Santens[*1], Emma Depuydt[2], Elissa-Marie Cocquyt[2], Arnout Bruggeman[2], Dirk Van Roost[1], Pieter Van Mierlo[2], Miet De Letter[2]*

[1] Ghent University Hospital, Ghent, Belgium

[2] Ghent University, Ghent, Belgium

Introduction: Subthalamic nucleus (STN) activity occurs in the early stages after presentation of auditory stimuli. It is unclear if this activity is modality-specific and related to linguistic features or rather aspecific.

Aim: To investigate and compare responses to linguistic and non-linguistic auditory stimuli within the STN and the cortex.

Method: Local field potentials (LFP) in the STN were investigated during a pre-attentive and attentive auditory oddball paradigm with linguistic and non-linguistic stimuli in 24 patients with Parkinson's disease who had electrodes implanted for deep brain stimulation. The analysis included averaging of LFP and spectrotemporal analysis. Similar data were obtained with scalp EEG and using the same oddball experiments in a cohort of 71 healthy controls.

Results: The attentive, but not pre-attentive, detection of relevant auditory stimuli resulted in patterned responses in the LFP of the STN. Spectrotemporal alterations in LFP, including an increase of delta and theta power and a decrease of alpha and beta power, were remarkably similar for linguistic and non-linguistic stimuli, coinciding with similar alterations in the EEG of healthy controls.

Discussion: These results suggests that STN activity in auditory perception is not modality-specific, but rather related to domain-general detection of relevant stimuli. Furthermore, the temporal coincidence of similar spectrotemporal alterations in the STN and cortical activity contributes to a hypothesis of cortico-STN connectivity involved in gating and domain-general monitoring of ongoing stimuli. These findings may potentially lead to a modification of the present model of basal ganglia function.

BASIC SCIENCE: Prevention, neuroprotection neuroplasticity

P11.01

Exercise-based rescue strategies in early-stage of PD: From preclinical to clinical studies

Federica Campanelli[*,1], Serena Fragapane*[*,1], Gloria Modica*[*,1], Gioia Marino[1], Giuseppina Natale[1], Elena Marcello[2], Fabrizio Gardoni[2], Maria De Carluccio[1], Federica Servillo[1], Anna Picca[3], Maria Rita Lo Monaco[3], Maria Teresa Viscomi[4], Anna Rita Bentivoglio[3], Veronica Ghiglieri[5], Paolo Calabresi[3]*

[1] Department of Neuroscience, Università Cattolica del Sacro Cuore, Rome, Italy., Rome, Italy

[2] Department of Pharmacological and Biomolecular Sciences, University of Milano, Milan, Italy., Milan, Italy

[3] Fondazione Policlinico Universitario Agostino Gemelli IRCCS, Rome, Italy., Rome, Italy

[4] Università Cattolica del Sacro Cuore, Rome, Italy., Rome, Italy

[5] Università Telematica San Raffaele, Rome, Italy., Rome, Italy

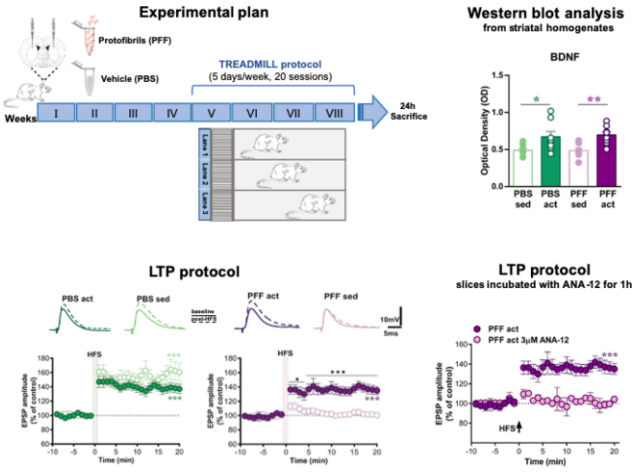
In Parkinson's Disease (PD) patients at the early stages, intensive physical activity improves motor function, reducing the need for drug escalation. Physical training has been shown to reduce the expression of α-syn and delay the formation of Lewy bodies in animal models of PD.

Based on our previous studies, we propose that α-syn impairs corticostriatal plasticity and motor learning through a synaptic mechanism that can be preserved by enhancing BDNF-TrkB as an adaptive response to non-pharmacological interventions. Using a toxic model with intracerebral administration of human α-syn-pre-formed fibrils (PFF), we tested the hypothesis that intensive exercise prevents striatal synaptic alterations caused by α-syn overexpression and spreading through the nigrostriatal system and exerts beneficial effects via a BDNF-dependent modulation of corticostriatal plasticity.

Our data show that corticostriatal long-term-potentiation (LTP), a form of plasticity lost in parkinsonian conditions, is restored in animals exposed to an intensive physical training program. This effect is associated with a reduced spreading of α-syn in the substantia nigra pars compacta, indicating slower neurodegeneration in the active animals. In line with our hypothesis, the TrkB receptor's blockade disrupted the exercise-induced LTP in the PFF active group, suggesting that an enhanced BDNF-TrkB pathway activity may underlie the rescue of synaptic plasticity. This exercise-induced BDNF plasticity depends on the activation of NMDA receptors bearing GluN2B subunits. These exercise-induced changes in neuronal functions resulted in beneficial effects on motor control and visuospatial cognition, compared with α-syn-PFF-injected parkinsonian animals of the sedentary group. These findings demonstrate that intensive physical exercise exerts beneficial effects by rescuing early synaptic alterations induced by α-syn.

These preclinical findings are supported by promising results obtained on PD patients. We examined whether an intensive rehabilitation treatment reduces motor disability in the early stages of PD and increases BDNF serum levels. PD patients subjected to 45 minutes three times a week of intensive physical activity showed a significant increase in BDNF serum levels and improved motor performances, reporting a beneficial effect of intensive treadmill exercise.

Taken together, these results demonstrate that intensive exercise has great efficacy as a non-pharmacological neurorehabilitation treatment for PD through BDNF-dependent mechanisms.



P11.02

Novel noninvasive gene therapy for Parkinson's disease using viral encoded single-chain antibody treatment

Anne-Marie Castonguay[*,1], Béatrice Morin[1], Thomas Durcan[2], Claude Gravel[1], Martin Lévesque[1]*

[1] Laval University - CERVO Brain Research Center, Québec, Canada

[2] McGill University, Montréal, Canada

Evidence in various animal and cell models suggest that pathological alpha-synuclein (aSyn) can be transmitted from cell-to-cell in a prion-like manner. Blocking either the aggregation process or the transmission of the pathological protein across the brain could therefore be effective therapeutic strategies. We generated small antibodies in the form of secreted single-chain variable fragments (scFv) and intracellular antigen-binding fragments (Fab) that bind to aSyn. We also generated a control antibody that targets GFP. We validated the specificity of our antibodies with dot blots and immunoprecipitation and identified one scFv specific for phosphorylated aSyn, and one recognizing both normal and phosphorylated aSyn. We also verified the efficiency of our intracellular Fabs to bind and degrade aSyn in vitro using HEK cells co-transfected with aSyn and by measuring the aSyn protein level. Our Fabs significantly reduced aSyn protein level compared to the control antibody. We then encoded the single-chain antibodies in an adeno-associated viral vector (AAV) of a serotype that can cross the blood-brain barrier when injected intravenously (IV). After IV injection, we verified the expression of the antibodies in the brain with immunohistochemistry for the Myc tag expressed by the antibodies. To model aSyn pathology spreading, we injected human pre-formed fibrils (PFF) of aSyn in the dorsal striatum of transgenic mice overexpressing human A53T-aSyn (M83) and 7 days later we injected IV the AAV encoding the aSyn scFvs or control scFv. Control groups were also injected with PBS instead of PFF. We closely monitored the motor impairments arising after the injections with a scoring system. Results show a strong protective function of the scFvs against motor impairments and aSyn brain pathology. In conclusion, we developed scFvs and Fabs targeting phospho- or total aSyn and proved that they engage their target. Our scFvs also show a great potential in reducing aSyn pathology in vivo in an aggressive Parkinson's disease mouse model.

P11.03

"Silver Snow Flake": Una iniciativa de prevención de caídas de Parkinson, "Silver Snowflake" Parkinson's Fall Prevention Initiative

Klaudia Cwiekala-Lewis[*,1], Brandon Parkyn[2], Ileana Feistritzer[3]*
[1] York College of Pennsylvania, Manchester, Pennsylvania, United States
[2] Translate Nursing LLC, Manchester, PA, United States
[3] YCP, York, PA, United States

The "Silver Snowflake Initiative" was created to educate globally Every Patient and Every Provider, about new research and intervention available to prevent falls in patients with Parkinson's Disease (PD).
This initiative presents evidence-based fall prevention. As an ongoing initiative to close the gap and to educate healthcare-provided, patients and their families about why patients with Parkinson's Disease are prone to falls and provide some interventions currently available to prevent falls in patients with Parkinson's Disease. The mission of this initiative is to globally educate patients and families about causative factors of falls in Parkinson's patients and existing modalities that can be utilized to minimize the risk of falling. Creators of the initiative strive to make the education material free and available in other languages to raise global awareness, this year we are translating all of the materials to Spanish.
Provided education includes free webinars. The materials provided present anatomy and Parkinson's disease symptoms that cause patients to lose balance and make them at risk of falling. Here we also introduce evidence-based research on complementary therapies such as Tai Chi, Yoga, Boxing, and dance that help prevent PD patient's falls. Education also highlights the importance of the home safety tip to prevent falls in patients with PD.

P11.04

Potential of exercise to modify the progression of prodromal Parkinson's disease

Malte Feja[*,1], Leonie Baldauf[2], Milos Stanojlovic[2], Julia Hankel[3], Christian Visscher[3], Eva Schäffer[4], Daniela Berg[4], Franziska Richter[1]*
[1] Department of Pharmacology, Toxicology und Pharmacy, University of Veterinary Medicine; Center for Systems Neuroscience (ZSN), Hannover, Germany
[2] Department of Pharmacology, Toxicology und Pharmacy, University of Veterinary Medicine, Hannover, Germany
[3] Institute for Animal Nutrition, University of Veterinary Medicine, Hannover, Germany
[4] Department of Neurology, University Hospital Schleswig-Holstein, Christian-Albrechts University, Kiel, Germany

Aims: Subtle motor and non-motor dysfunctions indicative of beginning Parkinson's disease (PD) progression are evident before clinical disease diagnosis, requiring a disease-modifying treatment to start during early prodromal stage. Persons of risk would be willing to determine their risk of developing PD and change their lifestyle in case of a concrete beneficial approach. Growing evidence indicates the potential of exercise in reducing components of PD-related pathology. We hypothesized that early intervention by exercise has a disease-modifying effect during prodromal phase in our PD mouse model and can be applied as a non-pharmacological preventive strategy for early-stage PD.
Methods: We examined exercise in transgenic mice that overexpress human wild-type alpha-synuclein (Thy1-aSyn mice) and replicate PD hallmarks by developing robust fine motor deficits at two months of age. Male wild-type and Thy1-aSyn mice were assigned to three groups receiving different intensity levels of exercise on a treadmill. Motor performance was assessed in the challenging beam and vertical pole test, activity was tested in the open field, and fecal and brain samples were taken for analysis of microbiota and PD-related pathology.
Results: Transgenic mice showed motor impairment on challenging beam and vertical pole, reflecting the expected progression of aSyn pathology at this age. Improved vertical pole performance under exercise in wildtypes suggests symptomatic effects, while slightly improved beam performance of transgenics might indicate a disease-modifying potential of exercise. Levels of phosphorylated alpha-synuclein at serine 129, a key feature of PD, were increased in the substantia nigra pars compacta in untrained, but not in trained, Thy1-aSyn mice, indicating a neuroprotective potential of exercise. Genotypes did not differ in locomotor open field activity, but untrained Thy1-aSyn mice exhibited an anxiety-like phenotype, reflecting one of the most frequent non-motor symptoms in PD patients. Intriguingly, intensive training reduced anxiety-like behavior in transgenic mice to wild-type level.
Conclusions: These results suggest that exercise is able to alleviate early sensorimotor and even non-motor deficits in Thy1-aSyn mice and demonstrate its potential as an early PD-modifying treatment. Increased fecal microbiota diversity in intensively exercised mice support a potential role of the gut-brain axis in the underlying pathological mechanisms of PD.

P11.05

Systematic balance exercise affects the level of Sirt1 and Sirt3 in older adults and persons with Parkinson's disease – pilot study

Jadwiga Kubica[*,1], Joanna Pera[2], Magdalena Wiecek[3], Justyna Kusmierczyk[3], Jadwiga Szymura[4]*
[1] Jagiellonian University Medical College, Kraków, Małopolskie, Poland
[2] Department of Neurology, Jagiellonian University Medical College, Krakow, Poland
[3] Department of Physiology and Biochemistry, Faculty of Physical Education and Sport, University of Physical Education, Kraków, Poland
[4] Institute of Clinical Rehabilitation, Faculty of Motor Rehabilitation, University of Physical Education, Krakow, Poland

Introduction: Ageing is a process that can be successfully modulated by some biomedical approaches including physiotherapy. In this manner it is possible to prevent or delay some age-related pathologies. One of the promising targets in slowing down the ageing process are proteins belonging to the sirtuin family.
Objective: Assessment as to whether moderate intensity systematic balance training (SBT) affects the level of selected sirtuins in healthy, elder people and in persons with Parkinson's disease (PD).
Participants and methods: The study involved 40 participants. Volunteers were randomly divided into 4 groups: training group with PD (PDT); group of training, healthy elder individuals (HT); non-training PD group (PDNT); group of non-training elder, healthy individuals (HNT). The study participants took part in twelve-week SBT based on exercises with an intensity of 60-70% HRmax (three 60-min sessions per week). Venous blood samples were taken before and at the end of twelve weeks of SBT. All data are expressed as mean ± SEM.

Results and conclusion: At baseline the level of sirtuins were similar in compared groups. In the HT group after 12 weeks of SBT the concentration of Sirt1 and Sirt3 was significantly higher than before (respectively: 2.87±0.36 ng/mL vs. 4.16±0.48 ng/mL, $p < 0.001$; 1.54±0.42 ng/mL vs. 2.84±0.54 ng/mL, $p = 0.002$). In the PDT group after training the concentration of Sirt1 was significantly higher than before (2.17±0.37 ng/mL vs. 3.08±0.61 ng/mL, $p < 0.016$). After 12 weeks, the level of Sirt1 was significantly higher in the HT group than in the HNT group ($p = 0.014$) and PDNT group ($p = 0.001$). The level of Sirt1 after the SBT was similar in both training groups ($p = 0.399$). Systematic balance exercise with moderate intensity increase blood levels of Sirt1 and Sirt3 in older adults, but the effect is different in healthy people and people with a neurodegenerative disease.
Acknowledgments: We sincerely thank the participants for their kind cooperation in this study.
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P11.06

Case series of PD patients with and without immobility symptoms and gait function – Three-dimensional motion analysis

Tadamitsu Matsuda[*,1], Kazunori Sato[2], Eriko Kitahara[2], Yuji Fujino[1], Toshiyuki Fujiwara[1], Nobutaka Hattori[1]*
[1] Juntendo University, Bunkyou-ku hongo, Tokyo, Japan
[2] Juntendo Hospital, Bunkyou-ku hongo, Tokyo, Japan

Parkinson's disease(PD) is characterized by immobility, which is more pronounced in the early stages of the disease and tends to become more rigid and less mobile as the disease progresses. This is especially strong in the gait movement, and by clarifying the characteristics of this symptom, a combination of pharmacotherapy and physical therapy for immobility is desirable from the earliest possible stage. The purpose of this study was to clarify the characteristics of gait in patients with and without pronounced immobility. Without features of immobility group, Case A 76-year-old male, HY Stage I, MDS-UPDRS 29 points (Off), 3 points (On) MiniBESTest 25 points; Case B 72-year-old female, HY Stage II, MDS-UPDRS 25 points (Off), 13 points (On) MiniBESTest 20 points. With features of immobility group, Case C 76-year-old woman HY Stage II, MDS-UPDRS 42 (Off) points, 4 (On) MiniBESTest 17 points, Case D 69-year-old male, HY Stage III, MDS-UPDRS 65 (Off) points, 6 (On) MiniBESTest 13 points. Three-dimensional motion analyzer was OptiTrack (Acuity Inc.), and imaging was performed with 8 infrared cameras. The markers were affixed according to the plug-in gait model, and comfortable walking movements were analyzed and compared using SKYCOM. Those with more pronounced immobility were characterized by greater left-right asymmetry in lower limb motion, extremely low normal stride length, and gradual decrease in stride length. Although immobility itself is characteristic of PD and improvement is sought with pharmacotherapy, the high frequency of immobility also produced characteristic changes in lower limb movements. Muscle stiffness associated with immobility and disuse due to the continuation of daily life may have affected gait. We believe that early treatment with exercise therapy for immobility will help prevent the gait characteristic of immobility.

P11.07

Regenerating dopaminergic neural circuits in Parkinson's disease through transplantation of super-resistant human neurons

Beatrice Morin[*,1], Anne-Marie Castonguay[1], Julia Obergasteiger[1], Tiago Cardoso[1], Valérie Watters[2], Claude Gravel[1], Samer Hussein[2], Thomas Durcan[3], Martin Lévesque[1]*
[1] CERVO Brain Research Centre, Quebec, Quebec, Canada
[2] St. Patrick Research Group in Basic Oncology, Oncology Division of CHU de Québec-Université Laval Research Center, Quebec, Quebec, Canada
[3] The Neuro - Montreal Neurological Institute, Montreal, Quebce, Canada

PD is a chronic neurodegenerative disease characterized by the extensive loss of dopamine (DA) neurons in the substantia nigra pars compacta through the accumulation of intraneuronal Lewy bodies containing misfolded fibrillar alpha-synuclein (aSyn). These toxic aggregates can spread the pathology to neighboring cells, contributing to disease progression. Neuroprotective therapy based on mini antibodies, such as single-chain variable fragments (scFv) is a promising treatment. They are efficient at an early stage of the disease when neurodegeneration is not too advanced. Cell replacement therapy is then an attractive option for more advanced PD to restore dopaminergic innervation. Although recent advances facilitate cell replacement therapy for PD, there are still hurdles to overcome. One major challenge is the survival of the grafted neurons in a brain environment containing toxic protein aggregates. Analysis of post-mortem brains from PD patients revealed that the grafted neurons acquire aSyn pathology, thus limiting their efficacy and survival, especially in the long term. Our main objective is to develop strategies to promote survival of transplanted DA neurons to restore the DA deficiencies efficiently. Here, we tested the efficacy of secreted and non-secreted scFvs against aSyn to protect human induced pluripotent stem cell-derived neurons from the spread of pS129aSyn pathology. To model PD, we used unilateral striatal injection of aSyn preformed fibrils (PFF). To control the production of our scFvs, we used the TeT-ON system. This system allows the expression of the scFv only in the presence of tetracycline or one of its analogs, such as doxycycline (DOX). To evaluate the efficiency of scFv in protecting grafted cells, we transplanted differentiated DA neurons into mice previously injected with PFF. DOX was then added to water to activate scFv transcription. Our preliminary data suggest that our scFvs can protect the graft from aSyn pathology. We believe that this neuro-regenerative approach will lead to a significant advance in cell replacement therapies for PD.

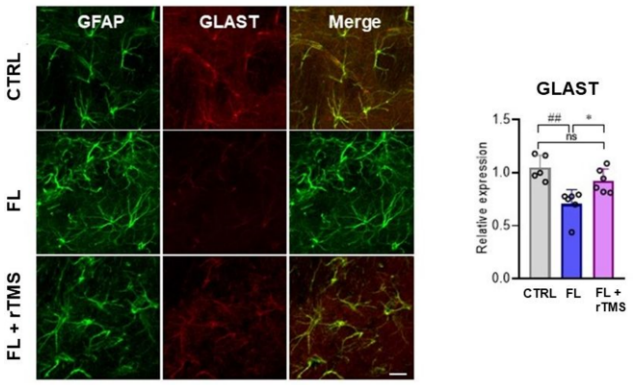
P11.08

Effects of magnetic stimulation in the rat brain plasticity: New insight in the astrocytes function in experimental parkinsonism

Giuseppina Natale[*,1], Maria De Carluccio[1], Maria Teresa Viscomi[1], Veronica Ghiglieri[2]*
[1] Università Cattolica del Sacro Cuore, Rome, Italy
[2] San Raffaele University, Rome, Italy

Excessive glutamatergic transmission in the nucleus striatum, the main input nucleus of the basal ganglia circuit, is implicated in the progression of Parkinson's disease (PD). Impaired glutamate uptake entails alterations of synaptic neurotransmission, neuronal excitotoxicity, and astro- and microgliosis. Reactive glial cells initiate a series of neuroinflammatory responses that increasing evidence indicates play a role in the early phases of neurodegenerative

diseases. Astrocytes, the predominant glia population in the central nervous system, can maintain glutamate homeostasis, protecting from neuronal excitotoxicity through the astrocytic glutamate transporter-1 (GLT-1) and glutamate–aspartate transporter (GLAST). Alterations in these transporters' expression have been reported as responsible for a perturbed astrocytic glutamate uptake function in both patients and experimental models of PD. Repetitive transcranial magnetic stimulation (rTMS) is a pain-free and non-invasive brain stimulation technique that allows functional recovery in the parkinsonian condition, characterized by aberrant forms of synaptic plasticity. Even at low intensities, rTMS has been shown to modulate neuronal plasticity and to influence, directly or indirectly, the activity of neurons and non-neuronal cells, communally known as glia. As PD is associated with decreased astrocytes functionality, rTMS application in the experimental condition may induce neuroprotection and, thus, recover synaptic plasticity and reduce peculiar symptoms of the disease. In this context, the objective of the present study was to explore the effects of rTMS on glial populations in a late symptomatic animal model of PD, highlighting the significant changes in the phenotype and function of astrocytes after the treatment. Morphological analysis from 6-OHDA-fully-lesioned rats showed that astrocytes are the most responsive glial cells after an in vivo acute rTMS treatment. In addition, this stimulation induced an increase of GLAST expression via ph-CREB activation, suggesting that astrocytes may have a crucial role in removing excessive extracellular glutamate in pathological conditions. These findings uncover a previously unknown role of iTBS on astrocyte modulation, advancing our understanding of the mechanism involved in rTMS neuroprotection. Overall, our study supports the view that correcting the altered properties of astrocytes is an appealing strategy for treating brain diseases characterized by a powerful neuroinflammation response, such as PD.



COMPREHENSIVE CARE: Caregiving, relationships, respite care, families

P12.01

Time critical medication on time every time: A right for all people with Parkinson's

Clare Addison[*1], *Jonny Acheson*[2], *Garth Ravenhill*[3], *Tincy Jose*[4], *Cormac Mehigan*[5], *Claire Leman*[6], *Ed Kirkham*[7], *Andrew Perkins*[8]
[1] Surrey and Sussex Healthcare NHS Trust, Oxted, Surrey, United Kingdom
[2] University Hospitals of Leicester NHS Trust, Leicester, Leicestershire, United Kingdom
[3] Retired from Norfolk and Norwich University Hospital, Norwich, United Kingdom
[4] Queen Elizabeth Hospitals NHS Trust, Kings Lynn, Norfolk, United Kingdom
[5] University Hospital Limerick, Dooradoyle, Co Limerick, Ireland
[6] NHS Dorset CCG, Dorset, Dorset, United Kingdom
[7] West Suffolk NHS Foundation Trust, Bury St Edmonds, Suffolk, United Kingdom
[8] Retired GP NHS Wakefield CCG, Wakefield, West Yorkshire, United Kingdom

The importance of managing time critical Parkinson's medication in NHS Hospitals across the UK is currently not fully appreciated, meaning that patients are not always getting these medications exactly when they need them. Time critical medication should be taken within 30 minutes of its prescribed time.
Failure to do so causes harm to patients living with Parkinson's (PD) as it disrupts what is usually a very complex bespoke medication regime designed to optimise that individuals motor and non-motor function. This often means the patient needs to spend longer in hospital while the symptoms that have been disrupted, are stabilised.
A small group of NHS professionals have launched a campaign driven by their own experiences of living with PD, and being dependant on time critical medication, to raise awareness of this important aspect of patient safety and care. The aim is to use their influence and credibility as healthcare professionals to educate colleagues across all health systems, and advocate for the wider Parkinson's community.
The launch on World Parkinson's Day 2022 of their video about Time Critical Medication on social media, and sent to senior healthcare executives asking for their pledge as leaders of change, has resulted in a whole system awakening to this vital agenda. With now over 50% of all acute NHS Trusts and 100% of all Ambulance Trusts committed to improving this aspect of their caring, with endorsement by Chief Nurses and senior executives across all four nations.
Slowly and steadily, using a top down and bottom-up approach, links are now being strengthened through partnership working, involving NHS England, the Health Boards of Scotland, Wales and Northern Ireland, Parkinson's UK, the Parkinson's Excellence Network and the patient voice, as together the work to address this need is developed and implemented. Influencing change takes time, but the journey has begun.
The power of the patient in influencing care quality and inspiring stakeholders is not to be underestimated.

P12.02

Some data on caregiving in advanced PD patients from Peru
Cintia Margoth Armas Puente*, Luis Torres, Yesenia Nunez, Miriam Velez, Gabriela Gushiken, Marcela Alvarado, Danilo Sanchez, Hugo Estrada, Rafael Suarez, Carlos Cosentino
Instituto Nacional de Ciencias Neurológicas, Lima, Peru

Background: Advanced Parkinson disease usually require assistance for daily living activities (DLA) and for accomplish adherence to treatment and caregivers play an important role. Little is known about these issues in advanced PD patients from Peru.
Methods: We reviewed the charts of PD outpatients with a disease duration of at least ten years followed regularly in our department. We tried to collect data about whether the patients need partial or full assistance in DLA and who is in charge of administrate anti-parkinsonian medication properly.
Results: We identified seventy-seven patients who fulfilled these criteria. Forty- one (53.2%) men and 36 women (46.8%). Mean age was 68 y-o (range 40-90). Mean disease duration was fourteen years (range 10 to 39 years). Nine patients were in Hoehn-Yahr stage II, 37 patients were in stage III, 23 in stage IV and 8 in stage V. Thirty -two patients (41.5%) were married; 14 patients (18.1%) were single, 13 (16.9%) were cohabitants and 19 patients (26.7%) were either widow or divorced.
Twenty-one patients (27.3%) needed no assistance at all for their DLA, 7 (9%) needed partial assistance and 49 patients (63.7%) needed a total assistance. This assistance was distributed into the espouse (33%), sons/daughters (24 %), and/or a caregiver with no parenthood with the patients.
Thirty-four patients (44.15%) admitted being in charge by themselves of their medication administration. Nine patients (11.6 %) needed partial assistance in this task and 34 (44.15%) needed complete assistance through a close family member or a non-relative caregiver.
Conclusions: As it was expected our results show that most patients with advanced PD need support for most DLA and this assistance is given mainly by close relatives who may not be fully trained. We think that this might be due to strong family relationships and cultural dynamics in Peru. Neurologists should be aware of potential consequences of caregiver burden and implement some preventive actions.

P12.03

Compassionate mind training for Parkinson's caregivers: A pilot study
Elena Berti[*,1], Silvia Della Morte[2], Carolina Lalli[2], Francesca Morgante[3], Nicola Modugno[4], Lucia Ricciardi[3]*
[1] St. George's University of London, United Kingdom, Roma, Italy
[2] ParkinZone Onlus, Roma, Italy
[3] Neurosciences Research Centre, Molecular and Clinical Sciences Research Institute, St George's University of London, London, United Kingdom; Medical Research Council Brain Network Dynamics Unit, Nuffield Department of Clinical Neurosciences, Oxford, United Kingdom, London, United Kingdom
[4] IRSSC Neuromed, Pozzilli, Italy

Introduction: Burden of Parkinson's disease (PD) nonmotor symptomatology impacts significantly caregiver's life quality, enduring physiological, psychological and emotional distress. PD caregivers can experience strain on maintaining relationships and validating their feelings. Emotional disregulation ultimately results in Heart Rate Variability (HRV) modifications. Compassion Focused Therapy (CFT) is a valid psychological approach to balance the three emotional systems: soothing (green), drive (blue) and threat (red) systems. CFT practices are effective at increasing HRV levels, heightening the parasympathetic response through the activation of the soothing system. Compassion has three-ways flow: for the self, for others and from others. CMT increases mindfulness and emotion regulation, building a compassionate self-perspective.
Objective: Using qualitative and physiological parameters, this pilot study aimed to test feasibility and effectiveness of CMT for PD caregivers.
Methods: Pre-post training tests: anxiety (STAI Y1-Y2), depression (BDI-II), caregiving burden (CBI) and Self-Compassion Scale (SCS); HRV detection via wearable device (Polar H10) with 3 different stimuli (baseline, trigger, deep breathing) during interview with clinicians.
Post training: self report on energy disposal changes in emotional systems and satisfaction.
Attendance of 6-week online CMT with therapist, 2 hours once a week.
Results: 16 PD caregivers attended (6 M, 10 F, mean age 59.9 ±9.2, mean assistance duration 10.1 ±4.9).
Preliminary and qualitative results show significant pre/post gains in BDI-II (p=0.00000141 ±19,5) and SCS Self-kindness subscale (p=0.05 ±0.35). Reported improvement in the Emotional burden subscale (p=0.35 ±0.18) of the Caregiver Burden Inventory (CBI).
PD caregivers highlighted increasing levels of Compassion three-ways flow, particularly compassion towards the self.
85% of participants perceived a significant change of energy disposal through their emotional systems (soothing system increase and threat system decrease); 90% considered the training useful and would continue practicing.
Conclusion: Compassionate Mind Training is feasible and engaging for PD caregivers. Considerable reduction of depression levels observed. It appears to be effective at enhancing self-kindness and self-compassion in order to regulate emotions recognition and expression. Slight impact reported on caregiver's burden. Further analysis is binding to inquire results of clinical scales and physiological parameters.

P12.04

Care partner preparedness courses with the BC brain wellness program: Fulfilling unmet need
Elaine Book[*,1], Julia Handra[1], Lakshmi Menon[2], Amanda Cama[2]*
[1] University of British Columbia, Vancouver, British Columbia, Canada
[2] BC Brain Wellness Program, Vancouver, British Columbia, Canada

Rational: Quality of life and wellness for people with health conditions is often dependent on the support received from family and friends commonly referred to as care partners. Supporting the care partners in their role and in maintaining their own wellness is critical to the success of supporting the person with the health condition. However, care partners often report feeling ill prepared for the role, lacking knowledge and skills on how to provide care.
Method: Based on a self-management model, the BC Brain Wellness Program developed and delivered two 5-week virtual psychoeducational care partner courses: "Care Partner Preparedness Course: Building skills while making connections" and "Preparing for the Future, practically and emotionally". The courses were designed to address common unmet needs through presentations, question/answer periods and self-care practice experiences. For increased accessibility, recordings of the courses were posted online and were supplemented with handouts summarizing key takeaways.
Results: A diverse group of care partners (spouses, adult children, friends) attended the courses who had been providing care between one and ten plus years to people with a variety of neurological conditions. Evaluation surveys revealed that the format was

effective in meeting care partners' need for acquiring practical information and new coping strategies as well creating a space for connecting with others in a similar situation.
Conclusions: The value of creating care partner programs that address unmet needs and that are accessible remotely (to allow for attendance while still providing care) is apparent and critical to supporting care partners in their role. Participant testimonials support that knowledge gained while making connections and learning new coping strategies led to feeling more prepared in their care partner experience.

P12.05

Caregiving through the progression: Themes from Parkinson's care partners from early to advanced stage partners living with Parkinson's

Anne Brooks[1], Courtney Malburg[1], Adolfo Diaz[*,2]*
[1] Parkinson's Foundation, New York, NY, United States
[2] Parkinson's Foundation, Miami, FL, United States

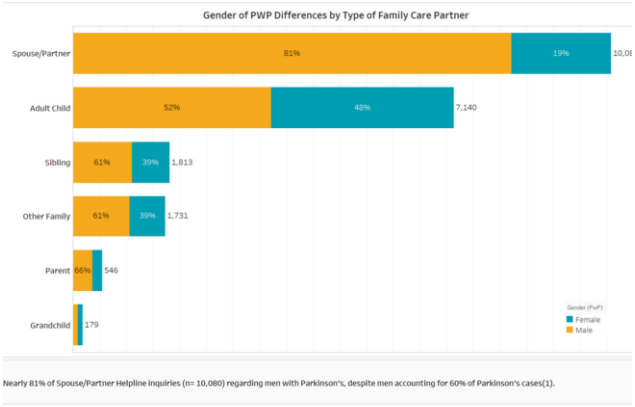
The Parkinson's Foundation conducted interviews with three Parkinson's Care Partners for the Care Partner Program online course "Caregiving Through the Progression." The following highlights the unique experiences of a diverse group of care partners throughout their Parkinson's journey.
Early Caregiving
Julia highlights the turbulent road to her husband Phil's diagnosis and the frustrations along the way. She also shares her experience of Black cultural norms around not disclosing a medical diagnosis and how this presented unique challenges, as well as the strength of their core family unit that allows for unique support.
Mid-stage Caregiving
Dick shares how he has prioritized his spiritual and emotional wellness as he cares for his wife Chris through regular support sessions through both his church and a men's group. He expresses his fears about the future as the disease progresses and how he and Chris have prioritized having conversations about advanced directives. He shares his experience as a male care partner expressing emotions in a healthy and productive way.
Advanced Caregiving
Edna shares the impact of her husband Mark's PD on their daughters, who grew up with Parkinson's as an everyday part of their childhood, and her perceived mistakes along the way as a mother and wife. She walks us through a realization that based on cultural norms as a Filipino woman in her 30's at the time of his diagnosis, she did not feel that divorce was an option though now, at 60, she recognizes that she would not want her daughters to feel that same obligations.
Self-care
Self-care is an important theme across all three interviews, but as expected it looks quite different in different contexts. Julia shares the role that partnership has played in her relationship with Phil, particularly as she initiated her own journey towards a healthier life. Dick acknowledges that he still finds it challenging to ask for help. Edna walks us through losing herself in the caregiving role, the moment she realized she needed help, and her "year of Edna" in her 20th year of caregiving which initiated a rare and revolutionary expression of self-care in advanced Parkinson's caregiving.

P12.06

Care partners in Parkinson's: Who calls the Parkinson's Foundation Helpline and why?

Adolfo Diaz, Anna Moreno, Sharon Metz, Linda Pituch, Jill McClure, Dianett Ojeda, Amanda Janicke, Michael Thompson, Colleen McKee, Leslie Mohr, Keisha Bermudez*
Parkinson's Foundation, Miami, FL, United States

The Parkinson's Foundation established its Helpline to provide the Parkinson's community with a place to find answers for general questions regarding Parkinson's disease, provide referrals to health professionals, support groups and wellness programs, provide educational materials in print and digital formats and to provide emotional support. Social workers, nurses and health educators staff the Helpline in English and Spanish Monday - Friday from 9am to 7pm EST.
This poster describes the reasons that care partners contact the Helpline and looks at whether there are gender differences in the reason for calling the Helpline, and the time since diagnosis, using data collected by the Helpline from phone and email inquiries during a seven-year period between 2016 to 2022.
The analysis found that:
• There were 21,489 cases of first-time callers and emailers where the gender of the person with Parkinson's was known. 46% were cases with a spouse/partner and 33% were from an adult child. This poster focuses on spouses/partners.
• People call the Helpline for many different reasons, and there were no major differences in spouses'/partners' reasons for contacting the Helpline or for the type of referrals given when analyzed by gender of the caller
• Nearly 81% of Spouse/Partner Helpline inquiries were regarding men with Parkinson's, despite men accounting for 60% of Parkinson's cases.
• Since most spouse/partner relationships are between men and women, spouses/partners of women with PD are mostly male, and they are contacting the Helpline less compared to female care partners. Other studies have seen similar results in both Parkinson's and other chronic conditions.
• Because male spouses/partners are contacting the Helpline less often than female, this study suggests a need for increased outreach toward male spouses/partners. The outreach could help male care partners gain information and resources to support their caregiving, and thus have a positive impact on the well-being of females with PD.
A similar poster reflecting a smaller sample of 14,189 cases (five years' worth of data), was submitted and accepted at the 2021 Movement Disorders Society Virtual Congress. The additional data is consistent with the original findings and further corroborates the conclusion.



P12.07

A call for more comprehensive approaches to Parkinson's, taking into account the voice of Uruguayan PwP and their families

*Paula Dodera**
Asociación Uruguaya de Parkinson y familiares, Montevideo, Uruguay

The Uruguayan Parkinson's Association (AUP) was born en 2002 in order to advocate for the rights of people with Parkinson's Disease (PD), particularly their access to health treatment. We also aim to contribute to the research on non-pharmacological interventions and their impact on the quality of life of people with PD (PwP) as well as their families. The AUP promotes rehabilitation, offering weekly activities, free of charge, led by a multidisciplinary team of volunteers.
Here, we present conclusions from a systematization on the psychological group methodology. These therapeutic groups (active since 2008) have the following goals: to aid in the process of accepting/adaptation to living with PD, and mourning the loss of health brought on by the diagnosis; to encourage mutual support by the group and the creation of new strategies to continue doing things they like; to work on interpersonal communication and expressing emotions, as well as providing a place to exchange relevant information about PD.
We made a thematic analysis taking into consideration contents from two therapeutic groups, one with PwP, the other with family members, during a period of two years. This aimed to comprehend the meanings attributed to Parkinson's, dependency, and care from their point-of-view.
In conclusion, we propose to understand PD as a complex and multi-dimensional situation, since it can impact on several aspects of everyday life. Therefore it is necessary an interdisciplinary, holistic approach.
There is need for more activities such as support groups, workshops, urban interventions, aiming to reflect on PD as a chronic illness in a lifecourse perspective, challenging the deficit model of disability, to deconstruct the negative prejudices against PD which produce discrimination and self-isolation.
For psy and social professionals, we suggest attending to the whole person instead of taking a patient-focused perspective. To understand "care" as a reciprocal relationship, between equals: it means to learn to accept help from others as well as giving aid. We could also help families or couples to avoid over-protection in their relationships, working out with each other what they expect and understand as proper care.

P12.08

Partnering with poise: Retention of cognitive, emotional, and physical benefits for care partners of people living with Parkinson's disease at 6 and 12 months after completion of an in-person Alexander-based group course

Monika Gross, BFA, RSME, m.AmSAT, m.ATI[*,1], Jaime Bellingham, M.S.*[2], Pepper Brisset*[2], Rajal G. Cohen, Ph.D, m.AmSAT*[2]
[1] The Poise Project, Candler, North Carolina, United States
[2] University of Idaho, Moscow, Idaho, United States

Objective: Care partners of people living with Parkinson's disease often experience emotional distress, role-engulfment, and decreased quality of life. We assessed the long-term effects of a standardized in-person group course based on Alexander technique (AT) principles, emphasizing whole-person health and taught in a fun, socially-engaging format.
Background: AT is a whole-person approach known for its physical benefits, including pain reduction and improved coordination. In addition, many studies have reported secondary non-physical benefits such as reduced anxiety and depression, increased wellbeing and confidence, and a greater sense of agency.
Design/Setting: Uncontrolled multi-site study. We delivered the program in community settings in seven North Carolina cities (USA); groups met for 90 minutes weekly over 10 weeks. Outcomes were assessed before and after the intervention and six and 12 months later.
Intervention: Practical self-regulation strategies to increase agency and pleasure during daily life were taught through enjoyable group, partnered, and individual activities. Teachers provided verbal, visual, and hands-on guidance. A unique feature of our program is the emphasis on individual choice. Participants practice interrupting their automatic reactions in a variety of practical daily contexts. Coursework includes embodied functional anatomy to improve body schema and facilitate skilled psychomotor functioning.
Outcome measures: Anonymous course evaluations, two measures of executive function, 12 self-report measures, and objective balance assessment.
Results: Participants enjoyed the course and interaction with other participants. Significantly improved pre→post: digit-span, Stroop, stress-burnout, emotional self-efficacy, positive affect, emotional distress, fear, mobility, MiniBESTest. Significantly improved pre→6mo: Stroop, stress-burnout, Zarit, emotional self-efficacy, positive affect, fear, fatigue, mobility, MiniBESTest. Significantly improved pre→12mo: Stroop, stress burnout, mindfulness & awareness, emotional self-efficacy, positive affect, emotional distress, fear, mobility, Mini-BESTest. Significantly improved post→12mo: Stroop. Not significantly improved at any time point: overall self-efficacy, perceived stress, pain interference. Inferior post→12mo: perceived stress and digit span backward.
Conclusion: Partnering with Poise, a fun, replicable AT-based group course for care partners of people living with neurodegenerative disease, shows promise as a self-management approach with long-term retention of benefits. Eight of nine significantly improved post-course measurements were maintained at 12 months. Further study with a randomized control group is merited.
Funding: Parkinson's Foundation, American Society for the Alexander Technique.

P12.09

Supporting the journey to empowerment for people with Parkinson's through the person-centred lens of those living with Parkinson's

Julie Jones[*,1], Alison Williams*[2]
[1] Robert Gordon University, Aberdeen, Aberdeenshire, United Kingdom
[2] Parkinson's UK -Edinburgh Branch, Edinburgh, Lothians, United Kingdom

A therapeutic challenge arises when, consciously or unconsciously, a person relinquishes their active sense of personal autonomy for the passive role of 'patient'. This is particularly problematic in Parkinson's, an incurable neurodegenerative condition, but where a good quality of life is possible through patient self-efficacy and empowerment.
Aims: To explore through secondary data analysis 1) people with Parkinson's experiences from diagnosis to living with Parkinson's, including enabling and hindering factors for successful living with Parkinson's; and 2) the role and impact of healthcare professionals within this journey.
Approach: The data were generated originally as part of a Live Project marketing exercise conducted by undergraduate marketing

students. Secondary analysis of this data was co-constructed by three people living with Parkinson's seeking to understand the impact of a Parkinson's diagnosis, and exploring internal and external factors influencing development of effective long term coping strategies.
Findings: Themes arising from this secondary analysis suggest that people with Parkinson's transition through four distinct stages to achieve empowerment, with progression and regression influenced by multiple variables, highlighting that the journey is not linear. Instrumental to progression is timely support from the Parkinson's community, healthcare professionals and peers. Levels of empowerment are associated with people with Parkinson's capacity to control their own management, and, crucially, the willingness and skills of healthcare professionals to adopt and encourage a partnership approach, grounded in person-centred practice. Paternalistic approaches reinforced patients' learned helplessness and deference, which risked blocking their journey towards self-empowered well-being.
Conclusions: Successful living depends upon developing empowered individuals facilitated through timely access to Parkinson's specialist healthcare professionals, support networks and peers. We suggest that services be reconfigured to promote true person-centred care, in which healthcare professionals:
• Adopt a person-centred approach to healthcare, fostering partnership
• Value people with Parkinson's lived experience,
• Provide them with knowledge and strategies for self-management.

P12.10

Getting Real!®: Addressing the educational, support and planning needs of Parkinson's caregivers through virtual formats
*Anissa Mitchell**
PMD Alliance, Longwood, Florida, United States

Objective: Provide care partners (CP) with multiple virtual formats and tools to enhance disease-state knowledge and care of a person with Parkinson disease (PwP) including addressing experiences related to burden and strain.
Background: Caregiving education has greatly increased over the last several years, however, access to real, honest conversations with experts into understanding symptoms and management, including how they might practically care-plan at different phases of Parkinson disease (PD), leave much opportunity. Available resources may provide education but lack a supportive and directional component. Caregivers who feel unprepared for the demands of long-term caregiving may lack understanding in how to provide care and fail to perform advanced-care planning. Failure to secure support along with feeling isolated creates significant caregiver strain which may lead to earlier institutionalization of PwP's. Parkinson and Movement Disorder Alliance, a US-based advocacy organization offers resources to support, educate and equip CP's through Getting Real!®.
Method: Getting Real!® provides a variety of program formats and tools including live, and on-demand education featuring movement disorder experts, facilitated support groups, and resource toolkits to address disease state knowledge gaps, stage-based planning, and caregiving strain. Surveys were conducted to assess length of caregiving, level of knowledge, support, and strain as well as usefulness of toolkit resources.
Results: In an initial survey of CP's assessing educational needs and current level of strain, of 158 responses, 88 were spousal CP's and 81.4% were female. 38.6% had been caregiving 0-5 years, 27.8% 6-10 years, and 33.5% more than ten years. 31% report family is not supportive, 33.5% did not know how to access support and 27% lack understanding of medications. 74.6% feel uncertain what to do with their PwP, 75.9% feel stressed providing care and balancing responsibilities, and 58.8% feel strained when around their PwP. Additional surveys (n=12) related to usefulness of toolkit resources indicate 63.6% currently use the resources provided and 45.5% have shared the resources.
Conclusion: While education for CP's is available, many CP's are still challenged with translating into action, may have limited support and resources available to them. Continued focus on pragmatic education and barriers care partners face, along with support is warranted.

P12.11

Relationship of psychological, financial and societal factors to Parkinson's disease
Elpida Panagiotounakou, Anastasia Bougea, Nikolaos Papagiannakis, Athina-Maria Simitsi, Chrysa Chrysovitsanou, Christos Koros, Leonidas Stefanis*
National and Kapodistrian University of Athens, Athens, Greece

Background and Objective: The influence that psychological, financial and societal factors may have on the quality of life (QoL) of Parkinson's disease (PD) patients is largely under-examined. This study aims to evaluate psychological, financial and societal factors that influence Health-Related QoL of people with Parkinson's (PwP). The study was performed as part of the ALAMEDA project, funded by the EU (https://alamedaproject.eu/), in order to take these factors into account in the eventual evaluation of indices collected by digital applications for the progression of PD.
Method: This is a cross- sectional study of 45 participants with PD who attended the Outpatient Clinic of PD and Related Movement Disorders at Eginitio Hospital in Athens from September 2021 to December 2022. All participants performed a neuropsychological battery including socio-demographic questions, the Parkinson's Disease Questionnaire (PDQ-39), Beck Anxiety Inventory (BAI), the Perceived Stress Scale and the Index of Personal Economic Distress.
Results: A total of 45 patients (28 men/17 women, age median 64 years) completed the survey. Low-income PwP report more mobility difficulties and worse emotional well-being, as well as difficulties in activities of daily living. The unemployed PwP report that they experience stigma more strongly. Retired PwP report more bodily discomfort, lack of social support and difficulties in communication with others.
Conclusions: Low income was associated with motor disability, distress and poor wellbeing. Our findings provide targets for clinician intervention and future research on social support strategies to optimize QoL in PwP.

P12.12

Close contact for couples with Parkinsons
*Judith Sachs**
Anyone Can Move, Philadelphia, Pennsylvania, United States

Keywords: movement, communication, cueing, partnering, mood, fall prevention, activities of daily living
Objective: To assist couples living with a movement disorder by teaching partnered movement techniques and types of support and body reliance that will alleviate dissention between partners, improve mood, and prevent falls.
Methods: Couples living with a movement disorder are often taught that exercise is essential to help with the symptoms of this progressive disease. Consequently, physical therapy and exercise modalities are prescribed for the patient. But the carepartner is often left in the dark.

At the point where real physical assistance is needed, even more emotional connection has to be made. The sense of touch can create an intimate pathway for stronger partnerships, and additionally, can lead to more physical aptitude. Patients will fare better if their partner is close, and if they can be allied in more ways than traditional physical therapy allows.
The addition of a social worker to the staff offers a private way of discovering how new forms of touch, communication, collaboration and intimacy in long-married couples can be facilitated by this program.
ACTIVITIES INCLUDE

- Learning base of support and center of gravity
- Momentum and rhythm-based interventions
- Leaning and shifting weight
- Conversations in movement
- Bed rolling together
- Floor rolling together
- Walking on uneven surfaces
- Entrainment on the wall
- Bed to chair to floor and back (transfers)
- Assist with kneeling, crawling
- Tandem walking; skater's walk
- Dual-tasking (walk and talk; walk and play ball; Stroop test)

Results: CLOSE CONTACT FOR COUPLES® teaches partners to talk out moves and transfers, just as dance partners do when they begin to work on new choreography. Rather than muscling their partner out of bed, out of a car, or down the street, a couple can learn to exchange weight to accomplish these feats.
Conclusion: We can achieve success in getting people who may not have had success in moving alone to find rewards in moving with a partner. Communication facilitates better mood, more self-confidence, and improved movement. It allows partners to play equal roles of helper and the one who receives help. Their success together can draw them closer.

COMPREHENSIVE CARE: Exercise and physical activity

P13.01

Mobile health technology, exercise adherence and optimal nutrition post rehabilitation among people with Parkinson's disease (mHEXANUT) – A randomized controlled trial
Sigrid Ryeng Alnes[*,1], Ellisiv Lærum-Onsager[2], Asta Bye[1], Annette Vistven[3], Erika Franzén[4], Mette Holst[5], Therese Brovold[1]*
[1] Oslo Metropolitan University, Oslo, Norway
[2] Lovinseberg Diaconal University College, Oslo, Norway
[3] Unicare Fram Rehabilitation centre, Rykkin, Norway
[4] Karolinska Institutet, Stockholm, Sweden
[5] Aalborg University Hospital, Aalborg, Denmark

Background: Exercise and physical activity, as well as dietary advice that aims to maintain nutritional status, have shown positive effects on physical capacity and function in people with Parkinson's Disease (PD). Unfortunately, adherence with such self-management recommendations over time may be difficult. It is therefore a need for interventions that help facilitate self-management. To the best of our knowledge, no earlier studies have combined exercise and nutritional interventions with an individual self-management approach in PD. Thus, we aim to examine the effect of a six-month mobile health technology-based follow-up programme, focusing on self-management in exercise and nutrition, after an in-service interdisciplinary rehabilitation programme.
Methods: A single-blinded, two-group randomised controlled trial. Participants are adults aged 40 and above, with idiopathic PD, Hoehn-Yahr 1-3, living at home. The intervention group receives a monthly, individualized, digital conversation with a physical therapist, combined with use of an activity tracker. People at nutritional risk get additional digital-follow-up from a nutritional specialist. The control group receives usual care. The primary outcome is physical capacity, measured by 6-minute walk test (6MWT). Secondary outcomes are nutritional status, Health related quality of life (HRQOL), physical function and exercise adherence. All measurements are performed at baseline and after 3 and 6 months. Sample size, based on primary outcome, is set at 100 participants randomized into the two arms, including an estimated 20% drop out.
Results: Study inclusion started in May 2021, and we expect to finish inclusion by the end of January 2023. By January 2023, 71 participants have completed the testing at 6 months, with a drop out rate of 10%, five from each group.
Discussion: The globally increasing prevalence of PD and the potentially huge negative impact of the disease, both for the individual and the society, calls for evidence-based interventions that can increase motivation to stay active, promote adequate nutritional status and improve self-management in people with PD. The digital follow-up programme, based on evidence-based practice, has the potential to promote evidence-based decision-making and to empower people with PD to increase adherence to exercise and nutritional recommendations in their daily lives.

P13.03

Exercise = delay Parkinsons + keep mental health in check
*Isaac Jose Alvarez Torres**
AYPSG, Stewarton, United Kingdom

My name is Isaac Alvarez and had PD since December 2017 wen i get the diagnosis, I have been invited to talk to you about my recent experience doing the camino Frances (The french way, that run

from France Saint jean pie de port to Santiago de Compostela) just over 500 Miles
At consequence of covid got made redundant from my Job, so as a result decided to do the camino, starting on June 2021 the 26 of June to be more precise.
* the preparations started back on march 2020 it took over a year to do the planing and at times was looking to be finished before starting due to the ever changing situation with covid and travel restrictions.
* the walk take us along the north of Spain, beginning in France (saint jean pie de port and finishing at Santiago de Compostela and this was to be covered over 29 days
* After all the travel arrangements where done and change flights 4 times due to cancelations we finally managed to get on the road to Manchester from Glasgow by bus to get a flight to Madrid
* we arrived on Madrid on the 24 of June and stayed with friends till next day the 25, that our flight to Pamplona also cancel and leaving now later on the day meaning we where not able to arrived at saint Jean till 11 O'clock at night
* on the 26 we started the camino with mix emotions excitement and fear to failure, but was clear from the first day that with the team i have with me it was going to be possible as they push me every day to do
* it and never give up, remind me the caption on our t-shirts. if you want it you find a way if you don't you find an excuse help us to beat Parkinson's and find a cure
* the purpose of this walk was to raise awareness of onset Parkinson's and also some money for Parkinson's research and for AJPOG.

P13.04

Modulation of neural activity in response to dance training in Parkinson's: A case study

Judith Bek[*,1], Royze Simon[2], Katayoun Ghanai[2], Karolina Bearss[2], Rebecca Barnstaple[2], Rachel Bar[3], Joseph DeSouza[2]*
[1] University of Toronto, Toronto, Ontario, Canada
[2] York University, Toronto, Ontario, Canada
[3] Canada's National Ballet School, Toronto, Ontario, Canada

Introduction: Recent evidence suggests that long-term participation in dance could delay the progression of symptoms in people with mild Parkinson's, but little is known about the neurobiological mechanisms of dance in Parkinson's. The present case study used functional magnetic resonance imaging (fMRI) to investigate potential neuroplastic effects of dance in a 69-year-old male with mild Parkinson's attending weekly dance for Parkinson's classes over a period of 29 weeks.
Methods: Neural activations were measured with fMRI at four timepoints (pre-training, 11 weeks, 18 weeks, and 29 weeks), while the participant listened to music from the dance classes and imagined dancing. Blood-oxygen-level-dependent (BOLD) signal modulation associated with the dance imagery was examined using region-of-interest analysis across the four timepoints.
Results. Significant changes over time were found in the supplementary motor area, right and left superior temporal gyri, and the right insula.
Conclusion: The findings indicate that regular dance participation modulated neural activity in regions associated with motor planning and learning, auditory processing, rhythm, emotion, and multisensory integration. This suggests the potential for dance to have neuroplastic effects across multiple domains in people with Parkinson's. Analysis of neuroimaging data from a larger number of participants is needed to further understand and interpret these findings.

P13.05

The effects of table tennis training on dual task performance in Parkinson's disease: Protocol for a pilot study

Pere Bosch-Barceló[1], Maria Masbernat-Almenara[2], Filip Bellon[2], Francisco José Verdejo-Amengual[2], Ares Alcaina[2], Helena Fernández-Lago[*,1]*
[1] Universitat de Lleida, Biomedical Research Institute of Lleida Fundació Dr. Pifarré (IRBLleida), Lleida, Spain
[2] Universitat de Lleida, Lleida, Spain

Introduction: Table tennis is a popular sport worldwide that can become an enjoyable and motivational activity for people with Parkinson's Disease (PD). It is also a challenging activity due to its characteristics, which combine constant motor adjustments with prediction of game actions and planning of responses. This combination of motor and cognitive tasks is known as Dual Task, which is known to be affected in PD, affecting aspects such as gait and balance and increasing fall risk. Table tennis for people with Parkinson's Disease has shown both its feasibility and safety by previous pilot studies, but no research has looked at its effects on Dual Task performance and how it affects balance and cognition in people with PD.
Aims: To investigate the effects of tennis table training on postural stability and cognitive performance under Dual Task conditions in people with PD.
Methods: The design for this study is a 10-week pilot study with pre-post assessment. The target study sample will consist of 15 participants with PD that attend the table tennis training sessions at Club Tennis Taula Borges Blanques, in Lleida, Spain. The experimental group will follow 2 supervised table tennis training sessions per week of 120min each, based on previous pilot studies. Participants will be assessed at baseline before the start of the intervention and after finishing the 10 weeks of training. The assessment will comprise a set of variables that include UPDRS, MoCA, MiniBEST and performance on postural tasks during Single and Dual Task situations.
Discussion: The development of this pilot study can provide information on how tennis table training affects postural stability and cognitive performance during Dual Task conditions for people with PD, and whether this type of training is beneficial for improving the integration of motor and cognitive tasks.

P13.06

The effectiveness of 'motor-motor' and 'motor-cognitive' dual-task training interventions on balance in people with Parkinson's disease: A feasibility study

Nesibe Cakmak, Jenny Freeman, Camille Carroll, Lisa Bunn*
University of Plymouth, Plymouth, United Kingdom

Objective: To test the feasibility and acceptability of a novel home-based programme, and the feasibility of a randomised clinical trial that explores the impact of motor-motor (M-DTT) and cognitive motor (C-DTT) interventions on standing balance and walking.
Background: Balance impairment is a major problem in Parkinson's disease (PD), often manifested at a stage of mild to moderate disease severity. Dual-task training (DTT) has demonstrated to be effective in enhancing balance control. However, there is a lack of evidence about the superiority of M-DTT versus C-DTT for improving balance. Our scoping review highlighted published evidence about home-based DTT, but no studies which investigated and compared the effectiveness of M-DTT and C-DTT on balance in people with mild-moderate PD.
Methods: This feasibility study design incorporates analysis of process measures alongside an embedded qualitative component. Approximately 10 participants with mild-moderate PD will be

recruited through Parkinson's UK. To be eligible participants need a safe home training environment and a volunteer supporter to act as a home-based training buddy. Standing body sway and functional balance (using the MiniBESTest) will be assessed at baseline. Participants will be randomly allocated to either M-DTT or C-DTT intervention group. Both groups will undertake 30-minutes of training, three times a week for 6 weeks. Both interventions include a face-to-face first session followed by home-based sessions led by pre-recorded online training movies. MiniBESTest scores and total body sway speeds (as well as velocity in mediolateral and anteroposterior directions) will explore any trends in data per group. Process measures relating to feasibility will include adherence to the programme (%movies streamed, self-reported exercise training logs), and intervention acceptability (self-report questionnaire). Safety will be monitored through adverse event recording. End-exit semi-structured interviews with participants and their training buddy will further explore feasibility and acceptability of operational aspects of the trial. Qualitative data will be analysed using thematic analysis.
Anticipated Results: The findings of this study will inform an anticipated future randomized control trial which investigates the superiority of the effectiveness of M-DTT and C-DTT intervention on balance in people with PD.

P13.07

Immersive virtual reality exergame for patients with Parkinson's disease: Feasibility and potential benefits
Pablo Campo Prieto, Jose Maria Cancela Carral, Gustavo Rodriguez Fuentes*
Universidad de Vigo, Pontevedra, Spain

Background: Exercise therapies have shown good results in PD, as rehabilitation and maintenance of physical and functional capacities are crucial aspects in these patients. Rehabilitation activities that are more engaging, e.g., virtual reality (VR), can be more effective compared to conventional rehabilitation, since they can enhance adherence and long-term use. Exergames require the active participation of the user in performing movements and physical tasks that can reproduce the results of traditional rehabilitation strategies in PD. This study aimed to investigate the feasibility and potential benefits of an immersive virtual reality (IVR) exergame program in patients with PD.
Methods: A heterogeneous sample of 20 volunteers (15 men; 66,7 ± 9,2 years) diagnosed with PD (I-II Hoehn and Yahr stage) and belonging to the Vigo Association of Parkinson (Vigo, Spain) were part of the study and were allocated to control group (n=6) and experimental group (n=14). We provided an IVR hardware (HMD Meta Quest 2) and a commercial software (FitXR) to the intervention and all the sessions were guided and supervised by a physiotherapist. Participants underwent 16 sessions (2 times a week; 6 minutes of a boxing exergame per session). Five-repetition sit-to-stand test (FSTS), Tinetti test, handgrip, Timed up and go test (TUG) [single and dual-task (cognitive and physical) conditions], and 39-item Parkinson's Disease Questionnaire (PDQ-39) were evaluated before and after intervention. Safety was evaluated using the Simulator Sickness Questionnaire (SSQ) and usability with the System Usability Scale (SUS).
Results: No adverse effects were observed during or after the training sessions (no SSQ symptoms). Usability was high (98.04%). A significant improvement was observed in Tinetti test total score ($p = 0.002$) and Tinetti test balance and gait scores ($p = 0.004$ and $p = 0.013$ respectively). TUG time and dual-task interferences showed positive changes, but these were only statistically significant in TUG dual task (physical-cognitive). No substantial changes were observed in FSTS and handgrip scores. Both groups generally maintain the PDQ-39 scores.
Conclusions: The results of our study support the use of this novel tool as a valid physical rehabilitation treatment in PD to improve balance parameters and reduce the risk of falls.

P13.08

Outdoor Adventure Program (OAP) for people with Parkinson's (PWP): Increasing activity through fun and salient community classes
*Joy Cochran PT, DPT, CEEAA**
JOY Explorations, Watertown, Wisconsin, United States

Background: Parkinson's Disease (PD) diagnosis often reduces expectations for community participation by: the PwP, their family, society, and even some healthcare provider(s). Evidence-based research highlights exercise principles which improve PD specific deficits so PwP can maintain or restore functional skills, minimizing the effect of PD on community involvement. Specialized PD community programs are often limited or not available in many geographic areas.
Objective: To help PwP live empowered, inspired, and active lives; and introduce the Activator® Poles to promote an ongoing active lifestyle and continued community participation with family and friends.
Methods: Group class 2x/week x12 weeks, plus 2 individual sessions for pre- and post- assessments. Program designed and led by a Doctor of Physical Therapy with specific PD certifications and experience. Small class sizes (~10) cultivated comradery and formation of an organic support group. Activities included evidence-based principles of high intensity aerobics, big amplitude, balance, strength, dual tasking, and flexibility training with a sport/game component such as hiking, kickball, baseball, basketball, and obstacle courses. Classes incorporated Activator® Poles proven to increase confidence, provide total body strengthening, improve balance and normalize gait. Sessions were conducted outside to simulate real world experiences and capture the benefits of sunshine, fresh air, and being in nature. Outcome measures collected: Trailmaking, 9 Hole Peg, Grip Strength, Core Strength, 1 minute Sit to Stand, Stand Prone Stand, 4 Square Step with & without Cognitive Task, 6 minute Walk, 10 meter Walk. The Parkinson Foundation Community Grant Program funded 20 participants; 10 have completed the program to date.

Results: 80% of the OAP graduates remain active in the class 3 months post program. All participants showed improvement in 4 or more of the outcome measures, many achieving scores within healthy older adult age/gender norms. Surveys indicated that 100% of participants increased their knowledge of PD, had fun, and plan to use their Activator® Poles outside of class. 100% report the program met expectations with 70% noting it exceeded expectations.
Conclusion: The Outdoor Adventure Program for People with Parkinson is a viable and impactful community exercise program that brings PD specific classes to underserved areas.

P13.09

Impact of active gait training programs on gait under daily life conditions and quality of life in Parkinson's disease
Bettina Debû*[,1], Pierre Pelissier[2], Nicolas Vuillerme[1], Matthias Chardon[1], Valérie Fraix[3], Elena Moro[4]
[1] University Grenoble Alpes, Grenoble, France
[2] Grenoble Alpes University Hospital, Grenoble, France
[3] University Grenoble Alpes Hospital, Grenoble, France
[4] University Grenoble Alpes - University Grenoble Alpes Hospital, Grenoble, France

While the efficiency of physical activity (PA) programs to improve gait in people with Parkinson's Disease (PD) has been well established based on laboratory assessments, few studies have examined their actual impact on gait in daily life. Yet, some data suggest that laboratory measures of gait do not reliably reflect locomotor behavior in daily life. This raises the issue of the actual benefit of PA programs in patients' real life. Our research aims at shedding light on this issue.
Fifty participants with PD (H&Y stage < 3), and with or without cognitive issues (Montreal Cognitive Assessments score 20 to 30) will be randomly assigned to treadmill gait training or to Nordic walking training. Both programs will involve three weekly sessions for twelve weeks. Gait and quality of life will be assessed before, immediately after intervention, and three and six months after the end of the supervised training. Gait spatiotemporal parameters will be collected in the laboratory while the amounts of daily PA and steps will be measured at home during one week at each period, using actimetry.
We expect that the two programs will yield improvements of gait as measured in supervised settings, that the level of PA and number of daily steps collected at home will be increased in the two groups after the end of the training, and that patients' quality of life will be improved. Specific hypotheses are that the Nordic walking program will yield greater benefits than the treadmill training as reflected by the level of PA and number of daily steps collected at home. However, this superiority may be modulated by participants' level of cognitive function.
Our results will better inform on the actual benefits of PA training programs in daily life, and help better define the objectives and modalities of prescribed PA within the framework of multidisciplinary care. Moreover, the outcomes will contribute to a better knowledge of the mismatches between gait characteristics measured in the laboratory and in daily life, contributing to further refining the design of training programs for people with PD.

P13.10

Step variability is decreased during ice skating approach to a door amongst people living with Parkinson disease
Jon Doan[*,1], Brittany Mercier[1], Claudia Steinke[1], Natalie de Bruin[1], Lesley Brown[2]*
[1] University of Lethbridge, Lethbridge, AB, Canada
[2] Yukon University, Whitehorse, YT, Canada

Freezing of gait phenomenon amongst people living with Parkinson disease often manifests during locomotion towards or through a doorway, a deficit that may be associated with the division of attention between locomotion and obstacle navigation. Conversely, some locomotor patterns and movement visualizations have been associated with decreased freezing at gait initiation and locomotion, notably ice skating. The purpose of this experiment was to combine the positive paradoxical kinesia of ice skating with the known locomotor challenge doorway passage amongst people living with PD. We hypothesized that locomotor rates would be increased and step variability decreased for skating locomotion compared to walking locomotion through a doorway.
Thirteen people living with Parkinson Disease and eight age-matched older adult controls completed GAIT trials on ground in shoes and SKATE trials on ice in skates. All trials took place on a 12 m with pathway markers placed every 2 m. Half of the 10 trials in each locomotion condition were challenged by a doorway outline (opening of 0.9 m x 2.2 m with 0.3 m of solid structure surrounding the opening on all sides). The presentation of DOOR trials was randomized within the locomotion trials. Digital video was used to capture the trials, and locomotor kinematics were compared for DURING door (0.5 m prior to 0.5 m past door), BEFORE door (approach; 4.0 m to 0..5 m prior to door), and AFTER door (0.5 m to 2.5 m past the door) phases of GAIT and SKATE trials.
Numerous locomotor differences existed between GAIT and SKATE trials and between BEFORE, DURING, and AFTER door. PD skaters decreased maximum step length and increased average step length DURING door for SKATE trials, leading to lower step variability. In addition, people living with Parkinson disease used relatively high BEFORE door velocity and increased double-limb support strategy DURING door for SKATE trials, compared to either GAIT trials or no DOOR SKATE trials. While these locomotor strategies are uniquely enabled by the mechanics of ice skating, they do provide interesting inference for both stimulation and resolution of freezing of gait, and for the paradoxical kinesia of ice skating amongst people living with Parkinson disease.

P13.11

Effectiveness of trampoline training in people with Parkinson's: preliminary study results

Josefa Domingos[*,1], Joao Gomes[2], Julio Belo Fernandes[3], John Dean[4], Joao R Vaz[5], Catarina Godinho[5]*
[1] Radbound University, Lisbon, Portugal
[2] Instituto Universitário Egas Moniz, Centro de Investigação Interdisciplinar Egas Moniz (CiiEM), Egas Moniz School of Health and Science, Almada, Portugal., Almada, Portugal
[3] Grupo de Patologia Médica, Nutrição e Exercício Clínico (PaMNEC) do Centro de Investigação Interdisciplinar Egas Moniz (CiiEM), Portugal., Almada, Portugal
[4] Triad Health AI, Aurora, CO, United States, Aurora, CO, United States
[5] Egas Moniz Physiotherapy Clinic and Research Centre, Centro de Investigação Interdisciplinar Egas Moniz (CiiEM), Portugal., Almada, Portugal

Background: Physical exercise is known to positively impact people with Parkinson's disease (PD) both in motor and non-motor domains. Activities that challenge balance will better impact gait and falls in PD. Trampoline training intervention can challenge the individual's control of balance to unexpected variations in their center-of-mass positioning while creating a safe environment in case of falling.
Goal: To investigate the clinical benefits, safety, and satisfaction of trampoline training in people with PD.
Methods: Participants underwent trampoline training three times a week for eight weeks (1-hour sessions). We recruited participants diagnosed with idiopathic PD, in stage 2-4 Hoehn and Yahr, with a clinical history of gait deficits and a fall history (at least one fall in the last six months) from a patient association. The intervention was led by specialized physiotherapists that provided progressive, challenging training and guaranteed safety. Participants were assessed at baseline and immediately after the intervention with a battery of tests. Preliminary results report on balance (Mini-BEST Test), fear of falling (Falls Efficacy Scale), balance confidence, walking ability and speed and quality of life (PDQ-8), cognition (Montreal Cognitive Assessment). and satisfaction with the program.
Results: Twenty-five people with PD (age: 69.3 ± 10.2 years; disease duration: 7.6 ± 5.6 years) participated. We observed significant improvements from baseline to post-intervention (T-test) for our primary outcomes –and– with participants exhibiting less fear of falling FES-I ($p < 0.001$) and better performance Mini-BEST ($p = 0.003$) post-intervention, respectively. We observed additional improvements in secondary outcomes, specifically Timed Up & Go (TUG) ($p = 0.003$), TUG Motor ($p = 0.001$), TUG Motor & Cognitive ($p < 0.001$), and Quality of Life ($p < 0.001$). No significant differences in the TUG Cognitive ($p = 0.069$) and MoCA ($p = 0.45$). Participants reported satisfaction with the training program through a self-assessment questionnaire, and adverse effects were mild (e.g., "feeling tired").
Conclusion: Our preliminary results show that trampoline training improves balance, walking ability, and quality of life in people with PD. Implementing such programs in community settings is feasible, safe, and has high satisfaction and adherence.

P13.12

Online zumba gold for people with Parkinson's disease: Acceptability study

Josefa Domingos[*,1], Sonia Gow[1], John Dean[2], Catarina Godinho[3], Julio Fernandes[4], Drew Falconer[1]*
[1] Inova Parkinson's and Movement Disorders Center, Alexandria, VA, USA., Alexandria, Virginia, United States
[2] Triad Health AI, Aurora, CO, United States, Aurora, CO, United States
[3] Egas Moniz Physiotherapy Clinic and Research Centre, Centro de Investigação Interdisciplinar Egas Moniz (CiiEM), Portugal, Almada, Portugal, Portugal
[4] Grupo de Patologia Médica, Nutrição e Exercício Clínico (PaMNEC) do Centro de Investigação Interdisciplinar Egas Moniz (CiiEM), Portugal., Almada, Portugal, Portugal

Background: Dance can benefit people with Parkinson's disease (PD) by improving physical, cognitive, and social well-being. Diverse types of dances have been studied in PD, yet patients' acceptability and safety of Zumba gold dancing delivered online are unknown.
Aim: To evaluate if online Zumba Gold dancing is acceptable and safe for individuals with PD.
Methods: People with PD were invited to participate in an online program consisting of a weekly 45 min dance session using Zoom. Patient acceptability was assessed at four months with an online questionnaire assessing satisfaction, perceived benefits, barriers, and willingness to continue and recommend it to others. Questions about adverse effects assessed safety.
Results: 25 participants responded (92% above 60 years old, the average time since diagnosis of 7,04 years (range 1-25). Findings from the questionnaire showed that participants enjoyed participating, with 68% very satisfied, 24% satisfied, and 8% neutral. Nine participants referred they would prefer the class to be twice weekly. The top 5 aspects participants most liked included "it's a fun way to do exercise" (76%), "instructor's competency and engagement" (72%), "helps me to stay active in my own house" (64%) and "allows me to improve my physical and mental well-being" (52%) and "the amount of physical workout I get in these classes" (52%). The aspects less liked included "the difficulty to follow the movements sometimes" (28%), "the difficulties perceived while I'm dancing" (24%), "limited social aspect with other people with PD" (4%), "Class time overlaps with physiotherapy" (4%) and "medication not working well at that time" (4%). Barriers to participation included: Fluctuations in health (32%), session timing (28%), lack of time to exercise (40%), personal demotivation (20%), and job restrictions (4%). Participants perceived the program's benefits, with 52% considering it extremely helpful for the current management of health, 24% very helpful, and 24% somewhat helpful. There were no adverse events reported. All said they would continue to participate and recommend it to others.
Conclusions: Our findings support online Zumba Gold program is an acceptable and safe form of exercise for individuals with PD. The program represents a new means to influence long-term adherence to regular exercise in PD.

P13.13

U-Turn Parkinson's: Empowering the pursuit of wellness ... for free

*Tim Hague**
U-Turn Parkinson's / PD Avengers, Winnipeg, Manitoba, Canada

U-Turn Parkinson's (UTP) is a Parkinson's Wellness Centre with the mission to 'empower people living with Parkinson's in their pursuit of wellness'. The mandate is to provide a holistic, evidenced based package of services to the Parkinson's community at no charge. What sets UTP apart in this space: we are not a sports specific gym or studio; we are not focused on a singular therapy model and all services are free. We evaluate our community and ask 'What is needed?' then move to meet those needs, all from a charitable, no charge perspective. This funding model helps ensure that the needs of the whole community are met and not just those who have the economic means for the services.

While the Parkinson's (PD) community and literature are awash in discussion of the research indicating the benefits of exercise in mitigating the symptoms of PD there has been little done to actually provide the services needed. Some might question the need for specialized PD gyms or wellness centres such as UTP but one need look no further than the stigma (the weak voices, stuttering, gait difficulties, unpredictable on/off periods, the looks and uncomfortable questions, etc.) associated with the disease to understand why many simply will not attend regular facilities. U-Turn Parkinson's was founded in the spring of 2016 with the intent to provide the resources needed to meet the many and varied needs of the person living with PD.
U-Turn Parkinson's programming includes exercise options addressing strength and conditioning, functional movement training, fall prevention, range of movement, flexibility, agility, coordination, balance, music and voice therapy, support groups, and health education sessions. Classes are offered in person, live online and via our studio of on demand videos. All free of charge.
With memberships in the hundreds U-Turn Parkinson's has an array of PD Athletes who daily take up the challenge to compete with PD and win. We stand together in the firm belief that we can slow the disease and ultimately see it eliminated from life. #uturnpd

P13.14

Utilizing the Parkinson's foundation five domains of exercise professional competencies to map five criteria for exercise education: A pilot study

Lisa Hoffman[*1], Miriam Rafferty[2], Lauren Krasucki[1]*
[1] Parkinson's Foundation, New York, NY, United States
[2] Shirley Ryan AbilityLab, Northwestern University, Chicago, IL, United States

The Parkinson's Foundation sought to develop condition-specific competencies for exercise professionals (personal trainers and group exercise instructors) who work with people with Parkinson's. These competencies built upon exercise guidelines and professional competencies for healthy populations. The purpose of this abstract is to describe the development of the professional competencies, continuing education criteria, and pilot accreditation process.
Competency development involved: (1) conducting an environmental scan of exercise professional education in Parkinson's and synthesizing condition-specific exercise guidelines with an expert panel, (2) surveying people with Parkinson's, and (3) constructing the competencies and curriculum criteria with psychometricians. The pilot accreditation process for Parkinson's exercise education programs and continuing education courses includes an application as well as baseline, 6- and 12-month assessments.
Utilizing psychometricians and a leadership committee, we developed a pilot accreditation process for Parkinson's exercise education programs and continuing education courses to validate the competencies. The goal of the 12-month pilot accreditation process is to understand the manner in which education programs/courses adhere to the professional and program competencies based on their individual missions and how these accreditations can inform employers of Parkinson's exercise professionals in the quality of their staff. Owing to the heterogeneity of those providing Parkinson's exercise instruction (personal trainers, group exercise instructors, physical therapists, other healthcare professionals), the accreditation process included documentation to assist different categories of exercise and healthcare professionals to meet the knowledge, skills, and abilities required to achieve competence. The pilot accreditation process was evaluated using the RE-AIM (Reach, Effectiveness, Adoption, Implementation, Maintenance) framework. A heterogeneous group of seven non-profit and for-profit entities were invited to partake in the pilot process. Accredited entities complete initial, 6-, and 12-month reports to monitor their experience, and we surveyed the exercise professionals (learners) with respect to their knowledge and confidence at the end of their education program/course and after 3 months to document change in practice.
This abstract will include data from the initial and 6-month program reports in addition to the Competency Framework and Criteria for Exercise Education Programs & Courses.

P13.15

Pathway to Parkinson's foundation exercise education accreditation program & competencies for exercise professionals and exercise education programs & continuing education courses

Lisa Hoffman[*1], Miriam Rafferty[2]*
[1] Parkinson's Foundation, New York, NY, United States
[2] Shirley Ryan AbilityLab, Northwestern University, Chicago, IL, United States

Exercise professionals play an important role in the care of persons with Parkinson's (PwP), but to date, there have been no unified guidelines or procedures in place to ensure that these professionals are competent to work with PwP. This leads to great variability in the knowledge, skills, and abilities (KSAs) of exercise professionals and makes it difficult for individuals with Parkinson's and their healthcare providers to evaluate the safety and effectiveness of exercise programs and instructors.
The Parkinson's Foundation, in collaboration with psychometric methodologists, created a two-phase process that would a) develop KSAs to define competencies for exercise professionals and b) develop a framework for an accreditation program to recognize exercise education programs and courses. Methods included: (1) convening subject-matter experts, (2) consolidating recommended exercise guidelines, (3) surveying stakeholders, and (4) convening a competency development task force. The process aligned with professional standards in testing articulated in the accreditation standards published by the National Commission for Certifying Agencies (NCCA, 2014).
The results include competencies for Exercise Professionals to describe the KSAs needed to provide optimal individual or group exercise sessions for individuals with Parkinson's as well as competencies for Exercise Education Programs & Continuing Education Courses to support the curricular development of these entities. Both sets of competencies are organized into five domains: (1) Foundational Information on the Diagnosis and Treatment of Parkinson's Disease and the Role of Exercise, (2) Screening for People with Parkinson's Disease to Participate in Exercise, (3) Group and Individual Exercise Design for People with Parkinson's Disease, (4) Exercise Leadership for People with Parkinson's Disease: Human Behavior and Counseling, and (5) Interprofessional Communication and Program Development.
The competency framework served as the foundation for a process by which the Parkinson's Foundation will accredit education programs and courses that provide the knowledge and skills necessary to create a safe and effective exercise experience for persons with Parkinson's.

P13.16

An exploration of service users perceptions of the Parkinson's beat program

Julie Jones[*,1], *Yoon Irons*[2], *Alison Williams*[3], *Jo Holland*[4]
[1] Robert Gordon University, Aberdeen, Aberdeenshire, United Kingdom
[2] University of Derby, Derby, Derbyshire, United Kingdom
[3] Edinburgh Branch Parkinson's UK, Edinburgh, Lothian, United Kingdom
[4] Parkinson's UK, Inverness, Scottish Highlands, United Kingdom

Background: Parkinson's is associated with reduced activity participation which initiates a vicious cycle of inactivity. Inactivity predisposes people living with Parkinson's (PLwP) to muscle atrophy and joint stiffness, leading to movement dysfunction, postural instability, and ultimately reduced physical capacity. Access to exercise interventions to attenuate the rate of decline of physical capacity of PLwP is essential. Parkinson's Beats is a form of cardio drumming, which encompasses aerobic, flexibility, balance and strength exercise combined with rhythmical cues and preferred music choices. The scope of this project is to undertake a preliminary evaluation of Parkinson's Beats to gain insight into the attendees' perceptions of Parkinson's Beats, including on-going motivation for sustained participation, and the attendees' perception of the impact of participation. Data gathered from this study will determine whether future research into its effectiveness is warranted. This study has commenced and will complete in June 2023.
Methods: Invitations to take part will be circulated through local Parkinson's UK branches and support groups in Scotland and will be promoted via Parkinson's social media channels. Parkinson's Beats will be delivered weekly online and face-to-face for 6-months. The research team aims to recruit 50 PLwP. Participants will be complete an online survey prior to commencing, and again at three and six months. The survey will assess Quality of Life and Health and Wellbeing using the EQ-5D and Warwick Edinburgh Mental Wellbeing Scale. Perceived impact of participation in Parkinson's Beats will be measured using Patient Global Impression of Change Likert scale. Satisfaction will be assessed using bespoke satisfaction Likert scales using a bespoke satisfaction questionnaire designed by the study team. Focus groups will be conducted at 6-months to explore perceptions of Parkinson's Beats and explore attendees' views on the costs associated with attending the classes to inform future provision of Parkinson's Beats.
Results: Quantitative survey data will be analysed descriptively. Focus group data will be analysed using Thematic Analysis as described by Braun and Clarke.
Discussion: the outcome of this study will inform whether a future effectiveness study of Parkinson's Beats is warranted and will also inform whether any adaptation of Parkinson's Beats is warranted to optimise future delivery.

P13.17

The impact of different time in bed calculations on activity measures in people with Parkinson's disease

Robyn Lamont[*,1], *Dion Scott*[1], *Sjaan Gomersall*[2], *Sandra Brauer*[2]
[1] School of Health and Rehabilitation Sciences University of Queensland, St Lucia, QLD, Australia
[2] University of Queensland, St Lucia, QLD, Australia

Background and aim: To meet the recognized definitions of sedentary behaviour, waking hours need to be identified and separated from sleep in passively collected activity monitoring data. This study aimed to determine the impact of different time in bed calculations on activity and sedentary measures in a population of people with Parkinson's disease.
Methods: Eighty-one people with mild to moderate Parkinson's disease wore an ActivPALTM accelerometer continuously for seven days. Participants were asked to self-report the time they went to bed, time they got out of bed and any time the device was removed using a daily wear diary. Daily activity summaries were generated using Pal Technologies proprietary software. MatlabTM was then used to process data into average daily awake time activity summaries using three different time in bed calculations: 1) 24-hour pattern; 2) PAL CREATM calculated time in bed (TIB); and 3) participant self-reported TIB. Total awake time spent sitting, standing, walking, and walking at >100steps/minute, and the number of transitions up, transitions down and step count were calculated. Differences between the activity outcomes for each of the different TIB estimations were determined using paired t-tests, using participants self-reported TIB as the comparator.
Results: Eighty-two people (mean age 64.8 years, SD 8.1) with idiopathic Parkinson's disease (disease duration 3.8 years, SD 3.2) participated. Activity outcomes calculated using the 24-hour pattern were significantly higher on all activity measures ($P < 0.001$) except time spent walking at cadences of >100 steps/minute ($P = 0.641$). Activity outcomes calculated using PAL CREATM TIB significantly differed from self-reported TIB for standing time only ($p = 0.015$) with time spent walking nearing significance ($p = 0.055$).
Conclusions: Different methods can be used to determine sleep and waking hours from passively collected activity monitoring data, which may be important for populations with disturbed sleep patterns, such as people with Parkinson's disease. Depending on the outcomes of interest, automated methods may be used with little impact on accuracy of activity outcomes.

P13.18

Can activity monitors be used to accurately detect time in bed in people with Parkinson's disease?

Robyn Lamont[*,1], *Dion Scott*[2], *Sjaan Gomersall*[2], *Sandra Brauer*[2]
[1] School of Health and Rehabilitation Sciences University of Queensland, St Lucia, QLD, Australia
[2] University of Queensland, St Lucia, QLD, Australia

Background and aim: To meet definitions of sedentary behaviour, waking hours need to be identified and separated from sleep in passively collected activity monitoring data. Automated algorithms for identifying start and end of time in bed have shown promise for healthy adults. This study aimed to compare existing and customized automated algorithms and self-report with manual data inspection in people with Parkinson's disease.
Methods: Thirty people with Parkinson's disease wore the ActivPALTM for seven days. Participants also completed a daily wear diary to record any time they slept, or the device was removed. A 24-hour self-report use of time recall tool (MARCA) was also completed. Time to bed (TTB) and time out of bed (TOOB) were determined using six methods: self-report determined from the MARCA, visual inspection of activity data, automated PAL CREATM analysis, and three customized algorithms with varied duration of sit/lie time, thresholds for breaks in sit/lie time and step count to estimate TTB and TOOB. Manual inspection of the data was considered the gold standard. Accuracy was determined by calculating absolute mean difference (MD) between visual inspection and each of the other methods.
Results: Thirty people (mean age 63.4 years, SD 8.4) with idiopathic Parkinson's disease (disease duration 4.1 years, SD 3.2) participated. Visual inspection returned TTB and TOOB times that most closely match self-report with a MD of 27.7 minutes (SD 34.3) and 34.1 minutes (SD 44.6), respectively. MD for TTB ranged from 31.6 (SD 116.2) to 50.7 minutes (SD 130.2), with the PAL CREA

calculation on average closest to the visual inspection. MD's for TOOB were larger, ranging from 37.2 (SD 76.1) to 45.0 minutes (SD 80.8) with a customized algorithm using 5 hours of sit/lie time with breaks less than 15 minutes and with less than 50 steps performing best.

Conclusions: Automated methods of calculating TTB and TOOB are convenient and may offer better accuracy than relying on self-report alone. However, rules applied to estimate TTB, may differ from those that accurately estimate TOOB. For populations with disrupted sleep or movement patterns self-report should still be collected to provide context and improve accuracy.

P13.19

Effects of an online 12-week Tai Chi intervention on the electromyography activity of the lower-limb muscles of individuals with Parkinson's disease during obstacle crossing

Nok-Yeung Law, Jing Xian Li*
University of Ottawa, Ottawa, Canada

This study examined the effect of an online 12-week Tai Chi (TC) intervention on the neuromuscular activity of the lower-limb muscles in people with Parkinson's disease (PD). Three 60-minute online TC classes were offered weekly to PD participants in Hoehn & Yahr stage 1-3. The electromyography (EMG) activity of the PD participants' lower limb muscles was assessed pre- and post-intervention and compared to age- and sex-matched healthy controls (HC). The ratio of the peak EMG activity, integrated EMG (iEMG) activity, and the ratio of the peak EMG and iEMG antagonistic pairs of the left and right lower-limb muscles were measured while the participants crossed a 20-centimeter-high obstacle. The rectus femoris (RF), adductor longus (ADDL), tibialis anterior (TA), semitendinosus (ST), gluteus medius (GMed), tensor fasciae latae (TFL), medial and lateral gastrocnemius (MG), and lateral gastrocnemius (LG) muscles were examined. Seventeen PD participants were enrolled; fifteen completed the 12-week TC intervention (88% completion; mean age: 72.0). No significant group differences were found in sex, age, weight, height, duration of exercise (minutes/week), or frequency of exercise (days/week) between the two groups. The PD participants had significantly higher peak EMG ratios of ADDL, GMed, and TFL in the leading limb than the HCs ($p < 0.05$). After the 12-week TC intervention, the PD participants significantly increased iEMG activity ratio of the TA in the leading and trailing limbs, decreased iEMG activity ratio in the TFL of the leading limb ($p < 0.05$), and decreased peak EMG ratio of the GMed and ADDL muscle pairs in the trailing limb ($p < 0.05$) compared to pre-intervention. No significant differences in the iEMG of GMed and TFL were found; however, the peak EMG ratio of the ADDL in the leading and trailing limbs was significantly different between the two groups ($p < 0.05$). Moreover, the iEMG ratio of the GMed and ADDL muscle pairs of the leading limb significantly increased. The biomechanical-based online 12-week TC program significantly improved the muscle activity of the GMed, TFL, and TA of the PD participants. The proposed intervention could be recommended to people with PD to manage the neuromuscular function of their lower-limb muscles.

Table 1. Comparison of the ratio of antagonistic muscle pairs for peak EMG and iEMG values before and after TC-intervention in the PD group ($n = 15$) and the comparison of the measures between PD group and health control (HC) ($n = 15$).

		peak EMG of muscle pairs						iEMG of muscle pairs					
		RF-ST		GM-TA		GMed-ADDL		RF-ST		GM-TA		GMed-ADDL	
Group	Session												
PD	0w	LL: 3.24 (324%)	TL: 0.54 (54%)	LL: 1.64 (164%)	TL: 0.96 (96%)	LL: 1.95 (195%)	TL: 2.13 (213%)	LL: 2.12 (212%)	TL: 0.84 (84%)	LL: 1.63 (163%)	TL: 1.14 (114%)	LL: 0.94 (94%)	TL: 0.59 (59%)
	12w	LL: 1.05 (105%)	TL: 0.71 (71%)	LL: 0.19 (19%)	TL: 0.22 (22%)	LL: 0.17 (17%)	TL: 0.51 (51%)	LL: 1.00 (100%)	TL: 0.72 (72%)	LL: 0.68 (68%)	TL: 1.08 (108%)	LL: 0.56 (56%)	TL: 0.78 (78%)
	p-value[a]	.426	.522	.095	.304	.483	**.043***	.347	.072	.191	.287	.431	.169
HC	control	LL: 1.26 (126%)	TL: 1.39 (139%)	LL: 0.85 (85%)	TL: 0.29 (29%)	LL: 1.70 (170%)	TL: 2.13 (213%)	LL: 0.64 (64%)	TL: 0.98 (98%)	LL: 0.92 (92%)	TL: 1.10 (110%)	LL: 1.42 (142%)	TL: 1.29 (129%)
	p-value[b]	.394	.110	.662	.505	.950	.319	.815	**.002***	.284	.417	.557	.572
	p-value[c]	.216	.124	.147	.123	.576	.123	.816	.923	.234	.159	.479	**.036***

[a]pre- vs post- TC intervention test in PD participants using paired sample t-test, [b] PD participants pre- TC intervention test (0w) vs. HC participants, [c] PD participants post- TC intervention test (12w) vs. HC (control).
*$p < .05$, **$p < .001$.

P13.20

Physical exercise interventions on balance and postural stability in Parkinson's disease: A network meta-analysis

Patricia Lorenzo-García[1], Iván Cavero-Redondo[2], Sergio Nuñez de Arenas-Arroyo[1], María José Guzmán-Pavón[3], Susana Priego-Jiménez[4], Celia Álvarez-Bueno[1]*
[1] Universidad de Castilla - La Mancha, Cuenca, Spain
[2] Universidad Autónoma de Chile, Talca, Chile
[3] Universidad de Castilla - La Mancha, Toledo, Spain
[4] Hospital Virgen de la Luz, Cuenca, Spain

Balance and postural stability are two of the most challenging and debilitating features for patients with Parkinson's Disease (PD). Some physical exercise-based physiotherapy interventions have already demonstrated effectiveness in improving balance and postural stability in patients with PD, but the specific effect of each type of physical exercise has not been reported. Thus, this network meta-analysis is aimed to assess which type of physical exercise intervention has the most beneficial effect on balance and postural stability in patients with PD assessed using the Berg Balance Scale (BBS) and Mini Balance Evaluation Systems Test (MiniBESTest). A literature search was conducted until August 2022 to identify randomized controlled trials on the effect of physical exercise interventions on balance and postural stability. The network meta-analysis included pairwise and indirect comparisons of results in the BBS and MiniBESTest for eight categories of physical exercise: sensorimotor training (SMT) including endurance, SMT not including endurance, resistance, endurance, dance, alternative exercises, body weight supported (BWS), and balance. Moreover, we estimated the probability of each physical exercise intervention of being the most effective for each scale. We included 51 studies with a total of 2779 patients. The highest effect sizes (ES) for BBS were for alternative exercises (1.21; 95% CI: 0.62, 1.81), BWS interventions (1.31; 95% CI: 0.57, 2.05), dance (1.18; 95% CI: 0.33, 2.03) and SMT including endurance interventions (1.10; 95% CI: 0.46, 1.75) versus control groups. The probability of being the best treatment for BBS was 32.8% for BWS interventions and 24.0% for dance. Indirect comparisons showing the highest ES for the MiniBESTest were balance exercises (0.75; 95% CI: 0.46, 1.04) and resistance interventions (0.58; 95% CI: 0.10, 1.07) versus control groups. Dance (36.2%) and balance (28%) interventions showed the highest probability of being the best for improving the MiniBESTest. Our results show that alternative exercises, balance, dance, BWS interventions, resistance, and SMT including endurance interventions, are effective in improving balance and postural stability. More research is needed to establish new treatment strategies for the consequences of PD, determining the types of physical exercise interventions that provide the most benefit for all the conditions of PD.

P13.21

Immediate effects of forced exercise cycling on core outcomes in individuals with Parkinson's disease

Daniel Miner[*,1], Kenny Harrah[2], Kevin Chui[1]*
[1] Radford University Carilion, Roanoke, VA, United States
[2] Warm Hearth Village, Blacksburg, VA, United States

Background: Evidence is lacking for non-pharmacologic management of motor symptoms in people with Parkinson's Disease (PD). Recent evidence suggests high intensity exercise may improve the motor symptoms of PD to a similar degree as dopaminergic therapy. However, there is limited evidence regarding the immediate impact of exercise on movement-based performance. The purpose of this study was to examine immediate effects of a single bout of forced exercise cycling on motor symptoms of PD and performance on movement-based outcomes.
Methods:
Design: Cohort Study with repeated measures
Subjects: 13 males, 7 females with idiopathic PD; Age 72.9±5.8 years; Years Since Diagnosis 6.1±3.6; Hoehn & Yahr Stages 2-3; "ON" medication (n= 10), "OFF" medication (n=10)
Baseline Testing: All subjects were assessed on a core set of outcomes across multiple domains of motor function, mobility, and balance. Outcomes included scores on the Unified Parkinson's Disease Rating Scale- Motor Exam, Mini Balance Evaluation Systems Test, Timed Up and Go Test (TUG), TUG-Cognitive, Five Times Sit to Stand Test, 10m Walk Test, and 9-hole Peg Test
Intervention: All subjects completed a single forced exercise cycling session: 30 min. (active-assisted cycling, minimum cadence of 80 rpm) with a 5 min. warmup/cooldown at 50 rpm.
Post-test: All outcome measures were reassessed immediately following the intervention.
Results: When controlling for medication status, a single bout of forced exercise cycling resulted in immediate improvements in motor symptoms of PD, performance across multiple balance systems, dynamic gait activities, and upper extremity coordination.
Conclusions: Individuals with PD demonstrate immediate improvements in performance on core outcomes across multiple domains of function following a single bout of forced exercise cycling. Given the immediate impact on motor symptoms and performance on movement-based outcomes across multiple domains of function, forced exercise cycling should be further explored as a possible adjunctive therapy for individuals with PD.

P13.22

Expanding on the brain-body connection through free, symptom-driven Parkinson's fitness programming

*Nina Mosier**
Power for Parkinson's, Austin, TX, United States

Objective: To stimulate neuroplasticity in people with Parkinson's by intentionally integrating complex cognitive challenges in a unique multi-formatted evidence-based virtual and in-person exercise program with classes that are also designed to be fun, energetic, and highly engaging to encourage retention.
Methods: Established free fitness program for Parkinson's in Austin, TX called Power for Parkinson's (PFP) successfully developed through collaboration of an innovative interprofessional team, including highly skilled group fitness instructors, co-founders from geriatric medicine and counseling backgrounds whose experiences with fathers with PD provided guidance and insight, an innovative, mission-driven staff, and 400+ PwP over the course of 7 years. Through extensive experience with PwP and an in-depth understanding of PD, instructors honed their approaches to remedy specific Parkinson's symptoms. Ultimately, instructors developed 9 distinct exercise formats in response to participant feedback. Underlying each format is an emphasis on cognitive challenges, sequencing, fun, variations in each class (such as new props, movements, and music) and the opportunity to communicate directly with staff and the PD community. Using these teaching techniques, each instructor empowers participants with the knowledge as to why they are doing specific exercises. With the onset of the pandemic and the drive to keep the PD population active and engaged, the team rapidly transitioned to a virtual format. Maintaining a focus on neuroplasticity and social engagement, the varied formats adapted to virtual programming on YouTube to accommodate a growing global community.
Results: The more symptom driven and cognitively challenging the classes became, the more involved the global community became. Class formats evolved in response to feedback from the PFP community. Beginner classes were created to help people get started with an exercise regimen and the PFP style. Standing series, YOPD, and Relax & Reset (mindfulness and yoga) became regular offerings along with Move & Shout, Brain & Body, Strength & Balance, Dance Exercise and Vocal Strength classes. In-person classes rapidly re-expanded when pandemic worries lessened, with growing class sizes and high participant retention. YouTube virtual classes continue to grow in popularity.
As engagement increases, we will continue to collect participant feedback to guide our programming and keep our classes accessible, symptom-focused and PwP-centered.

P13.23

Evaluation of functional capacity, body composition and VO2max in Parkinson's disease: Pre and post physical activity practice

Marcos Moura[*,1], Dirce Sanches Rodrigues[2], Miguel Soares Conceição[3], Katia Lousada Gouvea[4], Luiz Arthur Moreira Nunes[4]*
[1] São Francisco University, Atibaia, São Paulo, Brazil
[2] UNIFAAT University Center, Atibaia, São Paulo, Brazil
[3] São Francisco University, Bragança Paulista, São Paulo, Brazil
[4] Raimunda Moura Program for Parkinson's Patients, Atibaia, São Paulo, Brazil

Objective: To compare body composition, functional capacity and Vo2max in patients with Parkinson's disease, after three and six months of physical activity. **Method:** To measure body composition, we used a bioimpedance; for gait and balance, the timed up and go; for functional capacity, the six-minute walk test, and for Vo2max or Fitmate-Pro. Before starting the physical activity plan, evaluations of the studied variables were performed and also after 3 and 6 months with the practice, to collect the results. The intervention with physical activity focused on: Aerobic capacities and Strength resistance. **Results:** The participants were identified with letters A,B,C,D,E,F,G,H. In the weight variable, individuals H and E

reduced, on average, 7.35 kg after physical activity. B, F, C and D increased muscle mass by an average of 1.17 kg after six months. As for fat mass E, H, C, B and G reduced about 2.68 kg, as well as the percentage of body fat. B and F increased body weight, however, gained muscle mass, with an average of 1.6Kg and reduced body fat by 0.85Kg. In cardiorespiratory capacity, the eight assessed improved their six-minute walk results. D,E,F before the practice of physical activity were well below the cutoff threshold, 180, 270 and 180 meters. In the six- minute walk test, participants D, F and H after six months had an increase of 300 meters. B, C and E increased by 200 meters. In TUG, all participants had a reduction in time. F obtained in the pre-test 27 seconds and after six months 6 seconds. Three participants reduced it from 5 or 7 seconds. Regarding Vo2Max, C and D in the pre-test obtained 5 METs, B and A 6 and 7 METs.The others had values of 8 to 12 METs. A,B,D,E, F,H after six months with physical activity improved Vo2Max, highlighting B and E that in the pre-test obtained 6 and 10 MET and later 15 and 14 MET. **Conclusion:** In body composition, there was maintenance and gain in muscle mass, reduction in the percentage of body fat, improvement in metabolic rate and functional capacity. Regarding Vo2max, there was an improvement in their cardiorespiratory capacity.

P13.24

Does exercise attenuate indicators of disease progression in Parkinson's disease? A systematic review with meta-analysis

Jiecheng Alex Li[1], Marte Loevaas[1], Catherine Guan[2], Lina Goh[1], Natalie Allen[1], Margaret Mak[3], Jinglei Lv[1], Serene Paul[,4]*
[1] The University of Sydney, Sydney, Australia
[2] Concord Repatriation General Hospital, Sydney, Australia
[3] The Hong Kong Polytechnic University, Hong Kong, Hong Kong
[4] The University of Sydney, The University of Sydney, NSW, Australia

Introduction: Exercise has many benefits for people with Parkinson's disease (PD) and has been suggested to modify PD progression, but robust evidence to support this is lacking. This systematic review (PROSPERO registration: CRD42020169999) investigated whether exercise may have neuroplastic effects indicative of attenuating PD progression.
Methods: Six databases were searched for randomised controlled trials (RCTs) that compared the effect of exercise to control (no or sham exercise) or to another form of exercise, on indicators of PD progression (eg, brain-derived neurotrophic factor (BDNF), brain activation and connectivity from functional magnetic resonance imaging, "off" Unified Parkinson Disease Rating Scale (UPDRS) scores). Quality of included RCTs was assessed using the Physiotherapy Evidence Database scale. Random-effect meta-analyses were performed where at least three comparable trials reported the same outcome. The remaining results were synthesised narratively.
Results: Forty exercise RCTs involving 2104 PD participants were included. The RCTs included a variety of exercise types (ie, aerobic, strength, balance, dance, aquatic or combined programs) and exercise dosages. Compared to control, there was low certainty evidence that exercise may improve "off" UPDRS motor scores (Hedge's g -0.39, 95% CI -0.65 to -0.13, p=.003). There was very low certainty evidence for increased BDNF concentration (Hedge's g 0.54, 95% CI 0.10 to 0.98, p=.02), meaning we are unsure whether exercise improves this outcome. Narrative synthesis for the remaining outcomes suggested that compared to control, exercise may have neuroplastic effects. The exercise versus exercise comparisons were too heterogenous to enable pooling of results.
Discussion: This review provides limited evidence that exercise may have an attenuating effect on potential markers of PD progression. Future large RCTs are warranted to explore differential effects by exercise type, dose and PD stage, and should report on a core set of outcomes indicative of PD progression.

P13.25

Use of inertial sensors to measure the impact of a therapeutic boxing program in people with PD in Chile.

Miguel Pino[,1], Pablo Burgos[2], Lorena Bernales[3], Pablo Roa[3]*
[1] Parkinson Union of the Bío Bío, Chile., Concepcion, Chile
[2] Universidad de Chile, Santiago, Chile
[3] NBP Chile, Concepción, Chile

Background: Balance problems in PD improves with exercise. We implemented a physical exercise program based on Box (neuroboxing) with promising clinical results. However, the instrumentalized clinical test could improve clinical change detection. We evaluated the safety and applicability of Opal inertial sensors to measure balance in people with PD participating in the neuroboxing program to use this technology in a clinical trial that will be performed in 2023.
Objectives: Determine the safety and applicability of the inertial sensors to measure balance in people with PD participating in a neuroboxing program in Concepción, Chile.
Methods: 24 patients with PD were recruited in Concepción, from May to December 2022. Patients participated in a neuroboxing program once a week during December 2022 and were evaluated with clinical tests during January 2023. Clinical test applied were UPDRS-III, MiniBEST Test, FGA, and CTSIB. Subscores were analyzed for the lowest performance. Based on the above, a set of instrumentalized measurements was selected in the Mobility Lab (APDM) software. A sample of 7 patients with PD was selected to carry out the measurements with sensors and to evaluate the technical applicability and safety.
Results: Mean age of the sample is 66.4 and the H&Y stage is II (n=3) and III (n=4). The most altered elements of postural control were APAs, sensory orientation, turning, unipodal stance and gait stability in double task. We used three inertial sensors (lumbar and both feet) in the following test: Sit to Stand (5x), Instrumented CTSIB, single leg stance, 360 degree turn (1x), TUG/TUG-DT and SAW, that Patients tolerated well. The recording had some interruptions because the software could not detect some motions, paticularly in the Sit To Stand (x5) test. Application time was 17.2 minutes per person on average. Tests with the worst performance were the left single leg stance and TUG-DT. Test with the best performance was sway with eyes open on firm surface.
Conclusions: The use of inertial sensors was safe and well tolerated by people with Parkinson's disease, that will be incorporated for measuring clinical progress in participants of non-contact boxing-based exercise programs of our Parkinson foundation in Concepción, Chile.

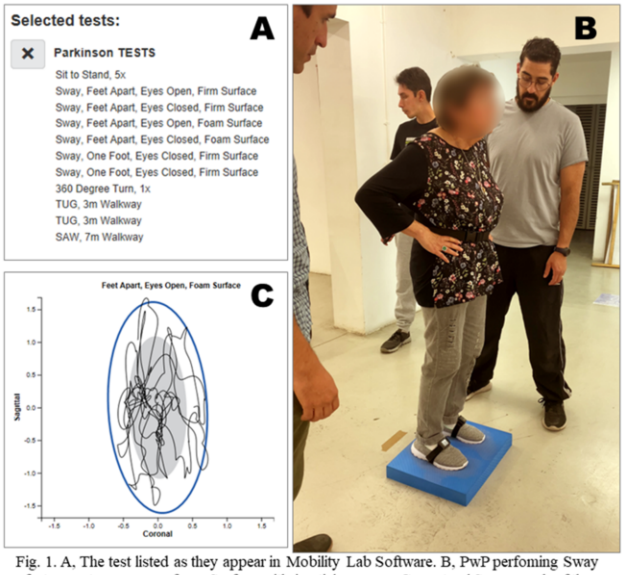


Fig. 1. A, The test listed as they appear in Mobility Lab Software. B, PwP perfoming Sway feet appart, eyes open, foam Surface with inertial sensors. C, postural Sway graph of the PwP in B.

P13.26

Relationship between habit strength of walking-related exercise behavior and real-world walking in persons with Parkinson disease

Franchino Porciuncula[*,1], Jenna Zajac[1], Nicholas Wendel[1], Dheepak Arumukhom Revi[1], Jaimie Gimis[1], Louis Awad[1], James Cavanaugh[2], Terry Ellis[1]*
[1] Boston University, Boston, MA, United States
[2] University of New England, Portland, ME, United States

Introduction/ purpose: The amplification of habitual daily walking-related exercise behavior is a key rehabilitation goal in persons with Parkinson disease (PD). Habit strength, an automaticity-based psychological determinant of health behaviors, substantially predicts physical activity in young healthy adults. How habit strength influences walking-related exercise behavior in persons with PD has not been investigated. In this preliminary study, we examined the relationship between habit strength and real-world walking activity in persons with PD.
Participants: Community-dwelling participants (N=12) with mild-to-moderate PD.
Method: Secondary analysis of baseline data of an ongoing study (NCT05421624) designed to examine the effects of a community-based walking program in persons with PD. At study entry, participants completed the Self-Report of Habit Index (SRHI), a widely used measure of habit strength in health behaviors. The SRHI included 12 questions related to the automaticity, frequency, and self-identity formed toward the behavior of "walking exercise." SRHI questions were scored on a Likert scale (0: strongly disagree to 10: strongly agree), averaged then reported as a total percentage score. Real-world walking activity was measured over 4 days using a research-grade step activity monitor (Modus Health, USA), providing metrics of walking amount (daily steps) and moderate walking intensity (daily minutes containing > 100 steps). Spearman's correlation was used to examine relationships between habit strength (SRHI total score) and daily mean values for each walking activity metric (amount, intensity).
Results/discussion: Participants had a mean SRHI score of 58.03 (28.07)%, walked 9,452 (3,752) daily steps, and accumulated 24.04 (22.66) daily minutes of moderate intensity walking. Habit was significantly correlated with daily steps (rs = 0.68, p =0.015) and moderate intensity minutes of walking (rs = 0.70, p =0.011).
Conclusion: Study findings demonstrate a link between self-reported habit strength of walking-related exercise and real-world walking activity in persons with PD.
Clinical implication: Habit-based assessments are needed to comprehensively understand the problem of diminished walking activity in PD. Study findings supported a habit-to-action link in persons with PD that warrants larger investigations on the role of habit formation as a mechanism for promoting walking-related behavior change.

P13.27

A retrospective evaluation of the brain and body fitness studio service on functional capacity and quality of life in people with neurological disorders

Joyce Ramos[*,1], Ranjay Chakraborty[1], Lance Dalleck[2], Kristina Sarunic[1], Jyoti Khadka[1], Tayla Haslam[3], Olivia Nassaris[3]*
[1] Flinders University, Adelaide, South Australia, Australia
[2] Western Colorado University, Gunnison, Colorado, United States
[3] The Hospital Research Foundation Parkinson's, Adelaide, South Australia, Australia

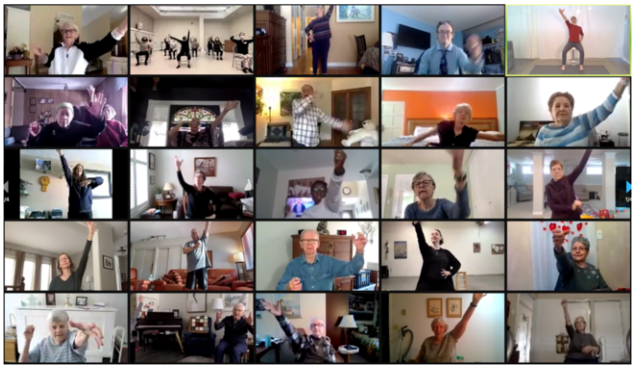
Background: People with neurological disorders (ND) are less physically active than the general population due to physical, sensory, and/or cognitive impairments. These individuals often feel intimidated to join mainstream health and wellness centers due to lack of specialised support for people with ND. The Brain and Body Fitness Studio (BBFS) is one of the first Accredited Exercise Physiologist-led interprofessional services in Adelaide South Australia to provide individualised evidence-based multimodal exercise prescription and social support for this population. This comprehensive retrospective study evaluated the impact of BBFS on functional capacity (FC) determined as the 6-min walk distance (6MWD) achieved during a 6-min walk test (6MWT), of its members with ND.
Methods: Sixty-two BBFS members (age, 66 ± 10 years; 60% male) with ND (85% Parkinson's Disease; average time since diagnosis, 4 years [IQR, 2 to 12 years]) and complete pre- and post-6-month clinical assessment of the primary outcome of the study, the 6MWD, were included in this retrospective analysis. A series of sub-analyses were also performed to investigate the effects of adherence to the recommended prescription of at least twice a week in the program (≥80 vs. <80% adherence), and disease stage (time since diagnosis; ≥6 vs. <6 years) on FC.
Results: Although there was no statistically significant change in 6MWD from pre- to post-6-month BBFS program (+15 ± 90 m, p = 0.19), a clinically meaningful improvement of >14 m was evident. Improvement in 6MWD was significantly greater in members who attended at least 80% of the recommended visits (≥80% visits, +37 ± 58 m; ≤80% visits, -1 ± 105 m, p=0.046). We also found a 6MWD improvement from pre- to post-6 months in those in the early years of their ND (<6 years since diagnosis, +39 ± 76 m), but not in those in the later years of their ND (≥6 years since diagnosis, -36 ± 123 m, between group difference, p=0.029).
Conclusion: A clinically meaningful 6MWD improvement may be elicited by services provided by BBFS in people with ND. Overall, the benefits appear to be more evident in members who attended the BBFS for at least 80% of the recommended visits and those who were in the early stage of their ND diagnosis.

P13.28

Evaluating dancing with Parkinson's (DWP) online dance classes

*Sarah Robichaud**
Dancing With Parkinsons, Toronto, Ontario, Canada

Background: Dancing With Parkinson's (DWP) is a not-for-profit organization based in Toronto, Canada that has been designing and delivering specialized dance classes for people with Parkinson's disease (PwP) since 2008 based on the Dance for PD Method. Prior to the COVID-19 pandemic, DWP provided 15 weekly in- person dance classes throughout the Toronto area. On March 15, 2020, DWP immediately began offering daily free online dance classes for the DWP community to keep them connected, active and engaged during the period of global isolation. The online classes also provided access to those in other regions of Canada and the US. The daily zoom classes continue today.
Objective: An evaluation was undertaken by The Evaluation Centre for Complex Health Interventions (TECCHI) at the University of Toronto to: 1) understand the benefits of the online classes, including impact on feelings of isolation, depression and anxiety, energy level, sleep, ease of daily activity; 2) understand the mechanisms by which the online classes might be conferring benefits to PwP; and, 3) obtain feedback from both clients and caregivers to improve the program.
Methods: Program participants were asked to complete a survey distributed in September 2020 which consisted of a series of closed- and open-ended questions.
Results: A total of 70 participants completed the survey, of whom 53% were PwP, 13% were caregivers of PwP, and 34% were other individuals who were neither PwP nor caregivers. Nearly 60% participated in 4 to 7 classes per week since March 2020. Participants reported improved energy levels (80%) and mobility (51%) plus reduced feelings of isolation (64%), depression (58%) and anxiety (51%). Moreover, 80% of respondents indicated that the virtual dance classes made the physical distancing during the pandemic more bearable. Similar results were observed for PwP, caregivers, and other individuals.
Conclusions: The virtual format of the DWP dance classes allow for increased participation. These online classes provided a clear positive impact during the pandemic. Interestingly, they were beneficial for both PwP and people without Parkinson's disease.



P13.29

Physical exercise and its impact on caregivers burden of people living with Parkinson's disease in a National Institute of Neurology and Neurosurgery from Mexico City

Diana Paulina Romero-Terán, Ana Jimena Hernandez-Medrano, María Fernanda Medina-Pérez, Andrea García-Hernández, Rodolfo Arturo Abundes-Corona, Amin Cervantes-Arriaga, Mayela Rodríguez-Violante*
National Institute of Neurology and Neurosurgery, Mexico City, Mexico City, Mexico

Introduction: Parkinson's disease (PD) is a systemic neurodegenerative disease with motor and non-motor symptoms that affect the quality of life (QoL) of people living with PD (PwP) (Santos García D, 2019). A comprehensive and integral care approach should include pharmacological and non-pharmacological strategies (Eggers C, 2018). Additionally, caregivers constitute a milestone in PwP wellbeing (Mosley P, 2017). There is strong evidence about the positive impact of physical exercise on motor symptoms, non-motor symptoms such as depression, and QoL (van der Kolk NM, 2019).
Objective: To describe the impact of physical exercise on motor and non-motor symptoms, QoL, and caregiver burden scales in Mexican people living with PD.
Methods: A prospective, cross-sectional, observational study was carried out. PwP were divided into two groups whether they reported practicing physical exercise on a regular basis or not. Mann-Whitney U test was used to compare: (i) PD motor dysfunction (Unified Parkinson's Disease Rating Scale [MDS-UPDRS3]); (ii) PD non-motor dysfunction (Non-motor symptoms scale [MDS-NMS]); (iii) impact on QoL (39-item Parkinson's Disease Questionnaire index [PDQi]), and (iv) the 22-item Zarit Caregiver Burden Inventory (ZCBI).
Results: 223 Mexican PwP (54.3% males; 63.28±11.74 years old) were included. 30% of PwP reported practicing physical exercise (see table 1). Mean MDS-UPDRS3, MDS-NMS, PDQi, and ZCBI scores were 33.74±15.56, 70.36±53.22, 22.28±14.15, and 25.24±13.10, respectively. PwP who exercise regularly had lower score in ZCBI compared to the no-exercise group (21.94±12.61 vs 26.64±13.09; p=0.018). There was no statistical difference in MDS-UPDRS3, MDS-NMS, PDQi (p=0.903, p=0.856, p=0.525). However, PDQi and ZCBI significantly correlated using Spearman's test (r=0.372, p<0.001).
Conclusions: Caregivers from Mexican PwP who do physical exercise regularly showed less burden using ZCBI. A positive correlation between caregiver burden and QoL in PwP might suggest the indirect impact of exercise on QoL. Exercise did not associate with lower motor and non-motor impairment. Further analysis is needed on our population to determine the factors contributing to this phenomenon.

Table 1. Proportion of different types of physical exercise among Mexican people living with Parkinson's disease (n=67).

Type of physical exercise	n (%)
Walking	30(13.5)
Biking	8(3.6)
Aerobic	7(3.2)
Yoga	6(2.7)
Weight training	5(2.2)
Tai-chi	2(0.9)
Others	
Dance	1(0.4)
Stretching	1(0.4)
Swimming	1(0.4)
Not specified	6(2.7)

P13.30

Case report: A dual tasking intervention for Parkinson's disease

*Darbe Schlosser**
Motorvation Foundation, Las Vegas, NV, United States

Background and aim: Dual tasking in Parkinson's disease (PD) can have negative impacts on set shifting and motor movement automaticity. Resources in the prefrontal cortex must be allocated effectively across executive functioning tasks and to assist in the automaticity of movement. Dual tasking interventions that target the prefrontal cortex to improve the allocation of these resources while providing strategies that address movement decrements is vital in thinking and moving well in Parkinson's disease.
Case presentation: The following case study illustrates a 49-year-old woman with young onset Parkinson's disease, marked by difficulties with attentional tasks requiring cognitive flexibility and learning and memory tasks requiring retrieval in the absence of prompts and cues. These difficulties were confirmed through a neuropsychological assessment summary evaluation on July 28th, 2022. This evaluation was performed as a screening to assess the patient's candidacy for deep brain stimulation (DBS). The results were presented to the patient on August 8th, and on Sept 7th the patient began virtual Brain Blast training with Motorvation. Brain Blast are virtual teams of 4 people who work together through a shared story that connects multiple mnemonics to the digits of Pi to improve working memory potential and cognitive flexibility. The goal is to increase awareness of how individual movement deteriorates when cognitive load is increased to effectively implement more optimal self-organization strategies.
The patient attended two group sessions per week and two solo sessions per month. In one month, she was able to recite from memory 51 digits of Pi while switching motor programs from marching to jogging. She was also able to rearrange the digits in multiple patterns retrieving them with 100 percent accuracy at different tempos while performing continuous and discrete movement skills.
Conclusion: This is the first case study demonstrating a cognitive and motor dual task intervention that is administered virtually using the methods of mathematics and storytelling while integrating motor learning principles that specifically address individual movement decrements and movement automaticity. The patient's improvement in retrieval accuracy, retrieval speed, and in set shifting while rearranging the digits demands further investigation of Brain Blast as an effective and easily accessible dual tasking intervention.

P13.32

Establishing the impact of aerobic exercise on biomarkers, mobility, and cognitive functioning of Parkinson's disease: A translational study

Isabel Soto[1], Vicki Nejtek[2], Gary Boehm[3], Paige Braden[3], Kelly Brice[3], Ella Kasanga[2], Robert McManus[2], Walter Navarrete-Barahona[2], Michael Salvatore[2]*
[1] University of North Texas Health Science Center, Fort Worth, TX, United States
[2] UNTHSC, Fort Worth, TX, United States
[3] TCU, Fort Worth, TX, United States

Parkinson's disease (PD) is a neurodegenerative disease characterized by a loss of mobility. A key premotor symptom of PD is cognitive decline, which often goes undetected in the prodromal stage. However, verifying cognitive loss in prodromal PD would benefit the patient if this loss was easier to recognize for treatment purposes. As an angle for detecting prodromal signs of PD, along with cognitive decline, we investigated whether the PD-associated biomarkers UCH-L1, GFAP, and s100b could provide a signature bio-cognitive profile. If so, these peripherally-obtained markers combined with cognitive testing would be highly valuable for enhancing diagnosis and therapeutic outcomes. Early and accurate disease detection would inform the clinician whether available non-pharmacological treatments (i.e., aerobic exercise) could help slow disease progression prior to initiating dopamine replacement therapy. While exercise may be a viable treatment for arresting PD progression, the CNS mechanisms associated with treatment efficacy are not well understood. To increase translation of CNS benefits of exercise, we implemented a cross-species translational paradigm between humans and a genetic PD rat model, the Pink1 knock-out (PKO) rat. Using a cross-sectional study design, we compared motor, cognitive and biomarker data from exercising and non-exercising early-stage PD (ESPD) subjects along with matched controls. We found that PD subjects participating in moderate intensity aerobic exercise showed significantly better cognitive flexibility and mobility than non-exercising PD subjects. Moreover, exercise also showed significantly higher serum concentrations of UCH-L1 ($p < 0.05$) and significantly lower concentrations of neuronal injury markers GFAP ($p < 0.0001$) and s100b ($p < 0.05$). To examine the translatability of the PKO rat, we longitudinally collected motor, cognitive data, and serum from PKO and wild-type (WT) rats and discovered premotor cognitive decline at 4 mo. old-with a decline in distance traveled at 6mo in PKO rats. Additionally, we found s100b

in PKO rats was significantly higher in SN (p=0.02) and serum (p=0.02) compared to WT rats. This is the first translational PD study to find that cognitive flexibility, mobility, UCH-LI, GFAP, and s100b are highly responsive to moderate intensity exercise in ESPD subjects. Our data also support that PKO rats may be a reliable model for cross-species translational research for ESPD.

P13.33

Post pandemic motor performance recovery among people with Parkinson's disease in a community-based wellness center

Elizabeth Stiles[*,1], Karen Jaffe[2], Cathe Schwartz[2], David Riley[3], Ben Rossi[2], Patrick Houlahan[2]*
[1] John Carroll University, University Heights, OH, United States
[2] InMotion, Beachwood, OH, United States
[3] David Riley MD, Beachwood, OH, United States

Objective: To present results of a series of performance assessments of participants in physical activity programs before and after Pandemic lockdown at a dedicated wellness center for Parkinson's disease.
Background: Previous evidence has established that exercise is effective for people with Parkinson's disease (PWP) in staving off motor and non-motor symptoms, and can ameliorate conditions such as dyskinesia and wearing-off resulting from long-term Parkinson's medication. Our research on exercise in a community center for PWP has shown short-term improvements or stability on a host of physical assessment measures used or adapted from the literature (Stiles et al, 2020; presented at WPC Kyoto (2019)).
Methods: Enrollment in the program is on-going. Participants all carried a diagnosis of PD and were able to complete gait and balance assessments independently. Enrollment was otherwise unselected. We include all clients who completed a pre-lockdown assessment and all 4 assessments after lockdown. Statistical significance was determined using paired Wilcoxon sign test (t-tests were not appropriate due to the presence of outliers).
Results: While the center was closed from March 2020 to May 2021, programs were broadcast so clients could continue to exercise using our protocol. When live workouts resumed after lockdown, however, our standard periodic assessments showed a significant decline in eight out of nine metrics assessing gait (Timed-Up-and-Go, Backward Mobility), balance (lateral balance test (Berg)), single arm press, single leg balance), functional mobility (sit-to-stand, rotational turns, stand-lie-stand) and cognition (Stroop). Our clients were subsequently assessed at 6-month intervals over the course of the next 16 months until October 2022. Comparing the first assessment after lockdown (May 2021) to the most recent assessment (October 2022), clients improved or stabilized on seven of nine assessments, halting the trend of deterioration in most gait and balance tests and showing strongest improvement in functional mobility.
Conclusions: Results suggest that group exercise programs for PWP in a community center have long-term beneficial effects and that clients who have discontinued or reduced their exercise regimens can return and halt or reverse disease progression.

Changes in Means Pre- Lockdown, First Assessment Post-Lockdown and Fourth Assessment Post-Lockdown

Assessment	n	Pre	Post	Post 4	Pre to Post	Post to Post 4
Functional Mobility						
Sit to Stand	28	40.4	32.2	34.1	362***	76.5*
Rotational Turns	27	53.9	44.9	47.4	343***	117.5*
Stand Lie Stand	25	4.8	6.5	6.2	22***	183
Gait						
Backward Mobility	27	15.8	19.9	19.9	22***	207
Forward Mobility (TUG)	28	9.3	10.5	12.1	182***	109@
Balance						
Standing Leg Balance	27	8.2	12.0	10.4	70.5*	163.5
Lateral Balance (Berg)	27	61.7	52.1	45.8	331.5***	219@
Standing Arm Press	27	33.1	30.7	32.4	214*	90.5*
Executive Function						
Stroop	27	29.1	27.2	28.3	250.5	145.5

Wilcoxon sign test (one-tailed, paired) (*p<=.05, **p<=.01, ***p<=.001, @p<.05 opposite of expected direction)

P13.34

Paradoxical relationship between handgrip strength performance and gait in subjects with Parkinson's disease

Eduardo Villamil-Cabello[*,1], Alfonso Jimenez-Gutierrez[2], Miguel Angel Fernandez-del-Olmo[1]*
[1] Universidad Rey Juan Carlos, Fuenlabrada, Spain
[2] Universidad Rey Juan Carlos & GoFit Lab, Fuenlabrada, Spain

Introduction: Handgrip strength deficit can be considered as an intrinsic feature of Parkinson's disease (PD). Individuals with worse performance in handgrip dynamometry, have worse scores in the UPDRS. Although, it has been suggested that the handgrip strength could be a predictor of PD severity there is not studies that explore the relationship between hand strength and gait performance. This is of relevance since gait disturbances are one of the principal and most incapacitating symptoms of PD. Therefore, we aimed to study the association between hand strength and kinematic gait parameters in a group of PD subjects.
Methods and procedure: Twenty-two subjects (14 males and 8 females, age 57±12) with PD (Hoehn & Yahr stages 1-3) participated in the study. All the patients were right-hand dominant, 8 with right-hand and 14 with left hand as the most affected hand.
Handgrip strength was measured in both hands through manual dynamometer (Vernier, 1Khz sample rate). Maximal peak of force (Pf), time to Pf (TPf), rate of force development (RFD) and Impulse (Imp) at 50 ms from the onset contraction (RFD0-50; Imp0-50), 50-100ms (RFD50-100; Imp50-100) and 100-200ms (RFD100-200; Imp100-200) were analysed for each hand.
Kinematic gait parameters were evaluated using an optical detection system (1 Khz sample rate) and software (v,1,11OptoGait; Microgait, Italy). Gait speed, step length and cadence were analysed at preferred speed and at maximal speed.
Results: There were not differences in the handgrip performance between the most and less affected hands. Maximal gait speed was significant and negative correlated with RFD50-100, RFD100-200 and Imp100-200 of the most affected hand ($t = -.45$, $p < 0.01$; $t = -.40$, $p < 0.05$; $t = -.39$, $p < 0.05$, respectively). Step length at maximal speed was also negative associated with RFD0-50 and Imp100-200 ($t = -.38$, $p < 0.05$; $t = -.31$, $p < 0.05$, respectively).

Conclusion: A greater ability to produce force more quickly in handgrip was associated with worse gait performance, suggesting that the relationship between handgrip performance and disease severity is more complex than previously described. Further research is need it in order to understand the nature of this relationship.

P13.35

Pass to Pass: Outdoor adventures with Parkinson's

A.C. Woolnough[*,1], Sarah Eltzman*[*,2], John Cunniff*[*,3], William Clugston*[*,4], Sandy Knudson*[*,4]*
[1] Pass to Pass, Sandpoint, ID, United States
[2] Pass to Pass, Mountain View, CA, United States
[3] Pass to Pass, Mountain, CA, United States
[4] Pass to Pass, Auburn, WA, United States

Pass to Pass is entering its 8th year of providing multi-day backpacking trips on the Pacific Crest Trail (and other trails) for persons with Parkinson's. A trip leader, support hikers and llamas (pack animals) round out each group. From a single hike in 2016 with four PWP hikers, the program expanded to eight hikes and forty PWP hikers in 2022. A total of 112 PWP hikers, from 20 states, have hiked a combined 7,549 miles.
There is no cost to participate. Hikers, however, must provide their own food and equipment--camp stools and sleeping pads are provided by PtP. Llamas carry about 35 pounds of gear and food for PwP hikers. Bill Meyer, a lifelong hiker with PD and DBS surgery, created Pass to Pass (utilizing pack animals and support hikers) to solve the problem of carrying a heavy pack with straps that interfered with his DBS generator.
Goals of the organization include building confidence, cultivating community, nourishing well-being, raising awareness and providing an achievable challenge.
John Muir might have said it best: In every walk with Nature one receives far more than he seeks.

COMPREHENSIVE CARE: Alternative & complementary therapies/Creativity

P14.01

CANNABAPA: CANNAbis-BAsed medicine for Parkinson's disease: patients' and health workers' points of view to pave the way

Tangui Barré[1], Christelle Baunez[*,2], Camelia Protopopescu[1], Fabienne Marcellin[1], Morgane Bureau[1], Géraldine Cazorla[1], Patrizia Carrieri[1]*
[1] Aix Marseille Univ, Inserm, IRD, SESSTIM, Sciences Economiques & Sociales de la Santé & Traitement de l'Information Médicale, ISSPAM, Marseille, France, Marseille, France
[2] Institut de Neurosciences de la Timone, UMR7289, Centre National de la Recherche Scientifique and Aix-Marseille Université, 13385 Marseille, France, Marseille, France

Background: People with Parkinson's disease (PD) suffer from an impaired quality of life. Existing treatments for PD have limitations in terms of efficacy and/or side-effects in the long term. Data from molecular, preclinical and few clinical studies suggest that cannabis and/or cannabidiol (CBD) have a great potential as therapeutic adjunct tools for PD management. Despite these potential benefits of cannabis-based medicine, PD was not retained as an indication for the French national experimentation on medical cannabis. To date, there is no data about cannabis or CBD use as self-medication and its impact on PD symptoms and quality of life among PD patients in France, where cannabis is illegal and CBD is legal. Along scientific evidence, how a potential medication is perceived is critical in order to be prescribed and taken. Our survey aims thus to document perceptions, positions and practices of both PD patients and healthcare professionals specialized in PD regarding cannabis and/or CBD use in France.
Methodology: A double-sided web-based survey targeting both PD patients (n=1000 expected) and concerned healthcare professionals (n=200 expected) will be used. Participants will be recruited through PD patients' and healthcare' networks. The main outcomes will be assessing acceptability of medical cannabis by PD patients and healthcare professionals, current use in PD patients, and its perceived/expected benefits and risks.
For both groups (i.e., patients and healthcare workers), we will conduct descriptive analyses for variables collected, including for specific sub-groups. For questions common to patients and healthcare workers, comparisons between the two groups will be carried out using appropriate statistical tests. We will explore the factors (demographics, symptom severity, perceptions etc.) associated with specific outcomes using generalised linear models with link function depending on the nature of the outcome.
Expected results: Our study will document the use of cannabis/CBD among PD patients and will provide an extensive overview of knowledge regarding cannabis and CBD, perceived barriers, benefits and harms by French PD patients and healthcare professionals. This work will provide a solid background for future studies and feed the debate around cannabis and PD by shedding light on the point of view of the most concerned.

P14.02

Patients with Parkinson's disease able of postural adaptation to the task performed but not as much as healthy controls

Cédrick Bonnet[*,1], Yann-Romain Kechabia[1], Arnaud Delval[2], Luc Defebvre[2]*
[1] SCALab, Villeneuve d'Ascq, France
[2] INSERM 1172, Lille, France

Introduction: Patients with Parkinson's disease (PD) have impaired postural and attentional abilities. As they oscillate more in the standing position, they need to more strongly reduce their postural oscillation than controls to succeed as well as controls in precise visual tasks (e.g. target location). During a precise visual task, we assumed that PD patients would be able of postural adaptation but not as efficient as controls.
Material and methods: Thirty-nine MP patients (± 59.32 years; H&Y I and II; ON) and forty healthy elderly controls (± 61.56 years) explored images of house rooms (100° visual angle) by performing two visual tasks: precise and non-precise (free viewing). The amplitude of displacement of the center of pressure (CoP) and of the body (Head-Neck-Pelvis) were analyzed.
Results: PD patients oscillated significantly more than controls in all tasks ($p=0.021$). For all participants, the amplitude of body and CoP displacements were reduced in the precise task vs. The non-precise ($p<0.001$). These reductions of displacements were greater in PD patients than in controls ($p=0.025$).
Discussion - Conclusion: In order to perform a specific visual task, PD patients at an early stages of their disease are not as able as controls to adapt their postural sway to the visual task performed. However, the positive point is that they are clearly still able to reduce their postural oscillations to perform the visual task as their reduction of postural sway is proportionaly greater than healthy controls. These results are promising as they show that attention to visual targets can greatly improve postural control. For rehabilitation perspectives, using visual cues or visual games (such as Wii

games) could greatly improve adaptation of postural control to the task performed.
Key words: Parkinson's disease, precise visual tasks, postural adaptation, cognitive resources.

P14.03

Why the fascia system needs to be addressed to manage and potentially reverse the effects of Parkinson's disease
Florencia Cerruti[*1], Deanna Hansen[2], Gary Sharpe[3]*
[1] Fluid Isometrics, Montevideo, Uruguay
[2] Fluid Isometrics, Winnipeg, Canada
[3] Out-thinking Parkinson's, London, United Kingdom

Fascia Decompression can improve the quality of life of persons with Parkinson's disease (PWP). Fascia tissue surrounds each cell in the body, including the nerve endings responsible for pain signals to the brain. Thus, it is very likely that fascia plays an important role in stiffness, pain and rigidity in the body, and indeed, its contractile nature under stress helps to explain its immediate and profound effects. As a consequence of injuries, or holding collapsed postural patterns for too long, many fibres grip to the underlying muscle, organ or bone. These grips will adhere with a force up to 2000 pounds per square inch, acting like barricades. Flow within the body becomes blocked, causing a deficient nutrition and oxygenation of the cells. Strengthening diaphragmatic breathing may be the most important practice one can do for overall health and well-being. The real challenge does not lie in exercises but to melt the adhesions that have sealed the diaphragm out of alignment. We will share the rationale of Block Therapy (BT), a self-administered method developed by Deanna Hansen in Canada, after working in the fascia system for over 60,000 hours for 23 years. She sees the fascia as the surface membrane of each cell, connected to every other cell. BT is designed to melt the adhesions between the layers of fascia, activate the diaphragm, train proper breathing and teach proper postural foundations to integrate cells back to life. Each individual sets their own pace, sequentially diving deeper through the layers while melting the adhesions along the way. In her work with PWP, Deanna has seen positive results beyond simply managing their symptoms, but also seeing improvements. Florencia Cerruti and Gary Sharpe are two PWP who have experienced the benefits of BT. We will share before and after images showing positive changes in short periods of time. For as complicated as this disease can be, this approach is simple, safe and continual with the benefits.

P14.04

Music and the native american flute – A tool for slowing Parkinson's disease progression
*William Clugston**
Self, Auburn, WA, United States

Background: Parkinson's Disease (PD) is a progressive disease that robs a person of cognitive and physical abilities. At least one tool allows a person with Parkinson's Disease (PWP) to slow and even reverse the decline in cognitive and physical skills. Music is such a tool. The brain needs to develop new cognitive skills to recognize notes, accurately gauge note sounds, and coordinate the movement of the hands on the instrument. A device for a PWP should be inexpensive, easy to understand, and sound good with little effort. The Native American Style Flute (NAF) is such an instrument.
The NAF's constant finger movement in intricate patterns is excellent for reducing micrographia. Blowing through the flute helps to exercise the muscles of the chest.
Objectives: Develop a training and distribution program for a simple, low-cost Native American Style Flute.
The goal is for the PWP to learn an enjoyable new skill that reinforces cognitive and physical skills. A secondary goal is social interaction for the PWP.
Methods: The methods for placing a simple flute in the hands of a PWP are straightforward. Using food-safe plastic pipe allows for the construction of a simple, inexpensive instrument. The plastic tube is the main barrel of the flute, while affordable 3D-printed parts compose the mouthpiece and other flute parts.
An illustrated information sheet detailing the care of the flute (minimal in this case) and how to play it accompanies the NAF. The sheet should contain two to three music examples to get the new owner started. Finally, the instructions should list available Internet resources. These items can be available at the World Parkinson's Congress for demonstration and display.
Results: Music is the body's rhythm. Parkinson's Disease is the loss of the body's rhythm. By placing an instrument in a PWP's hands, we can help to restore that rhythm to the body and slow PD's progression.
The Native American Style Flute is a simple, inexpensive instrument, but it can help to improve finger agility, cognition, and social confidence. The result is a Person with Parkinson's that remains engaged and active.

P14.05

Holistic complementary therapies for people with Parkinson's and their families in the open air in synergy with the nature
*Francesca De Bartolomeis**
FUERTE ES LA VIDA PARKINSON NO LIMITS, Corralejo, Fuerteventura, Canary Islands, Spain

In a normalizing, socializing, inclusive, antistigma and holiday setting in Fuerteventura, Canary Island, the professional team of Fuerte es la Vida Parkinson No Limits associacion, coordinated by the psychomotorist Francesca De Bartolomeis and the neurologist, propose innovative complementary therapies in natural settings (fundamental part of the therapeutic path).
The psychomotorist is the guiding thread throughout the course and thanks to the synergistic and transdisciplinary work of the team based on the Parkinson No Limits Method, the person, together with his family, is the absolute protagonist of his path of change and stimulation of his potential for health. The Parkinson No Limits Method is holistic, transdisciplinary and the association's consultants specialize in Parkinson's. In addition, some of them have or have had a family member with Parkinson's.
The settings are divided into 5 types: ocean, sand, earth, air and volcanoes (inactive).
Are carried out:

- in the ocean:Psychomotricity, Surf, Watermotricity, Art therapy in the water, Hydrotherapy, Ocean's Emotion (boat therapy and therapy assisted by cetaceans not in captivity), Meditation, Biodance
- on the sand: Psychomotricity, Biodance, Theater, Sound Bath, Art therapy, Phototherapy
- on the earth: Psychomotricity, Boxing, Qi-Gong, Holistic Nutrition, Music, Biodance.
- using the air: Psychomotricity, Iodine therapy, KyteSurf Therapy, Aerial-Acrobatic Yoga, Flytherapy, Screamtherapy.
- on the volcanoes: Pychomotricity, Art therapy, Trekking, Meditation, Theater, Screamtherapy.

The results are totally positive: objectives achieved in just one week and which persist in the following months. From the data collected, the benefits obtained have been maintained since people have lived the path, until today and persist. the emotional, motivational aspect and having experienced an immediate change in themselves

motivates people to adopt a more functional lifestyle for the quality of their daily life, even once the holiday is over.
Photographs, videos, questionnaires, evaluations by the neurologist and by the professionals involved, document these results.
The Association received an important nationally Spanish award Afectivo Efectivo 2022, organized by Janssen (Spain), Johnson & Johnson, for one of our projects carried out in 2021 that featured innovative complementary therapies linked to the Ocean element, in the category "Awareness and/or prevention initiative and/or intervention".

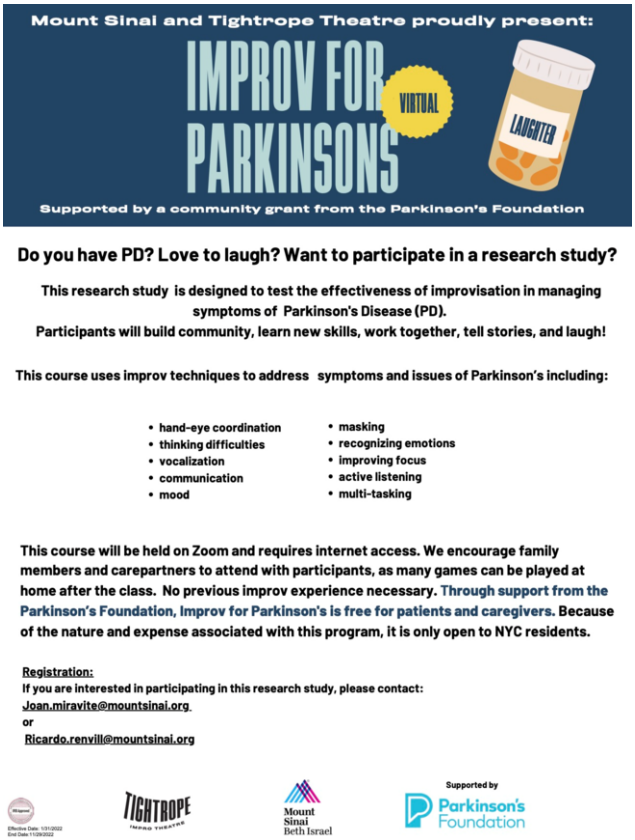
P14.06

Improv for Parkinson's: Creative skills for cognitive health
Daniel Dumsha*[,1], Peter Jarvis[2], Lucia Forward[2], Quinn Contini[2]
[1] Tightrope Improv Theatre, Vancouver, BC, Canada
[2] Tightrope Theatre, Vancouver, BC, Canada

Background: Tightrope Theatre has offered Improv for Parkinson's courses since fall 2019. More than 160 people with Parkinson's have taken these courses. We have founded North America's first Improv Performance Troupe entirely composed of PwP.

The classes are built on the Improvisational principle: Yes, and… Through our program, participants learn to accept their PD diagnosis (Yes,) and then how to participate more positively and expansively in life (and…) using creative skills.
Program partners include the Parkinson Society British Columbia, PD Avengers, Parkinson's Foundation, Mount Sinai Hospital, and University of British Columbia.
Program Objectives:
- Learn and apply improvisational skills to life with PD through games, exercises, and discussions
- Use improv to support cognitive health by targeting word search, working memory, creativity, and emphasizing facial and physical expression
- Foster positive social connection and community building

Methods: Evidence shows that regular and sustained physical exercise slows the progression of Parkinson's Disease. We use improvisational theatre as a means of exercising the mind.
Our six week virtual program introduces the following improvisational skills:
Week 1 - Presence and Acceptance
Week 2 - Listening
Week 3 - Spontaneity and Celebrating Mistakes
Week 4 - Teamwork and Collaboration
Week 5 - Clear Strong Offers
Week 6 - Putting It All Together
Results: Participants report primary outcomes of: enhanced creativity; increased self confidence; surmounting fear and anxiety through laughter; learning to better accept the risk of the unknown; improved sense of self as a PWP; and positive social connection and community.
Testimonials:
"Improv is an example of laughter that heals"
"Closing up is something that Parkinson's does to us, so anything to open us up is important"
"Humanizing"
Conclusions: Parkinson's Disease is characterized by loss. Our program allows participants to gain back some of the loss they experience living with PD by providing ways to open up, find connection, and exercise their minds.
Our goal is to extend the reach of this program as broadly as possible within the PWP community and to continue to empirically study and report on the effect of improv on the cognitive and physical health of PwP.



P14.07

Social work student knowledge and attitudes about medical cannabis use for Parkinson's disease
Offer Emanuel Edelstein[*,1], Alexander Reznik[2], Richard Isralowitz[2]*
[1] Ben-Gurion University of the Negev, Be'er Sheva, Israel
[2] Regional Alcohol and Drug Abuse Research Center, Ben Gurion University of the Negev, Beer Sheva, Israel

Background: Evidence is accumulating about the growing use of medical cannabis (MC) to treat neurological conditions like Parkinson's disease (PD). There is a lack of usable knowledge about social work student attitudes concerning MC use among individuals diagnosed with PD. The current study sought: (i) to explore whether social work students receive formal MC-education, feel prepared to answer questions about MC, and perceive MC as an effective therapy for individuals diagnosed with PD; and (ii) to explore the association between student background characteristics and beliefs regarding MC effectiveness for PD.
Method: A sample of 161 (146 female and 15 male) social work students voluntarily participated in an anonymous online survey.
Results: The vast majority (95.7%) of the participants indicated they had no formal education about MC and reported being unprepared to answer client MC-related questions (59.3%).
59.6% of the participants believed that MC is effective for use with individuals diagnosed with PD. 40.4% reported not knowing whether MC is effective in treating PD. Participants reported positive attitudes about the benefits of MC, the need for education, and the legalization of recreational cannabis use. Less supportive attitudes have been reported regarding MC-related risks. Multivariate analysis showed that personal recreational use of cannabis (self or

friends) was the only variable to increase the probability of a belief that MC is an effective therapy for PD [OR=3.123].
Conclusions: The results of this study highlight the need for MC-related training for social work students to provide future welfare providers with the fundamental knowledge and skills to answer client questions regarding the use of MC. Efforts to develop curricula and training programs are warranted.

P14.08

ES - Park: Evaluation of the effectiveness of the Parkinson's Specialized Teams intervention on the quality of life of Parkinson's patients in the territory of the Nouvelle-Aquitaine: ES-Park pilot study

Alexandra Foubert-Samier[*,1], Isabelle Benatru[2], Jean-Luc Houeto[3]*
[1] Institut des maladies neurodégénératives, Bordeaux, France
[2] Centre Expert Parkinson, Poitiers, France
[3] Centre Expert Parkinson, Limoges, France

This research is conduct with the support of Regional Health Agency of Nouvelle-Aquitaine and France Parkinson Association.
Parkinson's disease (PD) is the second most common cause of motor disability in the elderly after stroke. Progressively, the disability impacts the activities of daily living and social life of Parkinson's patients with a major impact on their quality of life. The diversity and complexity of the needs of parkinsonian patients and their caregivers justify a specific multidisciplinary approach. In France, the experience of specialized Alzheimer teams based on the same concept seems to have brought positive results on autonomy and resocialization. Based on this positive experience and in view of the data in the literature on Parkinson's disease, we would like to develop the same type of care with Parkinson's specialized teams (ESPark).
This study is a pilot experiment interventional study, randomized, multicenter (Bordeaux, Limoges and Poitiers), proposed in order to set up multidisciplinary team "ESPark" for Parkinson's patients at home. The aim of this study is to evaluate the effectiveness of this three specialized Parkinson's team (ESPark) intervention on the quality of life of patients with moderate to severe Parkinson's disease (Hoehn and Yahr Stage ≥3), without major cognitive impairment (MOCA score ≥21), living at home and with a primary caregiver. The intervention will include 15 sessions (1 session per week) and each team must systematically include an occupational therapist, a nurse and a psychologist.
Study design: Randomized 2:1 multicenter study with waiting list method.
The primary endpoint is the differences in progression of the score of quality of life scale (PDQ 39) between initial visit and 6 months visit after randomization between the both groups.
Number of subjects: 125 dyads (125 patients and 125 caregivers)

P14.09

"Those movements weren't moving anything to me": Investigating experiences and opinions about using motor imagery in people with Parkinson's

Charlotte Growcott, Ellen Poliakoff, Emma Gowen*
University of Manchester, Manchester, United Kingdom

Background: Motor imagery (MI) based interventions involve imagining movements without performing them and have been shown to improve motor skills in older adults. There is some evidence that MI can benefit the motor symptoms of people with Parkinson's (PwP). However, most papers reviewing the use of MI interventions agree upon the lack of standardisation and guidelines for the intervention. Similarly, MI is seen as an academic term, not easily understood by a lay audience and there is a lack of information helping to decipher and explain the topic. The aim of this study is to conduct follow up interviews to further investigate thoughts and experiences of MI from PwP.
Methods: Following an online survey (investigating MI ability and predictive factors such as Parkinson's severity and depression), 14 participants (aged between 54-75 and comprising of 8 females and 6 males) with mild to moderate Parkinson's were selected for an online follow up interview. The interview was semi-structured and ranged from 20-45 minutes long; participants were asked on their prior thoughts to MI and any experiences they may have had.
Results – The interview transcripts were thematically analysed and produced 4 main themes. These themes encompassed (1) the needs expressed by PwP for alternative treatments, (2) the need for clearer information and motivation in order to make MI a successful tool, (3) ideas to successfully use MI in research and/or interventions and (4) general thoughts on imagination, particularly that openness to a concept and willingness to practice are the most important components to imagining.
Conclusion: There is an obvious want for alternative treatments to help with motor symptoms in PD. MI could provide a successful strategy, but clearer information and guidance is needed to facilitate understanding as well as motivation and opening people up to the concept. Resources need to be developed to allow MI to be broken down from an academic or technical term to one that is accessible to the people it may benefit. This is something that may be best achieved by continuing to work with PwP in order to successfully co-develop such resources.

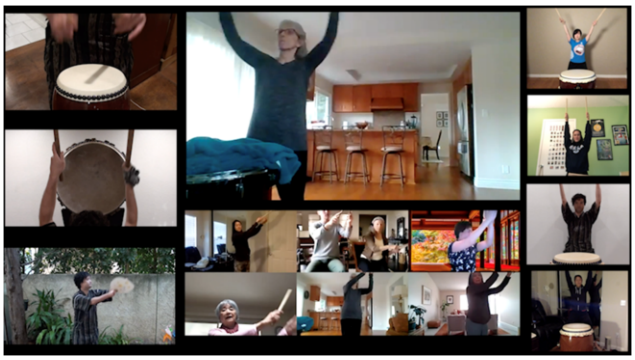
P14.10

Rhythmic flow taiko – Therapeutic drumming for people with Parkinson's

Vivian Lee[*,1], Yeeman Mui*[*,1], Galen Rogers*[*,2]*
[1] Rhythmic Flow Taiko, Los Angeles, CA, United States
[2] Rhythmic Flow Taiko, San Francisco, CA, United States

Rhythmic Flow Taiko (RFT) is a group of taiko drumming artists, educators, and health care professionals founded in 2020 that recognizes the benefits inherent in taiko for people with Parkinson's. RFT facilitators and participants aim to cultivate a practice that aligns the physical, cognitive, and social components of taiko with common therapeutic goals of people with Parkinson's. RFT also recognizes that taiko arts as a whole are enhanced by the participation of disabled individuals. Through weekly taiko zoom-classes, by sharing teaching resources, and by improving access for people with Parkinson's, RFT seeks to build community around the goal of cultivating more inclusive taiko opportunities.
Taiko means "large drum," and refers to many styles of drumming that have been used in Japanese festivals and ceremonies for centuries. In the wake of the Asian American Civil Rights Movement, taiko gained popularity in America and internationally as a form of ensemble drumming, community resilience and cultural empowerment. However, like many contemporary art forms, taiko has historically been represented solely by able-bodied individuals. For this reason, people with Parkinson's and other disabilities might feel that taiko is not appropriate for them.
Utilizing tools from physical/occupational therapy, health psychology, and music education, RFT instructors develop lesson plans and facilitate a weekly zoom-taiko class that is inclusive to individuals with various physical and cognitive conditions while maintaining the integrity of the art of taiko. Our classes integrate large amplitude movements, rhythmic exercises, fine/gross motor movements, breathing exercises, loud vocalizations called "kiai", and cognitive challenges. Participants are encouraged to stand or sit with a focus on core engagement.

After receiving the 2021 Taiko Community Alliance 2021 Grant, RFT developed an online resource library that taiko teachers can utilize in their curriculum to enhance accessibility. The video library is available at RhythmicFlowTaiko.org/resources.html. In 2022, RFT also started building a global directory of classes to help people with Parkinson's access taiko near their homes.
We continue to search for platforms to share our work in hopes of creating more accessible and inclusive taiko drumming spaces for people with Parkinson's and other disabled individuals.



P14.11

Dance for Parkinson in Iberian: Portugal and Spain methodologies

Anjos L. Macedo[*1], Rafael Alvarez[2], Annabel Barnes[3], Luisa Bento[1], Leonor Tavares[1], Cesar Casares[4], Paloma Alfonsel[4], Guillermina Bedoya[4], Sara Mora[4], Aurora Rodríguez del Barrio[4], Juvenal García[4]*
[1] Dançar com Pk, Portugal, Lisboa, Portugal
[2] Dançar com Pk, Portugal & BodyBuilders, Lisboa, Portugal
[3] Dançar com Pk, Portugal & CNB, Lisboa, Portugal
[4] Danza para el Parkinson, Asociación de Profesionales de la Danza en la Comunidad de Madrid, Madrid, Spain

The project Dançar com Pk Portugal, DcPk-PT, which started as a personal initiative driven by friendship, has very specific goals. The project was designed as a program of weekly dance sessions for people with PD, caregivers, family, and friends. It aims to create a unique artistic environment for people to enjoy music and dance.
The project Danza para el Parkinson, Spain, started as an initiative of a board member of the Professional Dancers Association in Madrid, proposed to Danza-T National network. The aim is to highlight the skills of dancers to be not only entertainment providers but a source of wellness for individuals and communities.
The very first step was organizing a workshop for professional dancers in Madrid in collaboration with DxPD and Mark Morris DG in which we met the founders of DcPk-PT.
The foundations of Dance for PD movement were the keystone to try to put in contact two communities that really had a lot to exchange: "If dancers are specialists in balance, movement, coordination… learning to think as a dancer has to be a good idea for a person with Parkinson disease", reinforced by all the medical literature that supports the positive effects of dance in the PD community.
The process of implementation in both countries is described in a concise way, showing its particularities and diverse possibilities, by comparing the analogies and differences of both projects.
The methodology for finding the perfect team, the appropriate facilities, and the right partners, will be presented from two different perspectives, considering how both projects create synergies and work together.
The experience of 8 years of the project implementation in both countries and the impact of the Covid-19 pandemic period, with online classes, is presented with a focus on social well-being and interaction, movement, cognitive knowledge, memory aspects, as some illustrative testimonials from PD patients, caregivers, and teachers.
Both Iberian teams will use the experience acquired in that long-term collaboration to expand the international initiative initiated by Dance for PD, setting up an active network at the European level as a vision for the near future.

P14.12

Mucuna: The power of nature

Patricia Maldonado[*1], Veronica Ruscio[1], Felix Jozsa[2]*
[1] Buenos Aires, Argentina
[2] National Hospital for Neurology and Neurosurgery, London, United Kingdom

I am 47 years old. In 2018 I was diagnosed with Parkinson's disease (PD) and, since then, I have dedicated myself to researching how to achieve disease remission, alongside becoming a yoga teacher. In this process, I discovered the existence of Mucuna and its use in the treatment of Parkinson's disease around the world.
Mucuna puriens is a plant containing high levels of L-Dopa. Despite randomised control trials demonstrating its efficacy when compared with synthetic L-Dopa medications (Cilia 2017; Katzenschlager 2004), it remains underrecognized as a therapeutic option for PD.
Having been initially prescribed pramipexol and then levodopa/carbidopa for 2 years, I was unable to tolerate these medications and experienced hallucinations, breast tenderness and discharge, vomiting, abdominal pain, and nightmares. I have been taking Mucuna for four years and, thanks to its use, I have noted progress in my motor coordination, balance, fluidity of speech, and I am sure that others could benefit from Mucuna if it were more widely recognised and offered.
We conducted a survey of PD patients using Mucuna in Argentina to assess their experience. 9 people responded, diagnosed between 4 months and 21 years ago. 50% were recommended Mucuna by a friend, 38% found it independently, and 12% were prescribed it by their neurologist. 2 (22%) used Mucuna as their only PD medication, 7 (78%) use it in combination with Levodopa, Madopar or Pramipexol. Most grind Mucuna and prepare it as a tea, others combining it with juice or pureed banana. Patients reported improvements in motor rigidity (75%), balance (12.5%) and improvements in emotional state (12.5%). 7 patients (78%) reported no side effects from taking Mucuna, 2 reported abdominal pain.
Our survey shows that in PD patients taking Mucuna experience symptomatic benefits with minimal side effects. As a cheap and natural alternative to synthetic L-Dopa preparations, Mucuna offers an effective treatment for patients living with PD.
I come to this congress with the humble yet profound intention to ask the scientific community to consider the use of Mucuna at the first consultation for new patients with Parkinson's disease, so that they may choose which type of treatment they want to pursue.

P14.13

Dance and Parkinson's: The effects on selected functional parameters during the 180 turning phase of the timed up & go test in people with Parkinson's

Aline Nogueira Haas[*,1], Leonardo Alexandre Peyré-Tartaruga[1], Marcela Dos Santos Delabary[1], Tina Smith[2], Yiannis Koutedakis[3], Matthew Wyon[2]*

[1] Federal University of Rio Grande do Sul, Porto Alegre, RS, Brazil
[2] University of Wolverhampton, Walsall Campus, Walsall, United Kingdom
[3] University of Thessaly, Volos, Greece

Introduction: Parkinson's disease (PD) is the fastest growing neurodegenerative disorder worldwide, characterized by a combination of motor and non-motor symptoms. Several studies have sought to investigate the effects of dance in PD, presenting significant results regarding improvements in functional mobility, motor symptoms and quality of life. However, few studies have investigated the effect of dance on turning ability or the biomechanical characteristics associated with a successful turn. **Purpose:** To investigate the effects of dance on selected functional parameters during the 180° turning phase of the Timed Up & Go test in people with PD. **Methods:** Subjects were 15 adults, both sexes, between 50 and 80 years, with clinical diagnosis of PD, staging between 1 and 4 of the Hoehn and Yahr Scale. Subjects were divided into two groups: dance group (n= 7) and control (n=8). The dance group (DG) participated in Dance for Parkinson's Groups in West Midlands, England, for 3 months, 2 times/week, 2 hours per week. The control group (CG) did moderate physical activity and, during three months, they not alter their personal lifestyle. At baseline, participants completed the Unified Parkinson's Disease Rating Scale and the Hoehn and Yahr scale. Pre- and post-intervention, while wearing the Xsens® full-body 3D motion suit, all participants performed the Timed Up & Go test twice (at a comfortable walking speed, and as quickly and safely as they could). The ANOVA test with mixed design analysis of variance was performed to detect statistical differences between pre and post-test ($p<0.05$). **Results:** We found a statistical difference in the number of steps, with large effect size, in the fast speed ($p=0.01$; $d=2.26$; CI= 0.367; 5.19). After the intervention period, the oscillation between pelvis and affect side shoulder reduced in the DG during the turning movement in the FS, changing the girdle dissociation pattern. **Conclusions:** During the performance of the 180° turning phase of the Timed Up & Go test, the number of steps and the total time of the turn reduced in the DG and, therefore, the oscillation between pelvis and affect side shoulder reduced too.

P14.14

Effect of vocal-dance program on speech, voice quality, and quality of life in persons with Parkinson's disease

Eunsun Park[*,1], Frank Boutsen[2], Betty Kollia[1], Justin Dvorak[3]*

[1] William Paterson University, Wayne, New Jersey, United States
[2] New Mexico State University, Las Cruces, New Mexico, United States
[3] University of Oklahoma Health Sciences Center, Oklahoma City, Oklahoma, United States

Approximately 89% of persons with Parkinson's disease manifest abnormalities of voice, speech, and prosody, referred to as hypokinetic dysarthria, as well as facial-expression impairment. Researchers and clinicians focus on the benefit of recreational group activities such as dancing, singing, and exercise, designed within the past decade to improve the quality of life for patients with PD. Theoretical and empirical evidence suggests that activities such as music, song, and dance can be therapeutic if presented intensively. To date, dancing programs do not focus on speech improvements. This project addresses this void in the newly developed vocal dancing program. This research aims to investigate changes in emotional speech and voice production, voice quality, and quality of life in people with Parkinson's disease (PD) who take part in vocal-dance therapy (total of eight sessions: 4 weeks, twice per week, each session 60 minutes). This vocal-dance class was offered through Oklahoma City Ballet's outreach division as a part of the Golden Swans program. The present study was approved by the IRB at William Paterson University. Six participants with PD (mean age 70.8 ± 5.2 years, mean duration of PD 2.9 ± 1.1 years) and five healthy (mean age 58.8 ± 10.8 years) participants took part in this study. This study compares changes in a) speech production b) depression, quality of life, and voice quality with survey questionnaires administering the Beck Depression Inventory (BID), Geriatric Depression Scale (GDS), Parkinson's Disease Questionnaire (PDQ), Voice Handicap Index (VHI), Voice Related Quality of Life (V-RQOL). All assessments were conducted before and after the vocal-dance training program while the participants with PD were evaluated in medication "on" condition. For survey questionnaires including BDI, GDS, PDQ, VRQOL, and VHI, all the results did not show statistical differences between pre- and post-vocal dance program. The mean scores for the acoustic voice quality index (AVQI) (Pre 0.5±0.3, Post 0.2±0.8) and median pitch during the reading task remained similar pre- and post-vocal dance program (pre 133.6±35.9, post 130.4±35.9 Hz). To our knowledge, this is the first study showing the effects of an interdisciplinary vocal-dance program on speech, voice, and quality of life in individuals with PD.

P14.15

Systematic review of the efficacy of traditional Chinese medicine in Parkinson's disease

Catarina Pereira[*,1], Jorge Rodrigues[2], Natália Oliveira[3], Jorge Machado[1], Maria Criado[4], Henri Greten[5]*

[1] ICBAS – Abel Salazar Institute for Biomedical Sciences, Porto, Portugal
[2] Research Department in Complementary Medicines, Portuguese Institute of Taiji and Qigong., Porto, Portugal
[3] CBSIn – Center of Biosciences in Integrative Health, Porto, Portugal., Porto, Portugal
[4] TOXRUN – Toxicology Research Unit, University Institute of Health Sciences, CESPU, CRL, Gandra, Portugal
[5] HSCM - Heidelberg School of Chinese Medicine, Heidelberg, Germany

Background: Parkinson's disease is a multi-system neurodegenerative disorder characterized by motor and nonmotor symptoms. To slow disorder progression, different treatment options are now available but in most of the cases these therapeutic strategies also involve the presence of important side effects. This has led many patients to pursue complementary therapies, such as acupuncture, to alleviate PD symptoms. Therefore, an update on the efficacy of this treatment for patients of PD is of great value. This work presents a systematic review of the efficacy of acupuncture treatments in relieving PD symptoms; **Methods:** EMBASE, Medline, Pubmed, Science Direct, The Cochrane Library, Cochrane Central Register of Controlled Trials (Central) and Scielo databases, were systematically searched 21 from January 2011 through July 2021. Randomized controlled trials (RCTs) published in English with all types of acupuncture treatment were included. The selection and analysis of the articles was conducted by two blinding authors through Rayyan application; **Results:** 720 potentially relevant articles were identified; 52 RCTs met our inclusion criteria. After exclusion of 35, we found 17 eligible. The included RCTs reported positive effects for acupuncture plus conventional

treatment compared with conventional treatment alone in the UPDRS score; **Conclusions:** Additional evidence should be supported by rigorous methodological strategies. Although firm conclusions cannot be drawn, acupuncture treatment, in the framework of an interdisciplinary care team, appears to have positive effects in PD symptoms.

P14.16

Moving mindfully: A mindfulness-based walking therapy program for people with freezing of gaip

Kerri Rawson[*,1], Tueth Lauren[1], Jeanne Kloeckner[2], Raina Foreman[3], Ryan Duncan[1], Allison Haussler[1], Sidney Baudenstiel[1], Keith Lohse[1], Gammon Earhart[1]*
[1] Washington University School of Medicine, St. Louis, MO, United States
[2] Mindful Solutions StL, St. Louis, MO, United States
[3] Washington University in St. Louis, St. Louis, MO, United States

Freezing of gait (FOG) is a debilitating symptom experienced by some people with Parkinson (PwP) and may be linked to anxiety. Mindfulness-Based Stress Reduction (MBSR) programs are used to reduce anxiety and improve quality of life. In this feasibility study, we developed a mindfulness-based walking therapy (MBWT) program based on MBSR, with the goal of improving FOG in PwP. This 14-week pilot of the MBWT program included pre-and post assessments. Each week, participants learned about a foundational attitude (e.g., beginner's mind, nonjudgement, self-compassion, etc.), formal and informal meditations, and participated in mindful walking exercises. Our feasibility aims included (1) Recruitment (12 participants); (2) Retention (80% of participants attending 80% of the sessions); (3) Satisfaction (minimum average rating of >.5 on Session Evaluation Form (SEF) and >1.5 on Client Satisfaction Questionnaire (CSQ); (4) Participant adherence (70% of participants complete 70% of home assignments); and (5) Internal validity as measured by increased pre-to post average scores on mindfulness scales. Participants also completed psychological, cognitive, and motor assessments.
After completing the program, the following aims were fully met. Participants expressed satisfaction with the intervention, evidenced by the minimum average rating of a session via the SEF as 1.7, with a max of 2.5 out of 3. Participants were satisfied with the program as a whole, with the minimum average rating on the CSQ being 1.6, and a max of 3.8 out of 4. The adherence aim was also met, with 71% of participants regularly reporting their home practice at 77% or greater. Recruitment and retention were promising with twelve participants recruited and nine passed the pre-evaluation. Seventy-eight percent of participants completed the program with 43% attending 80% of the sessions or more, and the average number attended being 11.3. Average scores on the mindfulness scales did not increase or decrease significantly. Scores on the other assessments will be presented.
Our next steps include consideration of these results along with feedback from the participants to further adapt the MBWT program. We will then conduct a randomized control trial. Future directions include conducting larger trials and combining conventional physical therapy content with the MBWT program.

P14.17

The use of music in every day life among people with Parkinson's: A mixed methods study

Dawn Rose[*,1], Ellen Poliakoff[2], William Young[3], Michelle Phillips[4]*
[1] Lucerne University of Applied Sciences and Arts, Luzern-Kriens, Switzerland
[2] University of Manchester, Manchester, United Kingdom
[3] Univeristy of Exeter, Exeter, United Kingdom
[4] Royal Northern College of Music, Manchester, United Kingdom

In Parkinson's care, medication does not adequately ameliorate symptoms leading to the need for adjunct therapies to improve quality of life. Music has organisational and motivational properties that have been explored in relation to Parkinson's rehabilitation. However, the reasons people with Parkinson's use music in everyday life has not been investigated.
The use of music as a potential health resource is a hot topic particularly as the prevalence of Parkinson's is predicted to increase by one fifth by 2025 (Parkinson's UK). Therefore, this project consulted with people with Parkinson's on the ways in which they use music in everyday life to self-manage motor actions and affective states in line with patient and public involvement (PPI) in research initiatives.
We developed an online survey to investigate how people with Parkinson's use music in everyday life. In addition to demographic and Parkinson's specific items, psychometric tests were included to: a) provide baseline data, and b) explore how use of music relates to musical and dance sophistication and quality of life. The sample (N=217) were mainly Caucasian (n=208) and British (n=190) with a mean age of 65.2 (SD=8.45) years (109 females). 64% reported a mild impact of Parkinson's on Activities of Daily Living. When asked how they listened to music, 69% reported a mixture of listening attentively and in the background, 77% used the radio, 52% played CDs. Regarding modern technology, 56% used a personal music listening device, 52% streamed their music and 34% used a 'smart device' (e.g. Alexa). Classical (74%), rock (65%) and pop (59%) were rated as the most popular music genres, though folk (45%), jazz (40%) were also well liked.
When asked why they used music, the top three categories were 1. Aesthetic Appreciation, 2. Motivation, 3. Relaxation. The bottom category was using music for Walking. The duration of attentive listening was significantly higher (W=1683.5, p<.01) for those who reported using music for managing their feelings than those who did not. The results suggest there is further scope for disseminating how people with Parkinson's can use music to manage their movement and mood to improve their quality of life.

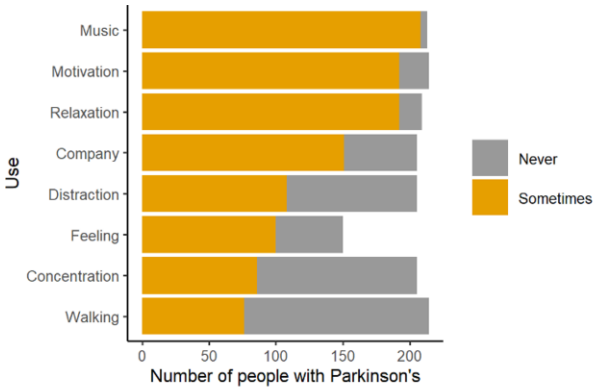


Figure 1. Depiction of participants use of music according to pre-classified themes.

P14.18

Songlines for Parkinson's: A new approach to co-developing a group-based music and movement intervention for and with people with Parkinson's, practitioners, medical professionals, and scientists

Dawn Rose[*,1], Marietta Ungerer[2], Sabrina Koechli[2]*
[1] Lucerne University of Applied Sciences and Arts, Luzern-Kriens, Switzerland
[2] Lucerne University of Applied Sciences and Arts, Lucerne, Switzerland

Research in Parkinson's suggests that, in addition to pharmacological and surgical treatment, interventions combining music/sound and movement within established frameworks for physical therapy, music therapy could positively impact both motor and non-motor symptoms for people with Parkinson's (PwP). As PwP tend to be up to 70% less active than their peers, it is important to develop interventions that appeal to PwP on a multi-modal level. Therefore, we took an inclusive Patient and Public Involvement (PPI) and transdisciplinary approach to co-develop a new group-based intervention that integrates musical activities with exercises to improve quality of life for PwP. This process involved 15 workshops and 28 interviews with Swiss and British PwP exploring the use of music in relation to potential rehabilitative mechanisms.
Each session of the 12-week Songlines for Parkinson's programme will involve 12-15 PwP and last for 90 minutes, plus refreshments (lunch) afterwards. Table 1 shows a basic outline of how the weekly sessions will run. The 5 group tasks include active rhythmic engagement exploring percussion with a guide, song sharing, group problem solving using music to help ameliorate Parkinson's symptoms, learning about rhythms from around the world and then trying out movements associated with rhythms from around the world. For example, in week 3, participants learn about different types of African percussion and African rhythms, before trying African dance steps and storytelling through music.
The intervention will now be evaluated as a clinical trial using a within-subject repeated measures mixed methods design (N=48) in the UK and Switzerland (2023-25).
We have also developed a new protocol that integrates a pressure sensitive gait mat with motion capture technology. This will enable us to probe clinical measures such as the Timed Up & Go to better understand change over time in the quality of functional mobility. Standardised measures (e.g., PDQ-39) and qualitative methods will track change over time in relation to motivation and mood. This project provides a framework for the development of non-pharmaceutical and low-cost intervention programmes. Our PPI approach will provide better individualised and targeted prevention strategies to counteract the increasing financial and personal burden of Parkinson's worldwide.

Table 1. Basic Overview of Weekly Sessions

Duration (minutes)	Name of Activity	Brief Description	Facilitator
0 - 5	1. Weather Scene Warm Up	Sensory, Body and Voice exercises	Practitioner
5 - 15	2. Active Rhythmic Engagement	Guided percussion (body/instrument)	Practitioner
15 - 25	3. Message Stick	Active rest; shared listening & reflection	PhD Student
25 - 35	4. Hive Mind	Group symptom problem solving using music cues + music and motor imagery	Whole group
35 - 45	5. Rhythms from Around the World	Active rest; mini 'psychoeducation' talk	Practitioner
45 - 65	6. Music & Movement	Practicing techniques using music to improve functional mobility	Practitioner & PhD student
65 - 70	7. Restore & Relax	Qigong breathing and gentle motion	Practitioner
70 - 90	8. Refreshments	Coffee & Cake/Lunch, Socialising	Whole group

P14.19

Sing a new song: Results from research on group therapeutic singing for people with Parkinson's disease

*Elizabeth Stegemoller**
Iowa State University, Ames, Iowa, United States

Singing is a popular activity in the Parkinson's disease (PD) community worldwide. Research has shown that group therapeutic singing (GTS) provides many benefits. This abstract will review the findings of recent research on GTS. In the first study, 30 participants with PD completed eight weekly one hour sessions of GTS, which included vocal exercises and group singing. Measures of voice, inspiratory and expiratory respiratory control, muscle activity associated with swallow, and quality of life were collected right before and after 8 weeks of GTS. Results revealed that there were improvements vocal loudness and pitch range, but only vocal duration was significantly improved. Moreover, there were significant improvements in both inspiratory and expiratory respiratory control, and significant changes in the muscle activity associated with swallow. Finally, results revealed significant improvements in quality of life. In qualitative interviews after this first study, participants reported that they felt less stressed and could move better after singing. Thus, in the second study, 17 participants with PD completed a single session of GTS to determine how GTS affected stress, inflammation, and clinical motor symptoms. Saliva and blood samples were collected immediately before and after the single session of GTS. In addition, the motor section of the MDS-UPDRS was collected and scored by Movement Disorders Specialists masked to the condition and time point. Results revealed no significant changes in cortisol, a measure of stress taken from the saliva sample, indicating that singing was not stressful. Results also revealed significant changes in peripheral cytokines IL-1β and IL-8, a measure of inflammation taken from the blood sample. Finally, results revealed a significant improvement in the clinical symptoms of gait, postural instability, and tremor after a single session of GTS. Taken together, the results of these two studies demonstrated that GTS has pervasive effects on multiple symptoms of PD. Future studies to better understand the long term effects 0f GTS and underlying neurophysiology are underway. In conclusion, including singing in the treatment of PD is a simple and cost-effective way to improve the overall health and symptoms of people living with PD.

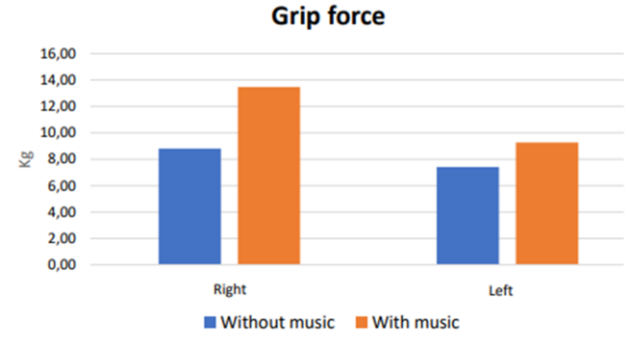
P14.20

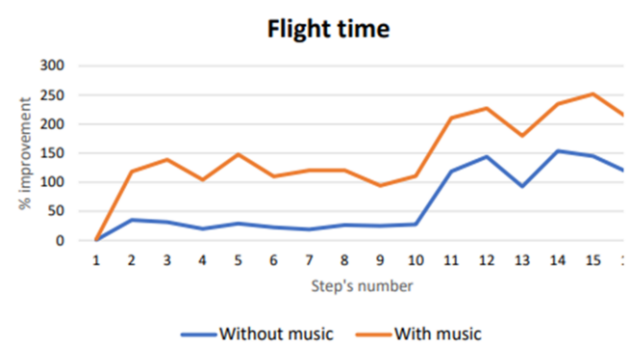
Music therapy improves strength and gait in Parkinson's disease patients: A pilot study and clinical case analysis

Cristina Tinajas Arrontes[*,1], Manuel García San Emeterio[1], Marta Méndez Olavide[1], Vanessa Bayo Tallón[1], Carlos Llobregat Delgado[2], Jordi Esquirol Caussa[3]*
[1] Escuelas Universitarias Gimbernat (adscritas a la Universitat Autònoma de Barcelona), Sant Cugat del Vallès, Barcelona, Spain
[2] Residencia Geriátrica Santa Rosalía, Sabadell, Bareclona, Spain
[3] Escuelas Universitarias Gimbernat (adscritas a la Universitat Autònoma de Barcelona) / ISADMU/Geriatria Centre Mèdic Teknon, Sant Cugat del Vallès / Barcelona, Barcelona, Spain

Introduction: Parkinson's disease (PD) is a progressive neurodegenerative disorder, highly frequent among elders, caused by degeneration and the consequent deficiency of dopaminergic neurons in the basal ganglia. Main motor symptoms are bradykinesia, rigidity, tremors, gait disturbances and postural instability, causing impairment in balance and motor coordination. These deficits decrease mobility and increase the risk of falls, negatively affecting patients' autonomy and quality of life.

Evidence shows that music therapy interventions may offer benefits on multiple functional parameters in PD patients.
Objectives: To analyse the effects of music therapy on muscle strength and gait parameters in patients with PD.
Methods: Pilot Test: one male participant diagnosed with PD (Hoehn & Yahr scale score ≥2). Variables: bilateral grip force (TakeiT.K.K.5401 GRIP-D handgrip dynamometer, three measurements), flight time, pace cadence and gait speed (4 Meters Walking Test, 4-MWT, digital analysis). Intervention: after obtaining informed consent, measurement of variables without (WoM) and with music (WM) with emotional attachment to the patient. Statistical analysis: descriptive and inferential.
Results: Pilot test: one male subject with Parkinson's disease (age: 93). Mean values of grip force: right hand (dominant) WoM 8.80kg (standard deviation SD=2.35kg) and WM 13.47kg (SD=1.06kg), aiming at an average increase in strength of 4.67kg (p=0.043); left hand WoM 7.40kg (SD=0.36kg) and WM 9.27kg (SD=0.23kg), evidencing an average increase in strength of 1.87kg (p=0.007).
Mean flight time values of each step: WoM 0.55sec (SD=0.42; Max=1.23; Min=0.15), WM 1.11sec (SD=0.15; Max=1.43; Min=0.83), significantly increasing the time in monopodial support (p=0.000).
4-MWT: 8.33s WoM and 7.39s WM times; WoM step cadence 146.67spm (steps per minute) and WM 133.33spm, showing improvements in both variables, although those results were not significant.
Discussion: Using emotionally meaningful music for the patient with Parkinson's disease can significantly increase grip strength both in upper extremities (dominant and non-dominant) and modify positively gait parameters (flight time).
Conclusions: The pilot study validates the proposed design and suggests that a larger clinical trial should be conducted to further investigate the effects of music therapy (cadence, rhythm and/or emotional attachment) on gait rehabilitation and strength in patients with PD.





P14.21

Can musical sonification improve motor control in Parkinson's disease? Results from a rehabilitation protocol
Lauriane Veron-Delor[*,1], *Serge Pinto*[2], *Alexandre Eusebio*[3], *Jean-Philippe Azulay*[4], *Tatiana Witjas*[3], *Bruno Nazarian*[3], *Jean-Luc Anton*[3], *Julien Sein*[3], *Marieke Longcamp*[4], *Jérémy Danna*[*,5]
[1] Centre de Recherches sur la Cognition et l'Apprentissage (CeRCA), Poitiers, France
[2] Laboratoire Parole et Langage, Aix en Provence, France
[3] Institut de Neurosciences de la Timone, Marseille, France
[4] Laboratoire de Neurosciences Cognitives, Marseille, France
[5] Laboratoire Cognition, Langues, Langage, Ergonomie (CLLE), Toulouse, France

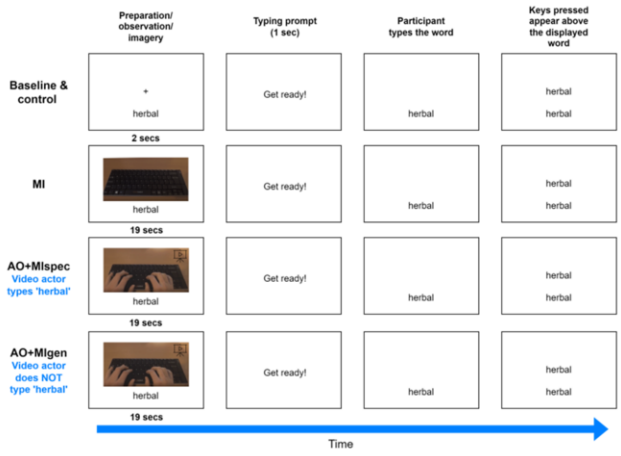
Music has been shown to activate a pathway that may compensate for the defective cortico-striatal networks in patients with Parkinson disease (PD), leading to motor improvements. In this study, we tested an original strategy of musical sonification. Technically, this method changes music as functions of handwriting kinematics in such a way that velocity distortions generate music distortions. Theoretically, the purpose of musical sonification is both to improve the perception of movement irregularities (when music changes) and to provide auditory guidance (when music does not change). Recently, we suggested that musical sonification would be more suitable than background music as a relevant auditory guidance allowing PD patients to improve control of writing movements (Véron-Delor et al., 2019). We are now seeking to evaluate the effects of such a method in a proper rehabilitation protocol lasting two weeks with 40 patients, using a pre-test/training/post-test design. The tests are strictly identical: participants are required to copy a text and some items, namely backward loops, the pseudo-word ''mune'', and their signature. The training consists of eight daily, one-hour, sessions during which patients perform different graphomotor exercises with musical sonification. Preliminary results from the first five patients included in the protocol showed that their writing height and velocity greatly improved after the training. If confirmed, this study will provide a novel argument to use musical sonification as an original, simple and easy to reach auditory guidance strategy for movement rehabilitation in PD patients. The interest of this study goes beyond the rehabilitation of Parkinsonian dysgraphia: this tool opens up promising new prospects for non-pharmacological treatments in Parkinson's disease (and maybe also other movement disorders). Ongoing neuroimaging investigations will contribute to determine whether such improvements could be related to the enhancement of the cortico-striatal network disrupted in PD, while involving the compensatory cortico-cerebellar pathway.

P14.22

Can action observation and/or motor imagery improve computer-based actions in Parkinson's?
Camilla Woodrow-Hill[*,1], *Emma Gowen*[2], *Stefan Vogt*[3], *Matthew Sullivan*[4], *Ellen Poliakoff*[2]
[1] University of Manchester, Chesterfield, United Kingdom
[2] University of Manchester, Manchester, United Kingdom
[3] Lancaster University, Lancaster, United Kingdom
[4] Person with Parkinson's, Manchester, United Kingdom

Computer-based actions, such as keyboard and mouse use, can be difficult for people with Parkinson's (PwP) due to motor symptoms such as rigidity, tremor and slowness. Computer use is becoming an ever more central part of daily life, particularly due to the COVID-19 pandemic; hence it is crucial to determine if low-cost tools could be developed to facilitate computer use in PwP. Growing research has indicated that action observation (watching movement; AO) and

motor imagery (imagining oneself move; MI) can be effective tools for facilitating movement in PwP and that they may be more effective when combined (i.e. imagining oneself perform a movement while watching someone perform it; AO+MI).
This study compared keyboard and mouse use after AO+MI, MI, and no training (baseline and control conditions) in two experiments using a within-subjects, counterbalanced block design. Typing and mouse cursor speed and accuracy were measured across all conditions and compared statistically using generalised linear mixed effects models. We hypothesised that keyboard and mouse use would be faster and more accurate after AO+MI compared to all other conditions; and faster in MI compared to the baseline and control conditions. We also performed exploratory analyses to determine whether self-reported imagery vividness or depression predicted performance differences between AO+MI/MI and baseline/control conditions using multiple linear regression.
Sequential analysis was performed half-way through data collection after data from 25 participants (aged 45-76 years; 17 males, 8 females; Hoehn & Yahr 1-3) to determine whether the results were conclusive enough to terminate data collection early. However, results did not meet the pre-determined cut-off thresholds so data collection will continue until the full sample of 50 PwP is achieved, which is expected to be March 2023. A sample of this size will mean the study has 90% power for statistical analysis. Data collection is currently ~70% complete and to prevent bias, the data cannot be analysed until the full sample of 50 participants has been achieved, as has been outlined in an embargoed pre-registration published on the OSF: https://osf.io/kp4gj
The final results and statistical analysis will be presented and discussed.



COMPREHENSIVE CARE: Lay/professional health literacy & public thought

P15.01

The early treatment phase in Parkinson's disease: Not a honeymoon for all, not a honeymoon at all?
Araceli Alonso-Canovas[*,1], *Jos Voeten*[2], *Larry Gifford*[3], *Omotola Thomas*[4], *Andrew J Lees*[5], *Bastiaan R Bloem*[6]
[1] Neurology Department. Hospital Universitario Ramón y Cajal, Madrid, Spain
[2] Patient advocate, Amsterdam, Netherlands
[3] Patient advocate, Co-founder PD Avengers, Toronto, Canada
[4] Founder/Director, Parkinson's Africa, Surrey, United Kingdom
[5] The National Hospital for Neurology and Neurosurgery, London, United Kingdom
[6] Radboud University Medical Center, Donders Institute for Brain and Cognition, Department of Neurology, Center of Expertise for Parkinson & Movement Disorders, Nijmegen, Netherlands

Background: Levodopa discovery was a 'golden moment' for people living with Parkinson's disease (PwP, PD). Unfortunately, after several years of treatment, motor fluctuations and dyskinesias developed. In the 70s neurologists introduced the term "honeymoon period", to describe the first period of uncomplicated response as opposed to the more complicated phase. This term caught on quickly and was commonly used in the PD scientific literature.
Methods: We analyse the use of the term "honeymoon period" and examine the reasons why it should be abandoned.
Results: In the last two decades alone, 22 articles in PubMed included "honeymoon period" among their keywords or abstract, as did over 3150 entries in Google Scholar. We found a widespread use in neurology textbooks, recent conferences, educational materials and podcasts.
Medical terms are now no longer restricted to professionals but are accessible to the general population. Although not meant to offend, "honeymoon" has been considered distasteful and inappropriate by many people with PD and medical professionals, and very few PwP relate to the notion of a "honeymoon" in their journey with PD. In a collective discussion with PwP and neurologists, we identified several reasons for this. The response to levodopa is variable and unpredictable, especially in symptoms like tremor, speech and balance problems, and non-motor symptoms, frequently unresponsive, with early onset, and a high impact in quality of life. Many PwP find it very complicated to personally adjust to a diagnosis of PD. Such a worrisome phase of grief is very hard to reconcile with a "honeymoon" feeling. Perhaps, if the early phase of PD is to be experienced by anyone as a honeymoon, it is rather by the treating physician, who needs to spend less time on adjusting complex medication regimes compared to the later phase.
Conclusion: We feel that the term honeymoon has become inappropriate and no longer useful, even for limited use within medical circles. Now that the lines between people with PD and their neurologists have blurred for the better we should continue to increase our efforts to adjust our clinical view of the disease to that of those who are best informed: namely PwP.

P15.02

Precision needed in Parkinson's advocacy: Healthy land and affordable food for people is always in desperate need
*Grant Burchnall**
Grant Burchnall - individual, Red Deer, Alberta, Canada

I am a part-time farmer from central Alberta, Canada. I have lived with a dopamine deficiency since at least 2010. My future is not intuitively predictable.
There really is little that is intuitive about Parkinson's diseases or much of the world's workings. Vigorous exercise was discouraged in decades past, considered intuitively detrimental; a theory now disproven by data. Other intuitive truths, disproven: the world was once flat, the sun once orbited the earth, those intuitive beliefs also dispelled. Then Einstein came along and told us that gravity bends light… actually true, if more difficult to believe. Another difficult truth, most pesticides protect our food and greatly protect our land. This counterintuitive requires an explanation; pesticides occupy a large space within PD advocacy.

First, I am grateful for the genuine people in our community who fight for PD support, research, and prevention. My contribution is to plea for more precision within advocacy. I will support my entreaty with a review of scientific, regulatory, trade papers, and personal experience. I'll argue:

- organic foods will not prevent disease
- bans on crop protection products may be too extreme
- food is a product of biology equally as complicated as disease

Respecting that complexity through precision advocacy will optimize our long-term impact, protect our credibility and help ensure affordable food and healthy land into the future.

Affordable food is a basic need for all people. Over 10% of people in developed countries, and many more in developing countries, are food insecure. Food unaffordability jeopardizes the health of too many with PD, and without. Organic food is not "cleaner" nor more nutritious yet at 20%-plus pricing premiums. Organic food production uses specified pesticides and often requires tillage. Tillage results in land-destroying erosion and a far larger carbon footprint. Most organic food is exported from countries where regulatory enforcement is questionable.

Hating PD is not enough. Love the land as well. If Organic strategies could kill weeds without tillage, the argument would be short. Tillage is an energy-hungry, soil-disrupting action. Tillage exacerbates climate change and causes soil erosion … soil is life, to people and nature.

P15.03

Teaching nursing students about Parkinson's disease using conversation mapping

*Marjorie Getz**
Methodist College, Peoria, IL, United States

Revalence rates are increasing for Parkinson's disease (PD) in the US. PD is chronic, progressive, and varies greatly across people. Research suggests that increased preparation of nurses can lead to significant improvement in well-being for those impacted by PD. To this end, the Edmond J. Safra Foundation has worked toward training nurse educators to enhance knowledge, skills and abilities of nursing students related to PD. We report on the expansion of a program developed with permission from Healthyi related to conversation mapping for persons with Parkinson's disease and their care providers. The purpose of a conversation map is to engage small groups in open discussions about PD to better educate people about their disease to promote treatment follow-through and self-efficacy for better control over symptoms. Although the conversation mapping process is structured and guided, sessions allow facilitators to focus on specific areas of PD education, allow patients/family members to ask about what they are most interested in knowing and learn from the experiences of others. A clinical facilitator also can learn how patients verbally conceptualize their disorder which can enhance care when the healthcare provider has greater insights into the lived experience of having PD or being close to a person with PD. Three separate upper-level social science courses (total of 49 students) worked on parts of this project. Students reviewed evidence-based resources and prepared two "elevator" conversations (casual 150-word conversations concerning their new knowledge about PD). One student group chose five broad topics that would have relevance to most people with PD (for the maps). The second group sketched conversation maps and began the process of assembling conversation enhancing resources (for example, prompts to help identify myths/truths about PD). The third group completed the resources. As experiential learning projects, students prepared reflections related to participating in the projects. Early qualitative analyses showed these themes: enhanced knowledge about PD, difficulty in identifying salient topics on which to focus discussion maps, positive experience when being part of a "bigger" project, developing skills related to life-long learning, appreciation for communicating/listening skills development when using the conversation map technique.

P15.04

Piece of mind: Bridging scientific research and the lived experience of Parkinson's with the performing arts

Naila Kuhlmann, Aliki Thomas, Natalia Incio-Serra, Stefanie Blain-Moraes*
McGill University, Montreal, Quebec, Canada

Introduction: Despite significant research advances in understanding and treating Parkinson's disease (PD), communication barriers continue to limit fruitful exchange between scientific researchers, clinicians and people living with PD. Traditional means of knowledge dissemination are inaccessible to non-academic audiences, hampering meaningful dialogue with and research uptake by community stakeholders. **Objective:** To explore alternative strategies for engaging diverse stakeholders, Piece of Mind brought together neuroscientists, people with PD and artists (musicians, dancers, circus acrobats) to co-create a multi-media knowledge translation (KT) performance based on scientific research and lived experience. We aimed to 1) facilitate knowledge exchange and empathy through participatory arts and 2) create a performance that could engage a wide audience on an intellectual and emotional level. **Methods:** Participants met regularly on Zoom over a 4-month period, in which creative, embodied approaches (e.g. dance, music) were used to explore scientific concepts, facilitate discussion regarding the lived experience of PD, and identify key issues to represent in the performance. Emergent themes were built on through structured improvisation, virtual and in-studio collaborations, and work-in-progress presentations. The resulting performance was filmed and disseminated on YouTube (>1600 views), with supporting materials to provide further context. To evaluate the potential of the performing arts as a KT tool, we examined both the process and the product. Semi-structured interviews were conducted to assess the impact of the creative process on participants, and an online questionnaire was used to evaluate the impact of the performance on viewers. **Results:** We found that our participatory, embodied and arts-based approach allowed participants to leave their comfort zones and disciplinary boundaries to engage with one another through curiosity and active listening, and move towards a common goal while integrating multiple perspectives. The resulting performance elicited strong emotional engagement, promoting increased understanding of PD, and empathy towards people with PD. We identified multiple factors influencing the audience's receptiveness to the performance's content. **Conclusion:** Our arts-based KT project bridged the experiences and knowledge bases of disparate PD stakeholders. By presenting an accessible and emotionally-engaging perspective on PD research and lived experience, Piece of Mind acts as an important complement to traditional means of knowledge production and dissemination.

P15.05

Supporting Parkinson's disease medication safety for nurses in the acute care setting through an educational intervention study

Diane M. Ellis, MSN, RN, CCRN[1], Elizabeth Burgess Dowdell, PhD, RN, AFN-C, FAAN[2], Johanna Romero de Slavy, MSN, CRRN, GERO-BC, NPD-BC[3], Louise Laufer Hummel, MSN, RN, CEN, GERO-BC, NE-BC[4], Lola Rene' Kropkowski, MSN, RN NPD-BC[5], Gwyn M. Vernon, MSN, RN, CRNP[,6], Heintje Calara, DNP, MA, RN[7], Erin Houton, BSN, RN[8], Katelyn Wackrow, BSN, RN[9], Natalia Matar, SN*[,2], Paul W. Bernhardt, PhD[10]*

[1] Biosion Inc., Villanova, PA, United States
[2] M. Louise Fitzpatrick College of Nursing, Villanova University, Villanova, PA, United States
[3] MedStar Good Samaritan Hospital, Baltimore, MD, United States
[4] Riddle Hospital, Main Line Health, Media, PA, United States
[5] MedStar Union Memorial Hospital, Baltimore, MD, United States
[6] Edmond J. Safra Visiting Nurse Faculty Program at Parkinson Foundation, Philadelphia, PA, United States
[7] Neurocrine Biosciences, San Diego, CA, United States
[8] Shady Grove Medical Center, Adventist Healthcare, Rockville, MD, United States
[9] Brigham & Women's Hospital, Boston, MA, United States
[10] College of Liberal Arts and Sciences, Villanova University, Villanova, PA, United States

Introduction: Patient medication safety in the acute care setting is a foundational action provided by nurses and healthcare providers for safe patient care. Hospitalization of patients with Parkinson's disease (PD) can be dangerous due to the unique and variable medication regimen required. The research question posed in this study was the following: does a PD medication educational intervention in the clinical setting enhance knowledge, comfort, and competence of practicing nurses in the care of patients with PD regarding their medication safety?
Design: A quantitative study design was used for this five-month, two-part study with a sample of practicing RNs at three different hospitals. Part one of the study assessed nurses' initial knowledge of PD and PD medication safety and included an educational intervention. Part two of the study occurred three months later and evaluated if knowledge from the educational intervention was retained.
Methods: The study was conducted in two parts and included a pre-test, educational intervention, post-test, and follow-up test three months later. The educational intervention consisted of a 15-minute video of two PD advanced practice nurses being interviewed regarding the general care of a patient with PD. The pre-test, post-test, and follow-up test were identical and consisted of six questions regarding knowledge, comfort, and self-perceived competency.
Results: A total sample of 252 RNs participated in this study. Statistically significant improvements in knowledge, comfort, and self-perceived competency were observed in the post-test scores compared to pre-test scores. These statistically significant improvements were retained after three months, despite a 42.9% decrease in the number of responders (n=252 vs. n=144). Additionally, compared to the post-test, there were no statistically significant declines in knowledge, comfort, or competency in the follow-up test.
Conclusion: A review of the literature and this study both support the need for increased education for practicing nurses as it relates to PD and PD medication safety. Healthcare systems, organizations, and associations that support continuing education for nurses create a stronger workforce. Education has been found to keep nurses up to date on the latest advances in care and treatment while also providing exposure to other areas of nursing beyond their clinical settings.

Table 1: Pre-test (n=252), Post-test (n=252), and Follow-up (n=144) scores for knowledge questions (Q1-Q3) and comfort/competency questions (Q4-Q6); percent increases and *p*-values for follow-up are based on n=144 responders to all three tests.

Knowledge Questions	Pre-test % Correct	Post-test % Correct (% increase)	*p*-value Pre vs. Post	Follow-up % Correct (% increase)	*p*-value Pre vs. Follow-up	*p*-value Post vs. Follow-up
Q1	57.8	98.4 (70.3)	<0.001	98.6 (63.2)	<0.001	1.000
Q2	29.0	48.8 (68.5)	<0.001	52.1 (87.5)	<0.001	0.450
Q3	90.1	92.8 (3.1)	0.296	97.9 (9.3)	0.002	0.021
Comfort/ Competency Questions	**Pre-test Mean Score**	**Pre-test Mean Score (% increase)**	***p*-value Pre vs. Post**	**Follow-up Mean Score (% increase)**	***p*-value Pre vs. Follow-up**	***p*-value Pre vs. Follow-up**
Q4	2.42	2.89 (19.5)	<0.001	2.81 (15.1)	<0.001	0.659
Q5	2.15	2.77 (28.4)	<0.001	2.72 (26.1)	<0.001	1.000
Q6	1.55	2.64 (70.2)	<0.001	2.55 (63.8)	<0.001	0.488

Figure 1: Pre-test, Post-test, and Follow-up test scores for the n=144 individuals completing all three tests. For Q1-Q3, standard errors ranged from approximately 0.7 to 4.2, while for Q4-Q6, standard errors ranged from 0.09 to 0.10.

P15.06

Certified Parkinson disease care (CPDC™): Improving the care of Parkinson's patients in long-term care

Anissa Mitchell[*,1], Andrea Merriam-Crespo[2]*

[1] PMD Alliance, Longwood, Florida, United States
[2] PMD Alliance, Chandler, AZ, United States

Introduction: Patients with Parkinson's disease (PD) are at greater risk for institutionalization as the disease progresses and symptoms become more complex. Issues such as falls, cognitive impairment, hallucinations, and other advanced motor and non-motor symptoms coupled with co-morbidities and caregiver burden are often predictors of institutionalization and decreased quality of life (QOL). Facilities that care for patients with multiple diseases may not understand the presentation and impact of these symptoms, the importance of timing of medications, and the management of neuropsychiatric behaviors resulting in decreased QOL for patients. With the expected rise of PD, aging of the population, and limited community resources, the number of institutionalized patients will likely increase.The lack of treatment guidelines or protocols for PD in facilities means patient care may be inconsistent and suboptimal.
Objective: Parkinson and Movement Disorder Alliance (PMD Alliance), a US-based advocacy organization, created Certified Parkinson Disease Care (CPDC™), an accreditation program aimed to improve the knowledge of long-term care (LTC) staff on Parkinson disease symptoms, medication, symptom and behavior management, disease process, communicating with family and providing optimum daily care with the goal of improving patient QOL.
Method: CPDC™ provides training through on-demand videos along with worksheets and evaluations. Additional educational tools and resources that providers can put into practice immediately are

included. Certification requires 80% of staff including 100% of leadership positions complete the training. Content covers disease-state education, medication timing, other treatment approaches, ADL considerations, the role of therapy, exercise, and the importance of sensitivity to and response to patient experience.
Results: Six facilities are currently CPDC™ certified. 474 (80%) staff was trained in 2021-2022. CPDC™ is additionally available to hospice programs, home care, and retirement communities. Comments from existing facilities include, "I gained valuable information on how to interact and care plan for someone with PD", "I am excited for the improvement in care", and "training will help me support our residents and their families".
Conclusion: Education of LTC staff in PD knowledge may improve care delivery and patient QOL. Additional data continues to be collected to support the efficacy of such programs to improve care.

P15.07

Doing DBS: Social considerations
*Daavid Shea**
Keio University, Tokyo, Japan

Most doctors think about Deep Brain Stimulation (DBS) in terms of medical conditions, but patient themselves probably consider the surgery on the basis of social factors. I know I did. I was particularly impressed to hear someone talk about DBS at the conference in Kyoto four years ago, as he demonstrated his situation prior to surgery with extreme contortions. "Before, I was like this." My neurologist told me told there was no general anesthesia which scared the living daylights out of me because I couldn't imagine having holes drilled in my head and someone poking around while I was awake. He dismissed my concerns as similar to going to the dentist but he introduced me to another a patient of his from Australia, who had the procedure. Perhaps it was because he was so diplomatically friendly that he was so persuasive.
In this paper, I basically outline my own experience with DBS beginning with the decision to undergo the procedure, what I went through during surgery, and my recovery afterwards. Success is a relative term, but it was the expected result even though the lesion effect seemed to have more affect than the surgery, especially at first. The neurologists was right about that at least.
Following a qualitative approach, I present data from doctors, colleagues, and family, whose testimony helps shed light on the decision. In conclusion, however, I argue, that until there is a cure for PD, it is the social connection with the neurologist that contextualizes the DBS and in fact keeps me alive.

P15.08

The Edmond J Safra visiting nurse faculty program at the Parkinson's Foundation
*Gwyn Vernon**
Edmond J Safra Visiting Nurse Faculty Program at the Parkinson's Foundation, Wallingford, PA, United States

Introduction: An observation study by Vernon and Bunting Perry (2007) showed there is a paucity of content in school of nursing curriculum on Parkinson's Disease (PD). Faculty surveyed voiced an overall lack of knowledge, comfort, and confidence in teaching content relative to PD. This concurred with a lack of educational opportunities and nursing journal articles on PD available at that time and concurs with more recent studies highlighting the errors in care that occur when a person with PD is hospitalized.
The Edmond J Safra Visiting Nurse Faculty Program was created to engage nursing professors in the nursing care for Parkinson's Disease. In turn, these professors provide learning opportunities for nursing students to learn about PD care, preparing them for entry into practice with evidenced based knowledge of care for PD.
Methods: A 50 nursing contact hours accredited course to immerse faculty in content on PD includes pathophysiology, signs and symptoms, disease progression, medical and surgical management, non-pharmacological management including PT, OT, ST, counseling and supportive services, nursing care and research. Importantly, 16 hours of work with patients alongside a PD expert physician or nurse is included. The faculty participant then completes an independent project to enhance nursing education and/or patient care.
Parkinson's disease centers of excellence host programs to meet geographical needs of nurse participants following a standard curriculum which is easily updated as new information on PD is released. Follow-up learning opportunities are key to keep our alumni engaged.
Outcomes: To date, over 350 nursing professors have completed the course and offer creative educational activities to over 26,000 student nurses yearly. New community programs, research projects and a dramatic increase in peer reviewed articles in journals are by-products as many nursing professors devote their scholarship to the topic of PD. Anecdotal stories support improvements in PD care.
Partipants evaluate the program highly.
Professors of nursing have the opportunity to make curricular changes by working with faculty colleagues and curriculum committees. As PD is becoming more prevalent and predicted to double by 2030, it is imperative that nurses are educated on the complex issues surrounding the vulnerable population of those with PD.

COMPREHENSIVE CARE: Disability and quality of life outcome measures

P16.01

Impact of sexual dysfunction in quality of life amongst Mexican population living with Parkinson's disease
Daniela Renee Aguila-Godinez, Etienne Reséndiz-Henríquez, Eduardo Ichikawa-Escamilla, María Alejandra Ruiz-Mafud, Gloria Itzel Cerda-Hernández, Ana Jimena Hernández-Medrano, Anna Paola Bazán-Rodríguez, Axel Antonio Herrera-Ruiz, Amin Cervantes-Arriaga, Mayela Rodríguez-Violante*
Instituto Nacional de Neurología y Neurocirugía Manuel Velasco Suárez, Ciudad de México, Ciudad de México, Mexico

Objective: Describe the impact of sexual dysfunction in the QoL of patients with PD.
Background: Parkinson's Disease (PD) has an impact on sexual activity for those who experience it (1,2), as sexual dysfunction (SD) is a Non- Motor manifestation of this pathology (3,6). It is often overlooked in Patients living with PD (1,2). The World Health Organization (WHO) defines Quality of Life (QoL) as "individuals' perceptions of their position in life in the context of the culture and value systems in which they live and in relation to their goals, expectations, standards and concerns"(4). Part of this QoL assessment is Sexual Activity. Sexual health and activity has been known to be a fundamental part of the overall welfare of humans. Defined by the WHO as ¨ a state of physical, emotional, mental and social well-being in relation to sexuality¨(5).
Methodology: We performed a retrospective longitudinal study in which we included Patients of both sexes with PD. SD was evaluated using the Movement Disorder Society Nonmotor Rating Scale (MDS-NMS) ¨I. Sexual¨Domain. Selecting the patients that answered 1 -3 in severity and 1-4 in frequency. QoL was assessed

with the Parkinson's Disease Questionnaire - 39 index (PDQ-39). The patients were divided into two groups, those with SD (>1 points in NMS.I. Total) and those without (<1 points NMS.I. Total).
Results: 136 Patients were included: 70 Males (51.5%) and 66 Females (48.5%). The mean age was 62 ±11.9 years. Hoehn and Yahr stage II was demonstrated in most (63.2%) patients. Kolmogorov-Smirnov normality test was performed, showing parametric variables. T-test was used to compare both groups showing p level of (0.983). Additionally, a Pearson Correlation was conducted between both groups and PDQ-39 index resulting in a (p= 0.611) and correlation coefficient of (r=0.044).
Conclusion: Although the comparison between groups did not show a statistical difference, we can see that there is no correlation between QoL and SD. Concluding, that the NMS Sexual Domain is not an specific tool for measuring the impact of sexual activity in the quality of life of patients with PD, hence a need for a more complete assessment tool in the Mexican population.

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P16.02

Introducing Project "Parkinson & Well": A study by Slovak Health Spa Piestany and Comenius University in Bratislava, Jessenius Faculty of medicine in Martin, Slovakia

Alena Korencikova[*,1], *Milan Grofik*[2], *Martin Kolisek*[3], *Boris Banovsky*[4], *Ivona Hrdinova*[1], *Michal Verchola*[5]
[1] Slovak Health Spa Piestany, a.s., member of Ensana Group, Piestany, Slovakia, Piestany, Slovakia
[2] Comenius University in Bratislava, Jessenius Faculty of Medicine in Martin, University Hospital Martin, Clinic of Neurology, Martin, Slovakia
[3] Comenius University in Bratislava, Jessenius Faculty of Medicine in Martin, Biomedical Center Martin, Martin, Slovakia, Martin, Slovakia
[4] Slovak Health Spa Piestany, a.s., Piestany, Slovakia
[5] Slovak Parkinson Society, Piestany, Slovakia, Piestany, Slovakia

The protective effect of the endogenous H2S has been extensively demonstrated with various in vitro and in vivo Parkinson's disease (PD) models (Cao et al. 2017). However, external H2S is also known to have positive effect on the muscle and peripheral nerve physiology. This is used for almost 200 years in rehabilitation of patients with muscle and neurological illnesses in world-renowned spa in Piestany, Slovakia. Unique composition of the sulfuric mineral water and of the river mud, which is one of the best and most famous peloids in the world, lead over the history of the spa in Piestany to development of the effective rehabilitation therapies for patients with multiple sclerosis, paralysis, paresis, polyneuropathies or various degenerative diseases of neuromuscular origin.
However, until present only isolated cases of patients with PD have been admitted for rehabilitation to our spa, being offered therapy generic for all neurological patients. In 2022, in cooperation with the Slovak Parkinson Society and Center for Diagnostics and Therapy of Extrapyramidal disorders in Martin, we have initiated development of a special rehabilitation program accustomed to specific needs of PD patients. This program consists of physio-therapeutic module (taking advantage of aquatherapy and balneotherapy), sensoric module (aiming to stimulate sensoric abilities of patients), and nutraceutical module (introducing patients to the basics of the "brain food" diet). The combination of these three modules should lead not only to rehabilitation and invigoration of PD patients, but also provide necessary knowledge base to introduce beneficial routine changes post rehabilitation in home settings.
Within the first quarter of 2023 three groups, each comprising ten PD patients, will undergo this unique rehabilitation program in spa Piestany. Our ambition is to report at the WPC forum the effect of our rehabilitation program on PD patients, based on the pre- and post-rehabilitation medical/neurological assessment and questionnaire-based data collection.
Development of this project was partly supported by grant APVV-19-0222 to MK
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P16.03

Flourishing in the face of Parkinson's: The question of well-being as it relates to Parkinson's disease

Neil Arvin Bretana[*,1], *Edward Shepherd*[2], *Dominic Rowe*[3]
[1] University of South Australia, Adelaide, SA, Australia
[2] It's Not Funny, New South Wales, Australia
[3] Macquarie University, Sydney, New South Wales, Australia

Background: To date most studies into Parkinson's disease (PD) have focused on the underlying causes, as well as management and treatment of the disease. However, as a chronic neurodegenerative condition, there is an equally important need to understand how people living with Parkinson's can continue living positive, healthy lives. A focus on salutogenesis including the factors that underly health and well-being may provide an answer. In this study, we examine whether people living with PD can live positively, and even 'flourish' in the face of Parkinson's.
Method: We generated an English-language survey based upon existing research into salutogenesis and well-being including existing theories on Flourishing and Mature Happiness. The survey utilised the Flourishing Scale (FS) designed to measure social-psychological well-being including items on engagement, optimism, and purpose. We also incorporated the Mature Happiness Scale-Revised (MHS-R) which includes items on acceptance, appreciation and harmony. The survey was deployed electronically via email and shared across several social media platforms. Participants included those diagnosed with the disease, but also others impacted by PD including carers, family members and health professionals.
Results: We collected 131 responses consisting of 79 (60%) women and 53 (40%) men from 14 countries. Of these 96 (73%) had been diagnosed with Parkinson's. The average number of years since diagnosis was 6.4 years, with a range of <12 months to 47 years. Responses indicated that most people living with PD felt significantly high levels of psychological and social well-being, with an average of 74% of respondents indicating that they "Agree" or "Strongly Agree" to each of the 8 positive statements in the FS. An average of 52% of respondents also indicated they experience

feelings of mature happiness “Most of the Time” or “All of the Time” across each of the 7 items in the MHS-R.
Conclusions: Our results show that people with PD are living positively with this chronic condition. This suggests there are strategies to transition from languishing to flourishing following diagnosis, highlighting the importance of a salutogenic approach to PD. Further research is needed to identify these factors that promote health and well-being for people living with Parkinson’s.

P16.04

Quality of life in Parkinson’s disease hypokinetic dysarthria and acoustic features in dialogical speech
Barbara Gili Fivela, Anna Chiara Pagliaro, Sonia d’Apolito*
University of Salento, Lecce, Italy

Hypokinetic dysarthria in Parkinson’s Disease causes changes in phonation, in the articulation of segments and in the production of prosody, with a marked variability in speech rate related to sudden accelerations and ‘inappropriate’ pauses [2,3,4,5]. The resulting speech characteristics play an important role in modifying communicative abilities, with consequences for the speaker’s perception of the quality of his/her life. The main goal of the present investigation is to verify if phonetic analysis of oral productions by Italian dysarthric speakers supports the self-assessment of their quality of life as measured by means of the Quality of Life in the Dysarthric speakers questionnaire - QoL-Dys [8], with a focus on interaction-related aspects.
Twelve Italian speakers particpated in the study: eight subjects suffering from Parkinson’s disease and mild hypokinetic dysarthria (PDs), together with four control speakers (CTRs). They were not cognitively impaired (MOCA >= 24), they were from and lived in the Apulia region and were age matched as much as possible (average age: PDs 63, CTRs 59 y.o.). The subjects were recorded while 1) participating in a Map-Task dialogue [9,10], and 2) describing, also through interaction with the experimenter, images corresponding to some of the icons also found in the Map-Task. Analyses regard (a) descriptive statistics on control and dysarthric speech, concerning a1) percentage and type of dialogic turns, a2) number and position of pauses, broken down into infra- and intra-speech turn pauses; b) acoustic measures, such as b1) dialogue duration; (b2) pause duration; (b3) articulation and speech rate; (b4) the disfluency index [13]). A Z test of proportions is used to statistically compare descriptive data (a) concerning PD and CTR speech, while Linear Mixed Effect Models are used to investigate acoustic measures (b), and correlations between QoL-Dys scores and acoustic measurements are investigated by means of the Kendall’s coefficient tau-b.
Results show that some investigated measures (e.g. b4 above – see figure 1) are affected by pathology and also seem to correlate with subjects’ self-evaluation. They point out the relevance of interactional aspects of speech, rather then just it accuracy or intelligibility, to preserve the speaker’s (perception of the) quality of life.

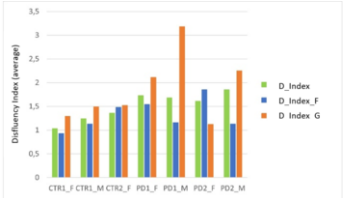
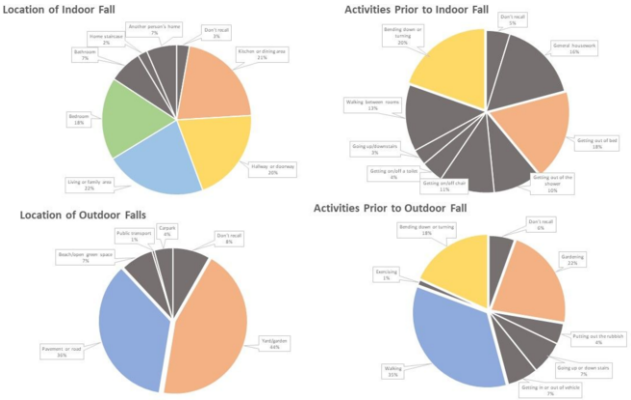


Figure 1. *Dysfluency index in Map-Task productions by 4 PDs and 3 CTRs: (F= follower, G= giver).*

P16.05

Understanding the circumstances and consequences of falls and near-falls in people with Parkinson’s disease
Dale Harris[1], Wei-Peng Teo[2], Gavin Abbott[3], Robin Daly[3]*
[1] Victoria University, Melbourne, Victoria, Australia
[2] Physical Education and Sports Science Academic Group, National Institute of Education, Nanyang Technological University, Singapore, Nanyang, Singapore
[3] Institute for Physical Activity and Nutrition (IPAN), School of Exercise and Nutrition Sciences, Deakin University, Geelong, Victoria, Australia

Background: Falls are a major health burden for people with Parkinson’s disease (PwP), however few studies have explored the precise circumstances and locations or falls and near-falls.
Objective: To explore the precise locations and circumstances (i.e., activities, causes and directions) of both falls and near-falls events among PwP.
Methods: A previously validated and reliable PD-specific questionnaire (PDFQ) was distributed online among the general community of PwP. 203 responses were provided for the questionnaire over a 1-year data collection period from January to December of 2017.
Results: A total of 138 (80%) participants reported having a fall(s) over the previous 12 months. Falls were mostly caused by tripping (27% indoor; 33% outdoor), slipping (25% indoor; 20% outdoor) or freezing (24% indoor; 29% outdoor) in a forward (37% indoor; 61% outdoor) or backward (32% indoor; 18% outdoor) direction. Indoor falls evenly occurred across the living/family (22.0%), kitchen/dining (21.3%), hallway/doorway (20.3%) and bedroom (17.9%) areas. Outdoor falls commonly occurred in the yard/garden (44.3%) or pavement/road (35.4%). A total of 159 (92%) participants reported a near-fall(s) over the previous 12 months, which were related to tripping (38%) or freezing (33%) and occurred while turning/bending (42%) or walking (35%), and commonly in a forward (45%) direction. There was a strong positive correlation between the total number of near-falls and the total number of falls, independent of location. There was no relationship between age, disease duration and BMI, however greater disease duration was correlated with near-falls and higher BMI was linked to fewer total and indoor falls.
Conclusions: The diverse characteristics of falls and near-falls explored in this study should help in the design of more targeted falls and near-falls prevention programs for PwP.



P16.06

Comparing the benefits of cognitive mapping and motivational interviewing with the Canadian occupational performance measure to provide better person-centered care

*Mary Grace Lagasca**
University of St. Augustine, Austin, Texas, United States

The purpose of this investigation is to identify the perceived benefits of using CM/MI compared to the Canadian Occupational Performance Model (COPM) in the delivery of PCC for PwPD. PD a progressive neurodegenerative condition that limits occupational engagement and quality of life (QoL) over time. There is a dearth of assessments to better capture PwPD's lived experiences and the challenges they face while engaging in activities of daily living. In the field of Occupational Therapy, the COPM is touted as an assessment of choice to provide PCC. This assessment is a standardized, semi-structured self-report, focusing on pre-determined categories of self-care, leisure, and work. The COPM is designed to capture change over time in perceived performance with intervention. The predetermined categories can limit understanding of the challenges PwPD face in general, due to the range of issues they experience. In contrast, CM/MI is a non-

structured, non-standardized method that requires a client to self-reflect, brainstorm, and discusses their specific challenge with the clinician. The CM/MI assessment tool method may have the potential to provide more insight into the needs of PwPD. The CM/MI process is a generic tool that can be used across disciplines. Methodology: A qualitative phenomenological analysis will be conducted to compare the above-mentioned assessments to better understand the needs of PwPD. Data collection will consist of the investigator/clinician's reflection on predetermined characteristics of PCC during and after administering the two tests. Data analysis will involve examining for emerging themes in the data. Findings: The themes emerging in this study may identify the benefits of using COPM compared to the CM/MI to deliver better PCC. Conclusions: Knowledge gained about the assessments will add to the body of knowledge about CM/MI and its potential to be used to deliver PCC.

P16.07

Correlation between functionality, motor and non-motor aspects of daily life experiences and the evolution of Parkinson's disease

*Isaíra Nascimento, Kátia Nobrega, Isabela Barone, Giovanna Checchio, Vitória Ponciano, Clara Paula, Natália Cardoso, Arieni Possani, Maria Elisa Piemonte**
University of Sao Paulo, Sao Paulo, Brazil

Background: People with Parkinson's disease (PD) show increasing physical disability over the course of the disease. Few studies have investigated the relationship between functionality, motor and non-motor aspects of daily life experiences of people living with PD. Measures that assess restriction in participation and not just activities are desirable. For such a purpose, WHODAS 2.0 (World Health Organization Disability Assessment Schendule) is an instrument of the World Health Organization (WHO) that assesses disability in different domains.
Objective: To investigate the relationship between functionality, motor and non-motor aspects of daily life experiences and the evolution of Parkinson's disease.
Methods: 337 individuals with PD, mean age of 58.0 years (SD=10.9), in stage 1 – 3 of disease evolution according to Hoehn and Yahr classification, living in 14 different cities representative of 5 different geoeconomic regions, participated in this study. Participants were asked to answer, through telephone interviews, a questionnaire about: (1) general information; (2) information associated with PD (i.e., Hoehn and Yahr estimated and dosage of medication); (3) perception of functionality (WHODAS 2.0); (4) perception of motor and non-motor aspects of daily life experience (MDS-UPDRS, Part I and Part II).
Results: Spearman's correlation test showed a positive correlation between variables. There was a positive correlation between the WHODAS and the MDS-UPDRS part I (r=.632, p <.050), the WHODAS and the UPDRS part II (r=.645, p <.050), as well as a positive correlation between WHODAS and disease progression, using the estimated Hoehn and Yahr variables (r=.301, p <.050) and daily dose of levodopa (r=.137, p <.050).
Conclusion: Functional disability is multidimensional. The early identification of the loss of functionality will provide us with preventive strategies for controlling and avoiding major disabilities. Therefore, multidisciplinary care should be instituted in the early stages of the disease and at all ages.

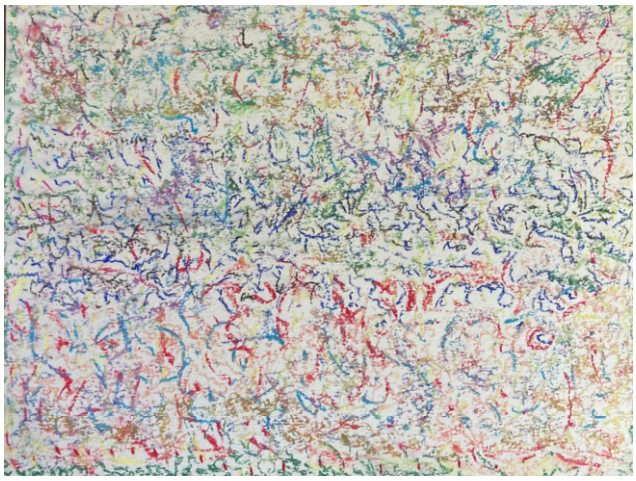
P16.08

Tracing quality of life in Parkinson's

*Fiona Navilly**
School of Sociology, Research School of Social Sciences, Canberra, Australian Capital Territory, Australia

My research examines what might be done through art to allay the diminished quality of life that haunts the diagnosis of

Parkinson's. Existing research on quality of life is often focused on a quantitative or a qualitative analysis. Research that depends on quantitative analysis, in simple terms, measures and records objective changes in physiology, and qualitative research records and measures subjective perceptions of the impact that the changes wrought by Parkinson's have on individuals. This knowledge guides decisions about treatment options and support needs. This much we know. Yet numbers and words are unable to contain all of life's qualities. Something escapes capture by the measures and records of both objective and subjective inquiry. My research responds to this problem and uses the process philosophy of AN Whitehead, and techniques developed in and the SenseLab collective at Concordia University, Canada, to expand our understanding of how we might conceptualise quality of life through examining the process of art making. Working over 18 months with 'Painting with Parkinsons', an art program for people with Parkinson's, I found that the perception of life's quality that is generated by existing quantitative and qualitative analysis is enriched by learning to register and value traces of the processes in which experience emerges. That is to say, in the experiences by which we account for "Quality of Life", there are myriad elements and forces present, only some of which, naturally, are collected into the accounts we make; that an analysis of parts alone, does not fully describe quality of life, but by locating experience in its processes, a fuller description is achieved. This research argues that what we "instinctively know" about life's quality can be registered in processes and traced through what is otherwise left out of the accounts recorded and accepted as "Quality of Life".



P16.09

Falls and quality of life in patients with Parkinson's disease

Kumar M Prakash[*,1], *Ee Chien Lim*[1], *Siew Lian Voon*[2]
[1] National Neuroscience Institute, Singapore, Singapore
[2] Singapore General Hospital, Singapore, Singapore

Objectives: Little research has been done to identify specific factors that contribute to fall risk and quality of life (QoL) in Singaporean and Asian Parkinson's disease (PD) patients. This study aimed to investigate the prevalence of falls, as well as demographic and disease characteristics that affect falls and QoL of local PD patients.
Design: This is a retrospective study.
Setting and Participants: All idiopathic PD patients seen at the Neurology and Movement Disorders Clinics from 2015 to 2019 were screened, and 136 patients satisfying the inclusion criteria were recruited.
Measures: Patients were evaluated for falls, non-motor symptoms [Non-Motor Symptoms Assessment Scale for PD (NMSS)], QoL [Parkinson's Disease Questionnaire 8 (PDQ-8)], disease severity and motor symptoms [Hoehn and Yahr stage, Movement Disorders Society-Unified Parkinson Disease Rating Scale (MDS-UPDRS) and gait assessment measures], other clinical and socio-demographic variables. Patients with 1 or more falls in the past 1 year were considered as fallers.
Results: A total of 257 falls were reported in the prior 12 months, with 39% of patients reporting at least one fall. Falls were associated with higher Hoehn and Yahr stage, freezing of gait, less social support and a lower QoL. Other factors associated with poorer QoL were higher total NMSS score and MDS-UPDRS Parts II and IV scores.
Conclusions and Implications: Differences in the effect of demographic characteristics such as social support on falls and QoL between Singaporean and Caucasian PD patients highlight the need to consider social and cultural factors when managing these patients. The findings have implications for patient care as increased educational efforts regarding fall risk factors and a multi-disciplinary approach to patient management may reduce falls and improve QoL in PD patients.

P16.10

Quality of life neurological disorders (Neuro-QoL) differences among individuals with Parkinson disease with and without freezing of gait

Lauren Tueth[*,1], *Raina Foreman*[2], *Ryan Duncan*[2], *Teresa Baker*[3], *James Cavanaugh*[4], *Tamara DeAngelis*[3], *Daniel Fulford*[3], *Jaimie Girnis*[3], *Michael Lavalley*[3], *Timothy Nordahl*[3], *Marie Saint-Hilaire*[3], *Cathi Thomas*[3], *Terry Ellis*[3], *Gammon Earhart*[2], *Kerri Rawson*[2]
[1] Washington University in St. Louis School of Medicine, St Louis, MO, United States
[2] Washington University in St. Louis, St. Louis, MO, United States
[3] Boston University, Boston, MA, United States
[4] University of New England, Portland, ME, United States

Background / Purpose: Freezing of gait (FOG), characterized by sudden arrests in walking despite intention to step, affects approximately half of individuals diagnosed with Parkinson disease (PD). While the cause of FOG is unclear, previous research suggested that FOG may be associated with anxiety, depression, and diminished quality of life (QOL). Because FOG is not well-understood, it is important to determine how individuals living with PD view their QOL and how the presence or absence of FOG may impact these self-report measures.
Methods: The sample for this cross-sectional, secondary analysis was taken from baseline data collected during a larger, prospective dual-site study titled "Walking Health is Paramount in Parkinson Disease" (WHIP-PD), which examined the effectiveness of a cognitive-behavioral, community-based, mobile health program to increase walking in persons with PD. The Quality of Life Neurological Disorders (Neuro-QoL) Measurement System was used to explore self-reported QOL across a variety of domains. The New Freezing of Gait Questionnaire was used to identify participants with and without FOG. Between-group differences in Neuro-QoL domain scores were analyzed using Welch's t-tests ($p = .05$)
Results: Of 119 individuals in the sample, 36 reported they experience FOG (mean age: 67.6±8.1; 27.8% female; MDS-UPDRS III score: 40.1±9.9) while 83 reported they did not (mean age: 67.2±8.7; 53.0% female; MDS-UPDRS III score: 36.1±12.2). Compared to non-freezers, freezers had significantly lower scores on the Lower Extremity Function survey (mean = 44.0 vs. 47.7, $p=.007$), indicating worse lower extremity function, and higher scores on the Stigma survey (mean = 48.61 vs. 45.88, $p=.031$),

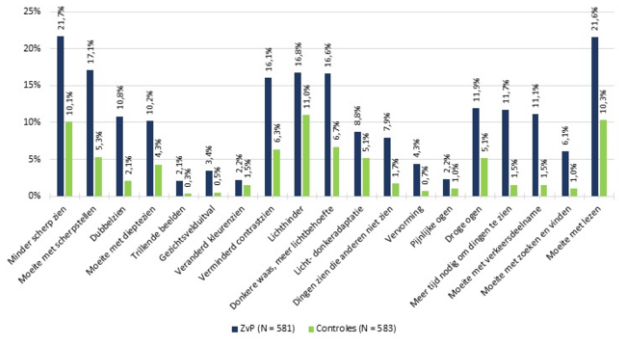
indicating greater perceived stigma related to PD. No significant differences were found on the remaining Neuro-QoL surveys (i.e., Ability to Participate in Social Roles, Anxiety, Cognitive Function, Fatigue, Positive Affect and Wellbeing, Communication, Emotional and Behavioral Dysfunction, Satisfaction with Social Roles, Depression, Sleep Disturbance, and Upper Extremity Function).
Conclusion: The results suggested that freezers may feel their QOL is more impacted with regards to mobility and stigma compared to non-freezers. The findings may assist clinicians and caregivers to understand how individuals living with PD may view their QOL and potentially inform a more patient-centered care approach.

P16.11

Prevalence and nature of self-reported visual complaints in people with Parkinson's disease – Use of the screening visual complaints questionnaire

Iris Van der Lijn[1], Gera de Haan[1], Fleur Van der Feen[1], Joost Heutink[1], Teus Van Laar[2]*
[1] University of Groningen, Groningen, Netherlands
[2] University Medical Center Groningen, Groningen, Netherlands

Introduction: Visual complaints can have a vast impact on the quality of life of people with Parkinson's disease (PD). In clinical practice however, visual complaints often remain undetected. A better understanding of visual complaints is necessary to optimize care for people with PD and visual complaints. This study aims at determining the prevalence of visual complaints experienced by an outpatient cohort of people with PD compared to a control group. In addition, relations between visual complaints and demographic and disease-related variables are investigated.
Method: The Screening of Visual Complaints questionnaire (SVCq) screened for 19 visual complaints in a large cohort of people with idiopathic PD (n = 581) and an age-matched control group (n = 583).
Results: People with PD experienced significantly more complaints than control subjects (see Figure 1), even when there was no underlying ophthalmological condition present. In addition, they experienced more limitations in daily life due to visual complaints. Most common were complaints regarding reading, unclear vision, trouble focusing, reduced contrast, blinded by bright light, and needing more light. Age, disease duration, and disease severity had a significant positive relationship with the prevalence and severity of visual complaints in people with PD. Most complaints did not differ between the sexes.
Conclusions: Visual complaints are highly prevalent in people with PD. These complaints progress with the disease and can only partially be explained by the presence of ophthalmological conditions. Standardized questioning is advised for timely recognition and treatment of these complaints.



COMPREHENSIVE CARE: PwP - Clinician partnership: Shared decision-making

P17.01

Why doctors should be talking about DBS with their YOPD patients early in their Parkinson's journey

*Christy Daniels**
Patient living with Parkinson's, Middlefield, CT, United States

Background: The appropriate time for Deep Brain Stimulation surgery (DBS) is when the needs and expected benefits outweigh individualized risks. The thresholds for these features may skew earlier in younger patients.[i] Optimizing quality of life when patients have the greatest response to dopaminergic therapy (and therefore neurostimulation) is critical to young-onset Parkinson's disease (YOPD) patients. Yet despite a study ("EARLYSTIM")[ii] that suggests DBS may be beneficial earlier in the course of Parkinson's treatment for patients with mild complications, it is not often discussed as an early treatment option for YOPD. DBS is typically used only after the disease has been present for 11 to 13 years or more, when quality of life, social adjustment (psychosocial competence) and professional activity are already severely impaired.[iii] Moreover, later in the course of the disease, features unresponsive to dopaminergic treatment often predominate.[iv] Despite this, DBS is currently only approved for people who have had PD for at least 4 years and experience certain complications (e.g., "off" time and dyskinesia)[v].
As a YOPD patient, I had to advocate for myself to opt for DBS surgery when my tremors were becoming levodopa-resistant and I experienced side-effects from higher doses of levodopa. But a Vanderbilt University Medical Center survey indicates that I wasn't alone in my persistence. The majority of respondents (72%) indicated they would consider learning more about participating in a trial testing DBS in early PD compared to standard medical treatment.[vi] In the EARLYSTIM trial, although patients had mild motor complications of recent onset (mean duration: 1-2 years), all were willing to undergo an invasive neurosurgical procedure.[vii]
Objective: To raise awareness in the Parkinson's medical community about the potential benefits of DBS at an earlier stage of YOPD and to encourage YOPD patients to consider DBS at a stage of the disease when medical treatment is still effective for motor function.
This abstract was written with support from Dr. David K. Simon MD, PhD Beth Israel Deaconess Medical Center and Harvard Medical School.

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P17.02

The complexity of Parkinson disease medication regimens may factor into treatment decisions: Results of a PMD alliance survey

Jill Farmer[1], Clarisse Goas[2], Jason Rivera[3], Anissa Mitchell[3], Andrea Merriam[3], Nikkilina Crouse[4], Andrea Formella[5]*
[1] Parkinson's Disease & Movement Disorder Program Global Neurosciences Institute, and Department of Neurology, Drexel College of Medicine, Philadelphia, PA, United States
[2] The Ohio State University Wexner Medical Center, Columbus, OH, United States
[3] Parkinson & Movement Disorder Alliance, Tucson, AZ, United States
[4] Supernus Pharmaceuticals Inc, Rockville, Maryland, United States
[5] Supernus Pharmaceuticals, Inc., Mooresburg, TN, United States

Objective: Identify factors affecting communication between people with Parkinson's disease (PwP), care partners. and health care providers (HCPs) when managing motor complications (dyskinesia and OFF episodes).
Background: The ongoing management of Parkinson disease (PD) requires clear and open communication between PwP, care partners and HCPs. However, treatment is often complex and there is a lot of information that needs to be shared. The Parkinson Disease and Movement Disorder (PMD) Alliance, a US-based advocacy organization, provides education and support to the PD community.
Methods: This online survey evaluated PwP and care partner perceptions about PD and its treatment, as well as the presence of motor complications and communication with HCPs about these symptoms.
Results: Of 562 respondents, 440 (78%) were PwP and 122 (22%) were care partners. Most PwP had PD ≥5 years (69%) and took PD medications at least 4 times daily (67%). Most respondents had experienced motor complications: 82% experienced occasional OFF episodes (39% daily), 50% experienced occasional dyskinesia (19% daily), and 28% said they had delayed starting, or avoided increasing medications because of dyskinesia or fear of developing it. Despite widespread acknowledgement of these motor complications, 72% felt PD was well-controlled by current medications. Overall, respondents perceived themselves as well-informed about PD and its treatment. Although 72% of PwP said they discussed motor complications with the HCP on most, or all visits, commonly reported challenges to these discussions included not wanting to take more medication (35%), difficulty describing symptoms (25%) and not remembering what they wanted to discuss with the doctor (18%). Additionally, care partners often noted that their loved one wants the HCP to think they are doing well, making it difficult for the care partner to raise concerns with the HCP in the presence of the person with PD.
Conclusion: Members of the PMD Alliance generally feel comfortable discussing PD symptoms and medications with their HCPs. However, even when PwP and care partners are well-informed, HCPs should be aware of potential barriers to open communication. The level of communication support needed may be even greater for individuals less well-informed about PD.

P17.03

What's your style? How personas can support personalized information provision for people with Parkinson's disease

Angelika Geerlings, Sanne Van den Berg*
Radboudumc, Nijmegen, Netherlands

Background: Providing personalized information is considered an important catalyst for empowering people with Parkinson's disease (PD) in becoming active partners in their own disease management. Understanding individuals' information style, describing i.e. how individuals seek, evaluate, select and use information, is thereby key to truly empower people with PD.
Objective: Applying a human-centered design approach to develop personas as visual representations of different information needs and preferences that support people with PD and their health care professionals in identifying personal information styles.
Methods: Six workshop sessions, each with the same group of four people with PD, were led by three researchers experienced in user experience and co-creation research. Using iterative workshop sessions, personas that mirror archetypes of information style of people with PD were co-created and visualized. In addition, for each persona tips and tricks for both patients and health care professionals were formulated.
Results: Four personas were identified: (1) Information Hunter, (2) Information Controller, (3) Information Observer and (4) Information Avoider. Personas differed by intrapersonal (personality, level of autonomy, skills and personal characteristics) and interpersonal (relationship with health care professionals, relatives as well as peers) characteristics.
Conclusion: A human-centered design approach yields valuable insights and might be used as a practical tool to identify personal information needs and preferences of people with PD. Information style personas are a first step towards personalized Parkinson care.

P17.04

The 55-word story to improve patient-provider communication

*Esme Trahair, Allison Allen, Sneha Mantri**
Duke University, Durham, NC, United States

Objective: To implement a pilot parallel charting initiative within a subspecialty interdisciplinary clinic.
Background: People with Parkinson disease and their care-partners often report difficulty communicating with their clinical team. Narrative medicine strategies, such as the parallel chart (documentation by patients/care partners), can improve communication but can require additional clinician time to review, limiting usability. The 55-word story, a short-form reflective journaling technique, can overcome time-related barriers to patient-centered communication, thereby improving clinician-patient decision-making and emphasizing the importance of the perspective of the person with Parkinson disease
Design/Methods: People with Parkinson disease seen in the THRIVE-PD (Transforming Health and Resilience through Interdisciplinary actiVities and Engagement in Parkinson Disease) interdisciplinary clinic were asked to respond to the following prompt: "What is important for your care team to know about you? Please take about 5 minutes to answer, using 55 words or less." Participants entered their response on a lined index card, using an iPad keyboard, or with dictation software. Responses were reviewed by each clinician and therapist during the interdisciplinary clinic meeting and were collected at the end of the day. Responses were transcribed and analyzed qualitatively by grounded theory methods to determine key themes. Participants also completed the PDQ-8 as an objective, validated measure of health-related quality of life.
Results: Themes reported by patients included non-illness identities (e.g. occupation, role in family or community), the psychosocial impact of living with Parkinson disease (e.g. losing independence, a changed sense of self), and the impact of clinical care (e.g. motor fluctuations, exercise, and access to rehabilitation therapy services). Correlations between qualitative responses and PDQ-8 are ongoing.
Conclusions: Short-form journaling, such as the 55-word story, is an effective way to enrich existing clinical data with the words of the patient. The concept can also be expanded to all patients and

carepartners, regardless of diagnosis, and potentially incorporated into the electronic health record for clinicians to review.

COMPREHENSIVE CARE: Palliative care/ advance planning/end of life care

P18.01

Parkinson's and palliative care – Are there different needs for women?

*Kathleen Armstrong**
St. Louis University, Saint Louis, MO, United States

Background: Men are over one and a half times more likely than women to develop Parkinson's Disease (PD), a progressive neurodegenerative disease characterized by impairments of movements, balance, and speech. Differences between men and women with PD exist in symptom presentation, progression of the disease, and response to treatment, and can have an impact on quality of life. Palliative care (PC) needs for women also differ from the needs of men. These needs are both emotional and physical.
Purpose: The purpose of this systematic review was to provide an overview of the literature concerning the gap in the literature relating to palliative care needs for women with PD at the end of life.
Methods: A systematic literature search was performed in the electronic databases PubMed, CINAHL, OVID Medline, Cochrane Library, and SCOPUS from January 2017 to December 2022. Search terms utilized were: female, females, women or women; palliative care, hospice, dying, end of life or terminal care; and Parkinsons, Parkinson's, pd, or parkinsonism.
Results: A total of 572 studies were found using the outlined search terms. After removing duplicates and non-relevant studies, fifteen studies were identified that addressed palliative care and women with PD for review. Inclusion criteria were studies addressing palliative care and included women of all ages and races with PD in the study.
Conclusions: While fewer women have PD than men, women report more disease severity and report more psychological distress with their disease. Women are less likely to seek treatment for PD symptoms, receive a lower quality of care, experience more symptoms including fatigue and pain, and tend to cease treatment earlier than men. In addition, more elderly women than men are widowed or live alone at the end of life. Women are largely underrepresented in studies focused on PD patients. The review of the literature uncovered that currently, no research studies exist addressing these and other specific needs of women with PD relating to the use of palliative care. With the incidence of PD projected to increase by 20% by 2025, globally there is a need to explore palliative care needs specific to women with PD.

P18.02

Continuous subcutaneous apomorphine infusion for the management of Parkinson's disease at the end-of-life

Matthieu Bereau, Mathilde Giffard, Anne-Laure Clairet, Marc Verin, Manon Auffret*
University Hospital of Besançon, Besançon, France

Objective: To describe the benefit of continuous subcutaneous apomorphine infusion (CSAI) for terminal care management in 10 PD patients.

Background: There are currently no recommendations for the therapeutic management of Parkinson's disease (PD) at the end of life. Progressive or sudden inaccessibility of the oral route is frequent at this stage and may result in complications such as aspiration pneumonia or the Parkinsonism-Hyperpyrexia Syndrome (PHS). These potentially fatal outcomes also considerably worsen the quality of life of PD patients and their relatives. Here, we described the benefit of continuous subcutaneous apomorphine infusion (CSAI) for terminal care management in 10 PD patients.
Methods: We retrospectively collected clinical data from 10 PD patients for whom CSAI was initiated in the context of terminal care. We analyzed the patient's comfort, analgesic and sedative drugs consumption, as well as the caregiver's burden. We also recorded side effects related to CSAI.
Results: All patients had a diffuse PD phenotype with severe motor and cognitive decline and dysphagia. Precipitating factors for end of life care were identified in all cases. Patients received CSAI for terminal care at low dosages (<3mg per hour) over 24 hours either at home or in care services. CASI was combined with neurological and palliative follow-up under the supervision of the PD nurse. Duration of treatment was between 2 and 10 days. In all cases, CSAI at low dosages markedly improved patient comfort (particularly axial rigidity and pain) and caregiver's burden. CASI also diminished analgesic and sedative consumption and allowed some patients to communicate with their relatives until death. No serious adverse events were noticed.
Conclusion: CSAI at low dosages was of great interest in PD terminal care for both patient's comfort and caregiver's burden, without serious adverse events.

P18.03

Terminal care for parkinsonian residents in French nursing homes: A 10-year longitudinal retrospective study

Mathilde Giffard[*,1], Corentin Geoffroy[2], Manon Auffret[3], Matthieu Béreau[4]*
[1] University hospital of Besançon, mobile palliative care team, Besançon, France
[2] University of Reims Champagne-Ardennes, Reims, France
[3] University hospital of Rennes, EA 4712, Rennes, France
[4] University hospital of Besançon, Neurology, Besançon, France

Background: Parkinson's disease (PD) affects approximately 6.5 million people worldwide. This progressive neurodegenerative disease causes a high institutionalization rate and a significant symptom burden leading to palliative care (PC) needs as significant as those of cancer patients. However, PC has not yet become an integral part of the care for these patients.
Aims: To increase PC development for parkinsonian residents in nursing homes, there is a need to scrutinize current practices during the terminal phase. Therefore, the present study aimed to describe (1) the clinical profile of the residents, (2) the medical team involved during the terminal care, and (3) the place of death, using data over 10 years.
Methods: This retrospective study included all nursing home residents who died between July 2012 and June 2022, suffering from PD or related syndromes in the Besançon area, France.
The following information was extracted from the medical files: gender, date of birth and death, place of death, parkinsonian syndrome, antiparkinsonian drugs, follow-up by a neurologist, general practitioner visits, PC mobile team, and neurologist referral during the terminal phase.
Results: The study included 109 residents from 7 nursing homes. Most patients had PD (94/109), followed by Lewy body dementia (12/109) and progressive supranuclear palsy (2/109). The mean age at death was 87±7 years. The duration of the terminal phase was 5.7 days. Most residents died in their nursing home (84/109), and

24/109 died in the hospital after a transfer occurring 6 days before death. Only 31/103 residents had follow-ups with a neurologist. During the terminal phase, 2/88 residents had a consultation with a neurologist, 10/90 had access to a mobile PC team, and 63/100 had a visit from their general practitioner. The dopaminergic treatment was stopped for 80/84 residents who died in their nursing home with no therapeutic alternative, 5.6 days before death.
Conclusion/Discussion: Many PD residents die in nursing homes. However dopaminergic treatments are often stopped without any alternative, raising questions regarding the quality of life during the terminal phase. Future studies should investigate how the integration of PD into the care of PD nursing home residents can be improved.

P18.04

The effect of a multidisciplinary blended learning program on palliative care knowledge for health care professionals involved in the care for people with Parkinson's disease
Herma Lennaerts, Anne Ebenau, Silvia Kanters, Bas Bloem, Kris Vissers, Bauke Dijkstra, Marjan Meinders, Marieke Groot*
Radboudumc, Nijmegen, Netherlands

Background: Parkinson's disease (PD) is an increasingly prevalent and progressive degenerative disease. Palliative care for PD should be integrated into the routine care for people with PD. However, PD health care professionals typically lack knowledge of palliative care, highlighting the necessity of educational programs in this field.
Objective: To determine the effectiveness of a multidisciplinary blended learning program for health care professionals specialized in PD in the Netherlands.
Methods: We used a pre-posttest intervention design. The intervention consisted of an e-learning in combination with an online network meeting in which the participating health care professionals discussed palliative care for PD with specialists from the field of palliative care. Outcome variables included self-rated level of knowledge (scale 1-10), familiarity with specialized palliative care services (5-point Likert scale) and the validated End-of-Life Professional Caregiver Survey (EPCS).
Results: A total of 1029 participants from sixteen different disciplines, all active in the care for people with PD, with a mean age of 45 years and 13 years of working experience, followed the blended learning program. Self-rated level of knowledge improved from 4.75 to 5.72 (0.96; $p < 0.001$; 95% CI change = [0.85 ... 1.08]. Familiarity with palliative care services also increased by 1.06 (from 1.85 to 2.90; p=<0.001; 95% CI change = [1.00 ... 1.12]).
Conclusion: A blended learning program can improve self-rated knowledge about palliative care and its services. Such programs might be a first step towards optimal integration of palliative care expertise and services within PD-care.

P18.05

Feasibility of a nurse-led advance care planning and care coordination intervention in Parkinson's disease – Results of a multicenter European study
Catharina Muente[1], Bauke W. Dijkstra[1], Marieke Groot[2], Marjan J. Meinders[1]*
[1] Radboud University Medical Center, Department of Neurology, Centre of Expertise for Parkinson & Movement Disorders, Nijmegen, Netherlands
[2] Rotterdam University of Applied Sciences, Research Centre Innovations in Care, Rotterdam, Netherlands

Background: Advance Care Planning (ACP) is a process which should help individuals understand and communicate their personal values, life goals and preferences in relation to future care. The use of ACP in healthcare for people with Parkinson's disease (PwPD) is rare. In the PD_Pal study, a nurse-led ACP and care coordination intervention for PwPD and their family caregivers (FCs) in various European countries was performed. Insights into the feasibility aspects of such an intervention from the perspective of PwPD, FCs and nurses involved should facilitate the future implementation of ACP and care coordination in clinical practice.
Methods: The intervention included multiple consultations with a trained nurse who conducted ACP discussions and supported care coordination, as well as the use of a patient-centred "Parkinson Support Plan Workbook". In a multicenter, randomized controlled trial, the intervention was evaluated in seven European countries (Austria, Estonia, Germany, Greece, Italy, Sweden and the United Kingdom). To assess feasibility, post-intervention qualitative semi-structured interviews were conducted with PwPD (n=39), FCs (n=30) and the nurses who delivered the intervention (n=6). Feasibility aspects included the design of the intervention, involvement of FCs, timing of ACP conversations, use of materials, as well as hindering and facilitating factors in general. The evaluation was based on a framework analysis.
Results: A major barrier for the implementation of ACP discussions was the tabooing of death and dying. Facilitating factors were the consideration of country-specific and cultural aspects, the creation of an atmosphere in which participants felt safe to talk about burdensome issues, and the empathetic guidance provided by the nurse. The design of the intervention, the involvement of FCs, the timing of ACP discussions and the use of materials should therefore be tailored to the PwPD's needs to better discuss end-of-life care wishes and improve care coordination.
Conclusions: The results highlight the importance of tailoring the intervention at multiple levels. In addition to country-specific and cultural factors, the PwPD should determine the timing and form of ACP discussions about end-of-life care wishes.
The PD_Pal project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No. 825785.

P18.06

Status report on palliative care in Parkinson's patients: Dark reality in resource poor nations
Shankh Pal[1], Ranjit Sharma[1], Tillotma Roy[1], Kaul Meghna[2]*
[1] SFCCP, Meerut, UP, India
[2] TNM, Meerut, UP, India

Issues: Social stigma, Fatigue, sexual dysfunction, Sleeplessness, depression commonly seen in Parkinson's patients. Palliative inaccessible in rural/tribal areas. Hence our NGO nurses took initiatives to help alleviate suffering of women with Parkinson patients since October 2018.
Objective: n=110. Of these statistically over 90% express sexual-dysfunction, 68% experience loneliness; 70% suffer social neglect/humiliation, 64% had depression. Importance of spirituality/religion in coping with terminal-illness is increasingly recognized Hence Our NGO-nurses involved community-leaders to make more women involved in our spiritual healing sessions.
Methods: We surveyed 110 subjects through QOL-questionnaires. After 22 weeks therapy with psychosocial support. Counseling & palliative care with anti-depressants/pain-killers/nutrition, QOL improved to statistically significant level. Requirement of palliative care evaluated by Palliative Care Problem Severity Scale (PCPSS). Traditional faith-healers involved for more psychological impact on patients community. Community leaders involved to reduce social stigma/discrimination among community.
Results: currently 210 specialist palliative care beds required for our Rural/tribal population of 16,00,000. But only 80 available. 60%

expressed that religious/community support/faith was most important factor that helped them to cope with Parkinson's. higher scores of QOL (ANOVA $p < 0.001$) correlated with lack of sexual dysfunction/pain. Our NGO-initiative suggests that over 70% patients will need well trained specialist for home-based-care.
Conclusions: Life-span/QOL of Parkinson patients-sufferers depends on social acceptance & appropriate-palliative-care. NGO-personals should be trained in Palliative-care-services. Field of Spiritual/psycho-social/community support is fertile ground for further investigations. We need focused platform like world Parkinson coalition to discuss our project ideas/concerns/difficulties with senior researchers.

P18.07

The role of telemedicine to support care in advanced Parkinson's disease
Robin van den Bergh, Pauline van Barschot, Bauke W. Dijkstra, Herma H. Lennaerts-Kats, Catharina Muente, Marjan J. Meinders*
Radboudumc, Nijmegen, Netherlands

Background: The care for people with advanced Parkinson's disease (PwP) faces several challenges such as managing increasingly complex medication schemes, coordinating care between healthcare professionals and providing palliative care. Telemedicine might be able to alleviate some of these challenges, for example by monitoring PwP remotely, reducing travel burden, and enhancing access to treatments and specialized care teams. Therefore, as part of the PD_Pal project (H2020 grant agreement No.825785), we aim to gain an overview of the opportunities of telemedicine to support care for people with advanced Parkinson's disease.
Method: We conducted semi-structured interviews with 58 people involved or interested in advanced Parkinson care including PwP (n=15), carers or family members (n=6), neurologists (n=4), nurses (n=7), physiotherapists (n=5), speech therapists (n=5), occupational therapists (n=6), specialists in elderly care (n=6), psychologists (n=3), and one ethicist. The interview guide was constructed together with a panel of patient researchers and covered teleconsultation, telemonitoring, and tele-information provision. We analyzed the data in a thematic analysis.
Results: Teleconsultations were perceived as a good adjunct to in-person consultations in specific cases. Participants stated that an in-person consultation more rapidly led to a trustworthy relationship and allowed for a more comprehensive picture of the other. This was especially important for conversations about palliative care, as they require a relationship of trust and understanding between the PwP and healthcare professionals. Although being a second best, participants stated they could talk about palliative care topics remotely. Especially when PwP were living far away, it was better to receive any form of palliative care than none.
Remote monitoring technology was generally perceived as useful by participants, for example when PwP were homebound. The specific monitoring information that was deemed useful varied considerably between participants, ranging from medication effects to cognitive functioning.
The participants desired a clear, reliable, and trustworthy online database with information about advanced Parkinson care. The technical skills and cognitive capacities of PwP in an advanced stage might prohibit the use of such digital information resources, but these resources can support relatives.
Conclusion: Our findings support the emerging initiatives to develop telemedicine solutions for the delivery of care for people with advanced Parkinson's disease.

P18.08

Symptoms at the end of life in patients with Parkinson's disease
Elisabeth Wilson, Emily King-Oakley, Edward Richfield*
North Bristol NHS Trust, Bristol, United Kingdom

Background: Parkinson's disease is a neurodegenerative condition affecting over 145,000 people in the UK. People with Parkinson's (PwP) are more likely to die in hospital, but this experience is not well documented, despite several factors likely to make it unique. Better understanding is important to alleviate suffering and achieve a "good death".
Method: Retrospective case note review of sequential in-hospital deaths in a tertiary centre in the UK, Feb '19 – Feb '21. Patients excluded if intubated at the time of death (n=5). Symptoms, medication and dopaminergic medication recorded in the last 72 hours of life.
Results: 51 patients, mean age 81 years (54-92).
Common symptoms; agitation 60.78%, pain 58.82%, shortness of breath 45.1% and respiratory secretions 43.14%. 2 patients had terminal rigidity. For agitation and pain this is higher than previously documented in the general population (52.4% agitation and 46.4% pain) and similar rates of respiratory secretions (44.6%).
Frequently administered breakthrough medications were; opiates 84.31%, midazolam 54.9% and hyoscine butylbromide 41.17%. Six patients received anti-emetic breakthrough doses (ondansetron 4, cyclizine 2, levomepromazine 1).
Patients with pre-existing cognitive impairment received higher mean total dose of midazolam than those with preserved cognition (29.18mg vs 11.4mg, median 7.5mg vs 2.5mg). Mean opiate doses were lower in this group (24.7mg vs 30.3mg), although median identical (10mg vs 10mg), requiring corroboration in larger study.
28 patients (54.9%) received rotigotine (off license indication) at time of death, for mean of 4 days. Less than a third of patients received correct OPTIMAL calculator dose of rotigotine (32.14% higher, 39.29% lower).
Conclusion: PwP have significant symptom burden at EoL with levels of terminal agitation higher than expected in the general population.
A trend towards higher doses of sedation, rather than pain relief in PwP and cognitive impairment, if corroborated elsewhere, is important, and may reflect difficulty in expression and recognition of pain in this vulnerable group. This warrants further exploration.
Terminal stiffness, despite seldom documented in the literature, is an important albeit infrequent symptom.
Rotigotine used off licence at EoL remains common place and better understanding of its effect, particularly with regard dosing and terminal delirium is required.

COMPREHENSIVE CARE: Health accessibility/underserved populations

P19.01

What can applicable Hoehn and Yahr five assessment measures tell us about people in advanced Parkinson's disease?
*Pâmela Barbosa, Maria Elisa Pimentel Piemonte**
University of Sao Paulo, São Paulo, São Paulo, Brazil

Background: People with Parkinson's Disease (PPD) in late-stage suffer from motor and non-motor symptoms that have a poor response to dopaminergic treatment, therefore non-pharmacological

treatment (NPT), such as physiotherapy (PT), assume an important role. However, not only this population faces many obstacles to access health care, but also healthcare professionals have limitations to approach them due to lack of evidence. **Purpose:** To access the motor function, cognition and quality of life (QOL) of six PPD in late-stage. **Methods:** Six PPD in stage 5 of Hoehn and Yahr classification (HY) were included in the study and assessed according to International Classification of Functioning Disability and Health using the Unified Parkinson Disease Rating Scale - II (UPDRS-II); Balance Evaluation Systems Test (BESTest); Nine-hole Peg Test (9HPT); and 5 Times Sit to Stand Test (FTSTS) as assessments for activity level. Measures of function included Geriatric Depression Scale (GDS-15); Montreal Cognitive Assessment (MOCA); UPDRS-III; and for participation level the Parkinson Disease Questionnaire (PDQ-39). **Results:** Firstly, BESTest; 9HPT; and FTSTS test were not applicable in this population. Actually, only 2 of the subjects were able to sit and stand 5 times with hand support. Further details about descriptive statistics are presented in the attached table. In function, visuoconstructive abilities, 0,66 (1,63); and memory 1,50 (1,76) were the most affected domains in MOCA. In participation level, the most affected domains was mobility, 80,41 (4,58); and daily life activities, 77,07 (12,84). Impairments of activity level and motor function can impact on QOL according to the most severely impaired domains in PDQ-39. Also, the most prominent deficits in cognitive function are important determinants for motor planning performance in everyday tasks. The ability to do basic daily functions are linked to a very important part of QOL and may jeopardize the emotional state, since this 6 PPD had high signs of depression. Even though NPT could have a key role to mitigate the impact of disease, only one subject had access to PT. **Conclusion:** UPDRS-II and III; MOCA; GDS-15; and PDQ-39 seems to be applicable and to bring valid information about PPD in HY 5 functionality.

Table 1. Descriptive statistics analysis based on mean and standard deviation using excel 2010 and Statisca programs.

Variable	Valid N	Mean	Standard Deviation
Age	6	77,00	6,32
Years of Study	6	10,33	5,95
UPDRS-II	6	32,50	3,14
5 FTSTS (seconds)	2	51,74	54,86
UPDRS-III	6	68,66	4,17
MOCA	6	14,67	4,96
GDS-15	6	10,50	1,87
PDQ-39	6	61,90	9,12

Unified Parkinson Disease Rating Scale (UPDRS); 5 Times Sit to Stand Test (FTSTS); Geriatric Depression Scale (GDS-15); Montreal Cognitive Assessment (MOCA); Parkinson Disease Questionnaire (PDQ-39).
Green - assessments for activity level
Blue - assessments for function level
Yellow - assessment for participation level

P19.03

Towards inclusion: Using integrated knowledge translation to design and implement a community-based assessment service for young people with Parkinson's disease

Sarah Davies[*,1], *Donna Rooney*[*,1], *Miguel Diaz*[*,2]
[1] The University of Queensland, Brisbane, Queensland, Australia
[2] Parkinson's Queensland Incorporated, Brisbane, Queensland, Australia

Parkinson's Queensland Incorporated (PQI) is leading the development of a novel health service to improve access to funding and support for young people with Parkinson's Disease (PwPD). In Australia, young PwPD are eligible for support through the National Disability Insurance Scheme (NDIS). The NDIS provides funding to support daily personal and household activities and access to therapies and equipment, with the goal of enabling greater independence and an improved quality of life. Access to such support systems for young PwPD is crucial in facilitating early intervention and ongoing care. Access to the NDIS also offsets the significant cost of Parkinson's in social and economic terms. Young PwPD frequently report challenges accessing and navigating the NDIS. The application process requires allied health assessments, particularly occupational therapy, to provide assessment reports in support of their application. The wait times for such assessments and the cost associated are significant barriers to access. Parkinson's organizations such as PQI provide valuable advocacy, support, information, and education and are often a main and early contact point for PwPD. In response to the frequent requests for support with the NDIS application process, PQI initiated a collaboration with researchers, occupational therapists and PwPD with the aim of developing a new service to improve access to the NDIS for young PwPD. Developing novel health services with the people they are intended to benefit leads to better outcomes and builds trust. Here we report on the design and implementation of an occupational therapy assessment service that will provide subsidized community-based assessments for young PwPD. This will ensure that all young PwPD in Queensland can access the NDIS and receive the early intervention and ongoing care support needed to live well with Parkinson's.

P19.04

Increasing Hispanic/Latino recruitment into Parkinson's genetics research

Priscila Delgado Hodges[*,1], *Rebeca DeLeon*[2], *Anna Naito*[2], *Roy N Alcalay*[3], *Juan Ramirez-Castaneda*[4], *Ruby Rendon*[5], *Claudia Martinez*[6], *Camila Gadala-Maria*[2], *Adriana Jimenez*[7], *Rossy Cruz-Vicioso*[8], *Henry Moore*[9], *Paulina Gonzalez Latapi*[10], *Valentina Caceres*[1], *Anny Coral*[2], *Ignacio F Mata*[*,11]
[1] Indiana University School of Medicine, Indianapolis, IN, United States
[2] Parkinson's Foundation, Miami, FL, United States
[3] Tel Aviv Sourasky Medical Center, Tel Aviv, Israel
[4] UT Health San Antonio, San Antonio, TX, United States
[5] Barrow Neurological Institute, Phoenix, AZ, United States
[6] Davis Phinney Foundation, Louisville, CO, United States
[7] Give for a Smile, Garden Grove, CA, United States
[8] Unión Médica del Norte Clínica Universitaria, Santiago de los Caballeros, Dominican Republic
[9] University of Miami, Miller School of Medicine, Miami, FL, United States
[10] Northwestern University, Feinberg School of Medicine, Chicago, IL, United States
[11] Genomic Medicine Institute, Cleveland Clinic, Cleveland, OH, United States

Our goal is to update the PD community about the strategies used to increase Hispanic/Latino recruitment into the Parkinson's Foundation (PF) PD GENEration study.
Current research has showed that Hispanics/Latinos are attracted to various research opportunities; however, unaddressed barriers limit their involvement. Some of these barriers include challenging work schedules, language, education, and transportation.
The PD GENE Latino Advisory Committee was created by the PF to increase study recruitment of Hispanics/Latinos. Members of the committee are key PD community stakeholders and focus on the minimization of barriers and expansion of research related resources. To address the language barrier, all study documents (i.e., advertising/marketing, study protocol, consents, letters) were culturally tailored and translated into Spanish. Recruitment of

bilingual staff, as well as the inclusion of sites with high Hispanic/Latino demographics was key. There is study enrollment flexibility (virtual & in-person) and we have expanded our community outreach to hybrid events. All event agendas are carefully developed to present relevant PD topics and engage the community with exercises, Q&A's, and personal stories.
Within 3 years and a pandemic, we have hosted 5 virtual/3 hybrid events with a total of 540 virtual/150 in-person attendees, and a total social media outreach of 3,059 individuals [table1]. Given the social media impact, there are additional efforts to engage the community through the Spanish PF Facebook page. The most successful post for December was a Christmas recipe book that encouraged research discussions among family members which had an average engagement rate of 10.3%. As of today, PD GENE has an 11.5% Hispanic/Latino representation which is a 4-fold increase since the creation of the AC.
Additional strategies are necessary in order to bolster Hispanic/Latino recruitment since virtual recruitment alone is not enough. Since current study strategies have proven successful, the Hispanic/Latino study representation goal has been increased to 20%. More in-person events are planned for this year that will be tailored to each community based on their needs and interests. It is our hope that by sharing these ever-evolving strategies we can help other researchers with their own research initiatives.

Table 1. List of events for the Hispanic/Latino community 2020-2022

Event Name	# Registred	# Attended	% AR*	In-person	Social media
La enfermedad de Parkinson y la genética	323	163	50	-	2696
Presentación a la Sociedad de Neurologia y Neurocirugia de la Republica Dominicana	87	63	72	-	-
Trabajando juntos hacia un mejor futuro en la enfermedad de Parkinson	19	8	42	-	-
GEN-EP Latino / La enfermedad de Parkinson y la genética	84	46	55	-	45
Rostros del Parkinson: Grupo de apoyo para pacientes con Enfermedad de Parkinson **	60	39	65	50	-
Hacia adelante: Un paso en frente del Parkinson **	144	130	90	50	
El Parkinson, los cuidadores y la investigación	115	51	44	-	318
Rostros del Parkinson_Cuidando tu bienestar emocional **	45	40	89	50	
Total	**877**	**540**	**507**	**150**	**3,059**

(*) AR= Attendance Rate

(**) Represents a hybrid event

P19.05

Academic-community partnership to develop a Parkinson resource center in the rural southern U.S.
Donna Hood, Denise Pyles*
Louisiana Tech University, Ruston, LA, United States

Background: Alumni of the Edmond J. Safra Visiting Nurse Faculty (VNF) Program at the Parkinson's Foundation gained heightened awareness of PD community needs and lack of resources in rural north Louisiana. Building on the support and expertise gained through participation in this program, the team established the Parkinson Resource Center (PRC) at Louisiana Tech in 2018. Louisiana Tech University is a comprehensive, public university located in rural, north central Louisiana.
Method: The four domains of community-based participatory research served as the implementation framework for the development of a mutually beneficial and sustainable academic-community partnership supporting the PD community. Bi-directional leadership across the academic and community context served to promote equal partnerships in every stage of development and implementation.
Results: Living with PD (individuals and care partners) and preparing the next generation of empathetic health care professional serve as the context for the model of the PRC. Partnership processes include community members with PD and care partners, academic faculty/staff from nursing, speech language pathology, nutrition and dietetics, music, and wellness, and program funders. Intervention and research processes include Rock Steady Boxing, Music & Movement, LSVT-LOUD, and PD Chorale. Outcomes include improving health, self-care, self-confidence and empathy, and sustainability. Shared leadership, promoting collective reflection, and empowerment are central to this model.

P19.06

Gaps in the literature for women with young onset Parkinson's disease
Kristi LaMonica[,1], Katherine Florian[1], Diandra Hennessy[1], Alexandra Iglesia[1], Britney Merwin[1], Eliza Whitman[1], Kate Murphy[2]*
[1] Russell Sage College, Troy, NY, United States
[2] The Albany Academy, Albany, NY, United States

We have identified gaps in the literature regarding women with YOPD. Anecdotal evidence shows women with YOPD during menstruation exhibit either an exacerbation of motor symptoms and menstrual symptoms, or loss of efficacy of medication. Furthermore, many women report their concerns are not acknowledged or taken seriously by care professionals. There are a number of groups working to address these issues. We are working towards evaluating scientific literature through pubmed with the search terms YOPD and quantifying mention of women, pregnancy, and menstruation. We show that only 71% of the articles mentioned YOPD with 27% mentioning women, with fewer papers even mentioning menstruation and pregnancy. Our goal is to provide data to help close the gaps on what is known about women with YOPD.

P19.08

The role of community neurology clinic
*Iku Moroo**
Mihama neurology clinic, Chiba, Japan

The Parkinson's disease pandemic is a looming problem for Japan, which has the fastest-aging population in the world. Japan does not have a polarized medical system consisting of specialists and general practitioners, and practitioners with experience as intermediate specialists support regional medicine. Clinic neurologists play an essential role in community medicine for Parkinson's disease. This survey clarified the actual conditions of Parkinson's disease patients who visited community neurological clinics.
The median age of outpatients was 76 years old, and outpatient visits for young-onset Parkinson's disease patients were rare. As neurological clinics that are active in the community are becoming known to the local community, residents have begun to visit clinics with suspected symptoms, indicating that community neurology clinics play a significant role in the early detection and intervention of Parkinson's disease.
Many people use walking, bicycles, and buses, and it turns out that they do not use trains when the H-Y grade reaches 4 degrees. We learned that community clinics are essential to provide medical care for older people who find it difficult to go to university hospitals, people who live alone, and patients with dementia with Parkinson's disease. The system has many advantages of being able to respond locally. From the perspective of maintaining appropriate medical care and improving the quality of life of Parkinson's disease patients, we provide home-visit nursing care, drug guidance,

cooperation with the government, vaccinations, and health checkups.
The study also showed that local clinics are playing a role as a receptacle for patients who cannot go to university hospitals due to the COVID-19 pandemic.
There is a dichotomy of debate over whether a movement disorder specialist should treat Parkinson's disease at a university hospital or whether general physicians should treat Parkinson's patients as home doctors. The Japanese system, in which doctors with experience in medical care at advanced medical institutions open their doors in the latter half of their careers and develop medical care in the community, helps raise the level of Parkinson's disease care.

P19.09

Leveraging design thinking to increase the accessibility of power for Parkinson's programming for underserved populations in Austin, Texas
Nina Mosier, Elena Eddington*
Power for Parkinson's, Austin, TX, United States

Objective: By using design thinking methodology, PFP will engage communities in the Greater Austin area that have historically experienced limited access to healthcare support and are not involved with Power for Parkinson's (PFP) free programming in order to diversify our outreach in a culturally relevant and community-informed way. Knowledge gained through direct community collaboration will help address health disparities by raising both general awareness of Parkinson's Disease (PD) as well as awareness of the free, evidence-based fitness and social support services offered by PFP.
Methods: Power for Parkinson's has innovation at the core of its work—offering free, PD symptom-focused exercise and dance classes, support groups, and social events to both the Austin community and a global audience. Continuing to center innovation in our efforts, PFP will use design thinking methodology to reach an expanded audience of people with Parkinson's in the greater Austin area, with an explicit focus on reaching African American, Latinx, and Asian communities. Design thinking is an iterative process of listening to, observing, and empathizing with people. The process involves the following steps:
Empathize: Learn about the target audience by observation and interviews.
Ideate: Brainstorm as many creative solutions as possible.
Prototype: Build a representation of one or more of your ideas.
Test: Share your prototyped idea with your audience.
Iterate: Take feedback into account and iterate on the prototype.
Implement final design
Results: Design thinking will produce community-informed solutions, ensuring improved access for traditionally underserved communities with increased engagement in both existing programming and newly developed programming. PFP will be to expand PD fitness programming to serve more diverse populations and coordinate culturally relevant social events and support services.
Future Goals: PFP has a long history of tailoring our programs to better serve our community as their needs change and as our bandwidth to support them expands. PFP will continue to gather community feedback in order to refine service delivery and enhance both PD awareness and the accessibility of our programs.

P19.10

www.PregSpark.com, introducing the International PregnancieS and Parkinson's Registry, an initiative of the Radboud UMC in co-creation with PWP
Annelien Oosterbaan, Willanka Kapelle, Bastiaan Bloem, Bart Post*
Radboud UMC, Nijmegen, Netherlands

Objective: PregSpark is an online prospective registry that aims to collect data on pregnancies in women all around the world living with Parkinson's disease (PD).
Background: Pregnancy in Parkinson's is rare, but with PD being the fastest growing brain disease worldwide combined with increasing maternal age, this combination will be more common in the future. However, the impact of pregnancy on PD or vice versa is not understood. Due to lack of available literature there is no evidence based periconceptional advise, guideline or management protocol available for PD women with a desire to have a child. This makes deciding on their child whish after diagnosis an insecure process. This has to change and therefore we have started this international online and ongoing registry to collect a significant amount of data and in the end create new guidelines.
Methods: From June 2023 all women with PD and pregnancy will be able to enroll at www.PregSpark.com. The registry is based on self-reported data, using Web-based questionnaires filled in by pregnant women. The participants are invited to fill in maximally six questionnaires during and after pregnancy. The amount of other questionnaires is dependent on the moment of enrollment. The questionnaires will cover issues concerning pregnancy and Parkinson's related topics and symptoms, medication use and general health, level of physical activity and so on. After birth important information concerning birth outcome will be collected. Women can participate from the beginning of pregnancy and at the latest 8 weeks postpartum.
Conclusion and Discussion: This registry for Parkinson's and Pregnancy is essential to fill the knowledge gap on this topic. By letting PD women all over the world enroll themselves, and by using web-based surveys, our goal to collect data on as many pregnancies as possible will best be achieved. Previous studies using web-based surveys with self-reported data have shown to validly collect data among pregnant women. In the future our data will provide PD women with the information they need to make an informed choice concerning their child wish. In addition, the data will serve to construct guidelines and management protocols on pregnancy, delivery and breastfeeding in women with PD.

P19.11

Novel initiative project for Parkinson's care by community contribution
Shankh Pal, Tillotma Roy, Bhindu Gupta*
SFCCP, Meerut, UP, India

Issues: Parkinson's patients Rehabilitation services aren't well-developed concept in resource-Poor nations due to poor economics & lack of expertise. With limited resources we wanted to explore these rehabilitation services in rural villages.
Aims: Rural/tribal areas of India lung Parkinson's patients [Ca] patients lack rehabilitation support available only in city hospitals. Our 12-year CBO is training youth volunteers & traditional faith halers in marginalized communities to provide rehabilitation.
Methodology: Around 1865 cases of Parkinson's will be in rural/tribal of India by 2025, but hospitals lack dedicated Rehabilitation program. patients returning to villages after onco-therapy in cities urgently need Rehabilitation support to suit their economic, social, cultural background. Since August 2018 Our NGO clinic started free advise on Rehabilitation. [n=112]. With 6 trained

nurses, two physicians, we screened patients. Average age 58.9 years, M:F ratio 68:32. Our support services devised as-per need of Patients in consultation with family & stretched over 14 months included conselling, physiotherapy and occupational therapy. Responses assessed with Quality of life scale by Flanagan Quality of Life Scale (QOLS) & psychological evaluation by Likert psychometric scale. This presentation demonstrates project in developmental stages & basic operational facts. Initially started as practically oriented guidance center & later developed in well-organized set-up offering free rehabilitation services in villages. It comprises NGO staff and traditional faith healers.
Results: Our program highlights variability of psychological & Socio-medical aspects in rehabilitation. Patents needed medical interventions in 10%, psychological approaches in 70% while remaining 20% needed combination of both.
Conclusion: This is pilot project running on community donation. We plan to document, evaluate this in large sample size, but resource restriction didn't permit. To overcome this, we plan networking of European NGO's at WPC-2023 Venue for better study design, technical support & collaborative efforts. I do not claim "I transformed whole community of Parkinson patients-patients but we had certainly taken initiative by this cost-effective approach".

P19.12

Improving equitable access to care through Parkinson Society BC (PSBC)'s innovative new programs of physiotherapy and healthcare navigation
*Shelly Yu**
Parkinson Society BC, Coquitlam, BC, Canada

Introduction: It is widely known that a multidisciplinary team approach, and having regular access to such a team, offers better outcomes than pharmacology alone in management of Parkinson's Disease. However, in British Columbia, Canada, People with Parkinson's (PwP) face financial, geographical and sociopolitical barriers in accessing allied health professionals. These can range from limited personal funds to pay for services, to living in remote areas without available services. Additionally, the province has five different regional health authorities, each with their own navigational complexities that can confuse users. This means PwP who are affected by these inequities are disadvantaged compared to those who live in urban areas and have the financial means to access services. PSBC's annually conducted surveys identified access to physiotherapy and the ability to navigate complex healthcare systems as main areas of inequity. PSBC addressed this through the provision of two complimentary virtual services: physiotherapy and healthcare navigation.
Methods: Services were made available through self-referral and set up on videoconferencing to ensure rapid access to care and to eliminate travel as a barrier. Physiotherapy was offered to those without financial means to access it elsewhere, or those living in rural areas without services available. Healthcare navigation was offered to those with multiple health challenges and limited supports to access multifaceted health services. Communication between PSBC and the individual's healthcare team was encouraged for continuity of care. Surveys were given out to service users to capture resulting feedback about the benefits and accessibility of programs.
Results: In 2022, 77 individuals accessed physiotherapy and 31 families accessed healthcare navigation. Surveys and testimonials identified themes of increased self-management efficacy, symptom improvement and confidence in navigating the disease.
Discussion: Although conducting these services virtually are not without their challenges, the overall feedback was positive on reducing health inequities and improving the lives of those touched by Parkinson's Disease. The number of people accessing the services highlights the need for more affordable care and availability of care outside of urban neighborhoods. Through this project, PSBC has demonstrated innovation can lead to meaningful change in dismantling inequitable access to care.

COMPREHENSIVE CARE: Sexuality & intimacy

P20.01

Approach to the management of sexual and intimate problems in patients with motor and non-motor manifestations of Parkinson's disease
Gila Bronner[*,1], Tanya Gurevich*[2]
[1] Tel-aviv Medical Center, Tel-aviv, Israel, Givatayim, Israel
[2] Tel-aviv Sourasky Medical Center, Tel-Aviv, Israel

Background: Difficulties in intimate and sexual life are well-known non-motor symptoms in Parkinson's disease (PD). Motor symptoms have also a significant negative effect. Despite their devastating impact on life satisfaction and quality of life, sexual problems and intimate issues are frequently ignored in clinical encounters between Health Care Providers (HCP) and people who live with PD. Our previous studies found that most patients experience such problems, and more than half are motivated to receive appropriate information regarding intimacy and sexuality from their HCP. Delivery of this sensitive information may well reduce stress and increase happiness among individuals and couples who live with PD.
Objective: To present contemporary and practical intervention program, which could benefit patients and their partners to ameliorate their intimate relations and better cope with these problems.
Methods: Based on our significant clinical experience and research data, we propose practical guidelines to assist HCP in the management of sexual and intimate problems in PD, as well as enable patients and their partners become more educated and proactive in this field.
Results: A flowchart algorithm is proposed including:
1. Classification of sexual dysfunction related to motor symptoms (e.g. tremor, hypokinesia, bradykinesia, dyskinesia), non-motor symptoms (e.g. depression, apathy, attention deficit, fatigue, urinary incontinence or pain) and medications' effects.
2. Description of intimate and sexual relations disturbed by motor symptoms, nonmotor symptoms, and by partners' burden or burn-out.
3. Presentation of treatment and interventional options.

Conclusions: The proposed guidelines will hopefully promote HCP-patient communication regarding sexual and intimate disturbances in PD and enable improvement of life satisfaction among individuals and couple who live with PD.

P20.02

LGBTQ, intimacy, sexuality and Parkinson's Disease (PD): Planning an observational pilot studd
Gila Bronner[*,1], Tanya Gurevich*[2]
[1] Tel-aviv Medical Center, Tel-aviv, GIVATAYIM, Israel
[2] Tel-aviv Sourasky Medical Center, Israel

Background: Concerns about sexual and intimate life are common among people with Parkinson's disease (PwPD). Motor as well as nonmotor symptoms negatively affect sexual function, impair

intimate relations, and significantly decrease life satisfaction. These concerns are rarely discussed by health care professionals.
It is important to emphasize that beside the erotic activities, sexuality has non-erotic aspects (e.g., being close emotionally, hugging and touching), which may boost self-esteem, reduce stress and increase wellbeing of PwPD and their partners.
PwPD who belong to the LGBTQ community may have problems and concerns as all PwPD, but they certainly have specific challenges in their intimate and sexual life, an issue which have not been studied.
Objectives:
(1) To understand the specific concerns of LGBTQ PwPD regarding their sexual function and intimate relations.
(2) To study how various motor and nonmotor symptoms impact these life aspects.
(3) To learn what changes have been imposed on the sexual and intimate life since the diagnosis of PD.
(4) To propose an intervention strategy appropriate for LGBTQ individuals and couples who cope with PD.
Methods: We plan a pilot study by interviewing 10-15 LGBTQ PwPD. Interviews will consist structured and open questions and will be performed by a sex therapist with >25 years of working with PwPD, and extensive experience in sex therapy with LGBTQ individuals and couples (without PD). Mixed quantitative and qualitive analysis methods will be used.
Results: Analysis of the interviews' responses will highlight the most bothering sexual concerns of PwPD of the LGBTQ community. Based on this information we plan to create a personalized intervention program for this community. Furthermore, the data will expand our understanding on the effects of motor and nonmotor symptoms on sexual and intimate life of LGBTQ individuals.
Conclusion: This pilot study focusing on this understudied and under-spoken issue, will enrich us with important information regarding the quality of life of PwPD who belong to the LGBTQ community, which could be used for further inquiries, resulting in intervention programs to improve life satisfaction among individuals and couples of this population.

P20.03

The cultural imaginary of disease: How those with Young-Onset Parkinson's disease are restricted in their relationships
*Lewis Johnstone**
Monash, Melbourne, VIC, Australia

Parkinson's disease can have significant impact on people's sexual wellbeing, but most of the research approaches this problem via an individual medicalised issue, if at all. Although Parkinson's disease is generally assumed not to be associated with the physiological dysfunction or neuronal damage that would interfere with sexuality, these research approaches persist. This article aims to explore how the body interacts within a broader cultural system with specific interest in why young-onset Parkinson's disease (YOPD) effects sexuality and relationships. Through in-depth semi-structured interviews with people who have been diagnosed with YOPD I will examine how the cultural imaginary of disability restricts those in experiencing their sexuality, relationships and aspirations for marriage and parenthood. To understand our social worlds, people draw upon a 'cultural imaginary', "a system of representation by which a subject gets captured or captivated by a ruling social and cultural formation" (Braidotti 2006, 85-86). It is a set of shared values and symbols which influence behaviours, including those around dating, sex, and relationships (Strauss, 2006). The purpose of this article is to continue the discussion of the sexual politics of disability with a focus on the lived experiences of young-onset Parkinson's disease. The potential significance of this research will aid in identifying new procedures to approaching sex and relationships when faced with a diagnosis of young-onset Parkinson's disease along with potential interventions that may assist those with young-onset Parkinson's disease to experience their sexuality, intimacy and continue relationships throughout the prognosis

P20.04

Biopsychosocial factors associated with the sexual health of women living Parkinson's disease
Katia Nobrega, Maria Elisa Piemonte, Thalyta Martins, Geovanna Santos*
Faculty of Medicine of the University of Sao Paulo, Sao Paulo, Sao Paulo, Brazil

Sexual disorders can cause distress in people with Parkinson's disease (PD). In addition, few studies have investigated the biopsychosocial factors that can affect the sexual health of women living with PD. Increased evidence on sexual dysfunction in women with PD is crucial to improving available interventions' specificity and efficacy. This study aimed to investigate the influence of several biopsychosocial factors on sexual health in women with PD. Ninety-five women with PD diagnosis, mean age of 53.31 years (SD=8.47), in stage 1 – 3 of disease evolution according to Hoehn and Yahr, living in 5 different geo-economic regions of Brazil, participated in the present study. The participants were asked to answer several questions through telephone interviews. The sexual function was evaluated by Female Sexual Function Index (FSFI) and Sex Quotient – Female Version (QS-VF). The motor impairment, evaluated by Section II of the MDS-UPDRS, and non-motor impairment, evaluated by Section I of the MDS-UPDRS, were included as biological factors. The depression severity, assessed by Beck Depression Inventory – BDI, was incorporated as a psychological aspect. The quality of partnership interaction, evaluated by Dyadic Adjustment Scale – DAS and socioeconomic level, assessed by the national socioeconomic inventory, were included as social factors. Considering that the results do not present a normal distribution, the Spearman and Kendall Tau non-parametric correlation tests were used. P-values below 5% were considered statistically significant. There was no statistically significant correlation between QS-VF and FSFI scores with age, H&Y stage, disease duration, levodopa dosages, socioeconomic classification, and MDS-UPDRS – Section II. There were statistically significant correlations of both variables used to assess the sexual health (QS-VF and FSFI) with scores MDS-UPDRS – Section I (p= 0,30; p= 0,12 respectively), BDI scores (p= 0,002; p= 0,000 respectively), and DAS scores (p= 0,000; p= 0,000 respectively). The sexual health of women with PD is negatively affected by non-motor impairment associated with disease, depression, and the quality of the couple's relationship. Considering the factors' complexity, regardless of age and disease evolution, interprofessional care to improve sexual health should be available for women living with PD from the initial disease stages.

P20.05

Association between motor, non-motor and sexual function in women living with Parkinson's disease in Brazil
Katia Nobrega, Maria Elisa Piemonte, Thalyta Martins, Geovanna Santos*
Faculty of Medicine of the University Sao Paulo, Sao Paulo, Sao Paulo, Brazil

Background: Sexual dysfunction (SD) is a common, yet under-reported, non-motor symptom (NMS) of Parkinson's disease (PD).However, few studies have investigated the motor, non-motor

that can affect the sexual function. Increased evidence on the sexual dysfunction in people with PD is crucial to improve the efficacy of available interventions. **Aim:** To investigate the relationship between sexual health and quality of life in PD. **Methods:** 95 individuals with confirmed PD diagnosis, women, mean age of 53.31 years (SD=8.47), in stage 1 – 3 of disease evolution according to Hoehn and Yahr classification, living in different cities representative of 5 different geo-economic regions of Brazil, participated in the present study. After presenting the informed consent form, and expressing agreement to participate in the study, participants were asked to answer several questions, through telephone interviews. The sexual function was evaluated by Female Sexual Function Index (FSFI) and by sex quotient – female version (QS-VF); motor aspect was evaluated by Section II of the MDS-UPDRS, non-motor aspect were evaluated by Beck Depression Inventory - BDI and Parkinson Disease Questionnaire - 39, PDQ39. Considering that the results do not present a normal distribution, the Spearman and Kendall Tau non-parametric correlation tests were used. P-values below 5% were considered statistically significant. **Results:** There was no statistically significant correlation between QS-VF or FSFI (particularly satisfaction of sexual life) with scores and age, H&Y stage, MDS-UPDRS – Section II. There were statistically significant correlations of both variables used to assess the sexual health (FSFI and QS-VF) with BDI scores (p = 0,002; p = 0,000 respectively), and PDQ39 scores (p = 0,008; p = 0,001 respectively). **Conclusion:** Among the non-motor aspects, depressive symptoms and quality of life in Parkinson's disease compromise sexual function in people living with PD. Thus, physicians should refer patients to sexual medicine specialists who can investigate and discuss problems fully, diagnose possible comorbidities, and suggest appropriate treatments.

P20.06

Development of a scale assessing sexual dysfunctions specifically experienced by patients with Parkinson's disease: "Parkinson's disease sexual experience scale" (PD-SES)

Emilie Wawrziczny[*,1], Kathy Dujardin[2], Luc Defebvre[2], Bérengère Flinois[2], Virginie Herlin[2], Nicolas Carrière[2], Clara De Groote[1]*
[1] Université de Lille, CNRS, UMR 9193 – SCALab – Sciences Cognitives et Sciences Affectives, Villeneuve d'Ascq, France
[2] Centre Hospitalier Regional et Universitaire de Lille, Lille, France

Background: Among the non-motor symptoms of Parkinson's disease, sexual dysfunctions are poorly recognized and therefore poorly taken care of, even though they play a major role in the deterioration of the quality of life of patients and their partners. Moreover, up to now, the available tools to assess sexual dysfunctions were not designed for Parkinson's disease and are not specific enough to capture problems experienced by persons with Parkinson's disease (PwPD).
Objective: The aim of this study was to develop and validate a scale to assess sexual dysfunctions in PwPD.
Method: Firstly, 14 PwPD (10 men and 4 women) were interviewed to develop a corpus of items based on their discourse to be as close as possible to PwPD's experience. Secondly, validity requirements of the corpus of items was measured to obtain a first selection of the most relevant items. Thirdly, the scale was completed by 140 patients and the structure of the scale was explored and the number of items reduced.
Results: Based on the interviews, a corpus of 59 items was created. Validity of this corpus was assessed by patients and clinicians working with PwPD leading to a 27-item version of the scale. After descriptive analyses of the responses to items and an exploratory factorial analysis, 15 non relevant items were eliminated. The 12-item version of the scale is able to assess four dimensions PD-related sexual dysfunctions, each with 3 items: "Sexual satisfaction", "Sexual self-esteem" "Impact of motor symptoms" and "Hypersexuality".
Conclusion: A final step will be to run a confirmatory factorial analysis to fully validate the scale. The « Parkinson's disease sexual experience scale » is a 12-item scale that allow to identify PD-related sexual dysfunctions and to propose an adapted support according to the problematic area and to monitor outcomes of support interventions.

COMPREHENSIVE CARE: Daily life activities including working & driving

P21.01

Impact of laser shoes on activities of daily living in people with Parkinson's and freezing of gait

Lauralei Dirks[*,1], Kalie Plesher*[*,2], Paige Rupiper[1], Sarah Moskowitz[2], Daniel Peterson[3], Linda Denney[4], Cindy Ivy[2]*
[1] Northern Arizona University, Scottsdale, AZ, United States
[2] Northern Arizona University, Phoenix, AZ, United States
[3] Arizona State University, Tempe, AZ, United States
[4] Tufts University, Phoenix, AZ, United States

Individuals with Parkinson's Disease (PD) commonly experience freezing of gait (FOG) which is characterized as a reduction or absence of effective forward steps. FOG has been associated with a higher fall risk, increased fear of falling, and lower quality of life. Therefore, individuals with PD and freezing of gait (PD-FOG) may encounter difficulty safely navigating their home and completing activities of daily living (ADLs). Visual cueing (VC) can improve functional mobility for individuals with PD-FOG, however, the most effective cueing device has yet to be determined.
This ongoing cross-sectional study assessed ten individuals (H&Y II-III, age 55-82, 6M and 4F) with idiopathic PD who reported one or more episodes of FOG in the prior month. Participants completed three functional mobility scenarios in a staged apartment. Scenarios include making tea in the kitchen, leaving the couch to answer the doorbell, and going to the bathroom. Each activity is completed both with and without the use of shoe-mounted lasers as a VC device, in pseudo-random order. Data was analyzed using Wilcoxon signed rank test to evaluate the change in completion time in lasers-on and lasers-off conditions. On average, the task completion time was shorter during lasers-on condition for all ADL tasks: "making tea" (-43.8±118.4), "answering the doorbell" (-2.5±46.4), and "using the bathroom" (-0.046±2.0); however this reduction was only statistically significant for the making tea scenario. Individually, 9/10 participants had shorter times "making tea", 6/10 "using the bathroom", and 5/10 "answering the doorbell". Additionally, participants were asked to report their satisfaction regarding use of laser-shoes for daily life. Participants rated general ease of use 6.4/10 (SD = 3) and willingness to use 7.9 (SD = 3), indicating potential future use of laser-shoes.
Together, these data indicate that laser shoes may be a feasible tool to improve functional mobility for ADLs in individuals with PD-FOG. Additional research is necessary to confirm and expand these findings.

	Task Completion Time in (seconds)								
	Making Tea			Doorbell			Bathroom		
Participant	Without Lasers	With Lasers	Change in Time	Without Lasers	With Lasers	Change in Time	Without Lasers	With Lasers	Change in Time
PM01	33.04	31.42	-1.62	17.69	18.57	0.88	25.63	22.89	-2.74
PM02	40.57	32.88	-7.69	11.81	13.04	1.23	16.16	16	-0.16
PM03	27.51	26.11	-1.4	11.12	10.33	-0.79	13.37	13.17	-0.2
PM04	33.34	33.52	0.18	19.63	14.98	-4.65	16.94	19.61	2.67
PM05	32.32	25.67	-6.65	13.39	11.16	-2.23	16.76	15.51	-1.25
PF06	118.31	103.93	-14.38	29.33	31.93	2.6	38.94	42.28	3.34
PM07	23.61	20.48	-3.13	10.98	10.75	-0.23	10.95	11.82	0.87
PF08	614.08	233.78	-380.3	226.34	117.33	-109.01	309.43	306.68	-2.75
PM09	45.8	28.17	-17.68	19.08	105.83	86.83	45.8	45.93	.13
PM10	33.31	28.12	-5.19	10.04	9.44	-.6	12.45	12.08	-.37
Mean (SD)	100.19 (182.61)	56.41 (66.81)	-43.786 (118.38)	36.94 (66.84)	34.34 (41.34)	-2.54 (46.42)	50.64 (91.68)	50.59 (90.81)	-0.046 (1.99)
Wilcoxon mean (SD)	67.31 (9.81)			23.9 (9.81)			34.64 (9.81)		
P-value	.007			.803			.646		

P21.02

Grip strength, motor symptoms, and ADL function pre-versus post-deep brain stimulation surgery

Nicole Tester[*,1], Samantha Witte[2], Orit Shechtman[2], Justin Mason[2], Lisa Warren[3], Charles Jacobson[3], Michael Okun[4], Kelly Foote[4], Justin Hilliard[4]*

[1] UF Health Rehabilitation - Norman Fixel Institute for Neurological Diseases, Gainesville, FL, United States
[2] University of Florida, Gainesville, FL, United States
[3] Norman Fixel Institute for Neurological Diseases, Gainesville, FL, United States
[4] University of Florida and Norman Fixel Institute for Neurological Diseases, Gainesville, FL, United States

Objective: To examine functional implications of deep brain stimulation (DBS) on grip strength and activities of daily living (ADL) in persons with Parkinson's disease (PD).
Methods: Data were retrospectively extracted from the Norman Fixel Institute for Neurological Diseases INFORM database following University of Florida Institutional Review Board approval. Twenty-nine persons with idiopathic PD who underwent DBS were examined at baseline (pre-surgery), acute follow-up (3-7 mos post-surgery), and chronic follow-up (12-18 mos post-surgery). The primary outcome was the mean grip strength of the hand contralateral to the surgical lead. Other outcomes included ADL, rigidity, and tremor scores from the Unified Parkinson's Disease Rating Scale (UPDRS); and health-related quality of life (HRQoL) from the Parkinson's Disease Questionnaire-39 (PDQ).
Results: There were no significant differences in the primary outcome of grip strength between baseline versus acute or baseline versus chronic follow-up. UPDRS II-ADL composite and subset scores demonstrated improvements between baseline and acute follow-up ($p=0.025$ and $p=0.009$, respectively). Significant reductions ($p<0.05$) in tremor and rigidity occurred between baseline and acute follow-up, as well as baseline and chronic follow-up. Improvements in HRQoL were acutely and chronically observed in the PDQ ($p=0.03$ and $p=0.02$).
Conclusions: DBS-related improvements in ADLs and quality of life were associated with reductions in tremor and rigidity but were not driven by changes in grip strength in this cohort. However, it remains unknown whether DBS may promote improvements in more sustained grip strength by reducing dopaminergic off states, motor fluctuations, and dyskinesia.

P21.03

Reading difficulties in Parkinson's disease – Guidance for assessment and rehabilitation

Iris Van Der Lijn*[,1], Gera de Haan[1], Pia Langenberg[1], Fleur Van der Feen[1], Joost Heutink[1], Teus Van Laar[2]
[1] University of Groningen, Groningen, Netherlands
[2] University Medical Center Groningen, Groningen, Netherlands

Introduction: People with Parkinson's disease (PD) frequently experience reading difficulties. However, little is known about the impairments underlying reading difficulties, which tests differentiate best between people with PD with and without reading difficulties, and how these should guide rehabilitation.
Method: This cross-sectional study included 74 people with PD in a neuro-visual rehabilitation setting. Each individual underwent assessment of visual, visual perceptual and cognitive functions, and outcomes were compared between those with (N = 55) and controls without reading difficulties (N = 19). Furthermore, reading aids and advice provided during rehabilitation were recorded.
Results: A distinction between the groups was found only for four functions, i.e., visual functions (i.e., contrast sensitivity, g = .76; reading acuity, g = .66; visual acuity, g = .54) and visual perceptual functions (i.e., lateralized visual attention, g = .58), with people with reading difficulties functioning worse than those without. Smaller effect sizes were found for non-visual cognitive functions.
Conclusions: The applied battery of tests is suitable to analyze visual, visual perceptual or cognitive impairment in PD in general, but not to detect reading difficulties. To differentiate between people with PD with and without reading difficulties, the battery can be reduced significantly. Applied rehabilitation methods seem to fit nicely with the most important impairments for reading difficulties, focusing mainly on a reduced visual acuity, contrast sensitivity and visual attention.

COMPREHENSIVE CARE: Self-management, empowerment, coping strategies

P22.02

Behaviour change techniques to reduce sedentary behaviour and increase physical activity in people with Parkinson's disease: A scoping review

Ghazi Alnajdi[*,1], Natalie Allen[2], Dr Serene Paul[2], Dr Sonia Cheng[2], A/Prof Zoe McKeough[2]*

[1] The University of Sydney, Camperdown, New South Wales, Australia
[2] The University of Sydney, Sydney, New South Wales, Australia

Introduction: Behaviour changes techniques (BCTs) have been used to increase physical activity (PA) and reduce sedentary behaviour (SB) in people with Parkinson's disease (PwPD). However, it is unclear which BCTs are most commonly used and whether they are used to target PA, SB or both. This scoping review (registration: https://osf.io/v72ag/) explored BCTs that have been trialled in PwPD to increase PA and/or reduce SB.
Methods: A scoping review was conducted. Seven databases were searched from January 1, 2000, up to April 15, 2022, plus additional papers were identified manually. Peer reviewed publications that investigated the effects of BCTs on PA and SB outcomes in PwPD were included. Pairs of reviewers independently screened titles/abstracts, then full texts, and subsequently extracted data. The

BCT Taxonomy v1 (Michie et al., 2013) was used to categorise BCTs.
Results: Twenty-one studies involving 2091 PwPD were included. Individual studies used 6 BCTs on average (range 2-12). BCTs were generally poorly described. Most studies (n=18) combined BCTs with exercises, three studies involved self-management, and three included interdisciplinary rehabilitation. Shaping knowledge, and feedback and monitoring, were the most used BCTs (Table 1). All studies reported PA outcomes; however, only four reported SB outcomes. Outcome measures included subjective measures through questionnaires, diaries and interviews, and objective measures from pedometers and accelerometers from body-attached devices including watches and phones.
Discussion: Since there was no standardisation of BCTs and measurement tools used, future studies should consider using standardised descriptions of intervention components to improve clarity and replication of the BCTs used. Shaping knowledge, feedback and monitoring were commonly used to increase exercise adherence rather than addressing PA and SB. Future research should focus on using BCTs to increase PwPD's participation in interventions specifically targeting PA and SB, as well as measuring SB outcomes.

Table 1: Summary of BCT taxonomy and frequencies of usage in the included studies (n=21)

BCT	Number of studies using this BCT (%)
Shaping knowledge (eg, information on how to perform the exercise)	21 (100%)
Feedback and monitoring (eg, by self or others or devices)	19 (91%)
Goals and planning (with problem solving, behavioural contract)	15 (71%)
Natural consequences (eg, health, social, emotional)	14 (67%)
Repetition and substitution (eg, practising, overcorrection, graded tasks)	14 (67%)
Social support (eg, practical, emotional)	14 (67%)
Antecedents (eg., changing physical/social environments, surroundings and body)	8 (38)
Comparison of behaviour (eg, demonstration, social comparison)	7 (33%)
Identity (eg., self-modelling, self-esteem)	6 (29%)
Associations (eg, cues, remove reward, exposure)	4 (19%)
Regulation (eg., medications, reducing negativity, conserving mental resources)	4 (19%)
Self-belief (eg, self-reflection on capability and performance, self-talk)	4 (19%)
Covert learning (eg., imaginary punishment/reward, vicarious consequences)	1 (5%)
Reward and threat (eg., social incentive, future punishment)	1 (5%)
Comparison of outcomes (eg., credible source, pros/cons, imagining of future outcomes)	0
Scheduled consequences (eg, behaviour cost, add/remove punishment or reward)	0

P22.03

Salutogenesis among people living with diagnosed Parkinson's disease

Alannah Beston[*,1], Edward Shepherd[2], Terry Boyle[1], Neil Arvin Bretaña[1]*
[1] University of South Australia, Adelaide, South Australia, Australia
[2] It's Not Funny, Sydney, NSW, Australia

Background: Salutogenesis focuses on the underlying assets and resources for positive health and health-promoting processes. It is understood to be a broad approach that includes multiple theories and concepts about health & well-being at the individual and collective levels. There has been increasing research in this area in the general population, however the concept of salutogenesis remains relatively underexplored among those living with chronic conditions such as Parkinson's disease. There is a need to focus on this research area particularly as the incidence of chronic progressive neurological diseases like Parkinson's disease increase. To date much of the research into Parkinson's has adopted a biomedical approach, focussed on understanding the underlying pathogenesis, risk factors and clinical management of the disease.
Method: A scoping review was done to examine emerging evidence surrounding salutogenesis in the Parkinson's community. A systematic literature search was then conducted across the MEDLINE database using 20 keywords from Lindström and Eriksson's salutogenic umbrella. Key search terms included: empathy, empowerment, coping, humour, optimism, flourishing, as well as Parkinsonian disorders and related terms. No restrictions with regard to country, age, or gender were applied. Results were screened for eligibility by ensuring abstract content indicated relevant content to both salutogenesis and Parkinson's disease. A full-text screening was employed to further narrow down the number of results to include only those relevant to the topic. A thematic analysis was applied on the final set of literature to identify key themes and categories from the resulting literature.
Results: A total of 32 published articles were included in the final analysis. Key themes identified included resilience, family dynamics, caregiver relationship, self-management, emotional stability, optimism, and communication.
Conclusion: The results of our literature search indicate there is a need for further research, policy and practice from a salutogenic perspective, when it comes to positive health & well-being among people living with Parkinson's disease.

P22.04

Examining leadership of Parkinson's disease support groups in rural and regional New South Wales: A qualitative descriptive case study

Vincent Carroll[*,1], Rachel Rossiter[2], Marguerite Bramble[3]*
[1] Mid North Coast Local Health District, Charles Sturt University, Parkinson's NSW, Coffs Harbour, New South Wales, Australia
[2] Charles Sturt University, Orange, New South Wales, Australia
[3] Charles Sturt University, Bathurst, New South Wales, Australia

Background and Aim: Research specifically examining leadership of disease-specific support groups such as cancer and dementia is widely available. However, research focusing on Parkinson's disease (PD) support groups and leadership is sparse. In New South Wales (NSW), Australia, more than 70 PD support groups are affiliated with the peak body, Parkinson's NSW. Fifty of these groups are in rural and regional areas. The study aimed to investigate and compare models of leadership in PD support groups across rural and regional NSW, specifically focusing on the skills, knowledge and attributes of the group leaders. The secondary aim was to identify factors impacting the function and sustainability of these support groups.
Methods: This study used a three-site case study design, each site defined by support group leadership type (person with PD, caregiver, health professional). Purposive recruitment was used to seek expressions of interest from all PD group leaders. Individual semi-structured interviews were conducted virtually with five leaders and 24 group members. Qualitative descriptive analysis of the data was undertaken.
Findings: People with PD and caregiver leaders described accidentally falling into the leadership role, as a result of social interactions among the group and members' collective perception that a particular person was more 'leader-like' and better able to lead the group than others. For the health professional leader, a deep understanding of people with PD and the caregivers' experience was incorporated in their own professional experience. PD support group leaders' displayed altruism in action and were committed to nurturing and guiding the group members on their

journey. A 'community of support' was created beyond the support group meetings, enabling self-empowerment and opportunities to foster, strengthen and nurture relationships.
Recommendations: It is recommended that PD peak bodies support and encourage health professional involvement and co-facilitation in support groups and provide training and education for support group leaders to enhance their knowledge and skills of leadership, corporate partnerships, relationship building and partnership maintenance. The development of a communication strategy to acknowledge and enhance the value of support group leaders, particularly their level of cooperation and altruistic approach to the leadership role is highly recommended.

P22.05

Lifestyle medicine for Parkinson's disease: Diet as a treatment tool

Rachel Dolhun[*1], Erin Presant*[2]
[1] The Michael J. Fox Foundation, New York, NY, United States
[2] Medicine of Yum, Santa Barbara, California, United States

Background: Parkinson's disease (PD) affects an estimated 6 million people worldwide. Without a proven cure, lifestyle factors take on greater importance for managing disease. Yet PD-specific lifestyle recommendations are scarce. To empower patients to use diet as a treatment tool, we created a thorough and practical guide on the topic.
Methods: An earlier version of the resource was developed in 2016 by movement disorder specialist Rachel Dolhun, MD, of The Michael J. Fox Foundation (MJFF). Since then, research has made significant strides in understanding how diet can support brain health and ease brain disease. The latest iteration, developed with culinary medicine specialist, Erin Presant, DO, and members of the Parkinson's community, offers useful information and tips to shop, cook and eat for brain health, PD symptom management, and much more. The free guide is shared with over 1 million followers of MJFF's social channels and with thousands of educational event attendees.
Results: Demonstrating the considerable appetite for this type of information, the guide has been downloaded 61K times — approximately 84 times per day — since 2020. Those who access the material include people at various stages of PD; their families and loved ones; and more than 1K clinicians, researchers and other health care professionals who serve the Parkinson's community.
Anecdotal feedback reinforces the need for and value of PD lifestyle resources. About the guide, one person commented, "This is a great read for me — even after 10 years of fighting Parkinson's." Another, "I was [recently] diagnosed. This has definitely helped me. I've always had a hard time eating healthy." To our knowledge, this is the most comprehensive, practical, Parkinson's-specific diet resource available to date.
Conclusion: This guide encourages patients and families to take action in promoting brain health and managing disease. It simplifies the use of diet as a treatment tool, making healthy eating inclusive and accessible. We now aim to raise clinicians' awareness of this resource and to expand Parkinson's-related lifestyle medicine offerings.

P22.06

Possible explanations for unexpectedly high functional mobility despite the presence of postural instability and gait disturbances. A longitudinal mixed-models analysis

Anne-Marie Hanff[*1], Christopher McCrum*[2], Armin Rauschenberger*[3], Gloria A. Aguayo*[4], Maurice Zeegers*[5], Anja K. Leist*[6], Rejko Krüger*[7]
[1] (1) Transversal Translational Medicine, Luxembourg Institute of Health, (2) Faculty of Science, Technology and Medicine, University of Luxembourg, (3) Department of Epidemiology, CAPHRI Care and Public Health Research Institute, Maastricht University Medical Centre+, Strassen, Esch-sur-Alzette, Maastricht, Luxembourg
[2] (4) Department of Nutrition and Movement Sciences, NUTRIM School of Nutrition and Translational Research in Metabolism, Maastricht University Medical Centre+, (5) Department of Rehabilitation Sciences, Neurorehabilitation Research Group, KU Leuven, Esch-sur-Alzette, Maastricht, Leuven, Netherlands
[3] (6) Biomedical Data Science, Luxembourg Centre for Systems Biomedicine, University of Luxembourg, Luxembourg
[4] Department of Precision Health, Luxembourg Institute of Health, Maastricht, Strassen, Luxembourg
[5] (3) Department of Epidemiology, CAPHRI Care and Public Health Research Institute, Maastricht University Medical Centre+, (8) Department of Epidemiology, NUTRIM School of Nutrition and Translational Research in Metabolism, Care and Public Health Research Institute, Maastricht University, Maastricht, Netherlands
[6] (9) Department of Social Sciences, University of Luxembourg, Esch-sur-Alzette, Luxembourg
[7] (1) Transversal Translational Medicine, Luxembourg Institute of Health, (10) Translational Neurosciences, Luxembourg Centre for Systems Biomedicine, University of Luxembourg, (11) Parkinson Research Clinic, Centre Hospitalier de Luxembourg, Strassen, Esch-sur-Alzette, Luxembourg

Background: Despite the presence of postural instability and gait disturbances (PIGD), not all people with Parkinson's disease (PwP) show impaired functional mobility (FM) [1]. Presumably, protective factors may also play an important role.
Objectives: We evaluated the interaction effects of potentially PIGD on patient-reported FM.
Methods: We included 778 people with either typical Parkinson's disease (PD) or PD dementia from the Luxembourg Parkinson's Study [2] with yearly follow-up and a total study duration from one to seven years. We assessed FM by the patient-reported FM composite score (FMCS) [3] (0 to 100, higher = better) and PIGD by the MDS-UPDRS-based PIGD score (higher = worse) [4]. A longitudinal two-level mixed models analysis (outcome: FMCS; fixed effects: disease duration, confounders, protective factors interacting with PIGD; random intercept [for the subject]) was performed with the R-package lme4 (function lmer) [5]. We created one model per protective factor and evaluated their interaction effect by testing the coefficient (t-test) at Bonferroni-corrected 5% significance level (alpha=0.05/12 = 0.0042). We controlled for confounders sex, age, education, assessor, depression, global cognition and the presence of a pathogenic GBA variant.
Results: For [a unit of increase] in PIGD, FMCS decreased [on average] by 2.39 points ($p<0.001$). Additionally, when body mass index and medication increased by one unit, the association of PIGD and FMCS significantly changed: Body mass index (-0.066, $p = 0.004$) and levodopa equivalent daily dose, LEDD (mg) (0.001, $p = 0.00003$). We detected no interaction effects of the Beck Depression Inventory, years of education, living in a rural area, bodily discomfort, Montreal Cognitive Assessment, urinary incontinence, lack of energy, lack of social support, widowed and children. Sensitivity analysis on baseline data identified no conflicting interaction effects.

Conclusion: Our findings identified a lower body mass index as a protective factor in the relationship between PIGD and FMCS. A higher LEDD was linked to a stronger association of PIGD and FMCS. Overall we found few effect modifiers in the relationship between PIGD and FMCS.

P22.07

Influence of neuropsychological care for the empowerment of patients with Parkinson's disease in managing their continuous subcutaneous apomorphine infusion

Jean-Françoi Houvenaghel, Marie Delliaux, Sophie Drapier*
CHU de Rennes, Rennes, France

Continuous subcutaneous apomorphine infusion (CSAI) is increasingly used as a second-line treatment in Parkinson's disease (PD). Its maximum benefit is however conditioned by the daily management of the equipment delivering the medication. Different procedures are necessary, from the preparation of the material to its removal, to ensure an optimal management. This care is rarely provided by the patient alone, and often requires the intervention of a relative and/or that of a nurse who comes to the patient's home every day. Our experience in the Neurology Department of the Rennes University Hospital led us to believe that the cognitive and psycho-behavioral difficulties of the patient constitute a major limit to the learning and application of these procedures. However, these aspects are rarely assessed and the neuropsychological methods to circumvent the patient's difficulties are never used. Our hypothesis is that individual care provided during hospitalization will promote efficient and independent management of the CSAI treatment and maximize its benefits. In addition, we estimate the impact of this training program on caregiver burden and care team satisfaction, an impact that we hope will be better. Our randomized controlled study aims to compare the level of autonomy in the management of the CSAI in 40 PD patients, at 10 days, 1 month, 3 months and 6 months after the introduction of the CSAI. These patients are divided into two groups, one group benefits from 6 individual learning sessions on the use the CSAI, the other group benefits from 6 individual psycho-information sessions about the daily lifestyle. This project aims to evaluate the interest of an individualized training program, adapted to the cognitive and psycho-behavioral skills of the patient, on the learning of these procedures. With this poster we show the method used and the preliminary results.

P22.08

Unique methods to alleviate freezing of gait that people with Parkinson's developed

*Yasuyuki Okuma**
Juntendo University Shizuoka Hospital, Izunokuni, Japan

Background and Objectives: Freezing of gait (FOG) is an episodic and disturbing gait disorder in people with Parkinson's (PwP) characterized by the inability to initiate or continue locomotion. Pharmacological treatment is only partially effective in reducing FOG, but auditory or visual cues are sometimes helpful. I herein present PwP who developed unique methods to alleviate FOG.
Methods: Among 300 PwP, several people were selected. They present methods to alleviate FOG by showing their home videos or in the outpatient clinic. A movement disorder specialist evaluated those methods.
Results: Methods developed by PwP were, (1) intentional kneeling to proceed, (2) pulling up the band looped around his right foot, (3) using visual cue with rope on cane, (4) using visual cue by putting rolled newspapers in front of him. (5) kicking a box to proceed.
Conclusion: The most stimulating point in these cases is that the PwP themselves developed the unique methods, and that they have been benefiting from them for a long time. Clinicians who learn a new method of overcoming FOG from the PwP have to extend the idea to other PwP or caregivers.

P22.09

Impower: Developing home-based digital training for people with Parkinson's to manage impulse control behaviours

Ellen Poliakoff[1], Jade Pickering[1], Judith Bek[2], Chris Kobylecki[3], Aansha Priyam[1], Jacob Hadfield[1], Jennifer McBride[1]*
[1] University of Manchester, Manchester, United Kingdom
[2] University College Dublin, Dublin, Ireland
[3] Salford Royal Hospital, Manchester, United Kingdom

Introduction: Dopaminergic medications required to treat the motor symptoms of Parkinson's can cause impulse control behaviours (ICBs) in a significant proportion of patients. ICBs, which include gambling and problem eating, can significantly impact quality of life for patients and their families. Clinical management of ICBs involves withdrawal of medication which can worsen motor symptoms, or psychological strategies, such as Cognitive behavioural therapy, which can be costly and/or difficult to access. We have developed an accessible alternative method to address ICBs. Drawing on extensive consultation with people with Parkinson's, we designed an intervention for independent computer-based home training, using an established inhibitory control task (go/no-go). The training involves responding quickly to neutral stimuli but withholding responses to personally relevant images associated with the individual's ICB (e.g., gambling logos). We hypothesise that this will translate to a reduction in ICBs in daily life, as previously shown in the general population using a similar approach.
Methods: We conducted a pilot study with 5 people with mild-to-moderate Parkinson's (4 female) to evaluate feasibility and the acceptability of the: (i) instructions and training tasks; (ii) training frequency and duration. Participants received a training task tailored to the ICB they wished to address. We also tested potential outcome measures including self-reported ICBs. Participants completed a 4-week training period, consisting of 3-6 short training blocks for 5 days per week. Outcomes were measured before and after the training and post-training interviews were conducted.
Results: Four participants completed the outcome measures and one dropped out of the study for unknown reasons (seemingly unrelated to the training). The participants were able to complete the training independently at home, indicating that the approach is feasible. Two participants described noticing improvements in their behaviour. However, participants reported that the training was not challenging or varied enough. Others participants felt it would be helpful and motivating to understand more about how the training might work.
Conclusion: This pilot study demonstrated the feasibility and acceptability of home-based digital training to manage ICBs. Further development of the task (clearer instructions, increased variety and challenge) should be conducted prior to evaluating efficacy of the intervention.

P22.10

Gaitkeeping: A Parkinson's telehealth training program

Pamela Quinn[*,1], Jeff Friedman[2], Colin O'Connor*[*,1], Natalie Schultz-Kahwaty[2], Lauren St. Hill[3], Roseanne D. Dobkin[3]*
[1] PD Movement Lab, New York, NY, United States
[2] Rutgers University, Integrated Dance Collaboratory, Dance Department, Mason Gross School of the Arts, New Brunswick, NJ, United States
[3] Rutgers–Robert Wood Johnson Medical School, Piscataway, NJ, United States

Background: People with Parkinson's Disease consistently rate gait disturbances as the number one issue affecting quality-of-life. Over the past decade evidence-based coping mechanisms, i.e., "cues," have shown efficacy in helping PWP overcome movement challenges, while telehealth has provided Parkinson's patients with greater access to high-level care. Gaitkeeping, a walking-focused behavioral health program, brings together these two developments to help PWP self-manage gait challenges. The program was designed by movement teacher and person with Parkinson's, Pamela Quinn, and emerged out of her novel use of cues in the context of her own life with PD. The program was recorded at Rutgers University and delivered remotely to PWP across New Jersey.
Objective: To gain pilot data for assessing benefits of Gaitkeeping for PWP. To identify further refinements for implementing a future larger study.
Methods: Individuals with confirmed Parkinson's diagnoses (PWP) were recruited through local support groups and dance classes led by Rutgers University Integrated Dance Collaboratory's instructor. Eligibility for participation was limited to individuals able to walk without support from canes or walkers. Participants completed self-report baseline measures of gait efficacy. Individuals were then given access to the web-based Gaitkeeping course, a progression of 20 short videos weaving together PD-specific physical analysis, sensory cueing, situational movement strategies, and Ms. Quinn's personal experience with PD. Individuals were encouraged to practice what they learned. One week later they had an hour-long in-person session with Ms. Quinn to refine use of coping mechanisms. Individuals practiced for another week, and then had a 45-minute phone session to further reinforce learnings. Participants practiced for two more weeks. Measures of gait efficacy were re-administered post-intervention. Three post-test focus groups, divided by random aggregation, were also held to further assess the program's impact on gait, mood, quality of life, and self-efficacy.
Results: 22 individuals with Parkinson's enrolled in the program. Participants demonstrated significant reductions in anxiety associated with walking and gait and reported improvements in gait stabilization, balance, self-efficacy, and quality of life. Ninety percent of participants (20/22) completed the intervention. Program satisfaction rates were very high.
Conclusion: Gaitkeeping gives PwP the means and autonomy to sustain their own walking health.

P22.11

Exercise with C.A.R.E.

*William Richard**
self, Vail, AZ, United States

I was diagnosed with PD on February 10, 2021. I had previously experienced several strokes and had sought a neurologist to oversee my care. What an unexpected shock when he told me it was Parkinson's symptoms, not stroke effects.
Within days I discovered the Parkinson Wellness Recovery Gym (PWR!Gym in Tucson, AZ, USA). Regular exercise helps me combat the physical symptoms of Parkinson disease, but exercise with my peers has provided more than just accountability. The members of our exercise class at the PWR!Gym have built a community that supports each other through Commitment, Awareness, Respect, and Encouragement (CARE).
The Problem: Many of us have other medical issues, family issues, and a plethora of diverse personal issues. Sadly, these issues have swept fellow PD patients from their involvement in the very exercise regime needed to impede the progression of PD. Total care for the PD patient is often compartmentalized. When the person undergoes any one of these life issues, the exercise regime is often sacrificed. When this involves illnesses, HIPPA regulations may also obstruct the sharing of this knowledge to concerned parties such as others in the exercise group or other support-type groups.
The Correction: We transitioned the members of our exercise group into an organized support group to provide the necessary CARE each of us needs. This was accomplished initially by creating a group directory containing personal data including, but not limited to, occupation, birthdates, family, hobbies and interests. Social interaction was further developed through quarterly social gatherings. In addition, we meet at the PWR!Gym once each month to plan future events and to assess the need for individual follow-up or personal visit.
The Results: C.A.R.E.
Commitment to one another and ourselves.
Awareness when Action is needed.
Respect and Regard for our status and our changes.
Encourage and Equip each other.
Conclusion: PD is progressive so we must be progressive in our plans. PD is aggressive so we must be more aggressive in our CARE for one another. For me and my peers, hope and purpose has been regenerated in this degenerative disease.

P22.12

A qualitative analysis of coping strategy patterns in Parkinson's disease

Caroline Seton, Aileen K. Ho*
University of Reading, Reading, United Kingdom

Background: Research on coping processes within Parkinson's disease (PD) populations suggest that individuals may use a pattern of various coping strategies as a repertoire of useful behaviours in different situations. Therefore, this study sought to further elucidate patterns or clusters of coping strategies by drawing on the lived experience of individuals with PD.
Methods: The study consisted of semi-structured interviews from a sample of eight female and three male participants (n = 11), with an age range of between 44 - 81 years and duration of illness varied from 5 - 23 years. The audio-recordings of each participants' interviews were transcribed verbatim and analysed thematically.
Results: We found four thematic categories relating to groups of coping strategies. The first theme, Internal Strategies, describing participants' use of mental or cognitive strategies to manage or overcome the challenges associated with living with PD and includes subthemes such as acceptance, avoidant thinking, developing awareness, positive appraisals, and managing emotions. The second theme, Activity-related Strategies, describes participants' use of activity-based or behavioural strategies that facilitate adaption to PD and includes subthemes such as seeking distractions, engaging in new activities, maintaining regular activities, and modifying activities. The third theme, Resource Utilisation, refers to coping strategies that participants enacted to identify formal and informal sources of support and includes subthemes such as information seeking and positive social interactions. The last theme identified, Attitude-based Strategies, describes the use of coping strategies informed specifically by an

adaptive attitude towards living with PD and includes subthemes such as confrontational coping, self-reliance, and self-advocacy.
Given the degenerative trajectory and variable nature of PD, the findings of this study emphasise that the utilisation of coping strategies which are flexible and informed by PD patients' understanding of their condition may best facilitate psychological adjustment. These findings support the conclusion that PD patients employ numerous adaptive coping strategies when approaching their disease management actively in a problem-oriented and cognitively structured manner.

P22.13

Detours of persons affected by Parkinson's disease in circumventing cognitive obstacles in daily life: The COPIED study

Ingrid Sturkenboom[*1], Edwin Barentsen[2]*
[1] Radboud university medical center, dept of rehabilitation, Nijmegen, Netherlands
[2] Parkinson Vereniging, Bunik, Netherlands

Background: Many people living with Parkinson's (PwP) experience difficulties in cognitive functioning. Although attention for cognitive deficits in PwP is growing, there is a lack of evidence-based, practically applicable tools for managing cognitive obstacles in daily life. The COPIED study aimed to identify and visualize detours that PwP and their care partners use for managing cognitive obstacles in daily life.
Methods: In individual telephone interviews and four online focus groups with PwP and care partners, we collected data on perceived cognitive obstacles in daily life and the detours used to manage these obstacles. The Perceive Recall Plan Perform System of Task Analysis was used as a theoretical framework for information processing in daily life, to categorize cognitive obstacles in the thematic analysis. The results were used to then design an online survey. This survey examined whether the identified obstacles and detours were recognizable to a larger group of PwP and care partners. After analysis, a self-help tool was designed based on the results by main researcher and project lead Marina Noordegraaf (PwP, †).
Results: 13 PwP and 5 care partners participated in both an individual interview and an online focus group. This provided rich data to set up the online survey. 357 PwP and 100 care partners participated in the online survey. Obstacles in the category 'Recall' were selected the most (58% of PwP); obstacles in the Perceive category the least (30%). For each obstacle, a wide range of detours and factors that enhance the use of detours were given.
The results of this research were compiled in a richly illustrated self-help book with detour maps for main 14 obstacles: 12 specific for and by PwP and 8 specific for and by care partners. Although a systematic evaluation of usability of the book has not (yet) been conducted, many positive comments have been received.
Discussion: This research carried out by and for PwP, higlights the creativity of PwP and care partners in finding detours to engage in daily activities despite cognitive obstacles. The published book can be used as an inspiration by PwP, their care partners and professionals to support PwP.

P22.14

Empowerment of people with Parkinson`s disease: development, testing and evaluation of a cross-sectoral, intervention-based self-management program

Trine Thomsen[*1], Sara Lyngby Skovbølling[2], Morten Møller[3], Vibeke W Grønlund[4], Maria Brønden[5], Bo Biering-Sørensen[1]*
[1] Movement disorder Clinic, Department of Neurology, Rigshospitalet, Copenhagen, Glostrup, Capitol Region, Denmark
[2] Department of Neurology, Bispebjerg-Frederiksberg University Hospital, Copenhagen, Copenhagen, Capitol Region, Denmark
[3] Holbæk Neurology Clinic, Holbæk, Region Zealand, Denmark
[4] The Danish Parkinson Association and Sano Rehabilitation Center, Skælskør, Region Zealand, Denmark
[5] Sano Rehabilitation Center, Skælskør, Skælskør, Region Zealand, Denmark

Background: Living with Parkinson`s disease (PD) involves living with a variety of symptoms, each of which affects many aspects of everyday life and quality of life (QoL). To support People with PD (PwP) and their caregivers to develop skills and provide them with tools to adapt to life with PD, increase QoL, as well as promote self-management, there is a need for education in all aspects of PD, including psycho-social aspects.
Objectives: The overall purpose of this study is to develop, test and evaluate the results of a self-management program targeted PwP in empowering both PwP and caregivers.
Methods: 85 PD-patients (Hoehn&Yahr score 1-3), and their caregivers will be included in the study. Participants are recruited consecutively from Movement disorder Clinics at two hospitals, neurologists in municipalities and a Rehabilitation Center.
The study is divided into three phases:
Study 1: Exploratory, qualitative study. Data on how PD-patients describe the needs in everyday life, self-efficacy, coping strategies, and ability to manage symptoms/challenges, and clinical perspectives, was obtained through workshops and focus-group interviews with PwP, caregivers, healthcare professionals and other stakeholders (13 participants in total)
Study 2: Intervention study. Based on the results in Study 1, an 8-week self-management program were developed. This consists of 6 educational sessions, monitoring of motor and non-motor symptoms by the Parkinson KinetiGraphTM (PKG At Home), individual goal-setting, home visits by PD-nurse and mindfulness-sessions. Primary oucomes are changes in scores of Health Education Impact Questionnaire (HeiQ) and Health Literacy Scale (HLS-14). Secondary outcome measures are changes in QoL-score (PDQ-39), The General Self-efficacy Scale (GSES), Unified Parkinson`s disease Rating Scale Part-II (UPDRS-II), algorithm outcomes regarding motor symptoms and fluctuation score measured by the PKG, and numbers of contacts to the clinics (evaluated 6 Months before and after the intervention).
Study 3: Follow-up study 3 and 6 Months after the intervention.
Results: Study 1 was completed in September 2022. From October to December 2022 the first group of PwP and their caregivers completed the self-management program (11 PwP and 9 caregivers) in Study 2.
Conclusion: The results of Study 2 and 3 will be analyzed when all 85 PwP have completed the self-management program.

P22.15

Registry of patients living with Parkinson: Active patient role in co-creating data-driven tools and solutions

Lucia Wang[*,1], Lucila Falcone*[2]
[1] Parkinson Joven Argentina, Buenos Aires, Buenos Aires, Argentina
[2] Parkinson Argentina, Buenos Aires, Buenos Aires, Argentina

In Argentina there are no official registries or figures that indicate Parkinson's disease prevalence and incidence. Clinical studies on PD are few in comparison with other countries in Latin America, Europe and the United States. Neither the government nor patient organizations have access to local clinical research information, and patient participation depends exclusively on physician invitation, or coordinating and being part of the study team in the country. As a result of this situation, people living with PD are not aware of research protocols nor know how we can participate.
From Parkinson Argentina (PA) we promote the creation of the Registry of people living with PD throughout the country. For this, we believe it is necessary to design a co-creation methodology that involves key actors to validate the objective and co-design the dataset, data collection and sharing strategies.
Objective: to present the co-creation methodology and the partial results obtained in the first workshops.
Results: the methodology includes 4 co-creation workshops aimed at 1) defining the objectives of the registry; 2) defining the data elements with specific and consistent data definitions; 3) identifying the data collection and sharing strategy; 4) discussing the main bioethical, security and privacy issues of individuals and their data. Regarding the registry, and as a result of the first workshop, the following objectives were defined by consensus: a) Know who we are, how many we are and what we need; b) Improve access to information and democratize access to studies; c) Streamline the patient recruitment process so that research is not delayed; and d) Promote the creation of policies for prevention, treatment and care for people living with PK.
Conclusions: Active patients can generate networks and reach out more effectively to the universe of people with PD; the great contribution of patient participation in research teams has been documented, and from PA we seek to provide evidence on the fundamental role of patients in the design of data-driven tools and solutions in all their phases.

P22.16

Patient experience and treatment satisfaction with continuous subcutaneous infusion of foslevodopa/foscarbidopa for treatment of advanced Parkinson's disease

Rajeev Kumar[1], *Michael Soileau*[2], *Connie H. Yan*[*,3], *Triza Brion*[4], *Alex Bellenger*[4], *Christina O'Donnell*[4], *Pavnit Kukreja*[3], *Maurizio F. Facheris*[3], *Anand Shewale*[3], *Jason Aldred*[5]
[1] Rocky Mountain Movement Disorders Center, Englewood, Colorado, United States
[2] Texas Movement Disorder Specialists, Georgetown, Texas, United States
[3] AbbVie, Inc., North Chicago, Illinois, United States
[4] ICON plc, Raleigh, North Carolina, United States
[5] Inland Northwest Research, Spokane, Washington, United States

Background: Foslevodopa/foscarbidopa (LDP/CDP) is a 24-hour/day continuous subcutaneous infusion (CSCI) delivered by an external portable device. LDP/CDP has demonstrated efficacy in controlling motor fluctuations in people with advanced Parkinson's disease (PwP) in Phase 3 trials. However, people's personal experiences using LDP/CDP, particularly integration of the device into their daily routines and satisfaction with treatment, are little known. The objective of this qualitative study was to understand patients' experience and satisfaction with long-term use of LDP/CDP.
Methods: PwP on at least 6 months of LDP/CDP treatment and living in the United States were recruited from the Phase 3 open-label extension trial (NCT04750226) through convenience sampling. Semi-structured interviews were conducted. Data was evaluated using content and thematic qualitative analysis.
Results: In this interim analysis of 9 PwP, patients on average (standard deviation) were 68.8 (10.0) years old, had been diagnosed with PD for 7.8 (1.6) years and were on LDP/CDP treatment for 13.1 (2.2) months. All patients were currently married and indicated their spouse was their caregiver. While some patients mentioned challenges transitioning to LDP/CDP (e.g., minor skin events, disconnection of the tubing/cannula, handling syringe), most felt the transition was easy once a routine was developed (e.g., set schedule for managing treatment, dedicated space for supplies and setup, learning to perform activities to accommodate the carrying device) and due to the sufficient support and instruction from their healthcare team. Motivations for patients to continue on LDP/CDP included improvement of symptoms (e.g., being functional, no OFF periods, wake up during night-time or in the morning without symptoms) compared to their prior treatment (i.e., oral medications), and ability to do normal activities (e.g., get life back, do hobbies). While some patients noted shortcomings to the delivery system (e.g., size and weight of device, tubing length), all nine patients rated high satisfaction with the device for treatment administration, indicated that the benefits of the treatment outweighed the negatives, and reported a high likelihood of continuing LDP/CDP outside of the clinical trial.
Conclusion: Patients' overall positive experience, high satisfaction and perceived benefit of CSCI LDP/CDP drove successful on-boarding and continued use of the novel treatment.

Table 1. Key themes with sample quotes

Transition to ABBV-951
▪ "It took me a while to kind of get it in my head that I needed to do it in the morning even with the morning rush of things, […] but I found the earlier that I do it in the mornings the better it was. I was doing it in the evening and then it was going off before I was able to go home and […] So, doing it in the morning, all of a sudden it became very freeing because the rest of the day was mine. I didn't have to worry about what time was it and when was this thing going to go off and things like that."
▪ "It's just, it's become like one of the first things that I do. I mean, I usually take a shower, and I usually have to […] stop my pump […] to take the shower and then I start it back and then […] right after the shower I go back downstairs and change it all out and then go up and dry my hair and things like that."
▪ "The infusion set, honestly, the cannula needs to get, changing that. I really didn't want to do it for a while, because it just, it seemed like I couldn't figure out the sequence of steps in the beginning, and I would get confused about what needed to be done, but now it's just like, like I said, second nature… I can do it in my sleep. I've done it enough times, believe me."
▪ "The first couple times when we got home, we were both a little – […] are we doing this right, are we doing this right, we gotta make sure we do this right. We were slower at it, […] it took us a little while longer to get it down to the art we have it down to, but […] they actually trained us pretty good. […] it was a little scary as far as at first. Yeah, because it was unknown. We didn't know what we were stepping into."
▪ "Having each other, having [NURSE NAME] to call if we had a problem. She always made herself completely available, and we took advantage of that when we needed to. So having professional support that we definitely had from [CLINICIAN NAME] office, and each other, and just time, doing it over and over and over again. Making all the mistakes and seeing that no mistake was incorrectable. You know, everything could be fixed."
Motivation to continue using CSCI LDP/CDP
▪ "The benefits are my life's back. I mean, most of it. There's still some things that we have to work on, but […] it's great, I love the thing. It's been a complete benefit towards me."
▪ "But after the first morning that I woke up, I got out of the bed and I walked to the bathroom and I didn't have any symptoms and I was like, I got the meds. […] I was pretty excited because I did get the medicine, and that's the best feeling, getting out of bed and feeling like, you know, you don't have symptoms of Parkinson's."
▪ "It's an easy thing to do, and enjoy the fact that you got something that you can wake up in the middle of the night and be just fine, just like you are during the daytime, and wake up every morning and get on with your business and don't have your wait while you got that medicine soak in and stuff like that."
▪ "Being vertical and functional and conversational and loving life, literally. […] I am just grateful for something that put me back in the world. […] Unless there's something better out. Then I'd drop it like a hot potato. As would anybody, but for what's out there now, I'm on it, and I'll be devastated […] if I don't get to use, I don't know […] how I'll transition back to […] oral medication. I don't think it'll work. I don't think I'll be able to…"
Shortcomings of the LDP/CDP delivery system
▪ "I am grateful for it. I hope that they continue to work on modifying it to be better, like making the pump smaller…"
▪ "I can live with this, but I mean, for some people it would probably be difficult, you know? Size-wise, if it was like half the size of this, that would be phenomenal."
▪ "…he wanted to figure out what to do with the extra tubing and you know he didn't want it hanging out of his shirt or when, we now know what shirts he has that he can wear over the top of the pump. So, like if we're going somewhere that it kind of is covered up, but then in the summertime he just wears short sleeve tops and so the pump hangs out and he, it's okay." - Caregiver
▪ "… one night around three o'clock in the morning it was beeping […] so I got out of bed and I turned the lights on and I'm looking at the pump and […] it said that the tubing was twisted, so somehow either he rolled over or whatever, so all I did was just remove the pump from the case and untangled the tubing, […] and put it back in the case and it was fine." - Caregiver

P22.17

P.D. PowerUp: A Comprehensive virtual program for managing pain in Parkinson's disease

*Apurva Zawar**
BeyondRehab, Seattle, Washington, United States

Pain is a common and often under-recognized symptom in Parkinson's disease (PD), affecting up to 80% of people with the condition. To effectively manage pain and improve quality of life, it is important to understand pain science and develop a range of skills to cope with pain without relying heavily on medication. The "P.D. PowerUp: Parkinson's Disease Pain Management Program" is a comprehensive virtual group program designed to empower individuals with PD, particularly those between the ages of 50-65+ with mild to moderate severity of the condition, to actively self-manage their pain using non-pharmacological approaches.
The program consists of eight virtual sessions delivered over 4 weeks in a small group setting of 6-8 people. The sessions are designed to be interactive and engaging and cover a range of topics to help participants better understand and manage their pain. Week one focuses on understanding pain neuroscience and ways to deconstruct the pain experience and optimize neuroplasticity through grounding practices. Week two focuses on re-connecting and re-training the mind-body connection through sensory training and the identification of appropriate exercise types and dosages for PD. Week three addresses flare-up pain and freezing episode management, helping participants understand potential causes and triggers and develop effective strategies to manage them. In the final week, participants learn how to advance their skills sets, engage in task-specific strengthening, and integrate into the community to facilitate a return to higher levels of function.
An initial evaluation is conducted to assess baseline condition, followed by biweekly progress reviews to track functional status, and monitor progress. Participants in the "P.D. PowerUp" have found it to be helpful and have reported decreased dependency on over-the-counter pain medications by 20%, increased use of active coping strategies by 35%, and improved confidence and engagement in physical activities. The program is effective in a group setting as it allows for sharing of experiences and learning from peers, fostering camaraderie and support. Overall, the program is beneficial for people with PD, helping them improve their confidence and skills in self-managing their pain and decreasing reliance on medical and surgical interventions while promoting healthy living.

P22.18

Investigating pain catastrophizing to improve treatment of pain and psychological distress in Parkinson's disease

Léonore Robieux[1], Sylvia Zimmers[,2], Catherine Bungener[2]*
[1] Université Paris 8-IED, Laboratory of Clinical Psychology and Psychopathology, 2 rue de la Liberté 93526 Saint-Denis cedex 02, Saint Denis, France
[2] Université Paris Cité, Laboratory of Psychopathology and Health Processes, F-92100 Boulogne Billancourt, France., Boulogne Billancourt, France

In Parkinson's disease (PD), a large number of patients are confronted with pain. This issue has been receiving increasing attention in literature in recent years, as the complexity of the painful phenomenon in this disease makes it difficult to evaluate and treat. In addition, pain in PD is often associated with anxiety and depression symptoms. However, the processes involved in the relationship between pain and psychological distress are not well understood.
The goal of this study was to explore in detail the experience of pain in participants, as well as to explore the links between pain and psychological distress. In addition, we aimed at identifying the psychological processes (pain coping strategies) which influence the links between psychological distress and pain.
A quantitative cross-sectional study was conducted among a cohort of participants (n=169) who had received a diagnosis of PD, using an online questionnaire. After collecting socio-demographic and medical data, the survey explored the severity of psychological distress (Beck Depression Inventory; Parkinson Anxiety Scale). Then the survey evaluated the participants' pain as completely as possible, with the King's PD Pain Questionnaire, the McGill Pain Questionnaire and the Brief Pain Inventory. The study also investigated the pain coping strategies, with a specific focus on catastrophizing (Coping Strategies Questionnaire; Pain Catastrophizing Scale).
The results allowed us to establish a pain profile for the participants. Overall, our results show that depending on the tool used, 83% to 95% of participants reported pain and levels of psychological distress were higher than those of the general population. In addition, psychological distress was significantly correlated with the severity of the sensory and emotional impact of pain, and inferential analysis highlighted a major result: the mediating role of catastrophizing in the relationship between psychological distress and pain.
These results allow a better understanding of the phenomenon of pain in PD and open new research perspectives. They offer both proposals for improving clinical practices and new possibilities of therapeutic intervention approaches to reduce catastrophizing. These latter can be aimed at modifying the perception of the experience of pain and thus facilitate adaptation to this particularly frequent and disabling symptom in patients with PD.

COMPREHENSIVE CARE: Multidisciplinary/interdisciplinary teams

P23.01

Parkinson's care clinic: "Outside the pill box" interdisciplinary rehab and wellness care: Improving access and efficiency of care for people with Pakrinson's disease (PWP) and their care partner(s) in underserved areas of North Alabama, USA

Erin Edmundson, Arantxia Wijngaarde*, Rebecca Rodgers*
Huntsville Hospital, Huntsville, Alabama, United States

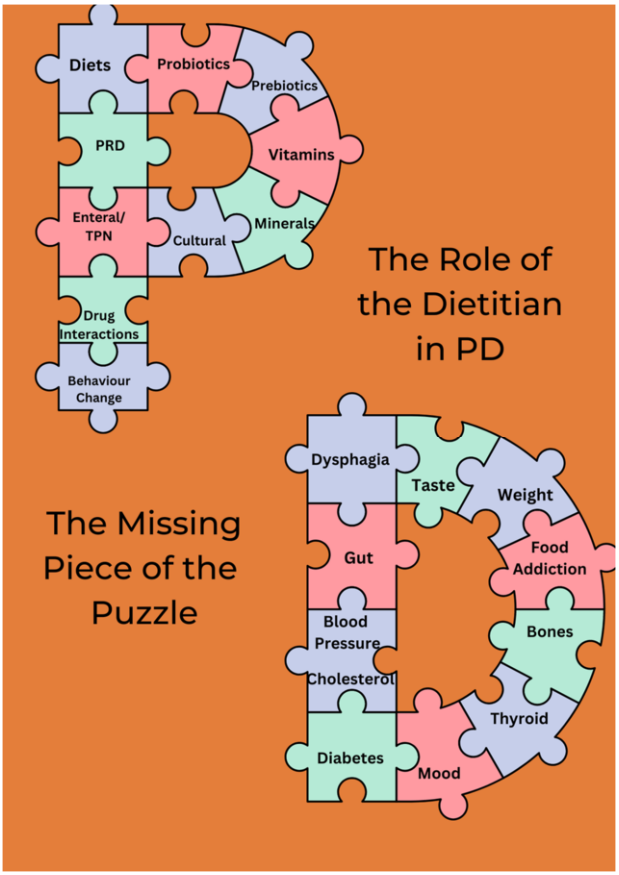
Objective: To assess patient outcomes and satisfaction of an interdisciplinary clinic (IDC).
Methods: Huntsville Hospital is the hub of a 14 hospital-affiliate health system across 15 underserved counties in North Alabama, USA, with 57% of its patients considered to be lower middle income. With no options for interdisciplinary care, in 2017, the "Outside the Pill Box" IDC was developed to improve access and decrease barriers of time, cost and transportation for PwP. Collaborating with a PwP, a "red light, yellow caution, green light" prioritized management plan was developed as a simple delivery of individualized clinic recommendations to a PwP. A pilot clinic completed, local and mobile IDCs connect PwP and their care partners to a physical therapist, occupational therapist, speech-language pathologist, a social services coordinator, licensed dietician, and an exercise physiologist, all with certifications and experience treating PwP. Clinic coordinators share the management plan, assisting with follow through, post clinic, and at three (3) and six (6) months. Feedback surveys measure patient satisfaction, value and efficiency.
Results: Since 2018 the Parkinson's Care Clinic has conducted 22 "Outside the Pill Box" IDCs across North Alabama, serving 124

PwP, 76 males and 48 females, ages 54 to 86 years, with an average age of 71. Red flags have improved by 77%, yellow caution items have improved by 23%, green light items have improved by 31%. Of the clinic participants with Parkinson's, > 90% were very satisfied with the location, environment, efficiency of the clinic, information and knowledge gained, and friendliness of staff. 100% of the PwP reported the time spent in the clinic was adequate and the IDC was valuable.
Conclusion: "Outside the Pill Box" IDCs have proven to be a valuable, efficient service, becoming an integral part of rehab and wellness care management for PwP and their carepartners in North Alabama, USA. Success of "Outside the Pill Box" interdisciplinary care encourages prioritizing continued development of interdisciplinary rehab and wellness service delivery for PwP and their carepartners across underserved areas of Alabama, USA.

P23.02

A missing piece of the Parkinson's puzzle: The critical role of the dietitian in the care of people living with Parkinson's disease (PD)
Richelle Flanagan[*1], Indu Subramanian[2], Carley Rusch[3]*
[1] My Moves Matter, Dublin, Dublin, Ireland
[2] UCLA Health, Los Angelos, United States
[3] Norman Fixel Institute for Neurological Diseases at UF Health, Gainesville, Florida, United States

There are misconceptions that nutrition only comes into play in the mid to late stage of PD and that it is only important in older people. In fact, nutrition plays a major role in the journey from diagnosis, regardless of age, to the end stage for the person with Parkinson's (PwP), their care partners and family.
Dietetic intervention can impact on non-motor symptoms such as constipation, weight, sarcopenia, dehydration, bone health and dysphagia, all of which have a significant impact on quality of life and mortality. Dietitians provide personalized guidance regarding diet, supplements, and food-drug interactions all within a cultural context. As a critical member of the multi-disciplinary team (MDT), Dietitians can alert team members to safety issues such as weight loss, swallow, or food addiction issues. They are specifically trained to facilitate behavior change through lifestyle modification.
Access to dietitians, however, remains woefully poor. A Belgian study of 82 PwP showed that only 11% of patients had ever seen a Dietitian with only 3% seeing a dietitian on an ongoing basis. A nationwide Irish survey of 1504 PwP showed that only 15% had access to a dietitian.
We propose a call to action to: improve access to dietitians, provide specialized training about PD and diet for Dietitians, provide nutrition for PD training for Dietitians and other health professionals. Inclusion of the dietitian as a core member of the MDT with inclusion in the Movement Disorders Society and team training. Updated guidelines for dietetic management of PD by global dietetic organizations and increased research into PD nutrition interventions including assessment tools for nutritional status. Inclusion of dietitians, diet and nutrition related topics in wellness strategies to help PwP.
As improved nutritional status is related to improved quality of life in PD, we propose the dietitian as a critical piece of the puzzle that has heretofore been underutilized in the management of PD. Improving access to dietitians may help dramatically improve the quality of life for PWP, their care partners and families. There is a dire need for dietary intervention research and universal up to date dietetic evidence-based guidelines for PD.



P23.03

Feasibility and efficacy of a multidisciplinary telemedicine intervention program to reduce falls and improve quality of life in Parkinson's disease (NCT04694443)
Álvaro García-Bustillo[*1], Florita Valiñas-Sieiro[2], Marta Allende-Río[2], Alicia Olivares-Gil[3], José Miguel Ramírez-Sanz[3], José Luis Garrido-Labrador[3], Álvar Arnaiz-González[3], José Francisco Díez-Pastor[3], Maha Jahouh[4], Josefa González-Santos[4], Jerónimo Javier González-Bernal[4], José María Trejo-Gabriel-Galán[2], Esther Cubo[2]*
[1] Fundación Burgos por la Investigación de la Salud, Burgos, Spain
[2] Hospital Universitario de Burgos. Neurology Unit, Burgos, Spain
[3] Universidad de Burgos. Computer Engineering Department, Burgos, Spain
[4] Universidad de Burgos. Health Science Department, Burgos, Spain

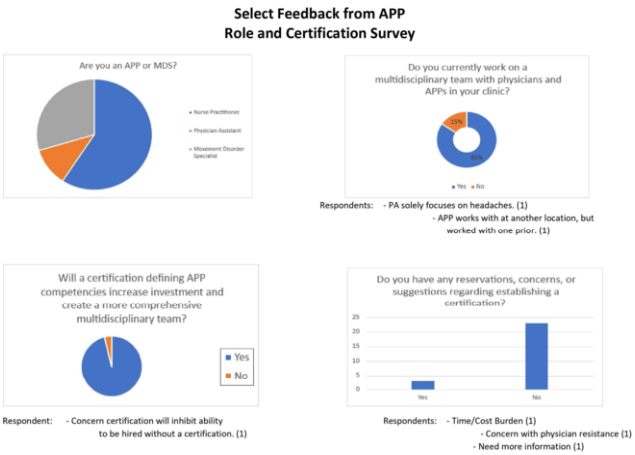
Objective: To evaluate the feasibility and effectiveness of a multidisciplinary telemedicine intervention program to reduce falls and improve quality of life (QoL) in patients with Parkinson's disease (PD).
Background: Falls in PD are very frequent, increase comorbidity, mortality, and socio-health costs, and decrease QoL. Many patients with PD, and especially those living in rural areas, have limited access to multidisciplinary interventions.
Methods: Ongoing, single-center, longitudinal, randomized, two-group study, involving patients with idiopathic PD, high risk of falls, without severe cognitive impairment, and without access to other multidisciplinary care services. Both groups were followed for 8 months in the Neurology Unit of the Hospital Universitario de

Burgos. The control group received the usual best clinical practice, and the study group received weekly remote Occupational Therapy sessions and monthly teleconsultations with neurologists and nurses for 4 months. Falls were recorded through a fall's diary, motor and non-motor symptoms were assessed with the MDS-Unified Parkinson's Disease Rating Scale (MDS-UPDRS), wearable sensors (STAT-On), Non-Motor Symptoms Scale (NMSS), Beck Depression Inventory (BDI-II), Lille Apathy Scale (LARS), Freezing of Gait Questionnaire (FOGQ) and Mini Balance Evaluation System Test (Mini-BESTest), and quality of life was assessed with EUROHIS-QOL 8 scale (WHOQOL 8).
Results: The clinical data of the first 41 PD patients were analyzed, 20 males (48.8%) and 21 females (51.2%), with a mean age 69.17±9.55 years old. There were no significant differences between both groups in the incidence of falls. Significant improvements were found in the study group compared to the control group in NMSS (p=0.024), BDI-II (p=0.0001), LARS (p=0.0001), FOGQ (p=0.019), total score of the MDS-UPDRS (p=0.042), Mini-BESTest (p=0.0001), and WHOQOL 8 (p=0.001).
Conclusions: Although the incidence of falls were not reduced, multidisciplinary telemedicine intervention was feasible and effective in reducing motor and non-motor symptoms including depression, and apathy, and in improving patient's QoL. Multidisciplinary telemedicine interventions represent an adjuvant clinical tool favoring greater equity in the distribution of resources and easier access to specialized health care in PD.

P23.04

Advanced practice providers central to managing patients with Parkinson disease and other movement disorders.
Sherrie Gould[*,1], *Kelly Papesh*[2], *Bruce Jones*[3], *Anissa Mitchell*[4]
[1] Scripps Clinic Center for Neurorestoration, La Jolla, CA, United States
[2] Association of Movement Disorder Advanced Practice Providers, Fort Collins, CO, United States
[3] Association of Movement Disorder Advanced Practice Providers, Chicago, IL, United States
[4] Parkinson & Movement Disorder Alliance, Orlando, FL, United States

Objective: Promote awareness of the increasing need to utilize advanced practice providers (APP) in management of patients with Parkinson disease (PD). Improve effectiveness of multidisciplinary teams and patient outcomes, creating a professional certification for APPs working with patients with PD.
Background: Limited access to advance-trained PD providers results in disparate diagnosis/management, especially considering annually new US cases are ~90,000 (PF, 2022), heavily burdening experts providing quality care. Roughly 40 new US-based movement disorder specialists (MDS) are entering practice annually (Dorsey, et al., 2021). In 2021, 24 fellowships remained vacant. MDS' mostly practice in metropolitan areas, leaving many patients without convenient access to specialists. APPs bridge the gap, providing management throughout a PD patient's journey. There are approximately 159,000 physician assistants and 355,000 nurse practitioners practice in the US (AANP, 2022). Most APPs (70%) practice in primary care settings (AANP, 2022), though others gravitate toward subspecialties. The data shows improving access to, and specialty care with APPs is crucial, as is APP professional development.
Methods: The Association of Movement Disorder Advanced Practice Providers, in conjunction with Parkinson & Movement Disorder Alliance, distributed a Survey Monkey survey in 2022 to APPs and physicians working in movement disorders to assess scope of practice and gauge interest in a certification for APPs managing patients with PD.
Results: Ninety-one percent of APPs and MDS survey respondents agreed an APP certification, with defined core competencies, will strengthen multidisciplinary teams and improve patient outcomes. Previous data demonstrates a positive correlation between nursing certification and clinical patient outcomes (Coelho, 2020). Similarly, enhanced skills and clinician confidence also predict improved patient outcomes (Vaughn, 2020).
Certification and opportunities for professional advancement become a voluntary investment by the APP, increasing their investment to their practice or specialty and improving retention.
Conclusion: One-hundred percent of participants agreed a sub-specialty certification for APPs, such as PD, will strengthen a more comprehensive multidisciplinary team by improving retention rates and job satisfaction among the certified clinicians. Similarly, poor retention can affect team cohesiveness, negatively impacting patient experience and outcomes. A multi-disciplinary team with APP certification will have greater capacity, skill set, and cohesion along patients' journeys through diagnosis and management.ce.



P23.05

ParkinsonNet Luxembourg – A multidisciplinary network adjusted to the healthcare environment in Luxembourg
Mariella Graziano[*,1], *Nicole Colson*[2], *Joëlle V. Fritz*[3], *Sylvia Herbrink*[4], *Anne Kaysen*[5], *Carole Simon*[6], *Jochen Klucken*[3], *Alexandre Bisdorff*[7], *Sanne Bouwman*[8], *Bastiaan R. Bloem*[9], *Rejko Krüger*[3]
[1] Neuro-Physiotherapy Practice, Esch sur Alzette, Luxembourg
[2] Occupational Therapy at home, Luxembourg, Luxembourg
[3] Luxembourg Institute of Health, Luxembourg, Luxembourg
[4] Speech and Language Therapy Practice, Warken, Luxembourg
[5] Luxembourg Centre for Systems Biomedicine (LCSB), University of Luxembourg, Esch sur Alzette, Luxembourg
[6] Speech and Language Therapy Practice, Niederdonven, Luxembourg
[7] Centre Hospitalier Emile Mayrisch, Esch sur Alzette, Luxembourg
[8] Radboud university medical center, department of Neurology, Nijmegen, Netherlands
[9] Department of Neurology, Centre of Expertise for Parkinson and Movement Disorders, Donders Institute for Brain, Cognition and Behaviour, Radboud University Medical Centre, Nijmegen, Netherlands

Introduction: ParkinsonNet is a patient-centred multidisciplinary network working according to evidence-based guidelines. This innovative network was initially founded in the Netherlands in 2004 to coordinate the activities of healthcare professionals (HCP) involved in care of people with Parkinson's (PwP) and to empower

them to take an active role in their respective treatment. ParkinsonNet takes care of PwP through all disease stages promoting early referral to and communication with the multidisciplinary HCP team.
Methods: Based on the Dutch model, implementation of ParkinsonNet in Luxembourg was started in 2018 after mapping Luxembourg-specific hurdles and obstacles. An effort was made to select therapists working in different geographical areas of Luxembourg. Occupational therapists, physiotherapists and speech and language therapists were trained by the Dutch team in a three-day basic training in 2018 and four of them followed a train-the-trainer course. To cover more of the Luxembourgish area and include more therapists working in close proximity to the PwP's home, a second training was organised in 2022 by the Luxemburgish team. All therapists and neurologists meet on a regular basis including multidisciplinary and monodisciplinary national and regional trainings with PwPs and carers to strengthen collaboration and increase their expertise.
Results: In 2019, a survey-based evaluation among ParkinsonNet members showed increased professional expertise and work satisfaction among the healthcare professionals one year after completing the training. The number of PwP seen by ParkinsonNet members increased over time, currently approximately 50% of PwP in Luxembourg are cared for within the network. The network started cooperating with researchers to incorporate digital tools in daily practice and for quality evaluation.
In 2020 the ParkinsonNet success amongst the Parkinson's community led to the identification of a patient ambassador, promoting ParkinsonNet by addressing PwP and decision takers in health politics.
Conclusion: ParkinsonNet Luxembourg developed as a main player for the care of PwP. It was selected as a model for integrated care in chronic diseases entering a pilot phase in 2023 to become the first evidence-based, quality monitored and digitally connected integrated care networks linked to reimbursement by the public health insurance in Luxembourg.
Reference: Sturkenboom et al Mov Disord. 2020; 35 (suppl 1)

P23.06

Temporal trends in the coverage of specialized allied health services for Parkinson's disease: 10 years of experience with the Dutch ParkinsonNet
Sanne Bouwman[*,1], Judith van Erkelens[2], Anja van Baardewijk-Joosten[1], Bastiaan Bloem[1], Johanna Kalf*[*,1]*
[1] Radboud university medical center, Nijmegen, Netherlands
[2] Vektis, Utrecht, Netherlands

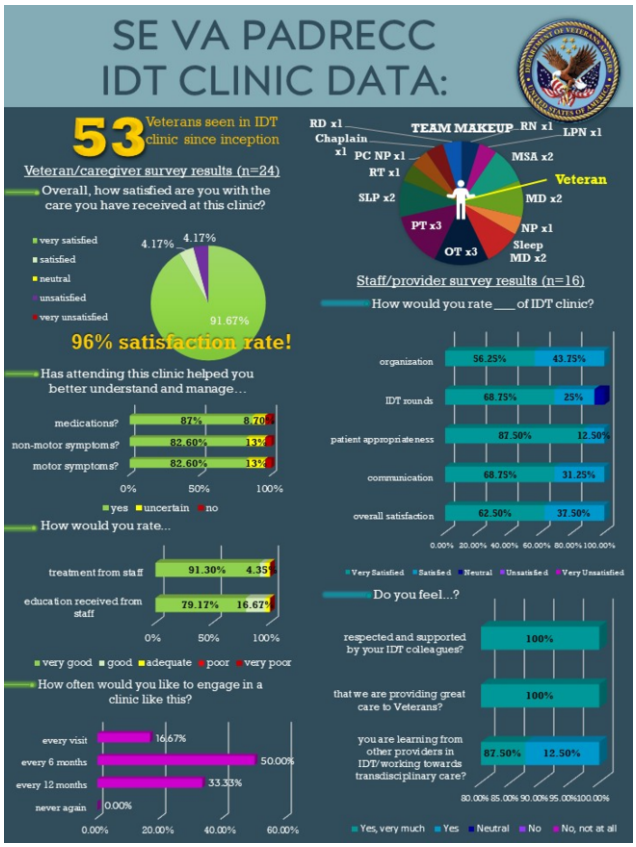
Introduction: ParkinsonNet is a nationwide system of regional multidisciplinary networks caring for people with Parkinson's disease (PwPD) or atypical parkinsonism in the Netherlands. Multiple studies have demonstrated that this care model improves the quality of care while saving cost. The ParkinsonNet concept has also been successfully implemented in other countries.
One element of the ParkinsonNet approach is the concentration of specialized care: specialized allied health care professionals (AHCP) enhance their clinical experience by treating a higher caseload compared to generically trained AHCPs.
Method: We monitored long-term temporal trends in the coverage of specialized allied health services for PD by analyzing health insurance claims. For this purpose, we used data from 2012 to 2021 obtained within the national independent registration of Dutch health care insurance claims (Vektis). We did this for four disciplines of community-based AHCPs: physiotherapists (PT), occupational therapists (OT), speech-language therapists (ST) and dietitians (DT) (data on AHC in hospitals and nursing homes is not available from this database).
Results: Between 2012 and 2021 the number of people diagnosed by a neurologist with Parkinson's disease or atypical parkinsonism increased with a mean of 2.4% per year.
In 10 years, the use of AHC by PwPD increased steadily: PT 62 to 66%, OT 10 to 21%, ST 7 to 11% and DT 2 to 11%. When comparing specialized AHCPs with generic AHCPs, increasing numbers of PwPD received specialized care: PT 36 to 73%, OT 61 to 79%, ST 59 to 88% and DT 24 to 50%.
In addition, the mean number of PwPD that are treated yearly in community-based practices by specialized AHCPs is higher (12 to 18) compared to PwPD in by generic AHCPs (2 to 4).
Conclusion: Concentration of specialized community care has substantially increased over a decade, demonstrating that the majority of PwPD in the Netherlands now profit from the ParkinsonNet approach. This suggests that a similar improvement can be expected for health care innovations in other countries.

P23.07

All hands on deck! Development and implementation of a nurse-driven, rehab-focused, in-person or telehealth interdisciplinary team (IDT) clinic for Veterans with PD and other movement disorders
Jessica Kaplan, Jessica Lehosit, Erin Buckley, Hall Emily, Serio Karissa, Brittany Reed, Lauren Sharpe-Payne, Abu Qutubuddin, Debbie Lindsey, Mark Baron, Cameron Jennings, Melissa Oliver, Alicia Sullivan, Hope Kumme, Mark Flores, Elsa Mathew, Leslee Hudgins, Kayla Thompson, Julie Thompson, Lesa Beatty, Christina Kausek, Mary Hamm, Miriam Hirsch, Michael Shapiro*
SE VA PADRECC, Richmond, Virginia, United States

The Southeast VA (Veterans Administration) PADRECC (Parkinson's disease Research, Education and Clinical Care Center) initiated an interdisciplinary team (IDT) clinic to help manage Parkinson's disease (PD) and associated disorders in June 2022. Our existing ALS (Amyotrophic lateral sclerosis) clinic model was adjusted for our PD Veteran population. Each week, two Veterans are seen in a 2.5–3-hour clinic by our team of physical therapist (PT), occupational therapist (OT), speech therapist (SLP), assistive technology OT, nurse, social worker, and chaplain. Depending on the needs of the Veteran, the nurse coordinator might also include an appointment with our movement disorder specialist or nurse practitioner (NP), palliative care NP, sleep neurologist, pelvic floor PT, registered dietician, music therapist, recreational therapist, or chaplain. The visit can be conducted in-person or also using our telehealth option from their home computer or smart phone. The goal of the clinic is to facilitate access to the vital therapists that can help manage their PD symptoms. After the clinic appointments, the providers round together and discuss goals and potential barriers to care. Open communication between providers allows greater understanding of the Veteran, providing patient-centered care. A discussion is held with the Veteran after rounds to discuss treatment plan. Depending on the treatment plan, the therapists will continue to work with the Veteran, either in-person or via telehealth. Veterans will follow-up with IDT every 6-12 months to create a preventative model of care. To date, 53 Veterans have been seen in our clinic (16 via telehealth and 37 in-person) with plans of further expansion in 2023. Veterans and their caregivers were sent an anonymous survey and 24 responded with largely positive results. 96% of respondents expressed overall satisfaction with IDT clinic, and majority indicated that IDT has helped them better manage medication, motor and non-motor symptoms. IDT clinic providers were also surveyed anonymously and 16 responded. Satisfaction was 100% (where 62.5% marked very satisfied and 37.5% marked satisfied). It is our ultimate goal to help integrate this model at other VA PADRECC Centers of Excellence and associated consortium sites, in order to increase access to vital

therapies and promote team-management in this movement disorder population.



P23.08

The role of social work in the delivery of integrated care for Parkinson's disease

Linda Kreitzer[*,1], Jessica Shurer[2], Elaine Book[3], Lisa Zerden[4], Ting Guan[5]*
[1] University of Calgary, Edmonton, Alberta, Canada
[2] CUREpsp, New York, New York, United States
[3] Parkinson's Foundation of Excellence, University of British Columbia, Vancouver, British Columbia, Canada
[4] School of Social Work, University of North Carolina at Chapel Hill, Chapel Hill, North Carolina, United States
[5] School of Social, Syracuse University, Syracuse, New York, United States

Background: Parkinson's Disease (PD) is the second most common neurodegenerative disease, affecting over 10 million people worldwide. The complex symptoms and long life expectancy of PD lend themselves to the need for multidisciplinary management over disease progression. Social workers have been part of integrated teams working with persons with PD and their families, offering support to address mainly non-motor symptoms such as cognitive and mood changes. Yet at present, little research has been conducted looking at the role of the social worker in PD care.
Methodology. A sequential mixed method study was conducted in 2020, early into the COVID-19 pandemic. A 30-minute online survey was administered with social workers who identified as working directly in PD care (N= 39). Of this sample, 11 social workers participated in follow-up qualitative semi-structured interviews to provide more in-depth description about their roles and functions in PD care.
Findings: Survey findings offer a clearer understanding of why referrals are made to social work services, social work interventions employed across disease progression, service delivery comparisons before and during COVID-19, interdisciplinary collaboration/communication practices, and barriers to the provision of social work care. The qualitative study illuminated the breadth of roles social workers play and how professional values inform their practice. Relationship-building between social workers and people with PD and their families, interdisciplinary team members, and community providers was found to be a central theme in the study and influential in the delivery of optimal services. Institutional barriers to the utilization of social work services were identified, including misunderstandings about the role of the social worker, lack of funding for positions, and the need for early social work intervention. Additionally, results from both the survey and interviews identified how COVID-19 changed social work practice with PD.
Implications: Findings from both the survey and interviews illustrate the breadth of social work roles in PD care, the application of the social work profession's value of human relationships with both people with PD and multidisciplinary teams, and the adaptability of social workers through COVID-19. This study underscores the integral role of social workers in the delivery of comprehensive care for PD persons and their families.

P23.10

CENPAR: Rehabilitaction area to 12 months

*Paola Alicia Riveros Cortés**
Cenpar Neurologyc Center To Parkinson Disease, Las Condes, Santiago, Chile

Abstract: During 2022, 120 people who maintained permanent therapies are compared. It is analyzed from the first session, held in previous years. Result: All the patients evaluated before and after 12 months of continuous therapy in CENPAR presented improvements in the abilities that presented alteration, however, some, due to personal condition, presented greater and faster improvement, and age.
Introduction: Rehabilitation is the care of various health areas that facilitate the functioning and reduce the alterations of people.
CENPAR, Neurological Center specialized in Parkinson's disease located in Chile
Material and method: This is a retrospective descriptive study obtained through the admission data of 120 patients with Parkinson's disease from the Parkinson's Neurological Center CENPAR.
Variables: Gait evaluated with the Gaitrite digital platform; sign of muscular rigidity with clinical test; clinically assessed aerobic capacity; balance tested with balance platform; fall risk assessed with timed up and go; state of cognition evaluated with Moca test; clinic-assessed swallowing; speech and voice evaluated by clinic; independence assessed with the Barthel test; signs of depression evaluated by Yesavage; social participation and free time evaluated by clinic.
Result: First session of 120 people,20% present dependent gait;100% muscle stiffness;100% alteration in cardiovascular capacity;100% balance disturbance; 76% a moderate or severe risk of falling;90% cognitive impairment;80% swallowing disorder;60% speech impairment;71% voice alteration;85% some degree of dependence in activities of basic daily life;63% present signs of depression;100% do not carry out social participation activities or free time. A re-evaluation of the skills of each person is carried out in December 2022: no person (0%) presents a walk dependent with

technical assistance;0% refer muscle stiffness;33% normal cardiovascular capacity;40% degree of balance disturbance;15% moderate or severe risk of falling;47% degree of cognitive impairment;43% swallowing disorder;0% speech impairment; 0% voice alteration;11% degree of dependence in activities of basic daily life;26% present signs of depression.
Conclusion: The results have shown that people with Parkinson's with 12 months to rehabilitation specific to their needs improve their quality of life, decreasing the fragility index, reducing the chances of hospitalization due to falls, fractures, aspirations or other consequences, secondary to abilities altered by the disease.

P23.11

Integrative treatment of Parkinson's disease including photobiomodulation: A case series
Anita Saltmarche[*1], Ann Liebert[2], Orla Hares[3], Brian Bicknell[4]*
[1] Saltmarche Health & Associates - Photobiomodulation Specialists, Caledon East, Ontario, Canada
[2] Faculty of Medicine and Health, University of Sydney, Sydney, NSW, Australia
[3] Gaitway Neurophysio, Parkinson's Wellness Innovation Centre, Hamilton, Ontario, Canada
[4] NICM Health Research Institute, Western Sydney University, Sydney, NSW, Australia

Parkinson's disease is a complex neurodegenerative disease that is highly heterogeneous in symptomology and progression. While no treatment can slow the progression of the disease, several interventions, such as exercise and nutrition, have been shown to slow the decline in the quality of life of some patients with Parkinson's disease. Exercise can maintain physical fitness, retard the loss of mobility, help with balance, reduce the harmful effects of inactivity and potentially diminish the deterioration in the quality of life. A healthy diet, for example, a Mediterranean or vegetarian diet, can maintain quality of life, reduce gastrointestinal symptoms such as constipation, and avoid secondary symptoms of Parkinson's disease. Photobiomodulation is the use of non-thermal light to improve cellular function. It has been used to alleviate pain, aid tissue repair, and reduce inflammation, including neuroinflammation. Two recent proof-of-concept clinical trials demonstrated that transcranial and abdominal applications of photobiomodulation using a laser and LED devices could alleviate some motor and non-motor symptoms of Parkinson's disease. These improvements have been shown to continue for three or more years with continued at-home treatment.
An interdisciplinary or integrative approach to managing the symptoms of Parkinson's disease may provide the optimal approach to maintaining health for as long as possible during the Parkinson's journey. This approach typically includes exercise, diet and carefully managed medication but might also include acupuncture, herbs, massage and (we would argue) photobiomodulation.
Here we present a case series of four patients from three countries (Canada, Germany, and Australia) at various stages of their Parkinson's disease journey and their responses to interdisciplinary intervention strategies, including photobiomodulation, exercise and medication. The photobiomodulation regimen consisted of home treatment with different combinations of abdominal application (class 1 "PDCare Laser") and transcranial application ("NeuroCare" LED helmet).

P23.12

Six month evaluation of a one year post graduate nurse practitioner (NP) fellowship focused on care for persons with movement disorders: An interdisciplinary approach
Kristen Matulis[*1], Patrick Walker[2], Abigail Corriveau[3], Christopher Hess[3], Christine Kim[4], Eli Pollard[5], Serge Przedborski[4], Janice Smolowitz[6]*
[1] Columbia University, Parkinson's Foundation Fellow, New York, NY, United States
[2] University of Florida, Parkinson's Foundation Fellow, Ganesville, FL, United States
[3] University of Florida, Ganesville, Florida, United States
[4] Columbia University, New York, NY, United States
[5] Parkinson's Foundation, New York, NY, United States
[6] Montclair State University, Montclair, New Jersey, United States

Background: The demand for healthcare providers, with specialist training, able to provide quality care for persons with movement disorders has been described. In the USA, neurology fellowships provide residents and graduates with advanced education in the diagnosis and treatment of persons with these conditions. Other healthcare professionals, such as NPs, may increase access to care through successful completion of advanced subspecialty education.
Objective:
Using an interdisciplinary model the objective of this NP fellowship is to educate, mentor, and promote expert clinician specialists who will devote their careers to the care of persons with Parkinson's disease and related movement disorders.
Methods:
NP fellows train alongside neurology fellows at two Parkinson's Foundation Centers of Excellence. This approach prepares graduates to participate in and facilitate collaborative interdisciplinary care. The NP fellows complete didactic, administrative, research, and clinical hours. Progress through the program is measured on a monthly and quarterly basis.
Results/Conclusion:
Three NPs are participating in the first cohort. During the first 108 clinical days they provided care for 1,041 persons. Sixty-five percent were 65 years and older and 25% were between 50 and 64. Fifty-nine percent reported male gender. The majority of patients received government insurance. Physician referrals accounted for 45% of encounters. Fifty-one percent of patients were self-referred. Seventy-six percent of encounters were recorded as routine follow-ups. The average time spent with patients was 54 minutes. Decision making was recorded as high complexity for 33% of the encounters and moderate for 39%. During this time, NP fellows participated in cross-site seminars, journal club, and interdisciplinary rounds. They report increased self-efficacy providing care during the first 6 months, which is consistent with site specific faculty report of fellows increasing independence, which met benchmark criteria. Positive relationships are reported among NP and MD fellows. Data monitoring and outcomes will continue through the remaining 6 months of this program.

P23.13

Multidisciplinary education transforming Parkinson's services

Susan Thomas[*,1], Sarah Gillett[2], Charlie Peel[2]*
[1] Healthcare Consulting, Tiverton, Devon, United Kingdom
[2] Parkinson's Academy, Sheffield, South Yorkshire, United Kingdom

Background: The UK is experiencing a workforce crisis, compounded by a lack of confidence amongst clinicians to tackle complex conditions like Parkinson's. This situation was recognised some 20 years ago prompting the development of a specialist training programme to develop new Parkinson's specialists the Parkinsons Academy. Initially developed for neurologists and care of the elderly physicians, the content has evolved to ensure relevance to nurses and allied health professionals (AHPs). To date 6,439 consultants, nurses, and Allied Health Professionals (AHPs) have attended events focused on improving Parkinson's services.
Methodology: Through 113 different events, 83 being in-person residential 'MasterClasses', an increasingly broad range of healthcare professionals (HCPs) have received targeted education across diagnosis, treatment and management of Parkinson's. Courses involve speakers from various disciplines and backgrounds, tiered to reflect key learning objectives whether a delegate is new to Parkinson's or a specialist in the condition. All courses feature sessions on service design, collaborative working and integrated management whilst all two-module courses include a mandatory workplace project to improve an element of their local Parkinson's services.
Results: 2,706 unique HCPs including consultants in neurology and medicine for the elderly, specialist nurses, AHPs and pharmacists, have attended one of the 113 educational events, with a gross total of 6,439 delegates attending an event with the Academy over the past two decades. 93% of delegates across 83 MasterClasses and conferences stated relevance to their learning needs was excellent or good, and 92% said they were highly likely or likely to modify their practice as a result of the education. Delegates go on to attend an average of two or more additional courses in Parkinson's, continuing to improve their knowledge and practice.
More than 500 mentor-supported workplace projects have impacted local services as a result of our education in more than 20 different categories or themes, from diagnosis to medication, cognition to exercise. Highly rated webinars addressing subjects like women's health, physical exercise, and delirium, have been attended live by over 3500 HCPs, and exceeded 10,000 views on demand; a recent survey suggests that these also impact people's personal practice. Case studies outlining outcomes will be highlighted.

P23.14

Home-based titration with duodenal infusion of levodopa in People with Parkinson's disease: An observational feasibility study

Trine Thomsen[*,1], Bo Biering-Sørensen[1], Nick Schou Nielsen[2], Asher Lou Isenberg[3], Michael Møller[2], Jesper Bøje Clausen[1], Louise Olsen[2], Mahsa Javidi[1], Marc Klee Olsen[2], Jeanet Roger Vilhelmsen[1]*
[1] Movement disorder Clinic, Department of Neurology, Rigshospitalet, Copenhagen, Glostrup, Capitol Region, Denmark
[2] Movement disorder Clinic, Department of Neurology, Rigshospitalet, Copenhagen, Glostrup, Denmark
[3] Department of Neurology, Nordsjællands Hospital, Hillerød, Hillerød, Capitol Region, Denmark

Background: Studies of duodenal infusion of levodopa (LCIG) on groups of parkinsonian patients (PD-patients) have reported beneficial effects on motor complications. The testing and titration of the right levodopa-equivalent dose has usually been completed during a hospital admission over a week. However, dose adjustment may depend on home environment, emotional stress, and normal physical activity in everyday life, which is why home-based titration (HBT) in a period of 4 days could be beneficial. Objectives: To assess the feasibility of LCIG home-titration with use of telemedicine-assisted (TM) technology, and evaluate safetyness and patient/caregivers satisfaction. Secondly, to establish practical recommendations for a HBT-program including characteristics for PD-patients suitable for home titration. Material and methods: Study design was an observational feasibility study assessing feasibility, safetyness and satisfaction of treatments with home-titration of LCIG-infusions with use of self-reported questionnaires. All eligible participants were screened consecutively from Movement disorder Clinic at Rigshospitalet, Denmark, from October 2017 to February 2022. Results: 10 PD-patients were included (6 male and 4 females). They all fulfilled the criteria of LCIG-treatment, lived in private homes and nursing homes respectively, mean age of 74 years, PD duration on 12.9 years, and varied in severity of cognitive impairments. PD-nurses spent in average 1 hour and 34 minutes at the participants` homes and made 3.2 video calls during the period. Results show that the HBT-program is feasible. PD-patients (mean 36.2, score 0-40) on average were more satisfied with the HBT-program than the caregivers (mean 31.8, score 0-40). Additionally, facilitators and barriers in completing an HBT-program were identified. Conclusion: This "real life" feasibility study indicates that TM-assisted HBT-programs are feasible, and rated satisfactory and safe by PwP and caregivers, and may be a substitute to in-hospital treatment. It was considered feasible due to numbers of contacts, time spent in private homes (based on individual needs) and quality of TM-assisted contacts. An extended focus and support should be given to the caregivers in both the decision-making and during the HBT-program. Subsequently, a RCT study comparing the HBT-program with in-hospital titration, will be initiated in Spring 2023, evaluating stress response, number of titrations, sleep, satisfaction and OFF/ON time measured with wearables.

P23.15

Frailty and risk for falling in Parkinson's disease. A longitudinal, randomized, multidisciplinary-based telemedicine intervention (NCT04694443)

Florita Valiñas-Sieiro[*,1], Marta Allende-Río[1], Álvaro García-Bustillo[2], José Miguel Ramírez-Sanz[3], Alicia Olivares-Gil[3], José Luis Garrido-Labrador[3], Álvar Arnaiz-González[3], José Francisco Díez-Pastor[3], Maha Jahouh[4], Josefa González-Santos[4], Jerónimo Javier González-Bernal[4], José María Trejo-Gabriel-Galán[1], Esther Cubo[1]*
[1] Hospital Universitario de Burgos. Neurology Unit, Burgos, Spain
[2] Fundación Burgos por la Investigación de la Salud, Burgos, Spain
[3] Universidad de Burgos. Computer Engineering Department, Burgos, Spain
[4] Universidad de Burgos, Health Science Department, Burgos, Spain

Objective: To investigate the relationship between frailty and risk of falling in Parkinson's disease (PD).
Background: Frailty can lead to increased vulnerability in patients with PD and worsen their health conditions. The prevalence and association of motor and non-motor symptoms (NMS) and other non-related PD factors with the risk of falling and frailty are still controversial.
Methods: This is a single-center, longitudinal, two group randomized study (NCT04694443). We recruited a cohort of non-demented PD patients with falls over the last 6 months. We conducted baseline, 4-months, and 8-months multidisciplinary evaluations. PD patients were randomized to receive in-office assessments versus alternating televisits including weekly Occupational Therapy sessions and monthly nurse and neurologist visits. The severity of motor symptoms was evaluated using the

MDS-Unified Parkinson's Disease Rating Scale (NMS-UPDRS) and Hoehn Yahr stage; NMS with the Non-Motor Symptoms Scale (NMSS), depression and anxiety with Beck BDI-II, apathy with Lille rating scale (LARS); frailty with FRAIL rating scale and Fried criteria, comorbidity with Geriatric CIRS-G, dysphagia with EAT10, quality of life with EUROHIS-QOL 8, and gait/balance with Mini-BESTest. Comparative and correlation analyses were conducted to analyze these associations.
Results: 41 PD patients were included, 20 males (48.8%) and 21 females (51.2%), with a median number of falls in the last month of 1 (range 0 to 20), mean MDS-UPDRS part III score of 40.17 ± 10.86, and frailty FRAIL and Fried scores of 1.10 ± 1.37, and 1.41 ± 1.36, respectively. Frailty (Fried criteria) was associated with age (r=0.34, p=0.03). FRAIL scores had a high correlation with FOGQ (r=0.67, p=0.0001), PDQ (r=0.66, p=0.0001), and MDS-UPDRS (r=0.62, p=0.0001), a moderate correlation with Mini-BESTest (r=-0.59, p=0.0001), EUROHIS-QOL 8 (r=-0.51, p=0.001), NMSS (r=0.43, p=0.005), CIRS-G (r=0.41, p=0.007), and BDI-II (r=0.40, p=0.010), and a low correlation with LARS (r=0.36, p=0.02), and EAT10 (r=0.31, p=0.04). There was a trend with Body Mass Index (r=0.27, p=0.08), and number of falls (r=0.25, p=0.11).
Conclusions: Frailty is associated with adverse health outcomes and increases the risk of falling in PD. Multidisciplinary telemedicine adjuvant interventions can improve access to vulnerable PD populations to prevent disability and dependence.

P23.16

Improving Parkinson's care in senior living communities and home care agencies in the US
Rose Wichmann, Joan Gardner*
Parkinson's Foundation, Minnetonka, MN, United States

Background: Current literature indicates that 90,000 Americans will be diagnosed with Parkinson's disease (PD) each year. As symptoms advance, many individuals living with Parkinson's seek care assistance through home care agencies and/or senior living communities. These organizations do not currently have adequate knowledge of the care needs of those with PD.
Objective: Struthers Parkinson's Care Network (now called Community Partners in Parkinson's Care) has worked to provide staff education and resources to enhance staff knowledge and confidence in the provision of PD care.
Methods: Training methods include site champion training of selected individuals, who were provided with an online curriculum to educate staff at their sites. Additional resources and discipline specific educational opportunities were also provided to member sites. Outcomes including staff surveys and medication audits of carbidopa/levodopa have been collected over time to assess awareness of PD care needs.
Results: Over 19,000 health care professionals across many disciplines, including direct care providers (nursing assistants, home health aides) have completed the online curriculum. Continued access to the online curriculum has helped to maintain awareness of PD care needs at member sites, decreasing knowledge loss due to staff attrition. Staff surveys have shown improvements in awareness of PD care needs following completion of the program's online education, including awareness of needs for PD medications on time. Lessons learned included need for greater education in ensuring all PD medications have documented scheduled times in the electronic medical record, greater awareness of timing separation between scheduled doses, and established goals of PD medications to be given within 15 minutes of the scheduled time. These results indicate continued need of expanded programming for home care agencies and senior living communities to receive ongoing PD education at all sites.

COMPREHENSIVE CARE: Digital health, E-health and technology

P24.02

Adherence and satisfaction of telemedicine in patients with Parkinson's disease. A longitudinal, randomized, multidisciplinary-based intervention (NCT04694443)
Marta Allende-Río[,1], Florita Valiñas-Sieiro[1], Álvaro García-Bustillo[2], José Luis Garrido-Labrador[3], José Miguel Ramírez-Sanz[3], Alicia Olivares-Gil[3], Álvar Arnaiz-González[3], José Francisco Díez-Pastor[3], Maha Jahouh[4], Josefa González-Santos[4], Jerónimo Javier González-Bernal[4], José María Trejo-Gabriel-Galán[1], Esther Cubo[1]*
[1] Hospital Universitario de Burgos. Neurology Unit, Burgos, Spain
[2] Fundación Burgos por la Investigación de la Salud, Burgos, Spain
[3] Universidad de Burgos. Computer Engineering Department, Burgos, Spain
[4] Universidad de Burgos. Health Science Department, Burgos, Spain

Objective: To analyze the adherence and satisfaction of patients with Parkinson's disease (PD) after participating in a multidisciplinary telemedicine intervention program at home using videoconferences and remote assessments with wearable sensors.
Background: Nowadays, new technologies are becoming a fundamental resource in everyday life. PD is more frequent in the elderly compared to the young, who often do not have the necessary skills to handle this technology and cannot easily access social and healthcare resources. On the other hand, remote assessments and telemedicine can facilitate access to social and healthcare services, especially for those living in rural, underserved areas. The Covid-19 pandemic has demonstrated the need to develop easy-to-use technologies for the entire population, including patients with PD, but adherence and acceptability of such resources are still unknown.
Methods: Single-center, longitudinal, randomized, two-group study (NCT04694443). PD patients were followed for 8 months via wearable monitoring sensors. In addition, the study group used a simple telemedicine system, with weekly remote Occupational Therapy sessions and monthly teleconsultations with neurologists and nurses. Adherence to the program was evaluated by quantifying the patients who successfully completed their participation in the program. Satisfaction with the telemedicine system, teleconsultations, and wearables, was assessed with the Telemedicine Usability Questionnaire (TUQ), satisfaction structured questionnaires from 1 (totally satisfied) to 7 (totally dissatisfied), and with the Quebec Users' Evaluation of Satisfaction with Assistive Technology (QUEST), respectively.
Results: To date, 38 patients have been included, and 36 patients (95%) have successfully completed their participation in this telemedicine program. After completing the program, the patients reported high satisfaction using telemedicine (mean TUQ score of 139.13±4.34), videoconferences including multidisciplinary health interventions (mean satisfaction in each session of 1.15±0.49), and with the wearable sensors (mean QUEST score of 4.35±0.44).
Conclusions: This multidisciplinary telemedicine program for patients with PD, including videoconferences and remote assessments with wearables, showed high adherence and satisfaction. These results demonstrate that telemedicine can be considered a valid and accepted resource for providing multidisciplinary care to PD patients.

P24.03

Use of a single inertial sensor on the thigh to assess gait quality during the 6-minute walk test in persons with Parkinson Disease

Dheepak Arumukhom Revi[1], Franchino Porciuncula[*2], Nick Wendel[2], Jenna Zajac[2], James Cavanaugh[3], Terry Ellis[2], Louis Awad[2]*

[1] Department of Mechanical Engineering and College of Health & Rehabilitation Sciences, Boston University, Boston, MA, United States

[2] College of Health & Rehabilitation Science, Boston University, Boston, MA, United States

[3] Department of Physical Therapy, University of New England, Portland, Maine, United States

Purpose: Wearable inertial measurement unit (IMU) sensors have the potential to quantify spatiotemporal gait characteristics during clinical walking assessments of persons with Parkinson disease (PD). However, current IMU systems require multiple sensors and extensive setup to assess gait quality, making their use challenging in clinical settings. Therefore, the purpose of the study was to assess the accuracy and feasibility of using a single thigh IMU to measure spatiotemporal parameters and performance changes during the 6-minute walk test (6MWT), a common walking capacity measure routinely used in clinical assessment.

Subjects: Community-dwelling participants (N=16) with mild-to-moderate PD.

Methods: This study was a secondary analysis of baseline data from a parent study (NCT05421624). Participants completed the 6MWT while instrumented with a single-thigh IMU. 6MWT distance was measured by a physical therapist using a hand-held measuring wheel. Using a modified version of an algorithm developed by our group, we used the IMU data to estimate stride-by-stride gait metrics of speed, cadence, and stride length. IMU-estimated stride lengths were summed to estimate distance traveled every 30m of the marked measurement walkway and the total 6MWT distance. These estimated distances were compared to the distances manually measured by the physical therapist. Distance-induced changes in each estimated spatiotemporal parameter were computed as the difference from the last 30 to first 30 seconds of the 6MWT.

Results: IMU-estimated mean total distance was similar to the therapist-measured distance (514 ± 96 m), with low mean absolute error (3.7m) and high inter-rater consistency (ICC = 0.99). Moreover, IMU estimates of distance traveled during each 30-m walkway also had a low error (2.4m) and high consistency (ICC=0.99). IMU estimates of distance-induced changes in spatiotemporal parameters revealed mean reductions in speed (Δ: -0.08 ± 0.11 m/s), cadence (Δ: -4 ± 5 steps/min), and stride length (Δ: -3.5 ± 7.3 cm).

Conclusion: A single-thigh IMU can accurately estimate distance walked and gait spatiotemporal characteristics in a clinical setting. IMU-derived metrics revealed a decline in spatiotemporal parameters during the 6MWT in persons with PD.

Clinical Relevance: The clinically-accessible, single-thigh IMU approach offers new opportunities to assess gait quality in persons with PD.

P24.04

Methods to quantify skin conductance in people with Parkinson's disease: A systematic review of observational studies

Mercedes Barrachina[*1], Laura Valenzuela-López[2], Marcos Moreno-Verdú[2], Yeray González-Zamorano[3], Juan Pablo Romero[4], Carmen Sánchez-Ávila[1]*

[1] Universidad Politécnica de Madrid (UPM), Madrid, Spain

[2] Universidad Francisco de Vitoria (UFV), Madrid, Spain

[3] Universidad Rey Juan Carlos, Madrid, Spain

[4] Universidad Francisco de Vitoria (UFV) y Brain Damage Unit, Hospital Beata María Ana, Madrid, Spain

Digital health is widely utilized to improve patient's quality of life. Biosignals are a key element to that purpose, and there are currently different biosignals utilized in people with Parkinson's disease (PD) to assess treatment effectiveness and accurately monitor patient's status. Traditionally, skin conductance assessment has been widely applied to evaluate autonomic (dis)function. However, its utilization has not been reviewed systematically yet. This work followed the PRISMA 2020 standards to investigate the use of this biosignal as a biomarker in people with PD. We searched for studies analyzing the use of skin conductance in IEEE Explore, PubMed and Science Direct, and collected information on the methods to acquire the signals, the specific device utilized, the pre-processing techniques and the features analyzed for each specific study. The STROBE checklist was used to assess the quality of the methodology used. A total of 24 studies were evaluated, involving 940 participants. The electrodermal activity (EDA) was used in 75% of studies, meanwhile the electrochemical skin conductance was used in only 25%. Their utilization was focused on assessing the autonomic and/or sudomotor disfunction, understand the decision-making and learning processes, detecting gait freezing or non-motor fluctuations or as a diagnostic tool. The EDA was analyzed in the temporal domain in 95.8% of the studies found, and the features of the ESC signal used in the analysis were very limited. The methodological quality was moderate. We conclude that there is a large heterogeneity on the devices employed to record the signals and in the processing methods applied to analyze them. Clinical utilization of skin conductance measures could result in a valuable element to identify non-motor fluctuations or to correlate with other observations, although there is still a lack of normative data that could impact its general application.

P24.05

Ability of electrodermal activity measures to detect non-motor fluctuations in Parkinson's disease

Mercedes Barrachina[*1], Laura Valenzuela-López[2], Marcos Moreno-Verdú[2], Yeray González-Zamorano[3], Francisco José Sánchez-Cuesta[2], Juan Pablo Romero[4], Carmen Sánchez-Ávila[1]*

[1] Universidad Politécnica de Madrid (UPM), Madrid, Spain

[2] Universidad Francisco de Vitoria (UFV), Madrid, Spain

[3] Universidad Rey Juan Carlos (URJC), Madrid, Spain

[4] Universidad Francisco de Vitoria (UFV) / Brain Damage Unit, Hospital Beata María Ana, Madrid, Spain

Background: Multiple biosignals are used to assess, treat, and monitor the status of people with Parkinson's disease (PD). Each signal is utilized to evaluate different organs/systems. To evaluate the sympathetic activation, the most used biomarker is the electrodermal activity (EDA). Previous studies have found a relationship between EDA and motor fluctuations in PD (Nene et al. 2019), but its usefulness to accurately detect them remains unexamined.

Objective: To determine the ability of EDA measures to detect non-motor fluctuations in people with PD by assessing changes of EDA values in ON and OFF states.
Methods: In this observational study, 18 people with PD participated (13 females, mean age = 60.12±12.41 years, Hoehn and Yahr (H&Y) 1-3). EDA was captured using the Empatica E4 device, placed on the wrist, and was continuously recorded in ON and OFF states. The raw EDA signal was pre-processed with a low pass Butterworth filter to clear noise and artifacts. The cleaned signal was analyzed with 3 different approaches, including analyses in the time and frequency domains and a convex optimization approach, which analyzed the signal distinguishing between tonic and phasic components.
Results: In the time domain, there were trends for higher EDA values in OFF state in comparison to ON state (mean = 2.07±2.2 µS vs 1.27±1.66 µS,) only in people with H&Y ≥ 2 (n=13). Similarly, in the frequency domain, higher power average values were found in OFF state in comparison to ON state (mean = 5.16±10.98 µS2/Hz vs. 10.77±19.84 µS2/Hz), only in people with moderate and severe PD. No relevant differences between OFF and ON states were found based on the tonic and phasic components of the EDA signal.
Conclusions: Sympathetic activation changes assessed with EDA measures could be of great value for the detection of non-motor fluctuations in PD and potentially could also be used to rate the evolution of the disease.

P24.06

Measuring rest-activity patterns using wearable devices in inpatients with Parkinson's and delirium: A nested feasibility study

Gemma L Bate[1], Sarah J Richardson[2], John-Paul Taylor[2], David J Burn[3], Louise M Allan[4], Alison J Yarnall[2], Silvia Del Din[2], Rachael A Lawson[2]*
[1] Newcastle University (Translational and Clinical Research Institute), Newcastle upon Tyne, England, United Kingdom
[2] Translational and Clinical Research Institute, Newcastle University, Newcastle, Newcastle-upon-Tyne, United Kingdom
[3] Population Health Sciences Institute, Newcastle University, Newcastle, Newcastle-upon-Tyne, United Kingdom
[4] Institute of Health Research, University of Exeter, Exeter, United Kingdom

Background: Delirium is a serious acute neuropsychiatric syndrome characterised by altered levels of consciousness and inattention. People with Parkinson's (PD) are at increased risk of delirium but delirium may be missed due to overlapping symptoms. Clinical scales for delirium cannot easily capture the fluctuating symptoms associated with delirium and are not validated for use in PD. Altered levels of arousal and activity are core features of delirium; wearable sensors can provide continuous objective monitoring. This feasibility study aimed to investigate differences in rest-activity patterns in PD inpatients with and without delirium and their relationship between clinically derived delirium severity.
Methods: A wrist sensor was worn by participants for at least 3 consecutive days. Delirium was identified using a standardized assessment based on the Diagnostic and Statistical Manual of Mental Disorders 5th Edition (DSM-V). Delirium severity was rated daily using an established clinical scale (Memorial Delirium Assessment Scale, MDAS). Recorded sensor signals were processed using a validated package (GGIR) [1] to provide rest-activity measures, including: Inter-daily stability (IS), time onset, average values for the most active five hours (M5) and ten hours (M10), the least active five hours (L5) and ten hours (L10), and the relative amplitude (RA) between the most and least active periods of the day. Rest measures included the percentage of rest at night-time (10pm-7am) and number and duration of rest periods during the day.
Results: Thirty-one out of 35 admissions (n=27 participants) had ≥3 days of valid sensor wear time. Delirium was identified in 66% (n=23) of admissions. Participants with delirium had significantly ($p<0.05$) lower IS, RA, % rest at night, earlier M10 and later L10 time onset. More severe delirium was associated with IS (r=-.500, p=.004, duration of rest periods (>15 mins during daytime, r=.488, p=.029), L10 onset time (r=.399, p=.029) and duration of all rest periods during daytime (r=.392, p=.029).
Conclusion: Wearable sensors can measure rest-activity patterns in inpatients with PD and delirium. Delirium was associated with increased daytime rest periods, suggesting PD participants had a more hypoactive presentation of delirium. These measures have potential utility in future clinical trials to determine improving delirium symptoms.
[1] van Hees VT, 2015, PLOS ONE, 10(11), p. e0142533.

P24.08

From research to home: Deployment of three web-based interventions types developed with people living with Parkinson disease and their caregivers in Quebec, Canada

Line Beaudet[1], Auriane Haegeman[2], Caroline Champeau[2], Dora Rodriguez[3], Marie-Neige Filteau[2], Renée Coulombe[1]*
[1] The University of Montreal Hospital Research Centre (CRCHUM), Montréal, Québec, Canada
[2] Parkinson Québec, Montréal, Québec, Canada
[3] The University of Montreal Hospital Research Centre (CRCHUM) and Parkinson Québec, Montréal, Québec, Canada

Background: Based on previous research works, as well as on the needs and preferences of people living with Parkinson disease (PWPD) and their caregivers (CA), three web-based interventions available 24/7, in French and in English, and offered free of charge, were deployed between 2021 and 2023 in Quebec, Canada. The first intervention, TAVIE in motion, offers 11 thematic sessions with a virtual nurse and experienced couples to better equip PWPD and CA to face the challenges associated with Parkinson's. The second intervention, Experts' advices, presents 8 capsules led by rehabilitation professionals including mentoring and specific exercises. The last intervention, Inspirational Testimonials, shares the experience, tips and tricks of 8 PWPD and CA recognized in the community for their empowerment.
Aim: Describe the three web interventions and their diffusion in the context of the COVID-19 pandemic, the strategies for optimizing the deployment as well as the evaluation of this process and its results based on users' perceptions.
Foundations: The web interventions are based on recognized methods to promote the satisfaction, self-efficacy and quality of life of PWPD and CA. The approach selected for this project allowes us to highlight the characteristics, place of origin, behaviors and perceptions of the users.
Results: So far, the results show that the pandemic, with its repercussions on PWPD, CA, audiovisual production firms and community organizations, has had an impact on the deployment of the web interventions. Positive interpersonal, technological and economic strategies have been implemented to reach the targeted users. Since the web interventions were gradually put online, preliminary results reveal that as of January 6, 2023, they had 31,171 unique visitors for the Experts' Advices, 11,112 for the Inspirational Testimonials and 923 for the TAVIE in motion program, 754 downloaded documents and a total of 58,341 views. Furthermore, the results reveal that the web interventions were viewed in 31 countries. Data collection is ongoing and additional available results will be presented.

Conclusion: This innovative project supports community organizations and health professionals interested in the development and deployment of web interventions in partnership with PWDP and CA.

P24.09

Video-assisted telenursing in patients with advanced Parkinson's disease treated with LCIG: Results from the Facilitate-Care study

Lars Bergmann[*,1], Tanya Gurevich[2], Andrew Evans[3], Georg Kägi[4], Dariusz Koziorowski[5], Juan Carlos Parra Riaza[6], Olga Sanchez-Soliño[6], Jaroslaw Slawek[7]*
[1] Abbvie, Ludwigshafen, Bavaria, Germany
[2] Movement Disorders Unit, Neurological Institute, Tel Aviv Sourasky Medical Center, Tel Aviv, Israel
[3] Royal Melbourne Hospital, Parkville, Australia
[4] Department of Neurology, Kantonsspital St. Gallen, St. Gallen, Switzerland
[5] Department of Neurology, Faculty of Health Science, Medical University of Warsaw, Warsaw, Poland
[6] AbbVie, North Chicago, United States
[7] Department of Neurological-Psychiatric Nursing, Faculty of Health Sciences, Medical University of Gdansk & Neurology and Stroke Department, St Adalbert Hospital, Gdansk, Poland

Introduction: A levodopa-carbidopa intestinal gel (LCIG) nurse support program provides education and troubleshooting for patients with advanced Parkinson's disease (aPD) treated with LCIG. Video-assisted telenursing may provide efficient resolution of issues and increase patient, caregiver, and physician satisfaction. The FACILITATE-CARE study assessed the feasibility and patient satisfaction of video-assisted telenursing in a real-world LCIG nurse support program (NCT04500106).
Methods: FACILITATE-CARE (Feasibility of video-Assisted Care for Intestinal Levodopa Infusion with Telenursing – observAtional Trial Evaluating patient and Caregiver Acceptance in REal life) was a multi-country, post-marketing, prospective, non-randomized, two-arm (audio and video), parallel-group study to evaluate patient, caregiver, and physician satisfaction of audio and video-assisted telenursing in the LCIG nurse support program. The primary endpoint was patient acceptance measured by satisfaction with the LCIG nurse support and communication access at week 12 (Visual Analog Scale [VAS] score from 1-10).
Results: Forty-one patients were enrolled, and the full analysis set included 39 patients (audio [n=15], video [n=24]). As the primary endpoint, mean patient VAS scores for satisfaction with nursing support and communication access at week 12 were 9.1 in the video arm and 9.3 in the audio arm. Mean patient and caregiver VAS scores for satisfaction with resolving issues using nursing support calls were similar, and physician satisfaction scores were aligned. Issues were resolved with remote education/guidance (video arm 60%, audio arm 49%), and remote troubleshooting (video arm 5%, audio arm 7%). Nurse support calls were on average longer in the video arm (71.6 mins vs 59.1 mins in the audio arm), but the mean total travel times by the nurse for unscheduled home visits during the 12-week study period were shorter in the video arm (126 mins vs 203 mins in the audio arm). Overall, most patients (86%) and caregivers (78%) would recommend the use of video conversations (VAS score 8-10). Safety events were consistent with the known LCIG profile.
Conclusion: Satisfaction with the nurse support program was very high and video-assisted telenursing resulted in high patient, caregiver, and physician satisfaction with the LCIG nurse support program.

P24.10

Digitised home-based care for people with Parkinson's disease

Katie Bounsall[*,1], Sue Whipps[2], John Whipps[2], Edward Meinert[3], Camille Carroll*[*,4]*
[1] University of Plymouth, Plymouth, United Kingdom
[2] Peninsula Excellence Network and Expert by Experience, Plymouth, United Kingdom
[3] Centre for Health Technology, School of Nursing and Midwifery, University of Plymouth; Department of Primary Care and Public Health, School of Public Health, Imperial College London; Harvard T.H. Chan School of Public Health, Harvard University., Plymouth, United Kingdom
[4] Peninsula Medical School, Faculty of Health, University of Plymouth; University Hospitals of Plymouth NHS Trust., Plymouth, United Kingdom

Background: Parkinsons's disease (PD) is the second most prevalent neurodegenerative disease worldwide. Complications can be serious, and symptoms negatively impact on quality of life for both the patient and care partner (CP). Working collaboratively with PwP and community teams, we have developed a new pathway that provides tailored self-management support with timely, triggered reviews, called Home Based Care (HBC). Digitisation of HBC will facilitate its capability to be used by other care networks, providing a potential model for the delivery of personalised, participatory and preventative care internationally.
Aim and Objective: We will conduct a pilot study of the enhanced digitised HBC (dHBC) pathway. The objectives are to assess uptake, engagement, feasibility, usability, and acceptability of dHBC.
Method: Mixed-methods incorporating quantitative measures coupled with qualitative evaluation of PwP, CP and healthcare professionals' (HCPs) experience will be used. Uptake and engagement will be assessed using rates of conversion and compliance with the digital platform/monitoring activities; usability will be assessed using the System Usability Scale. Feasibility will be assessed using process measures including waiting and administrative times, and staff hours. Semi-structured interviews will evaluate stakeholder perspectives of their experience with the pathway and explore themes of acceptability including reasons for decline or uptake failure, and usability including difficulty and perceived burden. 120 PwP enrolled on dHBC pathway and their CPs, and the associated HCPs will be invited to participate in the evaluation; 12-15 participants will be invited for interview. Rates of successful conversion to the digital pathway will be reported. Remaining quantitative data will be analysed using descriptive statistics. Qualitative data from system feedback will be examined using thematic analysis.
Results: Data collection is due to begin in late 2023. The results from this study will demonstrate if a digitised home-based care pathway is acceptable, feasible and usable by PwP, their care partners and HCPs.
Discussion: The findings of this study will inform further development, scaling and spread of dHBC, including its implementation in other organisations and with different populations, and whether the potential benefits for the patient, service and organisation can be realised.

P24.11

Evaluation of the Parkinson's Remote Interactive Monitoring System (PRIMS): Beta testing

Bronwyn Bridges[*,1], John Weber[1], Jake Taylor[2]*
[1] Memorial University of Newfoundland, St John's, NL, Canada
[2] University of Victoria, Victoria, British Columbia, Canada

The fastest-growing neurological disorder globally is Parkinson's Disease (PD), a progressive neurodegenerative disease that affects ten million people worldwide. PD is typically treated with Leva-Dopa: an oral pill is taken to increase dopamine levels and other dopaminergic agonists. However, as the disease progresses, the effects of the drug wane and adherence to this method are typically poor and do not provide meaningful information. Therefore, remote monitoring systems that can provide more detailed and accurate information about a patient's condition regularly are a valuable tool for clinicians and patients to manage their medication.
The Parkinson's Remote Interactive Monitoring System (PRIMS) developed by PragmaClin Research Inc. was designed to be an easy-to-use digital system that can accurately quantify motor and non-motor symptoms of PD remotely. PRIMS can engage with patients in real time and provide immediate, individualized results on a patient dashboard. The system can also be used by clinicians to oversee a patient's data. We released a beta version to 40 PwP to debug the system. From here, patients were monitored weekly and able to submit feedback on the system to improve development. This study was completed to finalize the software for Phase I clinical trials.

P24.12

Accelerating research on Parkinson's disease and empowering patients through digital health technologies

Yun-Hsuan Chang[*,1], Matt Wilson[1], Alastair J Noyce[2]*
[1] UMEDEOR LTD, London, United Kingdom
[2] Preventive Neurology Unit, Centre for Prevention, Detection and Diagnosis, Wolfson Institute of Population Health, Faculty of Medicine and Dentistry, Queen Mary University of London, London, United Kingdom

Parkinson's disease (PD) is a heterogeneous condition, both in terms of its clinical manifestations, progression and aetiological determinants. This calls for individualised treatment approaches and clinical trials that are designed to take account of the heterogeneity of PD. One of the key challenges faced by current PD studies is the difficulty in recruiting participants from diverse backgrounds that are truly representative of the PD spectrum. Limited ability to travel to trial sites due to physical disability, geographical distance, or financial constraints could further deter patients from participating in research studies. Access-PD is a fully remote, next-generation registry that is designed to tackle these challenges by incorporating digital solutions for identification and recruitment of patients, as well as collection of longitudinal data. Potential participants with a coded diagnosis of PD are identified using data held in primary care electronic health records (EHR) and engaged via a text message that takes them to a website for consent and registration. The process is simple and is supported by study nurses who act as the point of contact for any questions and issues related to participation. This approach ensures PD patients from different backgrounds can have equal opportunity to be invited to participate in the registry and those who are less familiar with remote research can be guided by a dedicated nurse. Once consented to the registry, participants are sent further questionnaires and home test kits (e.g. smell test kits) to collect additional data. By combining routinely collected EHR data with patient-reported outcome measures and home testing, Access-PD aims to create a comprehensive database that allows researchers to effectively stratify patients into meaningful subgroups, perform analysis and identify patterns that can guide the directions of future research, including trials. The pilot project has been well received by PD patients who feel empowered by an initiative that allows their voice to be heard. The first 100 participants were recruited within 2.5 months of launch which reflects enthusiasm from PD patients and confirms the feasibility of the Access-PD approach.

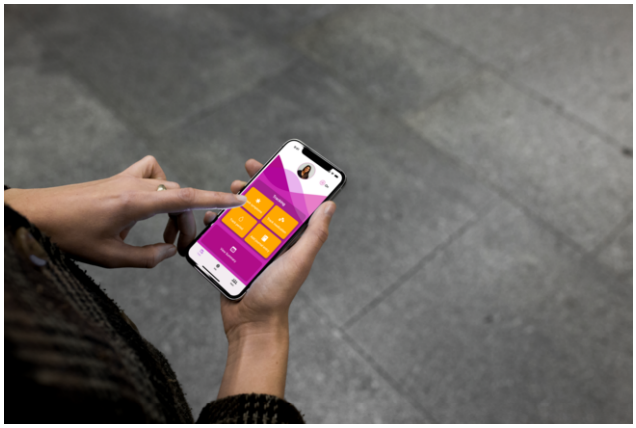
P24.14

Making my moves matter

*Richelle Flanagan**
My Moves Matter, Dublin, Dublin, Ireland

Aim: Development of an application for women with Parkinson's Disease (PD) that can track their symptom fluctuations in relation to their menstrual cycle, enabling clinicians to tailor their treatment and for women to better self-manage their symptoms to improve their quality of life.
Methods: As a woman living with Young Onset Parkinson's Disease (YOPD) and a health professional, I see the potential of technology to improve the lives of people living with PD. 4 million women are living with PD globallly with 20% (800,000) under 50 years. The motivation for this idea originated from a survey asking women with PD whether their symptoms fluctuated around their menstrual cycle. This survey showed that 81% of women reported worsening of their symptoms the week before their period and 51% the week of their period. Yet 95% reported that their neurologist had never adjusted their medications around their menstrual cycle.
I subsequently entered the Swiss based Day One patient centred digital health hackathon in November 2021.I set up a clinician focus group with 2 neurologists, 1 Specialist PD Nurse and a Gynaecologist and a patient focus group with five women with YOPD. An initial prototype was developed, and our project team won the hackathon. My Moves Matter was born.
Further research included women with PD workshops, in-depth interviews with 15 women of different ages and PD stages, in-depth interviews with 12 neurologists and a quantitative survey of 84 women. I applied for a feasibility grant in my local enterprise office in Ireland and also received funding through an Enterprise Ireland backed 6 month full time accelerator programme. These funds have enabled me to set up My Moves Matter to develop a self-care companion for women with PD based upon this women centred research.
One core element of the feedback has led to the development of a 'neuroaccessible' interface to facilitate women to log their symptoms when they are the most disabling, through voice navigation, voice and video logging and large button interfaces.

Conclusion: We are currently developing and testing the minimal viable product with women with PD, aiming to launch the beta version at WPC Barcelona 2023.



P24.15

Digital mobility outcomes derived from different wearable sensors and their link to clinically relevant scores in Parkinson's disease

Heiko Gassner[*,1], Sarah Seifferth[1], Teresa Greinwalder[1], Sabine Stallforth[1], Jelena Jukic[1], Patrick Süß[1], Alexander German[1], Franz Marxreiter[1], Martin Regensburger[1], Jochen Klucken[1], Alison Yarnall[2], Clemens Becker[3], Walter Mätzler[4], Lynn Rochester[2], Jürgen Winkler[1]*
[1] University Hospital Erlangen, Erlangen, Germany
[2] Newcastle University, Newcastle upon Tyne, United Kingdom
[3] Robert-Bosch-Krankenhaus Stuttgart, Stuttgart, Germany
[4] Christian-Albrechts-Universität zu Kiel, Kiel, Germany

Background: Parkinson's disease (PD) is characterised by gait impairment leading to loss of mobility and reduced quality of life [1]. Digital mobility outcomes (DMO) are considered to provide objective metrics of mobility collected in the hospital and real-life of patients. However, there is still a lack of robust, evidence-based anchors between DMOs and clinically relevant scores [2]. In terms of usability, it is not clear yet on which portion of the body wearable sensors should be placed in order to gain most relevant clinical outcomes with easy-to-apply systems that minimise the burden of patients.
Objective: Compare and clinically evaluate DMOs derived from two different sets of inertial sensors placed (1) on the shoes or (2) at the lower back (L5) of participants with PD.
Methods: For this purpose, during the Clinical Validation Study within the EU project "Mobilise-D" (https://www.mobilise-d.eu/), PD patients were instructed to perform standardised gait tests, e.g. 6-Min walk test in the hospital while wearing a hip-sensor, as per protocol, and two additional shoe sensors. The hip-sensor MoveTest® provided by McRoberts is an inertial measurement unit which is worn in a belt around the waist. The two shoe sensors on the other hand belong to the Mobile GaitLab System provided by Portabiles HealthCare Technologies. DMOs were correlated to established clinical scores such as the Unified Parkinson's Disease Rating Scale (MDS UPDRS-III), Falls Efficacy Scale, retrospective falls, and Montreal Cognitive Assessment.
Results: 130 individuals with PD in early to moderate disease stages (H&Y 1-3) were included in this study at the University Hospital Erlangen, Germany. Age (mean +/- SD 64,5 ± 8,6 years), gender (male/female: 89 / 41, Ratio 2:1), BMI (27,6 ± 4,7 kg/m2), MDS-UPDRS-III (19,9 ± 9,8 points), Montreal Cognitive Assessment, MoCA (26,4 ± 3,3 points), and walking distance in 6 Min (446,3 ± 98,7 m) are representative for a German PD cohort.
Conclusions: We correlate DMOs of two different sensor systems with established clinical scores in PD in order to detect most relevant digital parameters that may be used in future clinical trials. Additionally, usability aspects of both sensor systems are provided.
[1] Debu et al.2018
[2] Polhemus et al.2021

P24.16

Validation of mobility biomarkers in the assessment of Parkinsonian bradykinesia: Experience from a large real world data set

*Tiffany Jansen, Aiden Arnold, Witney Chen, Ro'ee Gilron**
Rune Labs, San Francsico, CA, United States

Sensors that detect various aspects of mobility are now widely available. Many smartwatches and smartphones provide not just the number of steps taken per day, but also other important mobility details such as walking speed and stability.
This study evaluates the performance of commercially available mobility algorithms in predicting Parkinsonian bradykinesia as measured by clinical labels such as MDS-UPDRS-III, without specific optimization for impaired gait. Previous studies that used inertial measurements to compute bradykinesia often relied on proprietary algorithms or devices worn for limited periods of time.
There are several benefits to using commonly available existing algorithms for assessing bradykinesia. One advantage is that many people have access to smartphones and smartwatches that can collect these metrics. Additionally, numerous initiatives are currently searching for early indicators of Parkinson's disease. Moreover, measuring the severity of bradykinesia during daily activities over an extended period is helpful in clinical trials and patient management, as bradykinesia is a key symptom of Parkinson's disease.
For algorithm validation we used the PPMI dataset which consisted of hourly estimates of patients' step count and amount of time walking per day paired to MDS-UPDRS-III bradykinesia scores. We evaluated the performance of state of the art machine learning algorithms such as LSTM (long short term memory) networks. Algorithm performance was evaluated using a leave-one-patient-out strategy as well as a separate validation set from another device.
This study may serve as a benchmark for future research into identifying early stages of Parkinson's and monitoring progression in naturalistic study populations.

P24.17

Usability and acceptability of a cognitive training application in Parkinson's

Julia Das[1], Gill Barry[1], Rodrigo Vitório[1], Lisa Graham[1], Claire McDonald[2], Brony Storey[2], Richard Walker[3], Samuel Stuart[1], Rosie Morris[1]*
[1] Northumbria University, Newcastle upon Tyne, United Kingdom
[2] Gateshead Health NHS Foundation Trust, Gateshead, United Kingdom
[3] Northumbria Healthcare NHS Foundation Trust, North Tyneside, United Kingdom

Background: Cognitive impairment is a common non-motor feature of Parkinson's disease (PD). Mobile applications delivering multidomain cognitive rehabilitation offer a potential means of delaying the worsening of cognitive deficits, but evidence for their feasibility of implementation in people with PD is limited.
Aim: This pilot study evaluated the acceptability and usability of a specific mobile application (Senaptec App) delivering cognitive

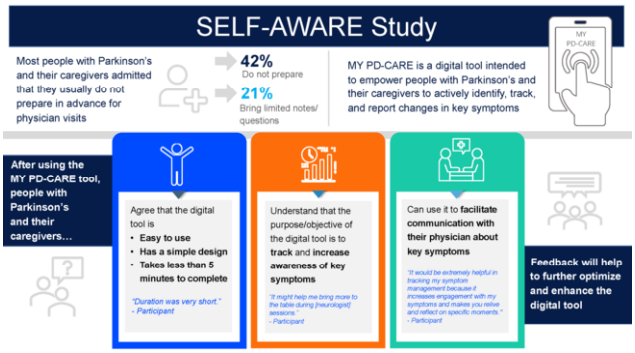
training drills as part of a visuo-cognitive training intervention for people with PD.
Methods: People with mild-moderate PD (H&Y 1-3) were included in the study. Participants used the application, downloaded on an iPad, at home with therapy supervision (two training sessions lasting 20-30 min/week for four weeks). The usability of the application was assessed with the System Usability Scale (SUS) after initial use and then again at the end of the intervention period. To supplement the SUS, acceptability and usability of the application was explored through semi-structured interviews.
Results: Twenty people with PD (15 male, 5 female; mean age 69.4±8.8 years; mean disease duration 6.7±6.0 years; mean MoCA score 26.6±2.6 points) were included in the study. After one use of the app, the mean score for the SUS (SUS; 0–100 range, higher scores indicating better performance) was 80.5±18 points (indicating "good" usability). After 4 weeks of use, the mean SUS was 88.6±11.3 points (indicating "excellent" usability). The SUS score at the end of the study was significantly higher than at baseline (P-value <0.001). Data from the interviews supported findings from the SUS, indicating that participants found the majority of drills "enjoyable" and "challenging". Participants were motivated by improvements in scores and the immediacy of feedback provided. By the end of the intervention, participants felt confident to use the app independently.
Conclusion: In our sample, the Senaptec App was deemed to have excellent usability after repeated use by people with PD. While this study does not provide efficacy data, it does suggest that cognitive training delivered by the Senaptec App is acceptable and feasible for use at home by people with PD. Further work is required to determine whether regular training with the Senaptec App can delay the progression of cognitive deficits in people with PD.

P24.18

Investigating usability, understandability, and acceptance of the MY PD-CARE digital tool for tracking and communicating symptoms of Parkinson's: The self-aware study

Angelo Antonini[1], Tove Henriksen[2], Amelia Hursey[,3], Lars Bergmann[4], Juan Carlos Parra[4], Per Odin[5]*
[1] Parkinson and Movement Disorders Unit, Center for Neurodegenerative Diseases CESNE, Department of Neuroscience, University of Padova, Padova, Italy
[2] Movement Disorder Clinic, University Hospital of Dispebjerg, Copenhagen, Denmark
[3] Parkinson's Europe, London, United Kingdom
[4] AbbVie Inc., North Chicago, Illinois, United States
[5] Division of Neurology, Department of Clinical Sciences, Lund University, Skane University Hospital, Lund, Sweden

Introduction: MY PD-CARE is a digital tool intended to empower people with Parkinson's and their caregivers to actively identify, track, and report changes in key symptoms and to facilitate discussions with physicians. MY PD-CARE was adapted from MANAGE-PD, a validated web-based tool to assist physicians to identify patients with inadequate symptom control. This study investigated if the MY PD-CARE tool was easy to use, understandable, and acceptable from the perspective of people with Parkinson's and their caregivers.
Methods: SELF-AWARE (Study on Ethnographic research and human factors evaLuation For a tool to increase AWareness, self-Assessment and Reporting of PD patiEnts uncontrolled on oral medication) enrolled people with Parkinson's (n=43) and their caregivers (n=31). MY PD-CARE was assessed during one-time virtual interviews conducted by ethnographic researchers using qualitative ethnographic and human factors evaluation methods.
Results: In 91% of people with Parkinson's and caregiver pairs, at least 1 individual was comfortable with using technology across multiple devices. Most people with Parkinson's and caregivers admitted that they usually do not prepare in advance for physician visits; 42% do not prepare and 21% bring limited notes/questions. Most participants understood that the purpose/objective of MY PD-CARE is to increase awareness of key symptoms, help track symptoms, and facilitate communication with physicians (Figure). Participants agreed that the MY PD-CARE tool is easy to use and has a simple design; it took 1–5 minutes to complete on the first try. Many participants found the medical terminology in MY PD-CARE not fully self-explanatory; however, half of the participants found the glossary helpful. Many (60%) participants indicated MY PD-CARE may have even more value if it allowed free text input and asked additional questions. Participants agreed that MY PD-CARE would be a useful tool to track symptoms and encourage discussions with physicians.
Conclusions: Interviews with people with Parkinson's and their caregivers found that the MY PD-CARE tool is generally useful and acceptable for increasing symptom awareness, tracking symptoms, and facilitating discussions with physicians. Structured feedback from people with Parkinson's and their caregivers will help to further optimize and enhance the MY PD-CARE digital tool.



P24.19

Mobilising patient and public involvement in the development of real-world digital technology solutions: Lessons learned from the Mobilise-D consortium

Alison Keogh[1], Riona McArdle[2], Mara Diaconu[3], Nadir Ammour[4], Valdo Arnera[5], Federica Balzani[6], Sara Buttery[7], Alma Cantu[2], Solange Corriol-Rohou[8], Laura Delgado-Ortiz[9], Jacques Duysens[6], Tova Gur-Arieh[6], Dominique Hamerelijnck[6], John Linnell[6], Leitizia Leocani[10], Tom McQuillan[6], Isabel Neatrour[2], Ashley Polhemus[11], Werner Remmele[6], Isabel Saraiva[6], Kirsty Scott[12], Norman Sutton[6], Koen Van den Brande[6], Beatrix Vereijken[3], Lynn Rochester[,2]*
[1] Insight Centre for Data Analytics, Dublin, Ireland
[2] Newcastle University, Newcastle, United Kingdom
[3] Norwegian University of Science and Technology, Trondheim, Norway
[4] Sanofi, Chilly-Mazarin, France
[5] Clario, Geneva, Switzerland
[6] Mobilise-D Patient and Public Advisory Group, Newcastle, United Kingdom
[7] Imperial College London, London, United Kingdom
[8] AstraZeneca, Paris, France
[9] IS Global, Barcelona, Spain
[10] San Raffele University, Milan, Italy
[11] University of Zurich, Zurich, Switzerland
[12] Sheffield University, Sheffield, United Kingdom

Mobility is an important indicator of physical health for people with various chronic conditions, including Parkinson's disease. As such there is potential clinical value in being able to measure mobility

accurately in a person's home and daily life environment to help researchers and clinicians to better track changes and patterns in a person's daily lives and activities. To do this, there is a need to create new ways of measuring walking. Recent advancements in digital technology are helping researchers to do this. However, before any new measure can be used, researchers, healthcare professionals and regulators need to know that the digital method is accurate and that it is both accepted and produces meaningful outcomes for the patients and clinicians. Researchers must therefore include patients, or members of patient organisations, in the development of such new tools in a process known as patient and public involvement and engagement (PPIE). Although the value and importance of PPIE activities is well-known, little guidance exists on how to do this in a meaningful way. This is particularly true within large research consortia that target multiple objectives, include multiple patient groups and work across many countries. Without clear guidance, the risk is that PPIE does not capture patient opinions and needs correctly, thereby reducing the usefulness and effectiveness of new tools. Mobilise-D is an example of such a large research consortium, that is looking to develop new digital outcome measures for real-world walking in patients with Parkinson's Disease, Multiple Sclerosis, Chronic Obstructive Pulmonary Disease, and Proximal Femoral Fracture. This abstract will outline the learnings derived from the work undertaken to establish meaningful PPIE structures within the consortium from the perspective of both the researchers and the patient advisors involved, specifically those with Parkinson's. Thus, it provides guidance around the work required to set up PPIE structures within a large consortium, to promote and support the creation of meaningful and efficient PPIE related to the development of digital mobility outcomes.

P24.20

Individualized smartphone-based exercise as a telemedical approach to reduce motor symptoms in Parkinson's disease

Lisa Lützow[*,1], Isabelle Teckenburg[1], Veronica Koch[2], Martin Regensburger[1], Franz Marxreiter[1], Jelena Jukic[1], Sabine Stallforth[1], Jürgen Winkler[1], Jochen Klucken[1], Heiko Gaßner[2]*

[1] Department of Molecular Neurology, University Hospital Erlangen, Friedrich-Alexander University Erlangen-Nürnberg (FAU), Erlangen, Germany

[2] Fraunhofer Institute for Integrated Circuits IIS, Erlangen, Germany

Background: Exercise therapy is considered effective for the treatment of motor impairment in patients with Parkinson's disease (PD). During the COVID-19 pandemic, training sessions were cancelled and the implementation of telerehabilitation concepts became a promising solution. The aim of this controlled interventional feasibility study was to evaluate the long-term acceptance and effects of a digital, home-based, high-frequency exercise program for PD patients. Training effects were assessed using patient-reported outcome measures combined with sensor-based and clinical scores.

Methods: 16 PD patients (smartphone group, SG) completed a home-based, individualized training program over 6 to 8 months using a smartphone app, remotely supervised by a therapist, and tailored to the patient's motor impairments and capacity. A control group (CG) received medical treatment without participating in digital exercise training. The usability of the app was validated using System Usability Scale (SUS) and User Version of the Mobile Application Rating Scale (uMARS). Outcome measures included among others Unified Parkinson Disease Rating Scale, part III (UPDRS-III), sensor-based gait parameters derived from standardized gait tests, Parkinson's Disease Questionnaire (PDQ-39), and patient-reported motor activities of daily life (M-ADL).

Results: Exercise frequency of 74.5% demonstrated high adherence in this cohort. The application obtained 84% in SUS and more than 3.5/5 points in each subcategory of uMARS, indicating excellent usability. The individually assessed additional benefit showed at least 6 out of 10 points (Mean=8.2±1.3). From a clinical perspective, patient-defined M-ADL improved for 10 out of 16 patients by 16% after the training period. The results of the UPDRS-III remained stable in the SG while worsening in the CG by 3.1 points (25%). The PDQ-39 score worsened over 6-8 months by 83% (SG) and 64% (CG) but the subsection mobility showed a smaller decline in the SG (3%) compared to the CG (43%) without reaching significance level for all outcomes. Sensor-based gait parameters remained constant in both groups.

Conclusions: Long-term training over 6-8 months with the app is considered feasible and acceptable, representing a cost-effective, individualized approach to complement dopaminergic treatment. This study indicates that personalized, digital, high-frequency training leads to benefits in motor sections of ADL and Quality of Life.

P24.21

Integration of a conversational agent in a mHealth solution to increase exercise adherence in Parkinson's disease

Patricia Macedo*, Pedro Mota, Ana Beatriz Rebola, Rui Neves Madeira, Carla Pereira

Instituto Politecnico de Setúbal, Setúbal, Setúbal, Portugal

Introduction: Mobile health (mHealth) apps to promote the exercise of people with Parkinson's Disease (PwP) have been emerging in recent years. However, adhering to the exercise practice on a regular basis to maximize benefits is challenging for this population. Recent studies have shown the potential benefits of integrating conversational agents in mHealth apps. Therefore, a conversational agent was developed according to key factors: empathic responses according to the user's state of mind, tailored content, information on goals status, and goals to achieve. Studying the viability of using this agent to guide and motivate PwP to exercise was important.

Methods: A study to evaluate the technical performance and the user experience of the conversational agent was conducted with physiotherapists and PwP, respectively. The technical performance consisted of tests to assess Domain Coverage, Coherence Response Capacity, and Dialogue Management Capacity. For usability tests, participants followed a protocol with pre-defined tasks, in a controlled one-day environment. They responded to a questionnaire (metrics included were Speech Recognition, Information Quality, Ease of Use, Perception of Usefulness, and Interaction Satisfaction) based on 5-Likert scale statements (1-totally disagree; 5-totally agree).

Results: Three physiotherapists (mean age: 34.0+15.7; mean experience years: 6.3+5.1) participated in the performance tests. Domain Coverage and Coherence Response indicators obtained a score of 100%, while Dialogue Management Capacity scored 87%. The usability tests were conducted with eight PwP (mean age=69.2+10.7; 7 male; Mean H&Y=2.0±0.76), who gave high scores to the metrics being evaluated. Two participants evaluated the solution with an average score of 4.9, two with 4.8, and four with 4.2. The metrics with the worst scores have been information quality and speech recognition. The latter was expected since it can be challenging for PwP because the disease can cause speech and voice changes, which can make it difficult for the technology to understand and transcribe their speech accurately.

Conclusions: Using a conversational agent to support and motivate exercise in PwP is viable and promising. The preliminary study with PwP indicates they consider it an added value. However, a thorough study is essential to investigate its effectiveness in increasing exercise adherence and self-management.

P24.22

Suppocial – Connect. Support. Inspire

*Blake Mackey**
Suppocial Inc., Bradford, Ontario, Canada

Do we truly grasp how critical the importance of being social and having a strong support system is ?
It can make a significant difference in the quality of life and in our ability to persevere. Socializing and connecting with others has a proven positive impact on mental and physical health. Life presents many challenges and obstacles that we need to overcome but there is one condition we can all relate to. The human condition. There is so much common ground between us, no matter the specifics of our personal "story". We all feel the same emotions throughout life and experience them in our own way. We can get overwhelmed and struggle to deal with them, especially in the absence of guidance/support. We have often heard or spoken the words "I feel better just knowing that I'm not alone". A powerful statement indeed. Unfortunately, a kind of stigma has been associated with support groups over the years. Fear itself, such as public speaking, one of the highest rated fears and even vulnerability can prevent people from benefiting from what they are designed to do. Bring people together, show them they're not alone, connect and support each other. The pandemic has not helped this. It has caused us to further isolate from each other.
Suppocial is a brand new way to experience all the benefits of the support group and more. Using the technology of today, we've modernized support by putting it at your fingertips, anywhere and anytime. Our mission, to unlock the power of the support group by making it accessible and relatable to everyone.
The user can customize their support to their unique needs, allowing them to connect on their own terms. Suppocial will bridge the gap between the different communities and also include care partners in the conversation to create a support network where there is currently little to no structure at all. Links to resources, educational information, posts about trials which helps further research and the list goes on.
It will cut through the fog, in a time where uncertainty and confusion can be overwhelming and allow us to find each other.

P24.23

Development of an evaluation framework for digitally enabled integrated care: Connected care PD

Ivana Paccoud*[,1], Liyousew Borga[1], Joëlle V. Fritz[1], Jochen Klucken[2]
[1] Luxembourg Institute of Health, Luxembourg, Luxembourg
[2] University of Luxembourg, Luxembourg, Luxembourg

Background: Digital health is increasingly recognized as a major driver of quality in healthcare by offering scalable tools to improve health, healthcare delivery, as well as supporting integrated care networks. Digitalisation in medicine also generates a large volume of real-world healthcare data that offers the potential for new ways of measuring health and consequently providing personalised care and precision medicine. However, the wider implementation of digitally enabled integrated care models depends on the provision of credible evidence on their health effectiveness, cost-effectiveness and the adoption of digital technologies by patients and healthcare professionals. Thus, in this study we outline an evaluation framework by providing a standard set of indicators that incorporate both medical and socioeconomic dimensions along a patient's journey. We use the Connected Care PD (Parkinson Disease) programme in Luxembourg as a case study of an integrated and multidisciplinary environment where currently digital solutions are being implemented in order to monitor and evaluate patient health and healthcare performance.
Methods: To arrive at this first set of standardized and patient-centred indicators, we first looked at the established set of guidelines and standards in the literature. Next, we used a consensus driven method by engaging different experts from the Parkinson disease field such as health professionals and academics from different backgrounds (medicine, social science and health economics). Patients' voices will also be included in defining the final set of outcomes.
Results: We provide a comprehensive list of medical and socioeconomic indicators that can be used to monitor healthcare quality for people with Parkinson disease, identify potential sources, and highlight current challenges in the healthcare system that impede the integrated collection of healthcare data. We recommend practical ways of designing efficient and timely ways of collecting healthcare data through an integrated system of healthcare claims-based data, electronic health records and patient relevant outcomes (PROMs/PREMs). In the future these sources could be supplemented by wearable devices and patient apps. Such integrated data sources based on real world data are vital for identifying the delivery of precision health and evaluating digitally enabled healthcare interventions.

P24.24

Compliance and satisfaction of Parkinson's disease patients from a pilot smart devices-enabled study

Nikolaos Papagiannakis[,1], Anastasia Bougea[1], Athina-Maria Simitsi[1], Elpida Panagiotounakou[1], Chrysa Chrysovitsanou[1], Minas Badounas[2], Ioannis Ladakis[2], Hara Stefanou[2], Panos Tsakanikas[3], Christos Koros[1], Leonidas Stefanis[1]*
[1] National and Kapodistrian University of Athens, Athens, Greece
[2] Wellics Ltd, Athens, Greece
[3] National Technical University of Athens, Athens, Greece

Background: The ALAMEDA study is a European Union funded project (https://alamedaproject.eu/). Its aim is to bridge the early diagnosis and treatment gap of brain diseases, including Parkinson's Disease (PD), via Smart Technological Interventions. PD patients were fitted with a smart watch and provided with a smartphone with a preinstalled customized application with questionnaires to answer daily, weekly or monthly. Questionnaires pertained to motor complications, emotional state, overall level of activity, dietary habits and degree of social interaction.
Objectives: To assess the overall compliance and satisfaction of the enrolled patients.
Methods: Fifteen patients were enrolled. A questionnaire with twenty-nine likert questions (scored 0-4) about patient satisfaction with the overall project and with the specific devices used was administered to all participants.
Results: In total, fourteen patients completed the satisfaction questionnaires. The average overall satisfaction score was 3 out of 4. Participants believed the accompanying app and smart devices were easy to use (3.2) and unobtrusive (3.5). No difficulties were reported with the smart device except occasional disconnections, and they considered the app easy to use (3.1). Most patients had problems with responding in the appropriate time to the daily questionnaires and considered the number of questions jarring. Additionally, although the app was interactive, the patients expressed the need for more regular and easy to follow feedback (2.7). More than 800 questionnaires were completed in the first six months of the study.

Conclusions: Tracking symptoms and quality of life through specialized apps with the use of smart sensors is an easy, feasible and unobtrusive way of monitoring PD patients. A balance must be sought to obtain sufficient information without overburdening patients with chronic brain diseases.

P24.25

Alameda study protocol: Bridging the early diagnosis and treatment gap of brain diseases via smart, connected, proactive and evidence-based technological interventions for Parkinson's disease

Nikolaos Papagiannakis[*,1], Anastasia Bougea[1], Athina-Maria Simitsi[1], Elpida Panagiotounakou[1], Kostas Lourentzos[1], Chrysa Chrisovitsanou[1], Christos Koros[1], Panagiotis Kokotis[1], Constantin Potagas[1], Anastasios Bonakis[1], Alexandru Sorici[2], Minas Badounas[3], Hara Stefanou[3], Sofia Segkouli[4], Christoniki Manga-Nteve[5], Nikos Tsolakis[5], Stefanos Vrochidis[5], Iphigenia Kapsomenaki[6], George Koutalieris[6], AdaneNega Tarekegn[7], Muhammad Sajjad[7], Faouzi Alaya Cheick[7], Konstantina Giannakopoulou[8], Panos Tsakanikas[8], Leonidas Stefanis[1]*
[1] National and Kapodistrian University of Athens, Athens, Greece
[2] University Politehnica of Bucharest, Bucharest, Greece
[3] Wellics Ltd, Athens, Greece
[4] Information Technologies Institute, Centre of Research & Technology, Thessaloniki, Greece
[5] Information Technologies Institute, Centre of Research & Technology, Athens, Greece
[6] ENORA, Athens, Greece
[7] Norwegian University of Science and Technology, Trondheim, Norway
[8] Institute of Communication and Computer Systems, Athens, Greece

ALAMEDA is a collaborative project of the European Research and Innovation Program Horizon 2020 (alamedaproject.eu/). Its aim is to create the next generation of personalized systems for monitoring people with Parkinson's Disease (PD), Multiple Sclerosis (MS) or Stroke. Advanced PD in particular requires monitoring of motor and non-motor symptoms and frequent changes in treatment approach.As part of ALAMEDA, the PD Pilot Study will enroll 15 patients with advanced PD, followed at the relevant Specialty Outpatient Clinic at the First Department of Neurology of the National and Kapodistrian University of Athens (NKUA), at Eginitio Hospital, between June 2022 and September 2023.Data collection will include: (i) a continuously running process of Patient Reported Outcome (PRO) submissions through daily, weekly or monthly digital questionnaires or scales set up in a mobile application (informing on motor complications, emotional state, overall level of activity, dietary habits and degree of social interaction) and use of a smartwatch to obtain digital information on daily activities, (ii) sets of one to two-week more intense monitoring periods at 3-month intervals, with minimally intrusive wearable devices (accelerometer bracelet, IMU sensor belt, ground force measuring insoles, sleep mattress), and (iii) Trimonthly in-person examinations with a full battery of questionnaires and scales for motor and non-motor aspects of the disease, including tablet-based tests for cognitive function (Virtual Super Market and Line Tracking test). Polysomnography and Autonomic Function Testing will also be performed to obtain objective measurements of sleep and autonomic function. The aim of the study is to identify digital variables that alone or in combination may predict disease progression at the end of the study, as defined by deterioration in the in-person evaluations at the end compared to the beginning of the study. Data analysis will be performed by novel Machine Learning algorithms. The design of the study, including its duration and intensity, and the degree of tolerance and acceptability of the sensors, was discussed with the stakeholders and study implementation took their suggestions into account.ALAMEDA highlights the importance of new technologies and algorithms in monitoring of neurological patients, in particular aiming to inform future efforts to improve long-term management of advanced PD.

P24.27

MoveONParkinson: Development of an innovative motivational solution for personalized exercise through the ONParkinson platform

Carla Pereira, Ana Beatriz Rebola, Daniela Sineiro, Pedro Alburquerque Santos, Ricardo Carmo, João Carreira, Patricia Macedo, Rui Neves Madeira*
Instituto Politécnico de Setúbal, Setúbal, Portugal

Introduction: The ONParkinson solution is a platform comprising mobile and web interfaces, which resulted from a previous survey undertaken on people with Parkinson's Disease (PwP), informal carers and healthcare professionals. The mobile app aims to increase PwP and carers' self-management skills, with a prototype showing high acceptance from potential end-users. MoveONParkinson project aimed to improve and evaluate the exercises module of the platform in order to promote long-term exercise adherence.
Methods: The development of the ONParkinson solution was based on the IDEAS framework for developing effective digital health behaviour change interventions. The second stage comprises an iterative design process based on the insights provided. This study aimed to gather feedback on the mobile app and evaluate the Web platform's usability, following a concurrent mixed methods study, with quantitative (System Usability Scale (SUS)) and qualitative (thinking aloud method and semi-structured interviews) data. A purposive sample comprised of PwP and physiotherapists was used. All participants gave informed consent in the study approved by the ethical committee [76/CC/2021].
Results: The study included 28 participants, with 20 physiotherapists (mean age= 34.5±10.47; mean years experience= 10.7±9.17) and 8 PwP (mean age= 65.75±8.63; average years since diagnosis= 11.63±6.8; mean H&Y= 2.0±0.76). Physiotherapists assessed the web platform's usability as "good" (mean SUS= 79.50 ± 12.40), considering it is a valuable resource for working on telerehabilitation and exercise prescription for PwP, with suitable exercises to be performed at home without supervision. Some recommendations were identified, including the importance of export and print exercise programs in case patients do not have access to the app or prefer paper. From the perspective of PwP the mobile app may be a valuable resource to promote exercise practice in their daily routines, whether to perform alone or with supervision. They found it easy to understand and follow instructions. Participants reported being interested in using the app when available.
Conclusion: Potential end-users' feedback and SUS score indicate that the platform is perceived as acceptable for telerehabilitation, including providing exercise programs and performance feedback through PwP data provided by the mobile app. These results are encouraging and make ground for the effectiveness study.

P24.28

Stepping outside the clinic: Gait detection using wrist-worn sensors for remote arm swing analysis in Parkinson's disease

Erik Post[*1], Twan Van Laarhoven[2], Yordan Raykov[3], Max Little[4], Peter Kok[5], Pablo Rodríguez-Sánchez[5], Tom Heskes[2], Bastiaan Bloem[6], Luc Evers[6]*
[1] RadboudUMC, Nijmegen, Netherlands
[2] Institute for Computing and Information Sciences, Radboud University, Nijmegen, Netherlands
[3] University of Nottingham, Nottingham, United Kingdom
[4] University of Birmingham, Birmingham, United Kingdom
[5] Netherlands eScience Center, Amsterdam, Netherlands
[6] Center for Expertise for Parkinson and Movement Disorders, department of Neurology, Donders Institute for Brain, Cognition and Behaviour, Radboud University Medical Center, Nijmegen, Netherlands

Objective: To assess the ability to discern gait reliably from other activities using wrist-worn sensors in unconstrained environments, as a prerequisite for subsequent free-living arm swing analysis in patients with Parkinson's disease (PD).
Methods: In the Parkinson@Home validation study, including 25 individuals with PD and 25 age-matched healthy controls (HC), participants wore the Physilog 4 on each wrist for at least one hour before and after the intake of dopaminergic medication, while conducting unscripted activities in and around their home environment. Here, we focus on the accelerometer and gyroscope signals of the most affected side for the PD group and a similar dominant vs non-dominant side distribution for the HC group. Manual video annotations for the presence of gait and other activities were used as ground truth labels. Effects of gravity were filtered using a 4th order 0.3 Hz cutoff high-pass Butterworth filter, after which the following features were extracted from 6-second Hann windows with 5 seconds overlap: standard deviation of the Euclidean norm, dominant frequency in each of the three axes, total power in prespecified frequency bands (0.3 to 0.7, 0.7 to 3.5 and 3.5 to 8 Hz), cepstral coefficients, and the mean of the gravitational component for each axis as a proxy for arm position. Using leave-one-subject-out nested cross-validation, we assessed gait detection performance of logistic LASSO regression and random forest for the PD pre-medication, PD post-medication, and HC populations.
Results: The mean [± standard deviation] across folds of the area under the receiver operating curve (AUC) of the logistic LASSO regression was 0.95 [± 0.07] for PD pre-medication, 0.96 [± 0.06] for PD post-medication, and 0.97 [± 0.02] for HC. The random forest classifier resulted in minimal improvements with AUCs of 0.96 [± 0.04] for PD pre-medication, 0.97 [± 0.03] for PD post-medication, and 0.97 [± 0.02] for HC.
Conclusions: The results show that free-living gait of PD patients can be detected reliably using wrist-worn sensor devices, independent of motor state. This paves the way for longitudinal free-living arm swing analysis, which is a promising strategy to unobtrusively monitor PD progression in daily life.

P24.30

A system for measuring akinesia via handheld momentum sensors

*Venkateshwarla Rama Raju**
CMR College of Engineering & Technology, jawaharlal Nehru Tehnological University, Hyderabad, Telangana, India

Background: The human-wearable-sensors plus sophisticated algorithmic-techniques might offer substantial decision-support in clinical-procedures. Mostly, the features of Parkinson`s often examined visually and estimated, that might result around and individual computation.
Objective: To apply tiny inertial—wearable-sensors, monotonous and prognostically significant activities/movements can be obtained also assessed scientifically-objectively for scientific-objective evidence as.
Methods: A different method is devised for scientific-objective estimation computationally and pointing bradykinesia automatically in monotonous and rhythmic finger-tapping-movements/actions and activities in subjects thru advanced-idiopathic Parkinson's disease (PD) plus different-parkinsonism's in this study. Our method consists of some easy but elegant also echo signal-analysis methods and processing-techniques and imaging modalities which are employed to extrapolate vital features of Parkinson movement. The system comprises easy but elegant procedures aimed to meet commonly defined principles that are assessed in clinical-procedures.
Results: Precision of proposed-system is simulated and evaluated depending on the source-scores given by the expert-neuro-physicians. The system attained the precision of 88.7 % for records-on that the neuro physiologists approved by their-scores. The introduced system is simple, repeatable, easy to implement, and can provide good assistance in clinical practice, providing a detailed analysis of finger-tapping performance and decision support for symptom evaluation.
Conclusions: Our system-study is objective, which can be employed as an aid-tool sturdily in clinical procedures for finding the symptoms-simplicity, checking the progression of disease and a Parkinson's reaction to treatment, plus disparities among new subjects(patients). An instinctive and insightful user-interface for an application-software - custom-built programmes can be built to give a graphical-visual performance, statistical-outcomes for feature-manifestations, scores, sub scores, plus simulation and clinico—statistical inferences. Extension involves diagnosing with tests applied to measure akinesia(bradykinesia) plus other motoric symptoms. We will propose a system of measurement to be applied for other effective disparity-diagnostics-of standard unusual Parkinsonism's.
Keywords: decision-support-system devices; human-wearable inertial-sensors; fingers-tapping`s; automatic-online-scoring; Parkinson's disease; unusual Parkinsonism's.

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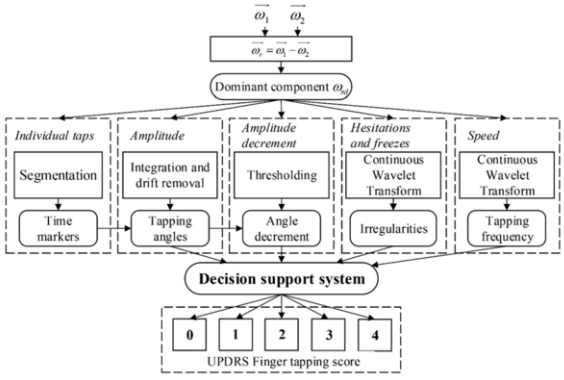


Figure 1. A pictorial representation of the of the system for the U.P.D.R. Scaling finger-tapping scoring computation.

P24.31

Consultation preparation: A pilot study to improve Parkinson's disease patients' perception of their doctor visit

Laura Carrasco[1], Damaris Alvarez[1], Manuel Perez[1], Chiara Capra[2], Daniel Rodriguez-Martin[,2], Marina Mata[3], Monica M. Kurtis[4], Carmen Borrue[3], Lydia Lopez-Manzanares[5]*
[1] Asociación Parkinson Madrid, Madrid, Spain
[2] Sense4Care, Cornella Llobregat, Spain
[3] Hospital Universitario Infanta Sofía, San Sebastián de los Reyes, Spain
[4] Hospital Ruber Internacional, Madrid, Spain
[5] Hospital Universitario La Princesa, Madrid, Spain

Many Parkinson's disease (PD) patients often suffer from stress and anxiety during the consultation with their neurologist and cannot describe their symptoms accurately. In turn, physicians have to quickly evaluate patients' conditions on the spot. Thus, clinical history can be confusing, leading to unsatisfying treatment adjustments from the patients' perspective. A need to improve the patient's consultation experience was identified by various PD patient associations in Spain and a Consultation Preparation Service (CPS) was proposed. We present the preliminary results of a CPS pilot study performed in the Madrid Parkinson Association.
The CPS prepared a report for the neurologist with a completed Non-Motor Symptoms Questionnaire (NMS-Quest) and information from the STAT-ON (an inertial waist-worn medical device that provides objective information on motor symptoms, such as motor fluctuations, bradykinesia, dyskinesia, freezing of gait, and activity measurements). The patients visited the Association 2-3 weeks before the doctor's visit to receive the STAT-ON sensor, which was worn for 1 week. Patients and neurologists were surveyed about their experience with the CPS.
A total of 44 patients with PD participated. From 43 responses, 54.5% of patients recognized previously non-identified symptoms; 23.3% stated they were more relaxed and ready for consultation; 51.2% felt more confident; and 32.6% felt they had organized the information they wanted to convey. Most (95.3%) patients expressed that their experience with the sensor was good or very good, and null patients reported it as a negative experience. Also, 90.7% of patients considered the CPS a good or very good experience. Thirty-two neurologists answered the survey. Only 3.2% found the sensor useless. In 56.3% of cases, there was a therapy adjustment.
The CPS was reported as a positive experience by the majority of PD patients, who felt more prepared and confident to face their doctor consultation. The information obtained by physicians was well received and resulted in some therapy adjustments.

P24.32

Co-designing digital medical devices for living well with Parkinson's disease

Isabel Schwaninger*[,1], Alexandre Kloos[2], Fozia Noor[3], Sandrine Lavalle[3], Anne Kaysen[4], Jochen Klucken[5]
[1] Université de Luxembourg, Belval, Luxembourg
[2] Université de Luxembourg, Luxembourg, Luxembourg
[3] Luxembourg Institute of Health, Luxembourg, Luxembourg
[4] Université de Luxembourg; ParkinsonNet, Belval; Luxembourg, Luxembourg
[5] Luxembourg Institue of Health; Université de Luxembourg; Centre Hospitalier de Luxembourg, Luxembouerg, Luxembourg

Data-driven digital medical devices (DMDs) are being developed to support people with Parkinson's (PwP) in self-management and in living well with Parkinson's disease (PD). However, there is still a low adoption rate of these technologies. Given that their use is entangled with the everyday life of PwP, there is a need for methods to design solutions reflecting the needs of people using DMDs. To design patient-centered solutions, we propose participatory design as an approach to involve PwP early in the design and development of DMDs. Based on a review of existing literature, four phases of participatory design (i.e., co-design) can be proposed: Ideation & contextualization, conceptualization, prototyping, and evaluation.
After a conceptual outline of the co-design phases, we present key aspects/challenges as identified from the literature which should be addressed when involving PwP. This is important, as traditional co-design techniques need to be tailored to PwP's needs, and to technical particularities of DMDs in the context of PD.
Key challenges to be addressed include:
- (1) defining user groups among PwP,
- (2) considering eHealth literacy of PwP,
- (3) tackling methodological challenges regarding data-driven DMDs for PwP.

(1): Given both the diversity of PwP and the use of qualitative methods in co-design, defining the actual target users among PwP and inclusion criteria (e.g., disease phase) is key. Also, while DMDs often target the patient as an individual, support networks should be considered as well. The target group should be defined at ideation and contextualization phases.
(2): To support the agency of PwP, data-driven DMDs should provide health information to PwP and support networks. Therefore, considering eHealth literacy (and designing for people with low eHealth literacy) is key for user-friendly and inclusive DMDs. Relevant aspects should be considered at conceptualization and evaluation phases.
(3): Data-driven DMDs are often challenging to co-design, as they can change at usage time. This requires a combination of top-down and bottom-up approaches, multidisciplinary collaboration, and effective collaboration between professionals and PwP throughout the four co-design phases.
The poster will support the WPC community to involve PwP and support networks into designing data-driven DMDs, aiming to reflect the needs of PwP.

P24.33

A 26-week case study of long-term adherence to a smartphone-based patient reported outcomes (PRO) platform: Enhancing measurement and improving outcomes for an individual living with Parkinson's

Benoit Tas[,1], Benoit Duvivier*[,2], Heiko Mueller[1], John M Dean[3]*
[1] NeuroPath SRL, Enghien, Belgium
[2] Person with Parkinson's, Registered Nurse, Wommelgem, Belgium
[3] Triad Health AI, Aurora, Colorado, United States

Introduction: We outline the utilization habits and resulting data from a six-month pilot of a PwP using NeuroPath Insights™ on a smartphone and digital platform in real-life.
Methods:
• Single male user, age 64, H&Y 1, neurologist-verified diagnosis of idiopathic Parkinson disease (June 2018)
• NeuroPath Insights™ implemented on iPhone and Apple Watch (June-December 2022)
• Multiple active and passive data entries regarding motor/non-motor symptoms and activities.
Data collected:
• E-diary (written/voice activated) with symptoms tracking
• Well-being
• Medication diary and adherence
• Health biomarkers (activity/cardio/energy/breathing/saturation)
• Mobility analysis (steps/walking distance/- speed/- asymmetry)
• Dyskinesia, tremor

- Physical therapy/sports
- AI analysis of marker-less video capturing of exercises
- Clinically-validated PROM on Quality of Life with score and classification (Neuro-QoL™)

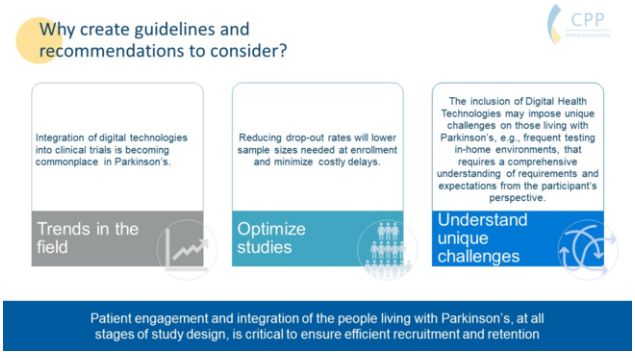
Results: User implemented NeuroPath Insights™ for a total of 460 entries over 146 out of 182 days, resulting in 80.2% compliance over 26 weeks. Participant used NeuroPath Insights™ at least once per day for six days of every seven-day window, including 97 Neuro-QoL™ questionnaires entries and 146 notes.
These insights were combined with passively captured data and reported on a dashboard via iPhone and Apple Watch.
The participant tracked significant improvements in mobility, flexibility and cognitive function, which motivated him to adhere to his medication - and physical exercise regimen. On average, it took him about five minutes of active tracking of symptoms per day, typically over two or three sessions.
Discussion: NeuroPath Insights™ allowed for active and passive monitoring which provided relevant insights to the user and his neurologist. User reported making use of the information provided to identify relevant information that he shared with his neurologist.
Recognizing the limitations of a single case design, utilization and compliance above 80% provides encouraging signaling towards wider implementation.
This may be due to a combination of the motivation of the user due to the information being provided by the NeuroPath Insights™ platform in conjunction with the ease of use of the interface, which includes passive monitoring functions and a voice interface that extends to the Apple Watch.
According to the participant, “using NeuroPath Insights™ increases my understanding in my Parkinson’s and helps me to anticipate and manage my mental and physical activities.

P24.34

Patient-centered recommendations for Parkinson’s clinical trials using digital health technologies

Kimberly Ward Barowicz[1], Marjan Meinders[2], Mark Frasier[3], Johan Hellsten[4], Tairmae Kangarloo[5], Matthew Sullivan[6], Cindy Zadikoff[7], Martijn Müller[1], Diane Stephenson[1]*
[1] Critical Path Institute, Tucson, AZ, United States
[2] Radboud university medical center, Nijmegen, Netherlands
[3] The Michael J. Fox Foundation, New York, NY, United States
[4] H. Lundbeck A/S, Valby, Denmark
[5] Takeda Pharmaceuticals, Lexington, MA, United States
[6] Parkinson’s UK, London, United Kingdom
[7] AbbVie Inc., North Chicago, IL, United States

Background: Digital health technologies hold significant potential for transforming healthcare, research, and clinical trials. However, the use of these technologies introduces unique complexities in clinical study design and operations. Parkinson’s disease is a slowly progressing disease with daily symptom fluctuations. Therefore, it is ideally suited to the deployment of digital health technologies providing objective and longitudinal data, in contrast to the snapshot view gathered at a single visit. Global regulatory agencies have embraced patient-focused drug development and recommend that people living with Parkinson’s are included in all stages of drug development. Study sponsors and clinical researchers must integrate the needs, expectations, and wishes of people with Parkinson’s disease participating in trials that use digital health technologies.
Objectives: To present the work of a worldwide pre-competitive collaboration, led by the Critical Path for Parkinson’s consortium’s Digital Drug Development Tool (3DT) initiative, that outlines how all stakeholders are working together to advance the development of digital health technologies by placing people with Parkinson’s at the forefront. A 3DT-led task force representing all stakeholders produced recommendations and considerations for integration of digital health technologies in Parkinson’s clinical studies from a participant-centered perspective.
Methods: Experts from industry, advocacy and academia joined forces with people with Parkinson’s to develop a presentation of consensus recommendations for industry sponsors and researchers conducting Parkinson’s clinical studies deploying digital health technologies in a participant-centered manner.
Results: Recommendations were driven by feedback from people with Parkinson’s who had participated in digital health technology studies, along with results of a literature review of 13 relevant device studies. The recommendations focused on three key areas: protocol design, enrollment, and protocol compliance & participant retention. There was universal consensus to follow regulators’ advice to assess the people with Parkinson’s perspective of how they function and feel by performing qualitative studies.
Conclusions: The recommendations gathered from the assessment of clinical digital health technologies in Parkinson’s studies have been shared broadly. Formalization and implementation of these recommendations to prioritize the input of participants at all stages of trial design and execution promise to improve efficiencies in drug development and expedite the approval of needed treatments for people with Parkinson’s.

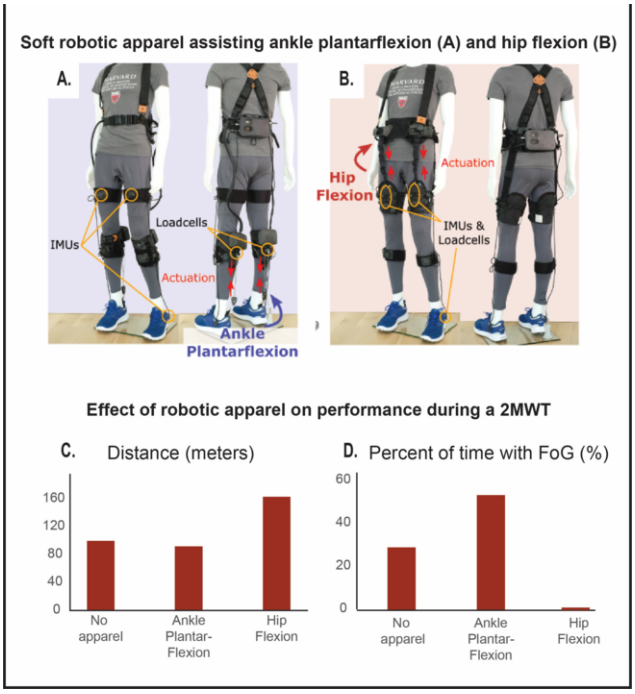


P24.35

Soft robotic apparel and freezing of gait: A targeted approach

Nick Wendel[*,1], *Jinsoo Kim*[2], *Franchino Porciuncula*[3], *Teresa Baker*[3], *Hee Doo Yang*[2], *Sungwoo Park*[2], *Conor Walsh*[2], *Terry Ellis*[3]
[1] Boston University, Boston, MA, United States
[2] John A. Paulson School of Engineering and Applied Sciences, Harvard University, Boston, Massachusetts, United States
[3] Boston University College of Health and Rehabilitation Sciences: Sargent College, Boston, Massachusetts, United States

Purpose: Freezing of gait (FoG) is a common and disabling symptom in people with Parkinson Disease (PD) that negatively impacts mobility and quality of life while increasing fall risk. Given the limited benefits of pharmacological and surgical treatments for FOG, innovative rehabilitation approaches are needed to address this debilitating problem. In this study, we sought to assess the potential of soft robotic apparel in ameliorating FoG by exploring the effects of a hip flexion versus ankle plantarflexion assistance.
Subject: Male, age 74 with a 11-year history of PD, who presented with moderate FoG (New FoG Questionnaire 19/28).
Methods: Effects of the robotic apparel were evaluated by having the participant walk with and without the robotic apparel during a two-minute walk test (2MWT), performed on a long straight hallway (~90 meters) – with all measurements completed in a single session. Assistance from soft robotic apparel was applied either at the ankle or the hip via flexible cable driven actuators and sensors on the waist and thighs. Hip flexion assistance was provided at a magnitude of 80 N and initiated at the pre-swing phase of gait, continuing throughout the swing phase. Ankle plantarflexion assistance was provided at a magnitude of 220 N in the terminal stance and pre-swing phases of the gait cycle.
Results: Without soft robotic apparel, the participant walked 100.02 meters and experienced FoG 29.2% of the time. With ankle plantarflexion assistance, the participant walked 92.20 meters and experienced FoG for 53.5% of the time. In contrast, with hip flexion assistance, the participant walked 163.12 meters and experienced FoG 0% of the time.
Conclusions: Soft robotic apparel, applied in a targeted fashion, prevented FoG in a single participant with PD. Preferential benefit was observed in favor of hip flexion assistance but not ankle plantarflexion assistance. Additional research is needed with participants with a range of FoG phenotypes to assess generalizability and to more fully understand the mechanisms underpinning these effects.
Clinical Relevance: Soft robotic apparel has the potential to help prevent FoG in individuals with PD. Evaluation of the effects in home and community settings is needed to determine potential benefits in the real-world.



COMPREHENSIVE CARE: Rehabilitation sciences (PT, OT, SLP)

P25.01

Fisior sequential squares mat as a stable environment to reeducate gait in patients whit Parkinson disease

José Alegre Tamariz[*,1], *Nuria Toledo Martel*[2], *Leticia Martínez Caro*[3], *Alberto Bermejo Franco*[4]
[1] Fisior Fisioterapia, Las Palmas de Gran Canaria, Las Palmas, Spain
[2] Asociación Parkinson Gran Canaria, Las Palmas de Gran Canaria, Las Palmas, Spain
[3] Universidad Internacional de la Rioja, Madrid, Pozuelo de Alarcón, Spain
[4] Faculty of Sports Science Universidad Europea de Madrid, Madrid, Villaviciosa de Odón, Spain

Introduction: Within the physiotherapy approach to rehabilitation, motor learning theories highlight the importance of interpreting environmental features for the development of movement strategies. Directing the program within specific environmental constraints provides information that is relevant to our actions and movement control.
Implementing as a treatment tool a Fisior® sequential squares mat (SSM) as a complement to conventional outpatient physiotherapy in patients with Parkinson's disease to generate movement strategies, is our proposal to favor motor learning in gait reeducation programs for these subjects.
General objective: To analyze the influence of a gait re-education program on a Fisior® SSM, as a complement to conventional physiotherapy, to improve ambulation in PD patients.

Specific objectives: To evaluate the efficacy of a gait re-education program on a Fisior® TCS as an adjunct to conventional physiotherapy, in improving gait speed and functional capacity.
Methodology: Randomized clinical trial in over 65 years old, diagnosis of mild or/and moderate PD, duration 12 weeks, 3 times per week, 30 minutes per session. Two differentiated types of intervention. Condition A, 3 sessions of 30 minutes per week of conventional physiotherapy. Condition B, conventional physiotherapy plus gait re-education program on Fisior® TCS. Gait speed was evaluated with the Timed Up and Go (TUG) test and functional capacity with the Short Physical Performance Battery (SPPB).
Results: Twenty-eight patients (n=28) participated, 14 experimental group (n=14) and 14 control group (n=14). Women 42.9%, men 57.1%, mild diagnosis 46.4% and moderate diagnosis 53.6%.
The analysis of the variable TUG for gait speed between the experimental group PRE (0.56±0.17) vs. experimental group POST (0.66±0.17) results with statistical significance (p=0.003).
The analysis of the SPPB variable for functional capacity between the PREexperimental group (70.8±11.8) vs. POST (87.1±17.6) results with statistical significance (p=0.007). Experimental group versus control group in PRE no significant results (p=0.170), in POST, statistical significance (p=0.012).
Conclusions: A gait re-education program using Fisior® sequential squares mat as a complement to conventional physiotherapy is an effective method to improve spatial gait parameters of PD patients and allows improving gait speed and functional capacity of the intervention group.

P25.02

Fisior® sequential square mat as a stable environment to improve the risk of falls in patients with Parkinson's disease
José Alegre Tamariz[*1], Asier Arrizabalaga Otaegui[1], Leticia Martínez Caro[2], Alberto Bermejo Franco[3]*
[1] Fisior Fisioterapia, Las Palmas de Gran Canaria, LAS PALMAS, Spain
[2] Universidad Internacional de la Rioja, Madrid, Pozuelo de Alarcón, Spain
[3] Faculty of Sports Sciences, Universidad Europea de Madrid, Madrid, Villaviciosa de Odón, Spain

Introduction: Aging produces a series of changes in the individual that may predispose to falls. Falls are one of the most important components of the geriatric syndrome, and one of those that most affects the elderly population in general.
Implementing as a treatment tool a sequential squares mat (TCS) Fisior® as a complement to conventional outpatient physiotherapy in patients with Parkinson's disease in order to generate movement strategies, is our proposal to promote motor learning in fall prevention programs for these subjects.
Objectives:
General objective:
To analyze the influence of a gait re-education program on a Fisior® TCS, as a complement to a conventional physiotherapy program, to improve the approach to ambulation in PD patients.
Specific objectives:
To evaluate the efficacy of a gait re-education program on a Fisior® TCS as an adjunct to a conventional physiotherapy program, in improving gait speed and fall risk.
Methodology: Randomized clinical trial in over 65 years old, diagnosis of mild or/and moderate PD, duration 12 weeks, 3 times per week, 30 minutes per session. Two differentiated types of intervention. Condition A, 3 sessions of 30 minutes per week of conventional physiotherapy. Condition B, conventional physiotherapy plus gait re-education program on Fisior® TCS. Gait speed was evaluated with the Timed Up and Go (TUG) test and FallSkyp inertial sensors for fall risk.
Results: Twenty-eight patients (n=28), 14 experimental group (n=14) and 14 control group (n=14) participated. Women 42.9%, men 57.1%, mild diagnosis 46.4% and moderate diagnosis 53.6%.
The analysis of the variable TUG for gait speed between the experimental group PRE (0.56±0.17) vs. experimental group POST (0.66±0.17) results with statistical significance (p=0.003).
The analysis of the FallSkip variable for fall risk did not show statistical significance in the PRE experimental group (p=0.100) vs. the POST control group (p=0.198). However, the control group PRE (4.57±1.34) versus POST (4.14±1.46) results gave statistically significant changes (p=0.034).
Conclusions: The application of a gait re-education program using Fisior® sequential frame mat as an adjunct to conventional outpatient physiotherapy is an effective method to improve spatial parameters of gait in PD patients. Secondarily, this program allows to improve gait velocity in patients with PD.

P25.03

Visual perturbation training to reduce fall risk in people with Parkinson's disease

Remco Baggen[*1], Anke Van Bladel[2], Maarten Prins[3], Katie Bouche[2], Leen Maes[2], Miet De Letter[2], Dirk Cambier[1], Patrick Santens[2]*
[1] Ghent University, Ghent, Belgium
[2] Ghent University/Ghent University Hospital, Ghent, Belgium
[3] Militair Revalidatie Centrum Aardenburg, Doorn, Netherlands

Background: Falls during dynamic tasks such as gait are common in people with Parkinson's disease (PD). This is due to a decrease in automaticity, leading to increased reliance on sensory cues to enable performance of locomotor tasks. However, the quality of this input from different sensory systems is often compromised in PD, particularly that of the vestibular system. This causes a stronger reliance on visual cues, which can cause a mismatch in perceived and actual self-motion, which in turn increases fall risk in conditions where balance is challenged. Visual perturbation training (VPT) is a novel rehabilitation method that mimics high-risk situations in real life using sudden movements of virtual reality (VR) environments. We hypothesize that VPT can reduce visual dependency and reduce fall risk, and that this effect is mediated by baseline vestibular function.
Aims: 1) To assess the effects of six weeks VPT on indicators of fall risk and self-reported falls. 2) To investigate the link between vestibular function and (training-based improvements of) gait parameters in people with PD.
Methods: Fifty people with PD (Hoehn & Yahr II-III, age 50-65y) will be recruited and randomly assigned to either the intervention (VPT) or control (normal treadmill training) group. The intervention will consist of 6 weeks (2x week) VPT training on a treadmill in a 3D projected VR environment of the Gait Real-time Analysis Interactive Lab. Visual perturbations will consist of medio-lateral translations and rotations around the anteroposterior axis of the projected environment. Pre- and post-tests will assess visual dependency (correlation between trunk- and screen movements), gait quality (speed, step time/length/width, cadence, trunk sway), margins of stability, and vestibular function (cervical and ocular vestibular evoked myogenic potentials). Falls will be monitored using fall diaries up to 6 months post-intervention.
Results and conclusion: Preliminary results indicate a link between vestibular function and quality of gait in people with PD, results from the intervention are pending. However, previous research using a similar VPT paradigm in vestibular patients without PD shows a clinically relevant and significant decrease in visual dependency. This indicates a strong potential of VPT to decrease fall risk in people with PD.

P25.04

Relationship between self-efficacy and real world walking activity in persons with Parkinson's disease

Teresa Baker, PT, DPT[*1], Kerri Rawson, PhD[2], Jaimie Girnis, PT, DPT[1], Ryan Duncan, PT, DPT, MSCI[2], James Cavanaugh, PT, PhD[3], Tamara R. DeAngelis, PT, DPT[1], Daniel Fulford, PhD[4], Martha Hessler[5], Michael Lavalley, PhD[6], Timothy Nordahl, PT, DPT[1], Marie Saint-Hilaire, MD[7], Cathi Thomas, RN MS, CNRN[7], Jenna Zajac, PT, DPT[1], Gammon Earhart, PT, PhD[8], Terry Ellis, PT, PhD[1], Franchino Porciuncula, PT, DScPT, EdD[1]*
[1] Department of Physical Therapy, Sargent College of Health and Rehabilitation Sciences, Center for Neurorehabilitation, Boston University, Boston, Massachusetts, United States
[2] Program in Physical Therapy, Washington University in St. Louis School of Medicine, Department of Neurology, Washington University in St. Louis School of Medicine, St. Louis, Missouri, United States
[3] Department of Physical Therapy, University of New England, Portland, Maine, United States
[4] Department of Occupational Therapy, Sargent College of Health and Rehabilitation Sciences, Boston University, Boston, Massachusetts, United States
[5] Program in Physical Therapy, Washington University in St. Louis School of Medicine, St. Louis, Missouri, United States
[6] School of Public Health, Boston University, Boston, Massachusetts, United States
[7] Department of Neurology, Parkinson's Disease and Movement Disorders Center, Boston University, Boston, Massachusetts, United States
[8] Program in Physical Therapy, Washington University in St. Louis School of Medicine, St. Louis, Missouri, USA; 3Department of Neurology, Washington University in St. Louis School of Medicine, Department of Neuroscience, Washington University in St. Louis School of Medicine, St. Louis, Missouri, United States

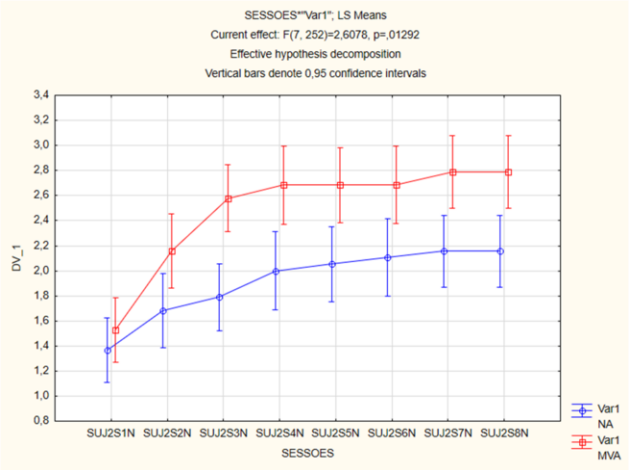
Purpose: Physical activity is an important rehabilitation target for persons with Parkinson Disease (pwPD) due to its influence on disability and quality of life. Self-efficacy, the belief in one's ability to perform a task, has been identified as a potential contributor to walking behavior in pwPD. However, the extent of its influence is not well understood. We sought to examine the influence of self-efficacy in pwPD on real-world walking activity.
Participants: 116 pwPD with a mean (SD) age of 67.1 ± 8.4 years, 45.3% female, Hoehn & Yahr (H&Y) 2-3 (H&Y 2: 49.6%; H&Y 2.5: 40.2%, and H&Y 3: 10.3%), and with mean disease duration of 5.38 ± 4.53 years.
Methods: The study was a secondary analysis of baseline data from an ongoing clinical trial designed to examine effects of a connected behavioral approach on walking in pwPD. Using the Self-Efficacy of Walking Duration (SEW-D) measure, pwPD rated their confidence (0-100%) in their ability to walk at a moderately fast pace across a range of walking durations at 5-minute intervals (i.e., 5, 10,… 50 minutes). Walking activity was measured over a seven-day period using a StepWatch Activity Monitor, capturing daily walking amount (steps) and minutes of moderate intensity walking (minutes in which ≥ 100 steps/min were taken). Separate linear regression

analyses were conducted to examine relationships between SEW-D mean score and daily mean values for each walking behavior metric.
Results: Participants had a mean SEW-D score of 54.46 ± 30.75%, walked 8,258 ± 3,544 steps per day, and accumulated 8.1 ± 9.3 daily minutes of moderate intensity walking. SEW-D was significantly associated with and explained 9.5% of the variance in daily steps (p <.001). SEW-D was significantly associated with and explained 15.3% of the variance in daily minutes of moderate intensity walking (p<.001).
Conclusions: Self-efficacy of walking duration explained a modest, yet significant percentage of variance in walking activity for this sample of persons with mild to moderate PD.
Clinical Relevance: Clinicians should consider assessing self-efficacy of walking, especially for sedentary pwPD, to determine its potential influence on a patient's community walking activity. Future studies are needed to determine the modifiability of self-efficacy.

P25.05

Can augmented feedback facilitate learning in serious games in People with Parkinson's Disease? A single-blind randomized clinical trial.
*Pâmela Barbosa, Amarilis Falconi, Matheus D'Alencar, Erika Okamoto, Maria Elisa Pimentel Piemonte**
University of Sao Paulo, São Paulo, São Paulo, Brazil

Background: Evidence has shown that augmented feedback (AF) improves the learning process's efficacy. However, the effect of AF offered through the physiotherapist (PT) during motor training with video games in people with Parkinson's Disease (PPD) has not been investigated yet. **Purpose:** To compare the effects of motor training with VR with and without AF supported by a PT manual movement guidance (MVG) versus identical training in the absence of MVG (NO MVG) on learning of PPD. **Methods:** A blind randomized clinical trial in PPD was performed. Both groups received 8 individual sessions, twice a week, for 4 weeks, and 40 minutes of video game balance training using XBOX 360 plus Kinect®. In the MVG Group, PT provided AF by assisting manually the participant's movements. While NO MVG Group, PT's involvement was restricted to ensure participant safety. Games from Your Shape Fitness Evolved® were chosen: Light Race (large step); Stach'em up (balance under multitasking); Wall Braker (dynamic balance) and Run the World (stationary gait). The score of each game was monitored throughout the session for learning analysis. **Statistical analysis:** ANOVA to repeated measures was used, one for each game, having as the main factor the group (MVG and NO MVG Group) and as repeated measure the training session (8 sessions). The post-hoc Tukey test analyzed the pair-to-pair comparison. A significance of 5% was considered. **Results:** 40 PPD participated in this study, staging from 1 to 3 according to Hoehn and Yahr scale, mean age of 63.78 years (SD 7.58). Significant session effects were found for both groups for Light Race (F7,25 = 0,33; p=0,93; ES=0,95), Stach'em up (F7,24 = 1,09; p=0,36; ES=0,95), and Run the World (F7,25 = 1,73; p=0,10; ES=0,95). There was a statistically significant interaction between group factor and session for Stach'em up game only (F7,25 = 2,60; p=0,012; ES=0,95). The post-hoc test confirmed that MVG reached higher scores than NO-MVG. **Conclusion:** PT's manual intervention during video game training can facilitate learning in more challenging games and consequently, improve the therapeutic results.



P25.06

Differences in gait between clinical subtypes in Parkinson disease
Sidney Baudendistel*, Scout Hizer, Allison Haussler, Kerri Rawson, Meghan Campbell, Gammon Earhart
Washington University in Saint Louis, St. Louis, Missouri, United States

Among people with Parkinson disease (PD) spatiotemporal gait features are associated with freezing of gait and falling, but also with cognitive impairment and depression. We hypothesize gait characteristics may differ across clinical subtypes of PD. Prospectively identifying PD subtypes using gait signatures may allow for earlier interventions, as gait changes may emerge prior to neuropsychological symptoms. A first step in testing this hypothesis is to determine whether people with different clinical subtypes of PD exhibit different gait signatures.
Using an existing research database, this cross-sectional study identified differences in sixteen quantified gait variables between individuals with three different subtypes of PD, similar to those described in Campbell et al. 2020. Individuals (n=210) were categorized based on the Geriatric Depression Scale or Hospital Anxiety and Depression Scale-Depression Subscale and the Montreal Cognitive Assessment: MOTOR (individuals without depressive symptoms and without cognitive impairment), DEPR (with depressive symptoms and without cognitive impairment), and COG (with cognitive impairment and without depressive symptoms). Differences between PD subtypes were significant for step velocity, step length, step time, and stance time, as well as temporal variability (step-to-step variability of step, swing, and stance time). MOTOR walked with longer steps and reduced step time, resulting in faster walking speed, compared to DEPR and COG. There were no significant differences between DEPR and COG for step length, step time, and velocity. For the COG subtype, the time within and between steps was more variable compared to MOTOR. DEPR displayed intermediate values between MOTOR and COG, but was not significantly different from either subtype. Of note, large person-to-person variance within the gait measures, combined with a smaller group size, restricted the ability to establish differences between DEPR and the other subtypes.
As current research is scant regarding the effects of depression on gait for individuals with PD, these results represent an important first step in determining the viability of gait signatures relating to the prediction and progression of non-motor symptoms. If viable, gait

analysis could be used to identify subtypes early in the course of the disease, facilitating earlier implantation of tailored rehabilitation strategies.

P25.07

Assessment of upper limbs impairments in Parkinson's disease: A systematic review

Tamine Capato[*,1], Rubia Rodrigues[1], Beatriz Santos[2], Manoel Teixeira[1], Rubens Cury[1], Egberto Barbosa[1]*
[1] University of São Paulo, São Paulo, São Paulo, Brazil
[2] PHYSICAL Parkinson's Disease and Movement Disorders Rehabilitation, São Paulo, São Paulo, Brazil

Background: Parkinson's disease (PD) may lead to a progressive reduction of upper limbs functionality. A standard upper limbs functional capacity assessment in PD is unknown. **Objective:** to identify the outcome measurements to assess upper limbs in PD; to identify specific outcome measures to assess functional capacity. **Methods:** We systematically reviewed and analyzed the literature in English published from August 2012 to August 2022 according to PRISMA. The following keywords were used in our search: "upper limbs" OR "upper extremity" and "Parkinson's disease". Two researchers carried out the search independently and a consensus meeting was held when needed included or excluded studies accordingly our criteria's. Registered at PROSPERO CRD42021254486. **Results:** We initially found a total of 797 studies. According to the inclusion and exclusion criteria, 55 studies were included in this review. In total, 2.387 participants were included, mean age of 61.16 and in H&Y stage 2 (2-3). The most common upper limbs outcome measures found in the studies were: (i) MDS-UPDRS, Nine Hole Peg Test, Purdue Pegboard Test, Fahn-Tolosa-Marin Tremor Rating Scale used to assess severity and progression of PD motor symptoms (tremor e bradykinesia); (ii) Nine Hole Peg Test and Purdue Pegboard Test, to assess manual dexterity; (iii) Spiral test and Funnel test to provoke and assess freezing of upper limbs (FOUL). Technology assessments such as wearables sensors and Apps were also found. No studies were found to assess specifically upper limbs functional capacity in PD. **Conclusion:** The upper limbs' functional capacity is under investigated during people with PD functional clinical examination due to a lack of specific outcome measures. Current evidence is insufficient to recommend standard and outcome measures to assess upper limb functional capacity impairments in PD. This review highlights the need to develop a practical and standardized instrument to assess the functional capacity of people with PD in clinical practice. Further studies should investigate technological advances to refine and support the outcome of assessing upper limb impairments.

P25.08

Use of a novel comprehensive balance assessment to measure fall risk in people with Parkinson's disease

Patricia Carlson-Kuhta[*,1], Carla Silva-Batista[1], Anjanibhargavi Ragothaman[1], Jacqueline Ellison[1], Graham Harker[1], Giorgia Marchesi[2], Alice De Luca[2], Valentina Squeri[2], Fay B. Horak[1], Martina Mancini[1]*
[1] Oregon Health & Science University, Portland, OR, United States
[2] Movendo Technology, Genoa, Italy

Introduction: Falls are prevalent in people with Parkinson's disease (PD) and can result in injury and loss of independence. Accurate prediction of those at risk of falls is important to be able to intervene with rehabilitation to reduce future falls. A recently developed posturography system uses a comprehensive balance assessment to calculate a fall risk index, that has been validated for older adults (Silver index). We examined if the Silver Index can be applied to people with Parkinson's disease.
Methods. We tested 39 people with PD: nonfaller group (No falls in the past year; age=68.4±7.6, PD duration=7.0±5.1 yrs) and faller group (1 or more falls; age=68.1±6.7 yrs, PD duration=11.2±7.1 yrs). Participants completed (on medication) a series of balance tasks standing with the platform in static or moving condition, and while seated on the Hunova posturography system (Movendo Technology, Genova, Italy). The Silver Index was automatically calculated (0-25%= low, 26-50%= medium-low, 51-75%= medium-high, and 75-100% = high fall risk) comprised from sub-scores of: static balance, dynamic balance, sensory integration, reactive balance, sit-to-stand, limits of stability, and gait speed, as well as history of previous falls and age. Cognitive function was assessed by the Montreal Cognitive Assessment (MoCA) and a clinical balance assessment with the miniBESTest.
Results: The faller group had a higher Silver Index than the nonfaller group (faller=57.5±26%, nonfaller=22.9±15%, $p<0.001$), indicating a higher risk of future falls. The only significant sub-score was dynamic balance (faller=–0.44±1.5, nonfaller=0.41±0.8 z-scores, $p<0.039$). Correlation analysis showed the Silver Index was significantly correlated with MDS-UPDRS, part III ($r=0.65$, $p<0.003$), PIGD sub-score (0.67, $p<0.002$), and MoCA ($r=-0.52$, $p<0.015$), only for the Faller group. No significant correlation with the miniBESTest.
Conclusions: We found that people with PD in the faller group had a medium-high fall risk on the Silver Index, whereas the nonfaller group had a low fall risk score. Ability to maintain dynamic balance on the moving surface appeared to be important in people with Parkinson's disease. Our results suggest that the Silver Index may be useful beyond healthy older adults. Further research is being conducted to look at the relationship of Silver Index score to future falls in people with PD.

P25.09

The eyes have it: Persons with Parkinson Disease demonstrate poor performance on the King-Devick test

Valerie Carter, John Heick, Robert Gorman, Tarang Jain*
Northern Arizona University, Flagstaff, AZ, United States

Introduction: Persons with idiopathic Parkinson Disease (PwP) are shown to have deficits in somatosensory and visual systems leading to an increased risk for falling. Eye tracking, specifically saccades, is impaired and plays a significant role in balance. Due to the high incidence of injury, when compared to the general population, assessing the overall risk and cause for falls within this population is crucial to understanding disease severity and help to develop effective intervention strategies. The purpose of this study was to compare the King-Devick (K-D) Test in persons with Parkinson's disease to age-matched healthy older adults.
Methods: PwP (72.6±8.7 yrs., 10F, n=19) and healthy elderly individuals (69.6±11.9 yrs., 11F, n=24) participated in the K-D test while sitting in a chair. The K-D takes about 2 mins to complete and measures the speed and number of errors while the patient reads aloud single-digit numbers of 3 test cards spaced unevenly across each card.
Results: K-D test scores in the PwP group (65.52 ± 5.51 sec, n=19) was higher than the age-matched healthy older adults (50.59 ± 1.98 sec, n=24) ($t(37) = 2.98$, $p = 0.005$) with a difference of 14.93± 4.50 sec (95% CI, 4.81 to 25.06). An independent t-test found that K-D test scores in the PwP group (65.52 ± 5.51 sec, n=19) were significantly higher than the control group (50.59 ± 1.98 sec, n=24) ($t(37) = 2.98$, $p = 0.005$) with a difference of 14.93± 4.50 sec (95% CI, 4.81 to 25.06).

Clinical Significance: Impaired oculomotor performance is attributed to dopamine depletion. Increased latency during volitional eye movement in PWP has been correlated with postural instability. Therefore, PwP may benefit from performing postural exercises that emphasize oculomotor movements and visual processing during daily activities.
Conclusion: PwP do not perform as well as healthy older adults when completing the K-D test, indicating poorer oculomotor performance and deficits in attention, language, and possibly other aspects of cognitive functions.

P25.10

Talk the Walk: Dual tasking with walking and visual-verbal processing is more difficult for persons with Parkinson than for young and older adults.
Valerie Carter, John Heick, Tarang Jain*
Northern Arizona University, Flagstaff, AZ, United States

Introduction: Recurrent falls in persons with Idiopathic Parkinson disease (PwP) are often attributed to deficits in postural stability, gait, saccades, and cognition. When completing dual task while walking, PwP demonstrate decreased step length and velocity, as well as increased double-support time and freezing of gait. Currently there are no clinical tests that assess the PwP's ability to safely complete the dual task of walking, scanning, and processing the environment accurately and safely. The visual-verbal Stroops test can be used to measure a person's selective attention capacity and processing speed. The purpose of this research was to assess the PwP's ability to safely complete the dual task of walking 10 meters while scanning, reading, and verbally reporting visual-verbal Stroops compared to age-matched healthy older and young adults.
Methods: PwP (73.6±8.7 yrs., 10F, n=20), as well as young (29.4±9.1 yrs., 14F, n=20) and 20 older adults (71.6±8.7 yrs., 11F, n=19) were asked to complete the 10-meter walk test (10MWT) and the new 10-meter walk test with visual-verbal Stroops (10 MWT with Stroops).
Results: One-way ANOVA indicates time to complete 10MWT increased from the older adults to PwP (p=.224). The time to complete 10MWT with Stroops progressively increased from the young to older to adults, PwP (p = <.001). Post hoc analysis revealed that the increase from young adults to PwP was statistically significant (p <.001), and from older adults to PwP (p = .028). The average number of errors made during 10MWT with Stroops were similar in young and older adults but increased in PwP (p = <.01) and was statistically significant (p =.02).
Clinical Significance: There are no clinical tests that assess a PwP's ability to complete the dual task of scanning and accurately processing their environment while walking safely. The new 10-meter walk test with visual-verbal Stroops may be able to assess PwP's ability to safely navigate in the community. Further, this new test can be used to evaluate effects of interventions that target falls in PwP.
Conclusion: PwP were slower and made more errors than healthy older and young adults while completing the 10-meter walk test with visual-verbal Stroops.

P25.11

Effectiveness of a virtual physiotherapy for Parkinson's course using a mixed on-demand and live model: Lessons learned from Malta
Veronica Clark[1], Josefa Domingos[2], Victoria Masalha[3]*
[1] Malta Parkinson's, Marsa, Malta
[2] Donders Institute for Brain, Cognition, and Behavior, Center for Medical Neuroscience, Department of Neurology, Center of Expertise for Parkinson and Movement Disorders, Radboud University Medical Center, Nijmegen, Netherlands
[3] Physiotherapy Services, Malta; Faculty of Health Sciences, University of Malta, Malta, Malta

Introduction: Excellence in teaching and learning methods is vital in providing quality training among health care professionals. Online education training programs have gained popularity in recent years. Yet, finding the best model of delivery, with an effective format and relevant content, still needs to be achieved.
Goal: To test a virtual training model for physiotherapists with mixed recorded on-demand and live sessions.
Methods: The course was developed as a collaboration between Malta Parkinson's Association and public Physiotherapy Services in Malta. We invited physiotherapists, working in acute, rehabilitation, and community sectors in Malta, with some or no experience managing Parkinson's disease (PD), and interested in further education and (national) collaboration. The course was delivered by a Physiotherapist, internationally recognised as a Parkinson's Specialist clinician, educator, and researcher. It aimed to increase Parkinson-specific expertise among physiotherapists through interactions with experts in the field and each other. To maximise learning, we used two modules: 1) an on-demand recorded 8-hour webinar divided into eight videos. 2) a live 6-hour webinar including a case study challenge, allowing trainees to acquire hands-on skills and discussions with local physiotherapists.
We assessed the impact of the course on knowledge and learner change using an anonymous knowledge-based questionnaire completed before and after the course. Results were compared to produce a percentage of learner change by topic and overall. We assessed satisfaction regarding several aspects, namely: the registration process, the format of recorded training, the format of the live training, and the competency of the trainer. We assessed knowledge base and learning using more specific questions related to the content.
Results: 40 physiotherapists participated. There was overall satisfaction with the different aspects of the course (fig. 1). There was an overall change in knowledge (fig. 2). Several specific skills or knowledge gained from this course were reported and captured in fig. 3.
Conclusions: Our results show an appreciable educational impact and satisfaction. Participants considered that the program provided an excellent experience, with active learning and understanding via videos and case studies. This innovative training model facilitates sharing knowledge that will benefit patient care and may help shape future programs.

Fig. 1 Satisfaction with the different aspects of the course

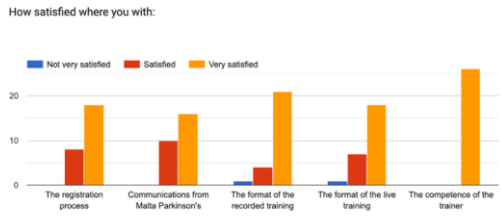


Fig 2. Overall change in knowledge - training impact

Q1	Parkinson's disease symptoms, how they progress, and how they may affect physiotherapy care.
Q2	Identifying Parkinson's-specific cognitive deficits, their management strategies, impact on the individual's performance and delivering care.
Q3	Specific evidence-based Physiotherapy interventions for Parkinson's Disease for critical areas: gait, falls, balance, transfers & posture.
Q4	Dual cognitive and motor task training in Parkinson's disease: recognizing the evidence, reasons to use it in clinical practice, whom to apply it to, and significant safety issues when applying it.
Q5	Early treatment options: when to start, what with, and why.
Q6	Recognize the primary differences between Parkinson's and Atypical Parkinsonism, as well as the specific physiotherapy interventions for the most frequent parkinsonisms (Multiple system atrophy (MSA), progressive supranuclear palsy (PSP), corticobasal degeneration (CBD), dementia with Lewy bodies (DLB), vascular parkinsonism (VP).
Q7	Exercise-based interventions for the home: How to keep people with Parkinson's disease motivated at home.
Q8	The overall level of competency in treating Parkinson's Disease.

Fig. 3 Several specific skills or knowledge gained from this course were reported by participants

Participants Skills or knowledge gained from this course
"More practical ideas on what exercise intervention can do in the early stages of PD"
"The importance of dual-tasking exercise for Parkinson's"
"How to think outside the box when formulating exercise sessions"
"Innovative treatment options"

P25.12

BeatMove: A personalized music-based gait auto-rehabilitation for persons with Parkinson's disease

Valérie Cochen De Cock[1], Loic Damm[2], Dobri Dotov[2], Simone Dalla Bella[3], Benoit Bardy[2]*
[1] Beau Soleil Clinic, Montpellier, France
[2] EuroMov Digital Health in Motion, Univ Montpellier, IMT Mines Ales, Montpellier, France, Montpellier, France
[3] International Laboratory for Brain, Music, and Sound Research (BRAMS), Montreal, QC, Canada, Montréal, Canada

Introduction: Musical auditory cueing has shown beneficial effects on gait in Parkinson's disease. However, its response varies a lot among patients, depending on their remaining rhythmic abilities (Cochen De Cock et al., 2018). To cope with this variability, we developed an individualized approach synchronizing the beat of the music to the persons' steps in real time (Dotov et al., 2019). We designed a mobile application coupled with ankle sensors, BeatMove, delivering interactive musical stimulations for gait auto-rehabilitation at home. The goal of our study was to evaluate the acceptability and the risks of BeatMove use. We also aimed for a pilot evaluation of its efficacy on falls and fear of falling.
Methods: Forty-five persons with PD used the BeatMove application (30 min/day, 5 days/week) during a one month, outdoor, gait auto-rehabilitation program. The music tempo was aligned step by step to the person's and then progressively increased at +20% of the spontaneous cadence. BeatMove was evaluated in open label through use measures, questionnaires and a six-minute walk test.
Results: Observance was at 78.8 % (±28.2) of the requested duration. Most of the persons enjoyed BeatMove use and 75% of them found it "easy to use". Falls and fear of falling were reduced by BeatMove use. Pain and quality of life were improved. At the end of the program, persons walked faster and had increased step length and cadence during the six-minute walk test performed without musical stimulation BeatMove users increased their "walk for exercise".
Conclusion: Using BeatMove at home is safe and enjoyable. It could be a useful tool to increase motivation to walk. Further studies are ongoing to confirm its efficacy on gait parameters, number of falls.

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P25.13

Voice self-assessment in Parkinson's disease: A comparison with different types of dysphonias

Francisco Contreras-Ruston[1], Jordi Navarra[2], Adrian Castillo-Allende[3], Jorge Saavedra-Garrido[4], Andrés Ochoa-Muñoz[5], Sonja Kotz[6]*
[1] Universidad de Barcelona, Barcelona, Barcelona, Spain
[2] Department of Cognition, Development and Educational Psychology, Universitat de Barcelona, Barcelona, Barcelona, Spain
[3] Department of Communicative Sciences and Disorders, Michigan State University, Michigan, Michigan State, United States
[4] Department of Statistics, Universidad de Valparaíso, Valparaíso, Chile
[5] Universidad de Valparaíso, Valparaíso, Chile
[6] Department of Neuropsychology & Psychopharmacology, Maastricht University, Maastricht, Netherlands

Aim: Voice self-assessment instruments apply to individuals with general vocal disorders (VD). Clinicians use such instruments in individuals with PD due to voice problems. However, individuals with PD seem to present a low disease awareness. For this reason, it is possible that certain voice deficits may be neglected, despite affecting the daily lives of these patients. For this purpose, this study compared the self-assessment of vocal symptoms between patients with PD and VD.
Methods: We administered participants a questionnaire (the Voice Symptom Scale; VoiSS) assessing the perception of their own voice in several domains (, physical, emotional, and impairment) related to voice symptoms (e.g., in loudness). We compared the total and domain scores and the voice loudness when vocalizing in a group of patients with PD and a group of non-PD patients with VD, using univariate and multivariate analyses. We also established several participant groups based on voice symptoms, using the Principal Component Analysis (PCA) and Hierarchical Clustering Analysis (HCA) approaches.

Results: Individuals with PD perceived fewer vocal symptoms than those with VD in all domains of VoiSS. The univariate analysis indicated significant differences between the two groups in the general score in each of the domains. Multivariate PCA showed that self-assessment of voice problems in individuals with PD did not correlate with total and domain-specific scores on the questionnaire, whereas there was a correlation between scores and vocal complaints in individuals with VD. However, difficulties in voice loudness problems (low intensity in PD and high intensity in VD) correlated poorly with the questionnaire scores in both groups. The HCA classified the participants into three groups, with PD and VD patients mostly falling into different groups.
Conclusions: Individuals with PD may have obvious voice problems (e.g., loudness), but their vocal self-assessment scores reflect they do not perceive their voice problem, impairing the reliability of these questionnaires. Therefore, we conclude that new voice self-report instruments specific to this clinical population should be developed.

P25.14

The priority goals and underlying symptomology related to goal-related performance of people with Parkinson's disease receiving a community-based rehabilitation program
Sarah Davies[*,1], Hannah Gullo*[*,1], Emmah Doig*[*,2]*
[1] The University of Queensland, Brisbane, QLD, Australia
[2] STARS Education and Research Alliance School of Health and Rehabilitation Sciences, The University of Queensland and Metro North Health, Brisbane, QLD, Australia

Purpose: Goal setting is a core practice in rehabilitation. Targeting therapy toward individualized, specific goals tailors therapeutic efforts to achieve meaningful outcomes. A holistic understanding of the goals of people with Parkinson's Disease (PwPD) undergoing rehabilitation may guide service delivery to ensure their needs and priorities are met. The aim of this study was to investigate the nature and priority of the goals self-selected by PwPD.
Method: Participants were receiving a community-based, goal-directed, metacognitive strategy-based intervention over 10 weeks. The goals, goal priority rankings and underlying performance component contributing to poor performance for each goal was extracted from each participant's documentation. The performance analysis diagnosis documented by the treating occupational therapist was used to determine the performance component problem (e.g. performance component 'tremor' as primary problem impacting on 'carrying a cup without spilling the drink'). Performance component problems were classified as either 'motor' or 'non-motor'. Goals were also classified by two independent raters using the International Classification of Function (ICF) as a framework on two levels: ICF component and ICF domain. Frequency of goals by ICF component, ICF domain and performance component classification were calculated and mean priority ratings for goals by component, domain and performance component domain were summarized.
Results: Twenty-two participants formulated a total of 88 goals. 72% of goals were related to non-motor symptomology. Goals related to motor symptomology tended to be ranked lower priority than non-motor symptomology goals, with only 30% of first priority goals related to motor performance. Participant's goals represented their motivations to improve or maintain their performance of everyday activities such as home organisation, time management and socialization for which barriers to their performance were primarily problems with executive function, fatigue and anxiety. 'Necessary' goals related to maintaining function for as long as possible were also common.
Conclusion: Goals of PwPD were primarily related to non-motor symptomology, which aligns with recent findings that non-motor difficulties are perceived as more restricting in daily life than motor problems for PwPD. This finding highlights the need to investigate rehabilitation approaches that can address both motor and non-motor symptomology impacting on the lives of PwPD.

P25.15

CO-OP feasible and promising for facilitating goal attainment in adults with Parkinson's disease: findings of a randomised controlled feasibility trial
Sarah Davies[*,1], Hannah Gullo*[*,2], Emmah Doig*[*,3]*
[1] The University of Queensland, Brisbane, QLD, Australia
[2] School of Health and Rehabilitation Sciences, The University of Queensland, Brisbane, QLD, Australia
[3] STARS Education and Research Alliance, School of Health and Rehabilitation Sciences, The University of Queensland and Metro North Health, Brisbane, QLD, Australia

Introduction: Despite major advances in the treatment and understanding of Parkinson's Disease (PD), people with PD (PwPD) have long-term difficulties with activities of daily living and quality of life due to PD symptomology. Non-motor symptoms, such as cognitive changes, have a hidden but significant impact on everyday functioning. Novel approaches to maximise quality of life, function, and participation in PwPD are needed. Occupation-based, meta-cognitive interventions are effective in populations with neurological conditions where cognitive impairments negatively impact functional goals, similar to that which occurs in PD. Occupation-based, meta-cognitive interventions therefore warrant investigation within the context of PD.
Purpose: This study investigated the preliminary efficacy and feasibility of an occupation-based, meta-cognitive intervention called Cognitive Orientation to daily Occupational Performance (CO-OP) for facilitating achievement of meaningful rehabilitation goals for PwPD. The intervention involved weekly sessions in participant's homes over 10 weeks.
Method: A parallel-group, randomized controlled feasibility trial (RCT) comparing a CO-OP treatment group to a waitlist-control group was conducted with community dwelling adults with PD in Brisbane, Australia. The Canadian Occupational Performance Measure (COPM) was used to measure perceived performance and satisfaction on self-selected goals. The Goal Attainment Scale (GAS) was used to objectively measure attainment of the participant's goals. GAS goal performance was rated by an independent, blinded assessor. Both the COPM and GAS ratings were obtained pre-post intervention and at 3 months follow up. The SEAR framework was used to assess feasibility of the approach for a larger scale trial.
Results: 20 PwPD completed the intervention, with 40 PwPD screened, 27 eligible and 22 randomised. Clinically significant improvements in goal attainment according to the GAS were recorded following the CO-OP intervention. Participants subjective occupational performance and satisfaction ratings on the COPM also recorded clinically significant improvements following the CO-OP intervention.
Conclusion: As the first RCT focused on CO-OP in PD, this trial has provided preliminary evidence for the feasibility and potential of the CO-OP approach for facilitating achievement of rehabilitation goals of people with PD, laying the foundation for future large-scale trials.

P25.16

"I didn't know I had executive functioning problems, but now I do… And there's something I can do about it" – Perspectives of people with Parkinson's disease about the Cognitive Orientation to daily Occupational Performance approach

Sarah Davies[*,1], Hannah Gullo*[*,2], Emmah Doig*[*,3]*
[1] The University of Queensland, Brisbane, QLD, Australia
[2] School of Health and Rehabilitation Sciences, The University of Queensland, Brisbane, QLD, Australia
[3] STARS Education and Research Alliance School of Health and Rehabilitation Sciences, The University of Queensland and Metro North Health, Brisbane, QLD, Australia

Purpose: Restrictions in occupational performance and participation in people with Parkinson's Disease (PwPD) are the result of both motor and non-motor symptoms. Therefore, approaches focusing solely on remediation of motor problems are inadequate to holistically address problems that PwPD experience. The Cognitive Orientation to daily Occupational Performance (CO-OP) approach is an occupation-based, metacognitive strategy approach with established efficacy in other neurological populations. The aim of this study was to explore and describe experiences of the CO-OP approach as reported by PwPD.
Methods: Interviews were conducted immediately following a 10-week CO-OP intervention, with open-ended interview questions about feasibility of the intervention based on Bowen's (2009) feasibility framework, exploring acceptability, implementation, practicality, adaptation and demand, and additional individualized questions exploring participant's perceptions and experiences of the intervention. A qualitative description approach using inductive thematic analysis of transcribed semi-structured interviews was carried out to understand participant's views and experiences.
Results: Interviews with 20 participants were completed. PwPD described the CO-OP intervention as a positive experience. They commonly expressed that learning and using the CO-OP strategies was worthwhile, meaningful, and useful over time. Concepts expressed by participants related to improved ability to manage daily life, changes in their ways of thinking and doing, improved insight, and self-efficacy for daily living in response to the intervention. PwPD described intervention structural elements as beneficial, such as a 10-week long intervention period allowing strong rapport development and consolidation of learned skills, the goal setting process and being in their own homes for the intervention.
Conclusion: This qualitative study describes the perspectives and experiences of PwPD following a CO-OP intervention. CO-OP was perceived as acceptable, worthwhile and valuable by participants, providing support for the benefit of and feasibility of the CO-OP approach for PwPD.

P25.17

The effect of rehabilitation interventions on freezing of gait in people with Parkinson's disease: A systematic review and meta-analyses

Lina Goh, Colleen G Canning, Jooeun Song, Lindy Clemson, Natalie E Allen*
The University of Sydney, Sydney, NSW, Australia

Background: Freezing of gait (FOG) commonly affects people with Parkinson's disease (PwPD) and may persist despite optimal medical intervention. Rehabilitation interventions may be used as an adjunct to reduce FOG but recent reviews examining the efficacy of rehabilitation were restricted to physical therapy interventions only and did not report prediction intervals (PIs), so the true effect in 95% of comparable studies is unknown.
Objective: To summarize the effects of rehabilitation interventions to reduce FOG in PwPD (PROSPERO registration: CRD42018116820).
Methods: Seven databases were searched for randomized trials of rehabilitation interventions (e.g., physical, cognitive, behavioural, occupational and psychotherapies) that reported a FOG outcome. Random-effects meta-analyses were performed for studies comparing an intervention to control and comparing two interventions. Quality of included studies and certainty of the pooled FOG outcome were assessed using the PEDro scale and GRADE framework.
Results: Sixty-five studies were eligible, with 62 trialling physical therapy/exercise, and five trialling cognitive and/or behavioural therapies. The overall mean PEDro score of the included studies was 6.1 out of 10. Thirty-two studies contributed to the meta-analyses; 20 compared physical therapy/exercise to control and 13 compared exercise interventions. Pooled FOG outcomes were measured using the FOG/New FOG Questionnaires (FOGQ/NFOGQ). All meta-analyses produced very low-certainty evidence. Physical therapy/exercise had a small effect on reducing FOG compared to control (Table 1). This effect represents a change of 1.1 points on the NFOGQ, whereas 9.95 points is considered the minimal detectable change1. The effect of exercise with cueing; action observation training plus physical movement strategy practice; and dance, when compared to exercise without cueing; physical practice alone; and multimodal exercise respectively, did not favour either intervention in 95% of comparable studies according to the PIs (Table 1).
Conclusion: We are uncertain if physical therapy/exercise, cognitive or behavioural therapies, are effective at reducing FOG. While there was a small, pooled effect in favour of physical therapy/exercise compared to control, its effect is unlikely to be clinically meaningful.

Table 1. Standardized mean difference, 95% confidence intervals (CIs), heterogeneity (I^2), and 95% prediction intervals (PIs) of effect of physical therapy/exercise interventions compared to control or another physical therapy/exercise intervention on freezing of gait post intervention.

Comparators	No. of studies	Hedges' g	95% CI	I^2 (%)	95% PI	GRADE
Physical therapy/exercise compared to Control	20	**-0.26**	**-0.38 to -0.14**	0	**-0.38 to -0.14**	Very low
Exercise with cueing compared to Exercise without cueing	6	**-0.58**	**-0.86 to -0.29**	28	-1.23 to 0.08	Very low
AOT plus physical practice of movement strategy compared to Physical practice alone	4	-0.56	-1.16 to 0.05	62	-3.01 to 1.89	Very low
Dance compared to Multimodal exercise	3	-0.64	-1.53 to 0.25	74	-10.98 to 9.70	Very low

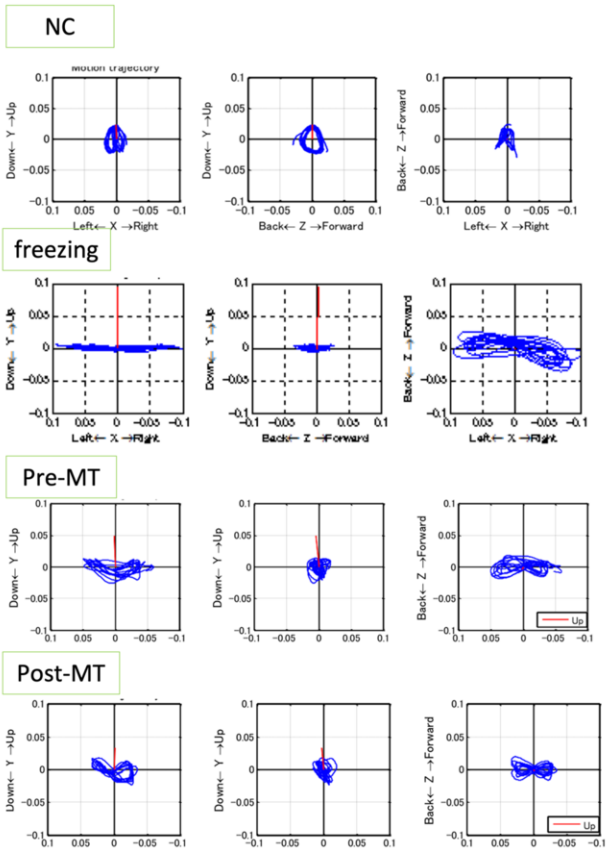
Significant findings ($p < 0.05$) shown in bold, in favour of physical therapy/exercise and exercise with cueing.
AOT = Action Observation Training, no. = number.

P25.18

Immediate effects of music therapy on gait disturbance in Parkinson's disease, and possibility to reduce the risk of freezing by analyzing the trajectory of center of body

*Emiri Gondo**
Juntendo University, Tokyo, Japan

External cues improve walking by evoking internal rhythm formation related to gait in the brain in people-with-Parkinson's-disease (PwP). The aim of this study was to investigate the immediate effect of music therapy (MT) on gait disturbance in PwP-without-freezing using a portable-gait-rhythmogram (PGR), and to examine the usefulness of MT by comparing it with gait in PwP-with-freezing.
Firstly, 19PwP who exhibited gait disturbance without freezing were evaluated for gait speed and step length during a 5m straight walking, and acceleration, cadence, and trajectory of the center of body (TCB) were estimated using PGR. Moreover, walking tasks were created while incorporating music intervention that gradually increased in tempo from 90 to 120 beats-per-minute (BPM). We then evaluated whether immediate improvement in gait could be recognized even without music after walking tasks by comparing pre-MT and post-MT values. Secondary, by using PGR, we examined gait acceleration and TCB in 43 PwP-with-freezing compared with 50 normal-control (NC) subjects on 5m walking.
Post-MT gait of PwP-without-freezing showed significant improvement in acceleration, gait speed, cadence, and step length. During transitions throughout the walking tasks, acceleration, gait speed, cadence, and step length gradually increased in tasks with music. On the other hand, for PwP-with-freezing, gait speed was significantly slow, the steps were small, the cadence was also slower compared as that of NC. In addition, the strength (acceleration) of PwP gait was apparently weak compared as NC. Furthermore, with regard to TCB, it was also found that PwP-with-freezing had a large ratio of amplitude of the medio-lateral direction (NC: Medio-lateral/Vertical=78.95% and Medio-lateral/Anteroposterior=107.14%, PwP-with-freezing: Medio-lateral/Vertical=277.78% and Medio-lateral/Anteroposterior=250%). The same tendency was observed in PwP-without-freezing, but we recognized a significant reduction the ratio of medio-lateral amplitude in post-MT (pre-MT: Medio-lateral/Vertical=194.31% and Medio-lateral/Anteroposterior=172.24%, post-MT: Medio-lateral/Vertical=157.0% and Medio-lateral/Anteroposterior=159.03%).
In this study, we evaluated the effects of MT and the characteristics of PwP's gait more objectively by using PGR. The MT was effective immediately on gait disturbance in PwP-without-freezing. In particular, by looking at changes in TCB, MT for PwP-without-freezing showed a reduction in medio-lateral amplitude, suggesting that, also for PwP-with-freezing who had greater medio-lateral amplitude, MT could reduce medio-lateral amplitude and subdue freezing.



P25.19

Effectiveness of transcranial direct current stimulation (tDCS) on clinical perceived pain and pain processing features in Parkinson's disease (PD) patients

Yeray González Zamorano*[,1], Francisco José Sánchez Cuesta[2], Aida Arroyo Ferrer[3], Marcos Moreno Verdú[2], Laura Valenzuela López[3], Josué Fernández Carnero[4], Juan Pablo Romero Muñoz[3]
[1] Department of Physical and Occupational Therapy, Rehabilitation and Physical Medicine, Universidad Rey Juan Carlos, Alcorcón, Spain
[2] Facultad de Ciencias Experimentales, Universidad Francisco de Vitoria, Madrid, Spain
[3] Facultad de Ciencias Experimentales, Universidad Francisco de Vitoria, Pozuelo de Alarcón, Spain
[4] Department of Physical and Occupational Therapy, Rehabilitation and Physical Medicine, Universidad Rey Juan Carlos, Alcorcón, Madrid, Spain

Background: Pain associated with PD is a common occurrence, affecting approximately 85% of patients. It significantly impacts their quality of life and is probably caused by changes in the way the brain processes and perceives pain due to the degeneration of dopamine and non-dopamine pathways that regulate pain. Both pain and PD can reduce activity in the primary motor cortex (M1). Transcranial direct current stimulation (TDCS) applied to the M1 has been shown to increase activity in brain regions involved in pain processing and reduce pain in other chronic pain conditions. However, its effectiveness for PD-related pain has not yet been studied.

Objective: To estimate the effectiveness of tDCS on perceived clinical pain and pain processing features associated with PD.
Methods: This is a randomized, triple-blinded, parallel-design study with 22 subjects (63.23±12.07). They were randomly assigned to one of two intervention groups: active-tDCS vs sham-tDCS. Active-tDCS group received 10 consecutive sessions of 20 min of tDCS with active anode on M1 at 2 mA intensity. The sham group followed the same protocol, but the tDCS stimulator was turned off at 30 seconds. King's Parkinson's Disease Pain Scale (KPPS), Pain Expansion, Temporal Summation (TS), and Conditioned Pain Modulation (CPM) were evaluated pre, post, and 15 days post-intervention.
Results: The results revealed significant differences in KPPS between groups in favor of active-tDCS group over sham-tDCS group at a follow-up of 15 days (p=0.014) but not immediately (p=0.059). Pain expansion also showed significant differences between groups in favor of active-tDCS group at 15 days (p=0.017) over sham-tDCS group. Moreover, the analyses showed significant differences in CPM between groups in favor of active-tDCS group post-intervention (p=0.002) and at 15 days (p=0.017) over sham-tDCS group. However, the results did not demonstrate statistically significant differences in the group-time interaction for TS.
Discussion: It seems that tDCS can potentiate the activation of the descending inhibitory pain systems through the improvement of the CPM immediately after 10 sessions. It is interesting that central desensitization of pain and reduction in the perceived pain require at least 15 days to occur after the end of treatment meanwhile improvements in the CPM are evident much earlier.

P25.20

Voice changes following deep brain stimulation in persons with Parkinson disease

Nicole Herndon[*,1], Karen Hegland*[2]
[1] UF Health, Gainesville, Florida, United States
[2] University of Florida, Gainesville, Florida, United States

Background: Nearly 1 million people in North America are now living with Parkinson disease (PD), and that number is projected to rise to nearly 1.2 million by 2030. With advancements in technologies, increasingly more of these individuals may elect to undergo deep brain stimulation (DBS) to control refractory and fluctuating motor symptoms in PD. Despite available research on motor symptoms after DBS, there is currently no consensus, and consequently no guidance, on whether communication related outcomes should be considered when selecting DBS target. Existing research suggests that voice production changes with DBS, however the nature, dynamics, phenotype(s) and extent of that change is not clear; this is due to substantial differences in methodologies across studies. Multiple groups have found high frequency stimulation (generally over 130 Hz) has a greater impact on voice versus low frequency stimulation.
Methods: Cross-sectional voice data was collected from forty-five persons with PD without DBS (n=10), with unilateral GPi DBS (n=9), unilateral STN DBS (n=8), bilateral Gpi DBS (n=8), and bilateral STN DBS (n=10). Speech tasks included spontaneous speech, sustained vowel phonation, and sentence repetition. Speech samples were analyzed using audio-perceptual ratings of voice (Consensus Auditory Perceptual Evaluation of Voice, CAPE-V) and acoustic measures (fundamental frequency, Jitter, Shimmer, harmonics-to-noise ratio, and smoothed cepstral peak prominence (CPPS)). Post hoc analysis of DBS stimulation spread in 12 patients who experienced no change, worsening voice, and improved voice was also completed.
Results: Significant differences for overall CAPE-V (p=.004), breathiness (p=.003), strain (p=.011), and loudness (p=.008) were found between the no DBS group and the bilateral STN group. There were also significantly higher CPPS on the sentence repetition task in the no DBS group compared to all DBS groups (p=0.02) was found. Preliminary data revealed relatively greater voxel overlap in subjects whose voice worsened compared to those who did not change or improved.
Conclusions: DBS was found to increase features of dysphonia, particularly following bilateral STN. Voice changes may be due to increased spread of DBS stimulation to the corticobulbar pathways.
Parts of this research were previously presented as a poster at the Fall Voice Annual Conference 2022.

P25.21

Speech and swallow trends following bilateral deep brain stimulation in persons with Parkinson disease: A retrospective chart review

Nicole Herndon[*,1], Karen Hegland*[2], May Smith-Hublou*[2]
[1] UF Health, Gainesville, Florida, United States
[2] University of Florida, Gainesville, Florida, United States

Background: Parkinson disease (PD) is a slowly progressive disease with a high prevalence of dysphagia and speech changes negatively impacting quality of life. As the prevalence of PD increases, so will the demand for advancing technology such as deep brain stimulation (DBS) to alleviate refractory or fluctuating motor symptoms of the disease. While it has been shown non-motor symptoms of cognition and mood can worsen with DBS, there continues to be inconclusive evidence on the impact of speech and swallow function following DBS implantation.
Methods: Retrospective chart review of 15 persons with PD who underwent a videofluoroscopic swallow study at our clinic between 2014-2019 before and after bilateral DBS implantation (Gpi= 10; STN=5) was completed. Video recordings were analyzed frame-by-frame and scored for functional outcomes of pharyngeal swallow safety, efficiency, and overall severity using the Dynamic Imaging Grade of Swallowing Toxicity (DIGESTv2, Hutchison et al., 2022). Additional retrospective chart review of 18 persons with PD who underwent an audio-perceptual speech evaluation at our center before and after bilateral Gpi DBS was completed. Descriptive statistics were used to analyze the data.
Results:
Pharyngeal Swallow Severity
Pre-DBS: normal=53%; mild severity=47%
Post-bilateral DBS: normal=53%; mild severity=40%; moderate=7%
Swallow Efficiency:
Pre-DBS: normal=53%; mildly inefficient=47%
Post-bilateral DBS: normal=53%; mildly inefficient=47%
Swallow Safety:
Pre-DBS: normal=93%; mildly unsafe=7%.
Post-bilateral DBS: normal=80%; mildly unsafe=13%; moderately unsafe=7%.
Speech Severity
All subjects demonstrated hypokinetic dysarthria (some with additional hyperkinetic features).
Pre-DBS: normal=5%; very mild=6%; mild=50%; mild-to-moderate=22%; moderate=17%
Post-bilateral DBS: very mild=11%; mild=22%; mild-to-moderate=34%; moderate=33% (worse: 50%; stable: 44%; improve 6%).
Conclusion: These findings indicate most of the subjects with PD who underwent bilateral DBS implantation did not experience worsening or improvement in functional swallow outcomes of pharyngeal safety and efficiency. There was a trend in worsening speech severity following post-bilateral DBS implantation with 50% of subjects noted to increase by at least one severity rating. Overall, speech and instrumental swallow evaluations are important for

determining patients comprehensive risk-benefit ratio for surgery and management of potential changes following the procedure.

P25.22

Effects of motor-cognitive training on dual task performance in people with Parkinson's disease: A systematic review and meta-analysis

Hanna Johansson[*,1], Ann-Kristin Folkerts[2], Ida Hammarström[3], Elke Kalbe[2], Breiffni Leavy[3]*
[1] Karolinska Institutet, Huddinge, Sweden
[2] University of Cologne, Cologne, Germany
[3] Karolinska Institutet, Stockholm, Sweden

Motor-cognitive training in Parkinson's disease (PD) can positively affect gait and balance, but whether motor-cognitive (dual task) performance improves is unknown. This meta-analysis therefore aimed to establish the current evidence on the effects of motor-cognitive training on dual task performance in PD. Systematic searches were conducted in five databases and 11 studies with a total of 597 people (mean age: 68.9 years; mean PD duration: 6.8 years) were included. We found a mean difference in dual task gait speed (0.12m/s (95% CI 0.08, 0.17)), dual task cadence (2.91 steps/min (95% CI 0.08, 5.73)), dual task stride length (10.12 cm (95% CI 4.86, 15.38)) and dual task cost on gait speed (-8.75% (95% CI-14.57, -2.92)) in favor of motor-cognitive training compared to controls. The GRADE analysis revealed that the findings were based on high certainty evidence. Thus, we can for the first time systematically show that people with PD can improve their dual task ability through motor-cognitive training.

P25.23

Occupational outcomes in individuals with Parkinson's disease using a small group functional skill training approach

Noelle Joyner[*,1], Heather Simpson*[*,2], Alison Kraus[2], Becky Farley[3]*
[1] University of Florida – Department of Occupational Therapy, Gainesville, United States
[2] UF Health Norman Fixel Institute for Neurological Diseases, Gainesville, United States
[3] Parkinson Wellness Recovery, Tucson, United States

Background: High-amplitude training in 1:1 rehabilitation interventions have been successful in recalibrating motor movements for people with PD. However, a singular focus on amplitude does not address the multiple motor and non-motor symptoms that interfere with everyday life. In addition, 1:1 rehabilitation hasn't shown the same psychosocial benefits observed in group exercise. In response, we piloted a multisymptomatic approach emphasizing functional skill training implemented as a group occupational and physical therapy (OT/PT) program to explore if the benefits of rehabilitation and group exercise were additive. For this abstract, results were focused on OT measures of hand dexterity, occupational performance, psychosocial impacts, and symptoms.
Methods: 5 participants over 50 years of age with a diagnosis of mild to moderate PD, participated in 1-hour group intervention sessions 3x/week for 6 weeks in a clinical outpatient setting. An exploratory, pre- and post-test case series design investigated standard rehabilitation measures in conjunction with clinical questionnaires. The intervention protocol introduced functional skills and salient movement sequences before progressing complexity to mimic the physical and cognitive challenges of daily life. PTs/Ots administered assessments to participants and sessions were billed to insurance.
Results: The group average for perceived performance on self-selected occupational goals improved 29.6% on the Canadian Occupational Performance Measure; indicating an increased ability for patients to perform daily activities ranging from hygiene to hobbies. This was corroborated by PDQ-39 results where the group improved 39.7% in PD-specific symptoms impacting quality of life. The Coin Rotation Task and Functional Dexterity Test (FDT) saw improvements in dexterity for either one or both hands in all participants; with all participants FDT scores improving 20-65% in their non-dominant hand. Additionally, participants reported high satisfaction and motivation to enroll in future group rehabilitation as well as reporting the social aspect of the sessions as important on a questionnaire designed for the study.
Conclusion: Findings suggest multisymptomatic functional skill training offered as group rehabilitation may transfer to more domains than previously tested, provide a novel solution for improving and sustaining the benefits of the more traditional 1:1 rehabilitation, and help address the growing demands for therapeutic intervention as the rate of disability in PD grows.

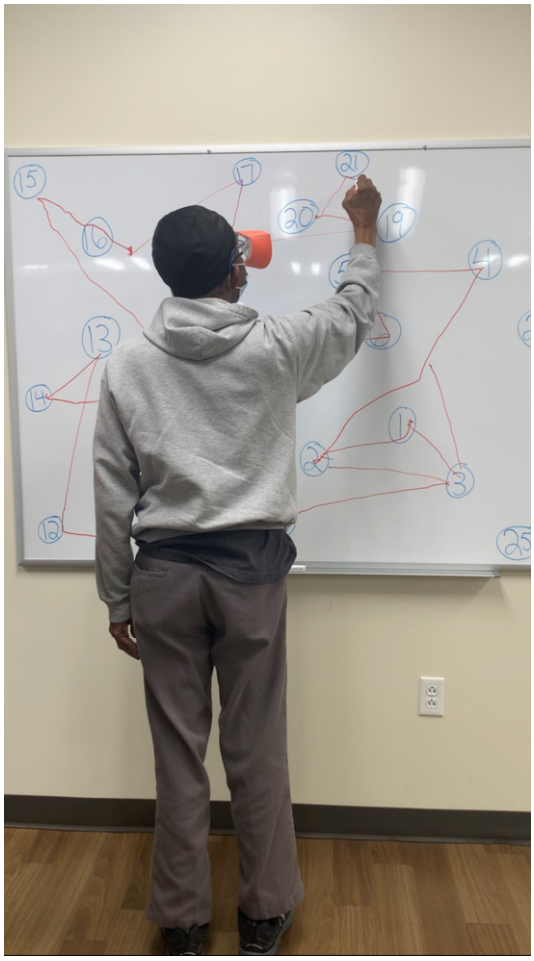
P25.24

Use of constraint induced goggles to manage dystonia and axial rigidity in Parkinsonism

Aison Kraus[*,1], Paul Auth[2], Nicole Tester[3], Michael Okun[4]*
[1] UF Health Rehab at Norman Fixel Institute for Neurologic Diseases, Gainesville, Florida, United States
[2] University of Florida, FL, United States
[3] UF Health Rehab at Fixel Institute for Neurologic Diseases, Gainesville, FL, United States
[4] University of Florida & Fixel Institute for Neurologic Diseases, Gainesville, FL, United States

Objective: Idiopathic and atypical Parkinsonism present with rigidity and bradykinesia, but also can include cervical dystonia, cognitive impairments, postural instability and vertical gaze palsy. Any combination of impairments can limit functional activities and community ambulation. Specifically, the ways in which these symptoms can impair the ability to scan the environment in a person with Parkinson disease (PwP) compromises or limits safe ambulation, communication, and participation in activities of daily living.
Rehabilitative approaches combine adaptive and compensatory techniques to promote maximum independence with functional activities to address impairments of dystonia, axial rigidity, and decreased visual scanning. Physical therapists often incorporate explicit cuing for prolonged benefits of interventions. Due to difficulties with cognition, however, implicit motor learning may offer a more effective strategy in some PWP. Constraint Induced Movement Therapy (CIMT), or forced use of the affected limb, post-stroke is widely accepted as a strategy to increase use of the affected limb during functional activities. A similar technique of forced use is being applied to persons with atypical Parkinsonism (PSP) and idiopathic Parkinson disease with similar symptoms.
Methods: Constraint Induced Goggles were trialed to promote increased cervical and trunk mobility as a strategy to address cervical dystonia, axial rigidity and gaze palsy. The goggles forced individuals to localize targets by rotating and extending their neck and trunk, versus compensating with use of peripheral vision. Individuals received 6 weeks of training (1-2x/week) with the goggles during physical therapy sessions. Pre- and post-intervention assessments included a modified Trails A test, balance and gait tests, and subjective questionnaires.
Results: With research ongoing, 2/2 individuals who have undergone training have shown improvements in the Berg Balance Assessment, 5 Time Sit to Stand, modified Trails A and subjective report of ADL performance. We believe the constraint induced

goggles address limitations in visual scanning by reducing rigidity and increasing active range of motion during functional tasks.
Conclusions: This ongoing case series demonstrates feasibility and efficacy of constraint induced goggles in high complexity atypical Parkinsonism. Its application may provide benefit to other PWP. Specifically, the use of implicit motor learning may be useful in addressing cervical dystonia and axial rigidity in Parkinson disease.



P25.25

The application of PD specific functional training in group rehabilitative sessions – Physical performance outcomes
Aison Kraus[*,1], Heather Simpson[2], Noelle Joyner[3]*
[1] UF Health Rehab at Norman Fixel Institute for Neurologic Diseases, Gainesville, Florida, United States
[2] UF Health Rehab at Fixel Institute for Neurologic Diseases, FL, United States
[3] University of Florida, Gainesville, FL, United States

Objective: High amplitude training in 1:1 rehabilitation has been successful in addressing bradykinesia and hypokinesia in patients with Parkinson disease. However, access to skilled neurologic physical and occupational therapists is limited, making it more difficult for individuals to access the care throughout the disease course. Community group exercise classes for functional movements, like PWR! Classes have become more popular, but patient outcomes have not been studied. The feasibility, safety and effectiveness of group rehabilitative sessions, administered by neurologic physical and occupational therapists, 3x/week for 6 weeks was assessed.
Methods: Five participants with idiopathic Parkinson disease completed a 6 week (18 sessions) group rehabilitative program emphasizing PD-specific, functional training (PWR! Classes). A wide range of patient presentation was incorporated into one single class based on patient need vs selecting patients of the same physical and cognitive baseline. The program worked to address rigidity, and bradykinesia affecting posture, transfers, and ambulation. As the weeks progressed, the complexity in training mimicked physical and cognitive challenges of daily life. The Timed Up and Go, Mini BESTest, 10MWT, 5 time sit to stand test, floor transfer test, and 3 meter backward walk test were administered to assess changes after group rehabilitative sessions.
Results: All 5 participants completed at least 16 visits of group rehabilitation over a 7 week period (1 week for makeup classes). Improvements in floor transfer test averaged 6.12 seconds with less assistance needed. A 10.65% improvement was the average seen in the Mini BESTest after 16 visits. 5 Time sit to stand test also improved with an average decrease of 3.418 seconds.
Conclusions: Application of functional task training is safe and effective in small group rehabilitative sessions. Despite the wide range of functional limitations in participant presentation, all participants demonstrated improvements in standardized assessments. These preliminary data demonstrate that functional improvements may be achieved in individuals with Parkinson disease working in a group rehabilitation setting. This may offer a solution to meet the growing demands for neurologic interventions compared to the more traditional 1:1 rehabilitation provided by a skilled therapist; addressing the increased rate of disability in Parkinson disease.

P25.26

Defining the components of an occupation-based intervention for people with Parkinson's with anxiety using Group Concept Mapping
Chris Lovegrove[*,1], Jon Marsden[1], Ingrid Sturkenboom[2], Katrina Bannigan[3]*
[1] University of Plymouth, Plymouth, Devon, United Kingdom
[2] Radboud University Medical Centre, Nijmegen, Netherlands
[3] Glasgow Caledonian University, Glasgow, Scotland, United Kingdom

Background: Anxiety is a common symptom of Parkinson's disease. The presence of anxiety in people with Parkinson's results in reduced quality of life, reduced participation in meaningful occupations, and increased health burden. There are no evidence-based interventions to reduce the impact of anxiety in Parkinson's on occupational participation. People with Parkinson's have expressed that new interventions should be focused on 'doing' as opposed to talking therapies. This study aimed to identify the key components required for the future co-production of an anxiety-focused intervention in Parkinson's.
Methods: A participatory mixed methods research study was conducted using an online Group Concept Mapping methodology. This involved five stages: brainstorming, idea synthesis, sorting activity, rating activity, and analysis. Based on participants' responses a cluster map, pattern match, and 'go-zone' charts were created through a multivariate statistical analysis. Stages were guided by questions generated by the research team in conjunction with stakeholder involvement.
Findings: Eighty-three people participated, with 64 taking part in more than one activity. Participants consisted of people with Parkinson's (n=72), care partners (n=6), and occupational therapists

(n=5). Following the 'idea synthesis' activity, 119 statements were included in the final map with eight clusters (stress value 0.252). There was significant concordance between the importance and feasibility rating activities (r = -0.07). 'Go-zone' charts highlight the statements considered priorities for intervention development.
Conclusion: This study used a systematic approach to identify important concepts for possible inclusion in a new intervention to help people with Parkinson's to live well with anxiety. The findings highlight eight priority components, presented as clusters and named using the participant's words, for consideration in the future intervention. These were: Access to information, Professional help, Peers and groups, Support from others, Coping, Self help, Lifestyle changes, and Exercise. Individual ideas rated highly on both importance and feasibility have been identified in go-zone graphs and are suggested starting points for future intervention development.
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P25.27

Developing an occupation-based complex intervention for living well with anxiety and Parkinson's (OBtAIN-PD): A logic modelling approach
Chris Lovegrove[*,1], Jon Marsden[1], Ingrid Sturkenboom[2], Katrina Bannigan[3]*
[1] University of Plymouth, Plymouth, Devon, United Kingdom
[2] Radboud University Medical Centre, Nijmegen, Netherlands
[3] Glasgow Caledonian University, Glasgow, United Kingdom

Background: Parkinson's is a neurodegenerative condition affecting around 10 million people worldwide. Anxiety is a common symptom in Parkinson's and is associated with reduced life quality, independence, and health outcomes. Current anxiolytic medications are ineffective. The results of studies into promising behavioural interventions are mixed and inconclusive. Occupational therapy is effective at promoting participation and is recommended in guidelines internationally. An evidence-based occupational therapy intervention for anxiety in Parkinson's does not exist. A new occupation-based complex intervention for anxiety was co-produced with people with Parkinson's, carers, and occupational therapists.
Objectives: To design an occupation-based complex intervention for living well with anxiety and Parkinson's (OBtAIN-PD) in co-production with people with Parkinson's, their carer partners, and occupational therapists.
Method: Logic modelling was used to prioritise and structure elements for the new intervention, using components identified from previous research and the participants' own lived experience. Participants were provided with 'information packs' prior to data collection sessions that consisted of a summary of the research team's findings to date. Online data collection was utilised following pilot testing.
Results: Participants (n=34) were recruited via purposeful sampling to engage in logic modelling to reach a consensus on the intervention design. Participants included people with Parkinson's (n=13), care partners (n=10), and occupational therapists (n=11). Included components include a focus on 'doing' as the means of delivering and measuring the intervention, the use of behavioural activation concepts to engage those receiving the intervention, and a lifestyle management approach to support living well with anxiety and Parkinson's. The OBtAIN-PD comprises an individualised intervention provided according to the criteria outlined in an accompanying manual. A review with eleven occupational therapists was performed to check content and comprehension.
Conclusion: This study led to the co-production of a new occupation-based complex intervention for living well with anxiety and Parkinson's (OBtAIN-PD), integrating current research findings with lived experience. The OBtAIN-PD will be explored in a feasibility randomised controlled trial.
Funding: National Institute for Health Research Clinical Doctoral Research Fellowship (NIHR301565).

P25.28

Evaluating the occupation-based complex intervention for living well with anxiety and Parkinson's disease (OBtAIN-PD): A feasibility cluster randomised controlled trial protocol
Chris Lovegrove[*,1], Jon Marsden[1], Chris Hayward[2], Joanne Hosking[1], Ingrid Sturkenboom[3], Katrina Bannigan[4]*
[1] University of Plymouth, Plymouth, Devon, United Kingdom
[2] Peninsula Clinical Trials Unit, Pymouth, United Kingdom
[3] Radboud University Medical Centre, Nijmegen, Netherlands
[4] Glasgow Caledonian University, Glasgow, United Kingdom

Background: Anxiety is a common non-motor symptom of Parkinson's and is associated with reduced life quality, independence, and health outcomes. Studies of anxiolytic medications and behavioural interventions to reduce anxiety provide inconclusive evidence. A new occupation-based and participation-focused complex intervention for living well with anxiety and Parkinson's (OBtAIN-PD) was co-produced with people with Parkinson's, carers, and occupational therapists. Feasibility testing is required to plan a future definitive trial.
Aim: To determine the feasibility of a cluster randomised trial design of the OBtAIN-PD in a real-world setting.
Methods: The study design was developed in collaboration with patient, carer, and healthcare professional stakeholders. The cluster RCT design was chosen to minimise potential contamination across intervention groups. We aim to recruit 50 participants across two clusters in the Southwest of England, UK. Eligible patients will have a formal Parkinson's diagnosis, score ≥10 on the GAD-7, without severe cognitive impairment, not receiving end-of-life care, nor another clinician-delivered non-pharmacological anxiety intervention. After screening, 1:1 cluster-level randomisation will allocate the participant to the OBtAIN-PD intervention or usual occupational therapy care. Participants will complete baseline clinical measures with a blinded researcher, undertaken remotely to minimise the risk of unblinding and to reduce patient burden, and remote patient-reported outcomes. Follow-up will be at 12 and 24 weeks. Feasibility outcomes comprise recruitment, intervention delivery, retention, and follow-up. A process evaluation will contribute to iterative intervention optimisation, implementation, and identifying contextual factors influencing OBtAIN-PDs delivery and uptake. An embedded qualitative study will interview 12 participants and the trial occupational therapists to explore their subjective experience of the OBtAIN-PD and trial design.
Discussion: We will evaluate the feasibility of conducting a cluster RCT of the OBtAIN-PD in a community population of people with Parkinson's. Key objectives will be to test the fidelity of trial design and intervention delivery, gather recruitment data to refine sample size calculation for the planned definitive trial, optimise data collection processes such as follow-ups, and optimise the intervention including training and delivery. A trial status update will be provided, such as current recruitment and participant dropout.
Funding: National Institute for Health Research Clinical Doctoral Research Fellowship (NIHR301565).

P25.29

Long-term effects of a 6-month brisk walking and balance program on physical performance and health-related quality of life in people with Parkinson disease: A randomized controlled trial

Margaret KY Mak, Irene SK Wong-Yu*
Department of Rehabilitation Sciences, The Hong Kong Polytechnic University, Hong Kong, Hong Kong

Background: Previous study indicated that a 6-month brisk walking and balance program alleviated motor symptoms, and increased fast gait speed and walking capacity at post-training in people with mild to moderate Parkinson's disease (PD) (Mak & Wong-Yu, 2021). However, the longer-term effects of brisk walking on comfortable gait speed (CGS), walking capacity and health-related quality of life (HRQoL) among people with PD have not been investigated.
Objectives: To examine whether the brisk walking and balance program would be effective in improving CGS, walking capacity and HRQoL in people with PD at post-training (Post6m) and 6-month follow-up (FU6m).
Methods: Eligible participants were randomized into either experimental (EXP) or control (CON) group. In 6 months, EXP group received 10 sessions of balance training and brisk walking exercise supervised by physiotherapist (targeting at 40-60% heart rate reserve using smartwatch heart rate monitor), while CON group received stretching and low-intensity strengthening exercises at same dosage. All participants performed home exercise 2-3 times weekly during intervention and until FU6m in the community. Outcome measures included CGS, six-minute walking distance (6MWD) and Parkinson Disease Questionnaire-8 (PDQ8) score.
Results: 142 participants (71 EXP, 71 CON) were randomized and 131participants (67 EXP and 64 CON) completed 6m training. Thirteen participants dropped out during 6m FU. Significant group*time interactions were found for all outcomes using 2-way ANOVA and intent-to-treat analysis (N=131). At Post6m, only EXP group significantly decreased PDQ8 score (-1.0 points), and increased CGS (+14.8 cm/s) and 6MWD (+41.6m) from baseline. At FU6m, only EXP group significantly increased CGS (+16.2 cm/s) and 6MWD (+36.4m) from baseline. Six-month attendance was 96.6% with very few adverse effects during intervention/follow-up.
Conclusion: Brisk walking and balance program enhanced gait speed, walking capacity and health-related quality of life at Post6m. This useful exercise protocol also enhanced longer-term improvements at FU6m in gait performance and walking capacity among people with mild to moderate PD.

P25.30

Does hand exercise and training improve dexterity and function in people with Parkinson's disease? A systematic review and meta-analysis

Jennifer McGinley[,1], Elizabeth Proud[2], Kimberly Miller[3], Meg Morris[4], Jannette Blennerhassett[5]*
[1] The University of Melbourne, Melbourne, Australia
[2] The University of Melbourne, Parkville, Australia
[3] BC Children's Hospital Research Institute, Vancouver, Canada
[4] La Trobe University, Bundoora, Australia
[5] Austin Health, Heidelberg, Australia

Introduction: Dexterity and hand function problems are frequently reported by people with Parkinson's disease (PD) yet there is limited evidence to guide physiotherapy and occupational therapy practice. This systematic review and meta-analysis investigated the effects of exercise and training programs on dexterity and hand function in people with PD. (PROSPERO CRD42018090284).
Methods: Five databases were searched for randomised controlled trials (RCTs) which 1) included participants with PD; 2) aimed to improve arm or hand function with exercise or training; 3) measured upper limb activity or participation, and 4) were published in English. Following screening, Cochrane Risk of Bias and GRADE tools were applied to assess risk of bias and quality of evidence, respectively. Data extracted were participant demographics, details of the interventions, and outcomes related to hand dexterity, self-reported hand function and handwriting performance. Meta-analyses were completed for dexterity (pegboard scores combined at the within hand level) and self-reported hand function outcomes. Handwriting performance data could not be pooled.
Results: Eighteen RCTs (n = 704) of variable quality were included. Most participants had mild to moderately severe PD. Interventions varied in their treatment focus, approach, and intensity. All studies delivered trained tasks, with varied use of strategies to promote skill acquisition. Three studies focused on handwriting, eight were home-based, and seven utilized technology to deliver training. Meta-analyses showed that training had positive, yet small, effects on dexterity (SMD = 0.25; 95% Cis 0.07, 0.44) (10 studies). Effects on self-reported hand function were not statistically significant (SMD = 0.67; 95% Cis -0.40, 1.75) (four studies). Handwriting studies reported improvements in performance following training. The GRADE strength of evidence was moderate (dexterity), low (handwriting) and very low (self-reported hand function).
Conclusions: Moderate certainty of evidence supports the use of exercise and training to improve dexterity but remains unclear for self-reported hand function. Application of task-specific training seems promising to improve handwriting, but current evidence cannot be pooled to assess certainty. More research is needed to inform clinical practice about the key elements and dose of exercise and training necessary to improve hand function in people with PD.

P25.31

Gait impairments in Parkinson's disease

Anat Mirelman[,1], Richard Camicioli[2], Terry Ellis[3], Jochen Klucken[4], Larry Gifford[5], Jeffrey Hausdorff[1], Elisa Pelosin[6], Paolo Bonato[7], Alfonso Fasano[8], Alice Nieuwboer[9]*
[1] Tel Aviv University, Tel Aviv, Israel
[2] University of Alberta, Edmonton, Canada
[3] Boston University, Boston, United States
[4] University of Luxembourg, Luxembourg, Luxembourg
[5] NA, Vancouver, Canada
[6] University of Genova, Genova, Italy
[7] Spaulding Rehabilitation Hospital, Boston, United States
[8] University of Toronto, Toronto, Canada
[9] KU Leuven University, Leuven, Belgium

Gait disturbances play a major role in the motor manifestation of Parkinson's disease (PD). Alterations in the gait pattern can already be detected in recently diagnosed, de novo patients, even before any visible or symptomatic gait disturbances are reported and these tend to deteriorate over time. However, there is a wide range in the manifestation of gait impairments among patients. In recent years, real-world gait assessment has provided more insight into how gait impairments affect function and the quality of life of people with PD during everyday life activities linked to regular healthcare routines. The mechanism of gait disorders has also been extensively evaluated over the years, increasing the understanding of the complex interplay between dopaminergic and non-dopaminergic contributions. However, the design of potential interventions to alleviate gait impairments remains a big challenge.
The GALOP committee is an advisory committee for the Michal J Fox Foundation for Parkinson's research. The committee comprises a person with PD living with gait issues and experts in the field of

gait, from academia and clinical care, who aim to progress research and treatment of gait impairments. In this work, we will summarize the evidence published in recent years (2022-June 2023) in three fields of gait research: mechanisms, assessment, and interventions, summarizing the most current and robust studies. We will focus on the promise of technology to facilitate ever more precisely delivered assessment and treatment for gait and practices that can differentiate care for different patients, moving beyond a "one-size-fits-all solution" towards personalized approaches. The summary will be made available for clinicians and people with PD and inform the direction of future research avenues.

P25.32

Effectiveness of balanceHOME program in functional mobility and cognitive performance in Parkinson's disease: A case study with mild cognitive impairment

Sara Monleón Guinot[*,1], *José M. Tomás*[1], *Joan Sánchez-Ortí*[2], *Vivina Aranda Asensi*[3], *Concepción de Salazar Antón*[3], *Manuel Villanueva Navarro*[3], *Constanza San Martín Valenzuela*[*,4]
[1] Deparment of Behavioral Sciences Methodology, Faculty of Psychology, University of Valencia., Valencia, Spain
[2] Unit of Personal Autonomy, Dependency, and Mental Disorders Assessment, INCLIVA Biomedical Research Institute., Valencia, Spain
[3] Asociación Parkinson Valencia Neurorehabilitation Center, Valencia, Spain
[4] Unit of Personal Autonomy, Dependency, and Mental Disorders Assessment, INCLIVA Biomedical Research Institute; Departament of Physiotherapy, Faculty of Physiotherapy, University of Valencia; Centro de Investigación Biomédica en Red de Salud Mental (CIBERSAM), Instituto de Salud Carlos III, Madrid, Spain., Valencia, Spain

Introduction: Studies with physiotherapy programs at home have been carried out so far in people with Parkinson's disease (PD) with normal cognitive status and with restrictive environments as well as balance evaluation conditions. We document a case study involving a 60-year-old male with idiopathic PD stage III, mild cognitive impairment (MCI), history of stumbling, and balance perturbances. The aim of this study is to analyze the effectiveness of balanceHOME program on balance and cognitive performance during 1-year of follow-up in a person with PD-MCI.
Methods: The participant followed the balanceHOME program (NCT04963894) which includes balance exercises incorporated into functional daily tasks, developed in-home, and conducted two times per week for 60-min over 8 weeks period. The assessment schedule study is shown in Figure 1. Static and dynamic balance was evaluated with a dynamometric platform through the Romberg tests, four functional tasks of daily life (visual, verbal, upper motor and lower motor), and two control tests over the center of pressure (CoP) movement during the limits of stability exploration (success and control) and the rhythmic displacement of CoP to side-to-side (ability). Cognition was measured through the MiniMental Parkinson (MMP) and the Frontal Assessment Battery test; the Scales for Outcomes in Parkinson's Disease-Cognition for the evaluation of cognitive performance (SCOPA-COG), and the Parkinson's Disease Questionnaire (PDQ-39) for the evaluation of quality of life.
Results and discussion: Once the intervention program was completed, an improvement of 36.25%, 71.24%, and 83.97% was observed in the variable CoP swept area in the Romberg test with eyes open (ROA), in visual and upper motor functional test, respectively. Regarding the stability limits exploration, an improvement of 4.62% and 57.56% was observed in directional control and success variables. Improvements in balance began to be observed from session 4 on balance performance during static functional test visual (23.94%), verbal (32.14%), lower motor (32.07%), and upper motor (104.44%). During follow-up, the effects lasted up to 2-months with a mean of 24.29% improvement on the CoP swept area during Romberg tests. The mentioned effect size can be explained by the fact that balance training has a greater impact in daily challenging environments than in clinical settings.

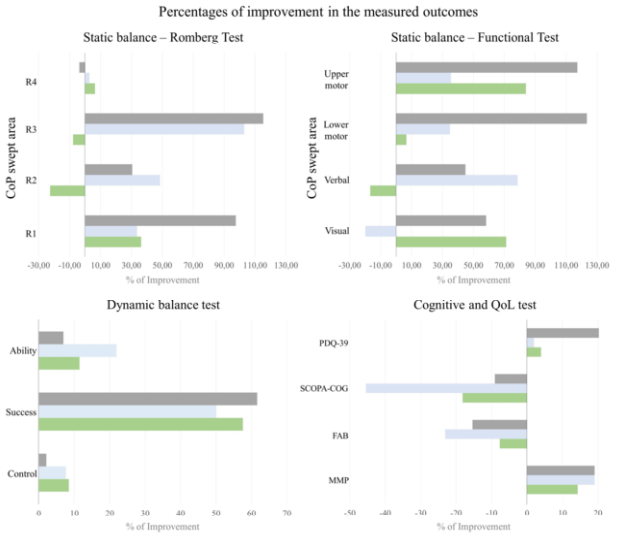

Figure 1 – Percentages of improvement in the measured outcomes. Green bars indicate improvement at post balanceHOME assessment compared to baseline; blue bars indicate improvement at 2-months follow-up compared to baseline; Grey bars indicated improvement at 4-months follow-up compared to baseline. CoP, center of pressure. R1, Romberg test with eyes open; R2, Romberg test with eyes closed; R3, Romberg test with eyes open on a foam rubber; R4, Romberg test with eyes closed on a foam rubber. QoL, quality of life test; MMP, Mini-Mental Parkinson; FAB, Frontal Assessment Battery; SCOPA-COG, Scale for Outcomes in Parkinson's disease-Cognition; PDQ-39, Parkinson's Disease Questionnaire.

P25.33

Crowdsourced perceptual ratings of voice quality in people with Parkinson's disease before and after intensive voice and articulation therapies: Secondary outcome of a randomized controlled trial

Tara McAllister[1], *Christopher Nightingale*[2], *Gemma Moya-Galé*[*,3], *Ava Kawamura*[4], *Lorraine Ramig*[5]
[1] New York University, New York, United States
[2] Gallaudet University, Washington D.C., United States
[3] Long Island University, Brooklyn, United States
[4] Georgetown University, Washington D.C., United States
[5] LSVT Global Inc., National Center for Voice and Speech/Boulder, New York, United States

Limited research has examined the suitability of crowdsourced ratings to measure treatment effects in speakers with Parkinson's Disease (PD), particularly for constructs such as voice quality. This study obtained measures of reliability and validity for crowdsourced listeners' ratings of voice quality in speech samples from a published study (Moya-Galé et al., 2022). We also investigated whether aggregated listener ratings would replicate the original study's findings of treatment effects based on the Acoustic Voice Quality Index (AVQI) measure.
This study reports on a secondary outcome measure of a randomized controlled trial (RCT) with speakers with dysarthria associated with PD, including two active comparators (LSVT LOUD and LSVT ARTIC), an inactive comparator, and a healthy control group. Speech samples from three time points (pre-treatment, post-treatment, six-month follow-up) were presented in random order for rating as "typical" or "atypical" with respect to voice quality. Untrained listeners were recruited through the Amazon Mechanical Turk crowdsourcing platform until each sample had at least 25 ratings.

Intrarater reliability for tokens presented repeatedly was substantial (Cohen's kappa .65-.70) and interrater agreement significantly exceeded chance level. There was a significant correlation of moderate magnitude between the AVQI and the proportion of listeners classifying a given sample as "typical.". Consistent with the original study, we found a significant interaction between group and time point, with the LSVT LOUD group alone showing significantly higher perceptually rated voice quality at post-treatment and follow-up relative to the pre-treatment time point.
These results suggest that crowdsourcing can be a valid means to evaluate clinical speech samples, even for less familiar constructs such as voice quality. The findings also replicate the results of Moya-Galé et al. (2022) and support their functional relevance by demonstrating that the effects of treatment measured acoustically in that study are perceptually apparent to everyday listeners.
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P25.34

Clinicians' self-perceptions of LSVT LOUD Globally: Data from Germany, France, and Japan

Gemma Moya Galé[*1], Thomas Brauer[2], Catherine Airiau[3], Masako Fujiu-Kurachi[4], Cynthia Fox[5], Heike Penner[6], Petra Benecke[7], Lorraine Ramig[8]*
[1] Long Island University, Brooklyn, United States
[2] Lehranstalt fuer Logopaeden, Universitaetsmedizin, Mainz, Germany
[3] Logotop, Medocentre, Vannes, France
[4] International University of Health and Welfare, Chiba, Narita, Japan
[5] University of Colorado-Boulder, National Center for Voice and Speech, LSVT Global, Inc, Tuscon, United States
[6] Abt. Logopaedie, Agaplesion-Bethanien-Krankenhaus, Heidelberg, Germany
[7] Abt. Logopaedie, Paracelsus-Elena-Klinik, Kassel, Germany
[8] LSVT Global, Inc., National Center for Voice and Speech/Boulder, New York, United States

This project was designed to evaluate the implementation of an efficacious voice treatment, Lee Silverman Voice Treatment (LSVT LOUD), into scope of clinical speech practice in Germany, France and Japan. 404 clinicians trained in LSVT LOUD were surveyed on a range of variables including training effectiveness and treatment outcomes.
Evidence-based rehabilitation without successful implementation has limited impact on patient care (Center for Research in Implementation Science and Prevention (CRISP), 2015). This proposal will describe the implementation of LSVT LOUD, which currently has five randomized controlled trials (RCTs) documenting its short and long-term efficacy in the USA, into the clinical speech practice in Germany, France and Japan.
The translation pathway recommended by CRISP was followed, with emphasis on treatment fidelity. Thus, a key element in the implementation process was standardized training of speech clinicians. A fundamental goal was maintaining the fidelity of the training while respecting the culture of the country.
Thirty-five LSVT LOUD Training and Certification Courses were held throughout Germany, France and Japan since 2000 resulting in more than 3,000 LSVT LOUD Certified clinicians. All training materials were translated into German, French and Japanese by native speakers and all training courses were delivered live with either simultaneous or subsequent translation.
To assess implementation and treatment fidelity of LSVT LOUD, an online survey was administered (Survey Monkey) to these LSVT LOUD Certified clinicians.
Preliminary results revealed 72-90% of clinicians surveyed felt they had received effective training in LSVT LOUD and 62-72% felt they were achieving better outcomes with LSVT LOUD than previous approaches. These findings were consistent with a pilot surveys of groups of German and French clinicians (Brauer et al., 2016; 2018).
LSVT LOUD is being implemented successfully into scope of clinical speech practice in Germany, France and Japan. This successful implementation of science into clinical practice model provides a road map for other countries where LSVT LOUD clinicians are trained (over 20,500 LSVT LOUD clinicians in 75 countries).
Funding Statement: Research reported in this publication was supported by the National Institute on Deafness and Other Communication Disorders Awards R01DC001150 (L. Ramig, PI) and by LSVT Global, Inc.

P25.36

Clinical practice guideline for the physical therapist management of Parkinson disease: An American physical therapy association and academy of neurologic physical therapy collaboration for quality improvement

Miriam Rafferty[*1], Beth Crowner[2], Jacqueline Osborne[3], Terry Ellis[4]*
[1] Shirley Ryan AbilityLab; Northwestern University, Chicago, Illinois, United States
[2] Washington University in St. Louis, St. Louis, MO, United States
[3] YouMeCare, Jacksonville, FL, United States
[4] Boston University, Boston, MA, United States

Best practice for people with Parkinson disease (PD) includes consulting with a physical therapist to address changes in physical function and to establish or progress an exercise program. To ensure best physical therapy (PT) interventions for people with PD, the American Physical Therapy Association convened a Guideline Development Group in 2019, which published a Clinical Practice Guideline (CPG) in 2021. The purpose of the CPG is to standardize PT interventions based on the best available evidence to optimize best practice globally to improve outcomes for people with PD.
The CPG recommends gait training, balance training, task-specific training, and external cueing to improve walking and functional mobility outcomes, including freezing of gait and fall risk (balance confidence). PT interventions that can improve motor disease severity include aerobic exercise, resistance training, and gait training. The CPG also strongly recommends inclusion of appropriately-dosed exercise interventions, including aerobic training, resistance training, and balance training. Flexibility training is recommended as a part of warm-up and cool-down activities. Physical therapists should use behavior change approaches to help improve physical activity and quality of life for people with PD. Physical therapists should work within integrated (interdisciplinary) care teams, should recommend community-based exercise, and may use telerehabilitation as a part of their physical therapy practice.
To facilitate dissemination and implementation of this CPG, the Academy of Neurologic Physical Therapy created a Knowledge Translation Task Force in 2021. The Task Force surveyed the knowledge, attitudes, and behaviors of over 300 physical therapists in the United States regarding CPG implementation. In response to the survey results, the task force is creating and disseminating freely-available knowledge translation tools for people with PD and physical therapists. These tools focus on appropriate exercise prescription, application of behavior change techniques, and handouts that physical therapists can provide to improve patient/care partner education and outreach. We will summarize the tools available in the virtual toolbox here:

https://www.neuropt.org/practice-resources/anpt-clinical-practice-guidelines/pt-management-of-parkinson-disease.
The clinical practice guideline and many of the education tools will be available in English and Spanish.

P25.37

Do dual-tasks affect gait asymmetry in people with Parkinson's disease?

Constanza San Martín Valenzuela[*,1], *Lirios Dueñas Moscardó*[2]
[1] INCLIVA Health Research Institute - Departament of Physiotherapy, Faculty of Physiotherapy, University of Valencia, Valencia, Spain, Valencia, Spain
[2] Departament of Physiotherapy, Faculty of Physiotherapy, University of Valencia, Valencia, Spain, Valencia, Spain

Introduction: The unilateral onset of Parkinson's disease (PD) causes asymmetric clinical signs that may last throughout the course of the disease. Although people with PD present asymmetrical adjustments in walking, there are unknown gait asymmetry changes during challenging conditions of walking as well its relationship with clinical tests. The aims of this work are to analyze the effect of different dual-tasks (DT) on the step length and step asymmetry (STEPasy), as well as the relationship between STEPasy and clinical outcomes.
Methods: Forty participants with PD (aged 66.72 [7.5] years, H&Y I-II-III) walked in the on-medication state under five gait conditions: single task (ST) and visual, verbal, auditory, and motor DT. The step length (m) of the most affected side (STEPa) and the least affected side (STEPb) were measured with a photogrammetry system. STEPasy (%) was also calculated using the equation [100 x |ln(STEPa/STEPb)|], where high percentages indicate greater asymmetry. Mobility, Risk of falls, and Quality of life were measured with the Time-Up-Go test (TUG), the Tinetti Mobility test (TMT), and the Parkinson's disease questionnaire-39 (PDQ39), respectively. Multivariate analysis of variance was conducted to analyze the effect of within-subject factor gait conditions. In addition, the Bonferroni correction was used for post-hoc (pairwise) mean comparisons. The relationship between STEPasy and clinical tests was explored using Pearson (r) or Spearman's rho (ρ) correlation tests according to normality distribution. Differences were considered statistically significant if $p<0.05$.
Results and conclusion: A significant effect of gait conditions was observed on STEPa ($F=13.21$; $p<0.01$). However, no effect was found in either STEPb ($p=0.15$) or STEPasy ($p=0.37$). The pairwise comparisons between conditions as well as the mean values of the variables are shown in Figure 1. On the other hand, significant correlations were observed between STEPasy in ST condition and TUG test ($\rho=0.41$; p=0,01), and between STEPasy in verbal DT condition and PDQ39 ($\rho=0.37$; p=0,01). In both correlations, low asymmetry percentages are related to low test scores and, therefore, better performance. Although in the initial stages of PD, challenging gait conditions did not alter gait asymmetry, this showed a significant correlation with mobility and quality of life.

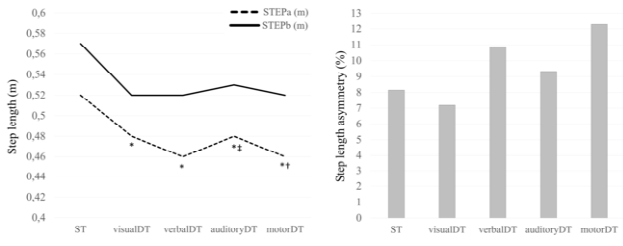


Figure 1 – Step gait assessment. STEPa, most affected side. STEPb, least affected side. ST, single-task. DT, dual-task. *statistical differences with single-task condition. †statistical differences with visual dual-task condition. ‡statistical differences with verbal dual-task condition.

P25.38

Comprehensive communication care for people with Parkinson's disease and their care partners

Lisa Sommers[*], Sara Mamo**
University of Massachusetts Amherst, Amherst, MA, United States

Given the high prevalence of hearing loss in adults over 70, and the reluctance to address this, it is often the case that both PwP and their partners have untreated hearing loss. The combination of hypophonia associated with PD, hearing loss, and cognitive decline results in significant relationship stress and poor quality of life. There is a lack of both research and evidence-based clinical service delivery by allied health professionals that focuses on this complex intersection of deficits. This study aims to address the problem of communication breakdowns between PwP and care partners, which are common and result in significant declines in quality of life. We have developed an innovative communication tool-kit for PwP and their communication partners that focuses on communication strategies and the hearing needs of this dyad. This program involves one in-person and two virtual sessions led by an audiologist, a speech-language pathologist, as well as audiology and speech-language pathology graduate clinicians. In the first session, PwP and care partners will complete voice, hearing, and cognitive screenings and will be fitted with a low-cost assistive listening device. They will be given a resource packet with instructions for device use and strategies for communication that will guide discussions during the virtual sessions. Two additional sessions will address communication strategies based on the specific individualized communication challenges of the dyads. Outcomes of interest include perceived improvements in communication and quality of life, as measured by standard questionnaires and qualitative interviews. In addition, student outcomes will track competencies and clinical confidence specific to the care and management of these complex communication challenges for PwP and their care partners. The initial cohort of participants will be enrolled in spring 2023. The ultimate aim of this study is to establish the efficacy of this person-centered approach and to develop a user-friendly communication tool-kit that could be provided to PwP and their care partners as an entry point for mitigating these challenges. This initial contact and education will further serve to establish connections with speech, language, and hearing professionals that can support them throughout the course of the disease.

P25.39

Developing an integrated guideline for allied health care in Parkinson's disease with decision support: Lessons learned

Ingrid Sturkenboom[*,1], *Anneli Langbroek-Amersfoort*[1], *Marten Munneke*[2], *Bastiaan Bloem*[3]
[1] ParkinsonNet, Radboud university medical center, Nijmegen, Netherlands
[2] ParkinsonNet, Nijmegen, Netherlands
[3] Center of Expertise for Parkinson and Movement Disorders, Radboud university medical center, Nijmegen, Netherlands

Background: Allied health care plays an important role in enabling people with Parkinson's (PwP) to manage the impact of the disease in daily life. Evidence-based guidelines for physiotherapy, occupational therapy, speech therapy and dietetics/nutrition are available. However, these have several shortcomings: 1) no support for personalized shared decision-making; 2) monodisciplinary nature, while there is considerable overlap between the treatment domains of different allied health professions; 3) not up-to-date; 4) limited use in clinical practice. We addressed these issues by

developing an innovative guideline for allied health care in PwP with an embedded decision support.
Methods: The development phase included two parallel processes:
1) Developing the guideline conform the GRADE approach including identifying key questions, performing a systematic literature search and analysis, and writing conclusions, considerations and actionable recommendations. Representatives of professionals and PwP were involved in this process.
2) Developing an online tool to support guideline development and continuous updates (every six months) and developing an interactive decision aid that presents the recommendations.
Results: We formulated 40 key questions with the general format 'What are effective allied health interventions to manage [problem X] in PwP?' The decision support is available in both a professional and lay version. Two main lessons are:
First, the decision support as a central product to present recommendations has many implications for the guideline development process and content. For example, one cannot be selective in choosing key questions, but must cover the many needs of PwP. We had to separate problems while many of the 40 'problems' are interrelated. For various interventions and subpopulations, we also needed to include more expert opinions in the recommendations to fill the gaps in the literature.
Second, the integration of guidelines across allied health professions revealed how much the jargon and understanding of concepts differed between professions, while the overlap in domains between professions was greater than expected.
Discussion: Developing this integrated guideline with decision support took a lot of time and effort. However, we expect it has high clinical relevance and it can easily be updated. The implementation and usability evaluation currently taking place will inform us about this.

P25.40

Feasibility of a combined intermittent theta-burst stimulation and video game-based dexterity training in Parkinson's disease
Manuela Pastore-Wapp[1], Brigitte C. Kaufmann[2], Thomas Nyffeler[2], Simona Wapp[2], Stephan Bohlhalter[2], Tim Vanbellingen[,3]*
[1] University of Bern, Luzerner Kantonsspital, Bern, Switzerland
[2] Luzerner Kantonsspital, Lucerne, Switzerland
[3] University of Bern and Luzerner Kantonsspital, Bern, Switzerland

Background: Persons with Parkinson's disease (PD) often exhibit difficulties with dexterity during the performance of activities of daily living (ADL), inter alia due to dysfunctional supplementary motor area (SMA). Combined intermittent theta-burst stimulation (iTBS) over the SMA followed by video game-based training (VBT) may therefore improve dexterity related ADL. The VBT may induce high flow levels related to high performance during the training. The aim of this study is to evaluate the feasibility of a combined iTBS-VBT intervention in persons with PD.
Methods: A total of nine persons with PD (mean age 63.3 ± 8.76 years) with self-reported difficulties with dexterity related ADL were included in this pilot iTBS-VBT study. All participants received either iTBS or sham stimulation over the SMA followed by a 45-min VBT, three times a week for a total of three weeks. Feasibility was measured by means of the adherence rate and the system usability (System Usability Scale). Moreover, flow was measured after the last VBT session.
Results: Adherence rate was excellent with 100%. High system usability scores (ie, mean 80%, range 55-97.5) and a significant Spearman's correlation with the Flow State Scale (r=.762, p=.017) further point to the high feasibility of the VBT. Neither demographic variables nor difficulties in dexterity related ADL affected the usability of the VBT.
Conclusion: This study demonstrates the high feasibility of a combined iTBS-VBT intervention. Moreover, the level of self-reported usability was related to flow experience. Whether this kind of combined iTBS-VBT intervention improves dexterity will be evaluated in a randomized controlled trial.

P25.41

No added effect of transcranial direct current stimulation on motor sequence learning in older adults
Britt Vandendoorent, Sanne Broeder, Moran Gilat, Evelien Nackaerts, Jean-Jacques Orban de Xivry, Alice Nieuwboer*
KU Leuven, Leuven, Belgium

Repeated sessions of transcranial direct current stimulation (tDCS) of the primary motor cortex could enhance the motor learning process in older adults, but so far existing studies are inconclusive and underpowered. It also remains unclear whether the tDCS effects depend on the delivery montage, as it was suggested that the conventional tDCS montage produces a relatively non-focal stimulation compared to high-definition tDCS. Therefore, this project examined the added effect of both tDCS montages on the primary motor cortex during motor sequence learning. Fifty-two cognitively-intact older adults (mean age: 68.4 ± 8.0 years; mean Mini Mental State Examination score: 28.8 ± 1.3) practiced a 12-item serial reaction time task while receiving two sessions of 20 minutes of tDCS in a double-blind randomized sham-controlled parallel study with a crossover for montage. Mean washout duration between montages was 25.43 ± 12.59 days. Stimulation intensity was set at 1 mA. We assessed reaction times during the twelve blocks of the two practice sessions of the serial reaction time task during tDCS or sham. The linear mixed model revealed that tDCS did not boost learning compared to sham (group*time: p=0.672). Also, learning was unaffected by tDCS montage (montage*time: p=0.651). Significant time effects showed that participants did react faster during all blocks of the second practice session compared to the last block of the first practice session (all p<0.05). We conclude that there is no surplus value of adding tDCS during two sessions of motor sequence learning in older adults. We did find that older people benefited from a second practice session to improve their motor learning. Future research should focus on the effects of multiple sessions of tDCS during motor sequence learning in people with Parkinson' s disease whose learning impairments are more pronounced compared to healthy, and therefore could benefit more from stimulation.

P25.42

Effects of a 6-month community-based Nordic walking program on alleviating motor and non-motor symptoms and improving balance performance in people with Parkinson's disease
Irene SK Wong-Yu[,1], Ken CK Poon[2], Margaret KY Mak[1]*
[1] Department of Rehabilitation Sciences, The Hong Kong Polytechnic University, Hong Kong SAR, China
[2] Hong Kong Sheng Kung Hui Welfare Council Limited, Hong Kong SAR, China

Background: Nordic walking (NW) is a moderate-intensity aerobic exercise using poles with special walking techniques. Nordic Walking program could improve dynamic balance in people with Parkinson's disease (PD) after 6-week training. However, its long-term effects on motor and non-motor symptoms and balance performance remains unknown.
Objectives: To examine whether a 6-month community-based NW program would be effective on alleviating motor and non-motor

symptoms and improving balance performance in people with mild to moderate PD at post-training.
Methods: Eligible participants with mild to moderate PD were recruited for the 6-month NW program. In 6 months, ten 90-minute NW training sessions were delivered by a physiotherapist with NW instructor certification. The protocol included six weekly NW classes followed by four monthly classes. Participants targeted to complete 150-minute exercise per week progressively at moderate intensity using smartwatch heart rate monitor. They also performed home exercise at same intensity for 2-3 times weekly during intervention in the community. Movement Disorder Society Unified Parkinson Disease Rating Scale motor (MDS-UPDRS Part 3) and non-motor (MDS-UPDRS Part 1) scores and Mini Balance Evaluation Systems Test (Mini-BEST) scores were assessed as outcomes before and after intervention.
Results: Twelve PD participants (age 62.9±4.0, Hoehn and Yahr stage 2.3±2.0) completed the 6m NW program with an attendance rate of 95%. There were no adverse effects or falls reported during the training period. At 6m post-training, there were significant decreases in MDS-UPDRS Part 3 score (by -3.8 points, $p<0.05$) and Part 1 score (by -2.1 points, $p<0.01$) and an increase in Mini-BEST scores (by +1.9 points, $p<0.01$) as compared with baseline measurements.
Conclusion: The 6-month community-based Nordic Walking program alleviated motor and non-motor symptoms and improved dynamic balance in people with mild to moderate PD after treatment completion.

P25.43

Experiences and future perspectives with two patterns of intensive online exercise training in early-stage Parkinson's disease

Yuya Yamaguchi[*,1], Junya Ogawa[2], Hiromi Masumori[2], Tadamitsu Matsuda[3]*
[1] Smile Space Corporation, Setagaya, Japan
[2] Smile Space Corporation, Tokyo, Japan
[3] Department of Physical Therapy, Faculty of Health Science, Juntendo University, Tokyo, Japan

Introduction: Intensive rehabilitation as a treatment for Parkinson's disease (PD) has been shown to be effective in improving motor symptoms. However, there are several problems with this intervention. These include, for example, requiring hospitalization and transportation. We have developed and conducted two patterns of intensive online training programs aimed at solving these problems. We are going to report on the findings of these experiences and our plans for developing better programs in the future.
Methods: The first, program we have developed is group online training (GOT). The GOT consists of a group of three to five participants who exercise independently at least three days per week for 12 weeks. It uses exercise video contents and weekly group lectures on exercise given by a physical therapist. The second program we developed is Personal Online Training (POT). The POT is designed to provide personal online training for four weeks, two to four times per week, 50 minutes each. The Parkinson's Disease Questionnaire (PDQ-39) and Modified Falls Efficacy Scale, standing posture, and gait were assessed, before and after these programs.
Results: Fifteen PD patients participated in the GOT and seven PD patients participated in the POT. PDQ-39 is 93.9 (±20.3) points before and 86.4 (±22.8) points after the program on the GOT. Those on the POT are 94.4 (±24.0) points before the program and 85.4 (±23.3) points after. There were no adverse events in each programs.
Discussion: Current study is the first to examine the effectiveness of two intensive online-based training programs for PD. Both programs improved the PDQ-39 before and after the program. However, we found some problems in each of the programs. For example, GOT is a group training program, which makes it difficult to address individualized tasks. The POT provides many opportunities for individual involvement, which can lead to over-dependence on the trainer in charge and fewer opportunities for independent training. We are going to continue to develop new programs through the experience of these two programs. Intensive personal training using video contents of exercise is planned with the aim of improving physical function and enabling the patient to continue exercising.

P25.44

Effect of transcranial direct current stimulation depending on stimulation sites to improve dual-task performance in Parkinson's disease

Seo Jung Yun, Sung Eun Hyun, Woo Hyung Lee, Byung-Mo Oh, Han Gil Seo*
Seoul National University Hospital, Seoul, South Korea

Background: Several studies suggested that transcranial direct current stimulation (tDCS) may be effective in improving the freezing of gait and motor/cognitive function of Parkinson's disease (PD). However, stimulation protocols including target sites, intensity, frequency, and duration, and the results of studies on the effectiveness of tDCS in PD have been inconsistent, and more research is needed to fully understand its potential benefits. Therefore, the study aimed to compare the effect of various tDCS target sites to improve dual-task performance in PD.
Methods: Participants underwent four sessions. Each session transferred 2mA current anodal tDCS for 20 minutes by random assignment through the primary motor cortex (M1), left dorsolateral prefrontal cortex (DLPFC), ventromedial prefrontal cortex, and sham stimulation. There was a wash-out period of at least 7 days between sessions. The timed-up and go test (TUG) under single- and dual-task (cognitive and physical) conditions, Stroop test, trail-making test (TMT), and digit span were evaluated before and after the stimulation. Every evaluation and intervention proceeded at the "on" state, which is the peak effect of PD medication.
Results: Fifteen idiopathic PD patients were enrolled and completed the entire study protocol. The mean age, disease duration, and Korean-Montreal Cognitive Assessment were 72.93 ± 5.65 years, 111.93 ± 49.13 months, and 24.13 ± 2.39, respectively. The modified Hoehn and Yahr stage was 2 in four patients, 2.5 in eight patients, and 3 in three patients. Left DLPFC tDCS induced significant improvements in cognitive dual-task TUG performance (15.13 ± 3.62 to 14.51 ± 4.10 sec, $p = .027$), and M1 tDCS enhanced single-task TUG performance (12.16 ± 3.33 to 11.74 ± 2.95 sec, $p = .031$). A significant improvement was observed in trail B of TMT in M1, Left DLPFC, and sham tDCS stimulation ($p < .05$).
Conclusions: Our study suggested that anodal tDCS on left DLPFC immediately improved cognitive dual-task performance. Further clinical trials are needed to validate the effectiveness and safety of multi-session tDCS on dual-task performance in PD patients.
Funding: This work was supported by the National Research Foundation of Korea (NRF) grant funded by the Korean government (MSIT) (No. NRF-2020R1C1C1012785).

Table 1. Changes in the outcome variables according to stimulation sites (N=15)

		M1	DLPFC	vmPFC	Sham
Timed up and go (sec)	*single-task*				
	Pre	12.16 ± 3.33	12.15 ± 3.27	12.28 ± 3.97	12.35 ± 3.89
	Post	11.74 ± 2.95	11.85 ± 2.92	12.25 ± 3.73	12.32 ± 4.23
	p-value	.031*	.300	.691	.691
	Cognitive dual-task				
	Pre	14.57 ± 4.77	15.13 ± 3.62	14.97 ± 4.03	14.43 ± 4.58
	Post	14.26 ± 4.33	14.51 ± 4.10	14.77 ± 4.20	14.85 ± 5.39
	p-value	.281	.027*	.609	.334
	Physical dual-task				
	Pre	18.04 ± 8.46	19.19 ± 9.62	18.41 ± 7.53	18.71 ± 8.66
	Post	17.99 ± 8.39	20.09 ± 11.87	19.49 ± 10.33	19.28 ± 12.14
	p-value	.910	.650	.460	.820
Stroop test†	*Word*				
	Pre	79.00 ± 21.97	76.27 ± 19.67	80.13 ± 21.22	79.33 ± 22.33
	Post	80.53 ± 21.62	77.60 ± 20.86	82.27 ± 19.63	82.73 ± 21.14
	p-value	.285	.513	.142	.382
	Color				
	Pre	64.67 ± 13.10	62.47 ± 16.66	64.73 ± 13.83	65.13 ± 15.64
	Post	66.33 ± 11.45	66.33 ± 15.97	66.33 ± 14.70	67.67 ± 13.22
	p-value	.130	.030*	.310	.181
	Color-word				
	Pre	40.27 ± 10.16	37.47 ± 9.94	40.13 ± 11.45	40.53 ± 12.58
	Post	43.33 ± 11.57	40.00 ± 10.99	40.27 ± 8.38	44.07 ± 12.97
	p-value	.027*	.064	.825	.078
Trail-making test (sec)	*Trail A*				
	Pre	44.00 ± 26.55	43.60 ± 26.66	39.80 ± 18.25	39.40 ± 15.27
	Post	36.93 ± 12.38	41.80 ± 21.33	40.87 ± 17.33	38.67 ± 18.14
	p-value	.268	.820	.593	.624
	Trail B				
	Pre	160.86 ± 75.55	173.86 ± 149.50	154.07 ± 137.07	171.00 ± 122.06
	Post	119.71 ± 75.55	129.00 ± 93.56	131.50 ± 101.57	107.86 ± 78.98
	p-value	.041*	.028*	.103	.048*
Digit-span†	*Forward*				
	Pre	6.93 ± 1.16	7.27 ± 1.28	7.47 ± 1.06	7.13 ± 1.19
	Post	7.67 ± 0.98	7.67 ± 1.05	7.60 ± 1.18	7.33 ± 1.23
	p-value	.018*	.083	.480	.429
	Backward (N=14)				
	Pre	4.33 ± 1.59	4.27 ± 1.44	4.33 ± 1.29	4.20 ± 1.27
	Post	4.13 ± 1.25	4.53 ± 1.60	4.60 ±1.77	4.33 ± 1.50
	p-value	.527	.206	.336	.739

†The higher the score, the more positive the result, Mean ± SD, *$p < .05$ by Wilcoxon signed-rank test

COMPREHENSIVE CARE: Nutrition and gastrointestinal issues

P26.01

Case studies documenting the interaction of antibiotics, photobiomodulation and Parkinson's disease

Brian Bicknell[1], Ann Liebert[2], Anita Saltmarche[3], Orla Hares[4], Hosen Kiat[5]*
[1] Western Sydney University, Westmead, Australia
[2] Sydney University, Sydney, Australia
[3] Saltmarche Health & Associates, Orangeville, Canada
[4] PhysioinMotion, Hamilton, Canada
[5] Cardiac Health Institute, Sydney, Australia

Over the past decades it has become apparent that there is a close association between the gut microbiome and metabolic and neurodegenerative diseases. This association is especially strong in Parkinson's disease, where gut bacteria appear to play a role in both the establishment and progression of the disease in a significant proportion of patients. Disruption of the gut microbiome and associated gastrointestinal symptoms is often an early indicator of Parkinson's disease, occurring 10 or more years before neurological symptoms. Disruption of the microbiome has also been shown to exacerbate symptoms and accelerate disease progression in both animal models of Parkinson's disease and in clinical studies. In fact, transplantation of faecal material from Parkinson's disease patients has been shown to induce Parkinson's disease symptoms in mice. Antibiotic use is one such way that the microbiome is disrupted with reduced and changed biodiversity. Somewhat paradoxically, some antibiotics can have a neuroprotective effect in Parkinson's disease models. There is, however, increasing evidence of a link between certain antibiotic exposure and the risk of developing Parkinson' disease. Accumulating epidemiological evidence has highlighted the increased risk of developing Parkinson's disease with the use and overuse of certain antibiotics, which may take 15 or more years to manifest as Parkinson's disease.
The potential of photobiomodulation to alleviate some of the motor and non-motor symptoms of Parkinson's disease has been demonstrated in multiple animal trials and two proof-of-concept clinical trials. Abdominal photobiomodulation has been shown to alter the microbiome in a mouse model of Parkinson's disease and there is an indication that photobiomodulation can benefit microbiome health in humans in clinical trials.
Here we present two case studies documenting the progression of Parkinson's disease over months and years and the interaction with antibiotic use and photobiomodulation therapy.

P26.02

Objective measures of gut dysfunction in Parkinson's disease

*Marta Camacho**
University of Cambridge, Cambridge, United Kingdom

Objective: To characterize gastrointestinal (GI) dysfunction in Parkinson's disease (PD) using objective measures.
Background: GI dysfunction is an important feature of PD and may play a role in disease onset and progression. However, studies examining gut problems in PD often involve only self-reported questionnaires hindering accurate estimates of prevalence.
Methods: 75 participants with PD (PwP) and 59 paired household controls (HC) ingested a blue food dye to measure GI transit time (length of time between ingestion of the dye and first appearance of blue stool). PwP also completed the Gastrointestinal Dysfunction Scale – Parkinson's Disease (GIDS-PD). In a small pilot study, 5 PwP and 5 household controls underwent a Small Intestinal Bacterial Overgrowth (SIBO) breath test that measures gases produced in the gut, hydrogen and methane.
Results: There was a significant difference in gut transit time between PwP (61.5 ±41.6 hours) and household controls (37.8 ± 26.9 hours, p<0.001). 29 PwP (39%) and 8 controls (14%) met criteria for slow transit time (≥59hours). There was a modest correlation between self-reported constipation (GIDS-PD Constipation score) and transit time (r=0.30, p=0.009). In the SIBO breath test pilot study, there was no significant difference in mean methane and hydrogen values between PwP and household controls, however, the prevalence of high methane producers was unusually high for both groups (40% for controls and 80% for PwP) vs. expected value of 20% for population studies. New recruitment to increase sample size for the breath test is ongoing.
Conclusion: Slowed transit time is common in Parkinson's disease, affecting 39%, but may not be accompanied by symptomatic constipation, underlining the heterogeneity of gut involvement in the disease, and the limitations of self-report instruments for assessing GI function. Non-invasive breath tests may be sensitive to alterations in gut microbiota in PwP, and warrant further investigation as a biomarker of gut function.

P26.03

The mealtime of people with Parkison's disease: A qualitative descriptive pilot study

Muriel Gabas[*,1], Estelle Harroche[2], Jean Paul Poulain[1], Virginie Woizard[3], Margherita Fabbri*[,4]*
[1] Laboratory CERTOP, UMR CNRS 5044, University Toulouse 2 Jean-Jaurès, Toulouse, France
[2] Centre Expert Parkinson, Neurosciences department of the University Hospital of Toulouse, CHU Purpan, Toulouse, France
[3] University of Toulouse-Toulouse 3, INSERM, UMR1214 Toulouse NeuroImaging Centre "TONIC", Toulouse, France
[4] CHU Toulouse, Toulouse, France

People with Parkinson's disease (PwP) may have swallowing disorders and eating difficulties (holding cutlery, carrying food to the mouth). Over disease progression, after 15-20 years, PwP are dependent for at least half of the activities of daily living (ADLs), and more than 60% are dependent for food tasks. Human assistance is necessary during the meal. P Formal or familial caregiver must develop strategies to prepare meals and feed the patient. The aim of our study is to describe the strategies designed by the familial caregiver and the patient (a dyad) to help with food intake. This is an observational qualitative prospective study that will be carried out by the Parkinson's disease (PD) Expert Centre at the Toulouse University Hospital (France). 10-15 dyads will be recruited. The study will consist of two phases; a) the production of a video-recorded meal followed by the interview with the two members of the dyad, during a follow-up hospitalization; b) 15 days later, on the basis of selected extracts from the video, using the technique of self-confrontation, a new interview will be conducted. The main objective is to use videotaped data and semi-directional interviews to write down the strategies designed and used by the dyad helping/aided to feed the "people who are dependent on the hand-to-mouth gesture, with swallowing disorders as part of Parkinson's disease or atypical parkinsonian syndrome during a meal." A lexico-semantic analysis will be used to identify the themes raised during the interviews. For the video, an analysis of the mimics, gestures and looks, both qualitatively and quantitatively, will be carried out, based on an adaptation of the CUED. Our findings could be helpful to propose a more personalized speech and therapist approach, being integrated into training modules for health-care professionals during Therapeutic Patient Education sessions for both patients and caregivers.

P26.04

The unmet nutritional needs of people living with Parkinson's Disease

*Richelle Flanagan**
My Moves Matter, Dublin, Dublin, Ireland

Aim: To identify nutritional care needs amongst the people living with Parkinson's Disease
Methods: A thirteen-question survey was distributed to people living with Parkinson's Disease through the Dublin branch of the Parkinson's Association of Ireland. All members were emailed an online survey and sent a postal option with a stamped addressed envelope for those who did not have access to the Internet.
Results: We received 82 responses, 50 postal and 32 online. 8 out of 10 respondents were over 64 years of age and most have had Parkinson's for less than 15 years. 87.5% and 79.5% reported that neither their GP nor neurologist, respectively, ever asked them about their diet. 82% said they had never been referred to a Dietitian since diagnosis and 88% of people had never requested a referral to a Dietitian (Figure 1). Of the people who had seen a Dietitian, 70% were happy with the advice they received.
61.2% and 59.3% reported that neither their GP nor neurologist respectively had never weighed them. Whilst 63% had lost weight unintentionally since their diagnosis. 36.4% had difficulty cutting food, 41.6% had difficulty holding utensils e.g., knife, fork, cup, and 28.6% had difficulty preparing/cooking food. Almost a quarter had difficulty choking/coughing on food/fluids whilst one-fifth had difficulty swallowing food. Almost 50% were not taking a Vitamin D supplement (Figure 2).
Conclusion: This survey identifies many of the nutritional needs of people living with Parkinson's such as weight loss, eating difficulties, and constipation all which are known issues within the clinical nutrition literature and guidelines. However, the survey also demonstrates a concerning gap between the nutritional needs of people living with Parkinson's disease and the delivery of nutritional care by their healthcare providers. A more comprehensive survey of the nutritional care needs of people with Parkinson's should be carried out for the whole of Ireland alongside a survey of healthcare providers' knowledge (e.g., GPs, neurologists) of the nutritional care needs of people with Parkinson's disease. This could inform the integration of better nutritional care for people living with Parkinson's disease within the multidisciplinary team.
https://irspen.ie/congratulation-to-our-irspen2021-poster-winners/ - not published in journal just on their website

Figure 1. Dublin PAI Nutrition Survey results – People living with Parkinson's Disease are not asked about their diet, not referred to a dietitian or requesting to be referred to a dietitian

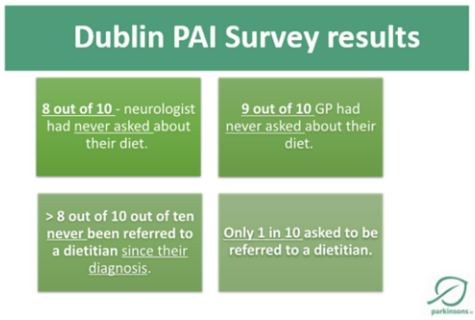
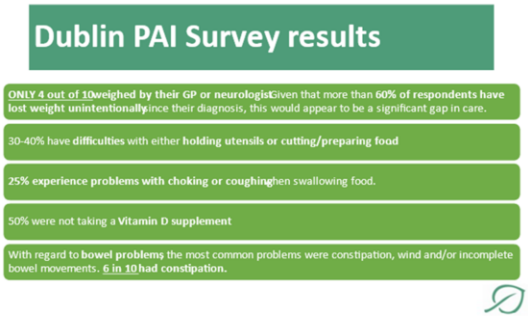


Figure 2 Dublin PAI Nutrition Survey results – nutritional related issues people living with Parkinson's Disease experience



P26.05

Comprehensive personalized nutrition approach for people with Parkinson's: A case study

*Sally Hillis**
(n=1)™, Lincoln, Nebraska, United States

Background: Comprehensive personalized nutrition (CPN) for people with Parkinson's (PwP) is needed. Though many studies

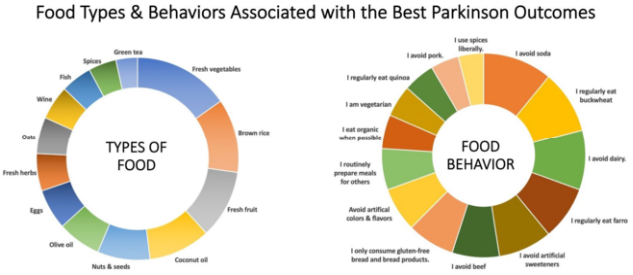
have utilized a variety of interventions, including diet, nutritional supplements, and/or exercise, few studies have incorporated multiple lifestyle factors together with personalized nutrition that integrates macronutrient and micronutrient assessments. Applying an advanced mixed methods protocol combining in-depth interview information and previous test results with added traditional and non-traditional lab results provides a better understanding of the disease process thus creating a comprehensive treatment plan.
Objective: To determine whether an integrated approach to providing comprehensive personalized nutrition is an effective treatment for PwP.
Methods: Comprehensive personalized nutrition protocol and tools used for assessment were outlined. A case study was completed by applying the protocol to a patient with Parkinson's Disease. Summary of Case Study: In May 2019 (UPDRS: 14), a patient recently diagnosed with late on-set Parkinson's Disease was subject to an in-depth interview, antecedent lab results were reviewed, and an evaluation for micronutrients, macronutrients, food allergies, behavior factors, toxin exposure, and vascular inflammation markers were performed. Patient was treated for 10 months, at which time micronutrients were retested. Treatment plan was adjusted, and patient continued the co-constructed protocol. September 2022 (UPDRS: 2), the patient reports "feeling better than before" and "is overall very happy".
Results: Overall, patient's micronutrient and macronutrient nutrition improved, as well as lifestyle factors. The patients PD symptoms did not progress.
Interpretation: Based on the improvement of the UPDRS score, the patient "feeling better" and changes in micronutrient levels, larger studies utilizing a comprehensive personalized nutrition approach for PwP warrant further investigation.

P26.06

The relationship between diet and Parkinson symptoms over time

Laurie Mischley[1], Joshua Farahnik[*,2]*
[1] Bastyr University, Parkinson Center for Pragmatic Research, Seattle, WA, United States
[2] Parkinson Center for Pragmatic Research; University of Washington, Seattle, WA, United States

Background: There is growing evidence that diet plays a role in Parkinson's disease (PD) pathophysiology. Numerous studies from around the world suggest diet is midlife is associated with subsequent PD diagnosis, but few studies have attempted to determine whether food choices following diagnosis impact the rate of PD progression. Aim: The goal of this study was to evaluate whether food intake frequency was associated with the accumulation of symptoms over time. Methods: Data of individuals with idiopathic PD that responded to The Modifiable Variables in PD (MVP Study) survey questions in 2022 were used for this cross-sectional analysis. The Patient-Reported Outcomes in PD (PRO-PD) was the primary outcome measure and regression models adjusted for age, gender, income, and years since diagnosis. Results: 2,176 individuals were available for analysis from 36 different countries (75% USA). The foods associated with fewer symptoms over time were fresh vegetables and fresh fruit, brown rice, oats, ancient grains (buckwheat, farro, quinoa), coconut and olive oil, eggs, fresh herbs and spices, wine, green tea, and non-fried fish. Protective food behaviors included avoiding soda, dairy, beef, pork, fried food, artificial sweeteners, colors, and flavors, gluten, trying to eat organically grown food when possible, being vegetarian, and routinely preparing meals for others (all $p < 0.05$). Discussion: The MVP Study is the world's largest and longest-running study evaluating the role of diet in PD progression. The high concentration of phytonutrients in these foods provides biological plausibility and the congruence of these findings with those from traditional epidemiological research related to PD risk lends further support for the integrity of these findings. Whether or not this diet based on Patient Reported Outcomes (PRO) can be adopted, and whether adherence is associated with improved outcomes over time cannot be determined from this cross-sectional analysis. Potential risks of this this PRO diet, such as additional financial costs and stress, have yet to be evaluated. Despite these limitations, these foods and food behaviors have a long record of safety and are readily accessible. The PRO diet may provide patients with a sense of empowerment and a potential strategy for disease modification.



CLINICAL SCIENCE: Symptoms, signs, features & non-motor manifestations

P27.01

The novel p.A30G SNCA mutation in Greek Parkinson's disease patients and asymptomatic family members

Ioanna Alefanti*[,1], Christos Koros[1], Chrisoula Kartanou[2], Athina Maria Simitsi[1], Maria Bozi[3], Stefanos Varvaressos[1], Athina Zachou[1], Roubina Antonelou[1], Matina Maniati[4], Sokratis Papageorgiou[1], Georgios Paraskevas[1], Constantin Potagas[1], Marios Panas[2], Konstantinos Voumvourakis[3], Georgia Karadima[2], Georgios Koutsis[1], Leonidas Stefanis[1]
[1] 1st Department of Neurology, Eginition Hospital, Medical School, National and Kapodistrian University of Athens, Athens, Greece
[2] Neurogenetics Unit, 1st Department of Neurology, Eginition Hospital, Medical School, National and Kapodistrian University of Athens, Athens, Greece
[3] 2nd Department of Neurology, Attikon Hospital, National and Kapodistrian University of Athens, Athens, Greece
[4] Laboratory of Neurodegenerative Diseases, Biomedical Research Foundation of the Academy of Athens, Athens, Greece

The SNCA gene is the first gene with mutations reported to cause heritable forms of Parkinson's disease (PD). In the Greek population, until recently, p.A53T was the only SNCA mutation that has been identified to cause autosomal dominant PD. According to a recent study, a novel heterozygous p.A30G (c.89 C>G) SNCA mutation was identified to segregate with the disease in three unrelated Greek families, causing an autosomal dominant form of PD. In the present study, genetic and clinical features of 6 additional carriers of the p.A30G SNCA mutation from four Greek PD families are described, providing further evidence on the phenotypic spectrum p.A30G SNCA mutation.
The patients were recruited from the Neurogenetics Unit's outpatient clinic of the 1st Department of Neurology of the National and Kapodistrian University of Athens and the specialist movement disorders outpatient clinics of the 1st Department of Neurology of NKUA. Restriction fragment length polymorphism (RFLPs) was

used for the genotyping and the positive findings were confirmed by Sanger sequencing.
The p.A30G mutation identified in 4 index cases of 4 unrelated Greek families, originated from geographically distant regions. The p.A30G-positive PD patients manifested typical PD motor dysfunction, with a good initial response to levodopa treatment and various non-motor symptoms including psychiatric disorders, RBD, autonomic dysfunction and hyposmia. The mean age at disease onset was 54 ± 6 years with a range of 48-61 years of age. The present study also describes the clinical and radiological findings of two asymptomatic siblings, carriers of the p.A30G mutation. On clinical examination the asymptomatic carriers demonstrated olfactory deficits, self-reported sleep disturbances and psychiatric manifestations (depression and anxiety).
The novel p.A30G SNCA mutation segregates with PD in 4 additional Greek families and, represents a relatively important, although uncommon, cause of Greek familial PD. The p.A30G patients present with typical PD phenotype, relatively late age of disease onset and various non-motor symptoms. Genetic testing of Greek PD patients should include not only the p.A53T founder mutation, but also the p.A30G mutation, especially among patients with autosomal dominant PD family history.
This research was funded by the National Precision Medicine Network for Neurodegenerative Diseases (EDIAN).

P27.02

Nature, degree of frequency and importance of the motor and non-motor disorders in 39 patients with Parkinson's disease
Etienne Baldayrou, Elodie Baroux-Petitperrin, Camille Beauger, Geneviève Merelle, Elise Maugras, Serge Merelle*
Quingey Health Center, Quingey, France

Introduction: The main diagnostic signs of Idiopathic Parkinson's Disease (IPD) usually include akinesia, tremor, hypertonia or rigidity and are grouped under the term "symptomatic triad". However, this disease is also characterized by a set of varied and frequent non-motor disorders.
Objective: The aim of our study, conducted in 39 patients suffering from IPD, is to highlight the nature, the degree of frequency and the importance of the motor and non-motor disorders identified by the patients with the Parkinson Well-Being Map™ (PWBM™)
Method: Since 2013 the physical rehabilitation department at the Quingey Health Center (Doubs, France) has been offering an individualized therapeutic education program for patients with IPD. To optimized patient care, the PWBM™, a tool for recording and monitoring 12 motor and 39 non-motor disorders grouped into 8 categories of symptoms, is completed by patients on their arrival. Patients are asked to identify the symptoms they are currently experiencing and then determine how often they experience them, before selecting the symptom and the 3 categories of symptoms that are the most troublesome for them.
Results: In terms of the nature of disorders, the most common symptoms identified by study patients regardless of their degree of frequency and importance are 3 non-motor symptoms (back and neck pain, feeling the urge to pass urine, nocturnal awakening) and 2 other motor symptoms (speech and posture disorders). Concerning their degree of frequency, nocturnal awakenings to urinate is the disorder with the highest degree of frequency, ahead of writing and postural disorders. Finally, regarding their importance, back and neck pain is the most distressing symptom identified, ahead of fatigue and constipation, and far ahead of the initial motor disorders (speech disorders and the feet feeling stuck to the floor). Nevertheless, movement is identified by study patients as the most distressing category of symptoms, followed by attention/memory, and urinary and sexual functions.
Conclusion: Our study reveals the high frequency of non-motors symptoms in IPD and their important impact on patient's quality of life. Interestingly, in nearly 25% of cases, the disorder identified as the most distressing is not the disorder with the highest degree of frequency.

P27.03

Compassionate mind training for people with Parkinson: A pilot study
Elena Berti[1], Silvia Della Morte[1], Carolina Lalli[1], Francesca Morgante[2], Nicola Modugno[3], Lucia Ricciardi[2]*
[1] ParkinZone Onlus, Roma, Italy
[2] Neurosciences Research Centre, Molecular and Clinical Sciences Research Institute, St George's University of London, London, United Kingdom; Medical Research Council Brain Network Dynamics Unit, Nuffield Department of Clinical Neurosciences, Oxford, United Kingdom, London, United Kingdom
[3] IRSSC Neuromed, Pozzilli, Italy

Introduction: People with Parkinson's disease (PD) can experience deficits of emotion recognition and expression, affecting life quality and their social cognition capabilities within relationships. Emotional disregulation ultimately results in Heart Rate Variability (HRV) modifications. Literature confirms that PD is associated with reduced HRV values, indicating that both sympathetic and vagal activities are decreased. Compassion Focused Therapy (CFT) is a valid psychological approach to balance the three emotional systems: soothing (green), drive (blue) and threat (red) systems. CFT practices are effective at increasing HRV levels, heightening the parasympathetic response through the activation of the soothing system. Compassion has three-ways flow: for the self, for others and from others. CMT increases mindfulness and emotion regulation, building a compassionate self-perspective.
Objective: Using qualitative and physiological parameters, this pilot study aimed to test feasibility and effectiveness of CMT for PD patients.
Methods: Inclusion criteria of MoCA>26.
Pre-post training tests: anxiety (STAI Y1-Y2), depression (BDI-II), life quality (PDQ-39) and Self-Compassion Scale (SCS); HRV detection via wearable device (Polar H10) with 3 different stimuli (baseline, trigger, deep breathing) during interview with clinicians.
Post training: self report on energy disposal changes in emotional systems and satisfaction.
Attendance of 6-week online CMT with therapist, 2 hours once a week.
Results: PD patients attended (11 M and 13 F, mean age 57.6 ±8.1, mean disease duration 8.9 ±3.36).
Preliminary and qualitative results show significant pre/post gains in 2 subscales of SCS: Self-kindness (p= -0.20 ±0.83) and Mindfulness (p= -0.0416 ±0.81). Registered improvement in the Stigma subscale (p=0.01 ±0.2) of Parkinson's quality life scale (PDQ-39).
PD patients reported increasing levels in the three-ways flow of Compassion, particularly compassion for the self.
Furthermore, 84% of participants perceived a significant change of energy disposal through their emotional systems (soothing system increase and threat system decrease); 88% considered the training useful and would continue practicing.
Conclusions: CMT is feasible and engaging for people with PD. It appears to be effective at enhancing self-compassion and mindfulness levels in order to regulate emotions recognition and expression. Slight impact on Parkinson's quality life. Further analysis is binding to inquire results of clinical scales and physiological parameters.

P27.04

Personality dimensions in Parkinson's disease patients with or without chronic pain

Mathilde Boussac[*,1], Fleur Lerebours[2], Nathalie Cantagrel[3], Margherita Fabbri[4], Clémence Leung[4], Fabienne Ory-Magne[4], Olivier Rascol[4], Estelle Harroch[4], Emeline Descamps[4], Christine Brefel-Courbon[4]*

[1] Toulouse NeuroImaging Center, University of Toulouse, Inserm, UPS, Toulouse, France
[2] Department of Neurology, University Hospital of Toulouse, Toulouse, Toulouse, France
[3] Department of Neurosurgery, University Hospital of Toulouse, Toulouse, France
[4] Department of Clinical Pharmacology and Neurosciences, Parkinson Expert Center, Clinical Investigation Center, University Hospital of Toulouse, Toulouse, France

Introduction: Parkinson's disease (PD) is also responsible of non-motor symptoms such as invalidating chronic pain that affects from 60 to 80% of PD patients (Nègre-Pagès et al., 2008; Silverdale et al., 2018). Pain may be related to psychological features (Ball et al., 2017) such as personality dimensions. Indeed, in patients with chronic pain such as fibromyalgia and chronic migraine, personality dimensions showed higher Harm Avoidance scores (a temperament associated with anxiety) and lower Self-Directedness scores (a character associated with less determination) (Conrad et al., 2007; Naylor et al., 2017).
Objective: To study the relationship between chronic pain and personality dimensions in PD patients and to compare with other chronic pain conditions.
Methods: Four groups of patients will be included: PD patients with (n=25) or without (n=25) chronic pain, patients with fibromyalgia (n=25) and patients with chronic migraine (n=25). The "Temperament and Character Inventory" (TCI) will be use to evaluate personality dimensions in each group of patients. It is an self-questionnaire allowing to obtain independent scores for seven personality dimensions (Cloninger et al., 1994) which was already used and validated in PD (Boussac et al., 2022). We will assess pain with a visual analogue scale, the brief pain inventory, the McGill pain questionnaire, the pain acceptance and the pain catastrophism scales. Other parameters (anxiety and depression) will also be evaluated.
Hypothesis: Some personality dimensions in PD patients with chronic pain could be different than PD patients without pain and similar than those of patients with other chronic pain conditions (fibromyalgia and chronic migraine). This might suggest the existence of "pain sensibility personality" in PD patients. This identification of specific personality may help to predict the emergence of future pain symptoms and to improve PD patients' care through personalised educational programs.

P27.05

Validation and replication of Parkinson disease behavioral subtypes

*Christina Lessov-Schlaggar, Peter Myers, Joshua Jackson, Baijayanta Maiti, Paul Kotzbauer, Joel Perlmutter, Meghan Campbell**
Washington University in St. Louis, St. Louis, MO, United States

Introduction: We recently identified three distinct behavioral subtypes of Parkinson disease: motor (predominant motor with intact cognition and psychiatric function); psychiatric & motor (prominent psychiatric symptoms with motor deficits); cognitive & motor (cognitive and motor deficits). Here, we used an independent cohort to validate and replicate these clinical behavioral subtypes of Parkinson disease.
Methods: We tested our original behavioral subtype classification of Parkinson disease with an independent cohort (N = 101) of Parkinson disease participants without dementia and the same comprehensive behavioral evaluations assessing motor, cognitive, and psychiatric function. Next, we combined the original (N = 162) and validation (N=101) datasets to test the classification model with the full combined dataset (N = 263). We also generated random split-half samples of the combined dataset to establish the reliability of the behavioral subtype classifications. Latent class analyses were applied to the validation, combined, and split-half samples to determine subtype classification; models were selected based on a combination of model fit indices, substantive meaning, and sufficient number of people per class to allow further statistical analyses.
Results: Latent class analyses revealed three behavioral subtypes in the original, independent validation, and combined data sets: motor; psychiatric & motor; cognitive & motor. The 3-class subtype model was also selected in 13/20 (65%) random split-half replications from the combined dataset.
Conclusions: These results demonstrate the validity and reliability of the Parkinson disease behavioral subtypes of motor, psychiatric & motor, and cognitive & motor groups.

P27.06

Does musculoskeletal pain impact physical activity in people with Parkinson disease?

Ryan Duncan[*,1], Timothy Nordahl[2], Teresa Baker[2], James Cavanaugh[3], Tamara DeAngelis[2], Daniel Fulford[4], Jaimie Girnis[2], Martha Hessler[5], Michael Lavalley[6], Marie Saint-Hilaire[7], Cathi Thomas[7], Jenna Zajac[2], Terry Ellis[2], Gammon Earhart[5], Kerri Rawson[5]*

[1] Washington University in St. Louis – School of Medicine – Program in Physical Therapy, St. Louis, Missouri, United States
[2] Department of Physical Therapy, Sargent College of Health and Rehabilitation Sciences, Center for Neurorehabilitation, Boston University, Boston, MA, United States
[3] Department of Physical Therapy, University of New England, Portland, ME, United States
[4] Department of Occupational Therapy, Sargent College of Health and Rehabilitation Sciences, Boston University, Boston, MA, United States
[5] Program in Physical Therapy, Washington University in St. Louis School of Medicine, St. Louis, MO, United States
[6] School of Public Health, Boston University, Boston, MA, United States
[7] Department of Neurology, Parkinson's Disease and Movement Disorders Center, Boston University, Boston, MA, United States

Introduction: Musculoskeletal (MSK) pain is a common non-motor symptom in people with Parkinson disease (PwP). However, it is unclear whether and how MSK pain impacts their physical activity. The purpose of this cross-sectional study was to determine if physical activity levels differed between PwP who reported MSK pain and PwP who did not. We hypothesized that PwP with MSK pain would demonstrate lower physical activity levels compared to PwP without MSK pain.
Methods: Data were collected from PwP during the baseline assessment of a randomized controlled trial. The King's Parkinson's Disease Pain Scale – MSK subscale was used to determine the presence of MSK pain. Participants with a score > 0 were deemed to have MSK pain. Physical activity was measured over a seven-day period using a StepWatch Activity Monitor. Variables of interest for physical activity were: 1) mean number of daily steps, 2) mean number of moderate intensity activity minutes (minutes in which ≥ 100 steps were taken), 3) mean number of active minutes (minutes

in which at least one step was taken), and 4) mean number of medium activity minutes (minutes in which 60-99 steps were taken). Independent samples t-tests compared physical activity variables between PwP with MSK pain and PwP without MSK pain.
Results: Of 118 participants completing the scale, 87 (mean age: 67.7 ± 8.1; 43.7% female; mean MDS-UPDRS III score: 38.3 ± 11.0) reported experiencing at least some degree of MSK pain, while 31 (mean age: 66.0 ± 9.7; 48.4% female; mean MDS-UPDRS III score: 34.7 ± 13.5) reported no MSK pain. Compared to PwP without MSK pain, PwP with MSK pain took fewer daily steps (9,661.7 vs. 7,716.9; p=.008), spent less time being active (356.1 vs. 295.7 minutes; p=.008), and had fewer medium activity minutes (32.4 vs. 22.6; p=.027). There was no difference in moderate intensity activity minutes between the groups (p=.71).
Conclusion: PwP with MSK pain may be less active compared to PwP without MSK pain. As such, it is important that clinicians recognize pain may be a barrier to their participation in physical activity.

P27.08

The hormonal impact on symptoms in women with Parkinson's
Richelle Flanagan[*,1], *Kat Hill*[2], *Sree Sripathy*[3], *Sabela Avion*[4]
[1] My Moves Matter, Dublin, Dublin, Ireland
[2] Women's Parkinson's Project & PD Avengers, Portland, Oregon, United States
[3] Women's Parkinson's Project and PD Avengers, San Francisco, California, United States
[4] Con P de Parkinson, New York, New York, United States

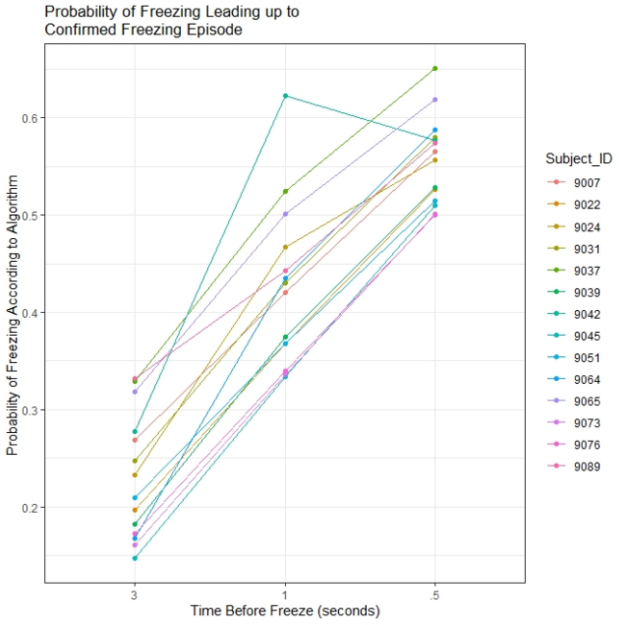
Aim: To identify gaps in hormonal care for women with PD
Methods: A fourteen question online survey in English and Spanish was distributed to women living with Parkinson's Disease (PD) through social media channels and through the Global women's advocacy group The Women's Parkinson's Project and the Spanish speaking women's advocacy group Con P.
Results: We received 218 responses, (173 English, 45 Spanish). 86% (84% English; 96% Spanish) answered the question 'Do you suffer from worsening of your PD symptoms around your menstrual period' with 75% (79% English; 74% Spanish) reporting to suffering from worsening of their PD symptoms around their menstrual period. The top three reported motor symptoms were rigidity, bradykinesia and tremor (81%, 72%, 49%) and were similar across the English and Spanish survey. The top three non-motor symptoms reported were fatigue, anxiety and insomnia (70%, 56%, 40%). 81% of women still menstruating reported worsening of their symptoms the week before their period and 51% the week of their period.
50% of the women answered the question "If you are perimenopausal do you notice your symptoms fluctuate randomly?" of which 66% reported that their symptoms did fluctuate randomly. 66% also reported it more difficulty in controlling their symptoms during perimenopause.
35% (77) women reported that they were post-menopausal. 49% reported their PD symptoms were about the same and 26% worsened. 145 women answered the question about HRT usage with 82% reporting they had never taken HRT. 30 women (28 English, 2 Spanish) reported being on HRT and 43% reported similar PD symptoms, 30% worse and 27% better. 74% of women reported starting HRT during the perimenopause.
95% of women answered the question "Has your neurologist ever discussed your hormones & the possible impact on PD symptoms?" with 88% reporting No to this question. 95% reported that their neurologist had never adjusted their medications around their menstrual cycle and 96% reported that their neurologist never suggested HRT.
Conclusion: This survey identifies the impact of hormones on PD symptoms in women and the lack of engagement by neurologists with women around this phenomena. This survey calls for further research to corroborate these findings.

P27.09

Exploring prediction of freezing of gait using sensor-based probability of freezing
Allison M Haussler[*,1], *Lauren E Tueth*[*,1], *David S May*[1], *Gammon M Earhart*[1], *Pietro Mazzoni*[2]
[1] Washington University in St. Louis, Saint Louis, MO, United States
[2] The Ohio State University, Columbus, OH, United States

Freezing of gait (FOG), characterized by sudden involuntary arrests of the feet while walking, is a debilitating symptom of Parkinson Disease. FOG leads to increased risk of falls, reduced quality of life, and potential increased levels of anxiety, as these episodes make walking difficult and time consuming. Treatment for FOG is challenging, as FOG is highly variable and often unpredictable. Because of the lack of reliable prediction of FOG, patients and clinicians have limited ability to implement prevention strategies. The purpose of this study was to determine if FOG episodes could be predicted in the seconds leading up to a freeze using an algorithm designed to calculate probability of FOG. Inertial measurement unit data were collected for walking and simulated IADL tasks designed to elicit FOG using wearable IMU sensors. Probability of FOG (pFOG) was calculated using sensor data and the pFOG algorithm developed by Prateek et al. The algorithm defines a freezing episode when pFOG > 0.7. For this analysis, freezing episodes were identified using the algorithm and verified by a trained human rater watching video of the tasks (current gold standard). Only episodes deemed true positive FOG episodes by both video rater and algorithm methods were utilized. After FOG episodes were identified, the pFOG values at 3 seconds, 1 second, and .5 seconds leading up to the FOG episode were averaged within subject. Data were then averaged within subjects to give a single average pFOG for 3 seconds, 1 second, and .5 seconds for all FOG episodes identified. Initial analysis illustrates a pattern of gradual increase in pFOG in the seconds leading up to a freeze,

with a particularly marked increase in pFOG occurring 1 second before the onset of freezing. This suggests the potential to predict a freezing episode before it happens using the algorithm in real-time. By the time of presentation, a time derivative analysis will be complete which will allow for identification of an inflection point where pFOG increases prior to the FOG episode. The ability to predict a FOG episode in real time may allow clinicians enough time to deliver a warning or intervention and thus inform future treatments.



P27.10

Apathy, gender and quality of life among Mexican people living with Parkinson's disease: An underrecognized non-motor symptom

Ana Jimena Hernández-Medrano, Diana Paulina Romero-Terán, María Fernanda Medina-Pérez, Andrea García-Hernández, Rodolfo Arturo Abundes-Corona, Daniela Renee Águila-Godínez, Axel Antonio Herrera-Ruiz, Amin Cervantes-Arriaga, Mayela Rodríguez-Violante*
National Institute of Neurology and Neurosurgery, Mexico City, Mexico City, Mexico

Introduction: Apathy is a prevalent non-motor symptom in Parkinson's disease (PD) [1], with impact on quality of life (QoL) of those who live with it (PwP) as well as their caregivers [2]. Apathy has been associated with advanced PD, older age, lower educational level, and being male [3]. Nevertheless, its clinical relevance is still controversial. Recognizing associated characteristics and detecting PwP who experience apathy could help guiding their therapeutic strategies in order to positively impact on QoL [5].
Objective: To compare the grade of apathy on women and men living with PD, as well as to correlate its impact on quality of life.
Methods: An observacional, retrospective, cross-sectional, analytic study was carried out (n=207; 57.5% males; 63.3±12.6 years). A comprehensive questionnaire, which included the Movement Disorders Society Unified Parkinson's Disease Rating Scale [MDS-UPDRS], the Movement Disorders Society Non-motor Symptoms Rating Scale [MDS-NMS], and the 39-item Parkinson's Disease Questionnaire index [PDQi], was used. Mann-Whitney U test was used to compare apathy scores between women and men.
Results: 34.8% and 43.5% of the participants reported some grade of apathy using the MDS-UPDRS (ítem 1.5) and the MDS-NMS (subdomain C), respectively. Means of educational years, years of PD evolution, levodopa daily dosage, MDS-UPDRS, MDS-NMS-C, and PDQ39i were 10.3±5.3, 7.2±5.2, 712.7±399.8, 59.0±26.7, 2.7±5.3, and 21.7±13.6. No statistical difference was observed on apathy between groups. Women showed higher PDQ39i (114.8 vs 96.0, p=0.026). Apathy scores (MDS-UPDRS 1.5 and MDS-NMS-C) significantly correlated with PDQ39i (r=0.29, p<0.01; r=0.44, p<0.01).
Conclusions: Apathy has a negative impact on quality of life in Mexican people living with Parkinson's disease, regardless of their gender. Moreover, the MDS-NMS prove to be a useful tool to assess apathy in our population.

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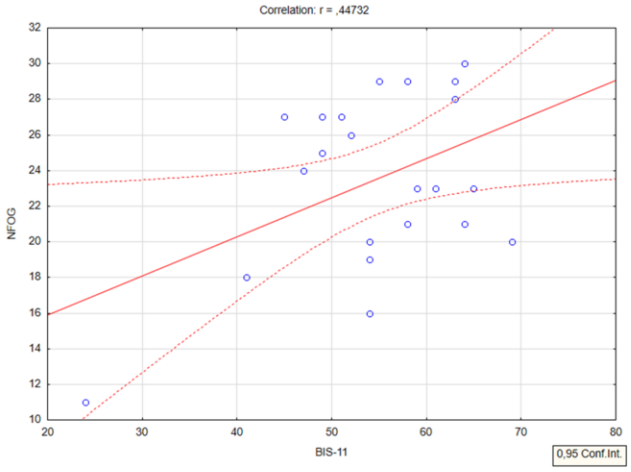
P27.11

Impulsiveness: A clinical aspect in Parkinson's disease with freezing of gait

Karina Yumi Tashima Honda, Nathalia de Brito Pereira*, Maria Elisa Pimentel Piemonte, Isaíra Almeida Pereira da Silva Nascimento, Katia Cirilo Costa Nobrega, Thayane Habache Barolli*
University of São Paulo, São Paulo, Brazil

Introduction: Motor and non-motor symptoms are very relevant to the decreased quality of life and functionality of individuals with Parkinson's Disease (PD). Although freezing of gait (FOG) and impulse control disorders (ICDs) are common symptoms in PD, their pathophysiology is still unclear. It is suggested that impaired inhibitory control may be a common mechanism, but the interrelationship of these factors remains inconclusive. Currently, there is no effective drug treatment to control FOG; therefore, a broad approach is important to investigate and intervene in the aspects that influence FOG to minimize the frequency of episodes.
Purpose: To investigate the relationship between FOG and impulsiveness. **Methods:** The study remotely evaluated 22 individuals with PD (18 women and 4 men), aged between 39 and 71 years (mean 54.09, ±8.45), with a mean time of 12.68 years (±6.78) diagnosis, with at least one episode of FOG per day, between stages I and IV in H&Y, using an average of 903.40 mg (±413.74) per day of levodopa. The mean score of the sample is 17.36 (±3.55) T-MOCA; 11.98 (±7.50) UPDRS part I; 14.56 (±8.92) UPDRS part II; 36.15 (±13.51) PDQ-39; 18.13 (±10.68) BAI. The instruments used to assess FOG and impulsivity were the NFOG and BIS-11 questionnaires, respectively. **Results:** A significant positive correlation was found between the NFOG scores and the BIS-11 total score (p=0.679, r=0.44), with an NFOG mean score of 21.43 (±4.87) and BIS-11 54.50 (±9.93). Furthermore, the BIS scores can predict more than 44% of NFOG variability (R=0.449, p<0.036, estimated SE=4.4694). **Conclusion:** The results showed that there is a positive association between the severity of FOG and the presence of impulsivity, independent of other clinical aspects. Therefore, impulsive behavior is associated with higher intensity or frequency of FOG episodes. Evidencing the importance of assessments and interventions based on non-motor aspects and

motor aspects to minimize FOG in PD. **Keywords:** Parkinson's disease, gait freezing, impulsive behavior.



P27.12

Parkinson's disease duration and motor symptom severity at baseline: An analysis of the Parkinson Progression Markers Initiative (PPMI) dataset

*Emily Houston**
The University of Vermont, Burlington, VT, United States

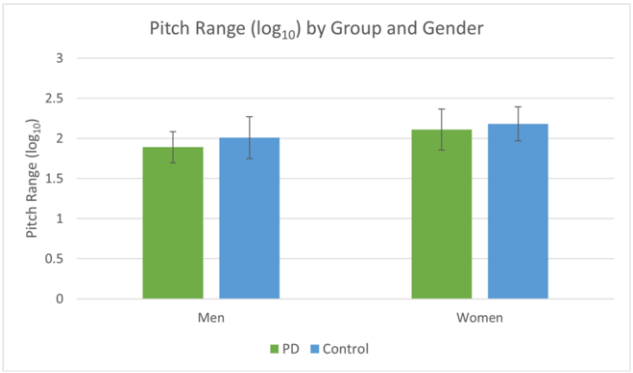
Objective: To examine the relationship between Parkinson's disease (PD) duration and motor symptom severity among patients with early, untreated PD while controlling for age at diagnosis, sex, and two prodromal markers, REM sleep behavior disorder (RSBD) and loss of smell.
Methods: We utilized baseline data from 423 participants with a confirmed clinical diagnosis of PD in the Parkinson's Progression Markers Initiative (PPMI) study. A linear regression was used to determine if an association exists between duration of PD and motor symptoms, as measured by the Movement Disorder Society Unified Parkinson's Disease Rating Scale Part III (MDS-UPDRS III). A multiple regression model was built to control for age at time of diagnosis, sex, loss of smell (UPSIT score), and REM Sleep Behavior Disorder Questionnaire (RBDSQ) Score.
Results: At baseline, the mean duration of PD was 6.65 □ 6.48 months and the mean MDS-UPDRS III score was 20.89 □ 8.854. In an unadjusted model, for every month increase in duration of PD, we found a 0.14 increase in MDS-UPDRS III score (p=0.04, 95% CI 0.005, 0.265). This association was weak (r = 0.1). After adjustment, the MDS-UPDRS Part III motor score remained positively correlated with duration of PD (p = 0.04). Further, age of diagnosis reached significance (p= 0.003) as did olfactory impairment (p = 0.04). Sex and RBDSQ score were not significantly related to MDS-UPDRS III score at baseline (p=0.86 and 0.18, respectively). Only 6% of the variance in the motor score could be attributed to the predictor variables included in our model, and the association was weak (r = 0.25).
Interpretations: In early, drug naïve patients with PD, the duration of PD at baseline is associated with a very slight change in motor symptoms. Our model, including two prodromes, indicates a weak influence of disease duration, age at diagnosis, sex, history of RSBD, and loss of smell on motor score, suggesting that other biomarkers should be explored for predicting change or severity of motor symptoms in this population.

P27.13

Patterns and consistency of speech changes in a diverse national sample of people with parkinson disease in the United States

Jessica Huber[1], Andrew Exner[2], Sandy Snyder[3], Hardik Kothare[4], Jackson Liscombe[4], Renee Kohlmeier[3], Shreya Sridhar[3], Brianna Coster[3], Kaylee Patterson[3], Helen Willis[3], Vikram Ramanarayanan[4]*
[1] Purdue University, Lafayette, IN, United States
[2] self-employed, Indianapolis, IN, United States
[3] Purdue University, West Lafayette, IN, United States
[4] Modality.AI, San Francisco, CA, United States

People with Parkinson disease (PD) have been reported to produce quieter and faster speech with reduced intonation in many, but not all studies. However, most studies have been conducted with small local cohorts that are heavily weighted toward White men. It is critical to examine whether the findings from earlier studies hold in larger, more diverse samples. For example, motor symptoms and progression differ between men and women, and in a small number of studies, speech deficits were reported to be more common in females. Further, no studies have examined how consistently people with PD perform on common speech assessment metrics. Understanding the consistency of performance is critical for determining how much assessment should be conducted when developing speech therapy goals. The aims of this study were to 1) determine how well commonly used speech assessment metrics differentiated people with PD from controls of similar age and gender in a more diverse sample and 2) examine the consistency of performance from week to week in these outcomes. Using a novel telemedicine platform (Modality.AI), we have collected a national sample from people in the United States, including 60 people with PD and 31 controls, with women comprising 50% of the PD sample and people identifying as Hispanic comprising 5% of the PD sample. We are continuing to collect and analyze data. Participants completed a standardized speech assessment once a week for four weeks. Assessment tasks included reading aloud, monologue, and an intonation task that elicited questions and statements using a contextual cue. Measurements included speech rate, articulation rate, pausing patterns, and pitch range and variability. Participants with PD demonstrated reduced pitch range and variability in the intonational task ($p<.001$), but they produced the correct contour direction (rise/fall) as often as controls. The figure presents pitch range, in log10 to reduce the effect of higher mean pitch in women. Differences were more significant in men than women. There were no significant differences in speech rate or articulation rate between PD and controls. The presentation will include consistency analyses which are currently underway.



P27.14

Women and Parkinson's disease: The impact of hormonal fluctuations during the menstrual cycle on parkinson symptoms

Willanka Kapelle, Esra Stuart, Hein Bogers, Bastiaan Bloem, Marjan Meinders, Annelien Oosterbaan, Bart Post*
Radboud University Medical Center (Radboudumc), Nijmegen, Netherlands

Introduction: Young women with Parkinson's Disease (PD) often report cyclic fluctuations of their PD symptoms, which could be related to hormonal fluctuations during the menstrual cycle. However, to date, research on this topic has mainly been limited to case reports. Gaps in knowledge result in vast shortcomings in providing young women with PD with the proper care. We explored the impact of hormonal fluctuations during the menstrual cycle on PD symptoms.
Methods: This sub-study was part of a larger study that was carried out in the Netherlands on women-specific matters and PD. We invited women to fill out an online questionnaire. All women were between 21 and 60 years of age, had been diagnosed with PD by a neurologist and were Dutch-speaking. For this particular sub-study, only women who were still menstruating were included.
Results: In total, 104 women completed the survey of whom 24 were included in the analysis. Two-third (67%; N=16) experienced worsening of PD symptoms around menstruation, most frequently in the week prior to their menstruation (75%; N=12). Women most frequently experienced worsening of energy problems (63%; N=15), rigidity, irritability and wearing off (46%; N=11 each). Almost half of the women (42%; N=10) had discussed these fluctuations in PD symptoms with a healthcare professional; they had all taken the initiative for addressing this topic themselves. In only four cases, it resulted in a change in hormonal or parkinson therapy and in only one case a gynaecologist was consulted.
Discussion: Although two-third of the women with PD, who are still menstruating, report fluctuations of their PD symptoms related to hormonal fluctuations during the menstrual cycle, most healthcare professionals do not address this topic. In order to provide women with PD with the proper care, women-specific care and interventions are essential. Women should have the option of consulting with both a neurologist and gynaecologist. To aid conversation with a healthcare professional apps could be used as a tool for tracking PD symptoms and the menstrual cycle. Moreover, hormonal therapy to decrease hormonal fluctuations could be explored since this may be an important treatment option.

P27.15

Measurement of dyskinesia in Parkinson's disease using a lower back sensor

Jennifer Kudelka[,1], Clint Hansen[1], Pia Reisdorf[1], Lisa Alcock[2], Philip Brown[2], Katharina Dirksen[1], Heiko Gassner[3], Pieter Ginis[4], Mark Gordon[5], Jeffrey M. Hausdorff[6], Hanna Hildesheim[1], Heather Hunter[2], Anat Mirelman[6], Alice Nieuwboer[4], Robbin Romijnders[1], Christian Schlenstedt[7], Alison Yarnall[2], Clemens Becker[8], Lynn Rochester[2], Walter Maetzler[1]*
[1] Department of Neurology, University Hospital Schleswig-Holstein, Kiel, Germany
[2] Translational and Clinical Research Institute, Newcastle University, Newcastle, United Kingdom
[3] Department of Molecular Neurology, University Hospital Erlangen, Friedrich-Alexander-Universität, Erlangen-Nürnberg (FAU), Erlangen, Germany
[4] KU Leuven, Department of Rehabilitation Sciences, Neurorehabilitation Research Group (eNRGy), Leuven, Belgium
[5] Innovative Medicine & Global Clinical Development, Neuroscience, Teva Pharmaceuticals, West Chester, PA, United States
[6] Center for the Study of Movement, Cognition and Mobility, Neurological Institute, Tel Aviv Sourasky Medical Center, Tel Aviv, Israel
[7] Institute of Interdisciplinary Exercise Science and Sports Medicine, Medical School Hamburg, Hamburg, Germany
[8] Robert Bosch Foundation for Medical Research, Stuttgart, Germany

Background: Levodopa-induced dyskinesias (LID) are a common therapy side effect in Parkinson's Disease (PD) after 5-10 years of treatment and represent excessive body movements that can affect the patients' trunk, limbs and face. To date, LID are mainly recorded by self-assessment, e.g. questionnaires. Multiple studies have indicated that investigators classify LID more accurately than those affected. Wearable digital technology that assesses movement has been shown to detect LID in PD (by use of data obtained from a wearable worn on the ankle).
Objective: To test, by use of a self-developed, validated algorithm for ankle LID detection, whether LID can also be detected using data obtained from a lower back sensor.
Methods: Data is currently collected from n=600 individuals with PD who participate in the Mobilise-D Clinical validation study. PD medication state is rated by a trained investigator as well as by the participants themselves using a scale from +3 (= ON with severe dyskinesia) to -3 (= severe OFF) in the beginning and in the end of the visit. Participants are subjected to various mobility tests (e.g. 6-Minute-Walk-Test (6MWT)) while wearing a MoveMonitor® lower back sensor. Area under the curves for the detection of presence and severity of LID will be obtained.
Discussion: This is to our best knowledge the first large study investigating the detection of LID by using a lower back sensor. We expect that LID detection using the MoveMonitor® worn on the lower back is effective and more accurate than by participants themselves. If this hypothesis holds true, this approach would open entirely new opportunities for the quantitative assessment of LID in the home environment.

P27.16

Clinical parameters associated with impaired self-awareness of levodopa-induced dyskinesias in Parkinson's disease

Jennifer Kudelka[*,1], Katharina Dirksen[1], Lisa Alcock[2], Philip Brown[2], Heiko Gassner[3], Pieter Ginis[4], Mark Gordon[5], Clint Hansen[1], Jeffrey M. Hausdorff[6], Hanna Hildesheim[1], Heather Hunter[2], Anat Mirelman[6], Alice Nieuwboer[4], Pia Reisdorf[1], Robbin Romijnders[1], Christian Schlenstedt[7], Alison Yarnall[2], Clemens Becker[8], Lynn Rochester[2], Walter Maetzler[1]*

[1] Department of Neurology, University Hospital Schleswig-Holstein, Kiel, Germany
[2] Translational and Clinical Research Institute, Newcastle University, Newcastle, United Kingdom
[3] Department of Molecular Neurology, University Hospital Erlangen, Friedrich-Alexander-Universität, Erlangen-Nürnberg (FAU), Erlangen, Germany
[4] KU Leuven, Department of Rehabilitation Sciences, Neurorehabilitation Research Group (eNRGy), Leuven, Belgium
[5] Innovative Medicine & Global Clinical Development, Neuroscience, Teva Pharmaceuticals, West Chester, PA, United States
[6] Center for the Study of Movement, Cognition and Mobility, Neurological Institute, Tel Aviv Sourasky Medical Center, Tel Aviv, Israel
[7] Institute of Interdisciplinary Exercise Science and Sports Medicine, Medical School Hamburg, Hamburg, Germany
[8] Robert Bosch Foundation for Medical Research, Stuttgart, Germany

Background: Levodopa-induced dyskinesias (LID) occur as a side effect in 50-60% of persons with Parkinson's disease (PwPD). LID is a risk factor for falls, but the association of LID with fear of falling (FOF) is not clear. Interestingly, impaired self-awareness (ISA) of LID is common (23-91%), and may contribute to increased risk of falls and FOF. To date, it is not fully understood which factors are associated with ISA in PD, which seems important for the management of LID and its consequences.
Objective: To compare motor and non-motor parameters, especially risk of falls and FOF, between PwPD with ISA of LID (ISA+), and PwPD without ISA of LID (ISA-).
Methods: From the Mobilise-D Clinical Validation study PD cohort (N=541), 65 ISA+ and 43 ISA- were identified by comparing the ratings from a Likert scale filled in by the trained assessor (gold standard) and the PwPD during an in-clinic visit. The Likert scale describes presence and severity of dyskinesia and hypokinesia on a scale from +3 (= ON with severe dyskinesia) to -3 (= severe OFF). During the visit, the Movement Disorder Society-revised Unified Parkinson's Disease Rating Scale (MDS-UPDRS), the Montreal Cognitive Assessment (MoCA), and the Falls Efficacy Scale – International (FES-I) were conducted. In the 6 months following, the number of falls was recorded in a monthly fall diary.
Results: No significant differences between the groups were found regarding demographic parameters (age, gender), disease severity, severity of LID and FOF. ISA+ showed significantly lower cognitive function (MoCA, p=0.042) and were less likely to fall within the next six months after the visit (p=0.01).
Discussion: Our results suggest that deterioration of cognitive function might play a role in the development of ISA of LID. Interestingly, ISA+ reported less falls in the following 6 months, which could indicate a better (unconscious) integration of LID into the movement patterns. Further monitoring of these groups, which to the best of our knowledge are unprecedented in terms of size, in upcoming follow-ups will allow a better understanding of ISA of LID and its impact on daily life.

P27.17

Discrepancy between self-awareness and objective measurements of olfactory function In patients with Parkinson's disease

Do-Young Kwon, Hwa Been Yang*, Minyoung Seo*
Korea University Ansan Hospital., Ansan-si, Gyeonggi-do, South Korea

Objective: Parkinson's disease (PD) is the second most common neurodegenerative disorders mainly affecting motor system. Importance of non-motor symptoms of PD such as REM sleep behavior disorder, constipation, affective disorders and hypo/anosmia is getting emphasized as those are known prodromal biomarkers of PD. olfaction is sensitive biomarker reflecting underlying neurodegeneration but there are lots of discrepancy of self-reporting olfactory function scale and the laboratory data in clinical practice. This study is performed to elucidate the correlations between self-awareness of olfactory function and results of objective olfactory test and investigate the factors influencing the differences in PD patients.
Methods: Cross-sectional clinical study was performed with 164 newly diagnosed non-demented drug-naive PD.
Basic epidemiological and clinical data were collected. Self-rating olfaction scale by visual assessment of rating) and Korean version Sniffin' stick test II (KVSS II) results were compared. Above 80% of self-rating score was considered as normal by self-rating and The KVSS-II TDI score ranged from 1 to 20 for anosmia, 20.25–27 for hyposmia, and ≥27.25 for normosmia
Results: 47 (28%) of the subjects had normosmia on KVSS II. Among 117 (72%) subjects had hypo/anosmia on KVSS II, 69 (59%) patients reported having normal olfaction by self-rating (VAS >8). Subjective self-rating olfactory function of PD patients showed correlation with TDI total score (p=0.021) and threshold (p<0.001), but not with discrimination (p=0.362) and identification (p=0.547) score on KVSS II.
Conclusion: Odor identification and discrimination requires complicated process within central nervous system that is not just simple sensory perception. Odor identification might be attributable to cognitive function and is representatively affected in various neurodegenerative disorders. Self-awareness of olfactory function is largely determined by perception of the smell, while more complicated odor process was not perceived by the subjects in this study. Self-rating scale to check olfactory function is not suitable to detect prodromal non-motor symptoms in elderly PD patients.

P27.18

Association between dizziness and clinical features in patients with de novo Parkinson's disease?

Kyum-Yil Kwon, Jihwan You, Rae On Kim, Eun Ji Lee*
Soonchunhyang University Seoul Hospital, Seoul, South Korea

Introduction: Clinical implications of dizziness in patients with Parkinson's disease (PD) remain to be little known. Herein, we aim to investigate an association of dizziness and motor or non-motor features especially in those with de novo PD.
Methods: We carefully reviewed medical records of patients clinically diagnosed with de novo PD in our hospital between 2017 and 2021. Motor symptoms were evaluated using the Unified Parkinson's Disease Rating Scale – Part 3 (UPDRS-III) and the modified Hoehn and Yahr (HY) stage. Non-motor symptoms including anxiety, depression, fatigue, and autonomic dysfunctions, were assessed using each representative measurement. In addition, the existence of dizziness was checked in those people to figure out the relationship between dizziness and clinical characteristics.

Results: Eighty patients with de novo PD were finally enrolled for the study. Compared with non-dizzy patients with de novo PD, dizzy patients with de novo PD were more women (69.5%, p= 0.008) and had worse scores in anxiety (p=0.001), fatigue (p= 0.011), cardiovascular (p <0.001) and thermoregulatory dysautonomia (p= 0.042). To predict the relationships between dizziness and clinical features, we conducted a logistic regression analysis and found that dizziness was significantly associated with females (Odds Ratio, OR= 4.167, 95% CI: 1.535 – 11.313, p= 0.005), anxiety (OR= 1.192, 95% CI: 1.065 – 1.334, p= 0.002), fatigue (OR= 1.192, 95% CI: 1.008 – 1.071, p= 0.002), cardiovascular dysautonomia (OR= 17.314, 95% CI: 3.573 – 83.890, p< 0.001). A subsequent multivariable logistic regression analysis revealed that dizziness was significantly related to females (OR: 8.421, 95% CI: 1.560 – 45.472, p= 0.013) and cardiovascular dysautonomia (OR: 22.141, 95% CI: 3.345 – 146.576, p= 0.003)

Conclusion: We revealed that dizziness in patients with de novo PD was highly related to women and cardiovascular dysautonomia. Therefore, when encountering patients with PD complaining of dizziness, cardiovascular dysautonomia need to be identified and managed in more detail.

Table 2. Univariate logistic regression analysis on dizziness in patients with de novo Parkinson's diseases

	Odds ratio	95% CI	*P*-value
Age, yr	1.006	0.955 – 1.058	0.829
Gender (female/male)	4.167	1.535 – 11.313	**0.005**
BMI (kg/m2)	0.958	0.819 – 1.121	0.592
Level of education	0.955	0.896 – 1.048	0.331
Disease duration, yr	1.102	0.702 – 1.729	0.674
UPDRS-III score (motor)	1.003	0.960 – 1.048	0.891
Tremor score	0.985	0.806 – 1.203	0.879
Rigidity score	0.976	0.841 – 1.132	0.748
Bradykinesia score	1.014	0.929 – 1.107	0.754
PIGD score	1.142	0.962 – 1.355	0.130
Hoehn and Yahr stage	0.967	0.334 – 2.802	0.951
Motor subtype (TD/non-TD)	0.440	0.166 – 1.169	0.100
MoCA-K (global cognition)	0.915	0.828 – 1.011	0.080
BDI (depression)	1.053	0.987 – 1.124	0.120
BAI (anxiety)	1.192	1.065 – 1.334	**0.002**
PFS (fatigue)	1.039	1.008 – 1.071	**0.014**
SCOPA-AUT (total dysautonomia)	1.057	0.996 – 1.122	0.070
Gastrointestinal (GI) domain	1.145	0.984 – 1.332	0.080
Urinary (UR) domain	1.004	0.912 – 1.107	0.928
Cardiovascular (CV) domain	17.314	3.573 – 83.890	**<0.001**
Thermoregulatory (TR) domain	1.709	1.001 – 2.919	0.050
Pupillomotor (PM) domain	1.231	0.689 – 2.199	0.484
Sexual (SX) domain	1.002	0.744 – 1.350	0.989
Orthostatic hypotension	0.974	0.234 – 4.053	0.971
Common comorbidity			
Diabetes mellitus	1.250	0.426 – 3.670	0.685
Hypertension	1.154	0.443 – 3.007	0.770
Coronary disease	3.200	0.599 – 17.102	0.174
Urinary diseases	0.524	0.182 – 1.504	0.229

P27.19

Sex differences in motor and non-motor symptoms among Spanish patients with Parkinson's disease

Ariadna Laguna*[,1], Jorge Hernández Vara[2], Diego Santos-García[3], Teresa de Deus Fonticoba[4], Carlos Cores Bartolomé[3], Maria J. Feal Painceiras[3], Maria Cristina Íñiguez-Alvarado[3], Iago García Díaz[3], Silvia Jesús[5], Maria Teresa Boungiorno[6], Lluís Planellas[7], Marina Cosgaya[8], Juan García Caldentey[9], Nuria Caballol[10], Ines Legarda[11], Iria Cabo[12], Lydia López Manzanares[13], Isabel González Aramburu[14], Maria A. Ávila Rivera[15], Víctor Gómez Mayordomo[16], Víctor Nogueira[17], Víctor Puente[18], Pablo Martinez-Martin[2], Pablo Mir[5], COPPADIS Study Group[19]

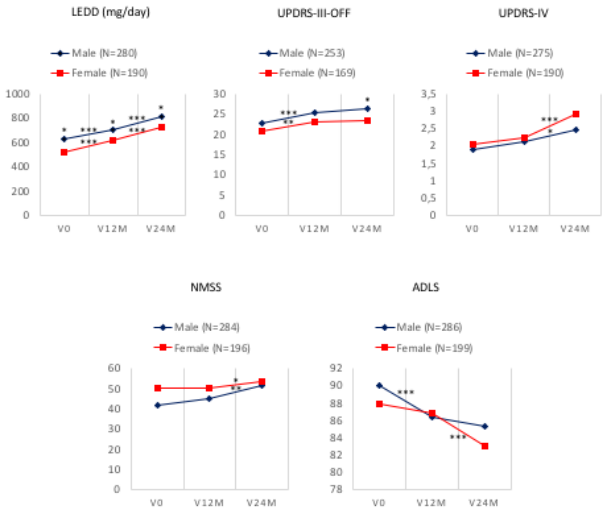
[1] Vall d'Hebron Research Institute, Barcelona, Spain
[2] Neurodegenerative Diseases Research Group, Vall d'Hebron Research Institute (VHIR), Barcelona, Spain
[3] CHUAC, Complejo Hospitalario Universitario de A Coruña, A Coruña, Spain
[4] CHUF, Complejo Hospitalario Universitario de Ferrol, A Coruña, Spain
[5] Unidad de Trastornos del Movimiento, Servicio de Neurología y Neurofisiología Clínica, Instituto de Biomedicina de Sevilla, Hospital Universitario Virgen del Rocío/CSIC/Universidad de Sevilla, Sevilla, Spain
[6] Hospital Universitari Mutua de Terrassa, Terrassa, Spain
[7] Clínica del Pilar, Barcelona, Spain
[8] Hospital Clínic de Barcelona, Barcelona, Spain
[9] Centro Neurológico Oms 42, Palma de Mallorca, Spain
[10] Consorci Sanitari Integral, Hospital Moisés Broggi, Sant Joan Despí, Spain
[11] Hospital Universitario Son Espases, Palma de Mallorca, Spain
[12] Complejo Hospitalario Universitario de Pontevedra (CHOP), Pontevedra, Spain
[13] Hospital Universitario La Princesa, Madrid, Spain
[14] Hospital Universitario Marqués de Valdecilla, Santander, Spain
[15] Consorci Sanitari Integral, Hospital General de L'Hospitalet, L'Hospitalet de Llobregat, Spain
[16] Hospital Universitario Clínico San Carlos, Madrid, Spain
[17] Hospital Da Costa, Lugo, Spain
[18] Hospital del Mar, Barcelona, Spain
[19] COPPADIS Study Group, COPPADIS Study Group, Spain

Background and objective: Sex plays a role in Parkinson's disease (PD). We analyzed sex differences among Spanish patients with PD.

Patients and Methods: PD patients who were recruited from the Spanish cohort COPPADIS from January 2016 to November 2017 were included. A cross-sectional and a 2-year follow-up analysis were conducted. Univariate analyses and general linear model repeated measure were used.

Results: At baseline, data from 681 PD patients (mean age 62.54 ± 8.93) fit the criteria for analysis. Of them, 410 (60.2%) were males and 271 (39.8%) females. There were no differences between both groups in the mean age (62.36 ± 8.73 vs 62.8 ± 9.24; p=0.297) or in the time from symptoms onset (5.66 ± 4.65 vs 5.21 ± 4.11; p=0.259). Symptoms such as depression (p<0.0001), fatigue (p<0.0001), and pain (p<0.00001) were more frequent and/or severe in females whereas other symptoms such as hypomimia (p<0.0001), speech problems (p<0.0001), rigidity (p<0.0001), and hypersexuality (p<0.0001) more in males. Women received more antiparkinsonian agents (p=0.011) and drugs overall (p=0.029) per day but fewer dopamine agonist (p=0.005) and levodopa (p=0.002) equivalent daily dose. Perception of quality of life was worse in females (PDQ-39, p=0.002; EUROHIS-QOL8, p=0.009). After the 2-year follow-up the NMS burden (Non-Motor Symptoms Scale) increased more significantly in males (p=0.012) but the functional capacity (Schwab & England Activities of Daily Living Scale) was more impaired in females (p=0.001).

Conclusion: The present study supports the idea that there are sex differences in the manifestation and progression of PD motor and non-motor symptoms, as well as in the usage of antiparkinsonian agents and drugs overall. All in all, long-term prospective comparative studies are needed to better understand the differences between males and females with PD, their causes, and their implications for clinical management.
Figure 1. Mean at V0, V12M and V24M in males vs females in the LEDD (mg/day) and the score on UPDRS-III-OFF, UPDRS-IV, NMSS and ADLS; *, p<0.05; **, p<0.001; ***, p<0.0001. The symbol above the line represents the significance of the change between one visit and another while the symbol above the point/diamond represents the difference in that visit between men and women.



P27.20

Cardiac perception task demonstrates interoceptive precision is impaired in Parkinson's disease

Senegal Alfred Mabry[1], Samantha Moss[2], Jeffery Bauer[2], Eve De Rosa[1], Adam Anderson[1]*
[1] Cornell University, Ithaca, New York, United States
[2] SUNY Cortland, Cortland, New York, United States

Precision, the Bayesian term for weighing the strength of your beliefs against evidence, may underlie neuropsychological diseases like Parkinson's disease. Promising theoretical arguments for how the body sets precision point to the neuromodulator dopamine, which has receptor and context-specific effects. This study will characterize Bayesian precision in people diagnosed with Parkinson's disease (PD) through computational models of data from people performing an interoceptive heartbeat detection task. We predict differences in Bayesian precision for people with PD and healthy controls.
Theoretical neurobiologists hypothesize that decreased dopamine transmission from substantia nigra cell death causes poor interoceptive precision setting, which leads to the disease symptoms. Clinicians treat PD by adjusting dopamine transmission in the brain by prescribing the dopamine precursor L-dopa or pharmacological inhibitors. In this study, 40 subjects (20 with PD, 20 age and sex-matched controls) will perform a interoception heartbeat detection task. The heartbeat task has been used to create a computational model of participants precision of interoceptive precision. Bayesian inference is a powerful tool for estimating the probability of an event using prior knowledge and collected data. This research will help clarify dopamine's roles in the competing hypotheses on Bayesian inference in the brain. It may help explain how changes in dopamine transmission led to PD symptoms.
Participants are asked to perform 200 trials of heartbeat detection under three different sets of instructions. First, participants are told they are allowed to report when they guess they feel their heartbeat. Then participants will perform the task but are told only to report if they are sure they felt their heartbeat, not their guesses. Finally, the participants will be told to hold their breath during the task to increase the precision of the cardiac signals, and they are only to report if they are sure they felt their heartbeat, not their guesses. Between the guess and initial no-guessing task, participants will complete a control condition where they will be asked to tap the key when they hear a 100-millisecond audio tone. The guess and no guess conditions adjust participants' prior beliefs about their cardiac signals, and the breath-holding increases the precision of cardiac signals.

P27.21

Observational study to investigate the relationship between stress related disorders and dysautonomic symptoms in Parkinson's disease

Esrom Jared Acosta Espinoza[1], Ilse Alejandra Ortiz Marroquin[1], Daniela Itzel Salinas Leal[1], Adriana Salinas Blancas[1], Hannia Mariana Macias Cruz[1], Daniel Martinez-Ramirez[2]*
[1] Tecnologico de Monterrey, Monterrey, Mexico
[2] Tecnologico de Monterrey, Escuela de Medicina y Ciencias de la Salud, Monterrey, Mexico

Background: Post-traumatic stress disorders are associated with an increased risk of developing Parkinson's disease. Studies demonstrate that these disorders share physiopathological characteristics with dysautonomic symptoms of Parkinson's disease. Dysautonomic symptoms have a negative impact on disease progression, morbidity, and mortality in patients. The relationship between post-traumatic stress disorders and dysautonomic symptoms in Parkinson's disease is unknown. We aimed to find a relationship between stress disorders and dysautonomic symptoms in Parkinson's disease.
Methods: A cross-sectional study was designed. Patients were selected from PI's clinic from July to September 2022. Patients were excluded if presented dementia, psychosis, TBI, DBS or missing data in medical files. Non-probability convenience and consecutive sampling was applied. SCOPA-AUT scale was used to identify dysautonomic symptoms and arbitrarily categorized into two groups, predominance of dysautonomic symptoms (total score ≥ 10), and without a predominance of these symptoms (total score <10). Patients were interrogated about personal experiences of a traumatic event. The psychiatric PCL-5, ACE, ASDS scales and a structured interview were applied to explore disorders related to post-traumatic stress.
Results: Thirty-two patients with Parkinson's disease were included, 16 with SCOPA-AUT ≥ 10 and 16 with SCOPA-AUT < 10. We observed a significant difference in PCL5 between groups, SCOPA-AUT ≥ 10 group scored 23.06 (SD 24.5) vs SCOPA-AUT < 10 group 3.2 (SD 9.8), p = 0.007. Among those in SCOPA-AUT ≥ 10, a positive correlation was observed between PCL5 and total SCOPA-AUT score, p = 0.002, rho = 0.530. A higher prevalence of a previous traumatic event (OR 4.84, p = 0.034) or of any stress-related disorder (OR 15.4, p = 0.003) was also observed in those with in SCOPA-AUT ≥ 10 group.
Conclusions: The present study suggests that Parkinson's patients with stress-related disorders have a higher prevalence of dysautonomic symptoms. Further studies with better design are required to confirm our results.

P27.22

Respiratory dysfunction in Parkinson's Disease: Prevalence and determinants

Maarten J. Nijkrake, Veerle A. van de Wetering-van Dongen, Philip J. van der Wees, Joanna IntHout, Sirwan K.L Darweesh, Bastiaan R. Bloem, Johanna G. Kalf*
Radboud University Medical Center, Nijmegen, Netherlands

Background: The prevalence of respiratory dysfunction remains understudied in people with parkinsonism, which includes both Parkinson's disease (PD) and atypical parkinsonism (AP). A better understanding of respiratory dysfunction and early recognition may prevent late-stage complications such as (aspiration) pneumonia.
Objective: To examine the prevalence and determinants of respiratory dysfunction among people with parkinsonism.
Methods: A cross-sectional study in which data was gathered through a self-administered questionnaire among a population-representative sample of people with parkinsonism. Respiratory dysfunction was defined as experiencing at least one of the following symptoms: experiencing breathing difficulties, breathlessness/shortness of breath, tightening of the chest, frequent throat clearing, frequent coughing and coughing difficulties. We also defined composite constructs of respiratory dysfunction through a principal component analysis (PCA). We assessed the association of participant-reported determinants with measures of respiratory dysfunction using multivariable logistic regression models, with adjustment for pulmonary diseases, coronary artery diseases and covid-19 symptoms.
Results: The overall prevalence of respiratory dysfunction was 45% in a sample with 982 people (939 with PD, and 43 with AP). The prevalence was 42% after excluding pulmonary diseases or covid-19. The PCA resulted in two constructs of respiratory dysfunction: 'dyspnea' and 'impaired coughing', which together explained 68% of the total variance. Female gender (OR = 1.43; 95% CI [1.03-2.0]), a higher BMI kg/m2 (OR = 1.05; 95% CI [1.01-1.09]), longer disease duration in years (OR = 1.34; 95% CI [1.13-1.58]), more self-reported rigidity (OR = 1.16; 95% CI [1.06-1.26]), previous pulmonary disease(s) (OR = 6.87; 95% CI [4.21-11.19]), and anxiety (OR = 1.04; 95% CI [1.02-1.06]) were independently associated with 'dyspnea'. Pulmonary disease(s) (OR = 1.85; 95% CI [1.17-2.92]), covid-19 symptoms (OR = 2.03; 95% CI [1.41-2.93]), swallowing complaints (OR = 1.45; 95% CI [1.22-1.72]), drooling complaints (OR = 1.06; 95% CI [0.94-1.20]) and speech complaints (OR = 1.02; 95% CI [1.01-1.03]) were independently associated with 'impaired coughing'.
Conclusions: Symptoms of respiratory dysfunction are common among people with parkinsonism and can be separated into dyspnea and impaired coughing. Clinical assessment of the determinants associated with dyspnea and impaired coughing may contribute to timely recognition and treatment of respiratory problems to prevent late stage complications.

P27.23

Clinical and cognitive characteristics in Parkinson's: The role of white matter injuries is decisive?

Daniela Ortiz Zacarias, Ingrid Eloisa Estrada Bellmann*, Christopher Cerda, Roberto Estrella Silva, Juan Roberto Trejo Ayala, Beatriz Chavez Luevano, Fernando Góngora Rivera*
Hospital Universitario Dr José Eleuterio González, Monterrey, Mexico

Background: In recent decades there has been a growing interest in the significance of leukoaraiosis evidenced in neuroimaging studies in elderly population, whether it is related to age or is a consequence of vascular diseases, In neurodegenerative diseases such as Parkinson's the real impact is still unknown but it has been associated with a worse grade of the total UPDRS and all sub-scores, worse cognitive results, greater cardiovascular risk, and less response to treatments such as levodopa.
Methods: The database of the population with Parkinson's from the outpatient service of the University Hospital was used. Clinical, demographic and paraclinical data were collected from January 2014 to October 2020. Patients with Parkinson's over 18 years of age, were included, had to have a magnetic resonance study and FLAIR sequence. 4 scales were evaluated by magnetic resonance: Fazekas et al, modified Scheltens, Ylikoski and ARWMC, the cognitive sphere was valued through the Moca scale, the activities of daily life using the Schwab e England index and the degree of disability with Hoehn-Yahr stages.
Results: 49 patients with Parkinson's disease were recruited. Spearman's ratio coefficient was used to demonstrate the convergent validity of the different leukoaraiosis visual scales and volumetric measurements. The leukoaraiosis visual scale most correlated with leukoaraiosis volume was the Ylikosky scale for PD. 60% of the population was masculine males with median of age 58 (27-87); 36% hypertensive and 40% smokers. Clinical characteristics 63.3% tremor dominant, 32% stages II and 24% Stage III of H&Y. The correlation of the coefficients between the volume and the scales was moderate (0.30-0.59). Spearman's coefficient reported a high correlation between the scales (>0.60). The total periventricular score of the Scheltens and Ylikoski scales was moderately correlated (R=0.320, p=0.039, R=0.334, p=0.031, respectively) with the MDS-UPDRS part III motor score. no significant correlations were found when comparing the volume of leukoaraiosis with the MOCA score.
Conclusion: Moderate correlation with motor clinic valued by MDS-UPDRS III was found, unlike the proposed in literature there was no difference in cognitive sphere with could be due to a poor mediation of vascular mechanisms in Parkinson's dementia. Limitations was the lack of a control group.

P27.24

Association between anxiety and freezing of gait in Parkinson's diseases

Nathalia de Brito Pereira, Karina Yumi Tashima Honda*, Isaíra Almeida Pereira da Silva Nascimento, Katia Cirilo Costa Nobrega, Thayane Habache Barolli, Maria Elisa Pimentel Piemonte*
University of São Paulo, São Paulo, SP, Brazil

Introduction: Anxiety is a non-motor symptom correlated with episodes of freezing gait (FOG). The interaction between these two factors of high prevalence and great impact on quality of life has been described as a vicious cycle, where the anticipation of an episode of FOG can trigger a panic experience, and the consequent increase in anxiety symptoms, can trigger or exacerbate FOG. However, both the pathophysiology and the interrelation of these factors are still not well elucidated in the literature.
Purpose: To investigate the relationship between anxiety and FOG in individuals with Parkinson's Disease (PD)
Methods: The study remotely evaluated 24 individuals with PD (19 women and 5 men), aged between 39 and 71 years (mean 53.75, ±8.24), with a mean time of 12.04 years (±6.83) since diagnosis, with at least one episode of FOG per day, between stages I and IV in H&Y, using an average of 874.12 mg (±445.38) per day of levodopa. The average score of the sample is 16.58 (±4.30) T-MOCA; 12.59 (±7.50) UPDRS part I; 15.72 (±8.92) UPDRS part II; 35.66 (±13.51) PDQ39; 54.50 (±9.93) BIS-11. The instruments used to assess FOG and anxiety were the NFOG and BAI questionnaires, respectively.
Results: A moderate and positive correlation was found between the NFOG scores and the total BAI score (p=0.017, r=0.48); with an

average NFOG of 23.66 (±4.72) and BAI 18.13 (±10.68). Furthermore, the BAI scores can predict more than 48% of NFOG variability (R=0.482, p<0.022, estimated SE=4.3758).
Conclusion: The results showed that anxiety is associated with greater intensity or frequency of FOG episodes, regardless of other clinical aspects. Therefore, this association reinforces the importance of a broad and multidisciplinary approach to motor and non-motor aspects in PD.
Keywords: Parkinson's disease, freezing of gait, anxiety

P27.25

Atypical Parkinsonism and psychiatric disorder in hereditary diffuse leukoencephalopathy with spheroids: A novel variant in the CSF1R gene
Neus Rabaneda Lombarte[*,1], Belén Flores Pina[1], Dolores Vilas Rolan[1], Ana Castillo Gandía[2], Cristina Carrato Moñino[2], Katrin Beyer[3], Martí Paré Curell[1], Anna Massuet[4], Lourdes Ispierto González[1], Mireia Gea Rispal[1]*
[1] Neurology Department, Hospital Universitari Germans Trias i Pujol, Barcelona, Spain
[2] Pathology Department, Hospital Universitari Germans Trias i Pujol, Barcelona, Spain
[3] Pathology Department, Hospital Universitari Germans Trias i Pujol, Health Sciences Research Institute Germans Trias i Pujol, Universitat Autònoma de Barcelona, Barcelona, Spain
[4] Radiology Service, Institut Diagnòstic per la Imatge (IDI), Hospital Universitari Germans Trias i Pujol, Barcelona, Spain

Background: Hereditary diffuse leukoencephalopathy with spheroids (HDLS) is a rare disease with autosomal dominant inheritance caused by mutations in the colony stimulating factor 1 receptor (CSF-1R) gene. The clinical presentation is heterogeneous and includes atypical parkinsonism, psychiatric disorder, cognitive decline and seizures.
Objective: We describe the clinical, radiological and neuropathological phenotype of a patient carrying a novel variant in the CSF1R gene.
Case description: A 56-year-old male presented with severe apathy and abulia syndrome associated with bilateral asymmetric akinetic-rigid parkinsonism and pyramidal signs for the last six months, as well as a rapidly progressive multidomain cognitive decline consisting of a severe frontal lobe syndrome, and language, memory and orientation deficits. He had a first-degree relative with history of dementia with frontal lobe syndrome at the age of 65.
The brain magnetic resonance imaging (MRI) showed moderate subcortical atrophy and an extensive fronto-parieto-temporal leukoencephalopathy affecting the corpus callosum, with involvement of the pons. The cerebrospinal fluid and serum analysis, including the determination of antineuronal and onconeuronal antibodies was normal. Given the fast clinical decline, the atypical extrapyramidal and pyramidal signs with red flags and the extensive leukoencephalopathy, we aimed to rule out other treatable conditions with an atypical presentation, such as progressive multifocal leukoencephalopathy and intravascular lymphoma. Accordingly, a brain biopsy was performed demonstrating loss of myelin, glial reactivity, foamy macrophages and mild lymphocytic inflammation with T (CD3+) and B (CD20+) cells affecting mainly the white matter. The immunohistochemistry for neurofilaments revealed abundant neuronal spheroids. The ubiquitin, phosphorylated tau and amyloid-beta immunohistochemistry was negative. The genetic analysis identified the novel p.Leu672Pro variant in the CSFR1 gene.
Conclusions: In the presence of atypical parkinsonism, behavioral changes and rapidly progressive cognitive impairment with extensive leukoencephalopathy, especially in patients with positive family history, HDLS should be considered as part of the differential diagnosis. The p.Leu672Pro variant in the CSFR1 gene might be responsible for HDLS in this patient.

P27.26

Compliance with national and international guidelines in treatment of non-motor symptoms in late stage Parkinson's disease
*Kristina Rosqvist**
Lund University, Skåne University Hospital, Lund, Sweden

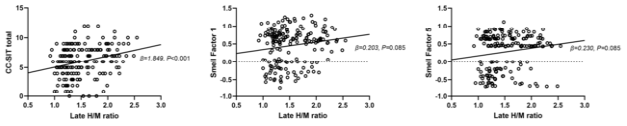
Background: National as well as international Parkinson's disease (PD) treatment guidelines are available. Previous research has shown that a large range of non-motor symptoms (NMS) and particularly neuropsychiatric symptoms are pronounced in late stage PD. It is therefore of high importance that NMS are screened for and adequately treated. Multinational analyses have suggested that current treatment in late stage PD is insufficient and could be improved.
Objective: Against a background of the national and international PD treatment recommendations, this study aims to investigate to which degree the guidelines are followed in the treatment of NMS in late stage PD.
Methods: This cohort constitutes the Swedish part of the European multicenter study Care of Late Stage Parkinsonism (CLaSP). Late stage PD was defined: Hoehn and Yahr stages IV-V in "on" and/or ≤ 50% on the Schwab and England ADL Scale. NMS were assessed with the NMS Scale (each item scored 0-12). Cognition was assessed with the Mini-Mental State Examination (MMSE). Depressive symptoms were assessed with the Geriatric Depression Scale (GDS-30).
Results: The study consisted of 107 patients, median age 78 years and median disease duration 15 years, the majority in HY IV (74%). All individuals exhibited presence of NMS to various degree and severity. NMS burden was median 91. The results showed that among symptomatic individuals (defined as ≥ 6 on item of the NMSS): 25% were treated with hypnotics for insomnia; 3% were treated with psychostimulant drugs for daytime sleepiness; 64% were treated with antihypotensives for orthostatic hypotension; 5% were treated with botulinum toxin for sialorrhea; 54% were treated with laxatives for constipation. For dementia (≥ 18 on the MMSE), 33% were treated with rivastigmine (cholinesterase inhibitor), 4% with donepezil (cholinesterase inhibitor), 37% with memantine. For hallucinations, 50% of symptomatic individuals were treated with antipsychotics; 11% with clozapine and 39% with quetiapine. For depressive symptoms, 57% of symptomatic individuals (≥ 10 on the GDS) were treated; 14% with SNRI (venlafaxine), 0 with TCA, 25% with NaSSA and 18% with SSRI.
Conclusions: Optimizing treatment of NMS according to the national and international treatment guidelines may improve symptomatology and enhance quality of life in late stage PD.

P27.27

Correlation of olfactory dysfunction in total and selective smell factors with cardiac sympathetic degeneration
Dong-Woo Ryu, Sang-Won Yoo, Ko-Eun Chol, Joong-Seok Kim**
Department of Neurology, College of Medicine, The Catholic University of Korea, Seoul, South Korea

Objective: It has been demonstrated that hyposmia is associated with autonomic failure in Parkinson's disease. The smell identification test for measuring olfactory function consists of multiple items to discriminate specific scents. We aimed to conduct the factor analysis of the smell identification test and investigate the

correlation of those with the degree of cardiac sympathetic denervation on MIBG myocardial scan.
Methods: We assessed olfactory function using Cross-Cultural Smell Identification Test (CC-SIT) and cardiac sympathetic function using 123I-MIBG myocardial scintigraphy in 183 patients with Parkinson's disease. Factor analysis of 12 items in CC-SIT was processed using the computed correlation matrix for the binary items. Five smell factors extracted over 1 of the sums of squared loadings were factor 1 (Soap, Pineapple), factor 2 (cinnamon, resin), factor 3 (gasoline, paint thinner), factor 4 (chocolate, lemon), and factor 5 (Onion). Multiple linear regression was performed to determine the correlation of CC-SIT total score and their 5 factors with a late heart-to-mediastinum ratio of MIBG uptake.
Results: In the enrolled subjects, the mean CC-SIT was 6.05 ± 2.58, and 133 patients (72.7%) had cardiac sympathetic degeneration. CC-SIT score and 5 smell factors were associated with neither dopamine transporter uptake on FP-CIT PET nor cognitive functions. CC-SIT score was significantly correlated with age (P<0.001) and the heart-to-mediastinum (H/M) ratio of MIBG uptake at the late phase (P<0.001). Factors 1 and 5 showed an increasing tendency as a larger H/M ratio but were not statistically significant (β=0.203, P=0.085; β=0.230, P=0.085; respectively).
Conclusions: This study demonstrated that olfactory dysfunction is associated with cardiac sympathetic burden in PD. The tendency in the soap and pineapple-dominant and onion-dominant smell factors suggests the possibility of selective hyposmia of odors in PD.



P27.28

The impact of freezing of gait on daily life mobility
Christian Schlenstedt[*,1], Jennifer Kudelka[2], Jonas Müller[2], Paul Fritz[2], Pia Reisdorf[2], Katharina Dirksen[2], Heiko Gassner[3], Clemens Becker[4], Anat Mirelman[5], Jeff Hausdorff[6], Lynn Rochester[7], Pieter Ginis[8], Alice Nieuwboer[8], Walter Maetzler[2]*
[1] Medical School Hamburg, Hamburg, Germany
[2] Department of Neurology, University Hospital Schleswig-Holstein, Kiel, Germany, Kiel, Germany
[3] University Hospital of Erlangen, Erlangen, Germany
[4] Robert-Bosch-Krankenhaus Stuttgart, Stuttgart, Germany
[5] Sackler School of Medicine and Sagol School of Neuroscience at Aviv University, Tel Aviv, Israel
[6] Tel Aviv University, Tel Aviv, Israel
[7] Translational and Clinical Research Institute, Newcastle University, Newcastle, United Kingdom
[8] KU Leuven, Department of Rehabilitation Sciences, Neurorehabilitation Research Group (eNRGy), Leuven, Belgium

Background: Freezing of Gait (FOG) in Parkinson's disease (PD) is a disabling symptom which impacts patients' quality of life [1]. FOG is usually assessed by self-reported outcomes retrospectively or by motor examination in the clinic. Little is known about when FOG occurs during the day and how it impacts daily life mobility.
Objective: To investigate how often and when FOG occurs over a period of 7 days and how it relates to daily life mobility. First, we hypothesize that the more periods of FOG during the day, the less active during the day. Second, we hypothesize that hours with FOG can be characterized by impaired gait kinematics such as higher gait variability.
Methods: This is a substudy of the Mobilise-D clinical validation study, a large European Union longitudinal study. In this sub-anaylsis, the baseline assessment of n=161 individuals with PD was included. The occurrence of FOG was assessed on an hourly base for 7 days with diaries. Additionally, severity of FOG was measured with the New Freezing of Gait Questionnaire (NFOGQ). Daily life mobility was assessed for the same period of 7 days with a wearable sensor (MoveMonitor, McRoberts) worn at the lower back.
Results: A total amount of n=1057 diaries were analyzed from the baseline assessment. FOG most often occurred during the early morning and during the afternoon, but data were highly heterogenous on an individual base. When comparing the data of the diaries with the data of the NFOGQ we found 4% of the participants reporting FOG in the diaries but not in the NFOGQ, and vice versa, respectively. Data analysis of the wearable sensor is currently ongoing and results will be provided at the conference.
Discussion: This study will provide information about the impact of acute hours with FOG on daily life mobility. The comparison of gait kinematics during hours with and without FOG will help understand the underlying mechanisms of the FOG symptom and will provide helpful information for the development of FOG detection algorithms.

P27.29

Visual dysfunction and performance in activities of daily living among persons with Parkinson's disease
Nicole Tester[*,1], Chiung-ju Liu[2], Yun Chan Shin[2], Aparna Wagle-Shukla[3]*
[1] UF Health Rehabilitation - Norman Fixel Institute for Neurological Diseases, Gainesville, FL, United States
[2] University of Florida, Gainesville, FL, United States
[3] University of Florida & Norman Fixel Institute for Neurological Diseases, Gainesville, FL, United States

While motor symptoms have long been the clinical focus to diagnose and treat Parkinson's Disease (PD), non-motor symptoms such as visual dysfunction have received growing attention. In Persons with PD, visual dysfunction ranges from dry eyes, blurriness, and double vision to deficits in contrast sensitivity, visual perception, and ocular movement. Although, intuitively, visual dysfunction could exacerbate limitations in activity and participation, studies examining correlations are sparse. This study aimed to investigate the prevalence of general awareness that PD can impact vision, describe visual dysfunction, and examine the association between visual dysfunction and performance in activities of daily living. Persons with PD from our Institute's research database were invited to complete a self-report survey containing items related to visual difficulties, diagnosed eye conditions, and general awareness about disease-related visual dysfunction. Ophthalmological symptoms and performance in activities of daily living were measured with the Visual Impairment Parkinson's Disease Questionnaire (VIPDQ) and the Revised Self-Reported Functional Visual Performance Scale, respectively. Data from 92 Persons with PD were analyzed. Nearly half were unaware their disease could impact vision. Awareness was not associated with disease duration. Individuals reporting awareness that their PD could affect visual functioning tended to report having trouble with vision relative to those who were unaware. Respondents who lived with a longer history of PD tended to report more symptoms based on the VIPDQ. However, age was not correlated with the VIPDQ. Functional activities requiring vision were mildly impaired; and the frequency of ophthalmologic symptoms was low. Despite this, a higher frequency of ophthalmologic symptoms was positively associated with a higher degree of disability in activities of daily living. This study demonstrates that Persons with PD with awareness tend to notice changes of vision and that there is a direct relationship between visual dysfunction and the ability to perform activities of daily living. It appears even mild changes in vision can impact independence in activities of daily living; yet general awareness that PD can impact

vision remains relatively low. Actively evaluating visual function may increase awareness, aid rehabilitation therapists in addressing functional independence, and allow timely intervention for Persons with PD.

P27.30

Relationship between cognitive functions and motor performance in patients with Parkinson's disease

Olena Tsurkalenko[*,1], Patricia Martins Conde[2], Claire Pauly[2], Sonja Jonsdottir[1], Stefano Sapienza[2], Laure Pauly[1], Anne-Marie Hanff[1], Jochen Klucken[1], Rejko Kruger[1]*
[1] Luxembourg Institute of Health, Strassen, Luxembourg
[2] University of Luxembourg, Esch-sur-Alzette, Luxembourg

Background: Although Parkinson's disease (PD) is primarily characterized by motor symptoms, cognitive impairment can occur at all stages of the disease. The cognitive performance is closely related with other functions and could worsen quality of life, motor and nob-motor symptoms in PD. At the same time, several types of motor impairments (akinetic-rigid, axial) are associated with a faster rate of cognitive decline in general and a greater risk of developing dementia.
Objective: To investigate the relationship between cognitive function and different motor or non-motor symptoms and establish its impact on the quality of life in people with PD.
Methods: We recruited 386 people with idiopathic PD from the Luxembourgish Parkinson Study who completed the basic assessment including Montreal Cognitive Assessment (MoCA), Trail Making Test A and B (TMT)], Hoehn & Yahr Scale (H&Y), MDS-UPDRS, Timed Up and Go (TUG), Parkinson's Disease Questionnaire – 39 (PDQ-39) and Beck Depression Inventory (BDI-I) on the thirst visit. Presence and severity of rigidity was computed as the sum of items 3.3 UPDRS; bradykinesia – 3.4-3.8, 3.14; axial symptoms (posture/balance/gait) – 3.9-3.13; freezing of gait (FOG) – 2.13, 3.11, tremor – 3.13-3.18. Pearson's correlation coefficients for multiple testing was used to evaluate the association between cognition and other parameters. To minimize effects of confounders (age, education, disease duration) a multivariate linear regression analysis was performed.
Results: Our analyses showed a positive correlation between cognitive deterioration and rigidity (r= 0.432, p = 0.034). TUG and presence of FOG correlated significantly with mental flexibility (TMT-B – TMT-A) (r= 0.382, p = 0.042; r= 0.324, p = 0.023 respectively) but not with global cognition. Worse cognitive performance was also correlated with a higher depression score and decreased quality of life.
Conclusion: A comprehensive understanding of the general neural systems underlying cognitive and motor control will hopefully lead to more concise and reliable explanations of distributed deficits. These findings highlight the importance of a parallel deep assessment of motor and cognitive function in PD. In future, we are planning a longitudinal analysis to develop cognitive predictors of motor impairment.

P27.31

Applications of acoustic analysis in the evaluation of the prosody in people with Parkinson

Alejandro Cano Villagrasa[*,1], Beatriz Valles-González[1], Cristina Agudo[2], Leticia Moreno[3]*
[1] Universidad Internacional de Valencia VIU, Valencia, Valencia, Spain
[2] Universidad de Valladolid, Valladolid, Castilla y León, Spain
[3] Asociación Parkinson Albacete, Albacete, Castilla-La Mancha, Spain

Introduction: In the context of logopedic care, it is necessary to have objective data on the characteristics of speech prosody in PwP in the different stages of this disease described by Hoehn and Yahr (1967), which will allow evidence-based care.
Objectives: The general objective is to quantitatively evaluate the prosodic speech alterations present in the different stages of PD, through the use of acoustic analysis. The following are proposed as specific objectives: (I) Identify prosodic speech disorders in PwP that are detected through the use of TEPHA (test de evaluación prosódica en el habla / prosody evaluation test), (II) Acoustically analyze the samples recorded during the application of TEPHA using the PRAAT program (Voice analysis software), (III) Compare the data obtained with the application of the TEPHA with the results of the acoustic analysis, (IV) Describe the results obtained with the two tools according to the different stages of PD and (V) Know the prevalence of dysprosody in the different stages of the PD.
Method: It is an investigation with a descriptive, cross-sectional design, with a single evaluation moment. The sample is constituted by 60 PwP distributed in three groups according to the stages of the PD. The inclusion criteria are having a diagnosis of idiopathic PD, being between stages II and IV, being between 50 and 70 years of age, and following adequate medical control. The exclusion criteria are: having an affected level of cognitive functioning, presenting a psychiatric diagnosis or using a deep brain stimulator. All the participants were recorded when they were evaluated with the TEPHA, later these recordings were analyzed using the PRAAT. The results were compared intragroup.
Results: The initial results show that prosody and intonation are progressively compromised as PD progresses, making it difficult for their interlocutors to understand the speech of PwP. The PwP showed better control of their oral expression in the initial stages, which allowed them to self-monitor and correct prosody and intonation.
Keywords: PD, Intonation, Dysprosody, Acoustic analysis.

P27.32

The impact of faecal microbiome transplantation (FMT) on gut physiology in Parkinson's disease patients with abnormal gut microbiota composition

Nora Vetkas[*,1], Lotta Luiskari[2], Tatyana D Fedorova[3], Reeta Levo[1], Berta Bosch[4], Riitta Korpela[2], Perttu Lahtinen[5], Rebekka Ortiz[6], Valtteri Kaasinen[7], Reetta Satokari[4], Perttu Arkkila[8], Filip Scheperjans[1]*
[1] Department of Neurology, Helsinki University Hospital and Clinicum, University of Helsinki, Helsinki, Finland
[2] Department of Pharmacology, Faculty of Medicine, University of Helsinki, Helsinki, Finland
[3] Nuclear Medicine and PET, Aarhus University, Aarhus, Denmark
[4] Human Microbiome Research Program, Faculty of Medicine, University of Helsinki, Helsinki, Finland
[5] Department of Gastroenterology, Päijät-Häme Central-Hospital, Lahti, Finland
[6] Department of Neurology, Tampere University Hospital, Tampere, Finland
[7] Clinical Neurosciences, University of Turku, Turku, Finland
[8] Department of Gastroenterology, Helsinki University Hospital, Helsinki, Finland

Background: Parkinson's disease (PD) has a heterogenous manifestation between individuals. However, a large body of research indicates that gastrointestinal dysfunction is a key aspect of PD and that the gut microbiota is involved in the symptoms, initiation, progression, and drug availability of PD. Modulation of the gut microbiota is becoming more widely recognised as a possible treatment option. Faecal microbiome transplantation (FMT), a therapeutic approach based on the gut microbiota, aims to replace a

dysfunctional microbiota with a healthy one. Animal studies and uncontrolled trials in humans have shown encouraging indications that FMT can be used to control gastrointestinal motility and motor symptoms.
Objective: The purpose of this research is to analyse the effect of FMT on objective and subjective markers of gastrointestinal function in PD patients.
Method: 47 Parkinson's patients aged 35 to 75 who tested positive for PD-dysbiosis in their faeces have been recruited from Helsinki, Turku, and Tampere University Hospitals. Patients were randomised to receive intracaecal infusions of donor FMT or placebo FMT in a 2:1 ratio. Follow-up visits occurred at 1, 2, and 3 weeks and 1, 3, 6 and 12 months after baseline visit. Gut dysfunction was assessed using computed tomography-based volume estimation and colonic transit time, stool diaries, and assessment of intestinal permeability using the Iohexol test.
Results: The impact of FMT on subjective and objective constipation as well as intestinal permeability will be assessed and reported as the primary outcome from baseline to 6 and 12 months.
Conclusions: In this study, the prospective therapeutic approach of FMT for treating both subjective and objective constipation and enhancing GI physiology in PD patients is investigated. The outcomes of this trial, which employs a personalised targeted therapy, are expected to shed light on the function of the microbiota in PD treatment and prevention.

P27.33

Safety and tolerability of adjunct non-invasive vagus nerve stimulation in people with Parkinson's: A randomised sham-controlled pilot trial

Alison Yarnall[*,1], Hilmar Sigurdsson[1], Heather Hunter[1], Lisa Alcock[1], Ross Wilson[1], Ilse Pienaar[2], Elizabeth Want[3], Mark Baker[1], John-Paul Taylor[1], Lynn Rochester[1]*
[1] Newcastle University, Newcastle upon Tyne, United Kingdom
[2] University of Birmingham, Birmingham, United Kingdom
[3] Imperial College London, London, United Kingdom

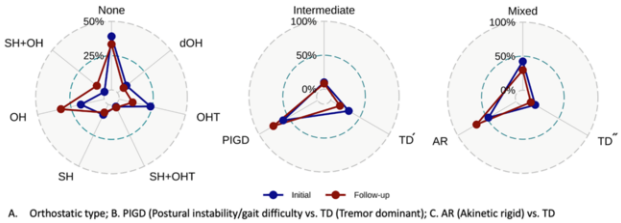
Background: Parkinson's disease (PD) is the fastest growing neurological condition worldwide. Recent theories suggest that symptoms of PD may arise due to spread of Lewy-body pathology where the process begins in the gut and propagate transynaptically via the vagus nerve to the central nervous system. In PD, gait impairments are common motor manifestations that are progressive and can appear early in the disease course. As therapies to mitigate gait impairments are limited, novel interventions targeting these and their consequences, i.e., reducing the risk of falls are urgently needed. Non-invasive vagus nerve stimulation (nVNS) is a neuromodulation technique targeting vagus nerve. We recently showed in a small pilot trial that a single dose of nVNS improved (decreased) discrete gait variability characteristics in those receiving active stimulation relative to those receiving sham stimulation. Further multi-dose, multi-session studies are needed to assess the safety and tolerability of the stimulation and if improvement in gait is sustained over time. **Design:** This will be an investigator-initiated, single-site, proof-of-concept, double-blind sham-controlled randomised pilot trial in 40 people with PD. Participants will be randomly assigned on a 1:1 ratio to receive either active or sham transcutaneous cervical VNS. All participants will undergo comprehensive cognitive, autonomic and gait assessments during 3 sessions over 24 weeks, in addition to remote monitoring of ambulatory activity and falls, and exploratory analyses of cholinergic peripheral plasma markers. The primary outcome measure is the safety and tolerability of multi-dose nVNS in PD. Secondary outcomes include improvements in gait, cognition and autonomic function that will be summarised using descriptive statistics. **Discussion:** This study will report on the proportion of eligible and enrolled patients, rates of eligibility and reasons for ineligibility. Adverse events will be recorded informing on the safety and device tolerability in PD. This study will additionally provide us with information for sample size calculations for future studies and evidence whether improvement in gait control is enhanced when nVNS is delivered repeatedly and sustained over time. **Trial registration:** This trial is prospectively registered at www.isrctn.com/ISRCTN19394828. Registered August 23, 2021.

P27.34

The natural history of orthostatic blood pressure instability in early Parkinson's disease

Sang-Won Yoo, Joong-Seok Kim*
Department of Neurology, College of Medicine, The Catholic University of Korea, Seoul, South Korea

Background and Objectives: Blood pressure (BP) lability is a frequent feature of early Parkinson's disease (PD), even in the prodrome. Cardiovascular dysautonomia accumulates with disease progression, but studies are lacking on the mechanism and prognosis behind each subtype except orthostatic hypotension (OH). This study aimed to describe the features of orthostatic subtypes in early de novo PD and investigate how each subtype progress during the follow-up.
Methods: Two hundred sixty-seven drug-naïve and de novo PD patients were included in this study. Their cardiovascular functions, particularly adrenergic functions, were assessed by head-up tilt-test and 123I-metaiodobenzylguanidine myocardial scintigraphy. All patients were classified as having supine hypertension (SH), orthostatic hypertension (OHT), delayed OH (dOH), or OH according to consensus criteria. The patients were assigned to one of three groups: extreme BP lability (BPextreme), mild BP lability (BPmild), and no BP lability (BPnone). The catecholamine deficits of 237 patients were re-assessed at 29.3 ± 9.4 and 30.0 ± 9.6 months with above respective tools.
Results: Overall, 61.8% of the initial population showed impaired adrenergic regulation: 29.6% (n=79/267) in the BPextreme group and 32.2% (n=86/267) in the BPmild group. At initial presentation, 23 (8.6%) had SH, 48 (18.0%) had OH, 22 (8.2%) were included in the dOH group, and 64 (24.0%) had OHT. At follow-up, the BPextreme group increased in number, while the BPmild group diminished. Most of the initial BPextreme patients maintained their initial subtype (67.0%) at follow-up. In comparison, 40.7% of the initial BPmild patients progressed to the BPextreme group, while 22.1% in the BPmild group. In the initial BPnone group, 32.4% and 14.7% progressed to BPextreme and BPmild, respectively. Non-tremor-dominant motor phenotype was the most frequent, however, was not associated with orthostatic subtype progression. Cardiac denervation was most severe in the BPextreme group, and linear gradient of impairment was observed across the subtypes.
Conclusions: Various forms of positional BP lability were observed during early disease stage. Subtypes SH and OH increased with disease progression, while OHT and dOH decreased, converting primarily to SH and/or OH.



A. Orthostatic type; B. PIGD (Postural instability/gait difficulty vs. TD (Tremor dominant); C. AR (Akinetic rigid) vs. TD

P27.35

Striatal dopaminergic depletion is related with cardiovascular non-motor symptom in drug-naïve patients with Parkinson's disease

Minkyeong Kim[1], Eugene Jeong[2], Jong Hyeon Ahn[2], Jin Whan Cho[2], Kyung-Han Lee[2], Seunghwan Moon[2], Jong Kyu Park[3], Jinyoung Youn[,2]*
[1] Gyeongsang National University Hospital, Jinju, South Korea
[2] Samsung Medical Center, Seoul, South Korea
[3] Soonchunhyang University Hospital, Cheonan, South Korea

Background: Despite the usefulness of dopamine transporter (DAT) imaging for the diagnosis of Parkinson's disease (PD), clinical interpretation is controversial, especially in terms of non-motor symptoms. This study aimed to investigate the correlation of striatal DAT uptake with motor and non-motor symptoms in drug-naïve, early-stage PD.
Methods: We enrolled drug-naïve, early-stage PD patients from Samsung Medical Center, Seoul, Korea. At the baseline, all PD subjects performed [18F] N-(3-fluoropropyl)-2β-carbonethoxy-3β-(4-iodophenyl)nortropane (18F-FP-CIT) positron emission tomography. Parkinsonian motor and non-motor symptoms were evaluated with Unified Parkinson's Disease Rating Scale (UPDRS) part 3 and non-motor symptoms Scale for Parkinson's disease (NMSS). We also checked levodopa equivalent daily dose (LEDD) after 5 years as a marker for the progression. We performed correlation analysis with stratal 18F-FP-CIT uptake and the scores from the aforementioned scales.
Results: We enrolled 41 drug-naïve, early-stage PD patients in this study. There was a significant correlation between putaminal DAT uptake and bradykinesia among motor symptoms, striatal uptake and cardiovascular symptoms among non-motor symptoms, and striatal uptake with LEDD after 5 years as a progression marker.
Conclusions: DAT scan could be useful not only for the diagnosis of PD but also as a potential biomarker for disease progression in PD patients. Additionally, DAT uptake is related to cardiovascular symptoms as well as motor symptoms in PD.

P27.36

The experience of pain in people diagnosed with Parkinson's disease at an early age: An interpretive phenomenological analysis

Sylvia Zimmers, Catherine Bungener*
Université Paris Cité, Laboratory of Psychopathology and Health Processes, F-92100 Boulogne Billancourt, France, Boulogne Billancourt, France

Parkinson's disease is a disabling neurodegenerative condition characterized by motor and non-motor signs. Pain, considered by patients as the most disabling non-motor symptom, is undervalued and undertreated. Models for understanding the phenomenon of pain are gradually emerging, highlighting diverse and particularly complex pain profiles. In addition, the first studies on pain identified that women, patients diagnosed at an early age, those with motor complications, with a longer disease duration and depressed and anxious patients, experienced more pain. However, few studies have focused on the subjective experience of patients.
The aim of our study was, therefore, to analyze the processes of making sense of the experience of pain through the exploration of representations of the disease and pain in PD.
Non-directive interviews were conducted with individuals with pain who had received a Parkinson's disease diagnosis. Four French-speaking participants (diagnosed at an early age and with various pain profiles) were included in this study.
Qualitative analyses conducted in IPA (Interpretive Phenomenological Analysis) identified four major themes: the history of the disease, adaptation to the disease, losses related to pain and strategies deployed to regain control over pain.
These qualitative results offer a better understanding of the subjective experience of pain in individuals diagnosed with the disease at an early age, and highlight the processes of adaptation implemented by the participants, despite the major identity upheaval caused by the disease and pain. They also shed light on how the relational dimension of pain takes place in this painful experience.

CLINICAL SCIENCE: Progression & prognosis

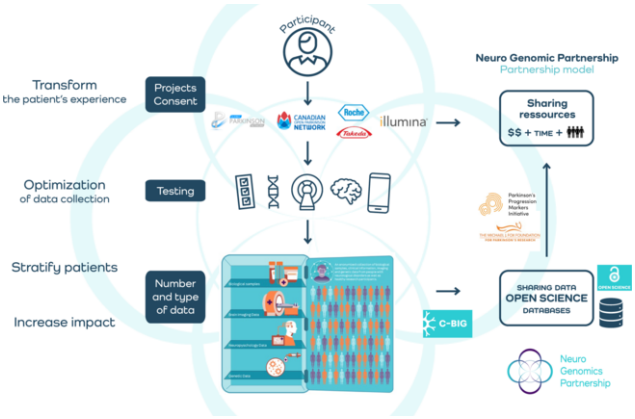
P28.01

The neuro genomics partnership: A new consortium dedicated to a fully open patient to patient (P2P) integrative R&D approach

Clotilde Degroot[,1], Kirsten Taylor[2], Sandor Szalma[3], Vincent Mooser[4], Ziv Gan-Or[4], Madeleine Sharp[4], Thomas Durcan[4], Caitlin Taylor[5], Marc Lussier[4], Edward Fon[4]*
[1] The Montreal Neurological Institute, Montreal, Quebec, Canada
[2] Roche, Bâle, Switzerland
[3] Takeda, San Diego, United States
[4] McGill University, Montreal, Canada
[5] Illumina, Toronto, Canada

Objective: The Open Science Neuro Genomics Partnership (NGP) has been established in 2021 by The Montreal Neurological Institute (The Neuro) in order to bring together several public and private actors including Takeda and Roche around the common objective of better understanding the nervous system and deliver much needed early diagnostic modalities and effective treatments for neurological diseases.
Background: The NGP brings about a step change in the discovery process for brain diseases by harnessing and integrating recent advances in genomics, big data and the unique patient populations recruited and followed at the Neuro and in Quebec.
Methods: The initial focus of NGP is on prodromal synucleinopathies including REM Behavioral Disorders (RBD), Parkinson's Disease (PD) and related syndromes. NGP's activities are possible thanks to the Neuro ecosystem: The Clinical Biospecimen Imaging and Genetic Repository (C-BIG-R), The Early Drug Discovery Unit (EDDU), The Clinical Research Unit (CRU), The Canadian Open Parkinson Network (C-OPN) and The Quebec Parkinson Network (QPN).
The NGP's activities consist of distinct modules. Module 1: Genomic studies - Perform a comprehensive genetic analysis involving whole genome sequencing (WGS) in iRBD patients to identify rapid converters and stratify them for enrolment into clinical trials. Module 2: Deep clinical phenotyping - Prospectively deeply phenotype a proportion of iRBD patients and a comparable group with PD and controls. Module 3: New diseases models - Identify disease phenotypes in microglia (MGLs) of LRRK2 PD patients.
Results: Module 1: 1200 samples with completed WGS (1140 RBD and 60 PD). Module 2: 60 PD, 60 RBD and 60 HC with deep clinical phenotyping: MRI, MDS-UPDRS, Neurospych assessment and PBMCs. Module 3: PBMCs obtained from PD or controls can be used as source of MGLs. From multiple runs (n=3 independent tests) with different vials of PBMCs, MGLs were successfully generated.

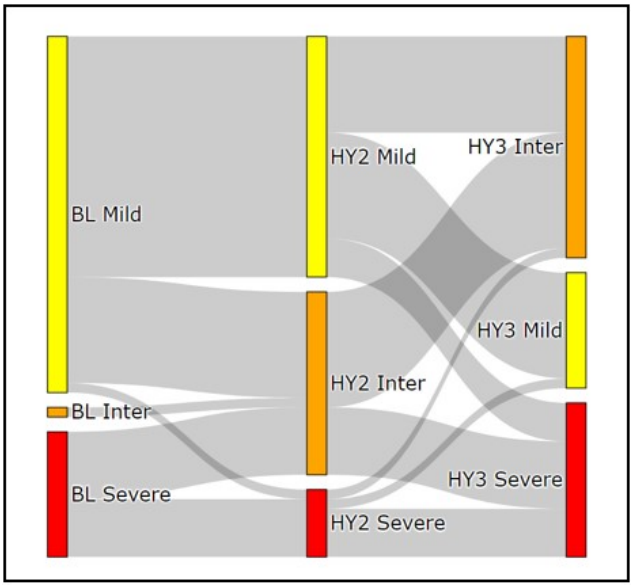
Conclusions: The model of the NGP involves a partnership between The Neuro and a number of key stakeholders. Each Member contributes to funding the Scientific Program. It is fully executed according to The Neuro Open Science Principles and, as such, all results generated will be deposited into the C-BIG-R and will be shared openly.



P28.02

Parkinson's: One disease or several? The fallacy of subtypes
*Jodie Forbes**
King's College London, London, United Kingdom

Background: Parkinson's disease (PD) is highly heterogenous in its clinical presentation and progression, suggesting that there may be several subtypes.
Objectives and Methods: We used machine learning techniques on two large datasets, PPMI (n=1,095) and CPP (n=9,145), over periods of up to 10 years, to provide insights into four questions, focusing on idiopathic PD: (1) based on clinical presentation, are there distinct PD clusters? (2) are the clusters stable over time? (3) are there distinct patterns of disease progression? (4) can the progression of PD be predicted?
Results:
(1) Patients can be grouped into clusters based on clinical presentation. We generated various cluster models, confirming the findings of several previous studies.
(2) Clusters are unstable. We demonstrated this by showing how a significant number of patients switch clusters between baseline and transition to Hoehn & Yahr stages 2 and 3.
(3) We developed an 8-state model of disease progression based on different elements of the MDS-UPDRS scoring process and found that there was a continuum rather than a discrete set of progression paths through this model.
(4) Some aspects of progression can be predicted, but not with high levels of confidence. For example, we identified a negative correlation (r=-0.64) between the severity of PD at baseline and the subsequent rate of increase in overall MDS-UPDRS score; and a positive correlation (r=0.49) between mild cognitive issues at baseline and more severe subsequent cognitive decline. However, a variety of supervised machine learning algorithms did not yield any useful predictive models.
Conclusion: Whilst it is possible at any stage of PD to allocate patients to clusters based on their clinical presentation, these clusters will be unstable and our analysis suggests that they likely relate to a common underlying pathology. The heterogeneity of PD phenotypes and progression is then a function of disparate individual response to multiple incremental genetic, physiological, environmental and therapeutic factors, rather than a set of distinct underlying disease pathologies. Consequently, prognostic capability is limited without additional biomarkers.



P28.04

Pure autonomic failure developed parkinsonism without changes in 18F-FP-CIT PET: A case study
*Oh Dae Kwon**
Daegu Catholic University Medical Center; Daegu Catholic University School of Medicine, Daegu, South Korea

Background: Primary autonomic failure is a rare neurodegenerative disease.
Case: The course and combined symptoms of the illness are variable. A 42-year-old woman developed orthostatic dizziness and was diagnosed as a pure autonomic failure. The Brain MRI & MRA were normal and the 18F-FP-CIT PET taken two times in two-year intervals were within the normal range. Initial and follow-up cognitive function tests were normal. The autonomic function test shows an abnormality in the tilt table test, showing significant orthostatic hypotension and loss of consciousness after 2 minutes of standing position. Midodrine was prescribed but she developed hypertension and a throbbing headache. Pyridostigmine was applied instead of midodrine and her activities of daily living were fairly maintained. She developed voiding symptoms and constipation after 5 years of onset. After 10 years of pure autonomic symptoms, asymmetric bradykinesia, and decreased arm swing developed on her right side. Her gait was slurred and her posture was stooped. Pramipexole was applied and her parkinsonism symptoms were partially improved. Interestingly, the third 18F-FP-CIT PET also shows normal findings.
Conclusion: We report a case of pure autonomic failure who developed parkinsonism after 10 years of onset without abnormality in the follow-up 18F-FP-CIT PET.

P28.05

Larger ventricle may predict the development of freezing of gait in Parkinson's disease

Jae-jung Lee[*,1], Young Bok Yong[1], Jong Sam Baik[2]*
[1] Ilsan Paik Hospital, Inje University College of Medicine, Goyang-si, Gyeonggi-do, South Korea
[2] Sanggye Paik Hospital, Inje University College of Medicine, Goyang, Seoul, South Korea

Objective: To explore the impact of the cerebral ventricular dimension on clinical manifestations of Parkinson's disease (PD).
Materials and Methods: The current registry-based retrospective cohort study recruited 101 de novo patients with PD, whose Evans' index (EI) were < 0.3 and stratified by the cut-off value of 0.25. Morphometric parameters of the cerebral ventricle included EI, frontal-occipital horn ratio (FOHR), callosal angle (CA), callosal height (CH), and temporal horn width (THW).
Results: The larger-ventricle group demonstrated a significantly lesser improvement in the UPDRS III score (33.7 ± 9.5 to 28.9 ± 8.1) than that of the normo-ventricle group (32.5 ± 6.1 to 24.3 ± 5.8) over 1 year of medical treatment ($p < 0.003$), especially in the axial sub-domain. Furthermore, the larger-ventricle group presented a higher development rate of the freezing of gait (FOG) compared to the normo-ventricle group (17/48 (35.4 %) vs 5/53 (9.4 %); $p = 0.002$) during 51.8 ± 6.2 months of the mean follow-up duration. A larger ventricle was observed to be a significant risk factor for the future development of the FOG (HR, 3.04; 95% CI, 1.005 – 8.710; p, 0.046).
Conclusions: Our data demonstrated a larger ventricle to be a potential risk factor for the future development of the FOG in patients with PD, although being a lack of evidence for outright ventriculomegaly. Given heterogeneous etiology of the pathogenesis in PD, the dimension of the cerebral ventricle might play a negative role in the motor manifestations in PD.

P28.06

Development and validation of a 7-year prognostic model for institutionalization in Parkinson's disease: An individual-participant-data meta-analysis

Yan Li[*,1], David McLernon[1], Rachael Lawson[2], Alison Yarnall[2], David Bäckström[3], Lars Forsgren[3], Marta Camacho[4], Caroline Williams-Gray[4], Jodi Maple-Grødem[5], Guido Alves[5], Ole-Bjørn Tysnes[6], Carl Counsell[1], Angus Macleod[1]*
[1] University of Aberdeen, Aberdeen, United Kingdom
[2] Newcastle University, Newcastle, United Kingdom
[3] Umeå university, Umeå, Sweden
[4] University of Cambridge, Cambridge, United Kingdom
[5] University of Stavanger, Stavanger, Norway
[6] University of Bergen, Bergen, Norway

Background: People with Parkinson's disease (PWP) may need care in nursing homes or similar institutions (institutionalization) if they lose the ability to look after themselves and insufficient care is available at home. This has major social and financial implications. A better understanding of institutionalization in PWP and being able to predict admission to care would allow information provision, improve clinical risk stratification, and inform health care planning. We therefore aimed to describe the incidence of institutionalization in PWP and develop a prognostic model to predict individualised risk of institutionalisation.
Methods: Data was analysed from the Parkinson's Incidence Cohorts Collaboration, a pooled dataset from 6 prospective incidence cohorts in UK (CamPaIGN, ICICLE-PD, PICNICS, PINE), Norway (ParkWest), and Sweden (NYPUM). We visualised time to institutionalisation using Kaplan-Meier curves and calculated incidence rates. A Royston-Parmar flexible parametric survival model predicting institutionalisation over seven years was developed using one-stage individual-participant-data meta-analysis. ICICLE was excluded from the model due to follow-up being less than 7 years. We used internal-external cross-validation to assess discrimination (using Harrell's Concordance (C) statistic to test the model's ability to discriminate between patients at low and high risk) and calibration. Missing data was imputed with multiple imputation.
Results: Incidence rates ranged from 1.7 to 5.0 per 100 person-years with substantial heterogeneity between studies. 156 PWP were institutionalised within the 7-year time horizon in the five included studies. Baseline age, sex, MDS-UPDRS, Hoehn and Yahr scale, and MMSE were predictors in the model. Harrell's C ranged from 0.71 to 0.84 across the studies suggesting fair to good discrimination. Mean calibration (observed versus average predicted risk) ranged from 0.60 to 1.29. The calibration slope showed systematic underprediction in 3 studies (1.20–1.44) and overprediction in 2 studies (0.61–0.95). Recalibration was performed for four out of five studies. After recalibration, mean calibration improved (ranged from 0.86 to 0.94).
Conclusion: Key early predictors were age, MDS-UPDRS, and MMSE. We have developed valid prognostic models, but given between-cohort heterogeneity, these models are best used with recalibration to the institutionalisation rate in the relevant population.

P28.07

Machine learning-based prediction of cognitive decline in early Parkinson's disease using multimodal features

Hannes Almgren[1], Milton Camacho[1], Alexandru Hanganu[2], Mekale Kibreab[1], Richard Camicioli[3], Zahinoor Ismail[1], Nils D. Forkert[1], Oury Monchi[,4]*
[1] University of Calgary, Calgary, Alberta, Canada
[2] University of Montreal, Montreal, Quebec, Canada
[3] University of Alberta, Edmonton, Alberta, Canada
[4] Centre de Recherche, Institut Universitaire de Gériatrie de Montréal, Montréal, Québec, Canada

Patients with Parkinson's Disease (PD) often suffer from cognitive decline. Accurate prediction of cognitive decline is essential for early treatment of at-risk patients. Previous machine learning studies mainly focused on prediction of conversion between categories. However, prediction of longitudinal change in cognitive test scores could be more informative. Here, we used demographic variables, clinical test scores, brain volumes, CSF biomarkers, and genetic variants (107 input features in total) for the prediction of decline in continuous global cognitive scores in patients with early PD.
Data were obtained from the Parkinson's Progression Markers Initiative database (PPMI). A total of 213 PD were selected based on: (1) a diagnosis of PD at the start of the study, (2) availability of a T1-weighted MRI scan and all other features at baseline used in the present study, and (3) completeness of a Montreal Cognitive Assessment (MoCA) test score at baseline and approximately 4 years post-baseline. Cortical volume was estimated for each region using Freesurfer. Features were ranked using the RReliefF algorithm, and random forest regression was used for prediction. Predictive performance was assessed using 10-fold cross validation. The outcome of the model was the difference between the baseline MoCA score and the score four years after.
Our best machine learning model for cognitive decline in de novo PD consisted of sixteen features: four genetic mutations, two CSF biomarkers, two clinical test scores, baseline cognition, four cortical regional volumes, total brain volume, and two subcortical regional volumes (Table 1). Pearson correlation between predicted and observed MoCA change was 0.38.

Next, we tested linear associations between selected features and cognitive change. Statistically significant positive associations with change in MoCA score (indicating that higher scores are related to less cognitive decline) were found for right hippocampal volume and total brain volume, while significant negative relationships were found for baseline MoCA, CSF total tau, and RBD questionnaire scores.
The predictive features in our model included features that have been linked to Alzheimer's disease (AD), such as hippocampal volume, APOE ε4 and CSF tau concentration, adding to the body of evidence showing an important overlap between features related to cognitive decline in PD and AD.

Features	
1. Baseline cognition	9. GBA (N370S)
2. CSF phosphorylated tau	10. Right inferior parietal volume
3. Right hippocampal volume	11. Left parahippocampal volume
4. APOE ε4	12. Total brain volume
5. MAPT (rs17649553)	13. Left middle temporal volume
6. Daytime sleepiness[1]	14. REM sleep behavior disorder[2]
7. CSF total tau	15. SNCA (rs356181)
8. Left hippocampal volume	16. Right parahippocampal volume

Table 1. The predictive features in our study. [1]Score on Epworth Sleepiness Scale. [2]Score on REM Sleep Behavior Disorder Questionnaire. *Abbreviations:* APOE = apolipoprotein E, MAPT = microtubule associated protein tau, GBA = glucosylceramidase beta 1, SNCA = Synuclein Alpha, CSF = cerebrospinal fluid.

P28.08

Effects of dihydropyridines on the motor and cognitive outcomes of patients with Parkinson's disease

Jin Ho Jung[1], Han Kyu Na[2], Seong Ho Jeong[3], Seok Jong Chung[4], Han Soo Yoo[5], Yang Hyun Lee[2], Kyoungwon Baik[2], Sang Jin Kim[6], Young H Sohn[2], Phil Hyu Lee[2]*
[1] Busan Paik Hospital, Inje University College of Medicine, Busan, South Korea
[2] Yonsei University College of Medicine, Seoul, South Korea
[3] Sanggye Paik Hospital, Inje University College of Medicine, Seoul, South Korea
[4] Yongin Severance Hospital, Yonsei University Health System, Yongin, South Korea
[5] Gangnam Severance Hospital, Yonsei University College of Medicine, Seoul, South Korea
[6] Busan Paik Hospital, Inje University College of Medicine, Seoul, South Korea

Background: Dihydropyridines are suggested to exert neuroprotective effects against Parkinson's disease (PD). This study investigated the effects of dihydropyridines on nigrostriatal dopaminergic denervation and longitudinal motor and cognitive outcomes in PD.
Methods: We classified 476 patients with drug-naïve PD who had undergone dopamine transporter (DAT) imaging, into three groups. They were selected according to a prior diagnosis of hypertension and use of dihydropyridines, and matched using propensity scores: patients without hypertension (HTN-, n=50) and patients with hypertension treated without dihydropyridine (HTN+/DHP-, n=50) or with dihydropyridine (HTN+/DHP+, n=50). Multiple linear regression and linear mixed model analyses were performed to determine intergroup differences in baseline DAT availability and longitudinal changes in the levodopa-equivalent dose, respectively. Using Kaplan–Meier analyses, we compared the risks of levodopa-induced dyskinesia, wearing-off, and dementia-free survival during the 5.06 years of the mean follow-up period. The Cox regression model determined the independent effects of dihydropyridines on dementia conversion.
Results: DAT availability in all striatal subregions was comparable between the HTN-, HTN+/DHP-, and HTN+/DHP+ groups. The risks of levodopa-induced dyskinesia and wearing-off, as well as longitudinal changes in the levodopa-equivalent dose, did not differ between the groups. The HTN+/DHP+ group had a lower risk of developing dementia than the HTN+/DHP- (Bonferroni-corrected p=0.036) group. The use of dihydropyridine was independently associated with a lower risk of dementia conversion after controlling for other antihypertensive drugs and confounding factors (hazard ratio, 0.242; 95% confidence interval, 0.087-0.668; p=0.006).
Conclusions: Dihydropyridines appears to be associated with better long-term cognitive outcomes in hypertensive patients with PD.

P28.09

Clinical evidence and upcoming neuroprotective strategies for Parkinson's disease: An update

*Olivier Uwishema**
Oli Health Magazine Organization(OHMO), Kigali, Kigali, Rwanda

Background: Parkinson's disease (PD) is a progressive neurodegenerative disease, clinically characterized by motor symptoms, such as rigidity, tremor, bradykinesia, and non-motor symptoms, like cognitive decline, depression, and anxiety. Early detection is crucial for the management of PD; as a result, it can be achieved by examining genomic make-up, associated epigenetic indicators, and integrating them with already employed clinical PD diagnosis techniques.
Aim: To analyse upcoming modalities of therapeutic clinical trials in an attempt to outline possible treatment options for PD.
Method: Literature was screened using the databases PubMed, Web of Science, Science Direct, Scopus and the National Library of Medicine. Articles comprising information on PD and its latest therapeutic modalities to cure the disease were considered.
Result: The ongoing research into new therapeutic alternatives has been sparked by the lack of a permanent cure for PD. Diverse medications are now being formulated on nanoparticles, which provides several benefits over traditional therapies. Due to its size and makeup, this form of multifunction carrier interacts differently with biomolecules, which can reduce its capacity to penetrate the blood-brain barrier. Clinical trials with intrastriatal transplantation of human fetal mesencephalic tissue, rich in dopaminergic neurons, in PD patients, have also been considered, revealing that cell replacement could induce major, long-lasting improvement.
Conclusion: While there are currently treatments available that aim to lessen or control the disease, researchers are also working on future therapies, including clinical trials to evaluate the effectiveness of promising therapeutic modalities like epigenetic modulation, LRRK2 inhibition, and intravenous N-acetylcysteine administration. Constraints in clinical trial design and the restricted emphasis on biological targets for therapy can be credited for the failure of drug development for PD which needs to be urgently addressed.

CLINICAL SCIENCE: Behavioral disorders

P29.01

Cognitive behavioral therapy for anxiety in Parkinson's disease induces functional brain changes

Guillaume Carey[1], Renaud Lopes[1], Anja Moonen[2], Anne Mulders[2], Joost de Jong[2], Gregory Kuchcinski[1], Defebvre Luc[1], Mark Kuijf[2], Kathy Dujardin[,1], Leentjens Albert[2]*

[1] Univ. Lille, Inserm, CHU Lille, U1172 - LilNCog - Lille Neuroscience & Cognition, Lille, France, Lille, France

[2] School for Mental Health and Neurosciences (MHeNS), Maastricht University, Maastricht, The Netherlands, Maastricht, Netherlands

Background: Cognitive behavioral therapy (CBT) reduces anxiety symptoms in patients with Parkinson's disease (PD).

Objective: The objective of this study was to identify changes in functional connectivity in the brain after CBT for anxiety in patients with PD.

Methods: Thirty-five patients with PD and clinically significant anxiety were randomized over two groups: CBT plus clinical monitoring (10 CBT sessions) or clinical monitoring only (CMO). Changes in severity of anxiety symptoms were assessed with the Parkinson Anxiety Scale (PAS). Resting-state functional brain MRI was performed at baseline and after the intervention. Functional networks were extracted by an Independent Component Analysis (ICA). Functional connectivity (FC) changes between structures involved in the PD-related anxiety circuits, such as the fear circuit (involving limbic, frontal, and cingulate structures) and the cortico-striato-thalamo-cortical limbic circuit, and both within and between functional networks were compared between groups and regressed with anxiety symptoms changes.

Results: Compared to CMO, CBT reduced the FC between the right thalamus and the bilateral orbitofrontal cortices and increased the striato-frontal FC. CBT also increased the fronto-parietal FC within the central executive network (CEN) and between the CEN and the salience network. After CBT, improvement of PAS-score was associated with an increased striato-cingulate and parieto-temporal FC, and a decreased FC within the default-mode network and between the dorsal attentional network and the language network.

Conclusion: CBT in PD-patients improves anxiety symptoms and is associated with functional changes reversing the imbalance between PD-related anxiety circuits and reinforcing cognitive control on emotional processing.

P29.02

Jumping to conclusions (JtC) and its association with psychosis and impulsivity in early stages of Parkinson's disease

Ioanna Pachi[,1], Vasilis Papadopoulos[2], Christos Koros[2], Athina-Maria Simitsi[2], Anastasia Bougea[2], Maria Bozi[3], Nikos Papagiannakis[2], Rigas-Filippos Soldatos[2], Dimitra Kolovou[2], George Pantes[2], Nikolaos Scarmeas[2], Georgios Paraskevas[3], Konstantinos Voumvourakis[3], Sokratis Papageorgiou[2], Konstantinos Kollias[4], Nikos Stefanis[4], Leonidas Stefanis[2]*

[1] KAT Attica General Hospital, 1st Department of Neurology, Aeginition Hospital, National and Kapodistrian University of Athens, Athens, Greece

[2] 1st Department of Neurology, Aeginition Hospital, National and Kapodistrian University of Athens, Athens, Greece

[3] 2nd Department of Neurology, Attikon University Hospital, National and Kapodistrian University of Athens, Athens, Greece

[4] 1st Department of Psychiatry, Aeginition Hospital, National and Kapodistrian University of Athens, Athens, Greece

Objective: The aim was to identify whether the presence of Jumping to Conclusions (JtC) tendency is associated with the onset of psychotic symptoms or impulsive-compulsive behaviors (ICBs) in patients with early Parkinson's disease (PD).

Background: The JtC bias refers to a decision-making style characterized by reaching certainty after limited data gathering. According to few reports, PD patients with ICBs have the tendency of an impairment in working memory tasks including JtC bias. Until present, it has not been determined whether the presence of JtC tendency is associated with the occurrence of psychotic features in PD.

Methods: The design of the study was cross-sectional. Healthy controls and patients within three years of PD onset were recruited. Participants were examined for psychotic symptoms using a 10 question PD specific psychosis severity scale. JtC was measured in both groups by a probalistic reasoning scenario, known as the Beads Task. In the PD group, medication use, motor and non-motor symptoms were documented. Impulsivity was evaluated using the Questionnaire for Impulsive-Compulsive Disorders in PD (QUIP).

Results: 74 healthy individuals (37% male, mean age: 68±7.9 years) and 70 PD patients (67% male, mean age: 63±11.9 years) participated in the study. The prevalence of psychotic features was 3% (2/74) in healthy controls, compared to 33% (23/70) in PD patients [p<0.001], while the JtC bias was noticed in 9% (6/70) of the healthy group, compared to 32% (22/68) of PD group [p=0.001]. No association was detected between the presence of JtC tendency and PD-associated psychosis (p=0.216). Regardless of the dopaminergic therapy, the JtC bias was associated with a seven-fold increasing risk of impulsivity in the PD group, (adjusted OR: 7.3, 95% CI:1.7-30.4, p=0.007), despite the small number of PD individuals presenting ICBs (n=12).

Conclusions: We found a highly significant seven-fold increase of impulsivity in PD patients with JtC bias, despite the small sample size. There was no association between psychotic features and JtC tendency. Additional studies are needed to confirm our results and further elaborate on the underlying pathophysiological neural mechanisms that correlate impulsivity with JtC tendency, which are likely to be different from those mediating psychotic features in early PD.

P29.03

Multidisciplinary approach as key to successful management of functional disorders in patients treated with deep brain stimulation – A report of two patients

Marijan Masic[,1], Valentino Racki[2], Elisa Papic[2], Ines Toric[1], Vladimira Vuletic[2]*

[1] Department of Neurology, Clinical Hospital Center Rijeka, Rijeka, Croatia

[2] Department of Neurology, Faculty of Medicine, University of Rijeka, Rijeka, Croatia

Introduction: Functional disorders after deep brain stimulation implantation are beginning to be recognized as the number of patients and physician experience grows, even though it is present in a small number of patients.

Case series: We present two cases of patients that developed functional symptoms following deep brain stimulation implantation and treatment. First is a 62-year-old female who had bilateral STN-DBS done in 2019., seven years after disease onset. Patient was referred from another centre after the inability to regulate severe

right-sided tremor that occurred after levodopa reduction. Upon initial examination, it was noticed that sham stimulation helped the patient symptoms consistently, with tendencies for increased depressive symptoms as noted by our psychologist and psychiatrist. Second patient is a 54-year-old male who had bilateral STN-DBS done in 2021., seven years after disease onset. He had an excellent initial response to DBS and regained working capability as a butcher. In the months after implantation, he reported for numerous emergency visits of worsening that improved even after sham stimulation changes. Trained movement disorder physiotherapist and nurse noticed that the symptoms subside in distraction of everyday care. Likewise, for both patients the basis for worsening was the sudden increase in functionality after implantation and stimulation, which led to a change in family dynamics and a decrease of “care” from family members. Both patients improved after psychological support, with no significant changes to parkinsonian therapy and stimulation.
Conclusion: Multidisciplinary approach with a team consisting of experienced movement disorder specialist, trained nurses and physiotherapists, as well as psychologists and psychiatrists are best suited to deal with functional disorders after deep brain stimulation. Each team member is instrumental in tackling this problem, through a thorough exam that detects the functional aspect of the symptoms, to treatment and continuous care that is the role of the whole team.

P29.04

Mindfulness-based cognitive therapy for anxiety and depression in people with PD

Andreea Seritan[*,1], Ana-Maria Iosif[2], Prarthana Prakash[3], Sarah Wang[1], Stuart Eisendrath[1]*
[1] University of California, San Francisco, San Francisco, California, United States
[2] University of California, Davis, Davis, California, United States
[3] Rhode Island Hospital, Providence, Rhode Island, United States

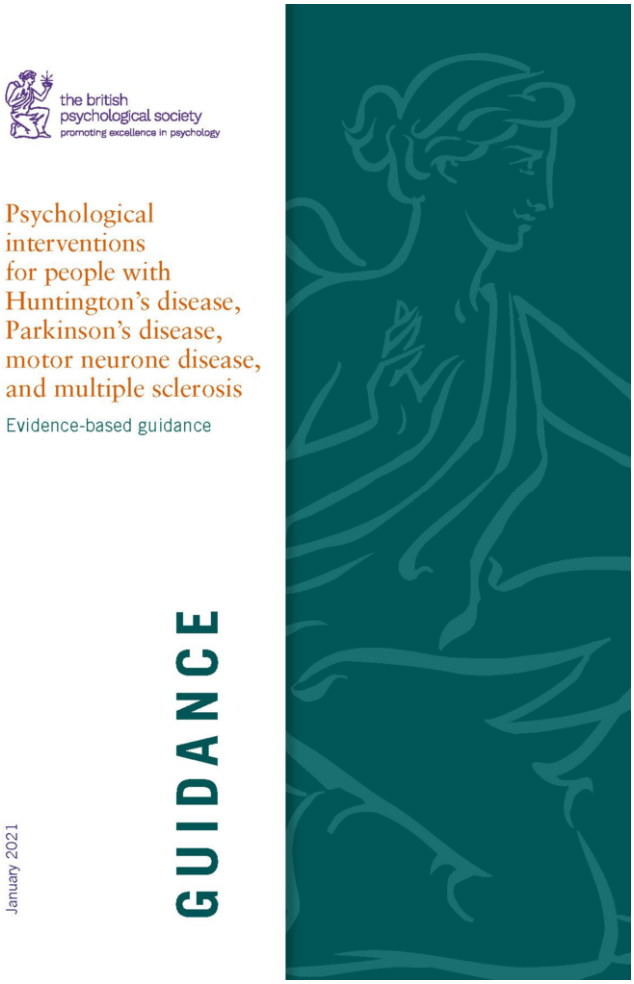
Introduction: Anxiety and depression are common nonmotor symptoms of Parkinson’s disease (PD). Mindfulness-based cognitive therapy (MBCT) is a mindfulness intervention conducted in 8-week group sessions plus participant independent practice. MBCT prevents recurrent depression relapse and improves anxiety and has been studied in patients with PD, although not extensively. Using a modified MBCT protocol, we investigated MBCT effectiveness in reducing anxiety and depression for people with PD in two pilot trials (NCT03904654, NCT04469049).
Methods: People with PD and mild-to-moderate anxiety and/or depressive symptoms participated in one of two studies. The first study was in-person (September 2019-March 2020, limited to San Francisco Bay Area residents). The second study was virtual (November 2020- June 2021, recruited people with PD from across the U.S.). Participant demographic, clinical variables, and pre- and post-intervention Generalized Anxiety Disorder-7 Item (GAD-7) and Patient Health Questionnaire-9 (PHQ-9) scores were collected. Descriptive statistics were used to summarize the demographic and clinical variables. Linear mixed-effects regression models with fixed effects for time (Pre-, Post-) and study (Study 1, Study 2) and a random effect for person-specific intercept were used to assess pre- to post - changes in GAD-7 and PHQ-9 scores. This study represents a secondary analysis of combined data from the two clinical trials, restricting the analysis to people with PD and more than minimal anxiety and/or depressive symptoms (GAD-7 and/or PHQ-9 scores ≥ 5).
Results: 5 MBCT groups (2 in-person, 3 virtual) were conducted. The subsample analyzed included 15 (8 women, age 64.2+/-7.4) people with PD in Study 1 and 13 (7 women, age 61.6+/-6.4) in Study 2. One participant withdrew. At baseline, 25 participants had anxiety symptoms (GAD-7 score mean 7.9, SD 2.9) and 22 had depressive symptoms (PHQ-9 score mean 9.8, SD 3.4). There were significant reductions in both anxiety and depression measures at the conclusion of the MBCT intervention. Post- to pre- estimated difference (95% CI) was -2.1 (-3.9 to -0.4) for GAD-7 and -3.8 (-6.0 to -1.5) for PHQ-9 (both $p < 0.05$). Participants reported high satisfaction with the intervention.
Conclusion: MBCT may be effective in improving anxiety and depressive symptoms in people with PD. Larger, randomized-controlled studies are needed.

P29.05

Minds & movement: Evidence-based guidance for psychological interventions for people with Huntington’s disease, Parkinson’s disease, motor neurone disease, and multiple sclerosis

Jane Simpson[1], Fiona Eccles[1], Nicolò Zarotti[*,2]*
[1] Lancaster University, Lancaster, United Kingdom
[2] Manchester Centre for Clinical Neurosciences, Manchester, United Kingdom

Minds & Movement is a project led by Lancaster University and the Faculty of the Psychology of Older People and Division of Clinical Psychology of the British Psychological Society to produce the first UK national guidance on psychological approaches for people with motor neurodegenerative disorders. More specifically, its aim was to offer evidence-based recommendations for providing psychological support to individuals living with the following four motor neurodegenerative conditions: Huntington’s disease, Parkinson’s disease, motor neurone disease, multiple sclerosis.
The overarching focus of the guidance was on psychological interventions for specific psychological outcomes in people experiencing each of these four neurological conditions. For people with Parkinson’s in particular, cognitive behavioural therapy (CBT), mindfulness-based approaches, and psychodrama may be recommended for the treatment of depression, anxiety, and sleep difficulties. However, the current evidence is too sparse to recommend any specific therapy for Parkinson-specific psychological issues such as impulse control disorders and apathy, thus highlighting a strong need for further investigations.
The guidance is now published available for free for all psychologists and any other health professionals who wish to have easy access to up-to-date evidence-based recommendations on Parkinson’s and other motor neurodegenerative conditions.



P29.06

Psychosocial interventions affecting global perceptions of control in people with Parkinson's disease: A scoping review

Nicolò Zarotti[*,1], Katherine Deane[2], Catherine Ford[2], Jane Simpson[3]*
[1] Manchester Centre for Clinical Neurosciences, Manchester, United Kingdom
[2] University of East Anglia, Norwich, United Kingdom
[3] Lancaster University, Lancaster, United Kingdom

Purpose: Perceived control is an important construct for the psychological well-being of people affected by chronic conditions, and higher perceived control is associated with better outcomes. Psychosocial interventions have been trialled in these populations to improve both global and specific perceptions of control. However, most interventions involving people with Parkinson's have focused on single-domain forms of control, while those addressing global perceived control are yet to be reviewed. This study aimed to identify and map the types of psychosocial interventions in individuals with Parkinson's which have included forms of global perceived control as an outcome.

Materials and Methods: Scoping review based on a search across MEDLINE, PsycINFO, CINAHL, Academic Search Ultimate.
Results: From an initial return of 4388 citations, 12 citations were eventually included. These consisted of 8 quantitative and 4 qualitative studies, and covered 4 overarching categories of psychosocial interventions. Mixed results were found for cognitive, educational, and physical interventions, while a randomised controlled trial on mindfulness-based lifestyle programme showed more positive evidence.
Conclusions: Further rigorous research is required on the topic to build on these preliminary findings. In the meantime, clinicians may need to consider programmes which proved effective with populations similar to people with Parkinson's.

CLINICAL SCIENCE: Cognition/mood/memory

P30.01

Investigating the effects of COVID-19 and the first UK lockdown on anxiety and mood in people with Parkinson's

*Moudhi Al Twaijri**
University of Manchester, Salford, United Kingdom

Background: Anxiety is common in people living with Parkinson's (PwP) and a key contributor to poor quality of life. Anxiety has been related to the emotional and physical stress of living with Parkinson's. In this study we examined how anxiety and mood were affected in PwP during the UK's first COVID-19 lockdown.
Methods: 166 PwP (79 female) and 50 healthy controls (HC; 32 female) participated in an online survey. Standardised scales included anxiety during (state) and prior to (trait) lockdown, apathy, and depression. In addition, qualitative data from open questions about lockdown experiences was analysed using thematic analysis.
Results: Both groups reported significantly higher anxiety during compared to before lockdown; however, PwP had significantly higher anxiety overall (state and trait) and a higher proportion isolated early compared to HC. Depression and trait anxiety were both significant predictors for state anxiety in PwP. Additionally, PwP reported feeling vulnerable and experienced increased motor symptoms during lockdown, sometimes linking these effects to increased anxiety. Many described being negatively affected by lockdown, attributing this to low mood as well as reduced access to medical support, physical activities, personal space, and physical and social contact. Notably, some reported a positive experience during the lockdown due to fewer social obligations, and others reported no change in their lifestyle.
Conclusion: Both PwP and controls experienced higher anxiety during than before lockdown and some PwP thought this exacerbated their motor symptoms. While many PwP described negative effects during the lockdown, others reported positive experiences or described little change since living with Parkinson's was already a lockdown of its own. This highlights the need for remote support in general as well as in the case of another lockdown.

P30.02

Imitation of object-directed hand movements in Parkinson's

Judith Bek[*,1], Eamon Brockenbrough[1], Emma Gowen[2], Stefan Vogt[3], Trevor Crawford[3], Ellen Poliakoff[2]*
[1] University College Dublin, Dublin, Ireland
[2] University of Manchester, Manchester, England, United Kingdom
[3] Lancaster University, Lancaster, England, United Kingdom

Introduction: Observation of human movement has been suggested to provide an effective strategy to promote movement and to maintain and improve daily activities for people with Parkinson's. Previous studies using motion capture have demonstrated the ability of people with Parkinson's to imitate observed hand movements, but these have focused on intransitive actions (such as pointing), which are less relevant to functional ability. The present study examined imitation of simple object-directed hand movements in individuals with Parkinson's compared to age-matched controls.
Methods: Eighteen participants with mild to moderate Parkinson's and twenty-one neurologically healthy participants observed and immediately imitated sequences depicting a human hand reaching for a cube-shaped object and transferring the object to a new location. The observed movements followed either an elevated or a non-elevated (i.e., direct) trajectory. Kinematics were recorded from the participant's index finger and modulation of vertical amplitude in relation to the observed movement (elevated vs. direct) was analysed for reach and transfer segments of the movement sequences. Peak velocity and dimensionless jerk (a measure of smoothness) were also analysed.
Results: Participants in both groups significantly modulated the vertical amplitude of their hand movements when imitating elevated vs. direct trajectories, although the control group exhibited modulation to a greater extent. The pattern of modulation was similar for both reach and transfer segments of the movements, but the imitated reaching movements were faster, lower in vertical amplitude, and smoother overall compared to the imitated transfer movements.
Conclusion: This study provides quantitative evidence that people with mild to moderate Parkinson's can imitate the kinematics of object-directed movements (both reaching and transferring), but their imitation may be reduced compared to neurologically healthy older adults of a similar age. The findings suggest that interventions using observation of object-directed actions may be beneficial for people with Parkinson's.

P30.03

Impact of cognitive impairment on quality of life in Mexican persons living with Parkinson's disease

Gloria Itzel Cerda Hernández, María Alejandra Ruiz Mafud, Anna Paola Bazán Rodríguez, Etienne Reséndiz Henríquez, Eduardo Ichikawa Escamilla, Daniela Renee Aguila Godinez, Axel Antonio Herrera Ruiz, Ana Jimena Hernández Medrano, Amin Cervantes Arriaga, Mayela Rodríguez Violante*
National Institute of Neurology and Neurosurgery, Mexico City, Mexico

Objective: Describe the correlation between cognitive functions and quality of life in Mexican persons living with Parkinson's disease.
Background: Parkinson's disease is related to cognitive impairment [1], so it is important to identify the specific cognitive functions that are most affected in relation to disease progression and that can affect the patient in their daily life as well as motor symptoms.
Methods: Patients treated at the National Institute of Neurology and Neurosurgery in Mexico City were evaluated in 2022. An observational, descriptive and cross-sectional study was conducted. Spearman's Rho correlation was used to evaluate the correlation between MoCA subdomain scores (I: Visuospatial/Executive, II: Denomination, III: Attention, IV: Language, V: Abstraction, VI: Deferred Recall and VII: Orientation), PDQ-39 and MDS-UPDRS.
Results: 165 patients (61.2% men, 38.8% women) were evaluated, whose average age was 62.8 ±12.2 years, with an average of years of diagnosis of Parkinson's disease of 7.1 ±5.2 years. The mean scores of PDQ-39, UPDRS, H&Y and MoCA were 33.5 ±18.2, 59.6 ±24.4, 2.2 ±0.8 and 21.57 ±5 respectively. The mean scores of the MoCA subdomains were I (2.79 ±1.5), II (2.88 ±0.4), III (4.30 ±1.7), IV (1.48 ±0.9), V (1.70 ±0.5), VI (2.13 ±1.5) and VII (5.7 ±0.8). Spearman's Rho correlation showed a negative correlation with statistical significance between MDS-UPDRS scores and subdomains I (rs=-0.32, p=0.000), II (rs=-0.16, p=0.039), III (rs=-0.18, p=0.021), IV (rs=-0.20, p=0.009), V (rs=-0.15, p=0.048) and VI (rs=-0.22, p=0.003) of MoCA, as well as between PDQ-39 and subdomains I (rs=-0.27, p=0.000), II (rs=-0.24, p=0.002), III (rs=-0.29, p=0.000), IV (rs=-0.26, p=0.001) and VI (rs=-0.19, p=0.013) of MoCA.
Conclusions: It was found that cognitive alterations in the subdomains Visuospatial/Executive, Denomination, Attention, Language and Deferred Memory have correlation with a lower quality of life and progression of Parkinson's disease, so it is important to pay special attention to these cognitive functions when giving multidisciplinary care to patients.
References:
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P30.04

NeuroOrb: An accessible co-designed "Serious Games" system for targeted cognitive training in Parkinson's disease

Lyndsey Collins-Praino[*,1], Bianca Guglietti[1], Simon Drum[2], Angus McNamara[1], Benjamin Ellul[1], Bradley Wesson[2], David Hobbs[2]*
[1] The University of Adelaide, Adelaide, South Australia, Australia
[2] Flinders University, Bedford Park, South Australia, Australia

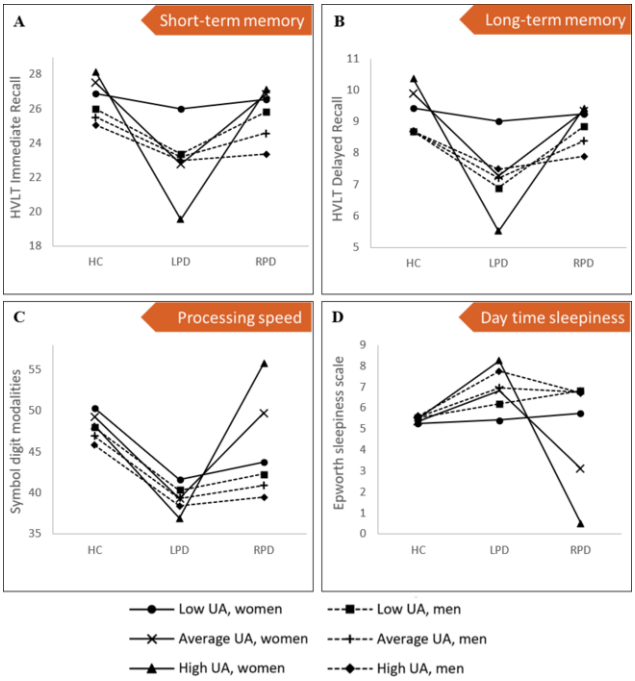
Background: More than 80% of individuals with Parkinson's disease (PD) develop dementia (PD-D), a major predictor of both quality of life and mortality, within 20 years of diagnosis. Despite this, PD-D treatment is a major gap in the field. Cholinesterase inhibitors, the only option currently available, have limited efficacy and may worsen motor impairment. Alternative strategies to prevent development of cognitive impairment are needed. While cognitive training (CT) presents a promising option, motor impairments may limit accessibility, and hence efficacy, of tools typically used to deliver CT. Further, many CT studies fail to investigate either long-term benefits or transfer effects of training.
Objectives: To address these gaps, we modified the highly accessible OrbIT gaming system, originally developed for children with cerebral palsy, to deliver targeted CT in PD.
Methods: Twelve custom "Serious Games" were developed, with each designed to target the executive function deficits common in PD. Following game development, a group of community-dwelling individuals (n = 13; mean age = 68.15 years; mean disease duration = 8 years), all within normal bounds on the MMSE, participated in three reiterative co-design loops: an initial series of three 60-minute sessions where participants trialled the system and two 60-minute follow-up sessions, one- and six-months later, following system modifications. Following each loop, participants completed a series of feedback surveys and interviews.

Results: During co-design, multiple outcomes, including enjoyment, accessibility, and usability of NeuroOrb, were evaluated. While initial impressions were positive, several key issues were identified. This led to major revisions of both the gaming suite and the system hardware. Following these changes, stakeholders rated changes to both the controller and the games extremely highly, and enjoyment and usability scores increased. A trial (n = 90 individuals; 30/group: NeuroOrb, "CogCafé" control group and normal activity control group) is currently underway to evaluate immediate and long-term benefits of NeuroOrb for cognition, as well as its effects on transfer to everyday ADLs and quality of life.
Conclusions: The engaging and targeted NeuroOrb system, optimised for use in PD through co-design with key stakeholders, may offer an exciting new option to deliver CT in individuals with PD.

P30.05

Moderating effects of uric acid and sex on non-motor symptoms in asymmetric Parkinson's disease
Ioana Medeleine Constantin, Philippe Voruz, Julie Anne Péron*
University of Geneva, Genève, GE, Switzerland

Introduction: Non-motor symptoms (NMS) are an important early feature of Parkinson's disease (PD), encompassing a variety of cognitive and neuropsychiatric symptoms, that seem to manifest differently depending on the asymmetry of motor symptoms. Different factors, such as uric acid (UA) and sex, also seem to influence NMS expression in PD. However, the interplay between UA, sex, and motor symptom asymmetry remains to be better understood in early-stage PD. Hence, the present study aims to investigate the interaction effects of UA, sex and motor symptom asymmetry on NMS in patients with PD.
Methods: A total of 413 patients taking part in the Parkinson's Progression Marker Initiative (PPMI) were studied based on the asymmetry of their motor symptoms, either predominantly right-sided (RPD) or predominantly left-sided (LPD), as well as sex. Clinical data was extracted over a 5-year follow-up period. Three-way interaction modeling was used to examine the moderating effects of sex and UA on the relationship between motor symptom asymmetry and NMS.
Results: The results highlighted significant three-way interactions between motor symptom asymmetry, UA and sex for immediate memory, long-term memory, processing speed and sleepiness in female patients only. Furthermore, female patients with RPD demonstrated the most preserved NMS in the presence of lower serum UA levels, while male patients with RPD showed the greatest vulnerability, regardless of UA levels.
Conclusion: These findings suggest that in the earliest stages of the disease, serum UA and sex moderate NMS expression differently depending on motor asymmetry. This holds important clinical implications for symptom management in patients with early-stage PD.



P30.06

Differential effects of motor task and executive demand on cognitive dual-task performance in people with Parkinson's disease and freezing of gait
Nicholas D'Cruz[1], Jana Seuthe[2], Femke Hulzinga[1], Pieter Ginis[1], Christian Schlenstedt[2], Alice Nieuwboer[1]*
[1] KU Leuven, Leuven, Belgium
[2] MSH Medical School Hamburg, Hamburg, Germany

Background: Daily-life mobility consists primarily of dual tasking situations. Although previous work has extensively studied cognitive interference on motor performance in Parkinson's disease (PD), cognitive performance during various motor conditions has received less attention. This is particularly relevant, as gait disorders such as freezing of gait (FOG) are more pronounced during high motor and cognitive demands, suggesting that insufficient cognitive reserves are responsible for gait breakdown. However, this is yet to be investigated during actual gait.
Objective: To investigate the effects of increasing motor and executive demands on cognitive task performance, in people with Parkinson's disease (PwPD) with and without FOG and healthy older adults (HOA).
Methods: A retrospective cohort sub-sample of 52 PwPD (34 with FOG and 18 without) and 12 HOA from were included. Participants performed two motor tasks – straight walking and turning in place, while responding to an auditory stroop task. In this task, the words "high" and "low" were presented in either a high or low tone, and participants were required to name the tone. Response time, variability and accuracy were separately assessed for stimuli with congruent and incongruent word-tone pairings. 3-way linear mixed models between Group, Task and Stimulus were performed.
Results: No interaction effects were found. Strong main effects of Task ($F(1,61) = 11.48$, $p = 0.001$) and Stimulus ($F(1,56) = 11.4$, $p = 0.001$) were found, with turning resulting in slower response times than walking, and lower accuracy on incongruent compared to

congruent stimuli. Group differences approached the significance threshold (accuracy - F(2,56) = 2.79, p = 0.069, variability - F(1,56) = 2.95, p = 0.059), with freezers being less accurate than non-freezers (uncorrected-p = 0.031), and both PD groups having higher response time variability than HOA (non-freezers uncorrected-p = 0.070, freezers uncorrected-p = 0.018).
Implications: Freezers did not have more difficulty responding to increasing motor and cognitive demands but did show a pervasive difficulty in resolving conflicting information. These results are largely in line with previous work. Interestingly, increasing motor complexity slowed response time, while increasing cognitive complexity mainly impaired accuracy. Results are preliminary and will be updated with the full-sample analysis.

P30.07

The impact of antidepressant treatment on disease-related disability: Preliminary findings from the Parkinson's progression markers initiative
Roseanne Dobkin[1], Nabila Dahodwala[2], Catherine Kulick[2], Meredith Bock[3], Ryan Cho[4], Chelsea Caspell-Garcia[4], Ethan Brown[3], Dag Aarsland[5], Daniel Weintraub[,2]*
[1] RUTGERS RWJMS, PISCATAWAY, NEW JERSEY, United States
[2] University of Pennsylvania, Philadelphia, PA, United States
[3] University of California at San Francisco, San Francisco, CA, United States
[4] University of Iowa, Iowa City, Iowa, United States
[5] Kings College, London, United Kingdom

Introduction: Depression is among Parkinson's disease's (PD) most prevalent and detrimental symptoms, often going undiagnosed or untreated. While this treatment gap undermines optimal PD management and accelerates long-term decline, there is more to learn about depression rates and symptom burden over time. In addition, little is known about the restorative effects of depression treatment on longitudinal motor, cognitive, and functional outcomes. The goal of this study was to explore the prevalence and impact of baseline depressive symptoms, and the longer-term (up to 7 years) benefits of antidepressant treatment initiation in the Parkinson's Progression Markers Initiative (PPMI) study.
Methods: PPMI is a longitudinal, observational study that evaluates how PD starts and changes over time, in order to advance therapeutic development. Participants complete motor, cognitive, and psychiatric assessments, and provide biological samples, on an annual basis. A positive (i.e., potentially clinically significant) depression screen was defined as a 15-item Geriatric Depression Scale (GDS-15) score ≥5 (range 0-15). Depression treatment included self-reported antidepressant use. The first 7 years of data from the de novo PPMI PD cohort (N=491) was utilized in the current study.
Results: 64 de novo PD (13%) endorsed depression at baseline, with 39 (61%) untreated. Depression at baseline was associated greater motor, cognitive, and functional impairment at baseline and across the 7-year follow-up period for the entire sample, controlling for relevant covariates (e.g., age, sex, race, and education). Ten participants (26%) in the depressed, but untreated, baseline cohort initiated antidepressant treatment sometime during the follow-up period, which significantly reduced the rate of subsequent motor and functional decline, and was associated with lower LEDD over time, compared with the period prior to antidepressant initiation.
Conclusion: Depression in PD is associated with multiple negative outcomes, both cross-sectionally and over time. Active screening and management of depression is required to optimize PD care, and antidepressant treatment may reduce disease-related disability.

P30.08

Is the ability to create motor images related to functionality and quality of life in people with Parkinson's disease and healthy control?
María del Rosario Ferreira-Sánchez[1], Marcos Moreno-Verdú[2], Yeray González-Zamorano[,3]*
[1] Catholic University of Ávila, Ávila, Spain
[2] Francisco de Vitoria University, Pozuelo de Alarcón, Spain
[3] Department of Physical Therapy, Occupational Therapy, Rehabilitation and Physical Medicine. Rey Juan Carlos University, Alcorcón, Madrid, Spain

Background: Motor imagery (MI) is defined as the cognitive process by which a person imagines executing an action without actually performing any movement and without producing muscular tension. This imagination process requires the activation of the brain regions responsible for the preparation and execution of the movement, as well as its voluntary inhibition. Systematic reviews have shown that the combined use of mental and physical practice is more effective than their isolated use, as MI training accelerates motor learning, although the relationship between the ability to create MI and functionality and quality of life has not been studied yet. Additionally, some studies suggest that the ability to create MI is altered or abolished in people with Parkinson Disease (PwPD) due to the sensory, perceptual and cognitive deficits associated with the disease.

Aims: To compare the ability to create MI between PwPD and healthy controls (HC) and to analyse its impact on functionality and quality of life.
Methodology: A case-control study was conducted comparing PwPD and healthy control groups. Socio-demographic data and clinical data of PD were collected. MI vividness and temporal accuracy were assessed using MIQ-RS and mental chronometry tests, respectively. Upper limb motor function (Box and Blocks test), balance (Berg Balance Scale), gait (Timed up and go test), and quality of life (QoL) (SF-36) were also assessed.
Results: 31 PwPD and 31 HC were recruited. Statistically significant differences in functionality and quality of life between groups (p=<.05) were revealed. No significant differences were found in the ability to create MI between groups, neither in terms of vividness (p=.106) nor temporal accuracy (p=.221). MIQ-RS and mental chronometry tests, and functionality and QoL measures were not significantly correlated, neither in PwPD nor HC groups.
Discussion: The results of the present study failed to find significant correlations between the ability to create MI and upper limb motor function, gait, and balance, suggesting that PwPD retain movement representation, but execution components hinder functionality.
Conclusions: PwPD retain the ability to create MI, although its relationship with functionality and quality of life has not been determined.

P30.09

Cognitive performance and depression in Parkinson's disease: A cross sectional analysis
*Emily Houston**
The University of Vermont, Burlington, VT, United States

Background: Cognitive impairment and depression are common non-motor symptoms that impact quality of life for people with Parkinson's disease (PD). Previous studies of the Parkinson's Progression Markers Initiative (PPMI) have shown that the Montreal Cognitive Assessment (MoCA) score decreases significantly over

two years, and that depression is more commonly reported in PD patients than healthy controls. This analysis aims to quantify the odds of having depression when cognition declines.
Methods: Cross-sectional analysis of Year 5 data from the PPMI, using the MoCA as a measure of cognitive performance and a score 5 on the Geriatric Depression Scale (GDS) to indicate clinically significant symptoms. A logistic regression was performed on a sample size of 312 participants with PD to determine an odds ratio (OR), and a t-test was used to compare the frequencies between each GDS group.
Results: At Year 5, 19.8% of people with PD met criteria for depressive symptoms, while 80.1% did not. The mean MoCA score was 26.55 (3.53). Among those without depression, the mean MoCA score was 27.01 (2.90), while the group with GDS score 5 had a lower mean MoCA of 24.71 (5.00), reaching statistical significance of p<0.001. The OR for depression was 0.849 per point of MoCA (p<0.001), making the change in odds 15%.
Conclusion: At Year 5, the frequency of depression in PPMI participants with PD increased considerable from the previously reported baseline prevalence of 13.9% to 20%. The mean MoCA score from Baseline to year 5 went from 27.14 to 26.55, less than a one-point change. Our analysis shows that participants categorized as depressed exhibited diminished performance on the MoCA, compared to the non-depressed group. The OR indicated that for every point decrease in the MoCA, the odds of experiencing clinically significant depression increase by 15%. In patients with PD, it is important to screen for changes in cognitive performance and depression, as they may co-exist, and both negatively impact quality of life. Further analysis of MoCA subsections or individual GDS items may be considered.

P30.10

The neuropsychological profile and other clinical characteristics in non-affected GBA-carriers versus non-carriers

Sonja R. Jónsdóttir[*,1], Claire Pauly[2], Valerie E. Schröder[2], Laure Pauly[1], Olena Tsurkalenko[1], Rejko Krüger[1]*
[1] Luxembourg Institute of Health, Strassen, Luxembourg
[2] University of Luxembourg, Esch-sur-Alzette, Luxembourg

Objective: We aimed to investigate the cognitive functioning and other clinical characteristics of at-risk individuals for Parkinson's disease (PD), previously also presented at the Precision Medicine Conference (26-01-2023).
Background: Variants in the glucocerebrosidase (GBA) gene are the most common genetic risk factor for PD. GBA Non-Affected Carriers (GBA-NAC) mostly remain healthy due to low penetrance, but could provide an insight into potential prodromal cognitive dysfunctions, that may indicate a higher risk for conversion into PD. Studies investigating prodromal cognition in GBA carriers show conflicting results that may be due to differences in methodology, sample sizes, heterogeneity of GBA mutations, thereby warranting further research.
Methods: 24 participants were identified from the Luxembourg Parkinson Study, to compare a GBA-NAC group to a matched Non-Carriers (NC) group. We used different scales to assess symptoms of depression, apathy, quality of life, autonomic features, REM-sleep behavior disorder, motor and non-motor PD aspects, respectively. Detailed descriptions of the assessment tools have been published elsewhere.
Results: 12 GBA-NAC (11 with low-risk, 1 with mild risk) and 12 age and years of education matched non-carriers without manifest Parkinsonism and other neurological comorbidities were included. Our results displayed that the GBA-NAC group performed significantly worse on the olfactory test than the NC group [12.25 (±1.66) versus 14.17 (±1.59) out of 16, pcorrected = 0.008], as well as on the episodic memory delayed recall test (CERAD Word List Memory) [6.50 (±2.11) versus 8.25 (±1.49) out of 10, pcorrected = 0.028]. No significant differences were found for the other scales and assessments.
Conclusion: Our results indicated that the GBA-NAC group performed significantly worse on the olfactory test and delayed recall of the episodic memory test than the NC group. Whereas both groups scored similarly for the other non-motor symptoms and global cognitive performance. These results need to be interpreted with caution due to the reduced sample size and high proportion of low-risk mutations among the GBA-NAC. We will conduct a longitudinal analysis to evaluate the evolution of the prodromal features of PD.

P30.11

Impairment in the behavioral synergic control of postural sway, gaze shift, and mental workload in Parkinson's disease

Yann Kechabia[*,1], Arnaud Delval[2], Luc Defebvre[3], Cédrick Bonnet[4]*
[1] Université de Lille, Lille, France
[2] Service de neurophysiologie clinique, Hôpital Salengro, CHRU, F-59000 Lille, France 4 Unité INSERM 1172, Faculté de médecine, Université de Lille, F-59000 Lille, France, Lille, France
[3] Service de neurologie et pathologie du mouvement, centre expert Parkinson, Hôpital Salengro, CHRU, F-59000 Lille, France 4 Unité INSERM 1172, Faculté de médecine, Université de Lille, F-59000 Lille, France
[4] Laboratoire de Sciences Cognitives et de Sciences Affectives, Université de Lille, CNRS, Lille, France

Introduction: Patients with Parkinson's disease (PD patients) exhibit impairments in postural control, eye movements and attention. We tested, while placing the subjective mental load as a covariate, whether these patients had impairments in the synergy between eye and body movements during visual tasks performed in the standing position.
Material and methods: Nineteen PD patients (58.47±10.9 years old, Hoehn & Yahr stage II and III, on usual dopaminergic treatment) and twenty healthy controls (HC; 62.15±8.55 years old) explored large images of rooms in houses in a virtual reality system (120° visual angle) by performing two visual tasks: precise (visual target location) and non-precise (free-viewing) with 6 trials of 45 sec per task. Eye (SMI) and body (Polhemus) movements as well as participants' attention to the task performed (oculometric data) were analyzed.
Results: The PD patients exhibited greater variability in both gaze shifts and postural sway than the HC (p<0.001). This impairement was stronger when performing the precise visual task (p=0.002) and it was associated with more attentional resources (p<0.001). Moreover, PD patients were less efficient than HC to locate targets in the visual display (p<0.001).
Discussion – Conclusion: Consistent with our expectation, Parkinson's Disease seemed to induce an impairment in the synergy between eye and body movements. Indeed, PD patients were less able than HC to engage attention to adjust their postural control to facilitate gaze shifts on precise location. Exercises using visio-postural tasks could be relevant to allow PD patients improving their stability and visual interaction with their environment.
Key words: Parkinson's disease, vision-posture synergy, cognitive load, synergistic model.

P30.12

In the direction of quantifiable objective psychopathology via cognitive neuropsychiatry: A fusion oriented hybrid-study

*Neerati Lavanya**
Osmania University, Hyderabad, Telangana, India

Cognitive neuropsychiatry (CNP) embodies a logical and hypothetically driven method to justify scientific (i.e.,clinical) psychopathologies regarding discrepancies to usual mental—mind mechanisms. An involvement through neuronal (neuronic) substrates-of-impaired cognitive processes connects CNP to the fundamental-neuroscience. The advent of CNP 3 decades ago (~1990) demonstrates the increasing reconciliation among CNP, objective medicine, also neurosciences in tackling widespread issues regarding misperceptions or uncertainties of the mental, mind, and mental illness of neurobiology and brain. So, we focus how this transdiscipline will make a unique and distinct role to psycho pathology. The aim is to get the innovative idea-of-scientific union which occur amid the cognitive-neuroscience plus psychiatry, plus to demonstrate by what means this union has started to offer a novel mental (neurobiology-based) reasoning policy with which we comprehend better psychiatric situations.Approached through hypothetical expectations, conceptual underpinnings, cognition, thought, symptoms, and cognitive mechanisms, followed by some of the initial evolution made through CNP. Then some developments on a variety-of-signs which span the neuro-psychiatric-field, next to offer a more comprehensive challenging and model expansions as of the field — misapprehensions of wrongly thinking plus aural delusions (i.e.,hallucinations). We conclude by referring to (future) prospects and the challenges that lie ahead. Following methods are applied and discussed in the study rigorously. Conceptual—underpinnings, cognitive reasons and justifications, the thought and lingua franca, human motor and its controls through basal ganglion-circuitry, emotions, anxiety, apathy, depression, dementia, symptoms and cognitive mechanisms, pathologies-of-belief, Capgras delusion, hallucinations followed by cognitive theory. This study is trying to link the disparity among cognition as well as neuroscience by 1. forming efficient association of psychiatric disorders in a structure-of-human CNP, then connecting the structure(framework) to appropriate brain—structures also pathos physiology. CNP timely offers the basis for a scientific psychiatric, disorders surrounded by the outline of human CNP and their psychopathology. The study (the CNP) can also give, can define the basis for cognition and cognitive-scientific psycho pathology timely and comprehensively.

P30.13

The effect of the social evaluative threat on substantia nigra functional connections to stress processing system regions of interest

Senegal Alfred Mabry, Marlen Gonzalez, Eve De Rosa, Adam Anderson*
Cornell University, Ithaca, New York, United States

Resilience, in the context of the human experience, describes being met with significant pressure but bouncing back from the stress without dysfunction or psychopathology. This study aims to contrast the stress recovery component of resilience in PD and healthy controls (HC) groups using the Social Evaluation Threat (SET) task. The study expects the SET task will create psychological and cardiopulmonary stress responses in people with PD. Further, we hypothesize changes in the functional connections of the Substantia Nigra (SN) to regions involved in stress processing, including the amygdala, the Ventromedial prefrontal cortex, and the thalamus for the PD and HC groups during stress recovery.

Resilience as a physiological and psychological framework has been operationalized in three ways (stress recovery, flexibility, and promotion) by neuroscientists using fMRI to study other diseases that impact brain structure and cognition, like depression and epilepsy. Stress recovery has been measured as psychological, cardiac, and neural changes after the stress event has occurred compared to before the event, and as a buffer, a person has during the stress experience changing the amplitude of the response. The study plans to collect data from 40 participants (20 PD, 20 age and sex-matched healthy individuals) performing the SET in the MRI.
During the task, functional connectivity scans are taken during the baseline, speech preparation, and recovery period. In the baseline, participants perform no task with their eyes not fixed on a cross for 6 minutes. During the speech preparation, the participant is told using the microphone and a screen projection they have 2 minutes to prepare a speech on a preselected topic they will be evaluated on by the experimenter. During recovery, participants are told they do not have to make the speech and can relax for 6 minutes in the scanner.
Differences in the functional connections between the SN and stress ROIs during stress recovery for participants in PD and HC groups may indicate the SN is sensitive to cardiovascular physiological, and psychological stress. It may also indicate that the SN plays a role in other stress and reward processes.

P30.14

Psychotic features in early PD: Prevalence, phenomenology and clinical correlates

Ioanna Pachi[*,1], Vasilis Papadopoulos[2], Christos Koros[2], Athina-Maria Simitsi[2], Anastasia Bougea[2], Maria Bozi[3], Nikos Papagiannakis[2], Rigas-Filippos Soldatos[2], Dimitra Kolovou[2], George Pantes[2], Nikolaos Scarmeas[2], Georgios Paraskevas[3], Konstantinos Voumvourakis[3], Sokratis Papageorgiou[2], Konstantinos Kollias[4], Nikos Stefanis[4], Leonidas Stefanis[2]*
[1] KAT Attica General Hospital, 1st Department of Neurology, Aeginition Hospital, National and Kapodistrian University of Athens, Athens, Greece
[2] 1st Department of Neurology, Aeginition Hospital, National and Kapodistrian University of Athens, Athens, Greece
[3] 2nd Department of Neurology, Attikon University Hospital, National and Kapodistrian University of Athens, Athens, Greece
[4] 1st Department of Psychiatry, Aeginition Hospital, National and Kapodistrian University of Athens, Athens, Greece

Objective: The aim was to evaluate the presence of psychotic symptoms using detailed scales and to assess their association with demographical, motor, non-motor, cognitive and other neuropsychiatric characteristics.
Background: Some reports suggest that psychotic features may occur in the early stages of Parkinson's disease (PD), but sensitive tools have not been utilized.
Methods: Healthy controls and patients within three years of PD onset were recruited in this cross-sectional study. Participants were examined for psychotic symptoms using two different instruments: a 10 question PD specific psychosis severity scale (10PDQ) and the Comprehensive Assessment of At-Risk Mental States (CAARMS). In the PD group, medication use, motor and non-motor symptoms were documented.
Results: Based on CAARMS and 10PDQ scales, psychotic features were present in 39% (27/70) of patients and 4% (3/74) of controls. The prevalence of passage hallucinations and illusions was significantly higher in PD compared to the control group. The presence of PD-associated psychotic features was not significantly affected by medication, motor severity or cognitive impairment. Higher prevalence of overall non-motor manifestations, REM sleep behavior disorder (RBD) and depressive symptoms was significantly

associated with the manifestation of psychotic features in PD [(adjusted OR:1.3; 95%CI:1.1-1.6; p=0.003), (adjusted OR:1.3; 95%CI:1.0-1.6; p=0.023) and (adjusted OR:1.2; 95%CI:1.0-1.4; p=0.026)].
Conclusions: Psychotic phenomena mainly of minor nature are highly common in early PD. Cumulative non-motor symptoms, RBD and depressive features are associated with the presence of psychotic symptoms in this non-demented, early-stage PD population. More studies are needed to clarify the mechanisms that contribute to the onset of psychotic features in early PD.

P30.15

Cognitive profile in prodromal Parkinson's disease – Cross-sectional and case-control study in an at-risk cohort of people with REM-sleep-behavior-disorder and hyposmia
Laure Pauly[*,1], Claire Pauly[2], Armin Rauschenberger[2], Valerie E. Schröder[2], Gilles Van Cutsem[2], Anja K. Leist[3], Rejko Krüger[2]*
[1] Luxembourg Institute of Health, Strassen, Luxembourg
[2] Luxembourg Centre for Systems Biomedicine, University of Luxembourg, Esch-sur-Alzette Belval, Luxembourg
[3] Institute for Research on Socio-Economic Inequality, University of Luxembourg, Esch-sur-Alzette Belval, Luxembourg

Introduction: We explored the cognitive profile in prodromal Parkinson's disease (PD) by comparing people with probable REM-Sleep Behavior Disorder (RBD) and hyposmia to an age- and gender-matched control group. RBD and hyposmia are strong risk factors for α-synucleinopathies such as PD. Previous findings reported that cognitive impairment may precede clinical PD diagnosis by up to 6 years.
Methods: A total of 98 participants from the Luxembourgish RBD cohort were included in the study. We excluded people with other neurological and severe psychiatric diseases. Participants were assigned to the prodromal PD group (probable RBD and hyposmia; n=49) or the control group (neither RBD nor hyposmia; n=49) based on the RBD Screening Questionnaire (RBDSQ)(cut-off ≥7) and an olfactory test (B-SIT/ Sniffin'Stick). Both groups were propensity-score matched for age and gender. Case and control groups were compared with the Mann-Whitney U test. No significant differences were observed for years of education. The Montreal Cognitive Assessment (MoCA), the CUPRO evaluation system, Trail-Making-Task (TMT), Digit Span, Corsi Block-Tapping task, Kaplan Stroop test, Frontal Assessment Battery (FAB), Semantic and Phonemic Fluency test, interlocking Pentagons, CERAD Word list, Isaacs Set test and Benton's Judgment of Line Orientation test were applied to assess diverse cognitive domains. The Beck Depression Inventory (BDI-I), Starkstein Apathy Scale (SAS) and Parkinson's Disease Questionnaire (PDQ-39) were applied to assess depressive, apathic symptoms as well as quality of life, respectively.
Results: The prodromal group presented significantly lower performances for global cognition (MoCA) and executive functions (TMT-B, TMT-ratio) at the nominal 5% level, but not at the Bonferroni-adjusted 5% level (p=0.01 respectively p<0.04). The prodromal group showed a significantly higher depression and apathy score and significantly lower quality of life (p<=0.05/9).
Conclusion: Individuals with both, RBD and hyposmia, had significantly higher levels of depression and apathy, lower quality of life, and non-significantly lower cognition and executive functions compared to the control group. Future research will complete these analyses with an increased sample size and in a polysomnography-validated RBD group and evaluate conversion rates to α-synucleinopathies.

P30.16

Facial emotion recognition is associated with MoCA score in patients with Parkinson's disease
Claire Pauly[*,1], Anne-Marie Hanff[2], Sonja R. Jónsdóttir[2], Olena Tsurkalenko[2], Nico J. Diederich[3], Rejko Krüger[2]*
[1] University of Luxembourg - LCSB, Esch-sur-Alzette, Luxembourg
[2] Luxembourg Institute of Health, Strassen, Luxembourg
[3] Centre Hospitalier de Luxembourg, Luxembourg, Luxembourg

Objective: To investigate the association between facial emotion recognition (FER) and non-motor symptoms in patients with Parkinson's disease (PD) compared to control subjects (CS).
Background: PD does not only involve motor symptoms but also a variety of non-motor symptoms such as autonomic dysfunction and impaired cognition. The latter may include reduced FER as well as emotional speech production and perception. These symptoms do not only impact the quality of life of PD patients but also of their family and caregivers.
Methods: 103 patients and 97 CS were recruited from the Luxembourgish Parkinson Study who completed the basic assessment including motor assessments (MDS-UPDRS part III), cognitive status (Montreal Cognitive Assessment, MoCA), as well as questionnaires about quality of life (Parkinson's Disease Questionnaire – 39), depression (Beck Depression Inventory, BDI) and apathy (Starkstein Apathy Scale, SAS) and who additionally underwent a social cognition assessment (Ekman 60 Faces test) to evaluate FER.
Results: 103 patients (74% male) with a mean age of 63.3±9.9 years and mean disease duration of 11.0±5.7 years were compared to 97 age-matched CS (61.6±8.1 years). Recognition of fear was significantly lower in both groups than for all the other emotions (5.4±2.5 for PD and 5.5.±2.5 for CS; p<0.001). However, FER was not significantly different in PD compared to CS. Bivariate correlations showed a positive association between MoCA total score and recognition of fear (r=0.29, pcorrected=0.002) in PD patients but not in CS. In both groups, we found no significant correlation between FER and sex, disease duration, MDS-UPDRS III, nor with quality of life, feeling of stigma, depressive symptoms and apathy, respectively.
Conclusion: In contrast with what was previously thought, we found that recognizing fear is equally difficult for PD patients and CS. The positive correlation found between MoCA and the recognition of fear only in PD may be indicative of a process that goes beyond normal aging, as the impairment in FER in older adults may be an age-related reduction in neural connectivity. Further research is needed to test this hypothesis and to investigate the potential role of other factors such as contrast sensitivity and color discrimination.

P30.17

Cognition and freezing of gait in Parkinson's disease: A systematic review and meta-analysis
Andrew Monaghan[1], Elise Gordon[2], Lisa Graham[2], Daniel Peterson[*,1], Rosie Morris[2]*
[1] Arizona State University, Phoenix, AZ, United States
[2] Northumbria University, Newcastle, United Kingdom

Freezing of gait (FOG) is a highly troubling symptom in those with Parkinson's Disease (PwPD). Cognition is thought to be impacted in PwPD who freeze. However, to date, a comprehensive evaluation of the relationship between FOG status and cognition has not been carried out. Such an analysis could inform future research and clinical care. We conducted a systematic review and meta-analysis that compared cognition in PwPD who do and do not exhibit FOG across a different cognitive domains. We also assessed whether disease severity or medication status moderated this relationship.

One hundred and forty five papers (n=9010 participants) were included in the overall analysis, with 144 and 138 articles assessing moderating effects of disease severity and medication status, respectively. PwPD and freezing exhibited worse cognition than PwPD who do not freeze across several cognitive domains, including global cognition, executive function/attention, language, memory, and visuospatial function. Greater disease severity and "ON" levodopa medication status moderated the relationship between FOG status and cognition in the global cognitive domain only. This meta-analysis confirmed that cognition is impacted in PwPD who exhibit freezing. Further, it highlights the importance of assessing disease severity and medication status to best understand this relationship.

P30.18

Screening for anxiety symptoms in Parkinson's disease in a Mexican cohort

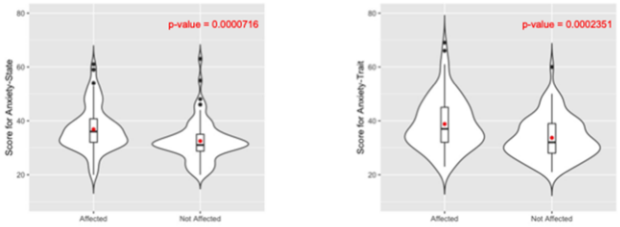
Paula Reyes-Pérez[*1], *Alejandra Medina-Rivera*[1], *Alejandra Ruiz-Contreras*[2], *Sarael Alcauter-Solórzano*[3], *Miguel Rentería*[4], *Luis García-Marín*[4], *Alejandra Lázaro-Figueroa*[2], *Eugenia Morelos-Figaredo*[5], *Damaris Vazquez-Guevara*[6]
[1] Laboratorio Internacional de Investigación sobre el Genoma Humano, UNAM, Querétaro, Mexico
[2] Facultad de Psicología, UNAM, Mexico City, Mexico
[3] Instituto de Neurobiología, UNAM, Queretaro, Mexico
[4] QIMR Berghofer Medical Research Institute, Brisbane, Australia
[5] Hospital Regional ISSSTE Morelia, Morelia, Mexico
[6] ISSSTE, Tijuana, Mexico

Anxiety is a common non-motor symptom among patients with Parkinson's Disease (PD), negatively impacting their quality of life. However, the characterization of anxiety disorders in PD patients, particularly in underrepresented populations such as Mexico, remains limited. The present study aimed to provide a deep phenotyping of anxiety in Mexican PD patients within the Mexican Parkinson's Disease Research Network (MexPD), a case-control cohort study established in 2021.
A total of 110 PD patients and 82 controls were recruited from public and private health centers in Mexico and assessed using the State-Trait Anxiety Inventory (STAI) and the Parkinson Anxiety Scale (PAS). Results revealed that 37.5% of PD patients reported feeling anxious for over 6 months at any point in their lives. The STAI inventory revealed that 25.9% of PD patients (19.7% of male and 36.5% of female patients) had clinically relevant levels of anxiety, compared to 11.25% of controls. Wilcoxon rank sum tests revealed significant differences between patients and controls in both trait and state anxiety subscales of the STAI (Figure 1). The total score for the PAS scale was slightly different between patients and controls (p-value = 0.04763), with persistent anxiety showing the highest scores in both groups. Overall, PD patients presented higher scores in these anxiety inventories compared to controls. Furthermore, specific manifestations of anxiety may be influenced y other factors such as age, sex, and disease stage.
Our findings provide evidence for distinct manifestations of anxiety in PD among Mexican patients and highlight the need for further characterization of PD-specific anxiety symptomatology to accurately assess and treat anxiety in PD. The MexPD cohort represents a valuable resource for continued research on the neuropsychiatric aspects of PD in underrepresented populations.

Sample description

		Sex composition		*Age at recruitment*		
	Registries	**Male (%)**	**Female (%)**	**Minimum**	**Maximum**	**Mean (SD)**
Cases	112	71 (63.4%)	41 (36.6%)	40	91	64.5 (10.8)
Controls	82	18 (22%)	64 (78%)	44	86	56.1 (9.2)
Total	194					

Score distribution for STAI-S and STAI-T subscales in cases and controls groups



P30.19

Agents and phases of stress and coping strategies in Parkinson's disease

Dirce Sanches Rodrigues[*1], *Marcos Antônio Moura*[2], *Adriana Aparecida Ferreira de Souza*[3], *Kátia Lousada Gouvea*[4], *Luiz Arthur Moreira Nunes*[4], *Miguel Soares Conceição*[5]
[1] UNIFAAT University Center, Atibaia, São Paulo, Brazil
[2] University of São Francisco, Atibaia, São Paulo, Brazil
[3] University of Mogi das Cruzes, Atibaia, São Paulo, Brazil
[4] Raimunda Moura Program for Parkinson's Patients, Atibaia, São Paulo, Brazil
[5] University of São Francisco, Bragança Paulista, São Paulo, Brazil

Objective: To identify the occurrence and the stressors as well as the coping strategies in individuals with Parkinson's Disease(PD) and relate it to the stage of the disease. **Method:** 36 elderly individuals with PD participated, three years of diagnosis and 41.66% of the participants are in Stage I, 38.88% in II and 19.44% in III.To measure the studied variables, the Lipp Inventory of Stress Symptoms for Adults (LSSI).The LSSI allows a classification of stress phases: alert, resistance, near-exhaustion and exhaustion; and the Systematic Framework to identify stressful situations/stimuli and coping strategies.The instruments were applied individually. **Results:** It was observed that of the 55.55% of the participants(n=36) presented stress, 50% are in stage I of the pathology, 35% in II and 15% in III. The stage with the highest number of people without stress was stage III(43.75%). Regarding the stress phases and pathology stage, it was observed that 66.66% were in the exhaustion phase and resistance phase(47%) in stage I.Only 17.64% in stage III and resistance phase. In stages I and II of the pathology, the participants were in the exhaustion phase, but in stage II with a lower incidence. Participants find stress in psychological symptoms(78.94%).The listed stressors were "being totally dependent" with 21.12%; "difficulties in carrying out daily activities"(19.71%), in which they reported and classified: putting on shoes, difficulty walking, cutting food and walking alone; "suffering with PD"(16.90%).Stress has a psychological component that involves behavior, thought patterns and emotions, it was found that the most frequent thoughts and feelings in people with PD were nervousness/irritability(17.85%), shame/embarrassment(17.85%), fear(17.85%), sadness(17.85%) and with 14.28% there is concern.Regarding the coping strategy, none of the individuals in the sample responded to the action they take in the face of the stressor they identified. **Conclusion:** It was found that 55% of the participants had stress and of these, 50% are in stage I of the pathology and these were, for the most part, in the phase of exhaustion and resistance. Stage III had a lower percentage of

people with stress and in the resistance phase. As symptomatology, it presented psychological factors. The thoughts and feelings that permeate them are nervousness/irritability, shame/embarrassment, fear, sadness and worry.

P30.20

Association between thyroid dysfunction and severity of cognitive impairment in de novo patients with Parkinson's disease

Iva Sarac[1], Helena Sarac[,2], Fran Borovecki[1], Neven Henigsberg[1], Ida Ivek[3], Lucija Bagarić Krakan[4], Mateja Iveta[5], Tea Sukobljevic[6], Zdravko Kresic[7]*
[1] University of Zagreb, Medical School, HR-Šalata 3, Zagreb, Croatia, Zagreb, Croatia
[2] University Hospital Centre Zagreb, Zagreb, Croatia
[3] Department of Internal medicine, University Hospital Center Zagreb, Kispaticeva 12, Zagreb, Croatia, Zagreb, Croatia
[4] Department of Psychiatry, University Hospital Center Zagreb, Kispaticeva 12, Zagreb, Zagreb, Croatia
[5] University of Zagreb, Faculty of Electronic and Engineering, HR-Unska 3, 10000 Zagreb, Croatia, Zagreb, Croatia
[6] University of Zagreb, Faculty of Humanities and Social Sciences, Department of Psychology, HR-Ivana Lučića 3, 10000 Zagreb, Croatia, Zagreb, Croatia
[7] General Health Center East, HR-Poljanice IV 8, Zagreb, Zagreb, Croatia, Zagreb, Croatia

Introduction: We demonstrated in our prior study that hypothyroidism and thyroiditis are more prevalent in Parkinson's disease (PD) than in control group.
Objective: The goal of this study was to investigate the association between thyroid disease and severity of cognitive impairment in Croatian residents with de novo PD.
Methods: This study comprised a total of 222 de novo PD patients, 121 women and 101 men (with mean age of 67,76), among whom 70 subjects (31,5%) also had thyroid disease (55 levothyroxin-treated.hypothyroidism, 54 thyroiditis, 7 hyperthyroidism, 2 subclinical hypothyroidism and 1 subclinical hyperthyroidism), 46 women and 24 men (with mean age of 69,2 years). Control group consisted of 152 PD patients without thyroid problems. Clinical severity of cognitive impairment were assessed by Montreal Cognitive Assesment (MoCA).
Results: Thyroid disturbance did not exhibited significantly higher scores for cognitive impairment assessed by MoCA in de novo PD patients compared with the non-thyroid disease-PD group (mean moCA score 24,28 vs. 24,9).
Conclusion: We demonstrated that neither levothyroxine-treated-hypothyroidism, thyroiditis nor hyperthyroidism had no impact on the cognitive impairment in de novo PD patients. Although thyroid disease may be associated with impaired regulation of TSH and thyroid hormones levels, and thyroiditis-associated-antibodies could lead to a local immune complex-mediated inflammatory reaction in the brain inducing neuronal tissue damage, it seems that thyroid disturbances do not more affect the severity of cognitive impairment in de novo PD patients than other etiopathogenetic factors. Further studies are needed to examine this impact.

P30.21

The effects of computerised cognitive training of executive functioning on emotion regulation in Parkinson's disease

Caroline Seton, Carien M. van Reekum, Aileen K. Ho*
University of Reading, Reading, West Berkshire, United Kingdom

Background: Striatal dopaminergic dysfunctions are suggested to contribute to working memory (WM) impairments and neuropsychiatric symptoms, such as depression, in individuals with Parkinson's disease (PD). WM has been shown to be crucial for coping with the cognitive challenges in everyday situations and facilitates the use of adaptive emotion regulation strategies such as reappraisal. This online, computerised cognitive training study presents a promising approach to targeting WM as a key mechanism for improving both executive functioning and emotion regulation in PD patients.
Methods: Per pre-registration (ISRCTN), a sample of 72 individuals diagnosed with PD are being recruited. Participants are randomly allocated to either an experimental group entailing the adaptive Paced Auditory Serial Attention Task (PASAT), or an active control group entailing an adapted visual search task. Both groups complete ten training sessions over a period of two weeks. Post-training assessments will be completed at 2-weeks, 1-month and 2-month intervals.
Participants complete pre-training assessments to establish baseline performance in executive function and emotion regulation including the Paced Auditory Serial Attention Task (PASAT), the Digit Span Task, the Colour-Shape Task, and the Go/No-Go task. Participants complete a reappraisal task – generating alternative interpretations of 13 negative images to reduce negative emotion - measuring productivity (number of reappraisals generated), difficulty (time taken to generate the first reappraisal per trial) and effectiveness (difference in self-rated emotion intensity on a Likert scale before and after reappraisal). The Emotion Regulation Questionnaire and Positive and Negative Affect Scale are also administered. Data collection is ongoing (current N = 42) and is projected to be completed by May 2023.
Discussion: We test the prediction that participants in the experimental group will show significantly improved reappraisal compared to the active control group. We also anticipate observing transfer effects on trained (non-adaptive PASAT) and untrained (Digit Span) tasks in the experimental group. Lastly, we hypothesise that at least one of the cognitive variables in which change in performance as a function of the intervention will predict reappraisal ability. The findings could highlight the utility of a low-cost intervention to enhancing executive function and wellbeing in individuals with PD.

P30.22

Motor symptom asymmetry predicts emotional and cognitive theory of mind outcome following STN DBS in Parkinson's disease

Philippe Voruz, Julie Péron*
University of Geneva, Geneva, Switzerland

The identification of potential phenotypes of people living with Parkinson's disease is an essential element of future management and could in basic research explain the heterogeneity of observed outcomes. One of the factors that could distinguish subgroups could be the asymmetric nature of the pathology.
In this context, our group has recently demonstrated distinct patterns and evolution of non-motor symptoms and biomarkers according to the asymmetry of motor symptoms1-3. Our researches have also demonstrated distinct effects of deep brain simulation of the subthalamic nucleus (STN-DBS) on cognitive performance4,5, psychiatric symptoms4,5, emotional processing4 and quality of life5. That said, to date, studies are not unanimous about the effects of STN-DBS on theory of mind6-8, but to the best of our knowledge no study has assessed the theory of mind in relation to motor symptom asymmetry. Therefore, the aim of our study in 34 patients with idiopathic Parkinson's disease was to assess cognitive and

emotional theory of mind at 3 months pre- and 3 months post-DBS as function of motor symptom asymmetry.
As expected our conservative and validated statistical methodology revealed a significant deterioration of performances for the emotional theory of mind only in patients living with an onset motor symptoms predominantly on the right side (RPD) at 3-months following the STN-DBS operation.
Interestingly, our results can be associated to those obtained previously by our group for the treatment of emotional prosody4, suggesting that RPD patients may not only be impacted by the STN-DBS operation in their performances for emotional processing4, but also in higher-level functions, such as social cognition. Those results are in contrast with our previous observations on cognitive performance in RPD patients, as well as an improvement in apathy symptoms 5, potentially suggesting the involvement of lateralized brain functions, as well as a dissociated (positive or negative) effect of the STN-DBS as function of motor symptom asymmetry and in interaction with the non-motor symptoms evaluated.
Evaluated in their entirety, the results from our group may be of importance for the improvement of the criteria of inclusion of the patients for surgery and open the way to new implication in personnalized medicine.

P30.23

Extending the BRAIN keyboard tapping test: To detect cognitive decline in a large community cohort of older Australians

Xinyi Wang[*,1], Rebecca J. St George[1], Aidan Bindoff[1], Alastair J Noyce[2], Katherine Lawler[1], Eddy Roccati[1], Larissa Bartlett[1], Son Tran[3], James Vickers[1], Quan Bai[3], Jane Alty[1]*
[1] Wicking Dementia Research and Education Centre, University of Tasmania, Hobart, Tasmania, Australia
[2] Queen Mary University of London, London, United Kingdom
[3] University of Tasmania, Hobart, Tasmania, Australia

Background: The Bradykinesia Akinesia Incoordination (BRAIN) test is a validated alternate-key keyboard tapping test to measure hand motor function in people with Parkinson's disease. Participants are asked to tap the 's' and ';' keys alternatively as fast and as accurately as they can. There is emerging evidence that impaired keyboard tapping may be associated with subtle cognitive decline. This is relevant in Parkinson's as 50% of people develop cognitive decline within 10 years of diagnosis and early detection would aid early recruitment to clinical trials. We have developed TAS test, a self-test online motor-cognitive battery, designed to be completed at home, that includes several keyboard tapping tests (including an adapted BRAIN test). We hypothesise that worse motor function measured by TAS Test keyboard tests will be associated with declines in cognitive function.
Methods: 1,177 community participants (65.8 ± 7.4 years old; 73% female) without any cognitive symptoms completed a 40-second single key tapping test and a 60-second alternate key tapping test from TAS Test and validated cognitive tests of episodic memory, working memory and executive function. Frequency, variability, key press duration and accuracy scores were calculated for each tapping test. Generalized linear models examined associations between keyboard tapping and cognitive performance, adjusted for confounders including age, sex, depression, anxiety and education.
Results: All motor features of the single key (R2adj = 8.8%, ΔAIC = 4.9) and alternate key tapping tests (R2adj = 9.1%, ΔAIC = 7.8; see Figure 1) improved estimation of episodic memory performance relative to models with demographic and mood confounders only (R2adj = 8.1%). No tapping features improved estimation of working memory. Only single key tapping features improved the estimation of executive function performance (R2adj = 16.0%, ΔAIC = 7.2).
Conclusions: Brief self-administered online keyboard tapping tests predict asymptomatic episodic memory decline. This provides a potential low-cost and brief home-based method for risk stratification of enriched cohorts for further assessment.

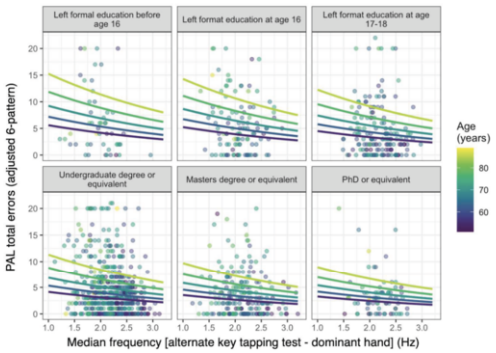


Figure 1. Episodic memory by dominant hand alternate key tapping frequency compared across age and level of education. The trend curves show expected episodic memory performance (PAL total errors adjusted for 6-pattern stage) with more errors associated with low tapping frequencies and older age. Non-dominant hand tapping variability, anxiety and depression scores, and gender are fixed at their respective means. This model predicts PAL total error scores significantly better than the covariate-only null model (ΔAIC = 7.8).

P30.24

Using keyboard motor tests in a cognitive clinic may help identify stages of the dementia continuum

Xinyi Wang[*,1], Aidan Bindoff[2], Rebecca J. St Geroge[2], Son Tran[1], Kaylee Rudd[2], Quan Bai[1], James Vickers[2], Jane Alty[2]*
[1] University of Tasmania, Hobart, Tasmania, Australia
[2] Wicking Dementia and Education Center, University of Tasmania, Hobart, Tasmania, Australia

Background: The process for assessing cognitive symptoms in clinic is time consuming, expensive and usually requires multiple clinicians. There is urgent need for accessible, quick and low-cost methods to aid identification of people at the early stages of the dementia continuum. Emerging evidence shows that simple low-cost keyboard tapping tests could aid risk stratification. This study evaluated the classification accuracy of the new TAS Test modified shorter version of the Bradykinesia Akinesia Incoordination (BRAIN) test for dementia, mild cognitive impairment (MCI) and subjective cognitive decline (SCD) from healthy controls.
Methods: 242 participants (68.9 ± 8.9 years old) were recruited in Tasmania, Australia: 107 from the ISLAND Cognitive clinic and 135 cognitively healthy controls. Clinic participants were diagnosed with dementia (n= 41), MCI (n= 45) or SCD (n= 21). Participants completed a 60-second alternate key tapping test on the TAS Test website. Frequency, variability, key press duration and accuracy scores were calculated for the tapping test. Area under the curve (AUC) was used to compare the model with combination of tapping features and the baseline model with age.
Results: Tapping feature data improved the differentiations of people with dementia (p=0.04) or MCI (p=0.01) from cognitively normal participants compared to the baseline model. The keyboard tapping features also helped distinguish MCI from SCD (p value = 0.03), but did not help distinguish cognitively normal controls from SCD (p value = 0.21).
Conclusions: A 60-second simple keyboard tapping test could help distinguish patients at the early stage of dementia continuum (i.e., at MCI stage) from cognitively normal participants, and also between participants with SCD and MCI. It could potentially be used as a

population screening test for identifying people at high risk of dementia for further medical assessments. This result is relevant to Parkinson's where there is increased risk of cognitive decline.

P30.25

Perceived control as a predictor of medication adherence in people with Parkinson's: A large-scale cross-sectional study

Nicolò Zarotti[*,1], *Katherine Deane*[2], *Catherine Ford*[2], *Jane Simpson*[3]
[1] Manchester Centre for Clinical Neurosciences, Manchester, United Kingdom
[2] University of East Anglia, Norwich, United Kingdom
[3] Lancaster University, Lancaster, United Kingdom

Purpose: Medication adherence is a multi-faceted construct associated with several positive consequences in people with chronic conditions. However, non-adherence currently represents a major issue in Parkinson's, potentially due to low perceptions of control. This study investigated the predictive ability of several aspects of perceived control on adherence in people with Parkinson's, while accounting for previously established predictors such as depression and medication variables.
Materials and Methods: An online cross-sectional survey was carried out with 1210 adults with Parkinson's from 15 English-speaking countries. Demographic and clinical questions, as well as measures of depression, aspects of perceived control, and medication adherence were included. Pearson's correlations and a 4-block hierarchical regression analysis were performed to assess the relationship between the variables.
Results: Perceived control explained a slightly higher amount of variance in medication adherence compared to medication variables when entered in the last block. Unexpectedly, depression was not significantly related with adherence. Internal locus of control was an independent negative predictor of adherence, while external dimensions of locus of control emerged as independent positive predictors.
Conclusions: In people with Parkinson's, perceptions of control may have a larger impact on adherence compared to medication variables. Implications for clinical practice and future research are discussed.

P30.26

Gait initiation in Parkinson's disease: Investigating the role of proactive and reactive inhibition with EEG

Déborah Ziri[*,1], *Laurent Hugueville*[2], *Claire Olivier*[2], *Marie-Laure Welter*[2], *Nathalie George*[2]
[1] Paris Brain Institute, Saint-Mandé, France
[2] Paris Brain Institute, Paris, France

Parkinson's disease is characterized by akinesia, that is, a difficulty to initiate movements. During gait initiation, this can lead to freezing of gait, which is highly disabling and responsible for falls. Akinesia has been linked to excessive inhibition, in particular proactive inhibition, which is set prior any movement, in the absence of any stimulus, in uncertain context. Proactive inhibition has to be lifted in order to initiate movement. Here, we studied proactive and reactive inhibitory processes associated with gait initiation in a modified Go-NoGo task performed on a force platform allowing gait parameter recording with high-density electroencephalography (EEG) recording. Go-certain trial blocks—with only Go stimuli—were added to a classic Go-NoGo task made of mixed (aka. uncertain) Go-NoGo trial blocks, in order to dissociate reactive inhibition (observed in response to the NoGo stimulus in the Go-NoGo blocks) and proactive inhibition (observed by contrasting the Go-uncertain with the Go-certain conditions). The results obtained in 23 healthy volunteers showed increased reaction time (RT) associated with the context of uncertain relative to certain gait initiation. This was accompanied by an increase of the N2-P3 evoked potential complex and modulations of oscillatory activities in the theta (3-7 Hz), alpha (7-13 Hz), and beta (low: 13-20 Hz and high: 20-30 Hz) bands, which reflected the executive—attention and response inhibition—processes associated with proactive and reactive inhibition. We further recorded data of 16 patients with Parkinson's disease with and without deep brain stimulation of the subthalamic nucleus (STN-DBS). On the behavioral level, patients showed the same pattern as healthy subjects, with longer RT in the uncertain than the certain contexts. RT was overall longer for patients than healthy subjects but improved with STN-DBS. For EEG data, after STN-DBS artifact correction, we are currently analyzing the N2/P3 complex and the oscillatory activities in order to test which stage of executive processes are affected and if STN-DBS allow normalizing the processes of proactive and/or reactive inhibition.

CLINICAL SCIENCE: Sleep disorders/fatigue

P31.01

Continuous dopaminergic stimulation to improve sleep disorders in Parkinson's disease with insomnia: Results from the Apomorphee study on subcutaneous night-time only apomorphine infusion

Valérie Cochen De Cock[*,1], *Pauline Dodet*[2], *Smaranda Leu*[2], *Cecile Aerts*[1], *Giovanni Castelnovo*[3], *Beatriz Abril*[4], *Sophie Drapier*[5], *Laurene Leclair-Visonneau*[6], *Marie Vidailhet*[7], *Isabelle Arnulf*[2], *Mohamed Doulazmi*[8], *Emmanuel Roze*[7]
[1] Beau Soleil Clinic, Montpellier, France, Montpellier, France
[2] Sleep Disorders Unit, Pitié-Salpêtrière University Hospital, Paris, France, Paris, France
[3] Department of Neurology, University Hospital of Nîmes, France, Nîmes, France
[4] Sleep Department, University Hospital of Nîmes, Nîmes, France, Nîmes, France
[5] Department of Neurology, Pontchaillou University Hospital, Université de Rennes 1, Rennes, France, Rennes, France
[6] Clinical Neurophysiology Department (L Leclair-Visonneau, PhD), University Hospital of Nantes, France, Nantes, France
[7] AP-HP, Salpetriere Hospital, DMU Neuroscience 6, Paris, France, Paris, France
[8] Adaptation Biologique et Vieillissement (UMR8256), Institut de Biologie Paris Seine, Sorbonne University, CNRS, Paris France, Paris, France

Insomnia is one of the most disabling non motor symptom in Parkinson's disease (PD). It has a severe impact on the person's and their caregiver's quality of life. Continuous dopaminergic stimulation through apomorphine infusion at night could be beneficial on PD-related insomnia.
We aimed to test the efficacy on sleep disorders of subcutaneous nigh-time only apomorphine infusion in PD with fluctuations.
From January 2017 to March 2021, 46 participants with fluctuating PD and moderate to severe insomnia were included in a randomised, multicentre, double-blind, placebo-controlled, crossover study (clinicaltrial.gov, NCT02940912). Night-time subcutaneous apomorphine (up to 5mg/h) or placebo were delivered during a10-night titration phase followed by a 7-night fixed-dose phase and separated by a 14-night washout period. We compared, in intention-to-treat, sleep complaints and measures at the end of each treatment period.

Compared to placebo, Apomorphine improved sleep disorders on Parkinson's disease sleep scale (PDSS) scores, insomnia severity and self-evaluated motor condition in the morning. Of note this improvement was present while most (62%) of the persons were already treated with prolonged release or transdermal dopamine agonists. Apomorphine did not improve sleep measures on polysomnography compared to placebo. Adverse events were not different between apomorphine and placebo except for dizziness, more frequent with apomorphine.
Night-time only sub-cutaneous apomorphine infusion improves sleep complaints and especially insomnia in PD. This result emphasizes the impact of a continuous and sufficient dopaminergic stimulation at night in fluctuating PD.
Cochen De Cock et al. Safety and efficacy of subcutaneous night-time only apomorphine infusion to treat insomnia in patients with Parkinson's disease (APOMORPHEE): a multicentre, randomised, controlled, double-blind crossover study. Lancet neurology 2022: 21:428-437.

P31.02

Do motor symptoms worsen Parkinson's disease insomnia? A videopolysomnographic study
Sarah Joanny, Smaranda Leu-Semenescu, Isabelle Arnulf*
Sleep Disorders Unit, Pitié-Salpêtrière University Hospital, Paris, France

Introduction: Most patients with Parkinson's disease (PD) experience difficulty maintaining sleep, but the mechanism of this insomnia is poorly understood and probably multifactorial. We aim at studying the role of motor symptoms (bradykinesia, resting tremor, dystonia) in poor sleep, by studying directly symptoms of parkinsonism during the night (wakefulness and sleep).
Methods: 20 participants with PD and 50 age- and gender-matched controls underwent a nocturnal videopolysomnography. Motor symptoms were investigated on the video plus 7 surface electromyographic sensors (chin, as well as left and right anterior tibialis, gastrocnemius and flexor digitoris muscles). Dystonia was measured by prolonged activity in legs and arms muscles and feet/arm postures. Resting tremor was visible on video and on muscles sensors. Bradykinesia was measured during by the time for changing position in bed and for urinating.
Results: People with PD fell rapidly asleep and slept as long as healthy subjects, but they woke up more often and for longer periods. Half of participants with PD (and no control) had a tremor at night, almost exclusively during wakefulness and sometimes during arousals, but very few had nocturnal cramps. Electromyographic activity typical of tremor without movement (isometric contraction) was very rarely observed in non REM sleep. The wakefulness after sleep onset time increased as daytime motor impairment (MDS-UPDRS-III, dopaminergic dose) and duration of the rest tremor at night increased, but not with the number of position changes (although they were fewer than in the healthy group), time spent supine on the back and duration for urinating.
Conclusion: The motor symptoms of PD (especially nocturnal tremor), and the frequent maintenance insomnia are correlated. The extrapyramidal involuntary motor activities disappear during sleep clinically, but may rarely persist in non REM sleep at a subclinical stage without causing awakenings, suggesting that these involuntary movements receive central inhibition during sleep.

P31.04

Examining the impact of sleep disturbances on lived experiences of persons with Parkinson's disease (PwPD)
Adriana Ornelas[1], Karen Aranha[1], Angela Blackwell[1], Nina Mosier[,2]*
[1] University of St. Augustine Health Science, Austin, TX, United States
[2] Power for Parkinson's, Austin, TX, United States

Introduction: This investigation aims to examine the lived experiences of PwPD who suffer from insomnia. Sleep disturbance affects up to 98% of individuals with PD. The non-motor symptom (NMS) significantly reduces HR-QOL, positively correlates with disease severity and duration, and increases the disease burden of care. Due to the nature of the disease, typical sleep hygiene protocols may not be the most effective intervention for this population. Understanding their challenges is vital to developing a sleep hygiene protocol tailored to their needs. **Methodology:** A pilot qualitative study using an interpretive phenomenological analysis (IPA) with PwPD (N=12). The study has received IRB approval. The qualifying criteria for the participants include a score of >18 on the MOCA, a score >82 on the PDSS, being older than 50, and having transportation to attend the focus group. Data collection will consist of two focus groups (n=6) using a semi-structured format. Data analysis will include open coding, memoing, fracturing the data, and examining emerging themes. The IPA methodology will allow the investigator to take a constructivist approach and examine the data generated from the extant literature to understand the unique experiences of PwPD and sleep issues prevalent with PD. Findings/ **Conclusion:** This study is currently underway. The saturated and unsaturated superordinate themes generated will be utilized to engage in a larger study to establish sleep hygiene recommendations unique to the PD population. It will also be used to increase awareness of sleep issues to advocate for a healthcare support system that caters specifically to the sleep needs of PwPD.

P31.05

Keyboard tapping performance in people with subjective REM sleep behaviour disorder
Cristina Simonet[,1], Harneek Chohan[2], Teresa Perinan Tocino[3], Laura Perez-Carbonell[4], Guy Leschziner[4], Aneet Gill[2], Jonathan Bestwick[2], Anette Schrag[5], Alastair Noyce[2]*
[1] Queen Mary University of London, London, United Kingdom
[2] Preventive Neurology Unit, Wolfson Institute of Population Health, Queen Mary University of London, London, United Kingdom
[3] Instituto de Biomedicina de Sevilla (IBiS). Hospital Universitario Virgen del Rocío, Seville, Spain
[4] Sleep Disorders Centre. Guy's and St Thomas' NHS Foundation Trust, London, United Kingdom
[5] Department of Clinical and Movement Neuroscience, UCL Institute of Neurology, London, United Kingdom

Background: The BRadykineisa Akinesia INcoordination (BRAIN) test is a 30-second web-based alternating finger keyboard tapping test which was validated to evaluate motor dysfunction in Parkinson's disease (PD). It is part of the online assessments in the PREDICT-PD study. In a previous study we found that patients with polysomnography (PSG)-confirmed REM Sleep Behaviour Disorder (RBD) had slow and erratic keyboard tapping.
Methods: A cross-sectional study was carried out to compare the BRAIN test performance of people with subjective RBD (sRBD, defined by RBD screening questionnaire score >5) to controls. BRAIN kinetic parameters included kinesia score (KS, taps over 30s), akinesia time (AT, mean dwell-time on each tap) and incoordination score (IS, variance of traveling time between taps). We undertook logistic regression models adjusted for age and sex

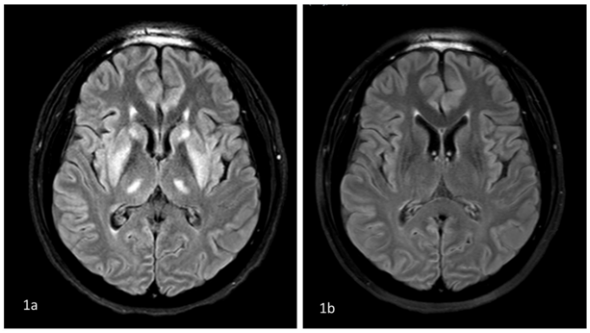
to determine the association between kinetic parameters (independent variable) and the presence of sRBD (dependent variable).
Results: We tested 2512 participants in PREDICT-PD (310 people with sRBD and 1907 controls). The sRBD group was younger (64.90 years (SD 9.07) vs 66.67 years (SD 6.84), p<0.001) and more likely to be male (51.2% vs 37.1%, p<0.001) than the controls. The sRBD group performed the BRAIN test more slowly than controls (KS: 57.05 taps vs 60.89 taps; 95% CI 2.32-5.36, p<0.001) and with greater incoordination (IS: 9.15 vs 8.91; 95% CI 0.12-0.36, p<0.001). Logistic regression analysis adjusted for age and sex showed that IS had the strongest association with sRBD. The odds of having sRBD was 1.13-fold greater per 1 unit change in the IS (95% CI 1.07-1.20, p<0.001). There was nominal evidence that AT was also associated with sRBD (OR, 1.01; 95% CI 1.00-1.01, p<0.001). KS did not show any association with sRBD after adjusting for age and sex.
Conclusion: There is some evidence that individuals with sRBD had an abnormal keyboard tapping which resembles what we found previously in patients with PSG-confirmed RBD. Remote keyboard tapping may have utility as a screening tool to select people with sRBD who might warrant a PSG study and subsequent closer monitoring.

CLINICAL SCIENCE: Diagnosis (differential, accuracy)

P32.01

Acute onset secondary Parkinsonism due to extrapontine myelinolysis
Cintia Margoth Armas Puente, Carlos Cosentino Esquerre*
Instituto Nacional de Ciencias Neurológicas, Lima, Peru

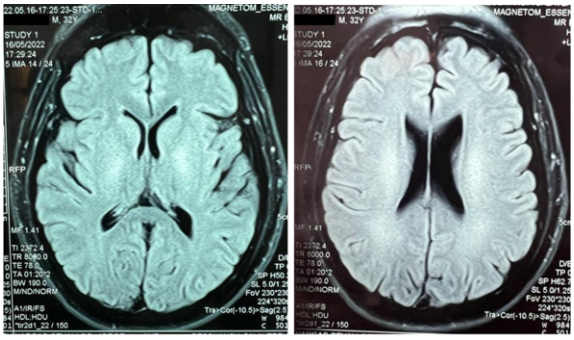
Background: Osmotic demyelination syndrome (ODS) is an uncommon neurological disorder caused by damage to the myelin sheath of brain cells. Central pontine myelinolysis is the classical presentation but extrapontine involvement is actually quite common affecting mostly thalamus and basal ganglia.
Case report: A 42-year-old man was admitted with headache and bitemporal hemianopsia due to a recent diagnosed pituitary tumor. On examination a clear parkinsonism was found with bradykinesia, resting tremor and severe rigidity involving fourall limbs. Medical dossier from other institution revealed that severe hyponatremia was found (106 mEq/Lt) and was rapidly corrected (125 mEq/L) over a period of 24 hours using hypertonic saline. Parkinsonism apparently developed a few days later. The T2/FLAIR sequences of brain MRI showed hyperintensities in both thalamus, globus pallidus, putamen and caudate nuclei suggestive of ODS (Figure 1a) as well as the pituitary macroadenoma compressing the optic tracts.
To treat his parkinsonism Levodopa/carbidopa was started (titrated to 625 mg/day). Steroids and levothyroxine were also started. Parkinsonian symptoms improved moderately and patient was discharged. He underwent tumor excision few months later and returned with us eight months after first evaluation with significant improvement, He was able to ambulate independently and to do activities of daily living. A new MRI showed almost complete disappearance of hyperintensities (Figure 1b). Levodopa was maintained at the same daily dose.
Conclusions: We report a case of levodopa responsive - acute onset parkinsonism caused by extrapontine myelinolysis after rapid correction of hyponatremia in a patient with pituitary adenoma. Extrapontine myelinolysis can involvement varied regions of the brain and can present with a wide spectrum of clinical manifestations as parkinsonism, tremor, dystonia, myoclonus, ataxia, chorea, mutism and catatonia. These manifestations can either occur early in the disease or as a delayed manifestation. Thus extrapontine myelinolysis should be always considered as a possible cause of acute onset secondary parkinsonism.



P32.02

Tacrolimus-induced Parkinsonism: A case report
Cintia Armas Puente, Carlos Cosentino Esquerre*
Instituto Nacional de Ciencias Neurológicas, Lima, Peru

Background: Drug-induced parkinsonism is the most common type of a movement disorder associated with drugs.
Tacrolimus is a very efficient immunosuppressive agent used especially in solid organ transplantation and despite a wide range of adverse effects tacrolimus still represents the cornerstone of immunosuppressive treatments after liver and heart transplantation.
There are very few reports of tacrolimus-induced parkinsonism so its pharmacologic management and functional impact remain poorly characterized in the literature. We present a case of tacrolimus-induced parkinsonism with a clear neuroimaging correlation.
Case report: A 32-year-old man a cardiac transplantation. He was discharged with prednisone, valganciclovir, mycophenolic acid, tacrolimus, diltiazem and atorvastatin. He complained of syncope-like episodes at home. Five months after transplantation he was evaluated in our hospital because of new motor symptoms as slowness and hands tremor. A clear parkinsonism was found with bilateral hypokinesia and rigidity, rest and postural hands tremor. Flexed posture, severe hypophonia and dysarthria. Mild limitation of ocular infraversion. Bradypsychic. No postural instability.
Diffusion-weighted and FLAIR sequence MRI showed symmetrical and bilateral hypersignal in globus pallidum and subcortical white matter (Figure 1).
Tacrolimus was withdrawn by cardiovascular surgeons and small doses of levodopa were initiated with very poor response. Poor clinical evolution delayed performing a new MRI and continue up titrating levodopa.
Conclusions: Tacrolimus is the preferred calcineurin inhibitor in case of primary transplants. Tacrolimus-induced neurotoxicity is usually manifested as encephalopathy mainly as posterior reversible encephalopathy syndrome (altered consciousness, seizures, visual abnormalities, headache and focal neurological signs). There are very few reports of tacrolimus-induced parkinsonism in the literature. We add here another case of parkinsonism as a dominant sign of encephalopathy induced by tacrolimus with abnormalities on MR images.



P32.03

Parkinson's disease: A new metabolic biomarker for early diagnosis and development of potential therapeutic target

Sabrina Boulet[*,1], *David Mallet*[1], *Raphael Goutaudier*[1], *Thibault Dufourd*[1], *Sebastien Carnicella*[1], *Emmanuel Barbier*[2], *Florence Fauvelle*[2], *Véronique Sgambato*[3], *Pierre-Olivier Fernagut*[4], *Jerry Colca*[5]

[1] University Grenoble Alpes, INSERM, U1216, Grenoble Institut Neurosciences, Junior group 'Physiopathology of motivation', Grenoble, France
[2] University Grenoble Alpes, INSERM, U1216, Grenoble Institut Neurosciences, Team 'fonctionnal neuroimaging and brain perfusion', Grenoble, France
[3] Université de Lyon, CNRS UMR5229, Institut des Sciences Cognitives Marc Jeannerod, Bron, France
[4] Université de Poitiers, INSERM U1084, Laboratoire de Neurosciences Expérimentales et Cliniques, Poitiers, France
[5] Metabolic Solutions Development Company, Kalamazoo, United States

Parkinson's disease (PD) remains an incurable neurodegenerative pathology affecting almost 1% of the population beyond the age of 60. The two main factors that account for this therapeutic failure are the late diagnosis, based on the characteristic motor symptoms of the disease appearing when neurodegenerative process has already past rescue, and an incomplete understanding of PD pathophysiology.
In this context, using proton nuclear magnetic resonance, we investigated serum and brain metabolic markers in three different animal models of PD, mimicking different stages of the disease assessed by behavioral and histological evaluation, and in 2 cohorts of de novo PD patients.
From our translational study, we first highlighted common metabolic dysregulations in serum of the different animal models and PD patients. We propose a promising biomarker exhibiting a high level of predictivity for PD diagnosis in its early phase, before motor symptoms appearance.
Moreover, mirrored brain and serum dysregulations strongly suggest dysfunctions in the pyruvate metabolism, a central metabolic node to supply cellular energy, as possible therapeutic target.

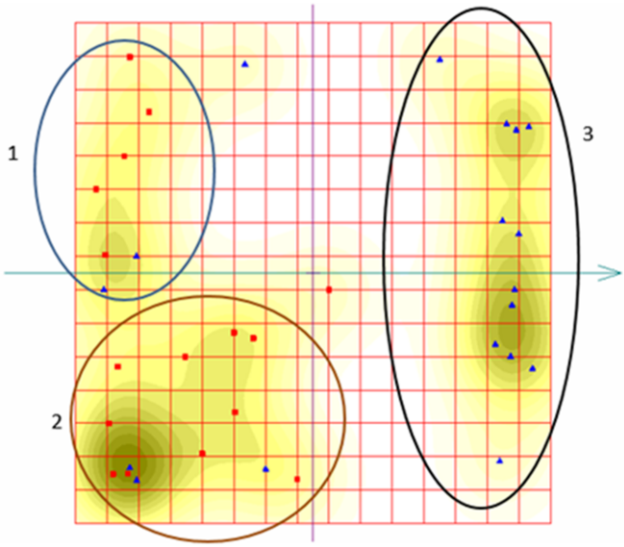
P32.05

Correlation between olfactory dysfunction and severity of tremor: New hypothesis

Denis Pokhabov[*,1], *Vladislav Abramov*[2], *Michael Sadovsky*[3], *Dmitrii Pokhabov*[1]

[1] Krasnoyarsk state medical university, Krasnoyarsk, Russia
[2] Federal Siberian Research Clinical Centre, Krasnoyarsk, Russia
[3] Institute of computational modelling of SB RAS, Krasnoyarsk, Russia

Objective: Our aim was to obtain tremor data of PD and ET patients and the results of their olfactory function, which can help verify our scientific hypothesis on the inverse relation between tremor manifestation and olfactory function decay:lower tremor is accompanied with worse smell perception,and vice versa.
Background: Millions of people suffer from neurological disorders worldwide. Parkinson's disease(PD) and essential tremor(ET) are among the leading diseases. Expected global PD rate is about 17 million people by 2040. Varying in manifestation,it exhibits some differences for PD and ET:rest tremor for PD and postural-kinetic for ET. Olfactory dysfunction has been reported as the first manifest of PD often preceding the movement disorders,however,it is not specific for ET. Thus, it becomes effective in early differential diagnosis. Tremor records of arms also supports correct diagnosis of the disease at early stage.
Methods: We had three groups of patients: suffering from PD, ET and healthy people. An examination procedure of olfactory function was based on extended olfactory Sniffin' sticks test to determine three parameters: threshold, identification and discrimination. For tremor testing we used wireless device to monitor electrophysiological signals. Four sensors recorded three main characteristics: skin electromyogram(SEMG), gyroscope and accelerations. We used an elastic map technique to cluster and analyze all data.
Results: Combination of tremor data and smell perception provides a clear and apparent distinction of PD patients from ET ones. Proven inverse relation between tremor level and olfactory function decay is the core result of our work. Indeed, ET patients showed better olfactory function results accompanied by stronger tremor, as compared to PD patients. Few ET patients occupy the cluster comprising PD patients, and the reason for that is the lower olfactory function observed on them. This fact forces to continue their observation in dynamics, keeping in mind that such patients have a high chance of PD development in the future.
Conclusions: Combination of olfactory testing and tremor records improves significantly the discrimination of PD patients from those with ET, as well from healthy people. The presented results could be implemented for early differential diagnostics of PD vs. ET, as well as for the improvement of individual therapy course for such patients.



P32.06

Transcranial sonography as a tool for the differential diagnosis of early stages of synucleinopathies

Neus Rabaneda Lombarte[*,1], Anna Planas Ballvé[2], Belén Flores Pina[1], Mireia Gea Rispal[1], Lourdes Ispierto González[1], Laia Grau[3], Ramiro Álvarez[1], Pau Pastor[1], Dolores Vilas Rolan[1]*
[1] Movement Disorders Unit, Neurology Service. Hospital Universitari Germans Trias i Pujol, Barcelona, Spain
[2] Movement Disorders Unit, Neurology Service, Complex Hospitalari Moisès Broggi, Barcelona, Spain
[3] Epilepsy Unit, Neurology Service. Hospital Universitari Germans Trias i Pujol, Barcelona, Spain

Background and objective: The diagnosis of synucleinopathies, such as Parkinson's disease (PD) and Dementia with Lewy bodies (DLB), is challenging, especially in the earlier stages. Our objective was to assess the usefulness of transcranial B-mode sonography (TCS) in the differential diagnosis of synucleinopathies at their earlier phases.
Methods: We prospectively include a cohort of newly diagnosed PD and DLB patients with less than 3 years from onset of symptoms and scoring 3-4 in the Global Deterioration Scale. For comparison purposes a group of recently diagnosed Alzheimer's disease (AD) patients and controls were included. TCS was performed in all individuals to assess the echogenicity of the substantia nigra (SN), the width of the third ventricle (IIIv) and the size of the frontal horn of lateral ventricles (LV). The medical image viewer Horos was used to analyze the intensity of the echogenicity of these structures.
Results: Ninety-eight participants were included (25 PD, 17 DLB, 25 AD, 31 controls). Mean age was 74±3,44 years for DLB and 69±6,63 years for PD patients. PD and DLB patients showed a higher percentage of hyperechogenicity of the SN (72.7% and 76.5%, respectively) compared to AD and controls (10.5% and 31%, respectively; p<0.001). The area of hyperechogenicity of the SN was significantly higher in PD and DLB patients (Right 0.205±0.085 cm2; Left 0.241±0.08 cm2 and R 0.213±0.097 cm2; L 0.253±0.09 cm2, respectively), compared to AD and controls (R 0.0134±0.054; L 0.125±0.066 and R 0.104±0.038; L 0.118±0.05, respectively; p<0.001). AD patients had the highest percentage of widened IIIv (23.8%) compared to the other groups (PD 0%, DLB 6.3%, controls 7.1%; p=0.046). The size of the LV was higher in AD and DLB patients (50% and 42.9%) compared to PD and controls (10% and 20.8%, respectively; p=0.034). No differences were found in the intensity of the echogenicity of the SN using the image viewer Horos.
Conclusions: TCS is a valid tool for the differential diagnosis of the early stages of synucleinopathies, especially combining the evaluation of the SN and the ventricle sizes. The application of an image viewer to quantify the intensity of the echogenicity of the SN does not seem to be useful.

P32.07

Whole-exome sequencing for Parkinson's disease: Tertiary single-center experience

Valentino Racki[*,1], Elisa Papic[2], Mario Hero[2], Anja Kovanda[3], Borut Peterlin[3], Vladimira Vuletic[2]*
[1] Clinical Hospital Center Rijeka, Rijeka, Croatia
[2] Department of Neurology, Faculty of Medicine, University of Rijeka, Rijeka, Croatia
[3] Clinical Institute of Genomic Medicine, University Medical Center Ljubljana, Ljubljana, Slovenia

Introduction: Parkinson's disease is a multifactorial disease, and an estimated 5-10% can be contributed to monogenic causes, and identifying those patients remains a diagnostic challenge. Whole-exome sequencing enables us to simultaneously analyse a large number of genes, although a lack of clear criteria for genetic evaluation and testing leads to reduced genetic testing in routine clinical practice. Our aim was to assess the clinical application of whole-exome sequencing Parkinson's disease patients.
Methods: Our study cohort includes patients from the Clinic of Neurology at the Clinical Hospital Centre Rijeka, referred to genetic testing during 2021 and 2022. Exome sequencing was performed at CIGM using standardized protocols in use at the time of processing. Identified variants were classified according to the ACMG and AMP 2015 joint consensus recommendation, along with ACGS recommendations where applicable.
Results: We have performed exome sequencing in 74 patients. Causative pathogenic mutations have been confirmed in 9 patients (12,16%, GBA n=8, PRKN n=1), while variants of uncertain significance were found in 17 patients (22,97%, ATP13A2 n=2, EIF4G1 n=2, PSEN1 n=1, SORL1 n=1, LRRK2 n=1, SNCA n=1, GCDH n=1, ATP7B n=1, THAP1 n=1, TBK1 n=1, ERBB4 n=1, ITM2B n=1, NOTCH 3 n=1, SETX n=1, NR4A2 n=1). Additonally, 3 patients have confirmed carriership of classically recessive genes (GCHD n=1, FIG4 n=1, RNF216 n=1).
Conclusion: Pathogenic mutation yield of 12% is comparable to current findings for european populations, with GBA as the most common pathogenic risk factor, similar to earlier reports in Czech and German population. Our findings show that whole-exome sequencing can be considered in the clinical evaluation of Parkinson's disease, as it can lead to the findings of causative pathogenic mutations, which can be of importance for clinical follow-up and is a significant information given to the patients and their families.
* This work has been submitted and will be presented at the AD/PD 2023 conference from 28th of March to 1st of April 2023. in Gothenburg, Sweden. This work has not been published.

P32.08

Impact of educational level on delayed diagnosis in people living with Parkinson's disease (PD): Treated at the National Institute of Neurology and Neurosurgery (INNN) during the year 2022

María Alejandra Ruiz - Mafud, Eduardo Ichikawa-Escamilla, Etienne Reséndiz - Henríquez, Gloria Itzel Cerda-Hernández, Axel Antonio Herrera - Ruiz, Daniela Renee Aguila - Godinez, Ana Jimena Hernández - Medrano, Amin Cervantes - Arriaga, Mayela Rodriguez - Violante*
Instituto Nacional de Neurología y Neurocirugía Manuel Velasco Suarez, Cuidad de México, Mexico

Objective: To determine whether the delay in diagnosis could be modified by the academic degree obtained in people with Parkinson's Disease. (PD)
Background: (PD) is the second most frequent neurodegenerative disease with systemic motor and non-motor involvement, affecting the quality of life of patients.(1) Although diagnosis is clinical, it is still a challenge. (2)The Mexican educational system is composed of 3 levels: basic (6 years), middle school (9 years) and high school (>9 years).(3) In general, only 44% reach a university degree.(4) A higher educational level will benefit the patient to identify and refer any symptom or complaint to the health professional seeking a quick diagnosis.(5)
Methods: Observational, cross-sectional and retrolective study, 185 PEP were included. A sociodemographic questionnaire was carried out, including years of schooling, years of evolution of the diagnosis and years of symptom onset. The population was divided into three groups, with the grouping variable being educational level. Group 1 had a basic educational level (≤ 6 years of schooling), group 2 had a high school level (7 to 12 years), and group 3 had a bachelor's

degree (>12 years). The difference in means of the mean diagnostic delay between the groups was performed with ANOVA test and with Games Howell post hoc. Subsequently, a bivariate linear correlation was performed with Spearman's test between educational level and diagnostic delay.
Results: A total of 185 PEP, of which 58.4% were men and 41.6% women with an average age of 62.2 ±12.2 years. An average educational level of 10.3 years of study. The average year for delay in diagnosis was 2.1 years.
ANOVA was used to compare between all groups. When comparing the delayed diagnosis between the 3 groups, it was found not to be significant (p=0.972). Subsequently, post hoc Games Howell was performed to compare between each group. The mean difference between groups 1 and 2 was (IJ -0.0445)(p=0.994), from 1 and 3 (IJ 0.0445)(p=0.994) and from 2 and 3 (IJ 0.1609) (p=0.980) similarly not significant.
Conclusion: It was concluded that the delay in diagnosis is not associated with the educational level or years of schooling possessed by the patients in our population.

Key words
Parkinson's disease, Schooling, Years of diagnosis.

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P32.09

Interpretable machine learning on metabolomics data reveals biomarkers for Parkinson's disease

J. Diana Zhang[*,1], Chonghua Xue[2], Vijaya B. Kolachalama[2], William A. Donald[3]*
[1] University of New South Wales, Sydney, NSW, Australia
[2] Boston University, Boston, United States
[3] University of New South Wales, Sydney, Australia

The use of machine learning (ML) with metabolomics provides opportunities for the early diagnosis of disease. However, the accuracy and extent of information obtained from ML and metabolomics can be limited owing to challenges associated with interpreting disease prediction models and analysing many chemical features with abundances that are correlated and 'noisy'. Here, we report an interpretable neural network (NN) framework to accurately predict disease and identify significant biomarkers using whole metabolomics datasets without feature selection. The performance of the NN approach for predicting Parkinson's disease (PD) from blood plasma metabolomics data was significantly higher than classical ML methods with a mean area under the curve of > 0.995. PD-specific markers that contribute significantly to early disease prediction were identified including an exogenous polyfluoroalkyl substance. It is anticipated that this accurate and interpretable NN-based approach can improve diagnostic performance for many other diseases using metabolomics and other untargeted 'omics methods.

CLINICAL SCIENCE: Co-morbidities

P33.01

PD and spine surgery: The importance of less-invasive surgery and potential of knowledge mobilizatil

Christian Carrwik, Anna Clareborn*
Uppsala University, Uppsala, Sweden

Background: Parkinson's disease (PD) is a well-known risk factor for inferior outcome after spinal surgery. Several studies show a high level of revision surgery, especially hardware failure when using implants. While these findings are important, they might withhold patients from potentially beneficial, less-invasive surgery. Overcoming the knowledge to practice gap and achieving knowledge mobilization is necessary to achieve the best outcomes for patients in this context.
Methods: We reviewed the literature on spinal surgery outcomes for patients with PD. The indications for surgery and the types of surgery were then compared to recent findings in the spine literature. We also reviewed the literature on knowledge mobilization through co-production in healthcare, with a specific focus on surgical interventions.
Results: The most common surgical indication for surgery in a recent meta-analysis was lumbar spinal stenosis (54%) and the most common surgical procedure was spinal fusion (55%). As several randomized studies demonstrate that lumbar fusion for patients with lumbar spinal stenosis is inferior to decompression alone, the choice of procedure for patients with PD could be questioned. In spite of numerous studies showing positive outcomes of co-production approaches in the wider field of healthcare, the concept has not been subject to significant investigation in the surgical context. In the field of spinal surgery specifically, there have been calls for future research focusing on outcome measures for the implementation of co-production strategies.
Conclusion: Patients with PD are at high risk for complications after spine surgery but surgery without implants removes the risk for implant-related failures. With proper patient counselling and adaption to findings in recent spine research, patients with PD should not be withheld from spine surgery. The considerable need for pre- and postoperative dialogue and planning suggests that the knowledge mobilisation elements of co-production can play a positive role in the management of spinal disorders in Parkinson's disease. Further research on knowledge mobilization in spine surgery as well as on outcomes for less invasive spine surgery for PD patients is needed.

P33.02

The prevalence of sarcopenia in an international Parkinson's disease cohort

Laura Cordova Rivera[*,1], Ashley Hart[1], Lisa Alcock[1], Philip Brown[1], Heather Hunter[1], Alice Nieuwboer[2], Ginis Pieter[2], Heiko Gassner[3], Jürgen Winkler[3], Jochen Klucken[3], Walter Maetzler[4], Jennifer Kudelka[4], Hanna Hildesheim[4], Christian Schlenstedt[5], Anat Mirelman[6], Jeff Hausdorff[6], Mark Gordon[7], Clemens Becker[8], Lynn Rochester[1], Alison Yarnall[1]*

[1] Translational and Clinical Research Institute, Newcastle University, Newcastle upon Tyne, United Kingdom
[2] KU Leuven, Department of Rehabilitation Sciences, Neurorehabilitation Research Group (eNRGy), Leuven, Belgium
[3] University Hospital Erlangen, Department of Molecular Neurology Movement Analysis, Erlangen, Germany
[4] Kiel University, Faculty of Medicine, Kiel, Germany
[5] Institute of Interdisciplinary Exercise Science and Sports Medicine, Medical School Hamburg, Hamburg, Germany
[6] Tel Aviv Sourasky Medical Center ICHILOV, Center for the Study of Movement, Tel Aviv, Israel
[7] Innovative Medicine & Global Clinical Development, Neuroscience, Teva Pharmaceuticals, Tel Aviv, Israel
[8] Robert-Bosh-Krankenhaus Hospital, Burgholzhof, Germany

Background: Sarcopenia (reduced skeletal muscle-mass and strength) appears to be increased in Parkinson's Disease (PD) and is associated with poorer outcomes. However, estimates of its prevalence according to definitions by the revised European Working Group on Sarcopenia in Older People (EWGSOP2) guidelines and its association with disease outcomes have been sparsely reported.
Mobilise-D (https://www.mobilise-d.eu/) is a large consortium comprising 34 partners based at leading international universities and some of the world's largest pharmaceutical and technical companies aiming to validate digital mobility outcomes (DMOs) that measure what matters to patients.
We aimed to evaluate the prevalence of probable and confirmed sarcopenia in this international PD cohort, and to determine its associations with measures of disease severity.
Methods: A longitudinal cohort study of 600 PD participants with mild-to-moderate disease severity is underway in five international sites. The EWGSOP2 guidance was used to evaluate the prevalence of probable [assessed by grip-strength or 5 sit-to-stand test] and confirmed [skeletal muscle mass (SMM) by bioimpedance analysis] sarcopenia. Descriptive statistics were used to determine associations between sarcopenia and disease severity [Movement Disorders Society Unified Parkinson's Disease Rating Scale Part III (MDS-UPDRS III)] and retrospective falls.
Results: 600 participants [64.8% men; mean(SD) 65.7(9.5) years; mean MDS-UPDRS III score 26.7(12.6)] were recruited at baseline assessment. Data on grip-strength [mean(SD) 33.8(11.2) kg] and SMM [mean(SD) 27.9(7.4) kg] were collected in 596 and 220 participants. Probable and confirmed sarcopenia was observed in 40.1% and 32.3% of participants, respectively. Mean MDS UPDRS III score was 30.1 in those with probable sarcopenia versus 24.5 in those without probable sarcopenia ($p<0.001$), while the mean difference between participants with confirmed versus nonsarcopenic participants was 4.3 points ($p<0.05$). 45.2% participants with probable sarcopenia reported to have fallen in the last 12-months versus 28.9% without sarcopenia ($p<0.001$). Participants with confirmed sarcopenia tended to fall more, but there was no significant differences compared to people without confirmed sarcopenia.
Conclusion: Probable and confirmed sarcopenia was common in a large, diverse and representative international PD cohort and was associated with measures of disease severity. This is of relevance as sarcopenia is potentially treatable and associated with adverse outcomes.

P33.03

A systematic review of the prevalence of sarcopenia in Parkinson's disease and related disorders

Laura Cordova Rivera[*,1], Ashley Hart*[*,2], Fred Barker[3], Avan A. Sayer[4], Antoneta Granic[3], Alison J Yarnall*[*,5]*

[1] Brain and Movement Research Group, Translational and Clinical Research Institute, Campus for Ageing and Vitality, Newcastle University, and Teesside University, School of Health and Life Sciences, Newcastle upon Tyne, United Kingdom
[2] Brain and Movement Research Group, Translational and Clinical Research Institute, Campus for Ageing and Vitality, Newcastle University UK and AGE Research Group, NIHR Newcastle Biomedical Research Centre, Newcastle University and Newcastle Upon Tyne Hospitals NHS Foundation Trust, Newcastle, UK., Newcastle upon Tyne, Tyne and Wear, United Kingdom
[3] AGE Research Group, NIHR Newcastle Biomedical Research Centre, Newcastle University and Newcastle Upon Tyne Hospitals NHS Foundation Trust, Newcastle, United Kingdom
[4] AGE Research Group, NIHR Newcastle Biomedical Research Centre, Newcastle University and Newcastle Upon Tyne Hospitals NHS Foundation Trust, Newcastle, UK and Newcastle upon Tyne Hospitals NHS Foundation Trust, Newcastle, UK, Newcastle, United Kingdom
[5] Brain and Movement Research Group, Translational and Clinical Research Institute, Campus for Ageing and Vitality and Newcastle upon Tyne Hospitals NHS Foundation Trust, Newcastle, United Kingdom

Background: The prevalence of sarcopenia (reduced skeletal muscle mass and strength), Parkinson's disease (PD) and Parkinson's related disorders (PRD) all increase with age and share risk factors and pathogenic features. Despite this overlap, estimates of the prevalence of sarcopenia in PD vary widely and research into sarcopenia in PD and PRD using standardised sarcopenia definitions is sparse.
We aimed to synthesise the published literature on the prevalence of sarcopenia, using definitions proposed by recognised sarcopenia working groups, in populations with PD and PRD, to compare it to estimates from the general population, and to assess the association of sarcopenia with motor severity in PD.
Methods: MEDLINE, EMBASE, Scopus and Web of Science were searched using predefined literature search strategies. Studies conducted in participants with PD or PRD reporting the prevalence of sarcopenia and those providing data to compute the prevalence were included. Pre-sarcopenia, probable/possible sarcopenia and confirmed sarcopenia were defined according to the main sarcopenia working groups. Risk of bias was assessed using the AXIS tool.
Results: 1978 studies were identified in three different searches; 97 assessed in full; 14 met inclusion criteria. The mean study quality score was 14.5/20. The range of probable sarcopenia was 23.9 to 66.7%, and it did not change after excluding PRD participants. The prevalence of confirmed sarcopenia in participants with any parkinsonian disorder ranged from 2 to 31.4% and most studies reported a higher estimates than those reported for the general population. Including just PD participants, the range was 10.9 to 31.4%. In studies with controls, sarcopenia was more prevalent in PD and PRD. There was a positive non-significant trend between severity of motor symptoms (using the Movement Disorders Society Unified Parkinson's Disease Rating Scale Part III) and prevalence of sarcopenia or components of sarcopenia. There was insufficient evidence to conclude whether sarcopenia is more prevalent in PD or PRD.

Conclusions: Sarcopenia is common in PD and PRD and may be associated with disease severity. This co-occurrence supports the value of screening for sarcopenia in PD and PRD.

P33.04

Association between history of SARS-CoV-2 infection and worsening of non-motor symptoms and non-motor fluctuations in Mexican people living with Parkinson's disease

Ana Jimena Hernández-Medrano, Diana Paulina Romero-Terán, María Fernanda Medina-Pérez, Andrea García-Hernández, Rodolfo Arturo Abundes-Corona, María Alejandra Ruiz-Mafud, Daniela Renee Águila-Godínez, Axel Antonio Herrera-Ruiz, Amin Cervantes-Arriaga, Mayela Rodríguez-Violante*
National Institute of Neurology and Neurosurgery, Mexico City, Mexico City, Mexico

Introduction: Parkinson's disease (PD) is characterized by a wide spectrum of motor and non-motor symptoms. Non-motor fluctuations (NMF) are common as PD progresses (1). According to the World Health Organization (WHO), the COVID-19 Pandemic has affected 666 million people worldwide with a total of 6.7 million deaths (2). Long-COVID manifestations, their impact, and therapeutic strategies are still being studied (3). In a case series reported by Leta et al, 85.2% patients with PD developed post–COVID-19 symptoms, being worsening of motor function the most frequent symptom in 51.9%, and some non-motor symptoms, such as fatigue and cognitive disturbances (4). Nevertheless, there is still no evidence on post-COVID-19 effect on non-motor fluctuations.
Objective: To analyze the association between history of SARS-CoV-2 infection and worsening of non-motor symptoms and non-motor fluctuations in PwP.
Methods: A prospective, cross-sectional, observational study was carried out. Sociodemographic data was collected. The population was divided in two groups, having a history of SARS-CoV-2 infection as grouping variable. Student's t-test was used to compare: (i) non-motor dysfunction (Non-motor symptoms scale [MDS-NMS]) and (ii) non-motor fluctuations (Non-motor fluctuations scale [MDS-NoMoFa]).
Results: 164 PwP were included (56.7% males; 62.6±12.1 years). 23.8% of PwP reported personal history of SARS-CoV-2 infection. Mean MDS-NMS and MDS-NoMoFa scores were 65.79±41.78 and 3.62±5.35, respectively. PwP with COVID-19 history showed higher rates of MDS-NoMoFa with statistical difference (5.3 vs 3.1, p=0.022), although no statistical difference was proven in MDS-NMS score (p=0.251).
Conclusions: Personal history of SARS-CoV-2 infection might have an impact on worsening non-motor fluctuations in Mexican people living with Parkinson's disease.
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P33.05

Association between type 2 diabetes mellitus with Parkinson's disease and the increase of the severity of neuropsychiatric symptoms in a Mexican institute

Axel Antonio Herrera-Ruiz[1], Eduardo Ichikawa-Escamilla[2], Etienne Reséndiz-Henríquez[2], María Alejandra Ruiz-Mafud[2], Ana Jimena Hernández-Medrano[2], Ana Paola Bazán-Rodríguez[2], Gloria Itzel Cerda-Hernández[2], Daniela Renee Aguila-Godinez[2], Amin Cervantes-Arriaga[2], Mayela Rodríguez-Violante[2]*
[1] Instituto Nacional de Neurologia y Neurologia, Mexico City, Mexico City, Mexico
[2] Instituto Nacional de Neurologia y Neurocirugia Manuel Velasco Suarez, Mexico City, Mexico City, Mexico

Background: Parkinson's disease (PD) is the second most common progressive neurodegenerative disorder affecting older adults. Resulting from a loss or degeneration of dopaminergic neurons in the substantia nigra. In Type 2 Diabetes Mellitus (T2DM) the response to insulin is diminished, and this is defined as insulin resistance2. Neuropsychiatric symptoms are highly prevalent nonmotor features and include cognitive impairment, depression, anxiety, psychosis, impulse control disorders, and apathy3.
Those with T2DM appear to be at increased risk of developing PD, as well as experiencing faster progression4. There are common underlying mechanisms in the pathophysiology of both diseases. These underlying mechanisms include mitochondrial dysfunction, oxidative stress, hyperglycemia, and inflammation5.
Objective: To describe the difference in the severity of the neuropsychiatric symptoms between people only living with PD and PD with T2DM.
Methods: An observational, cross-sectional, retroelective which included Mexican patients. A demographic and epidemiologic questionnaire where applied which determines gender, age and average evolution of PD for the descriptive statistics.
The population was divided into two groups. Group 1 patients with PD without T2DM and Group 2 patients with PD and T2DM. Both groups were applied UPDRS-NMS-A, HRSD, NMS-B,HRSA, NMS-K and MoCA.
Results: 60 patients were included, which 35(58.3%) were men and 25(41.7%) women. The average age was 63± 15.27 years old, with an average diagnosis of PD of 7.35± 5.98 years. The grouping variable was T2DM with an average evolution of 4.45± 6.88 years.
The results using U Mann-Whitney in HRSA scale (p=000.1) 21.93 for group 1 and 37.88 for group 2. HRSD (p=<0.001) 21.93 for group 1 and 39.07 for group 2. Moca total score (p=0.629) 31.58 for group 1 and 29.42 for group 2. NMS-A (p=0.021) 31.58 for group 1 and 35.1 for group 2. NMS-B (p=0.001) 21.93 for group 1 and 37.88 for group 2. NMS-C(p=0.022) 26.4 for group 1 and 34.6 for group 2. NMS-K(p=0.151) 26.87 for group 1 and 33.24 for group 2.
Conclusions: The results suggest that patients with PD and T2DM tend to increase the severity of depression, anxiety and apathy.

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P33.06

Pain and moods disorders as determinants of quality of life in Parkinson

Daniela Ortiz Zacarias, Ingrid Eloísa Estrada Bellman*, Roberto Estrella Silva, Juan Roberto Trejo Ayala*
Hospital Universitario Dr José Eleuterio González, Monterrey, Mexico

Background: Parkinson's disease (PD) is a neuropsychiatric disease that affect 10 million people. There are non-motor symptoms such as pain, anxiety and depression that directly affect the patient's quality of life.
Aim: Correlation of non-motor symptoms such as pain, anxiety, and depression in the quality of life and severity of the disease in patients living with Parkinson Disease in our population
Methods: Descriptive cross-sectional study, Consecutive patients were enrolled patients from the anormal movements clinic in our hospital. Sociodemographic and clinical data were collected. The quality of life of patients with Parkinson disease was assessed by Parkinson's Disease Questionnaire (PDQ-8) and the EuroQol-5D (EQ-5D). the presence of pain and moods disorders assessed according to the Unified Parkinson's Disease Rating Scale, part I (UPDRS-I). For the statistical analysis, chi square was used forma UPDRS-I variables with disease stage by H&Y, also compare means using quality life variables (PDQ-8 and EQ5) with presence of pain or mood disorders.
Results: A total of 104 patients with PD diagnosis were enrolled, 68.3% male, the initial side of the disease was right-handed in 61.2%, tremor was the most frequent initial symptom with 59.8% followed by rigidity in 33.3%. 43.3% presented a H&Y stage 2; EQ5 score median 70 points (50-85); UPDRS 62 (39-98); H&Y disease stage correlation with pain (p<0.001), anxiety (p=0.030), and depression (p=0.010) EQ5 with pain (p=0.016) and depression (p= 0.025) PDQ8 with anxiety (p=0.001) and depression (p<0.001)
Discussion: The presence of pain in PD is recognized in the literature in up to 40-85%, in our study 52.9% were evidenced with complaints of pain through MDS-UPDRS, as reported in the literature there is a significant correlation with the presence of pain and mood disorders in patients with more advanced stages of the disease on the H&Y scale, as well as presenting mood disorders correlated with greater presence of pain.
Conclusion: Pain and mood disorders in Parkinson's have not been well established. They can appear at any time during the disease, consistent with initial damage to the limbic system prior to motor circuits, frequent non-motor symptoms, and affecting quality of life in patients with PD.

	PDQ8	EQ5
Depresión	0.486 ($p < 0.001$)	-0.341 ($p < 0.001$)
Ansiedad	0.358 ($p < 0.001$)	-0.212 ($p < 0.032$)
Dolor	0.169 ($p = 0.089$)	-0.272 ($p < 0.006$)
SEND-PD	0.631 ($p = <0.001$)	-0.335 ($p = 0.001$)

CLINICAL SCIENCE: Biomarkers and neuroimaging

P34.01

Plasma ptau181 helps to identify amyloid-β co-pathology in Lewy body disease patients

Carla Abdelnour[,1], Melanie J. Plastini[1], Marian Shahid[1], Alena Smith[1], Edward N. Wilson[1], Katrin Andreasson[1], Victor Henderson[1], Geoffrey Kerchner[2], Kathleen L. Poston[1]*
[1] Stanford University, Palo Alto, California, United States
[2] Roche Pharma Research & Early Development, Roche Innovation Center, Basel, Switzerland

Objectives: Plasma phosphorylated tau181 (ptau181) levels have been associated with amyloid-β deposition in patients with Alzheimer's disease (AD). Amyloid-β co-pathology is frequently present in Lewy body disease (LBD) influencing disease progression, cognitive decline, and brain atrophy.
Our objective was to determine whether plasma ptau181 helps to identify amyloid-β co-pathology in patients with LBD, and whether plasma ptau181 levels in LBD are associated with AD cerebrospinal fluid (CSF) biomarkers.
Methods: We selected 203 Stanford research participants: 97 healthy controls, 37 Parkinson's disease with normal cognition, 39 on the LBD-spectrum (25 MCI-LB and 14 dementia-LB), and 30 on the AD-spectrum (10 MCI-AD and 20 dementia-AD). All participants had available plasma ptau181 and AD CSF biomarkers. AD CSF biomarkers and plasma ptau181 concentrations were measured using the Lumipulse G fully automated platform from Fujirebio Diagnostics. We evaluated diagnostic accuracy with area-under-the-curve (AUC) values from receiver-operating characteristic (ROC) analyses.
Results: Plasma ptau181 levels predicted amyloid-β positivity in LBD patients with an AUC=0.726. This model was improved by including age, sex, years of education, APOEe4 genotype, and global cognition (MoCA) (AUC= 0.881). Likewise, plasma ptau181 levels predicted amyloid-β positivity in MCI-LB patients (AUC=0.691). Combining plasma ptau181 levels with age, sex, years of education, APOE E4 genotype, and MoCA improved the prediction of amyloid-β positivity in MCI-LB patients (AUC=0.826).
Plasma ptau181 levels were negatively associated with CSF Aβ42/Aβ40 ratio and positively associated with CSF ptau181/Aβ40 ratio. There were no differences in plasma ptau181 levels between sexes. We did not find an association between plasma ptau181 levels with age, years of education, MoCA, or functional assessment measured with CDR.
Conclusions: Plasma ptau181 levels help to identify amyloid-β co-pathology and are associated with AD CSF biomarkers in patients with LBD, even at the MCI stage. These findings support the potential use of plasma ptau181 as a screening tool for amyloid-β co-pathology in LBD.

P34.02

The influence of gut microbiota as a potential regulator of amino acid metabolism and its' novel correlations in Parkinson's pathogenesis

Yasunthara Balalle-Deo, Nanthini Jayabalan, Kerry Roper, Helen Woodhouse, John O'Sullivan, Robert Adam, Richard Gordon*
The University of Queensland, Brisbane, Queensland, Australia

Neurodegenerative diseases are caused by the death of neurons and other cells within the brain, however various brain regions differentially affected between diseases. While Alzheimer's Disease

primarily affects memory, Parkinson's Disease and Huntington's chorea primarily affect movement. Parkinson's disease (PD) is characterised by resting tremor, rigidity and bradykinesia due to the death of dopaminergic neurons in the substantia nigra. Gastrointestinal dysfunction and microbiome alterations are emerging as key prodromal features of Parkinson's disease (PD) pathology. However, functional implications of gut dysbiosis on PD pathology and progression are still being defined. The aim of this study was to understand changes in host and microbial metabolism in PD patient biofluids which could reflect a transition from the healthy to diseased state. A total of 64 urine samples obtained from healthy control (n= 31) and PD (n= 33). Samples were deproteinised and analysed by reverse phase (RP)/UPLC-MS/MS methods with positive and negative ion mode electrospray ionization (ESI) and HILIC/UPLC-MS/MS with negative ion mode ESI. Welch's two-sample t-test was performed on log transformed data and p <0.05 was considered significant. Pearson R correlation was performed. We found many metabolites that were affecting the overall prognosis of PD patients, and these were classified into three main categories: polyamines, bile acids and fatty acids. A total of 7 polyamine metabolites were significantly altered in PD patients. Interestingly, the altered polyamines correlated with the levels of p-cresol sulfate in PD patients. Five metabolites were associated with bile acid metabolism and nine from the cholesterol pathway. Changes in secondary bile acid metabolism is indicative of microbial metabolism changes, specifically glycodeoxycholate and glycodeoxycholate 3-sulfate were upregulated and correlated in PD patients. With the tie between gut and brain health becoming ever more relevant, our results provide new insights into altered metabolism and gut dysbiosis in PD. The results of this study suggest potential changes in the expression levels of these gut bacteria in PD patients and potentially contribute for PD pathogenesis.

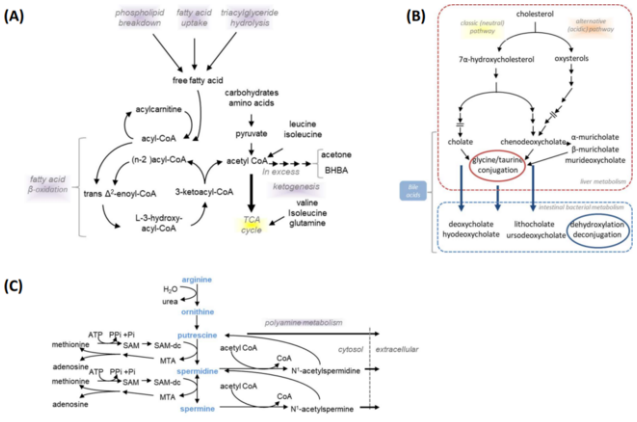


Figure 1. Amino Acid metabolic pathways that have correlated to altered gut microbiota in PD patients. (A) Fatty acid pathway, (B) Bile Acid pathway and (C) Polyamine pathways.

P34.03

Dopaminergic dysfunction is more symmetric in dementia with Lewy bodies compared to Parkinson's disease

Tatyana Fedorova[*,1], Karoline Knudsen[1], Jacob Horsager[1], Allan K Hansen[2], Niels Okkels[1], Hanne Gottrup[1], Kim Vang[1], Per Borghammer[1]*
[1] Aarhus University Hospital, Aarhus N, Denmark
[2] Aalborg University Hospital, Aalborg, Denmark

Introduction: The alpha-synuclein Origin site and Connectome model (SOC) suggests that alpha-synucleinopathies can be subdivided into two categories: brain-first Lewy body disease which is more asymmetrical, and body-first Lewy body disease which is more symmetrical. Here, we hypothesize that patients with Lewy body dementia (DLB) are more likely to conform to the symmetrical body-first subtype whereas patients with Parkinson's disease more often conform to the asymmetrical brain-first subtype. The objective of the study was to compare asymmetry of striatal dopaminergic degeneration in DLB and PD patients using [18F]-FE-PE2I positron emission tomography and computed tomography (PET/CT).
Methods: We looked at [18F]-FE-PE2I PET/CT scans from 76 PD patients and 29 DLB patients identified during a 5-year period at the Dept. of Neurology, Aarhus University Hospital. In-house imaging data from 36 healthy controls was used for age-correction and visual comparison.
Results: DLB patients had significantly more symmetrical decreases in specific binding ratios (SBR) in both putamen ($p<0.0001$) and caudate ($p=0.003$) compared to PD patients. Furthermore, PD patients had more severe degeneration in the putamen than the caudatus compared to DLB patients ($p<0.0001$) who had a more global striatal pattern of degeneration. Lastly, PD patients had lower putaminal SBR in the most affected hemisphere ($p=0.005$) compared to DLB patients.
Conclusion: DLB patients present with significantly more symmetric striatal dopaminergic degeneration compared to PD patients. These results support the hypothesis that most DLB patients conform to the body-first subtype characterized by a symmetrical spread of pathology whereas more PD patients conform to the brain-first subtype with a more lateralized initial spread of pathology.

P34.05

Ocular microtremor in Parkinson's disease: Protocol for an observational pilot study

Lisa Graham[*,1], Rodrigo Vitorio[1], Claire McDonald[2], Richard Walker[3], Alan Godfrey[1], Rosie Morris[1], Samuel Stuart[1]*
[1] Northumbria University, Newcastle Upon Tyne, Newcastle Upon Tyne, United Kingdom
[2] Gateshead Health NHS Foundation Trust, Gateshead, Tyne and Wear, United Kingdom
[3] Northumbria Healthcare NHS Foundation Trust, North Tyneside, Tyne and Wear, United Kingdom

Ocular microtremor (OMT) is a fixational eye movement that cannot be seen with the naked eye but is always present, even when the eye appears motionless/still. The link between OMT and brain function generates a strong rationale for investigation as there lies potential for its use as a biomarker in populations of neurological impairments. OMT frequency is typically 70-80Hz in healthy adults and research suggests that this will be reduced in those with neurological disease such as Parkinson's Disease (PD). This study aims to examine OMT in people with PD (PwPD) compared to healthy older adults. Identifying OMT as a PD biomarker could better support clinical assessment, enabling improved provision of care to patients with advanced disease monitoring.
This is an exploratory, observational study that will use a novel handheld device – The iTremor ONE, which has been developed to rapidly, non-invasively assess and evaluate OMT frequency. This device uses incident laser technology directed at the sclera. PwPD who meet the inclusion criteria will participate in a home-based assessment involving cognitive, motor (using the UPDRS-III) and OMT measures. With OMT as the primary outcome, assessment with the iTremor is incredibly quick, taking just three seconds to obtain a reading. PwPD will be assessed both off and on their anti-parkinsonian medication. PwPD will also be invited into the laboratory to perform extensive cognitive assessments along with an assessment of balance, gait, and turning using wearable sensors. We will recruit 30 PwPD and 30 age-matched healthy control participants for assessment of OMT. Ten PwPD will

complete a test-retest reliability assessment at the same approx. time, exactly one week after their initial visit.
This will be the first study of its kind to non-invasively investigate OMT frequency as a marker/monitor for PD with advanced technology that could be used within the clinic, laboratory, or home.
Agknowledgements and fuding: The authors acknowledge Head Diagnostics for providing the iTremor ONE device used within this study. This work is also supported in part by grants from the Parkinson's Foundation (PF-FBS-1898, PF-CRA-2073, PI: Stuart).
Keywords: Ocular microtremor, Parkinson's Disease, biomarker

P34.06

Assessing the biomarker potential of LRRK2 and GCase in Parkinson's disease monocytes
Laura Hughes[*,1], Nicolas Dzamko[1], Rebecca Wallings[2], Roy Alcalay[3], Alicia Garrido[4], Malú Gámez Tansey[2]*
[1] University of Sydney, Sydney, NSW, Australia
[2] University of Florida, Gainesville, Florida, United States
[3] Columbia University, New York, New York, United States
[4] Hospital clínic de Barcelona, Barcelona, Catalonia, Spain

There are presently no available cures or disease-modifying treatments for Parkinson's disease (PD), largely due to a lack of biomarkers to enable early detection, confirm diagnosis, monitor prognosis, or inform on stratification of PD patients into clinical trials. Leucine-rich repeat kinase 2 (LRRK2) and glucocerebrosidase (GCase) are two proteins highly expressed in peripheral monocytes. LRRK2 is a serine-threonine protein kinase and GCase is a lysosomal hydrolase that converts glucosylceramide into glucose and ceramide, and a wealth of evidence implicates the involvement of both proteins in the regulation of lysosomal function. Both proteins are of particular significance as mutations in LRRK2 are the most common cause of familial PD, and heterozygous mutations in GBA1, the gene encoding GCase, are associated with increased risk of developing PD. Increased LRRK2 kinase activity is pathogenically linked to PD, while GCase activity is seemingly reduced in PD patients. To determine the suitability of LRRK2 and GCase as PD biomarkers, the Universities of Sydney and Florida have worked together to develop and optimise a peripheral blood mononuclear cell (PBMC) processing protocol and downstream flow cytometry workflow (WHOPPA) to standardise the measurement of both proteins. LRRK2 levels and activity (via phosphorylation of the LRRK2 substrate, Rab10), as well as GCase enzymatic activity and lysosomal cathepsin activity via fluorogenic probes were then measured in PBMCs from carriers of LRRK2 and GBA1 mutations (n=10-20), as well as idiopathic PD patients (n=42) and matched healthy controls (n=36). Initial analyses revealed a reduction in GCase activity in total, classical, and intermediate monocyte populations from PD patients harbouring a GBA1 mutation and that LRRK2 kinase activity, as measured by pRab10 levels, was increased in classical and intermediate monocytes from LRRK2, GBA and idiopathic PD patients in a stimulation-dependent manner. Outcomes from this study may help to validate LRRK2 and GCase as peripheral blood PD biomarkers, inform on the recruitment for clinical trials targeting these enzymes for therapeutic development, and provide a better understanding of the relationship between LRRK2 and GCase activities in peripheral immune cells.

P34.07

Differential prognostic implications of cerebral hypo- and hyperperfusion in Parkinson's disease: Early-phase 18F-FP-CIT PET study
Seong Ho Jeong[*,1], Jong Sam Baik[1], Phil Hyu Lee[2], Young H. Sohn[2], Seok Jong Chung[2]*
[1] Inje University Sanggye Paik Hospital, Seoul, South Korea
[2] Yonsei University College of Medicine, Seoul, South Korea

Background: Patients with Parkinson's disease (PD) exhibit widespread brain perfusion or metabolic changes, which are known as PD-related pattern. This study investigated whether cerebral regions with hypo- and hyperperfusion have differential effects on motor and cognitive symptoms in PD using early-phase 18F-FP-CIT PET scans.
Methods: We enrolled 394 patients with newly diagnosed PD who underwent dual-phase 18F-FP-CIT PET scans. Indices reflecting associated changes in regional cerebral hypo- and hyperperfusion using early-phase 18F-FP-CIT PET scans were calculated as PD[hypo] and PD[hyper], respectively. The effects of PD[hypo] and PD[hyper] on motor and cognitive symptoms at baseline and longitudinally were assessed using multivariate linear regression, Cox regression, and linear mixed models.
Results: There was a weak correlation between PD[hypo] and PD[hyper] ($\gamma = -0.19$, $P < 0.001$). PD[hypo] was associated with the baseline Unified PD Rating Scale Part III scores ($\beta = -1.02$, $P = 0.045$), rapid increases in dopaminergic medications ($\beta = -18.02$, $P < 0.001$), and a higher risk for developing freezing-of-gait (hazard ratio [HR] = 0.67, $P = 0.019$), while PD[hyper] was not. In terms of cognitive function, PD[hypo] was more relevant to the baseline cognitive performance levels of visuospatial, verbal and visual memory, and frontal/executive function than PD[hyper]. However, greater PD[hyper] was associated with future PDD conversion (HR = 1.43, $P = 0.004$), whereas PD[hypo] was not.
Conclusion: This study suggests that PD[hypo] and PD[hyper] may be independent of each other and may differentially affect motor and cognitive function in patients with PD. In addition, PD[hypo] is relevant to baseline parkinsonian motor deficits, overall cognitive domains, and future development of FOG, while PD[hyper] is important for baseline visual memory function and future cognitive decline in patients with PD. Further studies investigating whether PD[hypo] and PD[hyper] can be used as an individual neuroimaging biomarker and therapeutic target are warranted.

P34.08

Adaptive closed loop deep brain stimulation in advanced idiopathic Parkinson's disease patients: A study with neuroengineering perspective
*Neerati Lavanya**
Osmania University, Hyderabad, Telangana, India

Deep brain stimulation (DBS) a well-derived provocative thought process surgical-procedure established as a binding—legal(valid) therapy for a range-of compulsive/uncontrolled (involuntary) obsessive, irrational and neurotic (pathological) conditions ranging from cardinal motor-symptoms to nonmotor cognitive disorders–impairment, dementia, delusional-hallucinations, axial (speech, and freezing-of-gait,FoG),etc. However, the induced stimulus linked process-of-action is much as of its being realized, plus few dyskinesias, the concept is ambiguous. The open-loop (DBS) limits were undertook by a range-of-methods which includes ACL-DBS which even on applying a persistently embedded microelectrodes (STN neural signals signature-patterns via MER-technique) and macro-leads (for testing macrostimulation) on sensing-mode to observe/perceive the neuronal-biomarkers of careful motoric-

symptoms(features) then to carry on-demand or modulate stimulus-parameters. This study enhances DBS modus-operandi with a variety-of-methods, encapsulates prime-disputes (tasks and tests) for progress of efficient adaptive-closed-loop DBS(ACL-DBS) therapeutic-efficacy. Model-paradigms of basal-ganglion (BG) circuitry disorders pathogenesis, computational enhancement for standard (open-loopDBS), also candidate neural and non-neural neuronal/non-neuronal features of Parkinson`s plus associated management-strategies for ACL-DBS. We determine key-operative tests concerning ideal-DBS, for instance, precise-target point, (ii) better stimulus spatio-temporals-region, building(constructing) the in-silico tests-for-DBS, (iv) detecting detailed motoric-feature-markers, specifically measuring in what way field-potential (i.e.,LFPs) oscillations correlate to developmental-dysfunctions, and simplify how stimulus involves cortico-basal-ganglion thalamic-network to create ideal stimulus-signatures. Using ACL-DBS method every Parkinson will experience an early calibration-measurement-period in which parameter-values of management-policy shall be adjusted/fine-tuned to different-qualities. In this connection, strength of neuro-bio-markers in excess-of-time will be of vital-consequence. These neuro-markers can be capable of coping over long-timescale through mystifying-factors as consequent treatment, Parkinson-aging, cycle of the disease. Our study to improves the stimulus-linked neuro-modulatory-plans. Once markers setting is done, the management-strategy must be customized stimulus-patterns corresponding to daily activities plus patients-behavior. In fact, understanding subject-behaviors like gripping, gait, speaking, napping can be improved beyond the purpose of optimum stimulus-model-paradigm. Like, higher-tremor Parkinson`s need lower stimulations while they are in sleep mode, and this is due to the lesser conditional problems. The Parkinson symptoms of disease can be altered marginally, nonetheless dopamine-cells even die; its evolution endures inevitably—inexorably to halt cell-death. The advent of available human-neuron assemblies in organoids possibly will offer a clearer log-on to the means inherent neuronal-downfall with the help of the adaptive closed loop deep brain stimulation devices.

P34.10

Characterizing Parkinson's clinical features in black americans and measuring the effect of non-impact lower body exercise on neuroimaging biomarkers and motor and gait function.

Senegal Alfred Mabry[*,1], Samantha Moss[2], Jeffery Bauer[2], Eve De Rosa[1], Adam Anderson[1]*
[1] Cornell University, Ithaca, New York, United States
[2] SUNY Cortland, Cortland, New York, United States

This study is a collaboration between neuroscientists and exercise scientists to characterize Parkinson's Disease (PD) clinical features in Black Americans and measure the effectiveness of short bouts of eccentric exercise training on reducing PD motor symptoms. The collaboration includes a 12-week exercise intervention with pre-and-post MRI scans on Black Americans recruited by a community research accelerator. The study expects differences in PD clinical features including functional connections between the Substantia Nigra (SN) and the peripheral vagus nerve, the primary connection from the heart to the brain. The study expects that eccentric training will be acceptable to both Black and white participants and will similarly reduce motor and gait symptoms, supported by communication between the Substantia Nigra (SN) and the cerebellum enabled by increased peripheral vagus nerve activity, measured through heart function health.
Conflicting findings on the prevalence and clinical features of PD in the Black community may be due to underrepresentation or may inform researchers how healthy autonomic nervous system (ANS) function is disrupted in PD. Our group has shown eccentric training to reduce PD motor and gait symptoms. We hypothesize this is mediated by engaging the heart-brain axis to enhance SN structure and function.
In this study, 20 Black participants (10 with Parkinson's Disease, 10 age-sex-matched healthy controls) will attend 24 training sessions over 12 weeks, with 2 sessions per week. During the training, participants will have motor and gait symptoms and success in training continuously accessed and later compare for differences between Black and white populations. In controlled studies, such training has improved gait and balance outcomes for 20+ white participants with PD over the past 4 years. Through nonimpact eccentric movement, the reACT trainer engages the lower body, targeting the quadriceps, as individuals safely balance on an oscillating platform holding onto support rails, keeping themselves in an upright fixed position. The study will compare the effects of eccentric training and features of PD neuroimaging biomarkers for Black and white participants, enabling more appropriate representation and generalization of the preliminary behavioral findings and their neural bases in the SN.

P34.11

Predicting progression of Parkinson's disease motor outcomes using a multimodal combination of baseline clinical measures, neuroimaging and biofluid markers

Angus McNamara[*,1], Benjamin Ellul[1], Dr Irina Baetu[2], Dr Stephan Lau[3], Professor Mark Jenkinson[3], Assoc/Professor Lyndsey Collins-Praino[1]*
[1] School of Biomedicine, The University of Adelaide, Adelaide, Australia
[2] School of Psychology, The University of Adelaide, Adelaide, Australia, Adelaide, Australia
[3] Australian Institute of Machine Learning (AIML), The University of Adelaide, Adelaide, Australia

PD is heterogenous, with diagnosis reliant on clinician assessment, corresponding to subjectivity and consequent high rates of misdiagnosis. Furthermore, forecasting disease progression on an individual basis is limited, contributing to a lack of personalised treatment strategies. Therefore, objective biomarkers of PD progression are critically needed, but must be validated prior to clinical deployment. We assessed the utility of various clinical, neuroimaging and pathological marker measures to predict motor outcome progression up to 5-years follow-up in early PD.
Data was extracted from the Parkinson's Progression Markers Initiative. As a proxy marker of substantia nigra (SN) integrity, manual masking of T2-weighted MRI scans was used to delineate the hypointense region adjacent to the SN. Enhanced hierarchal clustering was performed on Unified Parkinson's Disease Rating Scale (UPDRS) motor outcomes at 5-year follow-up. Models to predict cluster membership were developed via logistic regression and a stratified cross-validation machine learning pipeline comparing various classifiers. The utility of a multi-modal assessment was assessed by comparing two models: 1) only baseline motor assessments as predictors; and 2) incorporating additional measures including prodromal assessments (sleep, olfactory and autonomic function), neuroimaging (proxy SN volume, striatal DaT binding) and biofluid (CSF alpha-syn, p-tau, a-beta, and serum IGF-1) markers at baseline.
Two clusters were identified, with the second cluster (n=79) demonstrating higher rigidity, lower DaT binding, worsened cognitive and motor outcomes and increased mood dysfunction at 5-year follow-up compared to the first cluster (n=221), which displayed tremor dominance. Logistic regression determined that membership in the rigid-dominant cluster was predicted by higher difficulty in motor aspects of living, automatic dysfunction, and p-tau, along with lower smell and alpha-syn: predicting 49.1% of variance

(n=111). This was significantly higher (P < 0.001) than the model omitting additional measures, which accounted for only 27.4% of the variance. This was supported machine learning, whereby the inclusion of additional assessments corresponded to a classification accuracy of 72%, compared to 65% when omitted.
Utilising a multi-modal strategy demonstrated substantial improvements in prediction of 5-year outcomes, suggesting a combination of prodromal, pathological, and imaging markers can be used in conjunction with current clinical assessments to improve diagnosis and prognosis.

P34.12

Local field potentials in Parkinson's disease: Effect of lead type and target, peak detection, and contact selection

Alfonso Fasano[*,1], Thomas Witt[2], Sara Bick[3], Mya Schiess[4], Hideo Mure[5], Genko Oyama[6], Katsuo Kimura[7], Alexa Singer[8], Claudia Sannelli[8], Nathan Morelli[8]*
[1] Edmond J. Safra Program in Parkinson's Disease, Morton and Gloria Shulman Movement Disorders Clinic, Toronto Western Hospital, University Health Network, Toronto, Canada
[2] Department of Neurosurgery, Indiana University Medical Center, Indianapolis, IN, United States
[3] Department of Neurosurgery, Vanderbilt University Medical Center, Nashville, Tennessee, United States
[4] Department of Neurology, Movement Disorders and Neurodegenerative Disease Program, McGovern Medical School, University of Texas, Houston, Texas, United States
[5] Center for Neuromodulation, Department of Neurosurgery, Kurashiki Heisei Hospital, Kurashiki, Japan
[6] Department of Neurology, Faculty of Medicine, Juntendo University, Tokyo, Japan
[7] Department of Neurology, Yokohama City University Medical Center, Kanagawa, Japan
[8] Brain Modulation, Medtronic, Minneapolis, Minnesota, United States

Introduction: Local field potentials (LFP), recorded by deep brain stimulation (DBS) electrodes, in patients with Parkinson's disease (PwPD) provide biomarkers of motor dysfunction, pathophysiologic insights, and are currently leveraged for adaptive DBS commercially in Japan. However, the effect of electrode type and targeted nuclei on LFP measures, in addition to peak association to therapeutic contact selection, are not fully understood. Therefore, the objective of this study was to determine the difference in LFP peak and band power characteristics between the globus pallidus internus (GPI) and subthalamic nucleus (STN), as well as cylindrical and directional leads. The secondary objective was to determine real-world peak detection and the association of peak contact pairings to stimulation contact selection.
Methods: Real-world DBS and LFP data from 48 PwPD (age: 65.1[56.3-71.8] years, sex: 19 female, disease duration: 12.0[7.8-15.0] years) and 96 total nuclei recordings were collected as part of a prospective, post-market study. Peak characteristics and band power amplitude averages were calculated for each nucleus.
Results: Peaks were detected in a total of 76(81.7%) nuclei with a recording and at least 1 peak was detected in 93.3% of patients with bilateral recordings. Peaks were detected in 30/36 directional nuclei and 46/60 cylindrical nuclei (p=0.288). Peak amplitude (p=0.577) and frequency (p=0.962), as well as band power in the low-beta (p=0.104) and high-beta (p=0.213) ranges were similar between lead types. No differences were found in peak detection (p=0.078), amplitude (p=0.281), and frequency (p=0.506), as well as band power in the alpha (p=0.073), high-beta (p=0.314), and gamma (p=0.464) between targets. Therapeutic contact selection fell in between or on the lower contact of the peak bipolar contact pairing in 94.1% of cases.
Conclusion: Lead type appears to have minimal effect on peak detection and LFP characteristics when deployed in a real-world setting. LFPs were also similar between targets, however, the sample size for GPI was small. Importantly, LFP peaks are prominently detectable in real-world settings and demonstrate association to stimulation contact selection in PwPD. These data provide key insights into the real-world feasibility and interpretation of LFPs in PwPD.

P34.13

Real-world local field potential dynamics in patients with Parkinson's disease

Alfonso Fasano[*,1], Hideo Mure[2], Genko Oyama[3], Thomas Witt[4], Alexa Singer[5], Claudia Sannelli[5], Nathan Morelli[5]*
[1] Edmond J. Safra Program in Parkinson's Disease, Morton and Gloria Shulman Movement Disorders Clinic, Toronto Western Hospital, United Health Network, Toronto, Canada
[2] Center for Neuromodulation, Department of Neurosurgery, Kurashiki Heisei Hospital, Kurashiki, Japan
[3] Department of Neurology, Faculty of Medicine, Juntendo University, Tokyo, Japan
[4] Department of Neurosurgery, Indiana University Medical Center, Indianapolis, IN, United States
[5] Brain Modulation, Medtronic, Minneapolis, Minnesota, United States

Objective: Local field potentials (LFP) recorded from deep brain stimulation (DBS) electrodes provide salient biomarkers of pathologic oscillatory activity which could be leveraged for clinical implementation. Despite the large body of work on LFPs in patients with Parkinson's disease (PwPD) the longitudinal evolution of LFPs is less explored. Therefore, we analyzed LFPs recorded at routine follow-up visits to determine spectral peak and band power dynamics over time in PwPD and DBS.
Methods: A total of 26 PwPD (age: 67.0[56.8-73.1] years; sex: 8 females; disease duration: 12.0[7.8-15.0] years) with repeated LFP recordings (days between recordings: 33.9[11.0-65.1] were included in this analysis. PwPD with LFP recordings within 2-weeks of macroelectrode implant were labeled as Acute (N=12). Peak amplitude and frequency, in addition to alpha, low-beta, high-beta, and gamma band power, were calculated for each hemisphere.
Results: Peaks were detected in 41/51(80.4%) nuclei with recordings at the initial session and 43/51(84.3%) nuclei at follow-up. Of the patients with bilateral implants (n=26), 24(92.3%) at visit 1 and 25(96.2%) at visit 2 had at least 1 hemisphere with an identifiable peak. No differences were seen in peak amplitude (left hemisphere: p=0.695; right hemisphere: p=0.162) and frequency (left hemisphere: p=0.320; right hemisphere: p=0.576) between visits for the cohort. Right hemisphere low-beta (p=0.018) and bilateral gamma (left hemisphere: p=0.036; right hemisphere: p=0.014) band power demonstrated a significant increase at follow-up. No differences were found in the relative change of peak amplitude, frequency, or band power between patients with acute and chronically implanted macroelectrodes (p>0.05).
Conclusion: Our findings provide early, real-world evidence of LFP peak and band power stability in PwPD. Importantly, peak amplitudes and frequencies demonstrated no differences between visits or between patients with acute and chronic macroelectrode implants. Moreover, peak detection was stable across timepoints. These findings have fundamental implications as LFP recordings in PwPD are proposed to be a salient biomarker for guiding DBS programing and novel stimulation patterns. Nonetheless, continued research, with large samples sizes, is needed to determine the longitudinal dynamics of LFPs taken in real-world clinical settings.

P34.14

Cortical microstructural changes in Parkinson's disease and its correlation with clinical and neuropsychological performance

Jèssica Pardo[*,1], Victor Montal[2], Anna Campabadal[3], Javier Oltra[1], Ignacio Roura[1], Carme Uribe[4], Gemma Monté-Rubio[1], Maria J. Martí[5], Yaroslau Compta[5], Juan Fortea[6], Carme Junqué[7], Bàrbara Segura[7]*

[1] Medical Psychology Unit, Department of Medicine, Institute of Neurosciences, University of Barcelona; Institute of Biomedical Research August Pi i Sunyer (IDIBAPS), Barcelona, Spain
[2] Sant Pau Memory Unit, Department of Neurology, Hospital de la Santa Creu i Sant Pau, Biomedical Research Institute Sant Pau, Universitat Autònoma de Barcelona; Biomedical Research Networking Center on Neurodegenerative Diseases (CIBERNED), Barcelona, Spain
[3] Medical Psychology Unit, Department of Medicine, Institute of Neurosciences, University of Barcelona; Institute of Biomedical Research August Pi i Sunyer (IDIBAPS); Sant Pau Memory Unit, Department of Neurology, Hospital de la Santa Creu i Sant Pau, Biomedical Research Institute Sant Pau, Universitat Autònoma de Barcelona, Barcelona, Spain
[4] Medical Psychology Unit, Department of Medicine, Institute of Neurosciences, University of Barcelona; Institute of Biomedical Research August Pi i Sunyer (IDIBAPS); Research Imaging Centre, Campbell Family Mental Health Research Institute, Centre for Addiction and Mental Health (CAMH), University of Toronto, Toronto, Canada
[5] Institute of Biomedical Research August Pi i Sunyer (IDIBAPS); Biomedical Research Networking Center on Neurodegenerative Diseases (CIBERNED); Parkinson's Disease & Movement Disorders Unit, Neurology Service, Hospital Clínic de Barcelona, Institute of Neurosciences, University of Barcelona, Barcelona, Spain
[6] Barcelona Down Medical Center, Fundació Catalana de Síndrome de Down; Sant Pau Memory Unit, Department of Neurology, Hospital de la Santa Creu i Sant Pau, Biomedical Research Institute Sant Pau, Universitat Autònoma de Barcelona; Biomedical Research Networking Center on Neurodegenerative Diseases (CIBERNED), Barcelona, Spain
[7] Medical Psychology Unit, Department of Medicine, Institute of Neurosciences, University of Barcelona; Institute of Biomedical Research August Pi i Sunyer (IDIBAPS); Biomedical Research Networking Center on Neurodegenerative Diseases (CIBERNED), Barcelona, Spain

Background: Cortical mean diffusivity (cMD) has been described as a sensitive biomarker to detect early structural changes in different neurodegenerative diseases, but this measure has not been extensively explored in Parkinson's disease (PD) patients. This study aims to characterize cortical microstructural changes in PD using cMD, as well as to analyse their relationship with the clinical and neuropsychological data.
Methods: Magnetic resonance imaging (MRI) and clinical and neuropsychological assessments were acquired in a sample of 62 non-demented PD patients and 33 age, education and sex-matched healthy controls (HC). Z composite scores were calculated to obtain cognitive measures on attention and working memory, executive functions, memory, and visuospatial/visuopercetual performance. The MRI was carried out on a 3T scanner, including high-resolution 3-dimensional T1-weighted images and diffusion-weighted images. We computed cMD using a surface-based approach and analysed between group differences along with the clinical and neuropsychological correlates. Statistical significance threshold was set at $p<0.05$ for all the analyses.
Results: PD patients showed worse performance in memory ($t=2,580$, $p=0.01$) and visuospatial/visuoperceptual functions ($U=615,000$, $p=0,01$). After correction for multiple comparisons, PD patients showed increased cMD in left lateral occipital, right fusiform and inferior parietal gyri when compared with HC. The cMD in the left lateral occipital positively correlates with the MDS-UPDRS III ($r=0.27$, $p=0.04$) and PD duration ($r=0.29$, $p=0.02$); the cMD in the right fusiform positively correlates with the MDS-UPRS III ($r=0.27$, $p=0.04$) and the age at PD onset ($r=0.27$, $p=0.04$); and the cMD in the right inferior parietal positively correlates with the age at PD onset ($r=0.28$, $p=0.03$) and negatively correlates with the visuospatial/visuoperceptual performance ($r=-0.22$, $p=0.03$).
Conclusions: Our results identified posterior pattern of microstructural changes in PD patients, which was not only associated to clinical features but also with visuospatial/visuoperceptual impairment. These findings suggested that intracortical mean diffusivity is a valuable biomarker in PD and highlight the relevance of cortical involvement in non-demented PD phenotype.

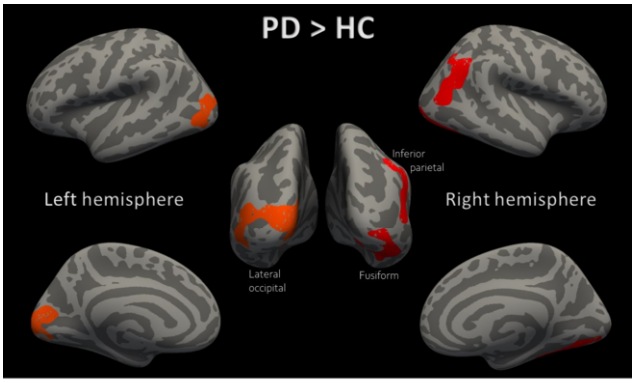


Figure 1. Cortical MD comparisons between PD patients and HC. The PD patients group showed significantly increased cMD values in the lateral occipital of the left hemisphere ($p<0.001$; X=-8.5; Y=-100.3; Z=8.6; size (mm^2)=3321.27), the inferior parietal of the right hemisphere ($p=0.02$; X=53.6; Y=-53.0; Z=36.4; size (mm^2)=1724.84) and the fusiform gyrus of the right hemisphere ($p=0.001$; X=39.4; Y=-69.8; Z=-13.9; size (mm^2)=2504.44), when compared with HC. Only clusters that survived Monte-Carlo corrections for multiple comparisons ($p<0.05$) are shown.

P34.15

Myocardial sympathetic denervation biomarkers for early detection of prodromal DLB

Mee Y Park, Dong S Shin*
Yeungnam University Medical Center, Daegu, South Korea

Background & purposes: Because of the time course of detecting DLB symptoms and signs, DLB is poorly diagnosed and hardly differentiate from AD, especially in early stage of dementia without the core clinical features of DLB.
We investigated patients with a clinical diagnosis of amnestic mild cognitive impairment (MCI) and early AD whether they had cardiac sympathetic denervation, detected by cardiac 123I-MIBG scintigraphy. And we also assessed presynaptic nigrostriatal dopaminergic system by 18F FP-CIT-PET imaging to distinguish between DLB and AD.
Methods: Thirty patients (72±9.0 yrs old: M:F 17:13) with a clinical diagnosis of amnestic MCI and early AD (CDR 0.5/SOB 3) who have been had visual hallucination and/or suspicious fluctuating cognition history without parkinsonism (n=20, prodromal DLB group, pDLB) and who have not been had visual hallucination and/or suspicious fluctuating cognition history (n=10, early AD group, eAD) enrolled in this study. 123I-Metaiodobenzylguanidine (MIBG) uptake was assessed using the ratio of the heart to the upper mediastinum (H/M ratio), and we also assessed presynaptic nigrostriatal dopaminergic system by 18F FP-CIT-PET imaging to distinguish between pDLB and eAD. Autonomic function tests and orthostatic vital signs were recorded.
Results: The H/M ratio were decreased in pDLB group, and the mean H/M ratio was significantly lower(early/delayed

uptake:1.72±0.61/1.65±0.63) compared with eAD group (early/delayed uptake:2.36±0.50/2.15±0.29) in 123I-MIBG scintigraphy ($p<0.05$). Presynaptic nigrostriatal dopaminergic deficits were founded in 18F FP CIT PET and orthostatic hypotension was evident only in pDLB group regardless of spontaneous Parkinsonism (n=17, 85%).
Conclusions: Myocardial postganglionic sympathetic denervation and autonomic dysfunctions especially orthostatic hypotension can be good biomarkers to predict DLB before core clinical symptoms appear, and may useful to distinguish from AD even in early stage. This study is under long term follow up.

P34.16

Evaluation of a clinically validated digital platform to provide diffusion MRI biomarkers in Parkinsonian syndromes
Vincent Perlbarg[*,1], Lydia Chougar[2], Jean-Baptiste Martini[1], Arthur Bezie[1], Julie Rachline[1], David Grabli[2], Florence Cormier[3], Marie Vidailhet[2], Jean-Christophe Corvol[2], Bertrand Degos[4], Stéphane Lehéricy[2]*
[1] BrainTale, Strasbourg, France
[2] Institut du Cerveau et de la Moelle épinière – ICM, INSERM U 1127, CNRS UMR 7225, Sorbonne Université, Team "Movement Investigations and Therapeutics" (MOV'IT), Paris, France
[3] Clinique des mouvements anormaux, Département de Neurologie, Assistance Publique Hôpitaux de Paris, Hôpital Pitié-Salpêtrière, Paris, France
[4] Dynamics and Pathophysiology of Neuronal Networks Team, Center for Interdisciplinary Research in Biology, Collège de France, CNRS UMR7241/INSERM U1050, Université PSL, Paris, France

Introduction: Parkinsonian syndromes include Parkinson's disease (PD) as well as heterogeneous disorders sharing some clinical features with PD including multiple system atrophy (MSA including a cerebellar – MSAc – and parkinsonian – MSAp – phenotypes) and progressive supranuclear palsy (PSP). Differential diagnosis of these disorders in clinical routine is crucial to adapt treatments. This study aims at testing whether standardized DTI biomarkers provided by brainTale-care, a software MDR CE-marked medical device, can discriminate between MSAp, MSAc and PSP from PD.
Methods: This analysis of prospectively acquired diffusion-weighted data from 46 patients with PD, 18 with PSP, 10 with MSAc and 7 with MSAp recruited in 2 previous studies (NCT00465790 and NCT01085253) have been processed with brainTale-care focusing on myelin-related markers within middle cerebellar peduncle and brainstem (MCPBS-RD) and on markers of white matter alterations within supratentorial regions (SUPRAT_FA). Kruskal-Wallis H-tests were used for group comparisons following by post-hoc Mann-Whitney tests in case of significant ($p<0.05$) group effects.
Results: Post-hoc performed tests showed significant decrease in SUPRAT_FA and increase of MCPBS-RD in MSAc and PSP groups compared to PD as well as significant increase of MCPBS-RD in MSAc compared to PSP groups (figure 1). No significant differences were found between MSAp and other groups.
Conclusion: This study shows that white-matter alterations related to different neuropathological mechanisms involved in Parkinsonian syndromes can be captured by brainTale-care platform of standardized DTI biomarkers. It paves the way for further exploration based on the differential diagnosis potential for Parkinsonian syndromes to enable better care in the clinic for patients. Objective patient population segmentation will also be of high interest for drug development addressing Parkinsonian syndromes.

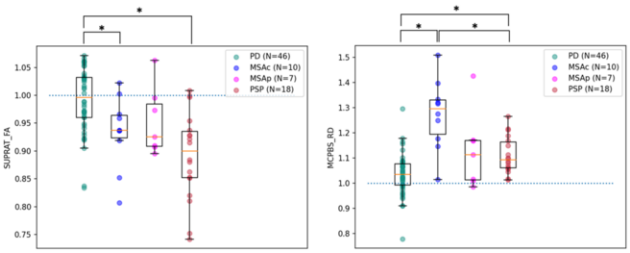


Figure 1. (Left) Boxplots representing the calibrated Fractional Anisotropy (FA) measured within supratentorial white matter regions for the four groups of patients. (Right) Boxplots representing the calibrated Radial Diffusivity (RD) measured within cerebellar peduncle and brainstem regions for the four groups of patients. * indicates that post-hoc comparison is significative ($p<0.05$).

P34.17

Multi-modal prognostic biomarkers for Parkinson's disease
Anne-Sophie Rolland[*,1], Ophélie Simonin[2], Romain Viard[3], Julien Labreuche[4], Jessica Carpentier[2], Petr Dušek[5], Markus Otto[7], Marie-Odile Habert[8], Stéphane Lehericy[9], Gregory Kuchcinski[3], Renaud Lopes[3], Jean-Pierre Pruvo[3], Christophe Scherfler[10], Jean-François Mangin[11], Marie Chupin[11], Caroline Moreau[12], David Devos[1], For the FAIRPARK-II study group[13]*

[1] Univ. Lille, Lille Neuroscience & Cognition, Team DVCD, INSERM UMRS_1172, CHU Lille, Department of Medical Pharmacology, Expert center of Parkinson's disease, LICEND COEN Center, NS-Park/FCRIN Network, Lille, France
[2] Univ. Lille, CHU Lille, Institut Pasteur de Lille, ULR4483-IMPECS - IMPact de l'Environnement Chimique sur la Santé humaine, Lille, France
[3] Univ. Lille, Lille Neuroscience & Cognition, Team DVCD, INSERM UMRS_1172, CHU Lille, Department of Neuroradiology, Lille, France
[4] Department of Biostastistics, Univ. Lille, CHU de Lille, Lille, France
[5] Department of Neurology and Center of Clinical Neuroscience. First Faculty of Medicine, Charles University and General University Hospital, Prague, Czech Republic
[7] Department of Neurology. University clinic, Ulm, Germany
[8] Sorbonne University, CNRS, INSERM, Laboratoire d'Imagerie Biomédicale, LIB. AP-HP, Pitié-Salpêtrière Hospital, Department of Nuclear Medicine. CATI, US52-UAR2031, CEA, ICM, SU, CNRS, INSERM, APHP, Paris, France
[9] Paris Brain Institute – ICM, Centre for NeuroImaging Research – CENIR, Sorbonne Université, Inserm U1127, CNRS 7225, Department of Neuroradiology, Hôpital Pitié-Salpêtrière, Assistance Publique Hôpitaux de Paris, Paris, France
[10] Department of Neurology Medical University of Innsbruck, Innsbruck, Austria
[11] Université Paris-Saclay, CEA, CNRS, Neurospin, Baobab, Gif-sur-Yvette, France; CATI, US52-UAR2031, CEA, ICM, SU, CNRS, INSERM, APHP; Paris Brain Institute - Institut du Cerveau (ICM), CNRS UMR 7225, INSERM, U 1127, Sorbonne Université, Paris, France
[12] Univ. Lille, Lille Neuroscience & Cognition, Team DVCD, INSERM UMRS_1172, CHU Lille, Department of Neurology, Expert center of Parkinson's disease, LICEND COEN Center, NS-Park/FCRIN Network, Lille, France
[13] For the FAIRPARK-II study group, Lille, France

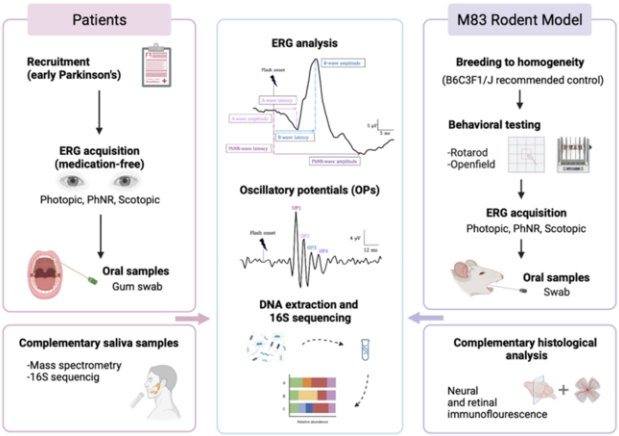
Objective: To determine a multi-modal panel of biomarkers significantly associated with the disease progression of Parkinson's disease.
Background: Detecting, monitoring and predicting the progression of neurodegeneration in Parkinson's disease (PD) is a major issue

with crucial relevance of patient's management and success of future therapeutical trials.
Methods: Sera samples and MRI were collected as part of a European prospective multi-centric cohort of naïve drugs PD patients (FairParkII: n=372, mean age: 62 years +/-9, disease duration since first symptoms: 416 days (266-618), disease duration since diagnosis: 105 days (47-116)). At baseline and nine months, clinical parameters to score motor symptoms were use as proxy of disease progression to assess the prognostic value of candidate multi-modal biomarkers. Markers related to neurodegeneration (NfL), lipid peroxidation (4-HNE), inflammation (Il-6, TNF-alpha, GFAP), iron dyshomeostasis (ferritin) and protein dyshomeostasis (alpha-synuclein) were assessed by electrochemiluminescence or Elisa on sera; markers related to iron accumulation, structural atrophy and dopaminergic loss by MRI measurement on 3DT2*, 3DT1 images and PET Scan images respectively. Statistical analyses with linear mix model were used.
Results: At baseline, 4-HNE, NfL, IL-6 and GFAP were correlated with MDS-UPDRSIII score, IL-6 and ferritin with MDS-UPDRS total score in multivariate analysis with adjustment on age, sex and disease duration since first symptoms. Also, level of iron (measured with IRM T2*) within the Substantia Nigra (SN), Putamen and Caudate nucleus were correlated with TNF-alpha, alpha-synuclein and ferritin; volume of the Putamen and Caudate nucleus were correlated with 4-HNE; denervation of the Putamen (measured with DAT Scan) was correlated with NfL and TNF-alpha in multivariate analysis with adjustment on age, sex and disease duration since first symptoms. We will now analyze and correlate biologic and imaging data at 9 months.
Conclusions: This multi-modal analysis will allow to propose a combination of biomarkers to predict the progression of the disease.

P34.18

Peripheral retinal and microbial biomarkers for the early diagnosis of Parkinson's disease
Victoria de los Angeles Soto Linan[*,1], C. Gora[1], M. Peralta[2], F-A. Guevara Agudelo[3], N. Dupré[4], M. Hébert[1], F. Raymond[3], M. Lévesque[1]*
[1] Laval University, CERVO Brain Research Center, Quebec City, Quebec, Canada
[2] CERVO Brain Research Center, Quebec City, Quebec, Canada
[3] Laval University, INAF, Quebec City, Quebec, Canada
[4] Laval University, CHU of Quebec, Quebec City, Quebec, Canada

Parkinson's (PD) diagnosis primarily occurs after severe neurodegeneration, despite early non-motor symptomatology being present decades prior. With the need to discover efficient biomarkers, we aimed to validate non-invasive techniques — electroretinography (ERG) and oral microbiota — to detect emerging peripheral effects reflecting early central dysfunction.
We used two-month-old homozygous M83 transgenic mice overexpressing human A53T α-synuclein (aSyn) as a PD model (n=40). Mice of both sexes underwent a battery of behavioral tests, ERG measurements, and oral swab collection. At four months, histological analyses were performed to assess synucleinopathies and neurodegeneration. Simultaneously, early-onset idiopathic PD patients (n=13, age 63.9±2.2; disease duration 3.6±0.3) and healthy age-matched controls (n=11, age 62.7±2.6) were recruited, including both sexes. They underwent ERG testing, Salivette swabs, and unstimulated saliva collection.
ERG analysis in mice revealed a 29.9%±0.2 and 39.2%±1 photopic b-wave amplitude reduction at two and four months, most prominent in females and indicating bipolar cell impairment. M83 mice also exhibited a 32.2%±0.2 PhNR-wave amplitude reduction at two months and a 23.7%±0.2 remaining reduction at four months. Based on retinal immunofluorescence imaging of M83 mice, ERG changes may be tied to outer retina aSyn phosphorylation. Echoing our animal model, women with Parkinson's consistently presented similar impaired parameters in ERG testing. In scotopic stimulation of the pure rod and mixed rod-cone response, a 31.7%±0.5 and 33.3%±0.2 b-wave amplitude reduction were found. The oscillatory potentials isolated from scotopic testing further detected an attenuated amacrine cell output, shown by a 49.3%±0.4 reduction of OP1 amplitude. Additionally, 42.1%±0.01 and 29.5%±0.2 reduction in the PhNR b-wave and PhNR-wave amplitude of women suggested hindered retinal ganglion cells. Lastly, the analysis of both swab and saliva samples exhibited group and sex-specific familial level abundance shifts of bacteria previously linked to PD onset and development.
Altogether, our results in mice and human cohorts suggest that in PD, retinal functional impairments and oral microbiota abundance shifts can be detected early in the pathology development, particularly in females. In the future, these tools may not only contribute to diagnosis establishment but also provide a wider window for therapeutic intervention and improved patient outcome.

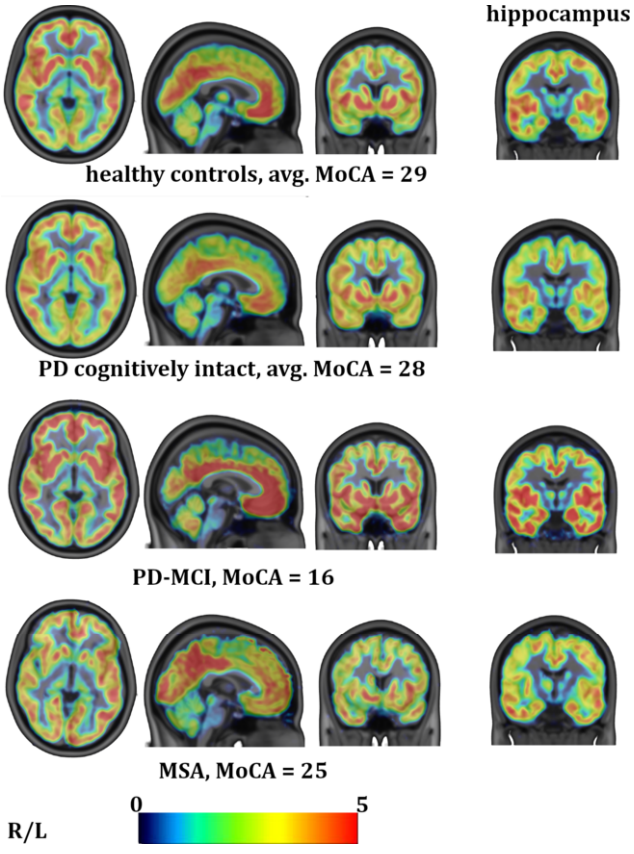


P34.19

Imaging presynaptic terminal integrity in parkinsonism: New findings from the 18F-SynVesT-1 tracer
Carme Uribe[*,1], Sarah Martin[1], Kelly Smart[1], Kimberly Desmond[1], Anthony Lang[2], Neil Vasdev[1], Antonio Strafella[1]*
[1] Centre for Addiction and Mental Health, Toronto, Canada
[2] Toronto Western Hospital, Toronto, Canada

Molecular imaging biomarkers are important for differential diagnosis among parkinsonisms, and for disease monitoring to improve clinical care. The synaptic vesicle protein 2A (SV2A) radioligand [18F]SynVesT-1 has been tested in healthy controls (HC) as a proxy for in vivo synaptic density quantification. Preliminary data displayed good in vivo binding distribution properties in PD. Here, we aimed at investigating the in vivo presynaptic terminal integrity in PD patients with and without mild cognitive impairment (PD-MCI/PD-noMCI) and in the brain of a Multiple System Atrophy (MSA) patient.
120-minute [18F]SynVesT-1 scans were acquired in 4 patients with PD (3M/1F, age=64.5y, disease duration=11.5y, 1PD-MCI/3PD-noMCI), 1 female MSA patient (66y, 2y disease duration), and 3 HC (2M/1F, age=54.3) on a GE Discovery MI PET-CT scanner after injection of 187±10MBq with arterial blood collection. Low-dose CT images were used for attenuation correction, and dynamic image reconstruction was performed using filtered back-projection. PET images were matched to the subject's T1-weighted MRI and processed using Pmod 4.2. We estimated binding potential (BPND)

using a Simplified Reference Tissue Model 2 (SRTM2) with the Centrum Semiovale as reference region.
PD-noMCI patients with different disease duration and severity (years range=4-15; LEDD:1,255mg, range=375-1,964mg; MDS-UPDRSIII:29, range=26-34) displayed lower distribution of SV2A in cortical and subcortical (putamen left:4.5, right:4.3; caudate left:3.7, right:3.4 nuclei) areas in comparison with HC (putamen left: 4.9, right:4.7; caudate left:3.9, right:3.9). The PD-MCI patient (left most affected side, 15y disease duration, MDS-UPDRSIII:29, LEDD:650mg) had higher SV2A distribution across the whole brain than the other groups, while an asymmetry in the hippocampus can be observed (right:3.5<left:3.8). Regarding the MSA patient with cognitive impairment (right most affected side, MoCA:25, UMSARSII:28, LEDD:400 mg), a lateralized density loss was found in cortical and striatal (e.g., putamen left:3.1/right;3.2; caudate left:1.9/right:3.0) areas with respect to PD patients and healthy controls (Fig.1).
We provide preliminary evidence of the fluor-labelled SV2A's tracer binding distribution properties in parkinsonian patients according to their cognitive status. The mechanisms underlying synaptic density distribution associated with cognitive impairment in parkinsonism are still unclear. The 18F-SynVesT-1 could be valuable for tracking asymmetry brain changes and ultimately assisting in clinical diagnosis.



P34.20

Peripheral immunophenotype and inflammatory changes in Parkinson's disease patients

Ana Florencia Vega Benedetti[1], Clara Porcedda[2], Tommaso Ercoli[3], Chiara Burgaletto[4], Giovanni Defazio[3], Alfonso De Simone[5], Giuseppina Cantarella[4], Valeria Sogos[2], Annarosa Carta[,2]*
[1] University of Cagliari, Cagliari, Italy
[2] Department of Biomedical Sciences, University of Cagliari, Cagliari, Italy
[3] Department of Medical Sciences and Public Health, Institute of Neurology, University of Cagliari, Cagliari, Italy
[4] Department of Biomedical and Biotechnological Sciences, University of Catania, Catania, Italy
[5] Department of Pharmacy, University of Naples "Federico II", Naples, Italy

Parkinson's disease (PD) is characterized by early peripheral events such as inflammation and misfolding of α-synuclein (αSyn), which may damage brain barriers resulting in chronic CNS infiltration of peripheral immunocytes and neuroinflammation. αSyn misfolding harbors the formation of toxic aggregates, among which small soluble oligomers (αSynO) induce neurotoxicity and inflammatory responses. We hypothesized that αSyn oligomers in peripheral circulation elicit inflammatory processes and alter brain barrier functions, thereby impacting CNS infiltration. In human PBMC from PD patients we investigated changes in cellular subpopulations as compared to PBMC from healthy donors, and cytokines expression after in vitro exposure to αSynOs. PD patients enrolled at the Cagliari University hospital were evaluated with classical motor (HY and UPDRS) and non-motor (MoCA and NMSS) scales. Fresh PBMCs isolated from healthy and PD donors were immunophenotyped by flow cytometry and exposed to αSynO (0.5 μM) for 24hs for multiplex ELISA (mELISA) analysis. Our results showed that peripheral immune cells displayed an altered phenotype in PD. Among PBMC subpopulations, the NK cell phenotype was mostly affected by the disease state, showing a highly significant increase of mature NK cells (CD16+/CD56-) and a dramatic decrease of immature NK cells (CD16+/CD56+), although a subpopulation of PD patients was refractory to such change of NK phenotype. The correlation analysis suggested that changes in NK phenotype correlated with the non-motor symptoms scale score. Cytokine analysis by mELISA showed that untreated PBMC from PD patients produced a highly dysregulated cytokine profile, that remained mostly unaltered after exposure to αSynOs. In contrast, PBMC from healthy donors drastically changed their cytokine profile in response to αSynOs. Changes in the PBMC phenotype may support the clinical diagnosis of PD. The increased inflammatory profile of PD-PBMC supports a role of peripheral inflammation in BBB function defects which may impact on disease progression.

P34.21

Characterisation of blood-derived extracellular vesicles in Parkinsons's disease patients

Alexander Weiss[*,1], Fanni Annamaria Boros[1], Philipp Arnold[2], Andreu Matamos-Angles[3], Verena Taudte[4], Friederike Zunke[1]*
[1] Department of Molecular Neurology, University Hospital Erlangen, Erlangen, Germany
[2] Insitute of Functional and Clinical Anatomy, Friedrich-Alexander-University Erlangen-Nürnberg, Erlangen, Germany
[3] Institute of Neuropathology, University Medical Center Hamburg-Eppendorf, Hamburg, Germany
[4] Insitute of Laboratory Medicine and Pathobiochemistry, Molecular Diagnostics, University Giessen and Phillipps-University Marburg, Marburg, Germany

Introduction: Up to today, no biomarker has been identified, which enables early and reliable diagnosis of Parkinson's Disease (PD). Thus, identification of potential molecules and establishment of a diagnostic method is urgently needed. Recently, extracellular vesicles (EVs) emerged as promising candidates for reflecting the disease states of the central nervous system, as they are able to cross the blood-brain barrier in both directions. As pathological forms of alpha-synuclein (a-syn) were detected in EVs, it has been proposed that they could also play a role in disease spreading mechanism.
Objectives: The aim of this study is the physical and biochemical characterisation of blood-derived EVs in PD patients in order to elucidate their potential as biomarkers.
Methods: Total EV fraction was extracted with the use of a commercially available isolation kit from blood samples of PD and control individuals collected at the University Hospital Erlangen. From the total EV pool neuron-derived EVs (NEs) were separated by immunoprecipitation with the use of antibodies against the neuronal surface protein NCAM-L1. The EV fraction was detected by biochemical characterisation using EV markers such as CD63. Transmission Electron Microscopy (TEM) and ZetaView© analysis was implemented for further validation of successful EV extraction and for the biophysical characterisation of the vesicles. The presence of pathological conformation of a-syn in the extracted vesicles was validated with dotblot analysis under non-denaturing conditions.
Results: EV and NE isolation was successful based on western blot results of positive EV and NE markers. This was further supported by TEM and ZetaView© analysis. TEM analysis shows no significant difference in the median size of the vesicles originating from PD and control samples. Furthermore, protocols for additional characterisation were established, including the a-syn seed amplification assay (SAA) to show the seeding of pathological forms of a-syn under in-vitro conditions.
Further perspectives: Our results pave the road for further characterisation of EVs by biochemical and biophysical analyses. Further studies in this direction will lead to a better understanding of molecular mechanisms in PD and will assess the potential of EVs serving as a valuable diagnostic tool.

P34.22

Delayed cardiac sympathetic denervation in Parkinson's disease: An intermediate gradient between CNS- and PNS-dominant subtypes

Sang-Won Yoo, Joong-Seok Kim*
Department of Neurology, College of Medicine, The Catholic University of Korea, Seoul, South Korea

Background and Objectives: Parkinson's disease (PD) is a multifaceted disease that encompasses diverse clinical phenotypes. The diversity of PD can be subtyped based on the dynamic status of cardiac sympathetic innervation. In the present study, how the subtypes of cardiac sympathetic denervation reflect the pathobiology and predict the progression of PD was investigated.
Methods: The study included 195 early PD patients. The subjects were followed up for at least 2 years and a maximum of 7.4 years (average follow-up duration; 4.7 ± 1.4 years). Cardiac sympathetic innervation was evaluated using 123I-meta-iodobenzylguanidine (123I-MIBG) myocardial scintigraphy and changes were re-assessed 2–4 times. PD severity was evaluated with the Unified Parkinson's Disease Rating Scale (UPDRS), part III and motor progression re-examined with Movement Disorder Society (MDS)-UPDRS, part III across disease duration. Patients were stratified based on the patterns of cardiac denervation: Scans with cardiac Norepinephrine Deficit (SND), Converter (delayed SND), and Scans with Preserved cardiac Norepinephrine innervation (SPN). The association between subtypes and the status of dopaminergic nigrostriatal degeneration was analyzed. The influence of cardiac denervation on motor progression was also investigated in this longitudinal analysis.
Results: Among the patients, 144 PD subjects were defined as SND, 16 as Converter, and 35 as SPN. The most severe nigrostriatal degeneration was observed in the SND group and the degeneration was the most asymmetric in the SPN group. Positive linear trends of nigrostriatal degeneration status and its asymmetric pattern among subterritories of striatum and globus pallidus were found across a pre-defined order (SND vs. Converter vs. SPN). The results indicated an increasing degree of asymmetric degeneration among the groups. The SND represented PNS-dominant biology of PD, the SPN supported CNS-dominant type, and the Converter the intermediate type. Longitudinal analysis of motor progression indicated each cardiac denervation developed a distinct progression trajectory.
Discussion: The gradient subtypes of cardiac sympathetic denervation in PD might indicate a dominant origin and seeding pattern of pathobiology. The characteristics of each group were confirmed by different progression of motor growth. 123I-MIBG myocardial scintigraphy might be a suitable alternative biomarker for subtyping PD and tracking its clinical development.

Table 1. Characteristics of Study Population

	ALL (n= 195)	SND (n= 144)	Converter (n= 16)	SPN (n= 35)	P value
Age at diagnosis, years	67.6 ± 8.9	67.9 ± 8.1	64.9 ± 8.1	67.8 ± 12.1	0.379
Sex, female, n (%)	97 (49.7)	75 (52.1)	8 (50.0)	14 (40.0)	0.462
Body mass index, kg/m²	24.2 ± 3.0	24.1 ± 3.1	23.6 ± 2.7	24.6 ± 2.9	0.504
Disease duration at diagnosis, years, median (IQR)	1.0 (1.0)	1.0 (1.1)	1.0 (0.54)	1.0 (1.3)	0.694
Total follow-up duration, years	4.7 ± 1.4	4.8 ± 1.5	4.6 ± 1.5	4.3 ± 1.3	0.158
Hypertension, n (%)	86 (44.1)	57 (39.6)	7 (43.8)	22 (62.9)	0.042
Diabetes mellitus, n (%)	29 (14.9)	24 (16.7)	0 (0.0)	5 (14.3)	0.215
Dyslipidemia, n (%)	60 (30.8)	48 (33.3)	3 (18.8)	9 (25.7)	0.405
Non-smoker, n (%)	189 (96.9)	139 (96.5)	16 (100.0)	34 (97.1)	1.000
UPDRS Part III	14.0 ± 7.9	14.5 ± 8.3	10.5 ± 4.4	13.8 ± 7.0	0.013
Converted MDS-UPDRS Part III$_{Converted}$, median (IQR)	17.8 (20.2)	18.5 (21.5)	15.0 (6.0)	15.5 (14.9)	0.184
UPDRS & HY each interval, years	2.21 ± 0.50	2.21 ± 0.52	2.30 ± 0.46	2.16 ± 0.48	0.644
Early H/M$_{Initial}$ ratio	1.53 ± 0.29	1.40 ± 0.18	1.96 ± 0.27	1.84 ± 0.20	<0.001
Delay H/M$_{Initial}$ ratio	1.50 ± 0.34	1.33 ± 0.18	2.05 ± 0.21	1.93 ± 0.23	<0.001
Early H/M$_{Delayed}$ ratio	1.46 ± 0.28	1.33 ± 0.15	1.63 ± 0.12	1.92 ± 0.17	<0.001
Delay H/M$_{Delayed}$ ratio	1.43 ± 0.33	1.27 ± 0.16	1.59 ± 0.11	2.02 ± 0.16	<0.001
^{123}I-MIBG scan each interval, years	2.31 ± 0.53	2.30 ± 0.55	2.33 ± 0.57	2.30 ± 0.38	0.983

P34.23

Evaluation of plasma levels of NFL, GFAP, UCHL1 and tau as Parkinson's disease biomarkers

Priscilla Youssef[*,1], Laura Hughes[1], Woojin Kim[1], Glenda Halliday[1], Simon Lewis[1], Antony Cooper[2], Nicolas Dzamko[1]*
[1] University of Sydney, Sydney, NSW, Australia
[2] Garvan Institute of Medical Research, Sydney, NSW, Australia

Objective biomarkers for Parkinson's Disease (PD) are critically needed for early diagnosis, effective monitoring of disease progression and interpretatation of clinical trial outcomes. In the present study we explored the biomarker potential of the neurology markers neurofilament light (NFL), glial fibrillary acid protein (GFAP), tau and ubiquitin C-terminal hydrolase L1 (UCHL-1) using the ultrasensitive Single Molecule Array (SIMOA) platform, alongside the measure of total alpha-synuclein using the MesoDiscovery (MSD) platform. Biomarker levels were assessed in plasma samples of a cross-sectional cohort comprised of 29 PD

patients and 30 matched controls. The control and PD groups did not differ in their mean NFL, GFAP, tau, UCHL-1 or alpha-synuclein plasma levels (t test p>0.05). When measured against disease severity scales, motor severity (MDS-UPDRS III) positively correlated with NFL (rho=0.646, p<0.0001), GFAP (rho=0.450, p<0.05) and alpha-synuclein levels (rho=0.406, p<0.05), while motor stage (Hoehn and Yahr) positively correlated with NFL (rho=0.455, p<0.05) and GFAP (rho=0.549, p<0.01), but not alpha-synuclein levels (p>0/05). Whilst none of the biomarkers were effective in discriminating PD patients from controls, NFL and GFAP appeared to be promising disease-state biomarker candidates of PD, given their correlation with motor features of the disease. Assessment of these two proteins within a longitudinal context will further validate their use as objective measures of PD motor progression.

CLINICAL SCIENCE: Pharmacological therapy

P35.02

May apomorphine be helpful for the axial symptoms of Parkinson's disease?

Araceli Alonso-Canovas[*1], Paula Pérez-Torre[2], Gema Sánchez[2], Angeles Patiño Paton[2], Nieves Monterde Fernández[2], Isabel Pareés Moreno[2], Juan Carlos Martínez Castrillo[2]*

[1] Neurology Department. Hospital Universitario Ramón y Cajal, Madrid, Spain

[2] Hospital Universitario Ramón y Cajal, Madrid, Spain

Background: Axial symptoms of Parkinson's Disease (freezing, falls, speech problems) may be severe and are commonly refractory to dopaminergic treatment. A possible benefit of apomorphine has been anecdotally reported in camptocormia and on-freezing.

Methods: Retrospective analysis of PD patients who started treatment with continuous subcutaneous apomorphine infusion (CSAI) in our Movement Disorders Unit 2020-2022.

Results: Thirteen patients, 6 female, 72±7 years old, with a PD duration of 11±5 years, were treated with CSAI. Basal levodopa equivalent daily dose (LEDD) was 1065±519, one patient was treated with deep brain stimulation. Nine reported on-freezing, 6 frequent falls, 5 posture abnormalities, 5 camptocormia, and 4 speech problems. One female was excluded due to COVID19 decease 2 weeks from onset. Twelve were treated with CSAI and followed for 14±8 months. LEDD was reduced to 508±321 (mean 50% reduction). Freezing improved in 7, posture in 5, speech in 4, and falls in 4. No improvement of camptocormia was reported. In 8 patients motor fluctuations improved, as did on-tremor (5) and dyskinesia (3). Clinical global impression was overall positive (very much improved in 4, much improved 6, improved 1, same situation 1). Three patients discontinued treatment in the first 3 months due to inefficacy (1), incomplete benefit (1), poor compliance with the device (1). Adverse events were common but mild (skin nodules in 6, dizziness 4, hypotension 3, oedema 4, somnolence 2) and did not lead to discontinuation.

Conclusions: In our experience with patients with advanced disease and disabling on-clinical symptoms, CSAI was useful, safe and maintained with sustained benefit after a long follow-up. It did not only improve motor fluctuations and some non-motor symptoms, but lead to an unexpected improvement of axial symptoms (freezing, posture and speech, but not camptocormia), usually associated with greater LEDD reduction and doses > 4 mg/h. These benefits may not be predicted by apomorphine test or previous levodopa response and warrant an empirical trial of CSAI.

	age	sex	disease duration	basal oral LEDD	follow-up oral LEDD	basal vs follow-up LEDD	Apomorphine dose mg/h	CGI (global)	Basal axial symptoms	Improved (axial)	Improved (non-axial)	Adverse events	follow-up (months)	Ongoing treatment
1	81	1	9	300	300	0	1	4	Campt	0	0	dizziness, hypotension	1	NO (inefficacy)
2	78	0	16	1575	625	-60%	4	4	Campt, Freez	0	0 (COVID19 admission and decease)	None		NO (exitus)
3	71	0	8	625	625	0	8	3	Campt, Falls	0	Tremor, Motor Fluct, urinary	mild nodules, dysk, mild hallucinations	18	YES
4	72	1	11	2087	850	-60%	6	2	Falls, Posture	Posture	Motor Fluct	mild nodules, oedema, mild confusion	21	YES
5	73	0	6	750	0	-100%	6	2	Freez	Freez	Tremor, sleep, pain	mild nodules, dizziness, vomiting	3	NO (poor adherence)
6	62	1	20	1930	450	-75%	6	2	Freez, Speech, Falls	Speech, falls	Motor Fluct, sleep, hiperse	dizziness, hypotension, low mood, low libido	1,5	NO (poor adherence)
7	58	1	5	1050	825	-21%	5	2	Campt	0	Tremor, Motor Fluct	mild nodules, dizziness, nausea	17	YES
8	79	1	16	600	400	-33%	7	1	Campt, Freez	Freez	Motor Fluct, pain	no	24	YES
9	81	0	8	900	150	-83%	7	1	Freez, Speech, Posture, Falls	Freez, Speech, Posture, Falls	Motor Fluct, Dysk, mood	oedema	22	YES
10	65	0	11	950	0	-100%	8	1	Freez, Speech, Posture, Falls	Freez, Speech, Posture, Falls	Tremor, Motor Fluct, anxiety	mild nodules, oedema, somnolence	19	YES
11	75	0	6	1000	700	-33%	6	1	Freez, Speech, Posture	Freez, Speech, Posture	Tremor, Motor Fluct, mood, sleep	no	15	YES
12	73	0	10	900	700	-22%	4,5	2	Freez	Freez	Motor Fluct, Dysk	blood pressure fluctuations	13	YES
13	72	1	16	1175	975	-17%	3	2	Freez, Posture, Falls	Freez, Posture, Falls	Motor Fluct, Dysk, anxiety, sleep,	mild nodules, oedema	10	YES

P35.03

Effect of cannabis on motor and non-motor symptoms of Parkinson's disease: A behavioral and pharmacological study in rats

*Elodie Giorla, Christelle Baunez**

Institut de neurosciences de la Timone, UMR7289 CNRS & Aix-Marseille Université, Marseille, France

Is cannabis or cannabidiol (CBD) beneficial for Parkinsonism is a currently often asked question. Although there is evidence from animal and human studies that cannabis has some symptomatic effects, many therapeutic challenges remain. Since the endocannabinoid system is largely expressed within the basal ganglia, most studies regarding Parkinson's disease (PD) and cannabis have focused on the cellular and molecular interactions between cannabinoids and dopamine. However, if cannabinoids have the potential to be beneficial for motor symptoms in various animal models of PD, the optimal treatment remains to be identified. The present study thus aims at highlighting the role of cannabis on motor and non-motor symptoms of PD.

The available data to suggest that cannabis could be beneficial for parkinsonian patients are inconsistent. One critical question remaining to be addressed is whether CBD alone could be sufficient or whether THC is required to obtain a therapeutic effect.

To address this question, we have run 2 different experiments in rats. First, in our model of haloperidol-induced catalepsy, we found that the combination of THC + CBD was most efficient to alleviate motor symptoms. THC alone, but not CBD alone, also seemed to be beneficial on this measure. Then, in a rat model of Parkinson's disease induced by a bilateral 6-OHDA injection in the striatum, we assessed both motor, attentional, impulsive and motivational processes in the 5-choice serial reaction time task. As for the catalepsy experiment, we here tested CBD, THC alone and CBD/THC mix at 2 various ratios. The results suggest that injections of THC+CBD is the best treatment to reduce the deficits induced by the DA depletion with no detrimental effect. CBD alone again in this task proved not to be efficient, while THC alone had some beneficial and no detrimental effects.

In conclusion, although it is currently trendy to consider therapeutic use of cannabis, the exact composition of what is available on the market is critical for efficiency. Our results suggest that CBD alone will not be efficient enough and it is important to have THC in the mixture, which raises legality issues in some countries.

P35.04

Deciphering cross talks of dopamine/insulin/NLRP3-Inflammasome signaling (DA/IN/NLRP3), metabolic syndrome(MeS) and cardiovascular risk (CVR) in drug-(antipsychotic)-induced Parkinsonism(DIP) and tardive dyskinesia(TD) mimicking Parkinson's disease(PD) motor/cognition symptoms: Neuroprotective effects of Panax ginseng: The prototypal NLRP3 regulator

Autumn Carriere[*,1], Simon Chiu[1], Jerry Hou[2], Edmund Lui[3], Mariwan Husni[4], John Copen[5], Robbin Campbell[6], Allison Foskett[7], Shad Mujeeb[8], Michel Woodbury-Farina[9], Ram Mishra[10], Yves Bureau[11], Amresh Srivastava[12]*

[1] University of Western Ontario, London, Ontario, Canada
[2] Dalian Fusheng Natural Medicine Development Co., Ltd., Dalian, Dalian Province, China
[3] University of Western Ontario Dept Pharmacology schulich School of Medicine, London, Ontario, Canada
[4] Arabian Gulf University Medical School, Bahrian Kingdom, Bahrain
[5] University of British Columbia, Victoria, BC, Canada
[6] University of Western Ontario /Eating Disorder Foundation Canada, London, Ontario, Canada
[7] University of Alberta, Edmonton, Alberta, Canada
[8] Touro University Nevada College of Osteopathic Medicine Psychiatry Residency Program, Las Vegas, Nevada, United States
[9] University of Puerto Rico, San Juan, Puerto Rico (US), Puerto Rico
[10] McMaster University school of medicine, Neurosciences program, Dept of Psychiatry, Hamilton, Ontario, Canada
[11] University of Western Ontario /Lawson Health Research Institute, Imaging/Biostatistics Division, London, Ontario, Canada
[12] University of Western Ontario Schulich School of Medicine, London, Ontario, Canada

Introduction: Growing evidence suggests spontaneous dyskinesia and drug-(antipsychotic)-induced-Parkinsonism (DIP) occurs more common among the elderly, and DIP predicts PD. Tardive dyskinesia (TD) and L-DOPA dyskinesia (LID) have negative impact on PD course. PD has higher prevalence of Type II-Diabetes-Mellitus(DM). DM drugs: Glucagon-like peptide-1 (GLP-1)-receptor agonists exhibit positive benefits in PD trials. Mechanisms of PD interacting with DM, Metabolic-Syndrome (MeS)-cardio-vascular risks(CVR) remain uncertain.
Objective/Method: We propose DM,MeS,CVR and PD converge on NLRP3-inflammasome, in orchestrating DA/IN-driven neural-immunity inflammation, in prefrontal cortical-limbic-nigral-striatal brain network and in pancreas-enteric plexus-gut-microbiome axis (PEGM), Our objective is twofold: i)to delineate interplay of DA/IN/NLRP3-signaling, cardio-metabolic risks related to DIP and TD mimicking PD; ii)to evaluate Panax Ginseng neuroprotective action in RCT and PD translational models
Results: We conducted post-hoc analysis of data from randomized placebo-controlled trial(RCT) of proprietary formulated Panax Ginseng: Ginsana-115 in treatment resistant schizophrenia (TRS) cohort. We used Simpson-Angus-Scale(SAS) for DIP and Abnormal-Involuntary-Movement-scale(AIMS) for TD and evaluated components of MeS: central obesity/BMI, dyslipidemia, hypertension, and DM, Insulin Resistance (IR) with HOMA model and Framingham risk score(FRS) for cardio-vascular risk burden. NCS: Neurcognitive-Screening Scale(University of PA, USA) was used for cognition. We recruited 44 chronic schizophrenic subjects: 38 years, male/female:29/15. Baseline SAS score was 4.2 (SD=3.9),: 52.3% SAS > 3.0, 34.1% > 6. Pearson correlation coefficients were used for correlative analysis. Both SAS and AIMS correlated directly and significantly with FRS scores (SAS:r=0.60, p<0.001; AIMS: r=0.36,p<0.05) but independently of BMI. SAS correlated directly with MeS components: Log-IR (r=0.44,p<0.008), LDL (r=0.50, p<0.001)and triglyceride (r=0.335, p<0.05), but inversely with HDL(r=0.57,p < 0.0001). SAS correlated significantly with impaired neurocognitive index (r=0.30; p<0.05), cognitive inflexibility and executive reasoning, AIMS scores correlated significantly with working memory (r=0.32; p,0.05). In tTRS cohort, Ginsana-115 significantly improved FRS score and IR, and reduced systolic blood pressure. In MPTP(1-methyl-4-phenyl-1,2,3,6-Tetrahydropyridine) rodent PD model, Ginsenoside Rg3 significantly antagonized glia inflammatory response and restored DA loss in striatum in parallel with motor improvement.
Conclusion: Our findings support DA/IN/NLRP3 signaling model highlighting cardio-vascular-metabolic dysregulation impact on PD, DIP/TD/LID phenotype. Preventive and therapeutic strategies targeting NLRP- activation-inhibitor: Rg3-ginsenoside, Exercises, PGEM-based Probiotics, and Epigenetics diets, can transform landscape of PD, PD-Dementia and PD-psychosis.

P35.05

Drivers of treatment decisions in advanced Parkinson's disease: A qualitative study among people with Parkinson's and caregivers

Josefa Domingos[*,1], Rajesh Pahwa[2], Angelo Antonini[3], Irene Malaty[4], Susanna Lindvall[5], Franceso De Renzis[5], Connie Yan[6], Krystallia Pantiri[7], Nancy Touba[8], Emily Evans[9], Ali Alobaidi[6], Anand Shewale[6], Pavnit Kukreja[6], Jorge Zamudio[6], K Ray Chaudhuri[10]*

[1] Radbound University, Lisbon, Portugal
[2] University of Kansas Medical Center, Kansas City, Kansas, United States
[3] Parkinson and Movement Disorders Unit, Study Centre for Neurodegeneration, Department of Neuroscience, University of Padova, Padova, Italy
[4] Department of Neurology, University of Florida, Fixel Institute for Neurological Diseases, Gainesville, Florida, United States
[5] Parkinson's Europe, Orpington, United Kingdom
[6] AbbVie Inc., North Chicago, Illinois, United States
[7] OPEN Health Group, Rotterdam, Netherlands
[8] OPEN Health Group, London, United Kingdom
[9] OPEN Health Group, Bernardsville, New Jersey, United States
[10] King's College and Parkinson Foundation Centre of Excellence, Kings College Hospital London, London, United Kingdom

Background: As disease advances, some people with Parkinson's (PwP) start responding poorly to oral therapies and must consider device-aided therapies, which include levodopa-carbidopa intestinal gel, deep brain stimulation, and continuous subcutaneous apomorphine infusion.
Objective: To understand drivers for treatment decisions in advanced Parkinson's disease (aPD).
Methods: A literature review was conducted to identify potential attributes of aPD treatments. Preference studies, qualitative research, and guidance documents on attribute selection for discrete choice experiments (DCEs) were consulted. Nine criteria were developed and applied to a list of 43 potential attributes, resulting in the selection of 14 attributes. These were reviewed in one-on-one qualitative interviews with 16 participants (14 PwP, 2 caregivers) across the US, UK, and Germany.
Results: [1] ON-time without troublesome dyskinesia, [2] early-morning OFF-time, [3] mild/moderate side effects that resolve without treatment, [4] severe side effects leading to hospitalization, and [5] route of treatment administration were confirmed as key attributes in driving participants' treatment decisions. [6] sleep disturbance and [7] pill burden were altered from the list of key attributes and [8] caregiver support was added based on participants' feedback (Table 1). The majority of participants valued ON-time as an efficacy attribute. Participants with sleep disturbance reported subsequent daytime drowsiness affecting their daily activities. Participants indicated that pill burden is better captured by

frequency of administration than with the number of pills per day. Although participants reported preferring to take less pills less often, they were willing to accept a higher pill burden to increase ON-time. Interestingly, participants were more concerned about the burden of treatment maintenance for their caregivers than for themselves. All PwP preferred a treatment that keeps them independent for as long as possible, even when the reported caregiver support did not exceed 3 hours/day.

Conclusions: Participants held attributes related to treatment efficacy, modality, and safety as important when considering aPD treatment choices. These qualitative findings can inform physician, PwP, and caregiver decisions in evaluating different treatment options for aPD. Further understanding of treatment preferences will be evaluated in a subsequent DCE survey to quantify how PwP's weigh risks and benefits of different aPD treatments.

Table 1 Participants' quotes supporting the key findings

ON-time without troublesome dyskinesia
"For me the more important attribute is the ON time. That is, how much time do I have effectively a day to work, to live, to spend time with the family? So, um, yes…My goal is to have an ON time that is as long as possible."
Early-morning OFF-time
"It is horrible. I literally had a doctor's appointment yesterday morning that I had to get up and get out the door within 15 minutes. It was terrible, I walked into the office and they're looking at me so pitiful. I'm like, "it'll be okay, my medicines going to kick in in a minute." I literally feel like an alien, I can't walk, I'm miserable, and see, I have some back issues going on right now too. So, I'm tremoring, I'm in a knot, my back's killing me, it's just horrible. The morning is the worst, but once it kicks in it feels really good, and it kicks in usually pretty fast and pretty good because I… my stomach is empty."
Treatment modality
"The less pain the better and I don't have to go through operation and more procedures that you described earlier. That would be better, and I would prefer it that way."
"That would definitely be an important point in the decision-making process. So, if I hear that the brain stimulator would have to be removed after all because of an infection… Because of severe side effects. I would have to think very carefully, …you would have to see how often that happens but … um … it definitely has an impact"
Sleep disturbance
"Well, sleep should be the most restorative thing after a strenuous day, right?, to gather the energy for a new day. When you have a phase with a lot of sleep disturbances, , then the entire ON time is effectively gone when you're tired, you know?"
"It was just a complete wash over feeling, I… I could literally blink my eyes, and if I blinked my eyes, I could find myself falling asleep, it was scary. That was scary, yeah, that wasn't like sleep deprivation there, it was just… that was weird.
Pill burden
"If I have to take them to feel better, I'll do it. That's not going to influence. If you said take two more pills, you'll feel better, I'll do it. I already take so many now, it's like whatever works."
[Most problematic of receiving pills]: "That I have to remember to take them on a schedule and that they sometimes don't seem to work as well as they should be."
"Very important, I would love to reduce those [i.e., number of times you need to take additional pill(s) in a day]*…Yes, because the reducing, yeah. Honestly though, those subcutaneous pump thing, those are brilliant ideas if they work properly. If you have the pump and you still take pills five times a day, that would stink."*
Caregiver support
"I would like if it was less burden to put on my family. I need their help; I hate asking for help."
"Anything to make you feel more independent and a little more freer is always better. You can do things for yourself, so you feel better about yourself."

P35.06

Apomorphine hydrochloride injection (Apokyn®) treatment initiations in the presence and absence of an antiemetic in people with Parkinson disease

Mindy Grall[*1], Cindy Happel[1], Andrea Formella[2]*
[1] Supernus Pharmaceuticals, Inc., Rockville, Maryland, United States
[2] Andrea E. Formella, Senior Director, Scientific Publications, Supernus Pharmaceuticals, Inc., Rockville, MD, United States

Objectives: Review real-world experience initiating apomorphine treatment with or without antiemetic prophylaxis.

Background: Subcutaneous injection of apomorphine hydrochloride (Apokyn®), is an "on-demand" therapy for rapid management of OFF episodes in People with Parkinson Disease (PWP). Pre-treatment with trimethobenzamide (Tigan®) has been recommended practice in the United States (US) to address the risk of nausea and vomiting during apomorphine initiation. However, trimethobenzamide is no longer manufactured in the US, and supplies were generally depleted in the summer of 2021. The product labelling for apomorphine subcutaneous injection was subsequently updated to recognize the ability to start treatment at a lower dose (0.1 mg) without trimethobenzamide. The Clinical Educator Program (CEP) is a comprehensive, company-sponsored support network that provides in-home visits and clinical educator support to PwP prescribed apomorphine therapy.

Methods: The CEP protocol requires clinical educators to schedule a visit with each patient prior to apomorphine initiation and during the post-initiation period. Clinical Educator Time Logs for the initiation of apomorphine injections were collected from the CEP database from 2019 to 2021. Treatment information, including trimethobenzamide use, initial dose of apomorphine, and patient outcomes were evaluated.

Results: Data were available for 1910 unique PwP. Subcutaneous apomorphine was initiated without trimethobenzamide in 32% of new patient starts in 2019 and 2020, increasing to over 80% of new patient starts by October 2021. Conversely, the apomorphine initiation dose did not substantially change across 2019, 2020 and 2021, with 34%, 34%, and 40% of PwP prescribed a 0.1 mg [0.1 mL] starting dose, and 59%, 61%, and 58% prescribed a 0.2 mg [0.2 mL] starting dose, respectively (the remainders initiated at other doses). Lack of trimethobenzamide pre-treatment did not appear to affect the percentage of PwP who discontinued therapy (for any reason) before completing 3 months of treatment (26%, 23%, and 23% in 2019, 2020, and 2021, respectively).

Conclusions: These data provide real-world support for the apomorphine label change, suggesting that patients can successfully initiate apomorphine injection without antiemetic pre-treatment using a 'start low, go slow' flexible titration strategy that is individualized to patient needs and backed by a comprehensive support network.

P35.07

Astrocytic networks as a novel therapeutic target in Parkinson's disease

Nataly Hastings, Saifur Rahman, Przemyslaw Aleksandr Stempor, Wei-Li Kuan, Maha Alfaidi, Matthew Wayland, Aleksandr Zakirov, Michael Whitehead, Mark Kotter*
University of Cambridge, Cambridge, United Kingdom

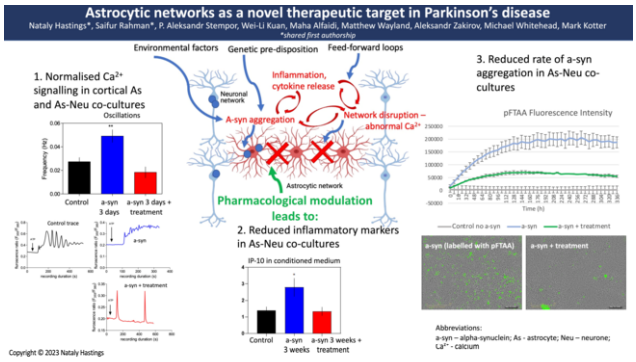
Parkinson's disease (PD) is a neurodegenerative condition with the highest rise in disability and is currently incurable. Dopamine replacement therapies reduce motor symptoms temporarily, but do not address non-motor symptoms (NMS) of PD, and often cause serious side effects; with up to 10 million people with PD worldwide and predicted economic burden of over £79 billion in the US alone by 2037, the unmet clinical need is large. Deeper understanding of PD pathology is required to create new transformative therapies.

One cell type that recently received increased attention in PD is astrocytes. Astrocytes express multiple familial PD-associated genes as much, or more than neurones, and develop alpha-synuclein (a-syn) immunoreactivity in human PD which correlates with dopaminergic loss. Their causal involvement in PD symptom development was demonstrated in vitro and in vivo, where healthy astrocytes could rescue functions of neurones carrying PD mutations and reduce motor symptoms in rodent models, and diseased astrocytes could induce PD-resembling dysfunction in heathy neurones or animals.

A key aspect of astrocyte biology is their ability to form large networks transmitting calcium signals. Abnormal calcium signalling is also a hallmark of PD. We hypothesised that astrocyte networks are dysregulated in PD, and normalising calcium transmission in astrocyte networks could reduce a-syn aggregation and inflammation. Our first target is connexin43 (Cx43) which connects astrocytes via gap junctions (GJs) and promotes calcium transmission.

We found that GJ communication and Cx43 expression were reduced in cultured astrocytes challenged with a-syn and inflammatory cytokines, and Cx43 expression was downregulated in rat models of PD induced by a-syn pre-formed fibril (PFF) injection,

and in human PD. Astrocytes from different brain regions were affected to varied extents. In humans, cortical Cx43 loss showed correlation trends with NMS such as depression. Cx43 downregulation in cultured astrocytes was casually linked to calcium disturbance which resembled that induced by a-syn.
Normalising GJ communication in cultured astrocytes pharmacologically had protective effects including calcium normalisation, reduced a-syn and phospho-a-syn aggregation, and lowered pro-inflammatory cytokine release.
Our results suggest that targeting astrocytic networks is a valuable therapeutic strategy in PD which can supplement dopamine replacement and address NMS and motor symptoms.



P35.08

Personalized dopaminergic treatment in a cohort of Parkinson's disease patients carrying autosomal recessive gene variants

Christos Koros, Athina-Maria Simitsi, Anastasia Bougea, Nikolaos Papagiannakis, Roubina Antonelou, Ioanna Pachi, Athina Zachou, Constantin Potagas, Leonidas Stefanis*
Eginition Hospital, National and Kapodistrian University of Athens, Athens, Greece

Introduction: Parkinson's disease (PD) patients harboring recessive gene variants exhibit a distinct clinical phenotype with an early onset disease and relatively mild symptoms. Previous studies have shown an overall favorable response to Levodopa treatment, however data concerning individualized therapy for autosomal recessive PD forms are still sparse.
Methods: Demographic and treatment data of a cohort of PD carriers of recessive genes (8 homozygous or compound heterozygous PRKN carriers, 5 Heterozygous PRKN carriers and 3 biallelic PINK1 carriers) followed in our Movement Disorders Outpatient clinic were evaluated.
Results: PRKN PD carriers (6M/7F) had an average age 50.4± 10.9, an average age at onset 37.6± 7.6 and disease duration was 14.3± 9.2 years. The average Levodopa Equivalent daily dose (LEDD) was 806.8± 453.5 (range 152-1810). In PINK1 carriers (2M/1F) mean age was 64.7± 11.4, average age at onset 35± 3, disease duration 29.7± 9.5 years and the average LEDD was 765± 96.6 (range 660-850). The majority responded to low/moderate doses of Levodopa and were prone to the development of motor fluctuations and dyskinesias. Nevertheless, certain patients could not tolerate even low Levodopa doses and alternative medication schemes were selected. The response to Dopamine Agonists (DA) was often favorable both as initial and longitudinal therapy, although side effects occasionally arose (7/16 patients needed to discontinue or reduce the dosage of DA due to impulse control disorders or psychiatric manifestations). Rasagiline was also a plausible add-on therapy (5/16). 8/13 PRKN and 1/3 PINK1 carriers were treated with amantadine successfully, and this also applied to patients who could not tolerate Levodopa or DA (Table 1).
Conclusions: In the era of personalized treatment, the therapeutic approach in recessive PD gene carriers might differ as compared to idiopathic PD. Lower LEDD doses were efficient even in patients with a very long disease duration, while a few patients were doing well without any Levodopa treatment decades after disease initiation. DA could be used as a first and main line treatment regimen if well tolerated. It furthermore appears that amantadine represents an attractive therapeutic option in PD with mutations in recessive genes, since it was generally effective and well tolerated.

	Age	Sex	Age at Onset	Duration (years)	H & Y	MMSE	LEDD	L-Dopa	COMT inhibitors	Dopa-agonists	Rasagiline	Amantadine
PRKN [1]	56	F	40	16	2	30	670	150mg	-	Ropinirole 6mg	-	400mg
PRKN [2]	67	F	47	20	3	29	1340	900mg	-	Rotigotine 8mg	-	200mg
PRKN [3]	41	F	29	12	1	30	320	-	-	Ropinirole 6 mg	-	200mg
PRKN [4]	65	F	45	40	3	30	793	250mg	Entacapone 1000mg	Ropinirole 8 mg	1mg	200mg
PRKN [5]	48	M	42	6	2	29	905	600mg	-	Pramipexole 1.05mg	-	200mg
PRKN [6]	66	F	45	21	3	30	320	-	-	Ropinirole 6mg	-	200mg
PRKN [7]	48	M	40	8	1	29	720	200mg	-	Rotigotine 4mg	-	400mg
PRKN [8]	40	F	32	8	2	30	1810	1600mg		Pramipexole 2.1mg	-	-
PRKN [9] (Het)	57	F	44	13	2	29	152	100mg	-	Pramipexole 0.52mg	-	-
PRKN [10] (Het)	35	M	29	6	1	29	660	200mg	-	Ropinirole 8 mg	1mg	200mg
PRKN [11] (Het)	40	M	24	16	2	29	833	350mg	Entacapone 600mg	-	1mg	300mg
PRKN [12] (Het)	42	M	31	11	2	30	705	600mg	-	Pramipexole 1.05mg	-	-
PRKN [13] (Het)	50	M	41	9	2	30	1260	1050mg		Pramipexole 2.1mg	-	-
PINK1 [1]	52	M	32	20	3	29	660	-	-	Ropinirole 8 mg	1mg	400mg
PINK1 [2]	74	F	35	39	2	28	785	500 mg	Entacapone 800mg	Rotigotine 4 mg	-	-
PINK1 [3]	68	M	38	30	2	25	850	750 mg	-	-	1 mg	

P35.09

Summative human factors validation of the foslevodopa/foscarbidopa (ABBV-951) continuous subcutaneous infusion drug delivery system by Parkinson's disease patients, caregivers, and healthcare professionals

Pavnit Kukreja[,1], Ed Halpern[1], Jill M. Giordano Farmer[2], Michael J. Soileau[3], Ji Zhou[1], Amy M. Spiegel[1]*
[1] AbbVie Inc., North Chicago, IL, United States
[2] Global Neurosciences Institute, Pennington, NJ, United States
[3] Texas Movement Disorder Specialists, Georgetown, TX, United States

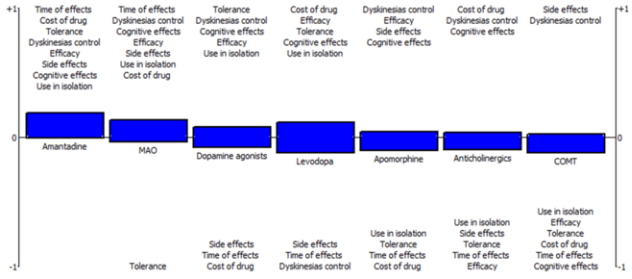
Objective: This human factors (HF) study utilized formative use testing to minimize risk and improve usability as well as a summative study to validate the safe and effective use of the delivery system for foslevodopa/foscarbidopa, an investigational therapy for advanced Parkinson's disease (aPD).
Background: The foslevodopa/foscarbidopa drug delivery system is a drug-device combination in development for motor fluctuation treatment in patients with aPD which delivers 24-hour continuous subcutaneous infusion of foslevodopa/foscarbidopa to the patient. The delivery system's design approach relied upon user-centered HF testing.
Methods: Formative and summative validation testing was conducted with representative intended user populations, including patients with aPD, caregivers, and healthcare professionals (HCPs). The delivery system, instructions for use (IFUs), training guides, and other supporting materials were evaluated, modified, and continually improved through iterative testing to enhance usability and minimize risk of patterns of use errors or compromised medical care. During summative validation testing, participants were assigned an overall performance score of "success" or "failure" for each use scenario, based on whether they could complete critical tasks successfully.
Results: Seven pump-focused formative studies resulted in iterative improvements in IFUs and pump hardware and software. Eight usability tests assessed infusion set and vial adapter usability. A final simulated-use HF summative validation study included 15 aPD patients (age range 47-74 years; 10 males, 5 females), 15

caregivers (30-74 years; 8 males, 7 females), 15 HCP trainers (28-66 years; 13 registered nurses, 2 nurse practitioners), and 15 HCP programmers (27-65 years; 9 pharmacists, 6 neurologists). The number of failures out of tested scenarios was 14/240, 10/240, 13/360, and 5/105 for aPD patients, caregivers, HCP trainers, and HCP programmers, respectively. The failures were further evaluated via a root cause analysis to determine the potential cause of the error, the clinical consequence/potential harms, and the mitigation strategy.
Conclusions: Most users were able to complete the scenarios in the final summative validation study. The summative validation study data suggested the foslevodopa/foscarbidopa delivery system was safe and effective for its intended users, uses, and use environment. However, clarifications were made to the patient IFUs to further improve future user experience.

P35.10

A comparative study for selecting the proper Parkinson's disease medication with Fuzzy PROMETHEE
Ilker Ozsahin[*,1], *Efe Precious Onakpojeruo*[2], *Berna Uzun*[3], *Dilber Uzun Ozsahin*[4], *Tracy Butler*[1]
[1] Weill Cornell Medicine, New York, NY, United States
[2] Near East Unuversity, Nicosia/TRNC, Turkey
[3] Carlos III University of Madrid, Getafe, Spain
[4] University of Sharjah, Sharjah, United Arab Emirates

Parkinson's disease (PD) is the most common cause of parkinsonism, a clinical syndrome of movement problems such as tremors, slowness, and stiffness. Selecting the most appropriate treatment alternative for controlling PD symptoms among currently available ones for the effective management of the disease is essential since no cure for PD exists and it is a neurodegenerative disorder. The currently available treatment methods for PD include medications, surgery, gene therapy, rehabilitation therapy, and focused ultrasound based on the pathologic stage. Considering the first line of treatment of PD is pharmacological therapy, finding the most appropriate medications that can be tailored to each patient's specific needs is crucial. However, for a neurologist, it is important to make the right decision for the benefit of the patients and it is potentially a difficult task to select the appropriate medication among many alternatives with many criteria. The aim of this study is to compare commonly used medications for PD, namely; monoamine oxidase (MAO-B) inhibitors, levodopa, catechol-o-methyltransferase (COMT) inhibitors, amantadine, anticholinergics, dopamine agonists, apomorphine in order to find the most appropriate alternative. Fuzzy preference ranking organization method for enrichment of evaluations (PROMETHEE) which is a multi-criteria decision-making (MCDM) method was used for the evaluation of the medications based on the following criteria; efficacy, tolerance, dyskinesias control, cognitive effects, cost of drugs, time of effect, use in isolation, and side effects. Results showed that amantadine with a net flow of 0.1735 is among the most preferred medication for the general management of PD symptoms, followed by MAO-B with a net flow of 0.0876 and then, dopamine agonist occupied the third position with a net flow of -0.0077. COMT ranked least among the alternatives with a net flow of -0.1043. Figure shows positive and negative aspects of the PD medications. A ranking for the choice of medications for PD was achieved by using a MCDM method. One can easily add more alternatives and criteria and assign weights of each criteria depending on specific patient profile and the physician's opinion.



P35.11

6 years of safinamide in the treatment of Parkinson's disease: Low rate of discontinuation and sparing of dopamine agonists
Anna Planas Ballve[*,1], *Nuria Caballol Pons*[2], *Isabel Gómez-Ruiz*[2], *Marta Balagué Marmaña*[2], *Alex Velazquez*[2], *Xavier Cardona*[3], *Asunción Ávila Rivera*[2]
[1] Complex Hospitalari Moisès Broggi, Barcelona, Spain
[2] Department of Neurology, Complex Hospitalari Moisès Broggi, Sant Joan Despí, Barcelona, Spain
[3] Department of Psyhicatry, Complex Hospitalari Moisès Broggi, Sant Joan Despí, Barcelona, Spain

Safinamide, a reversible monoamine oxidase-B inhibitor and modulator of abnormal glutamate release, was approved in 2016 as an add-on therapy for Parkinson's disease (PD) with motor fluctuations. We aimed to evaluate its effectiveness and discontinuation rate.
PD patients followed in our Movement Disorders Unit who have been treated with Safinamide since 2016 have been evaluated. For each patient, we collected the following clinical data: age, treatment duration, treatment discontinuation, UPDRS-III, Hoehn and Yahr scale (HY), levodopa equivalent daily dose (LED) and LED for dopamine agonists (LED-DA) at the visit when Safinamide was started (V0) and at the last follow-up visit (V1).
180 patients (mean age 72.34+-9.43 years) started safinamide, of which 14 (7.8%) discontinued it after 14.57+-4.44 months due to side effects or lack of efficacy. Among the 166 patients that were still taking Safinamide at the end of the observation (mean follow-up of 38.17+-14.57 months), presented in the V0 and V1: mean UPDRS-III 11.64+-7.34 vs 11.67+-10.14, mean HY 2+-0.6 vs 2+-0.85, mean DEL 364.9+-292.24 vs 509.43+-309.01mg, and mean DEL-AD 74.78+-120.22 vs 78.55+-114.87mg. In addition, after a mean follow-up of 33.37+-19.11 months, 89 patients that were still taking Safinamide, remained with stable doses of levodopa (mean LED in V0 and V1 respectively, 339.82+-262.27 vs 456.87+-293.98mg) and didn't require dopamine agonists.
Safinamide is a drug with a low discontinuation rate (7.80%), which allows us to stabilize the dose of levodopa and spare the use of dopamine agonists.

P35.12

May safinamide have a role in atypical Parkinsonism? A retrospective study in clinical practice
*Fernando Rodríguez Jorge, Paula Pérez Torre, Isabel Pareés Moreno, Jose Luis López Sendón, Samira Fanjul Arbós, Juan Carlos Martínez Castrillo, Araceli Alonso Cánovas**
Hospital Universitario Ramon y Cajal, Madrid, Spain

Background and aims: Safinamide (50-100 mg) has proved efficacy as an add-on treatment to levodopa in fluctuating Parkinson Disease (PD). Atypical parkinsonian syndromes (AP, progressive

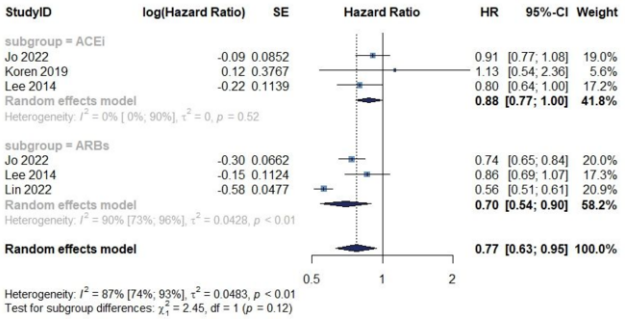
supranuclear palsy, PSP, Multiple System Atrophy, MSA, Corticobasal Syndrome, CBS) have a poor prognosis and lack specific treatment. Drugs approved for PD are commonly used off - label for symptomatic treatment in AP.
Methods: Retrospective study (2016-2020) of electronic records of our Movement Disorders Unit: patients with clinical diagnoses of AP with a safinamide prescription were registered. Clinical Global Impression of Improvement (CGI-I) was used for efficacy assessment.
Results: Twenty six patients, 10 (38%) male, mean 70±10 years, with diagnosis of MSA (14), PSP (11) and CBS (1), and disease duration 7±4 years were prescribed safinamide at 50 mg (1), 100 mg (21) or 200 mg (4). One patient was lost to follow-up before reassessment, and the remaining 26 were followed a mean of 8±9 months afterwards. Eight patients (32%) experienced mild adverse events (drowsiness, confusion, feeling unwell, headache). Nine patients (32%) (6 MSA, 3 PSP, 1 CBS) followed 13±11 months improved with safinamide (CGI-I 1 in 1, 2 in 6, 3 in 3), mainly in mobility (6), falls (5), mood (2), pain (2), sleep (1), dyskinesia (1). Fourteen cases did not improve (11) or minimally worsened (3), leading to discontinuation after 4±4 months.
Conclusion: In our experience with AP syndromes, off-label safinamide treatment was overall well tolerated, and had a clinical benefit in a subset of patients. Clinical trials are warranted to establish efficacy and safety of safinamide in this clinical setting.

P35.13

The impact of RAS inhibition on Parkinson's disease risk in hypertensive patients: A meta-analysis

Youssef Soliman[*,1], Mostafa Hossam[2], Basma Ehab Amer[3], Hadeer Elsaeed AboElfarh[4], Motasem Ayoub[5], Maged Elsayed Mohamed[6], Ahmed Nasr[7], Eman T. Salah[8], Omar Ahmed Abdelwahab[9], Mostafa Meshref[10]*
[1] Faculty of Medicine, Assiut University, Assiut, Egypt
[2] Faculty of Pharmacy Clinical department Alexandria University, Alexandria, Egypt, Alexandria, Egypt
[3] Faculty of Medicine, Benha University, Egypt, Benha, Egypt
[4] Mansoura Manchester Programme for Medical Education, Faculty of Medicine, Mansoura University, Mansoura, Egypt, Mansoura, Egypt
[5] Faculty of Medicine, Hashmite university, Jordan, Zarqa, Jordan
[6] Faculty of Medicine, Zagazig University, Egypt, Zagazig, Egypt
[7] Damietta Faculty of Medicine, Al Azhar university, Egypt, Damietta, Egypt
[8] Biochemistry department, Faculty of Science, Ain Shams University, Cairo, Egypt, Cairo, Egypt
[9] Faculty of Medicine Al-Azhar University, Cairo, Egypt, Cairo, Egypt
[10] Neurology Department, Faculty of Medicine, Al-Azhar university, Cairo, Egypt, Cairo, Egypt

Background: The presence of the renin-angiotensin system (RAS) in the nigrostriatal system has been confirmed in many studies. Animal studies indicated that dopamine depletion was associated with increased NADPH-oxidase complex activity and increased expression of angiotensin I and angiotensin II receptors, which decreased when dopamine levels returned to normal. Multiple clinical studies have examined the role of RAS inhibition in delayed PD progression, but they have conflicting results.
Objectives: Our meta-analysis aims to find whether RAS inhibition is associated with a decreased risk of PD or not.
Methods: We searched Web of Science, Cochrane Central, PubMed, and Scopus for all relevant studies. Our primary outcome is PD risk measuring using hazard ratio (HR). We used a leave-one-out meta-analysis to test the robustness of our evidence. Analysis was done using Rstudio, using the meta package.
Results: Seven studies were included in our study. We found that RAS inhibition led to a statistically significant lower risk of PD development (HR 0.77, 95% CI [0.63, 0.95], p =0.012). Analysis based on the type of RAS inhibitor used revealed that both angiotensin receptor antagonists (ARBs) (HR 0.70, 95% CI [0.54, 0.95], p =0.005) and angiotensin-converting enzyme inhibitors (ACEIs) (HR 0.88, 95% CI [0.7, 1.00], p =0.05) led to a statistically significant lower risk of PD.
Conclusion: Our study is the first meta-analysis to report that RAS inhibition might be associated with delayed PD progression. Therefore, we suggest that RAS inhibitors may be prescribed for hypertensive patients at high risk for PD as a regimen for their hypertension.



P35.14

Improvements in neuronal health by N-cyano pyrrolidine USP30 inhibitors in Parkinson's disease

Elezabeth Stephen[*,1], Fernanda Martins Lopes[2], Emma Green[1], Emma Murphey[3], Franziska Gunther[3], Katherine England[3], John Davis[3], Michael Clague[4], Sylvie Urbé[4], Laura Ferraiuolo[1], Heather Mortiboys[1]*
[1] University of Sheffield, Sheffield, United Kingdom
[2] UOS, Sheffield, United Kingdom
[3] BMS, New Jersey, United States
[4] University of Liverpool, Liverpool, United States

Involvement of mitochondrial defects in the aetiology of Parkinson's is widely accepted, particularly supported by the genetic forms Parkinson's including mutations in PINK1 and PRKN causing early onset Parkinson's. Both PINK1 and parkin are involved in mitophagy. Ubiquitin specific protease 30 (USP30) has been identified localised to mitochondria, with a specific function of inhibiting PINK1-PRKN mediated mitophagy by removing ubiquitin molecules from proteins targeted for degradation, hence this provides a potential therapeutic route to modify mitophagy. In this study, we aimed to investigate the basal levels of USP30 in induced neuronal progenitor (iNPC) derived dopaminergic neurons from patients with LRRK2, PRKN or SNCA mutations, and study the effect of pharmacological inhibition of USP30 on multiple parameters of mitochondrial and neuronal health. We found alterations in basal mitophagy, mitochondrial membrane potential (MMP), and mitochondrial reactive oxygen species (ROS) across the PD patient neurons. We found FT385 and related USP30 inhibitors boosted mitophagy rates across multiple PD patient lines and controls, as well as decreasing mitochondrial ROS levels. These mitophagy specific effects correlated with the specificity of the USP30 inhibitors Strikingly treatment of PD patient-derived neurons with USP30 inhibitor FT385 and related inhibitors also showed a significant improvement in neuronal morphology but this did not correlate with USP30 activity. We further investigated if the effects on neuronal morphology were being modulated by transcriptional changes in particular neuronal morphology

transcripts. We observed changes in NRP1 associated with compound treatment which could partially explain these neuronal morphology effects. These data suggest the USP30 inhibitors based on N-cyano pyrrolidine chemistry can increase mitophagy and cause improvements to neuronal morphology via mechanisms that are both dependent on and independent of USP30 inhibition.

P35.15

Passive immunization reduces propagation of alpha-synuclein pathology along gut-brain axis

Vasileios Theologidis[*,1], Jonas Folke[2], Tomasz Brudek[2], Richard Dodel[3], Alexander Ross[3], Hjalte Gram[4], Poul Henning Jensen[4], Per Borghammer[1], Nathalie Van Den Berge[1]*
[1] Department of Clinical Medicine, Aarhus University and Department of Nuclear Medicine and PET, Aarhus University Hospital, Aarhus, Denmark
[2] Centre for Neuroscience & Stereology and Copenhagen Center for Translational Research, Bispebjerg and Frederiksberg Hospital, Copenhagen University Hospital, Copenhagen, Denmark
[3] Chair of Geriatric Medicine, University Hospital Essen, Essen, Germany
[4] DANDRITE-Danish Research Institute of Translational Neuroscience and Department of Biomedicine, Aarhus University, Aarhus, Denmark

Parkinson's disease (PD) is characterized by spreading of pathogenic forms of the alpha-synuclein (asyn) protein, affecting multiple organs along the gut-brain axis. Beside a damaged brain, PD patients exhibit extensive nerve damage in peripheral organs, such as the heart and gut, causing debilitating non-motor symptoms up to 20 years before the onset of motor symptoms. Recent data suggest the existence of two PD subtypes: a body-first type, where damage to the cardiac and enteric nervous system precedes brain damage, and a brain-first type where neuronal loss in the brain precedes nerve damage to other organs. To date, no cure is available for PD and therapy is limited to symptomatic treatment of motor and non-motor symptoms. Recent advances in immunotherapy that target pathogenic asyn show great potential to block disease progression in patients with early stage 'body-first' PD. These patients have limited damage in the brain, and effective immunization could potentially stop disease progression by blocking the spread of misfolded asyn from peripheral organs to the brain.
Here, we use our established body-first PD animal model to investigate treatment efficacy of passive immunization to delay the stereotypic disease progression in 20-month-old wild-type mice. The initiation of PD in the gut of mice is achieved by injection of fibrillar asyn in the upper duodenum. The immunization is achieved by the administration of naturally occurring anti-asyn-antibodies (nAbs). The anti-asyn nAbs, or human albumin control treatment (high dose 10mg/kg, low dose 2.5 mg/kg), are administered i.p. once per week for 6 weeks. After euthanization, the brain and stomach are stained against phosphorylated and oligomeric asyn.
We observe reduced levels of pathogenic asyn in the dorsal motor nucleus of the vagus nerve and stomach of nAbs-treated mice, compared to control-treated mice.
Our preliminary results indicate that anti-asyn nAbs-treatment can effectively restrict both retro- and anterograde propagation of pathology along the gut-brain axis. Future validation studies should investigate long-term effect of nAbs-treatment on pathology, neurodegeneration and symptoms in our model. Positive results would contribute substantially to our knowledge of how to design human PD trials to increase treatment efficacy and may ultimately lead to a cure for early body-first PD patients.

CLINICAL SCIENCE: Surgical therapy, including cell and gene therapy

P36.02

Long-term motor outcomes of deep brain stimulation of the globus pallidus interna in Parkinson's disease patients: Five-year follow-up

Sun Ju Chung[*,1], Sungyang Jo[1], Seung Hyun Lee[1], Mi-Sun Klm[1], Yun Su Hwang[2]*
[1] Asan Medical Center, Seoul, South Korea
[2] Jeonbuk National University Medical School and Hospital, Jeonju, South Korea

Background: Deep brain stimulation (DBS) of globus pallidus interna (GPi) is an established treatment for advanced Parkinson's disease (PD). However, in contrast to subthalamic nucleus (STN)-DBS, long-term outcomes of GPi-DBS have rarely been studied.
Objective: We investigated the long-term motor outcomes in PD patients at 5 years after GPi-DBS.
Methods: We retrospectively analyzed the clinical data for PD patients who underwent GPi-DBS. Longitudinal changes of UPDRS scores from baseline to 5 years after surgery were assessed.
Results: Forty PD patients with a mean age of 59.5 ± 7.9 years at DBS surgery (mean duration of PD: 11.4 ± 3.4 years) were included at baseline and 25 patients were included in 5-year evaluation after DBS. Compared to baseline, sub-scores for tremor, levodopa-induced dyskinesia (LID), and motor fluctuation indicated improved states up to 5 years after surgery ($p < 0.001$). However, UPDRS Part 3 total score and sub-score for postural instability and gait disturbance (PIGD) gradually worsened over time until 5 years after surgery ($p > 0.017$ after Bonferroni correction). In a logistic regression model, only preoperative levodopa response was associated with the long-term benefits on UPDRS Part 3 total score and PIGD sub-score (OR = 1.20; 95% CI = 1.04–1.39; $p = 0.015$ and OR = 4.99; 95% CI = 1.39–17.89; $p = 0.014$, respectively).
Conclusions: GPi-DBS provides long-term beneficial effects against tremor, motor fluctuation and LID, but PIGD symptoms gradually worsen. This selective long-term benefit has implications for the optimal application of DBS in PD patients.

P36.03

Accuracy of the Guide ™ XT to determine the electrodes position according to the clinical outcome after subthalamic nucleus deep brain stimulation in patients with Parkinson's disease

Kirsys Del Giudice, Almudena Sánchez-Gómez, Pedro Roldán, Jordi Rumià, Esteban Muñoz, Ana Cámara, Francesc Valldeoriola*
Hospital Clinic of Barcelona, Barcelona, Spain

Introduction: STN-DBS is a well defined treatment for PD. The effectiveness of this therapy depends on several factors, especially on the correct anatomical position of the electrodes. Suboptimal placement can lead to propagation of the current into undesired pathways resulting in side effects and suboptimal antiparkinsonian effect. The Guide ™ XT is a visualization software that generates a postoperative model of the electrodes within the brain, by an automatic detection algorithm that allows a visualization of leads location within the target.
Objective: The aim of this study was to determine the accuracy of the GUIDE ™ XT to establish the anatomical position of the placed electrodes, based on the clinical outcome and side effects in patients with PD who underwent STN-DBS, and its utility in clinical practice.

Material and methods: Retrospective study of patients with PD diagnosis implanted with a STN-DBS system at the Hospital Clinic of Barcelona. Clinical assessment included the MDS-UPDRS III, PDQ 39, and LEDD. Stimulation was initiated one week postoperative. Standard monopolar review was performed in successive sessions, the appearance of immediate current related side effects was evaluated. The symptom control was tested on every contact and documented. In all patients, GUIDE ™ XT was used to evaluate the electrodes position.
Results: Nine patients with PD were included (age range 53 to 69 years and disease duration mean 10 years). All patients improved in the MDS-UPDRS III, QoL, and LEDD was reduced. We found a correlation between the electrodes position assessed by GUIDE ™ XT and the clinical outcome and side effects expected by anatomical relationship. Nine patients and eighteen electrodes were evaluated, we evidenced a clinical correlation between adverse effects and location in 14 electrodes (88.8%). Two electrodes were repositioned, only one of them (50%) correlated with the clinical outcome.
Conclusions: The GUIDE ™ XT software is an effective tool in clinical practice to evaluate the position of the DBS electrodes as it shows a very good correlation with clinical outcome and side effects related to stimulation. The use of this software can increase the confidence in DBS programming for a better outcome of patients.

Table. Lead position and side effects.

Patient	Side	Lead Position	Immediate side effects	Correlation between electrodes position and side effects	Clinical usefulness
1	Right	V	None	Yes	Confirm location
2	Left	O	Dyskinesias	Yes	Confirm location
	Right	L	Facial tightness	Yes	Direct current
3	Left	O	None	Yes	Confirm location
	Right	L	Facial muscle contractions	Yes	Direct current
4	Left	M	Dizziness	Yes	Confirm location
	Right	O	Dyskinesias	Yes	Confirm location
5	Left	O	Transient paresthesias	Yes	Confirm location
	Right	VP	Left hemicraneal stabbing sensation	Yes	Confirm location
6 -First intervention	Left	V	Mild dyskinesias	Yes	Confirm location
	Right	V	Facial tightness	No	Reposition
	Left	VL	Facial muscle contractions, dysarthria	Yes	Reposition
6 -Second intervention	Right	M	Facial tightness	No	Confirm location
	Left	M	None	Yes	Confirm location
7	Right	O	Transient paresthesias	Yes	Confirm location
	Left	O	Transient paresthesias	Yes	Confirm location
8	Right	O	Dyskinesias	Yes	Confirm location
	Left	O	None	Yes	Confirm location
9	Right	O	Mild dysarthria, muscular contractions left arm	No	No reposition
	Left	O	None	Yes	Confirm location

Abbreviations: O: optimal; M: medial; L: lateral; V: ventral; VP: ventral-posterior; VL: ventral-lateral.

P36.04

Enhanced differentiation of human induced pluripotent stem cells towards the midbrain dopaminergic neuron lineage both in vitro and in vivo through GLYPICAN-4 down regulation
Serena Corti[1], Remi Bonjean[1], Thomas Legier[1], Diane Rattier[1], Christophe Melon[1], Pascal Salin[1], Lydia Kerkerian-Le Goff[1], Rosanna Dono[,2]*
[1] Aix Marseille Univ, CNRS, IBDM, Turing Center for Living Systems, NeuroMarseille, Marseille, France
[2] DEVELOPMENTAL BIOLOGY INSTITUTE OF MARSEILLE (IBDM), Marseille, France

Enhancing the differentiation potential of human induced pluripotent stem cells (hiPSC) into disease-relevant cell types is instrumental for their widespread application in medicine. We have show that hiPSCs down regulated for the signaling modulator GLYPICAN-4 (GPC4) acquire a new biological state characterized by increased hiPSC differentiation capabilities towards ventral midbrain dopaminergic (VMDA) neuron progenitors. This biological trait emerges both in vitro, upon exposing cells to VMDA neuronal differentiation signals, and in vivo, even when transplanting hiPSCs at the extreme conditions of floor-plate stage in rat brains. Moreover, it is compatible with the overall neuronal maturation process towards acquisition of substantia nigra neuron identity. Of note, hiPSCs with down regulated GPC4 retain self-renewal and pluripotency in stemness conditions, in vitro, while losing tumorigenesis in vivo as assessed by flank xenografts. To investigate the functional relevance of these findings for Parkinson's disease (PD) therapy, we transplanted control and hiPSCs with down regulated GPC4 in the brains of rat models for PD following a short period of in vitro differentiation until the floor-plate stage. Immunohistochemistry of dissected brains indicated that hiPSCs with reduced GPC4 levels generate grafts with higher density of VMDA neurons in comparison to control cells. Interestingly, VMDA neurons with reduced GPC4 levels can establish graft host interactions as highlighted by retrograde transneuronal transport of rabies virus experiments. Finally, these findings correlated with a more efficient motor recovery of PD rats of transplanted with hiPSCs with reduced GPC4 levels versus controls. Taken together, our results highlight GPC4 down-regulation as a powerful approach to enhance generation of functional VMDA neurons both in vitro and in vivo. Outcomes may contribute to establish hiPSC lines suitable for translational applications.

P36.05

Improvement in quality-of-life and motor function during daily clinical practice using a directional DBS system
Jan Vesper[,1], Heleen Scholtes[2], Roshini Jain[3], Lilly Chen[3], Michael Barbe[4], Steffen Paschen[5], Andrea Kühn[6], Chong Sik Lee[7], Jens Volkmann[8], Günther Deuschl[5]*
[1] Heinrich Heine University, Düsseldorf Germany
[2] Boston Scientific Neuromodulation, Kerkrade, Netherlands
[3] Boston Scientific Neuromodulation, Valencia, CA, United States
[4] University Hospital Cologne, Cologne, Germany
[5] University Hospital Schleswig-Holstein, Kiel, Germany
[6] Charité-Universitätsmedizin Berlin, Berlin, Germany
[7] Asan Medical Center, University of Ulsan College of Medicine, Seoul, South Korea
[8] University Hospital Würzburg, Würzburg, Germany

Introduction: The main goal of Deep Brain Stimulation (DBS) therapy is to achieve optimal outcomes while avoiding side effects. The challenging anatomy surrounding DBS targets requires precise control of neurostimulation. Directional DBS systems can deliver specific amounts of current to each contact using Multiple

Independent Current Control (MICC), and this capability has been shown to increase therapeutic window under controlled study conditions. In so doing, vertical and horizontal steering of cathodic and/or anodic current can be achieved, thereby providing flexible programming options to deliver stimulation while minimizing side effects.
Methods: This is a prospective, multicenter (International), registry of up to 1500-patients implanted with directional MICC-based DBS systems (Vercise, Boston Scientific), per standard-of-care. Participants are being followed up to 3-years post- implantation whereby quality-of-life, motor symptoms improvement, overall satisfaction, and other disease aspects are measured. Adverse events and device-related complications are collected.
Results: A total of 815-patients have been evaluated. Quality-of-life as assessed by PDQ-39 out to 2-years demonstrated sustained clinically significant improvement (minimal clinically important difference [MCID] >4.7-points) despite an expected 5-point worsening due to disease progression ($p<0.001$). Improvement in motor function (MDS-UPDRS III Meds-OFF) versus baseline were also noted (35% reduction at 2-year; $p< 0.0001$). To date, with >1500 directional leads implanted, no lead breakages have been reported.
Conclusion: This on-going registry represents the first large-scale collection of real-world, long-term outcomes using MICC-based directional DBS systems. Use of directional DBS systems in clinical practice has been demonstrated to be beneficial per increases in therapeutic window and associated positive outcomes. Results from this on-going evaluation demonstrate sustained improvement in overall outcomes with the use of directional DBS systems.

P36.06

Real-world outcomes in USA using DBS systems with directionality and multiple independent current control
Michael Okun[*,1], Kelly Foote[1], Theresa Zesiewicz[2], Yarema Bezchlibnyk[2], Alexander Papanastassiou[3], Juan Ramirez-Castaneda[3], Jonathan Carlson[4], Jason Aldred[5], Vibhor Krishna[6], Aristide Merola[6], Corneliu Luca[7], Jonathan Jagid[7], Jennifer Durphy[8], Leo Verhagen-Metman[9], Sepehr Sani[9], Stephen Ojemann[10], Drew Kern[10], David Weintraub[11], Ritesh Ramdhani[11], Abdolreza Siadati[12], Bharathy Sundaram[12], Cong Zhao[13], Derek Martinez[13], Mustafa Siddiqui[14], Roshini Jain[15]*
[1] University of Florida – Normal Fixel Institute for Neurological Diseases, Gainesville, FL, United States
[2] University of South Florida, Tampa, FL, United States
[3] University of Texas, San Antonio, TX, United States
[4] Inland Neurosurgery and Spine, Spokane, WA, United States
[5] Selkirk Neurology, Spokane, WA, United States
[6] Ohio State University, Columbus, OH, United States
[7] University of Miami School of Medicine, Miami, FL, United States
[8] Albany Medical Center, Albany, NY, United States
[9] Rush University Medical Center, Chicago, IL, United States
[10] University of Colorado Anschutz Medical Campus, Aurora, CO, United States
[11] Northwell Health, New York City, NY, United States
[12] Texas Institute for Neurological Disorders, Sherman, TX, United States
[13] St. Luke's Regional Medical Center, Boise, ID, United States
[14] Wake Forest University, Winston-Salem, NC, United States
[15] Boston Scientific Neuromodulation, Valencia, CA, United States

Introduction: Randomized controlled trials have demonstrated that Deep Brain Stimulation (DBS) can be an effective strategy for reducing the motor complications in Parkinson's disease (PD) with potential for sustained improvement greater than 10-years. However, large, multi-center, real-world data can reveal insights in the care of PD patients when DBS is used per standard-of- care. In this study, we report real-world data (USA experience) with the use of directional DBS systems with multiple-independent current control (MICC) in the treatment of Parkinson's Disease (PD).
Methods: Prospectively enrolled participants are implanted with Vercise DBS systems (Boston Scientific), a multiple- source, constant-current system, and are assessed up to 3-years post-implantation. Clinical measures recorded at baseline and during study follow-up include MDS-Unified Parkinson's disease Rating Scale (MDS- UPDRS), Parkinson's Disease Questionnaire (PDQ-39), Global Impression of Change (GIC), and Non-Motor Symptom Assessment Scale (NMSS). Adverse events and device-related complications are also collected.
Results: A total of 111-patients (mean age: 64.1 ± 8.7 years, 73% male, disease duration 9.7-years) have been enrolled, and 93 have had their device activated. At 6-months ($n = 56$), an 8.4-point improvement in PDQ-39 Summary Index (25.8 to 18.0, $p<0.0001$) was noted, thereby representing a clinically significant improvement in quality of life (minimal clinically important difference, MCID >4.7-points). According to GIC, over 98% of patients and over 95% of clinicians reported improvement at 6-months. No lead breakage or unanticipated adverse events reported.
Conclusion: Real-world outcomes from this large, prospective, multi-center outcomes study demonstrate improvement in quality of life following DBS, and a high global impression of improvement among patients and clinicians. Data from this study will continue to provide insight regarding the application of the MICC-based directional DBS Systems for PD in clinical practice.

P36.07

Motor function and quality-of-life improvement following asleep versus awake deep brain stimulation (DBS) procedures
Jan Vesper[*,1], Günther Deuschl[2], Lilly Chen[3], Roshini Jain[3]*
[1] Heinrich Heine University Düsseldorf, Düsseldorf, Germany
[2] University Hospital Schleswig-Holstein, Kiel, Germany
[3] Boston Scientific Neuromodulation, Valencia, CA, United States

Introduction: Deep Brain Stimulation (DBS) procedures are typically conducted with patients being awake to allow for intraoperative clinical testing and/or micro-electrode recording to confirm lead location. However, asleep DBS procedures (i.e., under general anesthesia) are becoming increasingly popular due, at least in part, to technological improvements in imaging allowing alternative lead placement confirmation and shorter procedure duration. Here, we report real-world outcomes in patients with Parkinson's disease (PD) whose DBS leads were implanted using asleep procedures versus those patients that underwent the procedure using awake conditions.
Methods: A sub-analysis of patients receiving their DBS lead implant under asleep versus awake conditions was conducted in an ongoing, large, multicenter, prospective real-world outcomes study (Vercise, Boston Scientific). Motor function (MDS- UDPRS III), quality of life (PDQ-39) and related outcomes (GIC) were collected at baseline and up to 3-years. Safety events were also collected.
Results: To date, 157 patients (mean age 61.2±8.3 years; 69% male) were asleep and 433 (mean age 60.1±8.5 years; 66% male) were awake during lead placement. Patients in both groups presented with similar baseline age, duration of disease and disease state. Improvement in quality-of-life was noted in both groups with a 5.3- point improvement ($n = 104$) in asleep group and a 4.5-point improvement ($n = 319$) in awake group at 1-year. Similarly, an 18.8- and 20.9-point improvement in motor function was noted in the asleep and awake groups, respectively.
Conclusions: Outcomes from this large dataset of real-world outcomes examining the outcomes following asleep versus awake DBS demonstrate an alignment with results from previous studies. Patient outcomes show little to no difference between awake versus

asleep groups. Sleep DBS procedures may offer potential for shortening the total time taken for DBS procedures and offer a viable alternative for patients.

P36.08

Evidence-based correlates and predictors of medication reduction after DBS in PD

Jim Kirk[*1], Arthur Berg[2], Michele York[3], Jason Schwalb[4], Mustafa Siddiqui[5], Jim McInerney[2], Joohi Jimenez-Shahed[6]*
[1] Patient advocate, Boston, MA, United States
[2] Penn State College of Medicine, Hershey, PA, United States
[3] Baylor College of Medicine, Houston, TX, United States
[4] Henry Ford Health, Detroit, MI, United States
[5] Wake Forest University School of Medicine, Winston-Salem, NC, United States
[6] Icahn School of Medicine at Mount Sinai, New York, NY, United States

Objective: To explore predictors and correlates of LEDD reduction after DBS in a multi-center real-word registry of PD patients undergoing DBS.
Methods: RAD-PD systematically characterizes PD patients undergoing DBS through patient-reported outcomes and clinician-administered scales assessing disease features, medical/surgical treatments, motor/non-motor symptoms, quality of life, social determinants of health, stimulation parameters, and adverse effects. We analyzed 6-month outcomes according to LEDD change (decreased <75%/remained stable, decreased >/=75%, and increased LEDD). DBS outcomes, correlates of LEDD change at 6mos and predictors of LEDD change were investigated.
Results: Amongst N=32 with 6mo outcomes (N=29 STN, N=3 GPi), mean baseline LEDD=1268mg (SD 659.7) and mean 6mo LEDD reduction = 565mg (SD 855). 27/32 (84.4%) had reduced/unchanged LEDD at 6mos, of which N=10 (37.0%) reduced >/=75% [mean reduction 87% (SD 8%)] and N=17 (62.9%) reduced <75%/remained stable [mean reduction 27% (SD 21%)]. 5/32 (15.6%) increased LEDD by mean 200% (SD 147%). 6mos post-DBS, MDS-UDPRS part 3, EQ5D, PDQ39 summary index, MDS-UPDRS part 2, BDI, GAD-7, and NMSS significantly improved amongst all patients (Exact Wilcoxon signed rank test, $p<0.05$). When analyzed by degree of LEDD change, there were no statistically significant differences in PD motor phenotype or DBS target, but those who increased LEDD had significantly lower baseline LEDD (Table 1). Those who reduced LEDD>75% had significantly greater reductions in MDS-UPDRS 2, MoCA, and GAD-7 (Fisher's exact test, Kruskal-Wallis rank sum test, Table 1). Correlates of LEDD change at 6mos included starting amantadine after DBS, and the %changes in MDS-UPDRS 3 OFF, PDQ39 summary index, MDS-UPDRS 2, GAD-7, and NMSS (linear regression, $p<0.05$). Amongst pre-op features, only baseline MoCA correlated with LEDD change ($p=0.02$) at 6mos. Patient satisfaction and QoL at 6mos were not influenced by LEDD change.
Conclusions: A majority of patients reduced their LEDD 6mos after DBS with 31% reducing >/=75%, and 15% increasing. Motor phenotype and DBS target did not influence LEDD change. Those who increased had lower baseline LEDD but no clear baseline predictors of LEDD change were found. LEDD change at 6mos correlates with multiple motor and non-motor improvements, but does not influence patient satisfaction or quality of life. Long term follow-up and imaging are required.

Table 1. Treatment features and outcomes at 6mos according to LEDD change

	All (n=32)	Reduced LEDD >75% (N=10)	Reduced LEDD <75% or stayed stable (N=17)	Increased LEDD (N=5)	Significance (Fisher's exact test, Kruskal-Wallis rank sum test)
LEDD at baseline	1268 SD 659.6	1555 SD 756.7	1347 SD 467.4	425 SD 296.6	0.004
Mean change in LEDD at 6mos	-565 SD 855	-1397 SD 812	-405 SD 422	555 SD 270	<0.001
Phenotype at baseline	19 TD 1 intermed 12 PIGD	7 TD 1 intermed 2 PIGD	9 TD 0 interemed 8 PIGD	3 TD 0 intermed 2 PIGD	0.5
Mean % improvement in MDS-UPDRS III (pre-op OFF meds to 6mos OFF meds/ON stim)	36% SD 38	53% SD 27	30% SD 36	21% SD 58	0.3
Mean change NeuroQOL Ability	46% SD 88	64% SD 73	47% SD 103%	8% SD 60	0.3
Mean change EQ-5D VAS	18% SD 32	9% SD 28	25% SD 36	8% SD 20	0.7
Mean change PDQ-39 Summary Index	-30% SD 78	-50% SD 36	-45% SD 35	55% SD 162	0.11
Mean change Lawton IADL	3% SD 23	11% SD 25	1% SD 24	-5% SD 7	0.3
Mean change MDS-UPDRS II	-31% SD 40	-64% SD 28	-20% SD 36	-4% SD 40%	0.004
Mean change MoCA	1% SD 19	-9% SD 6	6% SD 23	5% SD 17	0.019
Mean change BDI-II	-26% SD 96	-66% SD 38	1% SD 119	-40% SD 61	0.2
Mean change GAD-7	-49% SD 53	-81% SD 34	-31% SD 46	-17% SD 118	0.053
Mean change NMSS	-16% SD 83	-50% SD 36	-14% SD 76	46% SD 141	0.2
Mean change QUIP-RS	3% SD 129	-38% SD 61	19% SD 160	56% SD 135	0.4
# NASS satisfaction scale score 1/2	23/9	9/1	12/5	2/3	0.13

P36.09

Effectiveness of lead-point using combined imaging driven by computed axial tomography and mer for targeting stn-dbs in Parkinson's

*Neerati Lavanya**
Osmania University, Hyderabad, Telangana, India

Combined MR imaging procedures led by stereotactic computed axial tomography(CAT) and micro electrode recording(MER) are largely applied to aim at subthalamic-nucleus(STN). But constantly MRI is not open. Therefore, goal of this study is to determine effectiveness of lead-point with STN-DBS by applying frame-based stereotactic CAT through MER driven, and whether targeting of STN in advanced idiopathic Parkinson's disease patients ("through ancillary or auxiliary") is effective or not.
34Parkinson disease patients enrolled and underwent DBS surgery. The patients are screened by the subjective method of Unified Parkinson's Disease Rating (stage-III) Scale score >5 and more clinical/ and/or diagnostic-profiles peri plus post operatively. The parallel plane and perpendicular spaces amid the center-point (mid-point) of the frame to the head, the brains mid-line on the (by the side of) level-of septum—pellucidum and higher edge-of the consensual (two-sided bilateral) lens, correspondingly. The CAT imaging is well-defined as the parallel-plane and perpendicular divergences, over the tinny bit of PD brain.
Results: Following the DBS surgical procedure, the Parkinson`s diseased patients UPDR (stage III) scale scores are progressed 48%±2.8% by ranging 20%-80% equated to patients' standard L-dopa "OFF" scores. There is no surgical difficulty aroused or provoked. The mean recorded difference in length of the subthalamic-nuclei amongst the primary and last mono micro electrode recording trajectory—paths are5.4±0.2mm ranging4.00–7.50. On application of multi regression-techniques it has shown

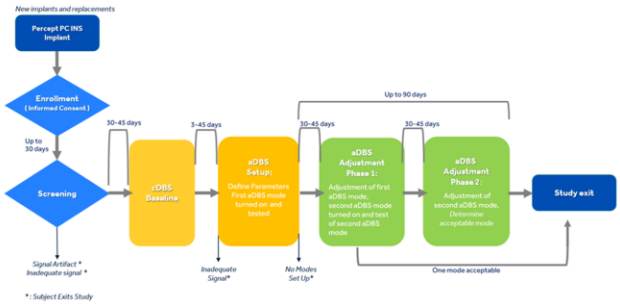
that the augmented measurements of the perpendicular, the regression-techniques coefficient B is−0.0635;i.e.,95% confidence-interval(CI) is −0.113and to−0.013) also parallel-plane differences are B is−0.0586 and the confidence-intervals95%, i.e.,−0.083 and to−0.017 are linked through a smaller amount of increase in the subjectiveUPDRS (stage-III) scaling scores.
Conclusion: Findings proved that the ancillary aiming of the subcortical STN intended for deep brain stimulation implantation of the electrode by applying the stereotactic computed-axial-tomography (frame-based CAT machine) as well as micro electrode recording direction in subjects with progressive idiopathic Parkinson disease(PD) is active and efficacious effectual as well as innocuous. Superior equilibrium or proportion of fixing the stereotactic-frame to the Parkinson head ensued in improved results of the subthalamic-nuclei DBS in Parkinson's diseased-patients, specifically while the parallel-plane difference is 2millimeter or a smaller amount plus the perpendicular aberration was 1millimeter or a smaller amount.

P36.10

Acceptability of adaptive deep brain stimulation for Parkinson's disease

Asuka Nakajima[*,1], Genko Oyama[2], Yasushi Shimo[1], Hikaru Kamo[2], Atsushi Umemura[3], Hirokazu Iwamuro[3], Yuta Sekiguchi[4], Ayumi Tsuchiya[4], Thomas C. Brionne[5], Kate Noel[5], Nobutaka Hattori[2]*
[1] Dept of Neurology, Juntendo University Nerima Hospital, Tokyo, Japan
[2] Dept of Neurology, Juntendo University Hospital, Tokyo, Japan
[3] Dept of Neurosurgery, Juntendo University Hospital, Tokyo, Japan
[4] Medtronic Japan, Tokyo, Japan
[5] Brain Modulation, Medtronic, Minneapolis and Tolochenaz, United States

Introduction: Adaptive Deep Brain Stimulation (aDBS) for Parkinson's Disease (PD) consists in adjusting stimulation amplitude based on local field potential (LFP) power. aDBS was released in Japan with two modes: dual-threshold mode, which adapts stimulation amplitude to maintain the LFP power between an upper and a lower threshold; and single-threshold mode, which adapts stimulation amplitude when the LFP power exceeds one threshold. The aim of the Early Adapter Part 1 (EA1) study was to characterize the proportion of subjects for whom at least one aDBS mode was acceptable to the subject.
Methods: EA1 was a prospective, open-label, observational, dual-center, post-market cohort study. Inclusion criteria included diagnosis of PD with motor impairment, implantation with Percept™ PC neurostimulator (Medtronic), stable continuous bilateral stimulation (cDBS) in the subthalamic nucleus and stable medications (see schematic).
Acceptability of an aDBS mode was determined using the Global Impression of Change (GIC) score and defined as aDBS efficacy greater than or equal to cDBS efficacy with minimal side effects.
Results: Twelve PD subjects (mean [sd]: 66.8 [7.36]yo, years with PD 12.5 [4.21], 5 women) were enrolled. All had at least one aDBS mode that was acceptable (see tables; blue: acceptable, red: unacceptable). Dual-threshold was acceptable in 12/12 (100%) subjects, single-threshold was acceptable in 10/10 (100%) subjects (2 subjects failed to set-up single-threshold). Compared to single-threshold mode, dual-threshold mode was preferred by a majority of subjects (9/12, 75%), perceived as best controlling disease-related symptoms (8/12, 66.7%) and resulting in the least number of side effects (8/12, 66.7%). There were no serious adverse events, and one adverse event of dyskinesia. Further analysis of clinical outcomes will be presented.
Conclusion: All subjects tolerated at least one mode of aDBS, most tolerated both, with a preference towards dual-threshold. Further research is ongoing to characterize the patients with PD who will benefit most from aDBS.
Disclosures: The study was sponsored by Medtronic. Yuta Sekiguchi, Ayumi Tsuchiya, Kate Noel & Thomas C. Brionne are employees of Medtronic.



P36.11

High-density noninvasive wired and wireless EEG electrodes and minimally invasive DBS in Parkinson's: A study with microelectrode recording

*Venkateshwarla Rama Raju**
CMR College of Engineering & Technology, jawaharlal Nehru Tehnological University, Hyderabad, Telangana, India

The aim is to divulge the effect of aging on β-oscillations and other oscillatory patterns in rest and movement, both at the cortical and sub cortical level. So, we aim to provide independent neuro physiological markers (the neural – neuronal biomarkers) that predict disease progression autonomously from calendar age. With the aging of our population the number of brain diseases and hence disorders is increasing rapidly, the number of patients with Parkinson's Disease grows even faster. Aging and PD both alter the electro physiological signature of the brain. In PD, beta (β) oscillations activity is measured as a neuronal biomarker that correlates with motor impairment, however β-oscillations may not occur or might not be generated in every PD subject. While PD is a persistent progressive disorder, the greatest significant factor of clinical progression is advancing age rather than disease duration. We hypothesize that the effects of the disease process and aging on electrophysiological activity, especially on β-activity, involve a biological-interaction.
We plan to unify EEG electrodes with minimally DBS electrodes. The MER signals of STN neural recordings will be conducted at rest and during a simple and elegant motor task. Individuals with PD and controls will be recruited for this study. We will blend HD-EEG and minimally invasive HD-DBS-electrode preops and all over time using innovative DBS system in PD patients undergoing surgery). Sample recordings will be acquired and repeated later two years of the study effects overall time. Though maximum clinical experiments in PD do not take the scale (diversity) of dissimilar age groups into account, this study purposely focusses on individuals with distinct age.
The unification of non-invasive and minimally invasive techniques will give unique insights on the changes in the neural web linked to ageing. The impact of aging on β-oscillations activity and other oscillatory patterns in rest and movement will be shown in normal aging and in Parkinson`s. Also, we will define if the neuro physiological changes occur at the cortical STN level. Initial results in Figures.
The neural/neuronal bio markers offered are potentially helpful in-patient counseling and therapeutic choices made.

Figures and Tables

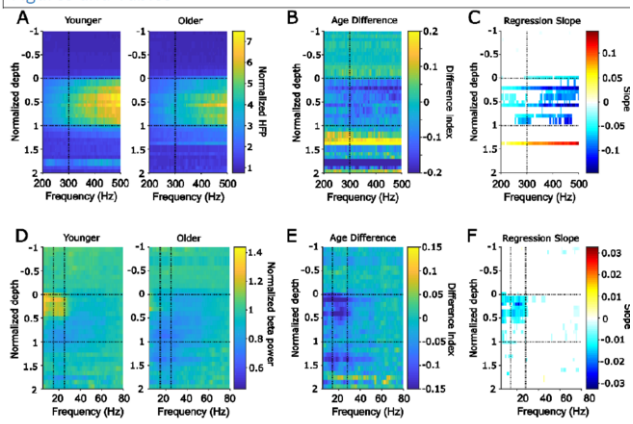


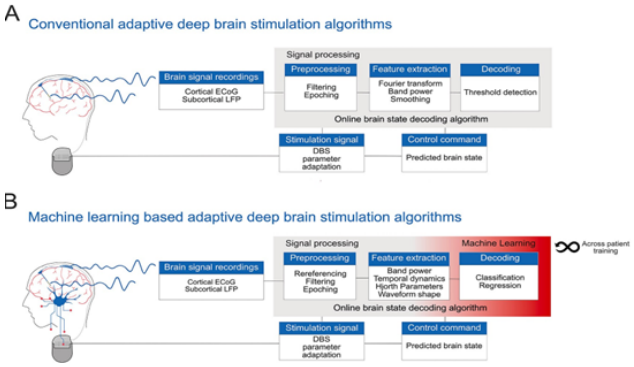
Figure 1. *Spectral analysis of age and depth differences in HFP (upper row) and Beta power (lower row) across the STN.* ***A)*** *mean depth-frequency power plot for younger (<median age) and older (>median) patients. Horizontal dashed lines represent dorsal boarder and ventral STN boarders. Vertical dashed line indicates lower cutoff for calculating HFP.* ***B)*** *difference index between groups, negative values indicate higher power in older patients.* ***C)*** *Age-power regression slope. Colored regions represent significant clusters (permutation test), negative values represent dropping power with age. White indicates non-significant regression.* ***D-F)*** *Spectral analysis for beta power. Conventions as in A-C, vertical dashed lines indicate beta band.*

P36.12

Refined cutting-edge adaptive closed loop smart deep brain stimulation in Parkinson's: A study with progressive machine learning decryption techniques

*Venkateshwarla Rama Raju**
CMR College of Engineering & Technology, jawaharlal Nehru Tehnological University, Hyderabad, Telangana, India

Background: Neuroprotection is the biggest issue and new frontier in Parkinson disease (PD) and movement disorders research and therapy which needs to be addressed.
This work addresses on the role of innovative closed loop smart adaptive deep brain stimulation (ACL-sDBS) system identification methods used to address the problems and focused on the development of tools-utilities and techniques for PD analysis. Detecting supported implantable devices and next generation vanguard neuro technology allow real-time adjustments of marginally invasive neuromodulation automatically without human intervention.
Objective: The characterization of signs, symptoms and feature manifestations and disease-specific bio markers (neural or neuronal-markers) in minimally invasive brain signal micro electrode recordings (MER) has motivated the notion of need determined ACL-sDBS.
Methods: Increasing the experimental utility of ACL-DBS through machine learning techniques (MLT) might hold the possible for the following breakthrough and innovation in the therapeutic success of scientific objective clinical (experimental) brain computer interfaces (BCI). To this end, classy ML algorithms/procedures (MLA/P) enhanced for decoding of brain states as of neuronal time-domain ought to be built. To support this effort, the study abridges o précises the existing state of ML research for minimally invasive neurology.
Results: The time-domain data to frequency transformation of brain recordings into meaningful features for encrypting the symptoms and behavior defined is also explained. Frequently applied ML models are elucidated plus examined following the notion of functionality for ACL-sDBS. This is observed by a perilous study on decent and refutable practices for imparting instructions and testing to ensure intangible and functional simplification for simultaneous change in clinical sets. Lastly, some findings fusing ML with ACL-sDB stimulations are underlined.
Conclusion: This study considers an indication and obsessed by the promising future of brainy and smart ACL-sDBS and accomplishes by classifying some significant elements on the path for effective clinical implementation. Future ACL smart DBS devices sturdily depends on transdisciplinary research, opensource data, and process resolutions plus sturdier research collaborations globally.



P36.13

Functional analysis of Parkinson`s disease using computational simulation models and systems control theory

*Venkateshwarla Rama Raju**
CMR College of Engineering & Technology, jawaharlal Nehru Tehnological University, Hyderabad, Telangana, India

Objectives: Firstly, to describe the system behavior with computationally efficient models which might help in detecting the best stimulus parameters for Parkinson`s disease patients. Secondly, to apply unfolding the functional-analysis to test the likely-mechanisms for computing oscillations while interacting nucleus and, finally, to study the clampdown (suppression)-of-oscillations via high-frequency stimulations.
Background: Parkinson disease (PD) is a complex-progressive, neuro degenerative disorder, categorized with hallmark motoric-symptoms features. The disease is connected by pathological, oscillatory-neural/ neuronal-activity within parallelly connected basal-ganglion (BG) motor circuitry. Deep brain stimulation (DBS) is successively applied to diagnose somatically deflective or refractile (refractive) PD. But choice of (induced) stimulus parameters is depending on skilled evaluation of Parkinson`s, ensuing in a long-lasting prolonged fine-tuning passé or retro as well as a sub optimum well-chosen (high-quality) superior parameter. Hence, the study reconnoiters third and fourth-order control theory-based systems models of oscillatory activity in basal ganglion motor circuitry.
Methods: Unfolding functional analysis techniques are applied to test plausible and probable mechanisms for generating oscillations while networking nucleus followed by exploring the clampdown-of-ripples thru high-frequency-stimulations (HfS). The hypothetical consequences (outcomes) to suppress the ripples activity gained by applying fourth order, also previous models, are enhanced to fit prognostically acquired local-field-potentials (LFPs) data attained as PD patients thru implanted pulse generators (IPGs) microelectrode recording (MER) via STN-DBS. Close agreement between the power of ripples computed for an array of stimulus-amplitudes is detected RMS:0-69-0.99.
Results: Our findings propose that the behavioral actions and performance of the system plus subjugation of pathological-

neuronal-oscillations thru DBS are greatly labeled by macroscopic-models demonstrated. Also, a third-order model is good enough to prototype the quantifiable model data clinically with no extra intricacy.

Conclusions: Unfolding the system behavioral actions, aspects and overall performance using computational simulation and statistical model can help in the affinity of finest stimulus parameters for PD subject constraints in irrefutable settings. Our prototype can be deciphered to clinical tool to help in setting DBS parameters, could be plausibly adjusted to signify distinct patient's pathological-state by means of a biomarker (LFP) of PD.

Table 1. Ideal parameters of a hypothetical third-order systems control-theory-based model detected for the data of local field potentials (LFPs) as of 4 PD subjects (patients) Figure 3 (a).

Subjects (PD Patients)	PDP-S_1	PDP-S_2	PDP-S_3	PDP-S_4
h-parameter	0.3176	0.3169	0.3186	0.3179
scale score on Axis-X	7.42	53.28	37.45	66.86
scale score on Axis-Y	0.0022	0.0016	0.0008	0.0004
pulse-width (μ-Sec) (Stimulus-intensity)	60	90	60	60
Stimulus-freq. (Hz)	130	130	130	130
Stimulus current (Volts)	1.5	1.5	1.5	1.5

Table 2. Ideal parameters of a typical hypothetical 4th-order time-series model-prototype (decreased)detected for fitting the data of LFPs as of 4 subjects demonstrated in Figure 3 (b).

Subjects (PD Patients)	PDP-S_1	PDP-S_2	PDP-S_3	PDP-S_4
h-parameter	0.1011	0.0999	0.1008	0.1011
scale score on Axis-X	44.66	91.25	71.25	151-74
scale score on Axis-Y	0.0001	0.0005	0.0002	0.0001
pulse-width (μ-Sec) (Stimulus-intensity)	60	90	60	60
Stimulus-freq. (Hz)	130	130	130	130
Stimulus current(Volts)	1.5	1.5	1.5	1.5

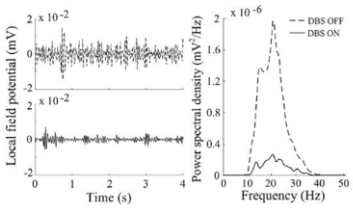


Figure 1. Filed potentials data acquired with embedded macro electrodes as of subthalamic-nuclei of PD subject demonstrated prior to 130 Hz stimuli at a current of 1.5volts plus 60μs pulse-width. Spectral-density was estimated with Welch's technique, is built on complete field potentials with MER recording for the given stimulus—settings.

P36.14

Computational simulation prototype-model of adaptive closed-loop deep brain stimulation (ACL-DBS) for curbing the low frequency β-oscillations in Parkinson's

Venkateshwarla Rama Raju[1], Lavanya Neerati[2]*
[1] CMR College of Engineering & Technology, jawaharlal Nehru Tehnological University, Hyderabad, Telangana, India
[2] Osmania University, Hyderabad, Telangana, India

Background/Objectives: In this study we present a prototype model of adaptive closed-loop control of deep brain stimulation (ACL-DBS) computationally designed for neurodegenerative Parkinson's disease (PD) patients to delve into clinically feasible mechanisms intended for curbing compulsive—β-band frequencyoscillations. ACL-DBS devices giving better outcomes in our observations and offering potential to get better management of PD-patient feature-manifestations (symptoms) also dyskinesias through high-speed/lower-power consumption than open-loopDBS. Yet, the model techniques testing is extensive and tough in Parkinson`s. It gives a means to discover a variety of preventive-algorithms in silico plus enhance DBSparameters prior-to-testing and incorporates field potentials, antidromic and orthodromic start of subthalamic-nucleus(STN)afferent nerve-threads (fibres), detecting LFPs, plus spatio-temporals disparity of β-oscillations motion net-work in the basal-ganglion circuitry.

Methods: The performance of "ON/OFF" and two-fold threshold-controls for β-oscillations by adjusting stimulus-intensity/amplitude is checked initially, showing levels-of β-oscillations decrease, also consumption-of-energy analogous to earlier research. ACL-DBS controls for stimulus-intensity(amplitude),pulse-width and frequency-modulation is examined then. A setting-rule is developed to choose useful device-control-parameters to hit long range β-fluctuations whilst acknowledging diagnostic-conditions which limit rate-of change-of stimulus-parameters. The controls attributed exceptional execution to normalize network β-activity.

Results: Relative-controllers ensued in objectionable fast oscillations of stimulus-device parameters that might surpass prognostically bearable time-limits. In general, PI-controller for regulating stimulus-DBS device frequency accomplished well, decreasing the mean-error with 83.2 % equated to "DBS-OFF" plus mean-power expended to 25.2 % of OL-DBS.

Conclusion: This model gathers adequate physiological features to act as a substitute for clinical observation of ACL-DBS techniques with a marker(bio-marker), offering a better way for prognostically fit ACL-DBS controllers.

Keywords: adaptive closed-loop deep brain stimulation (ACL-DBS), β-frequencies oscillations, computational simulation model-prototype, local field potentials (LFPs), Parkinson's disease, proportional-integral controller, subthalamic-nucleus (STN).

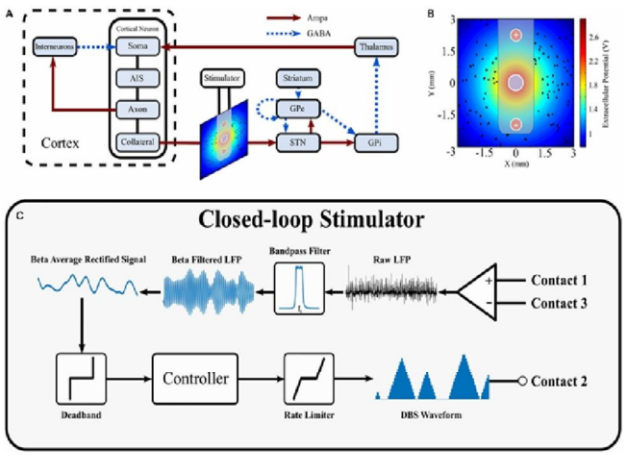


Figure. 1. Computational-model simulation of thalamo-cortical basal-ganglion circuitry net-work(NW). [A]. NW of thalamo-cortico basal-ganglion neural populace. Synaptic-links (Inhibition/exhibition(excitation)) inside the NW, signified as compact and dense indicated with pink-colored arrows connections, sapphire-arrows indicated with dotted-lines, individually. [B]. Field (current) delivery because of unipolar induced stimulus-electrode. Thalamocortical securities-(collaterals) depicted as dark-dots, that are sloping vertically to the folio. Bipolar-electrode signal acquisition/recording—contacts are indicated with +/- accordingly. [C] Model of ACL-DBS using field-potentials(i.e.,LFPs) ensuing restrained of NW β-oscillations/motion-activity. Interactions 1 and 3 showing bipolar-signal-recording electrode-contacts over the stimulus-electrode of DBS. Acquired potentials are filtered with band-pass filters. Filtered and be close to for computing the mean corrected-value of β-potential-activities. β-mean corrected-value which rectified is applied as an i/p (input) to the controller that quantifies an efficient and rationalized-value for stimulus-parameter (of DBS) that is being—modulated. Finally, the modernized stimulus signals with deep brain stimulator are then modeled by the contact2electrode and differs the field-distribution, i.e., the electric-field potentials supply.

CLINICAL SCIENCE: Complications of therapies

P37.01

Protocol to help neurologists manage subcutaneous apomorphine therapy skin nodules: Expert roundtable recommendations

Stu Isaacson[*,1], Mindy Grall*[*,2], Fiona Gupta[3], Daniel Kremens[4], Cuong Nguyen[5], Rajesh Pahwa[6], Marc Serota[7], Matthew Zirwas[8], Steven Feldman[9]*

[1] Parkinson's Disease and Movement Disorders Center of Boca Raton, Boca Raton, FL, United States
[2] Supernus Pharmaceuticals, Rockville, Maryland, United States
[3] Mount Sinai Health, New York, NY, United States
[4] Thomas Jefferson University, Philadelphia, PA, United States
[5] Northwestern Medicine, Chicago, IL, United States
[6] University of Kansas Medical Center, Kansas City, KS, United States
[7] University of Missouri Kansas City School of Medicine, Kansas City, MO, United States
[8] Dermatologists of Greater Columbus, Bexley, OH, United States
[9] Wake Forest University, Winston-Salem, NC, United States

Objectives: Develop a structured algorithm for the clinical evaluation and management of infusion site reactions (ISRs) in patients with Parkinson's disease (PD) treated with continuous subcutaneous apomorphine infusion (CSAI).
Background: ISRs are common in patients who are treated with CSAI. ISRs include subdermal nodules, cutaneous erythema, pruritus/pain, and others. The cause of CSAI-related ISRs is unclear, but evidence suggests local inflammatory reaction to apomorphine and/or excipients in the infused solution. Most ISRs resolve and do not lead to CSAI treatment discontinuation.
Methods: An expert roundtable consisting of US movement disorder neurologists with CSAI experience and dermatologists with expertise in inflammatory-mediated skin disorders was convened to review current knowledge of CSAI-related ISRs and to develop recommendations regarding clinical evaluation and management of ISRs that develop during CSAI treatment.
Results: Experts reviewed proposed steps to minimize the development of ISRs, including patient education of proper insertion technique, site rotation, skin hygiene, sterile procedure, and avoidance of problem skin areas. Some patients may be at higher risk of ISRs despite these methods. Experts suggested that a clearer classification system of CSAI-related ISRs be developed, and proposed presence of symptoms, timing, size, erythema, and fluctuance/drainage as factors to include. Based on classification, management would be determined. Most nodules can be managed conservatively. Because infections are uncommon, empiric antibiotics were not felt to be necessary in most circumstances. Patients should be instructed to report ISRs that are not improving, expanding, or associated with systemic symptoms to their healthcare provider.
Conclusions: ISRs are common with CSAI therapy, and probably reflect an inflammatory reaction in sensitized patients. Most ISRs resolve spontaneously, but some require evaluation to exclude infection. Simple steps to try to minimize ISRs are proposed. Although further research will help elucidate the underlying causes of ISRs, experts agreed that most CSAI-related ISRs are self-limited, resolve spontaneously, can be managed by a treating neurologist without dermatologic/medical referral, and do not limit successful continuation of treatment.

P37.02

Influence of continuous subcutaneous apomorphine infusion on cognition and behavior in Parkinson's disease: A systematic review

Jean-Françoi Houvenaghel[*,1], Virginie Czernecki[2], Kathy Dujardin[3], Emmanuelle Schmitt[4], Alexia Arifi[5], Eve Benchetrit[6], Céline Dillier[7], Elodie Lemercier[8], Cécile Cau[9], Amélie Bichon[4], Laura Lavigne[10], Mylène Meyer[10]*

[1] Neurology Department, CHU de Rennes, Rennes, France
[2] Neurology Department, Hôpital Pitié-Salpêtrière, Paris, France
[3] Univ. Lille, Inserm, CHU Lille, U1172 - LilNCog - Lille Neuroscience & Cognition, Lille, France
[4] Neurology Department, CHU Grenoble Alpes, Grenoble, France
[5] Parkinson Expert Center, Neurology Department, CHU Gui de Chauliac, Montpellier, France
[6] Department of Neurology and Movement Disorders, Timone University Hospital, Marseille, France
[7] Neurology Department, CHRU de Nancy, Nancy, France
[8] Department of Neurology, Caen University Hospital, Caen, France
[9] Neurology Department, Pays D'Aix Hospital, Aix-en-Provence, France
[10] Department of Neurology, CHRU Nancy, Nancy, France

The efficacy of continuous subcutaneous apomorphine infusion (CSAI) on motor fluctuations and dyskinesias in Parkinson's disease (PD) is demonstrated. However, the influence of this treatment on cognition and behavior remains debated. The main objective of this systematic review is to carry out an inventory of knowledges and the level of evidence concerning the influence of this treatment on cognition and behavior in PD.
The PRISMA recommendations are adopted. Only longitudinal studies statistically estimating the effect of CSAI in PD on cognition (global cognition, executive functions, visuo-spatial, language, memory, attention, emotion) and/or behavior (depression, anxiety, apathy, psychotic symptoms, impulse control disorders (ICD), non-motor fluctuations) are included. Pubmed, PsychInfo, Embase and Cochrane are queried. The quality of the studies is assessed using a 15-item scale.
22 studies are selected, none of which examines all of the cognitive and behavioral domains. Only four have an estimated good quality. Few studies investigated the influence of CSAI on cognition. Among them, the main result come from an uncontrolled study conducted on patients with major cognitive disorders, which showed cognitive deteriorations with CSAI. On the behavioral level, the results suggest a possible safety (TCI, psychotic symptoms) or even an improvement (depression, anxiety, apathy, non-motor fluctuations) with CSAI. However, the level of evidence is low for cognition and behavior.
In conclusion, CSAI rarely appears to negatively impact cognition and behavior in PD. However, there are significant methodological biases (lack of control group, limited domains assessed, small sample sizes, scales used, heterogeneity in disease severity). In this context, the current knowledge does not allow to conclude with certainty on the influence of continuous subcutaneous infusion of apomorphine on cognition and behavior in Parkinson's disease.

P37.03

Can Abilify cause disability?: A case series providing insight into parkinsonian symptoms experienced by Abilify users

Kristin Richey[*,1], Jacob Goforth[1], Paul Brill[2]*
[1] Medical University of South Carolina, College of Medicine - AnMed Health Satellite Campus, Anderson, South Carolina, United States
[2] AnMed Health, Anderson, South Carolina, United States

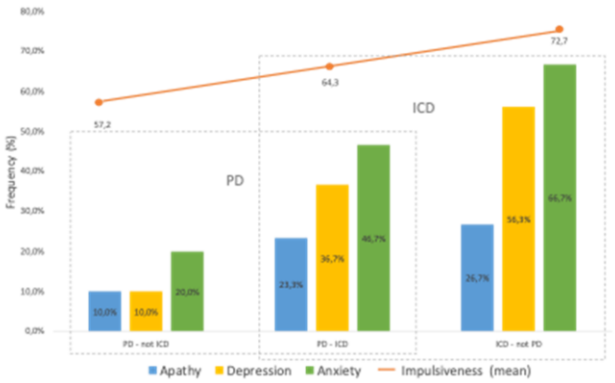
Objective: Aripiprazole (Abilify) has been endorsed as a relatively safe option when compared with other atypical antipsychotic medications that have a higher risk for evoking metabolic side effects. Additionally, when compared to typical antipsychotics it is less likely to cause extrapyramidal effects. Although its safety profile is better than many of its counterparts, it is possible for aripiprazole to cause extrapyramidal symptoms due to its partial antagonistic actions on D2 receptors. This case series was performed to provide further insight into Abilify's potential to induce parkinsonian manifestations and whether patients improve upon its discontinuation.
Method: Forty-six patients were identified in the EMR of a neurology practice as having been prescribed aripiprazole and having received a diagnosis of "Parkinson's", "parkinsonism" or "drug-induced parkinsonism". Exclusion criteria were 1) if the patient's diagnosis was later retracted, 2) the diagnosis was made by providers outside of the neurology practice and 3) if the patient started Abilify after the diagnosis was made. Twenty-three patients were chosen for inclusion in the study in accordance with these criteria. Patient demographic data and family history of Parkinson's was recorded. Additionally, patient information regarding symptoms experienced, recovery status and timeline after discontinuation of Abilify, and use of disease modifying therapies was recorded. This data was then analyzed for significant relationships.
Results: Average age of diagnosis was 69.2 years (range 38y-86y) with the primary diagnosis being parkinsonism/drug-induced parkinsonism (82.6%). Most patients had at least a partial recovery (78.3%) with average recovery rate of 8.9 months. Of those who noted significant recovery, 47.8% utilized disease modifying medications. Depression was the primary diagnosis qualifying patients for aripiprazole therapy (73.9%). Males seemed to have a higher rate of persistent side effects (80% vs 69.2% in females, $p > 0.1$), though they did not require medication as often for significant recovery (40% vs 53.8%, $p > 0.1$).
Conclusion: The findings in our study suggest that Abilify can induce parkinsonian manifestations that often improve or resolve upon discontinuation of the drug. Future studies encompassing larger sample sizes and studies that are prospective in nature are needed to add to the validity of the findings in this retrospective study.

P37.04

Apathy and impulse control disorders are not exclusionary behavioral conditions: Challenging a classical model in Parkinson's disease

Marta Vales Montero[*,1], Francisco Ferre Navarrete[2], Javier Conejo Galindo[2], Pablo Andrés Camazón[2], José Suárez Campayo*[*,2], Rubén Reyes Marrero[2], José Ramón López-Trabada Gómez[3], M Bayta Díaz Rodríguez[4], Pedro José Melgarejo Otálora[1], Francisco Grandas[1]*
[1] Department of Neurology. Hospital General Universitario Gregorio Marañón, Madrid, Spain
[2] Department of Psychiatry, Hospital General Universitario Gregorio Marañón, Madrid, Spain
[3] Department of Psychiatry, Hospital Universitario Ramón y Cajal, Madrid, Spain
[4] Asociación para la prevención y ayuda al ludópata (APAL), Madrid, Spain

Introduction: Impulse control disorders (ICD) and apathy are common in Parkinson's disease (PD) and classically thought to represent opposite extremes in a motivational spectrum. In order to assess this model, we aimed to analyze the coexistence of apathy and ICD in PD patients and in non-PD patients with pathological gambling.
Methods: This cross-sectional study included 30 patients with PD and ICD (PD-ICD), 30 patients with PD without ICD (PD-notICD) and 30 patients with pathological gambling without PD (ICD-notPD). All PD patients were previously exposed to dopamine agonists (DA). Demographic and clinical data were obtained by clinical records and formal interview. All 90 participants underwent a comprehensive neuropsychological evaluation including cognitive assessment, motor and non-motor status, and measures of impulsiveness, apathy, ICD, depression, mania and anxiety.
Results: The mean age was 59,5 (27,7% women). Hypersexuality and pathological gambling were the predominant ICD in PD-ICD group, although most patients (56,7%) suffered □2 ICD subtypes simultaneously. DA dose and subtype did not significantly differed in PD-ICD and PD-notICD groups. Prevalence of apathy measured by Lille Apathy Rating Scale was higher in PD-ICD compared with PD-notICD (23.3% vs. 10,0%; p=0,04) and in ICD-notPD compared with PD-notICD (26,7% vs. 10,0%; p=0,01). Past history of anxiety and depression were significantly higher in PD-ICD and ICD-notPD compared with PD-notICD. Measures of impulsiveness assessed with Barrat impulsiveness scale were higher in PD-ICD and ICD-notPD compared with PD-notICD.
Conclusion: In this study apathy was found to be higher in ICD groups (both PD-ICD and ICD-notPD) than in PD-notICD patients. This finding, in accordance with recent research, challenges the concept of ICD and apathy as opposite extremes in the axis of motivation. Interestingly, both apathy and depression were particularly prevalent among ICD-notPD patients. The dysfunction of reward systems might lead to the coexistence of both deficient and excessive motivational behaviors in the general population and in PD patients. Considering that ICD is a complication of dopaminergic therapy in PD, DA should be used with caution in patients with apathy or depression.



CLINICAL SCIENCE: Clinical trials: Design, outcomes, recruiting, etc.

P38.02

Phenotyping REM sleep behaviour disorder in a large community cohort in Tasmania, Australia: Baseline characteristics of the ISLAND Sleep Study

Samantha Bramich[*,1], Alastair Noyce[2], Anna King[1], Aidan Bindoff[1], Maneesh Kuruvilla[1], Sharon Naismith[3], Larissa Bartlett[1], James Vickers[1], Jane Alty[1]*

[1] University of Tasmania, Hobart, Tasmania, Australia
[2] Queen Mary University of London, London, United Kingdom
[3] University of Sydney, Sydney, Australia

Background: Isolated REM sleep behaviour disorder (iRBD) is a prodrome of neurodegenerative disease (NDD), and 90% of people with iRBD will develop Parkinson's disease (PD), dementia with Lewy bodies (DLB) or Multiple System Atrophy (MSA). iRBD prevalence is estimated to be 2% worldwide but few studies have calculated prevalence using the gold-standard method of video polysomnography (vPSG). There is little known about whether characteristics, such as slowed gait, olfactory dysfunction or autonomic symptoms influence whether iRBD progresses to PD, DLB or MSA. The Island Study Linking Ageing and Neurodegenerative Disease (ISLAND) Sleep Study aims to identify the population prevalence of iRBD in Tasmania, Australia using home-based vPSG, and determine how specific profiles of iRBD predict the risk of progression to PD and other NDD.
Methods: Adults aged 50+ years from the Tasmanian community were invited to complete a battery of online questionnaires including the REM Sleep Behaviour Disorder Screening Questionnaire (RBDSQ), RBD single question screen (RBD1Q), the Pittsburgh Sleep Quality Index (PSQI), and questions regarding sleep apnoea, autonomic dysfunction, Parkinson's symptoms, pain, and dreaming.
Results: 2905 participants have been recruited (mean (SD) age 64 (7.7) years; 26% male). 273 (9.4%) have 'probable' iRBD (pRBD) based on the RBD1Q and compared to those without pRBD, this group have poorer sleep quality (66% vs 57%), greater autonomic dysfunction (median score 18 vs 13), more pain symptoms (particularly stabbing, itching and heavy pain), higher risk for sleep apnoea (30% vs 13%), more intense dreams (21% vs 8%), and more early PD symptoms, including shaky limbs (16% vs 6%) balance problems (35% vs 26%.), and slurred speech (12% vs 6%).
Conclusions: This is the first study of iRBD prevalence in Australia and one of few worldwide that has phenotyped iRBD so widely. The next phase will include participants undertaking a home-based vPSG and objective tests of olfaction, circadian rhythm, and motor and cognitive function to stratify specific iRBD profiles and produce the first estimate of iRBD prevalence using a home-based vPSG system. Participants will be tracked over the next 10 years to improve understanding of phenoconversion to PD and other NDD.

P38.03

Onset of efficacy with continuous, subcutaneous levodopa/carbidopa infusion in patients with PD experiencing motor fluctuations

C. Warren Olanow[1], Fabrizio Stocchi[2], Aaron L. Ellenbogen[3], Liat Adar[4], Ryan Case[,4], Tami Yardeni[4], Alberto J Espay[5]*

[1] Clintrex, Sarasota, FL, United States
[2] University and Institute for Research and Medical Care IRCCS San Raffaele, Rome, Italy
[3] Michigan Institute for Neurological Disorders, Farmington Hills, MI, United States
[4] NeuroDerm, Rehovot, Israel
[5] James J and Joan A Gardner Center for Parkinson's disease and Movement Disorders, University of Cincinnati, Cincinnati, OH, United States

Objective: Evaluate the onset of efficacy for continuous 24-hour subcutaneous infusion of liquid levodopa/carbidopa (LD/CD) with investigational ND0612.
Background: Primary results from this Phase 2 study (NCT02577523) demonstrated that 28 days of treatment with 24-hour ND0612 infusion increased ON-time with no/mild dyskinesia (Good ON) by 3.7 [1.9, 5.6] hours ($p < 0.0001$) in patients with PD experiencing motor fluctuations (Olanow et al, 2022). However, less is known about the onset of efficacy following subcutaneous LD/CD infusion.
Methods: We report data from a secondary analysis of patients treated with the 24-hour ND0612 infusion regimen (N=19). Patients received the infusion at a rate of 0.64 mL/hour from 4AM to 10PM and 0.08 mL/hour between 10PM and 4AM to a total LD/CD dose of 720/90 mg. Motor status was determined by a blinded-rater at 30-minute intervals for 8 hours. Patients also assessed the time to full ON each morning in a diary. The first post-baseline efficacy evaluations were performed at Day 3.
Results: At Day 3, patients treated with 24-hour ND0612 infusion showed a significant increase from baseline in Good ON-time (+1.83 [0.30, 3.35] hours, p=0.02), and a significant reduction in ON-time with moderate-severe dyskinesia (-1.36 [-2.29, -0.42] hours, p=0.006). Improvements at Day 3 were also noticeable in the Subject and Clinician Global Impressions of change (SGI and CGI improvements were reported for 73.7% and 52.6% of patients, respectively). By the end of the first week of treatment, the proportion of patients who reported achieving a full ON at 9AM increased from 31.6% at baseline to 72.2%.
Conclusions: Results of this analysis demonstrate that patients experience statistically significant and clinically relevant improvements with 24-hour subcutaneous infusion with ND0612 at Day 3 after treatment initiation that improved further to Day 28 (primary endpoint).

P38.04

Descriptive case studies of patients in their fifth consecutive year of treatment with ND0612

Alberto J Espay[*,1], Tanya Gurevich[2], David Arkadir[3], Sophia Sopromadze[4], Liat Adar[4], Ryan Case[4], Tami Yardeni[4]*

[1] James J and Joan A Gardner Center for Parkinson's disease and Movement Disorders, University of Cincinnati, Cincinnati, OH, United States
[2] Neurological Institute, Tel Aviv Medical Center, Tel Aviv, Israel
[3] Hadassah Medical Center, Hebrew University of Jerusalem, Jerusalem, Israel
[4] NeuroDerm, Rehovot, Israel

Objective: Describe the long-term (up to 5 years) experience of individual patients with Parkinson's disease (PwP) treated with investigational ND0612 in an open-label clinical safety study.
Background: Continuous levodopa infusion is considered the optimal delivery route for treating PwP experiencing motor fluctuations (Olanow et al, Nat Clin Pract Neurol; 2006). ND0612 is in development as a 24-hour subcutaneous infusion of liquid levodopa/carbidopa offering patients the efficacy of continuous levodopa via a minimally invasive delivery system. Primary data from the BeyoND study showed that ND0612 is generally safe and well tolerated up to 1 year of treatment (Poewe et al, Mov Disord; 2021).
Methods: We report four individual cases (2 male/2 female) from the USA (2 study sites) and Israel (2 study sites). Eligible patients for the study were adults (≥30 years) with a diagnosis of Parkinson's

disease (PD) and experiencing ≥2 hours of OFF time/day despite receiving ≥4 levodopa doses/day and ≥1 other PD medication.
Results: Patients were aged 60-68 years old, BMI 22.8-32.5, Hoehn and Yahr Stage 2-3, and experiencing motor fluctuations for 2-7 years. All four patients showed relevant reductions from baseline in OFF time and increases in ON time without troublesome dyskinesia, which were maintained until last date of efficacy follow-up. All patients experienced infusion site reactions starting early after treatment initiation. Nodules and bruising were mild to moderate and well tolerated. One case had a serious infusion site infection which was managed successfully with antibiotics and abscess drainage. This patient decided to continue ND0612 treatment because of its favorable effect on motor fluctuations and gait.
Conclusions: Continuing into their fifth year of treatment, these patients exemplify the favorable long-term benefit/risk profile of ND0612 and will serve to inform future patient selection and education.

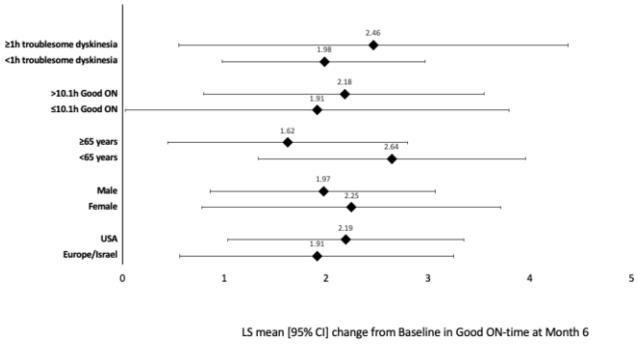
P38.05

Efficacy of 24-hour subcutaneous levodopa/carbidopa infusion with ND0612 for patients with Parkinson's disease experiencing motor fluctuations: Subgroup-analysis from the open-label BeyoND study

Werner Poewe[*,1], Stuart Isaacson[2], Fabrizio Stocchi[3], Liat Adar[4], Nelson Lopes[5], Ryan Case[5], Tami Yardeni[5], Nir Giladi[6]*
[1] Medical University Innsbruck, Innsbruck, Austria
[2] Parkinson's Disease & Movement Disorders Center of Boca Raton, Boca Raton, FL, United States
[3] University and Institute for Research and Medical Care IRCCS San Raffaele, Rome, Italy
[4] NeuroDerm, Rehovot, United States
[5] NeuroDerm, Rehovot, Israel
[6] Neurological Institute, Tel Aviv Medical Center, Sackler School of Medicine, Sagol School of Neurosciences, Tel-Aviv University, Tel Aviv, Israel

Objectives: Evaluate the efficacy of 24-hour subcutaneous levodopa/carbidopa infusion with investigational ND0612 for different subgroups of patients with Parkinson's disease (PD) experiencing motor fluctuations.
Background: Primary data from this Phase 2b study have shown that one year treatment with ND0612 infusion is generally safe and well-tolerated. Adjusted mean daily 'Good ON' time (sum of ON without dyskinesia + ON with non-troublesome dyskinesia) increased from baseline by 2.3 hours at Month 3 and was maintained for at least 12 months (Poewe et al., Mov Disord 2021). We evaluated the efficacy of 24-hour levodopa/carbidopa infusion with ND0612 in improving Good ON time in different subgroups of patients.
Methods: The BeyoND study is an ongoing open-label study (NCT02726386) of ND0612 treatment conducted in PD patients (n=214) with Hoehn & Yahr score of ≤3 during ON experiencing ≥2 hours daily OFF-time. We analysed the efficacy of 24-hour infusion in improving Good ON time in different subgroups categorized by age (≥65 years vs <65 years), sex (male vs female), geographic region (USA vs Europe/Israel) as well the amount of Good ON time (>median of 10.1 hours vs ≤10.1 hours) and troublesome dyskinesia (<1 hour vs. ≥1 hour) at Baseline.
Results:
All subgroups analysed showed increases in the amount of Good ON time throughout 1 year follow-up; with no significant differences in the increases in Good ON-time between the subgroups. The figure shows the LS mean [95% CI] change from Baseline in Good ON-time at Month 6.

Conclusions: Findings support improved Good On time for all patient subgroups treated with 24-hour subcutaneous levodopa/carbidopa infusion with ND0612.



P38.06

Enrollment characteristics for patients entering a Phase 3 study of subcutaneous levodopa/carbidopa infusion with ND0612

Olivier Rascol[1], Alberto Albanese[2], Aaron Ellenbogen[3], Joaquim J Ferreira[4], Tanya Gurevich[5], Sharon Hassin[6], Jorge Hernandez-Vara[7], Stuart Isaacson[8], Karl Kieburtz[9], Peter LeWitt[10], Lydia Lopez Manzanares[11], C. Warren Olanow[9], Rajesh Pahwa[12], Werner Poewe[13], Harini Sarva[14], Fabrizio Stocchi[15], Tami Yardeni[16], Liat Adar[16], Laurence Salin[16], Nelson Lopes[16], Nissim Sasson[16], Ryan Case[16], Alberto J. Espay[,17], Nir Giladi[5]*
[1] University of Toulouse 3, University Hospital of Toulouse, INSERM, Clinical Investigation Center CIC1436, Toulouse, France
[2] IRCCS Istituto Clinico Humanitas, Rozzano, Italy
[3] Michigan Institute for Neurological Disorders, Farmington Hills, MI, United States
[4] Laboratory of Clinical Pharmacology and Therapeutics, Faculdade de Medicina, Universidade de Lisboa, Lisbon, Portugal
[5] Sackler School of Medicine, Tel Aviv University, Tel Aviv, Israel
[6] Sheba Medical Center, Tel Hashomer, Israel
[7] Hospital Universitari Vall D' Hebron, Barcelona, Spain
[8] Parkinson's Disease and Movement Disorders Center of Boca Raton, Boca Raton, United States
[9] Clintrex Research Corp, Sarasota, FL, United States
[10] Departments of Neurology, Wayne State University School of Medicine, Henry Ford Hospital, Detroit, MI, United States
[11] Hospital Universitario de La Princesa, Madrid, Spain
[12] University of Kansas Medical Center, Kansas City, KS, United States
[13] Medical University Innsbruck, Innsbruck, Austria
[14] Weill Cornell Medical Center, New York, NY, United States
[15] University and Institute for Research and Medical Care IRCCS San Raffaele, Rome, Italy
[16] NeuroDerm, Rehovot, Israel
[17] James J and Joan A Gardner Center for Parkinson's disease and Movement Disorders, University of Cincinnati, Cincinnati, OH, United States

Introduction: The BouNDless study (NCT04006210) compared the efficacy, safety, and tolerability of subcutaneous levodopa/carbidopa (LD/CD) as an investigational ND0612 24-hour infusion versus oral immediate-release (IR)-LD/CD in patients with Parkinson's disease (PwP) experiencing motor fluctuations. Here we report patient enrollment characteristics; primary results will be available in 2023.
Methods: Following screening, PwP on ≥4 doses/day of oral LD/dopa-decarboxylase inhibitor (LD ≥400mg/day) and experiencing ≥2.5h daily OFF-time were consented and enrolled. They entered a 4-6 week open-label adjustment period during which oral LD

formulations and COMT inhibitor doses were converted to equivalent doses of IR-LD/CD and then adjusted to optimal clinical effect. Patients then entered an 4-6 week open-label ND0612 conversion period in which IR-LD/CD was replaced by ND0612 (LD/CD dose up to 720/90mg/day) with adjunct IR-LD/CD, as required, and adjusted until this combination regimen was optimal. Patients then entered a 12-week, double-blind, double-dummy period, during which they were randomized (1:1) either to their optimized regimen of ND0612 infusion (plus IR-LD/CD), or to the optimized IR-LD/CD-only regimen.
Results: Enrollment characteristics of randomized patients (N=259) were similar to other clinical trials in PwP experiencing motor fluctuations refractory (mean±SD age: 63.5±9.0y; 63.7% male; diagnosed 9.6±4.3y; motor fluctuations 4.5±3.3y, mean OFF time 6.1±1.7h). Levodopa equivalent daily doses at enrollment were 1029mg; 86% patient were receiving adjunct Parkinson's medications, mainly dopamine agonists (63%).
Conclusions: Enrollment characteristics of patients randomized in the BouNDless trial are consistent with those observed in other clinical studies in PwP experiencing motor fluctuations.

P38.07

Utilizing a variation of the train the trainer model to create best practice guidelines and to build a culturally sensitive and community educated team of ambassadors to increase diverse enrollment in clinical trial research studies
R Bernard Coley, Denise Coley**
Enable Your Vision, Morgan Hill, CA, United States

Background: The basic goal of this initiative is to increase the participation of communities of color in clinical research studies.
Understanding our approach begins with our view of the big challenges to meeting the ultimate goal: 1) gaining sufficient community trust to attract diverse participation, 2) overcoming historical biases and unethical treatments of diverse populations in clinical research trials, 3) reaching under-engaged communities in culturally sensitive ways, 4) providing the mutually needed education of both the target population and the targeting research organization, and 5) overcoming the structural preferences for quick fixes and one-and-done solutions. Removing the abstraction of these challenges, it is clear that custom solutions must be crafted for each target population. We focused on developing a generalizable program model, customized to make gains in the Black communities of the US around Parkinson's Disease.
Methods: We use a multi-disciplinary team of stakeholders which is patient community led and features a phased approach to developing best practices leading to desirable outcomes. Our value proposition is to produce meaningful outcomes (papers, guidance, and trained community ambassadors and research advocates) overall realistic period of time (3-5 years) of commitment. Critically, we allow solutions to evolve from deliberation of very diverse team constituency, requiring respect of diverse contributors as peers, deconstructing the big challenge into manageable components, facilitating community engagement beyond the core leadership, and mitigating constraints caused by institutional structural silos.
Results: A strong special interest group (SIG) of Black/community of color People with Parkinson's, Care Partners, Movement Disorder Specialists, social workers, and PD community engagement staff has been built and is producing communications tools, community engagement guidance and has modified a successful Learning Institute program to train and certify a cohort of Black Research Advocates.
Discussion and Conclusion: If we as a society want to realize the benefits of diverse clinical research trial participation, we must include the voices of patients and care partners from diverse communities in the planning and design for clinical research trials, we must intentionally address the specific barriers each diverse group faces, and we must embrace the novelty of solutions that inherently results from this inclusion.

P38.08

Targeted touchscreen training in people with Parkinson's disease: A pilot study
Joni De Vleeschhauwer, Evelien Nackaerts, Yifeng Zhang, Luc Janssens, Wim Vandenberghe, Alice Nieuwboer*
KU Leuven, Leuven, Belgium

Background: Previously, we found that sliding movements on a touchscreen are impaired in people with Parkinson's disease (PD) compared to healthy elderly. It is therefore imperative to develop and investigate training programs aimed to enhance these skills, so that patients can optimally partake in current technology-based society.
Objective: To examine the effectiveness of two-week home-based touchscreen training versus no training in PD.
Methods and materials: Thirty-one PD patients (HY I-III) (data collection ongoing), ON-medication, were randomized in a training (EXP, N=15, age 69.9±7) or a control group (CTR, N=16, age 69.1±8). EXP practiced the Swipe-Slide Pattern (SSP) task over a two-week period (5x/week, 10min/session), whereas CTR received no training. The SSP-task consisted of forming predefined patterns as fast and as accurately as possible by sliding over the screen. To facilitate variation during training, single and dual (i.e., counting red or green dots on the screen) training conditions were delivered in a random order throughout the training. Performance on the SSP-task (primary outcome) and a Mobile Phone task (MPT) to assess transfer, were tested at three time points: at baseline (T0), after two weeks (T1) and finally, four weeks after T1 at follow-up (T2). Outcome measures included SSP-time (ms), SSP-accuracy (% correct trials) and MPT-time (s). Between-group differences were assessed using separate ANCOVA's for immediate training effects (primary endpoint) and for retention effects (secondary endpoint), controlling for baseline performance and MoCA.
Results: At T1, we found a significant effect of training for SSP-time ($F(1,25)=4.383$, $p=0.047$, $\eta^2=0.149$) and for SSP-accuracy ($F(1,25)=5.352$, $p=0.029$, $\eta^2=0.176$). No significant effects of training were found at T2. Baseline performance had a significant impact on SSP-performance at T1 as well as T2 (all $p<0.001$). Finally, SSP-training did not transfer to the MPT-task.
Conclusion: This study showed some promising results as a short training program delivered at home improved touchscreen skills when compared to no training. To address the lack of retention and transfer effects and be able to personalize future programs, further investigation is warranted to understand which patients benefit more or less from training.

P38.10

An entirely home-based phase 3 clinical trial of specialized light therapy for Parkinson's disease – Rationale and design
Ray Dorsey[,1], Dan Adams*[,2], Suzanne Hendrix[2], Bradley Wyman[2], Jamie Adams[1], Meghan Pawlik[1], Melissa Kostrzebski[1], Karl Kieburtz[2]*
[1] Center for Health + Technology - University of Rochester, Rochester, New York, United States
[2] PhotoPharmics, American Fork, Utah, United States

Objective: To present the study rationale and design for a randomized, blinded, controlled trial of specialized light therapy for Parkinson's disease (PD).

Background: Current treatments do not adequately address many disabling features of PD, including circadian dysfunction. Previous studies suggest that specialized light therapy may enhance circadian function and safely improve sleep, daytime sleepiness, fatigue, motor symptoms, and psychological health. A previous phase 2 clinical trial suggested benefit on patient-reported endpoints, including parts I and II of the Movement Disorder Society – Unified Parkinson's Disease Rating Scale (MDS-UPDRS) and on a measure of quality of life, the Parkinson's Disease Questionnaire-39.
Methods: Given the heavy burden of traditional clinical trials on participants, favorable safety profile of light therapy, and desire for a broad, inclusive study population, we are conducting an entirely remote phase 3 clinical trial. All study activities, including the specialized light therapy, will occur in the home. No in-person clinical visits are required. Clinical assessments will be conducted remotely, and investigators will evaluate research participants via video visits.
We plan to recruit 300 individuals from the U.S. with stably treated PD. They will be randomized to receive specialized light therapy from a light-emitting box one hour daily in the evening for six months or low intensity light (control or placebo arm) from the same device. Randomized participants will receive a light therapy device, and a blinded study assistant will assist with home set-up. The phase 3 study's rationale and design was proposed and discussed with the U.S. Food and Drug Administration (FDA).
Results: In pre-submission inquiries, the home-based approach was discussed with the FDA, and they agreed with the approach. After discussions with FDA, a quality-of-life measure, the Parkinson's Disease Questionnaire-39, was selected as the primary outcome measure and parts I and II of the MDS-UPDRS as a key secondary outcome.
Conclusions: If the data confirm the earlier phase 2 results, specialized light therapy could provide a non-invasive, non-pharmacologic treatment option to improve the quality of life and reduce disabling features for individuals with PD.

P38.12

Key factors affecting participation in Parkinson's clinical trials

Rosie Fuest[*,1], Gary Rafaloff[2], Kevin McFarthing[3], Lyndsey Isaacs[1], Helen Bracher[4], Tim Bracher[4], Alison Anderson[5], Michele Bartlett[6], Zia Mursaleen[6], Georgia Mills[7], Marie-Louise Zeissler[8], Camille Carroll[8], Leah Mursaleen[1], Soania Mathur[9], Helen Matthews[1], Emma Lane[10]*
[1] Cure Parkinson's, London, United Kingdom
[2] Parkinson's Research Advocate, Miami, United States
[3] Parkinson's Research Advocate, Oxford, United Kingdom
[4] Parkinson's Research Advocate, London, United Kingdom
[5] Parkinson's Research Advocate, Gloucestershire, United Kingdom
[6] Parkinson's Research Advocate, Surrey, United Kingdom
[7] University College London, London, United Kingdom
[8] University of Plymouth, Plymouth, United Kingdom
[9] PD Avengers, Toronto, Canada
[10] Cardiff University, Cardiff, United Kingdom

Despite increasing numbers of clinical trials, data on factors influencing the decision making process of people with Parkinson's to participate is not well studied. Understanding these factors, and how they may be impacted by experience of trials, can inform clinical trial design to improve recruitment, retention and participant experience. The objective of this study was to ascertain key barriers, motivators and facilitators to participation in clinical trials from people with Parkinson's with and without trial experience, alongside insights on effective recruitment and communication processes.
The survey was developed in collaboration with people with Parkinson's and disseminated by groups including Parkinson's UK Take Part Hub, Van Andel Institute, PD Avengers and Cure Parkinson's. Respondents answered questions concerning their experience or perception of clinical trial participation, demographic information and details relating to their Parkinson's. The survey remained open for 3.5 months and has been quantitively and thematically analysed.
774 people with Parkinson's responded, of whom 19% (149/774) had clinical Trial Experience (TE) and 81% (625/774) had not (Trial Inexperienced, TI). Of those that answered optional demographic questions 51% of both the TE (56/106) and TI (241/417) groups were male. 88% (510/581) currently live in the UK with other respondents predominantly from Europe and USA. Both groups identified possible intervention side effects (TE – 42%, 63/149; TI – 52%, 324/625) and requirement for brain surgery (TE - 26%, 39/149; TI - 46%, 290/625) as significant barriers and a direct line of communication to the trial team as the top facilitator to participation (TE - 42%, 63/149, TI - 50%, 310/625). Other key factors considered in participation differ with experience, in particular TI respondents were more motivated by the intervention itself (74%, 462/625) than the TE group who typically ranked altruistic motivators higher (75%, 111/149).
Although there was some overlap between the barriers and facilitators reported by respondents with and without trial experience, experience impacts on the factors considered most important prior to embarking on a trial. This highlights the need to involve people with and without trial experience in trial design stages to aid broader recruitment of people who are not yet research active to clinical trials.

P38.13

The current experience of participating in Parkinson's clinical trials

Rosie Fuest[*,1], Gary Rafaloff[2], Kevin McFarthing[3], Lyndsey Isaacs[1], Helen Bracher[4], Tim Bracher[4], Alison Anderson[5], Michele Bartlett[6], Zia Mursaleen[6], Georgia Mills[7], Marie-Louise Zeissler[8], Camille Carroll[8], Leah Mursaleen[1], Soania Mathur[9], Helen Matthews[1], Emma Lane[10]*
[1] Cure Parkinson's, London, United Kingdom
[2] Parkinson's Research Advocate, Miami, United States
[3] Parkinson's Research Advocate, Oxford, United Kingdom
[4] Parkinson's Research Advocate, London, United Kingdom
[5] Parkinson's Research Advocate, Gloucestershire, United Kingdom
[6] Parkinson's Research Advocate, Surrey, United Kingdom
[7] University College London, London, United Kingdom
[8] University of Plymouth, Plymouth, United Kingdom
[9] PD Avengers, Toronto, Canada
[10] Cardiff University, Cardiff, United Kingdom

Only a small number of trials have sought to obtain participant views following completion. Capturing the experiences of people who have participated in trials is crucial to inform future study design, aid recruitment and retention, and improve participant experience.
This study surveyed people with Parkinson's (PwP) with and without experience of participating in pharmacological and surgical clinical trials. Developed in collaboration with PwP, questions covered factors influencing participant experience in terms of communication and procedures pre-, during and post-trial, alongside preferences on trial duration and assessment format. It was disseminated via groups including Parkinson's UK, Van Andel Institute, PD Avengers and Cure Parkinson's, remaining open for 3.5 months before analysis.
Of the 774 respondents, 19% (149/774) were Trial Experienced (TE) (the remainder Trial Inexperienced, TI), most participating in drug intervention trials (64%, 95/149). Whilst good communication

was reported as a major facilitator of participation, barriers often involved ineffective communication. Although most frequently selected as being well communicated, only 60-62% of TE respondents reported that data security (90/149) and consent procedures (92/149) were well communicated. Off-medication guidance for participants (19%, 29/149) and care-partners (8%, 12/149) alongside trial completion procedures, such as results dissemination (17%, 25/149) and feedback collection from care-partners (5%, 8/149) were infrequently reported as well communicated but also ranked as important. Both TE (52%, 51/98) and TI (47%, 292/625) respondents showed preference for a combination of in-person and online assessments but TE respondents (27%, 26/98) were more willing to have in-person assessments than TI respondents (12%, 77/625), and to participate in trials of 1-2 year duration (TE: 23%, 23/98; TI: 18%, 112/625).
This data illustrates the varied experiences and perceptions of clinical trials. Improving communication around aspects such as consent procedures and off-medication guidance should be explored with TE and TI patient input. Despite concerns around communication, TE respondents were still more willing to participate in longer studies, typical of disease-modifying trials. Sharing participation experiences with TI PwP, developing clear communication strategies pre-, during and post-trial, and implementing hybrid delivery may aid broader recruitment and retention to trials with longer duration.

P38.14

Building a coalition to advance engagement of black and African American communities in Parkinson's disease (PD) research using best practices in diversity, equity and inclusion (DEI), and patient engagement: A multidisciplinary approach

Bernard Coley[*,1], Denise Coley*[*,1], Casey Gallagher*[*,2], Tammyjo Best[3], Chantale Branson[4], Michael Fitts[5], Kimberly Gamble[6], Phil Gee[7], Angela Huckabee[8], Richard Huckabee[8], Reversa Joseph[9], Evelyn Lewis[10], Arita McCoy[11], Disep Ojukwu[12], Terrie Peacher-Ransom[13], Don Ransom[13], Nik Roberts[14], Lisa Seghetti[15], Hiral Shah[16], Karen Williams[17], Lance Wilson[18], Evelyn Stevens[2], Karlin Schroeder[2]*

[1] Parkinson's Foundation, Morgan Hill, CA, United States
[2] Parkinson's Foundation, New York, NY, United States
[3] Emory University, Atlanta, GA, United States
[4] Morehouse School of Medicine, Atlanta, GA, United States
[5] Parkinson's Foundation, Alabaster, AL, United States
[6] Parkinson's Foundation, Charlotte, NC, United States
[7] Parkinson's Foundation, Hilton Head, SC, United States
[8] Parkinson's Foundation, Macedonia, OH, United States
[9] Ohio State University, Columbus, OH, United States
[10] Parkinson's Foundation, Hainesport, NJ, United States
[11] Johns Hopkins University, Baltimore, MD, United States
[12] Stanford University, Stanford, CA, United States
[13] Parkinson's Foundation, Indianapolis, IN, United States
[14] Parkinson's Foundation, Atlanta, GA, United States
[15] Parkinson's Foundation, Jessup, MD, United States
[16] Columbia University, Eastchester, NY, United States
[17] Northwestern University, Chicago, IL, United States
[18] Thomas Jefferson University, Philadelphia, PA, United States

Background: Underrepresentation of Black and African American (BAA) communities in PD research is well-established. This dearth of experiences from BAA communities hinders research and improved understanding of PD. Exclusion of BAA communities results in bias, health inequities, and unjust distribution of research-specific benefits to participants. To our knowledge, there is no nationwide, multidisciplinary, patient-centered program focused on addressing underrepresentation of BAA people in PD research.

Methods: In 2020, the Parkinson's Foundation patient engagement team, twelve BAA people with PD and care partners (Research Advocates) and BAA clinicians, social workers, nurses, and researchers across 8 states in the United States developed a coalition to address research participation. Guided by best practices in DEI (e.g., trust, reciprocity and cultural humility) and patient engagement (e.g., shared decision-making and equal partnership), the first coalition goal was to rebuild and execute the Parkinson's Foundation Learning Institute in a culturally responsive way for BAA communities. The Learning Institute trains people with PD and care partners in research, creating collaborations with researchers to co-design and implement studies.
Results: During 2021-2022, the coalition met biweekly to redesign the Learning Institute to focus on health equity and DEI in PD research. A Community Day was added to engage community organizations in health partnerships. Atlanta, 2023 was chosen for the site and date. The following goals were set:

- learn more about, and respond to, the needs and priorities of BAA communities.
- build relationships between the Foundation, BAA people with PD and community leaders, health and faith-based organizations, historically Black colleges/universities and allies to advance health equity research.
- train 30 new BAA Research Advocates to spearhead research agendas/priorities and address research-related health disparities.

Discussion and Conclusion: Engaging BAA communities in research is a long-term multipronged endeavor. The coalition recognizes addressing care and resource needs of the BAA community, and trust and relationship building are essential to increasing DEI in research and addressing systemic bias faced by BAA people with PD and care partners. The formation of this nationwide, patient-driven, multidisciplinary BAA collation and implementation of the Learning Institute are first steps in the process of addressing these barriers.

P38.15

Outcomes and impact of capacity building for patient engagement in research on staff at academic research centers through a patient advisory board model

Casey Gallagher[*,1], Karlin Schroeder[1], Melissa Armstrong[2], Martie Carnie[3], Megan Dini[1], Megan Feeney[1], Benzi Kluger[4], Sandhya Seshadri[4], Lance Wilson[5], Jori Fleisher[6], Patricia Davies[7]*

[1] Parkinson's Foundation, New York, NY, United States
[2] University of Florida, Gainesville, FL, United States
[3] Brigham and Women's Hospital, Boston, MA, United States
[4] University of Rochester, Rochester, NY, United States
[5] Thomas Jefferson Univeristy, Philadelphia, PA, United States
[6] Rush University, Chicago, IL, United States
[7] Parkinson's Foundation, Washington, United States

Background: Involving people with Parkinson's disease (PD) and care partners in research co-creation alongside researchers has gained traction with implementation resources proliferating. However, research teams still seek tailored trainings on methods and best practices for this work. A scoping review of the PD community indicated interest in patient engagement training and implementation via a pilot patient advisory board (PAB) model for comparative effectiveness research (CER).
Methods: People with PD, patients from other disease areas with patient engagement expertise, researchers, clinicians, social workers and Parkinson's Foundation's patient engagement team co-created a training for staff at five academic research centers. This training provided online sessions on best practices in patient engagement, research basics, running a PAB and co-creating research questions. Centers then ran PABs to form a CER question.

Baseline and follow-up surveys measured knowledge, attitudes, intent and behavior about the training and PABs.
Results: 11 staff from 5 centers responded to the survey. 100% of staff felt the training covered all topics that came up in PAB meetings (33% strongly agree, 67% somewhat agree) and improved their ability to work with PAB members (67% strongly agree, 33% somewhat agree). Staff most commonly engaged PABs through Zoom (100%) in setting research priorities (86%). All staff (100%) felt patient engagement was important to the research process at baseline and follow-up. 83% of staff reported the PAB was beneficial to the organization's research mission and will continue meeting.
Discussion and Conclusion: Pilot trainings were generally successful in preparing staff to engage with participants in research co-creation through PABs, although there is room to improve. Staff felt confident in leading PABs in setting research priorities. Ongoing commitment of the centers to this work indicates a successful and satisfactory model. Results may have been impacted by pivoting from in-person to virtual due to COVID-19. Also, all staff participants believed patient engagement was important at baseline. A weakness in the data is potential selection bias as all sites volunteered for this project. The success of this pilot led to the Foundation dedicating new research money to CER and creating a second round of PABs at new centers.

P38.17

An outcome measure set for disease-modifying multi-arm multi-stage Parkinson's disease trials within the EJS ACT-PD initiative: Selection process and preliminary results

Cristina Gonzalez-Robles[*,1], Michèle Bartlett[2], Matthew Burnell[3], Rebecca Chapman[4], Caroline S Clarke[1], Romy Ellis-Doyle[1], Shlomi Haar[5], Michele Hu[6], Brook Huxford[7], Ashwani Jha[1], Michael Lawton[8], Georgia Mills[1], Alastair Noyce[7], Paola Piccini[5], Kuhan Pushparatnam[9], Lynn Rochester[10], Carroll Siu[11], Daniel Van Wamelen[12], Caroline Williams-Gray[13], Marie-Louise Zeissler[4], Henrik Zetterberg[14], Camille B Carroll[4], Thomas Foltynie[1], Rimona Weil[1], Anette Schrag[1]*
[1] University College London, London, United Kingdom
[2] Expert by experience, Guildford, United Kingdom
[3] MRC Clinical Trials Unit at UCL, London, United Kingdom
[4] University of Plymouth, Plymouth, United Kingdom
[5] Imperial College London, London, United Kingdom
[6] University of Oxford, Oxford, United Kingdom
[7] Queen Mary University of London, London, United Kingdom
[8] University of Bristol, Bristol, United Kingdom
[9] Expert by experience, London, United Kingdom
[10] Newcastle University, Newcastle, United Kingdom
[11] Expert by experience, Canterbury, United Kingdom
[12] King's College London, London, United Kingdom
[13] University of Cambridge, Cambridge, United Kingdom
[14] University of Gothenburg, Mölndal, Sweden

Objectives: To devise a set of outcome measures (OM) for a disease-modifying multi-arm multi-stage (MAMS) Parkinson's disease (PD) clinical trial as part of the Edmond J Safra Accelerating Clinical Trials in PD (EJS ACT-PD) initiative.
Background: EJS ACT-PD aims to accelerate the identification of disease-modifying PD drugs through a MAMS trial, testing several treatments against a common placebo arm and stopping futile interventions early to replace them with others.
Appropriate OMs are essential in clinical trials' success, to detect the most relevant effect of each intervention. This is particularly challenging with different treatment arms and the confounding effect of symptomatic therapy.
Methods: A range of experts and Patient and Public Involvement and Engagement (PPIE) representatives form the Outcome Measures Working Group (OM WG), to propose primary, secondary, and interim OM (i.e. for early stopping of futile interventions).
Primary and interim OM choice stemmed from expert opinion, literature review, PPIE input, and analysis of the Critical Path for Parkinson's (CPP) database to elucidate the natural history and rate of progression of PD as measured by different parameters.
Secondary OM were selected from a list created by the OM WG (motor and non-motor, health-related quality of life, digital, imaging, etc.). For each OM, the most relevant aspects were reviewed, such as feasibility, burden to patients and clinicians, clinical meaningfulness, and validity.
Results: The OM WG propose the sum score of parts I and II of the Movement Disorders Society Unified Parkinson's Disease Rating Scale (MDS-UPDRS) as primary OM. It is clinimetrically sound, captures non-motor symptoms, includes patient-reported outcomes, is sensitive and applicable remotely. The combination of parts I, II and the remotely deliverable items of part III of the MDS-UPDRS was selected as interim OM due to its high sensitivity to change over time. A set of core and supplemental secondary OM has been created to cover other relevant aspects.
Conclusions: OM selection in disease-modifying PD trials remains challenging. This framework considers the natural history of PD, existing OM, and PPIE input to achieve it. MAMS trials can aid validation of exploratory OM which may outperform current instruments, such as milestone-based measures.

P38.18

Disease-modifying drug selection in multi-arm multi-stage Parkinson's disease trials within the EJS ACT-PD initiative

Cristina Gonzalez-Robles[*,1], Rebecca Chapman[2], Sally Collins[2], David T Dexter[3], Susan Duty[4], Romy Ellis-Doyle[1], Edwin Jabbari[1], Keith Martin[5], Kevin McFarthing[6], Georgia Mills[1], Heather Mortiboys[7], Esther Sammler[8], Paula Scurfield[9], Simon Stott[10], George Tofaris[11], Li Wei[1], Alan Wong[12], Marie-Louise Zeissler[2], Camille B Carroll[2], Thomas Foltynie[1], Oliver Bandmann[7], Anthony HV Schapira[1]*
[1] University College London, London, United Kingdom
[2] University of Plymouth, Plymouth, United Kingdom
[3] Parkinson's UK, London, United Kingdom
[4] King's College London, London, United Kingdom
[5] Expert by experience, Nottingham, United Kingdom
[6] Expert by experience, Oxford, United Kingdom
[7] University of Sheffield, Sheffield, United Kingdom
[8] University of Dundee, Dundee, United Kingdom
[9] Expert by experience, London, United Kingdom
[10] The Cure Parkinson's Trust, London, United Kingdom
[11] University of Oxford, Oxford, United Kingdom
[12] Royal Free Hospital NHS Foundation Trust, London, United Kingdom

Objectives: To select promising compounds for the initial phase of a multi-arm, multi-stage (MAMS) Parkinson's disease (PD) clinical trial as part of the Edmond J Safra Accelerating Clinical Trials in PD (EJS ACT-PD) initiative.
Background: There are currently no disease-modifying PD interventions. With a growing number of strong preclinical candidates, it is crucial to accelerate the clinical trial process. The EJS ACT-PD initiative aims to achieve this through a MAMS trial, testing several treatments against a common placebo arm and stopping futile interventions early to replace them with others. This warrants a reliable system to identify the best candidates.
Methods: A Treatment Selection Working Group (TS WG) divided initial candidate compounds into 5 mechanistic subgroups in keeping with PD pathophysiology (mitochondrial, lysosomal, protein, inflammation, and "other"). Initial candidates were identified through

various sources (literature, similar initiatives (e.g. Cure Parkinson's International Linked Clinical Trials Initiative (iLCT)), expert suggestions), and a set of go/no-go criteria and a scoring system covering preclinical, pharmacological and clinical evidence was devised. Three experts applied this scoring system to enable quantitative rankings. Detailed dossiers, partly adapted from iLCT documents, were produced for the most promising compounds and discussion within the Steering Group (SG) regarding pragmatic and logistical issues guided the final decision. There were Patient and Public Involvement and Engagement (PPIE) representatives in the WG, providing feedback throughout the process.
Results: 336 interventions were identified and reduced to 52 after application of go/no-go criteria and review by the TS WG Chairs and SG. These were scored, resulting in 14 top-ranking interventions, with at least 2 from each subgroup. Detailed dossiers were reviewed and discussed by the SG, leading to the initial candidates. A reserve list is being created in case the selected compounds cannot be included in the trial for unanticipated reasons.
Conclusions: Drug selection in a disease-modifying PD MAMS trial requires consideration of scientific and practical issues, such as design-specific ones (e.g. shared placebo arm). We present a robust, multi-step system which will hopefully inform similar initiatives. The process is being reviewed to further refine the methodology and ensure ongoing prioritisation of the most relevant candidates.

P38.19

Funding and sustainability of a multi-arm multi-stage Parkinson's disease clinical trial: Challenges and progress within the EJS ACT-PD initiative

Cristina Gonzalez-Robles[*,1], Rebecca Chapman[2], Shona Clegg[3], Sally Collins[2], Eric Deeson[4], Romy Ellis-Doyle[1], Maryanne Graham[1], Vince Greaves[1], Joel Handley[5], Emily J Henderson[6], Karen Matthews[7], Laurel Miller[8], Georgia Mills[1], Marie-Louise Zeissler[2], Camille B Carroll[2], Thomas Foltynie[9], Sonia Gandhi[1], Joy Duffen[10]*
[1] University College London, London, United Kingdom
[2] University of Plymouth, Plymouth, United Kingdom
[3] Parkinson's UK, London, United Kingdom
[4] Expert by experience, Birmingham, United Kingdom
[5] Salford Royal Hospital, Salford, United Kingdom
[6] University of Bristol, Bristol, United Kingdom
[7] National Institute of Health Research Clinical Research Network, London, United Kingdom
[8] Expert by experience, Reading, United Kingdom
[9] University College London`, London, United Kingdom
[10] The Cure Parkinson's Trust, London, United Kingdom

Objectives: To secure funding and devise strategies which ensure the long-term sustainability of a disease-modifying multi-arm, multi-stage (MAMS) Parkinson's disease (PD) clinical trial in the UK as part of the Edmond J Safra Accelerating Clinical Trials in PD (EJS ACT-PD) initiative.
Background: The EJS ACT-PD initiative aims to accelerate the identification of disease-modifying drugs in PD through a MAMS trial, which will test several treatments against a common placebo arm and stop futile interventions early to replace them with others. This poses unique funding challenges, especially considering its open-ended nature and the need for long-term viability.
Methods: A Funding and Sustainability Working Group (FS WG) was created, including different experts and Patient and Public Involvement and Engagement (PPIE) representatives. The FS WG engages with potential stakeholders to identify funding streams, understand their requirements, and start contracting processes. The FS WG maintain an active communication with the other WGs to provide funding-related feedback for other decisions within the initiative.
Results: Provisional cost estimates for the trial were generated, to determine the funding requirements for the project, as well as the percentage of cost reduction per active arm added versus a regular 2-arm phase 3 trial.
An initial list of interested funders was obtained through active contact and surveys (charities, philanthropy, government). In-depth meetings will be organised with them in early 2023 to discuss practicalities and conditions required for their collaboration, also learning from previous platform trials in other areas. Round-table events will be organised to present the project to additional stakeholders, find out their views and improve funding strategies.
A commercial survey to potential funders also provided feedback on relevant aspects, such as the funding model (i.e. single funder versus consortium) and intellectual property considerations. Preliminary commercial information on the shortlisted compounds to be included in the first phase was also collected to inform the feasibility of their inclusion in the trial.
Conclusions: We provide a roadmap to approach funding of a MAMS trial in PD, which is a challenging but exciting endeavour. Once initial funding is secured, long-term sustainability will likely require demonstrating the savings associated with this trial approach.

P38.20

Piloting the PREDIGT score in a movement disorders clinic to distinguish Parkinson's patients from subjects with other diagnoses without a neurological examination

Kelsey Grimes[*,1], Juan Li[2], Joseph Saade[3], Julianna Tomlinson[4], Douglas Manuel[5], Tiago Mestre[6], Michael Schlossmacher[6]*
[1] Parkinson's and Movement Disorders Clinic, Division of Neurology, Department of Medicine, The Ottawa Hospital; Program in Neuroscience Ottawa Hospital Research Institute, Ottawa, ON, Canada
[2] Program in Neuroscience and Program in Clinical Epidemiology, Ottawa Hospital Research Institute; University of Ottawa Brain and Mind Research Institute, Ottawa, ON, Canada
[3] Parkinson's and Movement Disorders Clinic, Division of Neurology, Department of Medicine, The Ottawa Hospital, Ottawa, ON, Canada
[4] Program in Neuroscience, Ottawa Hospital Research Institute; University of Ottawa Brain and Mind Research Institute, Ottawa, ON, Canada
[5] Program in Clinical Epidemiology, Ottawa Hospital Research Institute, Ottawa, ON, Canada
[6] Parkinson's and Movement Disorders Clinic, Division of Neurology, Department of Medicine, The Ottawa Hospital; Program in Neuroscience, Ottawa Hospital Research Institute; University of Ottawa Brain and Mind Research Institute, Ottawa, Ontario, Canada

Introduction: The PREDIGT Score model was developed to predict incident Parkinson disease (PD). As a first step, we assessed its ability to distinguish subjects with early-stage PD from healthy controls without the reliance on a motor examination using two case-control cohorts (DeNoPA; PPMI); there, the model showed robust performance with area-under-the-curve values from 0.84 to 0.92 (Li et al., npg Parkinson's Disease 2022).
Objective: To further examine the PREDIGT Score's performance, we sought to recruit 200 new study participants in the setting of an outpatient Movement Disorders Clinic and compare PD subjects, with those carrying other neurological diagnoses and healthy controls, using a 2-step approach: Step 1: completion of an online questionnaire that comprises 69 questions from 5 risk categories in the PREDIGT Score model; step 2: completion of the University of Pennsylvania Smell Identification Test (UPSIT). Following subject

recruitment, both steps were completed virtually. Results: As of December 31st, 2022, we enrolled 208 subjects between the ages of 40 to 80 years from seven diagnostic categories: typical PD (n= 56; males 63%); non-PD-type parkinsonism (n=9; males 33%); dementia with Lewy bodies (DLB; n=1; males 0%); non-PD-type tremors (n=12; males 42%); non-DLB-type cognitive impairment (n=11; males 55%); other neurological diagnoses (n=15; males 33%); and persons without any neurological disorder (n=104; males 38%). All participants successfully completed the online questionnaire; the accuracy of their diagnostic classification was confirmed by an independent rater for all subjects carrying a neurological diagnosis, as guided by published criteria. Assessment of olfactory function by UPSIT is ongoing.
Conclusions: We present the results of a pilot study to prospectively test the performance of the PREDIGT Score model, as carried out in two steps at home, regarding its performance in discriminating patients with typical PD from those with other forms of parkinsonism, unrelated neurological conditions and from healthy controls. If further validated, the PREDIGT Score model could provide a useful screening tool for subjects with typical PD or those at high risk of PD.

P38.21

LRRK2 Inhibition by BIIB122: Trial designs for two efficacy and safety studies in Parkinson's disease patients with and without LRRK2 mutations (LIGHTHOUSE and LUMA)

Julia Shirvan[*,1], Danna Jennings[2], Pan Wang[1], Romeo Maciuca[2], Sowmya Chary[1], Katie Harrison[1], Angela Kay[2], Kyle Fraser[1], Sarah Huntwork-Rodriguez[2], Minhua Yang[1], Matthieu Levee[1], Peter Chin[2], Tien Dam[1]*
[1] Biogen, Cambridge, MA, United States
[2] Denali Therapeutics, Inc., South San Francisco, United States

Objective: Describe LUMA and LIGHTHOUSE, two studies that investigate efficacy and safety of BIIB122, a LRRK2 inhibitor.
Background: Increased LRRK2 kinase activity has been linked to lysosomal dysfunction and Parkinson's disease (PD) pathogenesis. Inhibition of LRRK2 kinase activity is a promising new approach to treat PD with and without a LRRK2 mutation. BIIB122 is a potent, selective, CNS-penetrant LRRK2 kinase inhibitor under investigation for treatment of PD.
Methods: Two multi-center, randomized, double-blind, placebo-controlled trials will investigate the efficacy and safety of BIIB122 in early-stage PD patients.
The LUMA study will enroll PD patients who do not carry a LRRK2 pathogenic variant (n~640 patients) diagnosis within 2 years, Hoehn and Yahr 1-2, untreated with symptomatic PD medications or stably treated with MAOB inhibitor or levodopa monotherapy. LUMA participants will be randomized (1:1) to BIIB122 225 mg or placebo administered orally daily for a 48-week minimum to 144-week maximum treatment period.
The LIGHTHOUSE study will enroll patients carrying a LRRK2 pathogenic variant (n~400 patients) diagnosis within 5 years, Hoehn and Yahr 1-2.5, untreated or stably treated with symptomatic PD medications. LIGHTHOUSE participants will be randomized (1:1) to BIIB122 at doses of 225 mg or placebo administered orally daily for a 96-week minimum to 180-week maximum treatment period.
Primary outcome measure will be a time to event endpoint using the Movement Disorders Society-Unified Parkinson Disease Rating Scale (MDS-UPDRS) for both studies. Secondary outcomes will include safety, Schwab and England Activities of Daily Living Scale, and MDS-UPDRS. Pharmacokinetics of BIIB122 will be examined through plasma levels. Pharmacodynamics will be characterized by phosphorylated serine 935 in whole blood for target inhibition, BMP in urine for downstream lysosomal pathway modulation, and total LRRK2 and lysosomal markers in cerebrospinal fluid for central target and lysosomal pathway engagement.
Results: Early studies on BIIB122 support its continued development through LUMA and LIGHTHOUSE.
Discussion: LUMA and LIGHTHOUSE are the first studies of LRRK2 inhibition in PD patients with efficacy endpoints that measure clinical progression of PD and biomarkers that measure the expected biologic impact of LRRK2 inhibition.

P38.22

Listening to the experience of participants on neurosurgical trials: Outcomes of the LEARN-GDNF and LEARN-transeuro studies

Cheney Drew[1], Kim Smallman[1], Suzette Shahmoon[2], Emma Lane[*,3]*
[1] Centre for Trials Research, Cardiff University, Cardiff, United Kingdom
[2] Cardiff University, Cardiff, United Kingdom
[3] School of Pharmacy and Pharmaceutical Sciences, Cardiff University, Caerdydd, United Kingdom

Clinical trials involving neurosurgical interventions (including growth factor, cell and gene therapies) are filling the horizon for Parkinson's disease. Whilst offering a lot of potential, these invasive trials are demanding on the participants, requiring them to undertake brain surgery and repeated brain imaging alongside a range of assessments of motor and non-motor function. Designing trials centering participants and their own support network, whilst balancing acceptable participant burden with the need for collecting clinically validated outcomes can be facilitated by understanding the lived experiences of those who have taken part in similarly invasive trials.
Semi-structured online interviews were conducted with participants and their family members/ care partners following a trial of Glial Derived Neurotrophic Factor (GDNF) infused via intra-cranially implanted drug delivery catheters (Whone et al) and also with participants of the TransEuro, a foetal dopaminergic neuron transplantation trial (Barker et al). Interviews were conducted on-line alone or in dyads, and observed by a second non-participatory researcher. Interviews were transcribed verbatim and analysed thematically using NVivo software.
The experiences of participants were largely positive, expressing strong feelings of collegiality and altruism. Specific issues surrounding the nature and timing of assessments and post operative care were identified. A common thread relating to negative experiences lay with the difficulties participants faced once the trial had ended and the transition from participant to patient. This included the impact of learning about the negative outcome of the trial and decreased interactions with health care professionals following an intensive study period.
Listening to the voice of lived experience from novel, complex trials is vital to inform the design of patient-centred studies to enhance recruitment and retention for maximum impact. Simple modifications to trial conduct can significantly improve the participant experience and advocates for the inclusion of broad and diverse patient experience in the development of future ATMP studies.

P38.23

The LEARN study: Tools to aid participant and support partner experience in clinical trials for Parkinson's disease

Cheney Drew[1], Kim Smallman[1], Lesley Gosden[1], Colin Gosden[1], Darren Calder[1], Jayne Calder[1], Helen Matthews[2], Emma Lane[,3]*
[1] Cardiff University, Cardiff, United Kingdom
[2] Cure Parkinson's, London, United Kingdom
[3] Cardiff University, Caerdydd, United Kingdom

With new potential therapies for Parkinson's comes new clinical trials. However, the complexity and multi-dimensional nature of Parkinson's and the novel interventions require good communication tools to support informed participation. A recent interview study (see Drew et al) and survey (see Fuest et al) identified several areas of clinical trial participation that lack user-friendly information.
Semi-structured interviews were conducted with trial participants and care partners, transcribed verbatim and analysed thematically using NVivo software. Four specific outputs were drafted: two documents and 4 videos were drafted by the research team, with the assistance of the participant advisory group and consultation with UK based Parkinson's charities and public contributors with Parkinson's.
A checklist for trials: Whilst all participants engaged with the consent process, recruiting more diverse participants means better supporting them to identify where they may lack knowledge or understanding. We developed a checklist (with supporting video) adaptable to different trial designs, for use by potential participants to check their understanding and ask the right questions of the trial team.
'Off medication assessments': what they are and how to cope: A major concern for participants, representing a significant barrier to trial entry, is the experience of being assessed 12 hours or more after their last dose of medication. This guidance document and supporting video explains what 'off medication' assessments with hints and tips from previous trial participants.
Brain imaging, what you will experience. Having MRI or PET imaging can be a daunting experience for trial participants. Knowing what to expect can alleviate those concerns or better inform participants to avoid retention issues. This video walks through the process of MRI and PET brain scanning as might be experienced on a trial.
Conversations with care partners: care partners are often crucial to participants taking part in trials but their experiences are often not prioritised by either trial staff or their partners with Parkinson's. This video provides an insight into that experience which may help both support partners and participants to recognise the important of sharing their clinical trial journey.
This is part of ongoing work to identify how the experience of participation in clinical trials can be improved.

P38.25

Case studies of a 3-year follow-up of abdominal photobiomodulation treatment for Parkinson's disease

Ann Liebert[,1], Brian Bicknell[2], Vincent Pang[2], Geoffrey Herkes[1], Hosen Kiat[3]*
[1] Sydney Adventist Hospital, Wahroonga, NSW, Australia
[2] Western Sydney University, Westmead, NSW, Australia
[3] Cardiac Health Institute, Sydney, Australia

Parkinson's disease is a relentlessly progressive neurodegenerative disease, with deterioration in the clinical signs and symptoms expected and anticipated. PD is also a complex disease and highly heterogeneous in symptomology and progression. The rate of progression is difficult to predict and various from person to person. While medication intervention early in the disease trajectory can create a so-called "honeymoon period" where symptoms can appear stable or even improve somewhat, the trajectory over years is inevitable deterioration in motor and non-motor symptoms, which significantly impacts health-related quality of life in all patients.
Photobiomodulation (PBM) is the use of non-thermal light to affect cellular processes. We have previously demonstrated that abdominal laser PBM treatment has the potential to improve some of the clinical signs and symptoms of Parkinson's disease for up to one-year in two clinical proof-of-concept trials. The objective of the study reported here was to assess the effectiveness of continued at-home abdominal laser PBM treatment (with a class 1 "PDCare" laser) over a three-year period. We report on 3 participants (of the original 7 from the clinical trial) who continued PBM treatment. Each was assessed for mobility, fine motor skills, balance, and cognition, as well as a novel blood marker (kynurenine/tryptophan ratio). The participants were compliant in their use of the treatment. No negative side-effects to the treatment were reported. Results suggested that continued at-home treatment with PBM effectively maintained the symptomatic improvements gained in the initial trial for as long as treatment continued. The results of this study warrant a larger, long-term, prospective randomised trial.

P38.26

A triple-blinded, sham controlled study of transcranial photobiomodulation (PBM) in Parkinson's disease

Claire McGee[,1], Ann Liebert*[,2], Brian Bicknell[3], Vincent Pang[3], Craig McLachlan[1], Hosen Kiat[4], Geoffrey Herkes[2]*
[1] Torrens University, Sydney, Australia
[2] Sydney Adventist Hospital, Wahroonga, Australia
[3] Western Sydney University, Westmead, NSW, Australia
[4] Cardiac Health Institute, Sydney, Australia

Objective: To determine the safety and efficacy of Transcranial Photobiomodulation (PBM) in Parkinson's Disease
Background: PBM is the use of non-thermal light to modulate cells and tissues. Animal and some pilot human studies suggest that PBM has positive outcomes on the symptoms and signs of Parkinson's disease. PBM is well tolerated but its overall efficacy is still under investigation. This study was performed predominantly in 2021, when Covid-19 meant that many face-to-face interactions were not possible.
Methods: We conducted a double-blind, randomised, sham controlled trial of an active PBM ("NeuroCare") helmet vs a sham helmet for 12 weeks (20 active, 20 sham), followed by a further 12 weeks of a no treatment phase for those on active therapy or active treatment for those who had been on sham. The coprimary endpoints were safety, and efficacy as assessed by the MDS-UPDRS-motor scale. Secondary endpoints were patient reported outcomes.
Results: The treatment was well tolerated, with no adverse events greater than classified as minor. Of the completers, there was a significant improvement in the UPDRS-motor scale in those who switched to active treatment. The relevance of these results, and the large placebo effect noted in the first 12 weeks, will be discussed. In addition, secondary outcome data will be presented. The issue of performing a clinical trial using video assessments is highlighted.
Conclusion. PBM was well tolerated. We present the largest sham-controlled blinded study in people living with Parkinson's disease to date.

P38.29

Exploring the disease-modifying potential of the probiotic Bacillus subtilis in Parkinson disease

Jodi Maple-Grødem[*,1], Veslemøy Hamre Frantzen[1], Conni McCarthy[2], Johannes Lange[3], Rachel Dakin[2], Guido Alves[1], Maria Doitsidou[2], David Breen[4]*
[1] Stavanger University Hospital, Stavanger, Norway
[2] University of Edinburgh, Edinburgh, United Kingdom
[3] Stavanger University Hospital, Norway, Norway
[4] Royal Infirmary of Edinburgh, Edinburgh, United Kingdom

Background: In people with Parkinson disease (PD), the protein α-synuclein builds up and forms toxic clumps which are associated with the death of dopamine producing nerve cells. Therefore, α-synuclein is a major target for drug development. We have recently shown that including a probiotic called B. subtilis in the diet of an animal model of PD (the roundworm C. elegans) could protect against the build-up of α-synuclein and remove some of the already formed protein clumps. B. subtilis is available for human consumption and has a low cost and an excellent safety profile and based on our pre-clinical work it is possible it could be a novel therapeutic strategy for PD.
Objective: Together, the University of Edinburgh and Stavanger University Hospital will test the potential of B. subtilis PXN21 to modify α-synuclein aggregation in patients with PD.
Design/Methods: We have initiated a twin site, placebo-controlled study to evaluate tolerability and target engagement of B. subtilis PXN21 in PD. A total of 52 PD patients (26 at each site) will be recruited and will be randomised to receive either B. subtilis PXN21 or matched placebo over 24 weeks. The primary outcome measure will be changes in gut and blood-based biomarkers relevant to the proposed mechanisms of action, as well as evaluating the acceptability of taking regular B. subtilis PXN21 in the PD population. Secondary outcome measures will be changes in gut microbiota and PD motor and non-motor symptoms.
Outlook: While PD is fundamentally a condition that affects the brain, it is increasingly clear that the gut microbiome plays a major role in the disease. This has driven the interest in investigating the use of probiotics as novel therapeutic strategies for PD. The results of our study will provide the first clues to understand if B. subtilis PXN21 can impact PD and could form the basis for larger future trials.

P38.30

Characterizing the frequency of clinically reportable variants in major genes established in Parkinson's disease (PD) in a large American cohort

Kamalini Ghosh Galvelis[*,1], Anna Naito[2], Lola Cook[3], Jennifer Verbrugge[3], Tae-Hwi Schwantes-An[3], Jeanine Schulze[3], Priscila Hodges[3], Amanda Miller[3], Rebeca De Leon[2], Rossy Cruz Vicioso[4], Anny Coral-Zambrano[2], Laura Heathers[3], Michelle Totten[3], Tatiana Foroud[3], Anne Hall[2], Anne-Marie Wills[5], Karen Marder[6], Ignacio Mata[7], Niccolo Mencacci[8], Marth Nance[9], Michael Schwarzschild[5], Tanya Simuni[8], James Beck[1], Roy Alcalay[10]*
[1] Parkinson's Foundation, New York, NY, United States
[2] Parkinson's Foundation, Miami, FL, United States
[3] Indiana University, Indianapolis, IN, United States
[4] Unión Médica del Norte Clínica Universitaria, Santo Domingo, Dominican Republic
[5] Massachusetts General Hospital, Boston, MA, United States
[6] Columbia University Irving School of Medicine, New York, NY, United States
[7] Cleveland Clinic, Cleveland, OH, United States
[8] Northwestern University, Chicago, IL, United States
[9] Park Nicollet Struthers Parkinson's Center, Minneapolis, MN, United States
[10] Tel Aviv Sourasky Medical Center, Tel Aviv, Israel

Background: Seven genes (LRRK2, GBA, PRKN, PINK1, SNCA, PARK7 and VPS35) are established as causative for PD. Those with PD are often unaware of their genetic status since clinical testing is rarely offered, limiting personal and clinical utilities, such as enrollment in precision medicine trials. Furthermore, the genetic yield in a large North American population is largely unknown.
Methods: PD GENEration is a multi-center, observational study, offering genetic testing and counseling to individuals with PD in Canada, Dominican Republic (DR) and the United States (US). DNA samples undergo next-generation sequencing and deletion/duplication analysis (CLIA-certified; Fulgent Genetics). Variants classified as pathogenic/likely pathogenic, and those considered clinically actionable, are disclosed.
Results: From September 2019 to January 2023, the study enrolled 7,500+ participants across 35 sites, 60+ referral centers in Canada, DR and the US. Overall, 11.5% of the cohort are Hispanic/Latino. As of January 1, 2023, 6,166 participants have completed testing. US cohort characteristics include: 41% female; 92% White, 3% Asian, 2% Black, 7% Hispanic/Latino; and a mean age of 66.5 years (S.D. 10.2). Sixteen percent had early-onset PD (age < 50 years), 15% were high-risk ancestry, and 22% had an affected first-degree relative. Of individuals tested, 829 (13.4%) participants had a reportable variant; 8.4% with variants in GBA1; 2.6% in LRRK2; 2.4% in PRKN; 0.2% in SNCA; and 0.1% in VPS35, PINK1, or PARK7. Twenty-seven (0.4%) participants had variants in more than one gene. Variants were more frequently identified among those with early-onset PD (onset at age <50), high-risk ancestry (Ashkenazi Jewish, Spanish Basque, or North African Berber), or a first-degree relative with PD, compared with those without these risk factors (18.6% vs. 9.4%; P<0.001).
Conclusions: Genetic testing of well-established PD genes in this cohort resulted in a genetic diagnostic yield of 13.4%, and, notably, 9.4%, in those without obvious risk factors. Together with the increasing utility of self-knowledge of PD gene status, our findings support a shift to universal testing in those with PD who are interested.

P38.32

APGS-ShakeItUp Australia Parkinson's registry: A catalyst for rapid testing of new therapies in clinical trials

Michael Katz[1], Clyde Campbell[1], Vicki Miller[1], Richard Balansan[1], Nicholas G. Martin[2], Miguel E. Renteria[*,2]*
[1] Shake It Up Australia Foundation, Sydney, NSW, Australia
[2] QIMR Berghofer Medical Research Institute, Brisbane, Queensland, Australia

The APGS-ShakeItUp Australia Parkinson's Registry is a new resource designed to enable the rapid testing of new therapies in clinical trials for Parkinson's disease (PD). PD is a neurological disorder that affects over 100,000 people in Australia and is the fastest growing, with 38 new cases diagnosed every day. Recent progress in genomics and biomarker discovery has led to the development of promising potential disease-modifying therapies for PD. However, many clinical trials for PD have failed in the past due to the lack of matching the right treatments with the right patients.
The Australian Parkinson's Genetics Study (APGS) is a nationwide cohort study supported by the Michael J. Fox Foundation for Parkinson's Research (MJFF) and Shake It Up Australia Foundations. APGS has enrolled more than 7,000 participants with PD as of December 2022 and has a target of 10,000 participants by mid-2023. Participants are recruited through a combination of methods, including targeted assisted mailouts to people identified as

having been prescribed Parkinson's medications in the last two years, according to government records in the nationwide Pharmaceutical Benefits Scheme database. These mailouts are managed by a specialized government agency, which maintains the confidentiality of the recipients. Participants who choose to participate are asked to learn more about the study, provide informed consent, and complete questionnaires about their clinical symptoms, family history, medical history, treatment history, lifestyle, and environmental exposures. They also provide a saliva sample via traditional mail for DNA genotyping. The recruitment strategy allows us to reach potential participants from a range of backgrounds form across the country.
Additionally, in partnership with the Shake It Up Australia Foundation, the APGS researchers have established the APGS-ShakeItUp Australia Parkinson's Registry, which allows a subset of consented patients to be screened for eligibility and invited to participate in clinical trials. Companies or institutions interested in running a trial can contact the Shake It Up Australia Foundation for further information (enquiries@shakeitup.org.au).

P38.33

Randomized, double-blind, sham-controlled study to evaluate effectiveness of photobiomodulation plus exercise, to enhance motor, cognition and quality of life in those with Parkinson's disease

Anita Saltmarche[*,1], Orla Hares[2], Ann Liebert[3], Brian Bicknell[4], Margaret Naeser[5], Geoff Herkes[6]*
[1] Saltmarche Health & Associates - Photobiomodulation Specialists, Caledon East, Ontario, Canada
[2] Gaitway Neurophysio, Parkinson's Wellness Innovation Centre, Hamilton, Ontario, Canada
[3] Faculty of Medicine and Health, University of Sydney, Sydney, NSW, Australia
[4] NICM Health Research Institute, Western Sydney University, Sydney, NSW, Australia
[5] VA Boston Healthcare System, Boston University School of Medicine, Boston, MA, United States
[6] Sydney Adventist Hospital, Sydney, NSW, Australia

Background: Parkinson's disease (PD) is the fastest growing and second, most common progressive neurodegenerative condition worldwide, resulting in significant motor and non-motor consequences. Current treatments are limited. Research and clinical studies suggest that photobiomodulation (PBM) - the application of red and near-infrared wavelengths of light (633nm to 1100nm) to cells, can optimize cellular activity to increase ATP, manage neuro-inflammation, and reduce oxidative stress. PBM may provide benefit for those with Parkinson's and other neurodegenerative diseases.
Objective: This single-centre trial investigates if following a series of Active or Sham PBM treatments, there is significantly greater improvement in motor, cognitive and quality-of-life measures in individuals with PD who receive Active PBM treatments plus exercise, compared to those with PD who receive Sham PBM treatments plus exercise.
Methods: Eligible participants (ages 55-75) will have moderate-stage PD (Hoehn & Yahr, Stages 2-3 scores). Sixty participants will be randomly assigned to either an Active PBM Group (n=30), or a Sham PBM Group (n=30). Each Group will receive a total of 24, self-administered home PBM treatments (Active or Sham), three times per week, eight weeks. Assessments will be performed at Entry, and at 1 and 4 weeks after the final PBM treatment (Active or Sham). Exercise will have been part of each participant's routine, before entering the study, and will continue during, and after the PBM treatment series. There is an option of Active PBM home treatment (open protocol), for those who completed the Sham PBM series.
Each PBM protocol (Active or Sham) has abdominal and cervical placements using the PDCare Laser (a hand-held, super-pulsed, near-infrared, 904nm laser); and transcranial (scalp) placements using the NeuroCare LED helmet (red and near-infrared LEDs). Participants receive three introductory PBM treatments/teaching sessions in the clinic, prior to initiating their home treatments. Weekly, follow-up telephone calls monitor adherence to the PBM protocol and exercise regimen. At completion of participation in the study, devices are returned to the centre, and two post-treatment, outcome measurement sessions are performed.
Results: Quantitative and qualitative results from the initial PBM series (Active and Sham) will be presented.

P38.34

The Vall d'Hebron Initiative for Parkinson (VHIP) cohort: a prospective, longitudinal and observational study enrolling de novo Parkinson's disease (PD) patients and carriers of PD-linked mutations for biomarker and pathophysiology studies

Daniela Samengo, Laura Domingo, Maria Camprodon, Silvia Enriquez, Mar Armengol, Victoria Gonzalez, Sara Lucas, Helena Xicoy, Jordi Riera-Heredia, David Montpeyó, Marta Martinez-Vicente, Ariadna Laguna, Jorge Hernandez-Vara*
Vall d'Hebron Hospital, Barcelona, Spain

Objective: To describe the study protocol of the Vall d'Hebron Initiative for Parkinson (VHIP) cohort, a prospective, longitudinal and observational cohort study aimed at deeply phenotyping de novo PD patients and carriers of PD-linked mutations. We anticipate this initiative will contribute to identify biomarkers for PD risk, diagnosis and prognosis, as well as to stratify disease subtypes and increase our understanding of pathophysiology at early PD stages.
Background: PD is a progressive neurodegenerative disorder causing a variety of motor and non-motor symptoms. To date, no disease-modifying treatment exists and diagnosis is based on the manifestation of the clinical motor symptoms, which occurs when the neurodegenerative process is already advanced. Studies designed to find diagnostic/prognostic biomarkers and pathophysiological pathways involved in disease onset/progression are needed.
Methods: Participants involving 150 de novo subjects and 150 aged- and sex-matched healthy controls are estimated to be recruited by the movement disorders specialists at the Vall d'Hebron University Hospital. After informed consent, subjects are evaluated to primarily assess objectives within four major domains of PD: motor, cognitive-affective, autonomic function and vision. First, an extensive clinical evaluation is performed by recording demographic, personal history, lifestyle and dietary habits, and by completing clinical scales covering motor and non-motor symptoms. Second, data from autonomic function and visual function tests, together with neuroimaging data, are acquired. Finally, a wide range of biospecimens such as blood, cerebrospinal fluid, urine, feces, oral and olfactory mucosa swab, and skin biopsy are collected for biochemical and molecular assessments, including the genotyping of all participants. The recruitment is ongoing since 2019 and participants will receive follow-up assessments at 2.5 and 5-year intervals.
Results/Conclusions: VHIP is the first study to establish a Spanish cohort combining clinical, imaging, biochemical and molecular data in de novo patients and PD-linked mutation carriers over time. To date, 74 participants have been recruited: 15 controls and 59 PD patients (10 previously diagnosed and 49 de novo). After genotyping, 2 GBA non-manifesting carriers were identified from the 11 controls genotyped and 16 PD patients with genetic mutations

from the 25 patients genotyped (8 with GBA, 5 with LRRK2 and 3 with ATP13A2 mutations).

P38.36

Development and validation of the Parkinson's Disease-Health Index (PD-HI): A disease-specific, patient-reported outcome measure for use in clinical trials

Jamison Seabury*[,1], Jennifer Weinstein[1], Spencer Rosero[1], Anika Varma[1], Charlotte Engebrecht[1], Nuran Dilek[2], John Heatwole[3], Michael McDermott[2], Abigail Arky[4], E. Ray Dorsey[1], Christine Zizzi[1], Chad Heatwole[5]
[1] University of Rochester Center for Health + Technology, Rochester, NY, United States
[2] University of Rochester Department of Biostatistics and Neurology, Rochester, NY, United States
[3] Pittsford Sutherland High School, Pittsford, NY, United States
[4] Des Moines University College of Osteopathic Medicine, Des Moines, IA, United States
[5] University of Rochester Center for Health + Technology; University of Rochester Department of Neurology, Rochester, NY, United States

Background: In preparation for Parkinson's disease (PD) therapeutic trials and to optimize the clinical care of patients with PD, it is critical for the PD research community to have access to valid, disease-specific, and responsive patient-reported outcome measures (PROs) that are accepted by patients. Properly validated, disease-specific PROs are an optimal way to bring the patient voice to the forefront of clinical trials and quantify clinically meaningful changes in patient health in response to therapeutic intervention. This research utilized large scale patient-reported data and published Food and Drug Administration (FDA) guidelines to develop and validate the Parkinson's Disease-Health Index (PD-HI), a novel PRO designed for use in PD clinical trials and clinical care.
Methods: We conducted semi-structured qualitative interviews and a national cross-sectional study of individuals with PD to identify the most important symptoms to this population. Symptoms with the highest prevalence and relative impact to the cross-sectional sample cohort were selected as questions in the PD-HI. We used factor analysis to group symptom questions into symptomatic themes of PD health, developing instrument subscales. We conducted beta interviews to assess the relevance and usability of the PD-HI to participants. We evaluated the test-retest reliability of the PD-HI over a 14-day period. We used known groups and area-under-the-curve (AUC) analyses to assess the ability of PD-HI scores to distinguish between subgroups of participants with differing disease severity.
Results: Twenty individuals with PD participated in the initial qualitative interviews. Four-hundred and four individuals with PD participated in the cross-sectional study, providing over 120,000 symptom rating responses. During beta testing, participants indicated that the PD-HI was comprehensive, relevant, and easy to use. The PD-HI demonstrated high internal consistency, test-retest reliability, and an ability to distinguish between individuals with differing disease severity. The final PD-HI consists of 13 subscales which comprehensively measure patient-reported disease burden in the areas of health that are most important to patients.
Conclusion: This research provides initial evidence that the PD-HI is a valid mechanism to quantify multifaceted patient-reported disease burden in PD.

P38.37

Worldwide collaborative framework for optimizing new Parkinson's treatment trials with patient centric outcome measures

Diane Stephenson[*,1], Yuge Xiao[2], Catherine Kopil[2], Karen Lee[3], David T. Dexter[4], Martijn Müller[1], Klaus Romero[1], Helen Matthews[5], Gary Rafaloff[6], Jodie Forbes[7], Sarah Zenner[8], Carroll Sui[7], Johan Hellsten[9], Mark Maybank[10], Tanya Simuni[11]*
[1] Critical Path Institute, Tucson, AZ, United States
[2] The Michael J. Fox Foundation, New York, NY, United States
[3] Parkinson's Canada, Ontario, Canada
[4] Parkinson's UK, London, United Kingdom
[5] Cure Parkinson's, London, United Kingdom
[6] PD Patient Researcher/Advocate, New York, NY, United States
[7] PD Patient Researcher/Advocate, London, United Kingdom
[8] PD Patient Researcher/Advocate, Evergreen, CO, United States
[9] PD Patient Researcher/Advocate, Malmo, Sweden
[10] PD Patient Researcher/Advocate, Toronto, Canada
[11] Northwestern University, Chicago, IL, United States

Background: Development of effective therapies for Parkinson's disease (PD) is a high priority with many promising new targets in the pipeline. Global regulatory agencies have embraced the concept of patient-focused drug development and recommend that people living with PD are included in all stages of drug development. There is a growing need for new sensitive, responsive patient-centric endpoints that are adequately validated for use in clinical trials to evaluate safety and efficacy of new treatments.
Objectives: To present a new pre-competitive collaborative worldwide network including the Critical Path for Parkinson's (CPP) consortium that outlines how all stakeholders are working together to advance the development of new outcome measures that are meaningful to patients and reflect what is clinically meaningful for use in Parkinson's trials.
Methods: Five global nonprofit research organizations have convened under the CPP consortium in partnership with industry and academic experts to participate in a working group with the goal of defining ways to optimize patient-centered endpoints for Parkinson's clinical trials. The working group objectives are 1) to identify what symptoms and measurements are important to people living with Parkinson's and 2) to assess the landscape of available measurement approaches including digital measurement of signs/symptoms by carrying out a comprehensive data inventory of studies being carried out around the world.
Results: The Michael J. Fox Foundation for Parkinson's Research, Parkinson's UK, and Parkinson Canada co-hosted the Parkinson's Disease Endpoints Roundtable convening November 2-3, 2022, in Washington, DC to discuss the current scientific and regulatory environment for clinical outcome assessment development in PD, define unmet needs and outline areas of collaboration. The global PD endpoints initiative recognizes the need to catalogue and inventory relevant Parkinson's studies where data collection has been carried out to date, is ongoing, or planned for the future.
Conclusions: The information gathered from the assessment of the landscape of clinical endpoints in PD studies promises to improve efficiencies across all stakeholders in the development of novel measures to improve Parkinson's clinical trials. A robust collaboration between all stakeholders around the world centered on data standards and sharing is key for success in the future.

P38.38

Parkinson's disease drug therapies in the clinical trial pipeline: 2020-2022

Kevin McFarthing[*,1], Sue Buff[2], Gary Rafaloff[3], Leah Mursaleen[4], Rosie Fuest[4], Marco Baptista[5], Brian Fiske[5], Richard Wyse[4], Simon Stott*[*,4]*

[1] Parkinson's advocate, Oxford, United Kingdom
[2] PDTrialTracker, San Francisco, United States
[3] Parkinson's advocate, Miami, United States
[4] Cure Parkinson's, London, United Kingdom
[5] The Michael J Fox Foundation, New York, United States

Introduction: For the last three years, we have provided an overview of the pharmacological therapies - both symptomatic and disease modifying – under clinical evaluation for Parkinson's disease (PD). The goal is to provide the research and patient communities with a better understanding of the pipeline for PD, to create greater awareness of the opportunities for engagement and collaboration.
Methods: Each January (from 2020 - 2022), we downloaded data on active clinical trials of PD drug therapies from the online U.S. National Library of Medicine clinical trials database (ClinicalTrials.gov). We then analysed the studies that fit our inclusion criteria. We sorted the trials into their different phases, grouping them based on mechanism of action or class of drug, and whether the study is symptomatic or disease modifying.
Results: Despite the COVID19 pandemic, we observed a relatively stable number of clinical trials during 2020, 2021 and 2022 (number of trials being 145, 142 and 147, respectively). This consistency was not due to trials being in limbo, as there was an annual turnover of approximately 1/4 of the studies (45 studies (31%) dropped out of the database between 2020 & 2021, and this number was 36 (24%) between 2021 & 2022). Stability was also observed in the distribution of trials in each phase of testing, with approximately 35% of trials each year in Phase 1, 45-50% in Phase 2, and only 15-20% at the Phase 3 level. Similarly, the overall nature of the trials remained stable, with approximately 40% of the studies focusing on disease modifying therapies each year. One area of concern is the low number of disease-modifying drugs in Phase 3. In general, 1/3 of the trials each year were testing repurposed therapies. Particularly encouraging was the broad range of approaches being tested in PD, from cell transplantation to GLP-1 receptor agonists.
Discussion: Despite significant global health constraints, the development of new drug-based therapies for PD over the last three years has remained diverse and robust. New efforts focused on speeding up the clinical trial process (such as the EJS-ACT-PD platform) should help to further stimulate progress.

P38.39

Ten years of drug repurposing for Parkinson's: The international linked clinical trials project

Richard Wyse[*,1], Simon Stott[1], Tom Isaacs[1], Roger A Barker[2], Jerry Callaghan[3], Mark R Cookson[4], Ted Dawson[5], David Devos[6], David T Dexter[7], Joy Duffen[1], Howard Federoff[8], Brian Fiske[9], Thomas Foltynie[10], Susan Fox[11], J. Timothy Greenamyre[12], Lyndsey Isaacs[1], Karl Kieburtz[13], Jeffrey H Kordower[14], Dimitri Krainc[15], Soania Mathur[16], Helen Matthews[1], Kevin McFarthing[17], Darren Moore[3], Leah Mursaleen[1], Gary Rafaloff[18], Michael Schwarzschild[19], David Sulzer[20], Caroline Tanner[21], Camille Carroll[22], David K. Simon[23], Patrik Brundin*[*,24]*

[1] Cure Parkinson's, London, United Kingdom
[2] University of Cambridge, Cambridge, United Kingdom
[3] Van Andel Institute, Grand Rapids, United States
[4] National Institutes of Health, Bethesda, United States
[5] Johns Hopkins University School of Medicine, Baltimore, United States
[6] Université de Lille, Lille, France
[7] Parkinson's UK, London, United Kingdom
[8] University of California, Irvine, Irvine, United States
[9] The Michael J Fox Foundation for Parkinson's Research, New York, United States
[10] University College London, London, United Kingdom
[11] University of Toronto, Toronto, Canada
[12] University of Pittsburgh, Pittsburgh, United States
[13] University of Rochester, Rochester, United States
[14] Arizona State University, Tempe, United States
[15] Northwestern University Feinberg School of Medicine, Chicago, United States
[16] Patient advocate, Toronto, Canada
[17] Patient advocate, Oxford, United Kingdom
[18] Patient advocate, Miami, United Kingdom
[19] Harvard Medical School, Boston, United Kingdom
[20] Columbia University, New York, United States
[21] University of California San Francisco, San Francisco, United States
[22] University of Plymouth, Plymouth, United Kingdom
[23] Harvard Medical School, Boston, United States
[24] Van Andel Insitute, Grand Rapids, United Kingdom

In an effort to speed up the search for disease modifying therapies, in 2012 the research charity Cure Parkinson's initiated the international Linked Clinical Trials (iLCT) project. It is a global clinical trial programme, centred around an annual two-day meeting at which a committee of 22 Parkinson's experts evaluate, rank and prioritise a selection of ~20 dossiers that have been compiled by Cure Parkinson's research team. The dossiers are focused on therapeutic candidates that have displayed evidence of disease modifying potential in the context of Parkinson's.
As well as iLCT committee members, Parkinson's patient advocates and representatives from major Parkinson's research charities and government regulatory institutes are invited to attend and contribute to the meetings. Everyone is part of the discussion, but only the iLCT committee members are allowed to score the dossiers.
The dossiers contain a comprehensive summary of the treatment being assessed. If a dossier is prioritised by the iLCT committee, Cure Parkinson's is mandated to support getting the associated agent into clinical testing for Parkinson's. This might occur by providing funding with the iLCT funding partners (such as the Van Andel Institute and the John Black Charitable Foundation) or by providing letters of support, guidance on clinical trial design, and/or support with patient involvement/communication.
Over the last decade, 205 dossiers have been presented to the iLCT committee, representing a total of 159 agents. 32 of these potential therapies have gone into clinical trials that have involved 4,745 people with Parkinson's (PwP) in 17 countries. There have been 20 completed studies of 17 agents (involving 1,439 PwP), and there are currently 21 trials of 18 drugs that are currently active (involving 3306 PwP), including two Phase 3 trials for exenatide and ambroxol.
Current/future plans include an expansion of the number of clinical trials with iLCT agents being tested via new platforms like the Australian Parkinson's Mission and the Edmond J Safra Accelerating Clinical Trials in PD (EJS ACT-PD) initiative. In addition, Cure Parkinson's has set up a new "pipeline research" programme to proactively accelerate the collection of missing preclinical research required to properly judge whether an iLCT agent of interest should be prioritised.

P38.40

Patient engagement in early drug development: Building target product profiles with patient experts and organisations, from validation to co-creation

Kate Trenam[*1], Kevin Kwok[2], Paula Scurfield[3], Nikul Bakshi[4], James Beck[5], Carl Vandeloo[1], Isabelle Wilputte[1]*
[1] UCB Pharma, Brussels, Belgium
[2] Patient Expert, Parkinson's Foundation, New York, New York, United States
[3] Patient Expert, Parkinson's UK, London, United Kingdom
[4] Parkinson's UK, London, United Kingdom
[5] Parkinson's Foundation, New York, New York, United States

UCB Pharma, Parkinson's Foundation and Parkinson's UK formed a Patient Engagement Council for Parkinson's Research, in partnership with patient experts (PEs), aiming to ensure patient insights are central to the overall activities across Parkinson's research and early clinical development. The Council identified target product profiles (TPPs, a planning tool for the progression of a medicine from discovery to clinical development, capturing expected and minimally acceptable features), as a key area of focus. The project aim is to bring patient perspectives early and consistently into the TPPs development process, moving from ad-hoc patient validation towards early co-creation with alignment to the Patient Focused Medicines Development Target Product Profile guidance. Here, we report best practices, learnings and successes from this project.

Five workshops were planned to discuss the new TPPs process, however, outputs from the first two showed a need to move away from industry structure and thinking, to an approach beginning with how people living with Parkinson's think. One-to-one interviews with two PEs and two patient organisations were conducted and review sessions with PEs are taking place. Two TPP outputs (a playbook and patient community guidance) containing key principles on when, who and how the patient community should be engaged and what they should engage with are being finalised, and will be shared with the Parkinson's community. Key to success will be changing mindsets and embedding this new approach towards TPP development.

We established the following guiding principles for TPPs: simplifying concepts that are relevant for patient discussions to enable universal understanding, ensuring representative patient insights; treating PEs like physician experts; documenting patient insights; and providing transparency about where there is flexibility for change throughout the process. PEs must be involved early in the process, and working relationships with the patient community should be established and maintained to ensure continuity throughout the drug lifecycle.

Building TPPs with PEs ensures that patient input is considered equal to other contributors' perspectives. The patient community endorses early and continuous inclusion of first-hand patient feedback in research of Parkinson's interventions and encourages regulatory agencies to factor this feedback into the drug submission process.

P38.41

Mobilising Parkinson's: Application of real-world digital mobility outcomes for clinical and research use

Alison Yarnall[*1], Lisa Alcock[1], Christian Schlenstedt[2], Pieter Ginis[3], Phillip Brown[1], Heather Hunter[1], Jurgen Winkler[4], Jochen Klucken[4], Jennifer Kudelka[2], Hanna Hildesheim[2], Mark Gordon[5], Lou Sutcliffe[1], Isabel Neatrour[1], Clemens Becker[6], Jeffrey Hausdorff[7], Heiko Gassner[4], Anat Mirelman[7], Alice Nieuwboer[3], Walter Maetzler[2], Lynn Rochester[1]*
[1] Newcastle University, Newcastle upon Tyne, United Kingdom
[2] Kiel University, Kiel, Germany
[3] KU Leuven, Leuven, Belgium
[4] University Erlangen-Nürnberg, Erlangen, Germany
[5] Teva Pharmaceutical Industries Ltd, West Chester, United States
[6] Robert Bosch Hospital, Stuttgart, Germany
[7] Tel Aviv Sourasky Medical Center, Tel Aviv, Israel

Objective: Validate and support widespread adoption of real-world digital mobility outcomes (DMOs) to monitor mobility performance, disease progression and predict falls in patients with PD.

Background: DMOs that remotely monitor Parkinson's disease (PD) remain an area of unmet need for research and clinical care. Mobility loss is a priority area for people with PD and its valid assessment relevant for patients. Supporting evidence also shows that DMOs may be used to monitor mobility performance, indicate changes in motor disease severity and falls risk. Robust evidence of clinical validity, however, is still lacking and remains a barrier to widespread adoption. Mobilise-D (https://www.mobilise-d.eu/) is a large consortium comprising 34 partners based at leading international universities and some of the world's largest pharmaceutical and technical companies aiming to validate DMOs that measure what matters to patients.

Methods: The Clinical Validation Study, a longitudinal cohort study of 600 PD (commenced April 12, 2021) is underway in 5 clinical sites in UK, Germany, Belgium and Israel. Participants with mild to moderate disease severity are being followed every 6 months for 24 months (5 assessments). Participants are asked to wear a lower-back body-worn device continuously for 7 days, undergo a series of clinical tests, and, complete monthly falls diaries. Data analysis will establish construct validity, ability to detect change, predictive capacity and clinical meaningfulness of DMOs. Here we describe the protocol and population.

Results: Updated results from those presented at [3] demonstrate that 602 participants have completed baseline assessment (T1) and as of 20th December 2022, 527, 374 and 98 have completed T2 (6 months), T3 (12 months), and T4 (18 months), respectively. 51 have been lost to follow up. Mean age at baseline was 65.7 (± 9.5) years, 64.8% were male, mean MDS UPDRS III score 26.4 (± 12.4) and median H&Y 2.

Conclusions: Results indicate compliance with and feasibility of remotely recorded digital mobility outcomes in a diverse and representative cohort of PD. The final results of the Mobilise-D Clinical Validation Study will provide supporting evidence for the use of DMOs as complementary tools in clinical research and healthcare.

[1] Yarnall et al., International Movement Disorders Conference, Madrid 2022.

P38.42

Designing a protocol to evaluate feasibility, acceptability and impact of patient and care partner engagement in the EJS ACT-PD initiative

Marie-Louise Zeissler[*,1], Nikul Bakshi[2], Michèle Bartlett[3], Amit Batla[4], Rebecca Chapman[5], Eric Deeson[6], Romy Ellis-Doyle[4], Jodie Forbes[7], Cristina Gonzalez-Robles[4], Anna Jewell[8], Emma Lane[9], Keith Martin[10], Helen Matthews[11], Laurel Miller[12], Georgia Mills[4], Miriam Parry[13], Kuhan Pushparatnam[7], Dorothy Salathiel[14], Paula Scurfield[7], Carroll Siu[15], Sue Whipps[16], Sheila Wonnacott[17], Thomas Foltynie[4], Camille B Carroll[5], Kevin McFarthing[18]*

[1] University of Plymouth, Plymouth, United Kingdom
[2] Parkinson's UK, London, United Kingdom
[3] Expert by experience, Guildford, United Kingdom
[4] University College London, London, United Kingdom
[5] University of Plymouth, Plymouth, United Kingdom
[6] Expert by experience, Birmingham, United Kingdom
[7] Expert by experience, London, United Kingdom
[8] Expert by experience, Winchester, United Kingdom
[9] Cardiff University, Cardiff, United Kingdom
[10] Expert by experience, Nottingham, United Kingdom
[11] The Cure Parkinson's Trust, London, United Kingdom
[12] Expert by experience, Reading, United Kingdom
[13] Kings College Hospital NHS Foundation Trust, London, United Kingdom
[14] Expert by experience, Southampton, United Kingdom
[15] Expert by experience, Canterbury, United Kingdom
[16] Expert by experience, Plymouth, United Kingdom
[17] Expert by experience, Portsmouth, United Kingdom
[18] Expert by experience, Oxford, United Kingdom

Objectives: To design a protocol to evaluate the feasibility and acceptability of the Edmond J Safra Accelerating Clinical Trials in Parkinson's disease (EJS ACT-PD) initiative's processes for patient and care partner involvement (PPI) and impact on the design of a UK multi-arm multi-stage (MAMS) platform trial for PD.
Background: The EJS ACT-PD PPIE working group (WG) comprises 2-3 people with Parkinson's (PWP) and care partners per each of five WGs to advise on the design of a MAMS trial. WGs address treatment selection, outcome measures, funding and sustainability, infrastructure and trial design. Co-designed processes are embedded within the project to facilitate understanding and communication. Here we present our planned evaluation of PPIE feasibility, acceptability and impact.
Methods: Thorough evaluation of PPIE involvement strategies was embedded within the terms of reference of the programme. A subgroup of PPIE WG members was convened to decide priorities for this evaluation. The final evaluation protocol and scope of work was reviewed and approved by the full PPIE WG. The project continues to be overseen by a project external PWP who advises on participant facing materials and communications.
Results: Operational aspects and processes such as standing agenda items, post meeting debriefs with chairs and completion of standard reporting forms will be evaluated annually. Bi-annual administration of a modified Patient Engagement In Research Scale (PEIRS) will allow quantitative comparison of professionals as well as patient and carer views on PPIE involvement. Semi-structured interviews will be conducted with four members per working group (two professional, two PPIE) midway through the programme and at the end. This will give insights into acceptability of processes and perceived impact on project outputs, as well as provide opportunities to identify and address areas requiring improvement.
Conclusions: Evaluating feasibility and impact of PPIE involvement in EJS ACT-PD will inform similar programmes on effective strategies to embed PPIE. This will help enable future patient-centered research.

P38.43

Towards a preliminary protocol for a multi-arm multi-stage trial of disease modify therapies in Parkinson's disease: the EJS ACT-PD initiative

Marie-Louise Zeissler[*,1], Matthew Burnell[2], Tom Barber[3], Yoav Ben-Shlomo[4], Rebecca Chapman[1], Caroline Clarke[5], Sally Collins[1], Carl Counsell[6], Mark Edwards[7], Romy Ellis-Doyle[5], Cristina Gonzalez-Robles[5], Anna Jewell[8], Georgia Mills[5], Dorothy Salathiel[9], Sue Whipps[10], Alan Whone[4], Thomas Foltynie[5], Camille B Carroll[1], Roger Barker[11], James Carpenter[2]*

[1] University of Plymouth, Plymouth, United Kingdom
[2] MRC Clinical Trials Unit at UCL, London, United Kingdom
[3] University of Oxford, Oxford, United Kingdom
[4] University of Bristol, Bristol, United Kingdom
[5] University College London, London, United Kingdom
[6] University of Aberdeen, Aberdeen, United Kingdom
[7] King's College London, London, United Kingdom
[8] Expert by experience, Winchester, United Kingdom
[9] Expert by experience, Southampton, United Kingdom
[10] Expert by experience, Plymouth, United Kingdom
[11] University of Cambridge, Cambridge, United Kingdom

Objectives: To design a patient-centered, multi-arm, multi-stage (MAMS) platform trial within the UK to identify disease modifying therapies in Parkinson's disease (PD) as part of the Edmond J Safra Accelerating Clinical Trials in PD (EJS ACT-PD) initiative.
Background: Identification of a disease modifying therapy for Parkinson's represents a major unmet need. Previous trials have been negative, with no consensus on effective designs to overcome challenges. MAMS trials offer efficiencies, increasing research pace by investigating multiple treatments in parallel and allowing the addition of new arms as well as cessation of ineffective treatments at interim stages. Here we present the proposed outline of the trial.
Methods: Our Trial Design Working Group (TDWG) included Parkinson's and methodological experts, people with Parkinson's and care partners. TDWG decisions were informed by an international Delphi study on trial design and modeling of data from existing data sets including Critical Path for Parkinson's Consortium database (CODR) and the Oxford Parkinson's Discovery Cohort (OPDC). Trial design decisions included criteria for participant selection, stratification and minimisation, study duration and planned analyses, and recruitment and retention methodologies.
Results: This will be an inclusive phase 3 trial for PD patients on stable Parkinson's medication without dementia, severe disability or major comorbidities. Participants will be stratified by sex, centre, age, and Hoehn & Yahr stage and randomized to each of two active treatment arms or placebo for three years. Three interim analyses are proposed at pre-specified recruitment milestones. Two futility analyses on the inverse variance weighted remote MDS-UPDRS parts 1, 2 and 3 score will inform discontinuation of ineffective treatments. One interim efficacy analysis on the primary outcome (MDS-UPDRS part 1 and 2 total score) will allow early identification of an effective treatment. A third pre-planned treatment arm will be added within the first two years of the trial. A hybrid design with both remote and in person study visits will increase deliverability and retention.
Conclusion: This trial promises to speed up clinical research to identify new disease modifying treatments for people with Parkinson's. Treatment specific adjustment to the trial design will be subject of future work.

P38.44

Understanding site capability to inform the delivery of an inclusive multi-arm multi-stage trial for disease modifying therapies in Parkinson's as part of the EJS ACT-PD initiative

Marie-Louise Zeissler[*,1], Jennifer Allison[2], Dilan Athauda[3], Sandra Bartolomeu-Pires[4], Gareth Baxendale[5], Kailash Bhatia[3], David Breen[6], Rebecca Chapman[1], Helen Collins[7], Rebecca Croucher[8], Romy Ellis-Doyle[3], Jodie Forbes[9], Cristina Gonzalez-Robles[3], Fleur Hudson[10], Rajeshree Khengar[11], Prasad Korlipara[3], Christian Lambert[3], Georgia Mills[3], Huw Morris[3], Monty Silverdale[12], Sheila Wonnacott[13], Alison Yarnall[14], Thomas Foltynie[3], Camille B Carroll[1], Stephen Mullin[1]*

[1] University of Plymouth, Plymouth, United Kingdom
[2] National Institute for Health and Care Research, London, United Kingdom
[3] University College London, London, United Kingdom
[4] University Hospital Southampton NHS Foundation Trust, Southampton, United Kingdom
[5] National Institute for Health Research Clinical Research Network, Leeds, United Kingdom
[6] University of Edinburgh, Edinburgh, United Kingdom
[7] National Institute for Health Research Clinical Research Network, Thames Valley and South Midlands, United Kingdom
[8] National Institute for Health Research Clinical Research Network, Wessex, United Kingdom
[9] Expert by experience, London, United Kingdom
[10] MRC Clinical Trials Unit at UCL, London, United Kingdom
[11] NIHR University College London Hospitals Clinical Research Facility, London, United Kingdom
[12] University of Manchester, Manchester, United Kingdom
[13] Expert by experience, Portsmouth, United Kingdom
[14] Newcastle University, Newcastle, United Kingdom

Objectives: To evaluate capacity of current UK PD-trial delivery infrastructure for the first multi-arm multi-stage (MAMS) platform trial for Parkinson's disease (PD) as part of the Edmond J Safra Accelerating Clinical Trials in Parkinson's initiative (EJS ACT-PD) ready for trial launch in 2024.
Background: The opportunity for research participation is not widely available in Parkinson's services. As a result few people with Parkinson's participate in clinical trials, particularly from under-served populations. EJS ACT-PD aims to deliver a MAMS disease modification trial in PD, recruiting a representative PD population across 50 UK sites.
Methods: UK National datasets were used to evaluate regional variation in Parkinson's prevalence and the availability of PD-research active sites. A survey disseminated to NHS hospitals assessed Parkinson's research capability regarding facilities, rater experience, imaging and biosample collection. Findings informed site categorisation into 3 tiers, with tier 1 having the least PD-research capability or experience, and tier 3 being experienced specialist centres. We mapped tiers to PD prevalence, social deprivation and ethnic diversity to identify gaps in infrastructure.
Results: 85 survey responses were received. Out of 66 PD-research active (RA) and 19 PD-research naive (RN) hospitals, 30/66 (RA) and all 19 RN were categorised as tier 1, 17/66 as tier 2 and 19/66 as tier 3. In England, tier 3 sites were present in 4/5 regions with high PD prevalence, 2/3 areas with high ethnic diversity and 5/5 areas with high levels of social deprivation. Most tier 2 sites lacked capacity for specialist imaging and CSF collection; most tier 1 RA sites lacked specialist rater capacity.
Conclusions: Initial EJS ACT-PD trial sites will be predominantly tier 2 and tier 3. Core funded staff, located at strategic tier 3 sites will upskill and mentor less experienced sites and support development of regional solutions for inclusive trial participation. The EJS ACT-PD IFWG is collaborating with the National Institute of Health and Care Research (NIHR) to develop a national rater training programme. The trial will utilise a hybrid model of in-person and remote study visits, which will ensure deliverability within existing UK trial delivery infrastructure.

P38.45

The effects of an on-demand auditory cueing device used in the home for freezing of gait in people with Parkinson's disease

Demi Zoetewei[*,1], Pieter Ginis[1], Talia Herman[2], Marina Brozgol[2], Pablo Cornejo Thumm[2], Luca Palmerini[3], Alberto Ferrari[4], Jeffrey Hausdorff[2], Alice Nieuwboer[1]*

[1] KU Leuven, Leuven, Belgium
[2] Tel Aviv Sourasky Medical Center, Tel aviv, Israel
[3] University of Bologna, Bologna, Italy
[4] University of Modena and Reggio Emilia, Modena, Italy

Background: DeFOG is an on-demand cueing device that delivers auditory cues upon freezing of gait (FOG) detection. This study investigated the effects of DeFOG as a training and rescue tool in the home to alleviate FOG in people with Parkinson's disease (PD). We also explored if DeFOG had a differential effect on akinetic versus trembling FOG+festination.
Methods: Sixty-three people with severe FOG were randomized into the Intervention (N=32) or Control (N=31) group. Both groups wore DeFOG for 4 weeks in daily life. DeFOG consisted of a smartphone and shoe-worn wearable sensors. All subjects received feedback on daily step counts, but only the intervention group received on-demand cueing to alleviate FOG. A FOG-provoking protocol was performed in ON and OFF (after >12h medication withdrawal) in the home before (T1) and after the intervention (T2) without cueing. At T2, the protocol was repeated with cueing for all subjects. Expert video annotations were carried out to determine percentage time frozen (%TF) in OFF+ON (primary outcome). Secondary outcomes included %TF during specific tasks (e.g. 360°-turns) and the number/duration of FOG. Also, akinetic and trembling FOG+festination were annotated separately. Linear mixed models were applied to assess the cueing effects.
Results: The groups were well-matched on baseline clinical and demographic outcomes. Fifteen (24%) patients dropped out of which 9 in the intervention group. Pre-post analysis without cueing revealed no significant Group*Time effect for the primary (p=0.98) and secondary outcomes. However, when comparing conditions with and without cueing at T2, positive effects of on-demand cueing were found on %TF (OFF+ON) ($F(1,45.0)=9.11;p=0.004$) as well as on most secondary FOG-outcomes regardless of group and medication state. For most FOG-outcomes, on-demand cueing reduced trembling+festination but not akinetic FOG.
Conclusions: Four weeks of using DeFOG in the home did not improve FOG when cueing was not applied. However, when comparing with and without cueing at T2, %TF was lower in both groups implying that cueing did not induce habituation in the Intervention group. Trembling FOG+festination was particularly responsive to on-demand cueing. We conclude that the DeFOG system is suitable as a rescue but not as a training tool to improve FOG.

CLINICAL SCIENCE: Rating scales

P39.01

Virtual low-cost quantitative continuous measurement of movements in the extremities of people with Parkinson's disease

James Brasic[*,1], Abdelwahab Elshourbagy[2], Mennatullah Eltaras[3], Hassan Abdalshafy[4], Samrah Javed[5], Ahmed O. Sadaney[6], Timothy Harrigan[7], Kelly Mills[8], Manuel Hernandez[9]*

[1] Johns Hopkins University, Baltimore, MD, United States
[2] MISR University of Science and Technology, Cairo, Cairo Governorate, Egypt
[3] Al-Azhar University, Cairo, Cairo Governorate, Egypt
[4] Cairo University, Giza, Giza Governorate, Egypt
[5] Jinnah Sindh Medical University, Karachi, Sindh, Pakistan
[6] Faculty of Medicine, Cairo University, Giza, Giza Governorate, Egypt
[7] Research and Exploratory Development, Applied Physics Laboratory, The Johns Hopkins University, Laurel, Maryland, United States
[8] Department of Neurology, The Johns Hopkins University School of Medicine, Baltimore, Maryland, United States
[9] Department of Kinesiology and Community Health, University of Illinois at Urbana-Champaign, Urbana, Illinois, United States

Background: Structured assessments of motor impairments common in people with Parkinson's disease (PD) were developed to be performed in person to utilize human observation by trained examiners. However, risks of infections, lack of transportation, and other environmental influences may prevent the conduct of live ratings. For these reasons we developed procedures for conducting motor assessments online.
Method: A low-cost quantitative continuous measurement of movements in the extremities of people with Parkinson's disease (McKay, et al., MethodsX 6 (2019) 169–189 https://doi.org/10.1016/j.mex.2018.12.017) (Figure 1) was performed in person by an examiner certified in the Movement Disorder Society-sponsored revision of the Unified Parkinson's Disease Rating Scale (MDS-UPDRS) (Goetz, et al., Mov. Disord. 23 (2008) 2129–2170) on cohorts of participants with PD (N=20) and healthy controls with typical development (TD) [N=8]. The original clinical scores were recorded by the trained examiner immediately after the administration of the protocol in person.
Rating of the videos of the original assessments was conducted by a team of six trained raters who were all in different physical locations. Rating sessions were hosted by the coordinator (AE) who presented the video clips of the individual tasks performed by participants for viewing providing only the code number of the participant without name, age, sex, diagnosis, or other identifying characteristics. After all protocol items were scored independently by the raters, the coordinator asked all raters to send him electronic copies of their score sheets. Then the coordinator conducted a consensus conference with all raters to attain agreement for the score for each item.
Results: Six trained raters on three continents provided the scores for each of the 22 tasks performed by five participants (Parkinson's disease aged 72 and 76 years and typical development aged 55, 58, and 70 years) including repeat administrations by two participants. Ratings were obtained by viewing on individual monitors the videos shown through screen sharing by the coordinator.
Conclusion: The proposed protocol provides the foundations for colleagues to expand the motor evaluation of people with PD throughout the globe. The proposed protocol will generate an optimal framework for clinical trials.

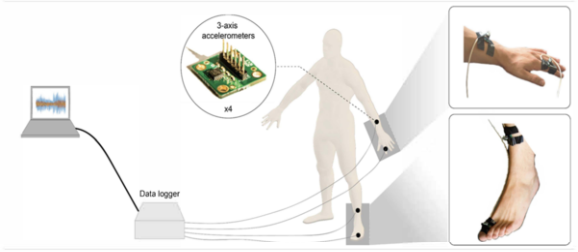


Figure 1. Schematic diagram of procedure to generate output from accelerometers on the extremities to record on a data logger to connect to a laptop computer for conversion to signals for further analysis (McKay, *et al.*, MethodsX 6 (2019) 169-189) (Courtesy of Jenny-Ann Phan, MD, PhD).

P39.02

Remote scoring of a low-cost quantitative continuous measurement of movements in the extremities of people with Parkinson's disease

Abdelwahab Elshourbagy[1], Menna Eltaras[2], Hassan Abd El shafy[3], Samrah Javed[4], Ahmed O. Sadaney[3], Timothy P. Harrigan[5], Kelly Alexander Mills[6], Manuel Manuel Enrique Hernandez[7], James Brasic[*,8]*

[1] Misr university for science and technology, Cairo, Egypt
[2] Al Azahar Universitry, Cairo, Egypt
[3] Cairo University, Cairo, Egypt
[4] Jinnah Sindh Medical University, Karachi, Pakistan
[5] Research and Exploratory Development, Applied Physics Laboratory, The Johns Hopkins University, Baltimore, Maryland, United States
[6] Department of Neurology, The Johns Hopkins University School of Medicine, Baltimore, Maryland, United States
[7] Department of Kinesiology and Community Health, University of Illinois, Urbana, United States
[8] Johns Hopkins university, Baltimore, Maryland, United States

Objective: To develop a procedure for trained raters to remotely score videotaped motor assessments.
Method: Five participants aged 66.2 + 9.2 (55, 76) years including four men and two people with Parkinson's disease (PD) underwent a low-cost quantitative continuous measurement of movements in the extremities of people with PD (McKay, et al., MethodsX 6 (2019) 169–189 https://doi.org/10.1016/j.mex.2018.12.017) administered in person by an examiner certified in the Movement Disorder Society-sponsored revision of the Unified Parkinson's Disease Rating Scale (MDS-UPDRS) (Goetz, et al., Mov. Disord. 23 (2008) 2129–2170). The procedure was conducted with the participant on a straight-back chair without wheels and recorded by a videographer. A technologist recorded the output of instrumentation.
Two trained raters edited the original videotapes to extract each of the 12 tasks for individual video clips. The coordinator then presented the edited videos once on his shared computer screen to six trained raters for independent scoring without knowledge of the age, sex, or diagnosis of the participants. After independently scoring each task, raters sent the their to the coordinator, who then conducted a consensus conference with the raters to agree on a score for each task. Lack of agreement was recorded by a period (.).
Results: Altogether 110 consensus conferences were conducted among the six raters of the 22 video clips of the protocol conducted on five participants. Raters on three continents agreed on 28 scores of 0, 14 scores of 1, 4 scores of 2, and 7 scores of 3. The raters did not agree on scores for 57 video clips indicated by periods (.) on Table 1. Interruptions and blurring of video images presented challenges for rating using the techniques of visual observation for live rating. Internet disconnections prevented some ratings during the experimental sessions.

Conclusion: The proposed protocol provides the means for trained raters in different locations to conduct ratings of structured motor assessments of videos. Future assessments may be improved with improved remote video collection and display.

Age	PD	Male	Ht	Wt	3.17UR	3.17UL	3.17UCR	3.17UCL	3.15R	3.15L	3.4R	3.4L	3.5R	3.5L	3.6R	3.6L	3.9U
76	1	1	72	178	0	.	0	0	1	.	.	.	.	.	.	.	1
70	0	1	61	122	0	0	0	0	.	.	.	.	.	.	.	.	0
72	1	0	64	177	1	1	1	1	1	1	.	3	.	.	.	.	0
58	0	1	71	215	0	0	0	0	2	2	.	.	3	3	3	3	0
55	0	1	67	159	.	.	.	.	.	.	1	.	.	.	1	1	.

Age	3.17LR	3.17LL	3.17LCR	3.17LCL	3.7R	3.7L	3.8R	3.8L	3.9L
76	.	.	0	.	.	.	.	.	1
70	0	0	0	0	.	.	2	2	0
72	1	0	1	0	.	.	.	.	0
58	0	0	0	0	3	3	.	.	0
55	.	.	.	.	.	.	.	.	.

Table 1. Demographic traits and consensus scores of six independent raters of videos of motor tasks of five participants.

Age: Age in years; PD: Parkinson's disease 1 = present, 0 = absent (healthy control with typical development); Male: Male 1 = present, 0 = absent (female); Ht: Height in inches; Wt: Weight in pounds; 3.17UR: 3.17 Rest tremor amplitude upper limbs right; 3.17UL: 3.17 Rest tremor amplitude upper limbs left; 3.17URC: 3.17 Rest tremor amplitude upper limbs right counting; 3.17ULC: 3.17 Rest tremor amplitude upper limbs left counting; 3.15R: 3.15 Postural tremor of the hands right; 3.15L: 3.15 Postural tremor of the hands left; 3.4R: 3.4 Finger tapping right; 3.4L: 3.4 Finger tapping left; 3.5R: 3.5 Hand movements right; 3.5L: 3.5 Hand movements left; 3.6R: 3.6 Pronation-supination movements of the hands right; 3.6L: 3.6 Pronation-supination movements of the hands left; 3.9U: 3.9 Arising from chair upper limbs; 3.17LR: 3.17 Rest tremor amplitude lower limbs right; 3.17LL: 3.17 Rest tremor amplitude lower limbs left; 3.17LRC: 3.17 Rest tremor amplitude lower limbs right counting; 3.17LLC: 3.17 Rest tremor amplitude lower limbs left counting; 3.7R: 3.7 Toe tapping right; 3.7L: 3.7 Toe tapping left; 3.8R: 3.8 Leg agility right; 3.8L: 3.8 Leg agility left; 3.9L: 3.9 Arising from chair lower limbs; period (.): absence of consensus agreement.
(McKay GN, Harrigan TP, Brasic JR. A low-cost quantitative continuous measurement of movements in the extremities of people with Parkinson's disease. MethodsX 2019; 6:169-189. https://doi.org/10.1016/j.mex.2018.12.017).

P39.03

The Ziegler test is a reliable and valid measure of freezing of gait in people with Parkinson's disease

Lina Goh[*,1], Serene S Paul[2], Colleen G Canning[2], Kaylena A Ehgoetz Martens[3], Jooeun Song[2], Stephanie L Campoy[4], Natalie E Allen[2]*
[1] The University of Sydney, Camperdown, NSW, Australia
[2] The University of Sydney, Sydney, NSW, Australia
[3] The University of Waterloo, Waterloo, ON, Canada
[4] No affiliation, Sydney, NSW, Australia

Background: Current tools to measure freezing of gait (FOG) severity are largely inadequate for clinical use. Self-report questionnaires may not be sufficiently responsive to detect changes in FOG and using video annotations or wearable sensors to measure FOG are resource-intensive. The Ziegler test may be suitable for quantifying FOG but its clinical utility remains unknown.
Objective: To determine the inter-rater and test-retest reliability of the Ziegler test to measure FOG severity in people with Parkinson's disease (PwPD). Secondary aims were to determine test validity, explore test duration as a proxy FOG severity measure, and evaluate test usability.
Methods: Twenty-four physiotherapists (PTs) watched 36 videos of PwPD who self-reported FOG performing the Ziegler test. The PTs rated FOG severity via video analyses in real-time using the Ziegler rating scale and determined test duration using a stopwatch. Two of these PTs rated an additional 12 videos and repeated the ratings at least one week later. All PTs also completed a test usability survey after the ratings. Inter-rater and test-retest reliability were calculated using intra-class correlation coefficients (ICCs). Correlations between Ziegler scores, duration, and percentage of time frozen (based on expert video annotations) were determined using Pearson's r.
Results: The Ziegler test showed good inter-rater reliability and excellent test-retest reliability (Table 1), with little differences in reliability when considering PTs' level of experience. The Ziegler test was a valid FOG severity measure, with a high correlation (r=0.72) between scores and percentage of time frozen. Test duration was moderately correlated (r=0.67) to percentage of time frozen and may be considered as a proxy FOG severity measure. Overall, PTs reported the Ziegler test easy to use, but several PTs found it difficult to interpret test instructions, identify the presence or type of FOG, and felt the scores were likely underestimating FOG severity in people with severe FOG.
Conclusion: The Ziegler test is a reliable and valid tool to measure FOG when used by PTs in real-time. Test duration may be used as a proxy for FOG severity. A more detailed rating scale that clarifies test instructions and accounts for frequency and duration of FOG episodes may improve its clinical utility.

Table 1. Overall inter-rater reliability ($ICC_{2,1}$ with 95% CI) and test-retest reliability ($ICC_{3,1}$ with 95% CI) of the Ziegler test, and reliabilities based on physiotherapists' clinical experience.

Inter-rater reliability	n	$ICC_{2,1}$	95% CI
Overall	24	0.80	0.65 to 0.92
Based on overall clinical experience (years)			
0.5-2	7	0.74	0.51 to 0.90
3-10	9	0.83	0.68 to 0.94
>10	8	0.83	0.67 to 0.94
Based on number people with PD seen in the past year			
0-10	10	0.81	0.63 to 0.93
11-30	11	0.81	0.66 to 0.93
>30	3	0.84	0.47 to 0.95
Test-retest reliability	n	$ICC_{3,1}$	
Overall	2	0.91	0.82 to 0.96
Based on overall clinical experience (years)			
0.5-2	1	0.88	0.70 to 0.96
>10	1	0.94	0.79 to 0.98

P39.04

Test-retest reliability of a low-cost quantitative continuous measurement of movements in the extremities of people with Parkinson's disease.

Samrah Javed[1], Abdelwahab Elshourbagy[2], James Brasic[*,3]*
[1] Omi Hospital, Karachi, Sindh, Pakistan
[2] Misr University for Science and Technology, Cairo, Egypt
[3] John Hopkins University, Baltimore, MD, United States

Purpose of Study: A low-cost quantitative continuous measurement of movements in the extremities of people with Parkinson's disease was developed to enhance the motor assessments by adding instrumentation to record the positions in space of movements commonly impaired in people with Parkinson's disease (McKay, et al., MethodsX 9 (2019) 169–189). We sought to assess the test-retest reliability of this instrument administered to cohorts of people with Parkinson's disease (PD) age, sex matched healthy people with typical development (TD).
Method: The protocol was administered to 19 participants aged 45 to 83 (mean = 65+10) years composed of cohorts with PD (N=11) aged 45 to 82 (66 +11.7) years and with TD (N=8) aged 55 to 74 (63.6+7.4) years and repeated one to 28 (7.4+8.8) months after initial testing. A table was constructed for each task of the procedure to provide a score of 0 if the test and retest scores were not identical and a score of 1 if the test and retest scores were identical. Percentage agreement was calculated for as the sum of the 1s divided by the sum of the 0s and 1s.
Result: Percentage agreements for the 22 tasks of the protocol were 49.5 + 14.2 (18, 82) for PD, 71.9 + 14.2 (22,100) for TD, and 58.8 + 14.0) for PD+TD (Table 1).
Conclusion: We developed a means to assess test-retest reliability for a structured motor assessment of people with PD. The attainment of 100% agreement for some items is evidence that this procedure can be developed to achieve good reliability in future studies correcting limitations of the current study. Test-retest reliability will be enhanced in future investigations when uniformity of the study variables is obtained. Therefore, future studies will be performed by the same examiner with participants in the same chair with arms without wheels in the same location of the same room at the same temperature at the same time on the same two

consecutive days of the week. This protocol will provide the means to enhance the diagnosis and treatment of PD.

Participant cohort	3.17UR	3.17UL	3.17UCR	3.17UCL	3.15R	3.15L	3.4R	3.4L	3.5R	3.5L	3.6R	3.6L	3.9U
TD	75	63	75	88	63	63	63	50	50	63	38	63	100
PD	45	45	73	45	64	55	45	36	36	18	45	45	82
TD+PD	58	53	74	63	63	58	53	42	42	37	42	53	89

	3.17LR	3.17LL	3.17LCR	3.17LCL	3.7R	3.7L	3.8R	3.8L	3.9L
TD	100	88	100	88	63	88	88	38	75
PD	64	64	45	45	36	36	55	55	55
TD+PD	79	78	68	68	47	53	68	42	63

Table 1. Percentage agreements for test-retest reliabilities of cohorts.

TD: Typical development; PD: Parkinson's disease; TD+PD: Typical development and Parkinson's disease; 3.17UR: 3.17 Rest tremor amplitude upper limbs right; 3.17UL: 3.17 Rest tremor amplitude upper limbs left; 3.17URC: 3.17 Rest tremor amplitude upper limbs right counting; 3.17ULC: 3.17 Rest tremor amplitude upper limbs left counting; 3.15R: 3.15 Postural tremor of the hands right; 3.15L: 3.15 Postural tremor of the hands left; 3.4R: 3.4 Finger tapping right; 3.4L: 3.4 Finger tapping left; 3.5R: 3.5 Hand movements right; 3.5L: 3.5 Hand movements left; 3.6R: 3.6 Pronation-supination movements of the hands right; 3.6L: 3.6 Pronation-supination movements of the hands left; 3.9U: 3.9 Arising from chair upper limbs; 3.17LR: 3.17 Rest tremor amplitude lower limbs right; 3.17LL: 3.17 Rest tremor amplitude lower limbs left; 3.17LRC: 3.17 Rest tremor amplitude lower limbs right counting; 3.17LLC: 3.17 Rest tremor amplitude lower limbs left counting; 3.7R: 3.7 Toe tapping right; 3.7L: 3.7 Toe tapping left; 3.8R: 3.8 Leg agility right; 3.8L: 3.8 Leg agility left; 3.9L: 3.9 Arising from chair lower limbs (McKay GN, Harrigan TP, Brasic JR. A low-cost quantitative continuous measurement of movements in the extremities of people with Parkinson's disease. MethodsX 2019; 6:169-189. https://doi.org/10.1016/j.mex.2018.12.017).

P39.05

Validation of the UCLA Loneliness Scale 8- and 3-item versions in a cohort of people living with Parkinson's disease and correlation with quality of life

Indu Subramanian[*,1], Bradley McDaniels[2], Devon Fox[3], Laurie Mischley[4]*
[1] UCLA/Veterans. Administration, Los Angeles, CA, United States
[2] U of North Texas, Denton, TX, United States
[3] Parkinson Center for Pragmatic Research, Seattle, WA, United States
[4] Bastyr University, Seattle, WA, United States

Background: Loneliness has recently been shown to be associated with worse motor and non-motor scores and Quality of Life (QOL) in people with Parkinson's disease (PWP), but there has not been a validated measure to use in this population. A short screening tool that could be administered proactively could help clinicians identify at-risk and affected individuals and help guide targeted social support interventions.
Goal: To validate two short forms of the UCLA Loneliness Scale (ULS-3 and ULS-8 in a cohort of PWP participating in a web-based survey (Modifiable Variables of Parkinsonism study -MVP) administered during the COVID-19 pandemic.
Methods: Participants with self-reported idiopathic PD completed the survey between August 2020 and July 2022. Data quality was determined by percent of missingness, skew, kurtosis and floor and ceiling effects. Linear regressions were used to determine correlation with demographics of age, age at onset, years with PD, gender, race/ethnicity, and income.
Results: 1,428 participants were included in this analysis. The mean age of this cohort was 66.42 (±9.08) with an average age of onset of 58.66 (±9.92) and an average length of time with PD of 7.74 (±5.41). The cohort was composed of 59.7% (n = 853) female and 91.6% (n = 1308) Caucasian. The scales show good reliability (= .90 and .84, respectively) and acceptable validity. ULS-8 scores were significantly associated with age, age at onset, years with PD and income with non-significant associations with race and education. The ULS-8 and ULS-3 were both strongly correlated with PROMIS QOL scale (r = 0.7, p <0.001).
Discussion/Conclusion: Each item of the ULS-8 and the ULS-3 was valid and strongly negatively correlated with worsened QOL. The three questions from the ULS-3 were most strongly correlated with QOL. Amidst an epidemic of social isolation and a growing body of evidence that loneliness is associated with worse PD outcomes, providers are encouraged to assess patients' social health during clinic visits and, the ULS-8 and ULS-3 are validated measures to consider. The ULS-3 has been validated for use on the phone and offers a shorter version (< 1min vs 1-2 min), which lends itself to the clinic setting.

	Data quality(<10%)*	Floor effect	Ceiling effect	Skew/kurtosis	Inter-item correlation
I lack companionship	9.0	41.5	6.09	0.69/-0.68	0.79
There is no one I can turn to	8.8	58.0	2.73	1.36/0.87	0.73
I am an outgoing person (reverse coded)	9.0	32.2	3.01	0.54/-0.36	0.44
I feel left out*	9.1	33.1	3.22	0.42/-0.84	0.80
I feel isolated others*	9.3	33.5	5.3	0.43/-0.89	0.84
I can find companionship when I want it (reverse coded)	9.5	61.9	1.12	1.66/2.48	0.67
I am unhappy being so withdrawn	9.6	44.7	4.20	0.78/-0.56	0.77
People are around me but not with me	9.6	33.8	4.97	0.48/-0.83	0.74
Total	13.0	0	0	0.56/-0.41	

Table #: Data quality for UCLA8 individual items and totaled score including percent of missing data, floor and ceiling effects and skew and kurtosis.

CLINICAL SCIENCE: E-health and technology

P40.01

TAS Test automatic hand movement analysis – Validation of a new self-assessment tool designed for home use

Jane Alty, Quan Bai, Xinyi Wang, Renjie Li, Guan Huang, Katharine Lawler, Rebecca St. George, Kaylee Rudd, Eddy Roccati, Aidan Bindoff, Larissa Bartlett, Saurabh Garg, Mark Hinder, Anna King, James Vickers*
University of Tasmania, Hobart, Tasmania, Australia

Background: Home-based methods that objectively measure motor function would help people with Parkinson's to track their response to medications more precisely and also to support telemedicine and personalised care. TAS Test is a new self-assessment motor-cognitive tool that uses standard home computer equipment such as webcams and computer keyboards. Advanced computer vision technologies have been developed to automatically track hand movements and extract features (rhythm, speed etc). This prospective validation study aimed to establish the accuracy, reliability and usability of TAS Test video- and keyboard motor tests.
Method: Adults aged 50+ years were recruited from the ISLAND Project in Tasmania, Australia. They all completed TAS Test at home and provided feedback via an online questionnaire. Some also completed TAS Test at a university research centre. To validate TAS Test computer vision technologies, a separate group wore movement sensors on their index finger and thumb whilst completing video-recorded finger-tapping. Accuracy and test-retest reliability were compared using intraclass correlation coefficients and Bland-Altman analysis. Participant feedback was analysed
Results: In 2021, 2,109 adults (mean [SD] age 67.6 [7.6] years, range 50-92; 72% female) completed TAS Test at home and 572 completed onsite (99 home first; 473 research centre first). In 2022, 1,679 (67.4 [7.8] years, 70% female) repeated TAS Test at home. The test re-test reliability was good for video (r = 0.78 – 0.80) and keyboard tapping features (r = 0.69 - 0.79). 96% of computer vision measures of finger-tapping tests were within +/−0.5 Hz of the wearable sensors. Hand gestures (e.g. finger-thumb opposed vs apart) were correctly detected in real-time with 0.782 mean average precision. Participants reported that TAS Test was easy to understand (95%), their attention was maintained (93%), test duration was about right (90%), the software functioned well (82%),

they preferred to do TAS Test at home (95%) and immediate availability of results to the participant is a priority for future development (92%).
Conclusions: Remote assessment of hand motor function using TAS Test is accurate, reliable and well accepted. This new tool has potential to facilitate home monitoring for clinical and research purposes. A validation study in people with Parkinson's has just begun recruitment.

P40.02

A 20-second home-based test helps detect prodromal Parkinson's in a community sample of older Australians
Jane Alty[*,1], *Samantha Bramich*[1], *Xinyi Wang*[1], *Renjie Li*[1], *Alastair Noyce*[2], *Guan Huang*[1], *Maneesh Kuruvilla*[1], *Rebecca St. George*[1], *Katherine Lawler*[1], *Mark Hinder*[1], *Eddy Roccati*[1], *Larissa Bartlett*[1], *Saurabh Garg*[1], *Quan Bai*[1], *Sharon Naismith*[3], *Anna King*[1], *James Vickers*[1]
[1] University of Tasmania, Hobart, Tasmania, Australia
[2] Queen Mary University, London, United Kingdom
[3] University of Sydney, Sydney, NSW, Australia

Background: Isolated REM sleep behaviour disorder (RBD) is considered a prodromal stage of Parkinson's disease (PD) as 90% of people with it will develop PD or a related disorder within 10 years. Identifying RBD thus provides an opportunity to intervene early before significant neurodegeneration. However, it is under-recognised and we need population-level tools to help develop enriched cohorts for clinical trials. TAS Test is a new online self-test motor-cognitive battery, designed to be completed at home using a standard home computer. The study objective was to assess which TAS Test motor assessments improved classification of probable RBD (pRBD) from healthy controls. We hypothesised that pRBD associates with impaired motor function.
Method: We assessed 2905 adults 50+ years in Tasmania, Australia with the RBD single question screen (RBDQ1) to identify pRBD and 362 (mean (SD) age 64 (7.7) years; 72% female) also completed TAS Test motor tests: video-recorded finger tapping with each hand separately and then bilateral +/- backwards counting (i.e. dual task) followed by 4 different keyboard tapping tests (single/alternate finger; 3-step sequences). Each task duration was 10-20 seconds. Key features of movement were extracted from videos and keyboard data. Classification accuracy was assessed with area under ROC curves (AUC). Models with hand movements features, adjusted for age and gender were compared with the baseline model with confounders only.
Results: 273/2905 (9.4%) screened positive for pRBD (45% male) and 40/362 (11.0%) of those completing TAS Test. The video dual task finger tapping test improved detection of pRBD compared to the baseline model of age and gender alone (AUC 0.79 vs 0.70; $p<0.01$). Discriminatory motor features from the dual task test were total tapping count, maximum speed and rhythm (COV of tapping frequency). No other motor tests aided detection of the pRBD above the baseline model.
Conclusions: A brief online dual task finger tapping test detected a subtle motor deterioration in the prodromal PD group (pRBD). This may be due to the greater cognitive load of a dual motor-cognitive task compared to standard motor tasks. TAS Test holds potential to aid enrichment of cohorts for clinical trials and a possible pre-diagnostic PD biomarker.

P40.03

Evaluation of the Parkinson's Remote Interactive Monitoring System (PRIMS): A usability study
Bronwyn Bridges[*,1], *John Weber*[1], *Jake Taylor*[2]
[1] Memorial University of Newfoundland, St John's, NL, Canada
[2] University of Victoria, Victoria, British Columbia, Canada

The fastest-growing neurological disorder globally is Parkinson's Disease (PD), a progressive neurodegenerative disease that affects ten million people worldwide. PD is typically treated with Leva-Dopa: an oral pill is taken to increase dopamine levels and other dopaminergic agonists. However, as the disease progresses, the effects of the drug wane and adherence to this method are typically poor and do not provide meaningful information. Therefore, remote monitoring systems that can provide more detailed and accurate information about a patient's condition regularly are a valuable tool for clinicians and patients to manage their medication.
The Parkinson's Remote Interactive Monitoring System (PRIMS) developed by PragmaClin Research Inc. was designed to be an easy-to-use digital system that can accurately quantify motor and non-motor symptoms of PD remotely. PRIMS can engage with patients in real time and provide immediate, individualized results on a patient dashboard. The system can also be used by clinicians to oversee a patient's data. We conducted a usability evaluation to determine the ease of use of the PRIMS and whether this product has appropriate functionality for users.
Participants were recruited from a user sign-up online database owned by PragmaClin Research Inc. 12 participants were selected based on the inclusion criteria: (1) diagnosed with PD, and (2) not diagnosed with dementia or any other comorbidities that would increase the risk of study participation (e.g., osteoporosis). Patient users complete a questionnaire based on the Movement Disorder Society revision of the Unified Parkinson's Disease Rating Scale (MDS-UPDRS). Interviews and field notes were analyzed for underlying themes. Thematic analysis of the observer's notes revealed six central themes associated with the usability and functionality of the PRIMS system. These are: (1) automated voice prompts are confusing, (2) the small camera is problematic, (3) the motor test is particular on positioning, (4) the system poses mobility challenges, (5) navigating the system is complex, and (6) the motor test is glitchy. This feedback is being used to upgrade the current PRIMS system.

Table 1: Mean motor examination and entire PRIMS questionnaire time for all participants.

Participant	Section	Time (mins)
P1	ME	58.82
	PRIMS	80.72
P2	ME	96.43
	PRIMS	112.18
P3	ME	48.87
	PRIMS	51.42
P4	ME	65.78
	PRIMS	82.33
P5	ME	90.9
	PRIMS	115.73
P6	ME	60.28
	PRIMS	68.8
P7	ME	75.95
	PRIMS	115.67
P8	ME	53.72
	PRIMS	67.2
P9	ME	76.3
	PRIMS	89.87
P11	ME	49.5
	PRIMS	58.17
Mean	ME	67.66
	PRIMS	84.21

Table 2: Number of times each motor test was skipped, tests ranked from most to least number of skips.

Motor Test	Skipped Tests
3.15	12
3.14	6
3.13	6
3.3	2
3.8	1
3.9e	1
3.10	1
3.1	0
3.2	0
3.4/3.5	0
3.6	0
3.7	0
3.9a-d	0
3.11	0
3.12	0

P40.04

Screening risk of falls in people with Parkinson's disease using a digital App: A feasibility study

Tamine Capato, Johnny Miranda, Venicio Graboi, Francielle Santos, Fabiana Almeida, Rafael Carra, Rubens Cury, Manoel Teixeira, Egberto Barbosa*
University of São Paulo, São Paulo, Brazil

Digital technologies promise to change research and treatment monitoring in people with Parkinson's Disease(PWPD). Center of Body Mass (COM) measurements such as accelerometers and gyroscopes data extracted from a smartphone have been studied due to their practicality in stabilometry assessments. However, it is unknown which is the better digital system to screening risk of falls. Objective: To verify the feasibility of the TechBalance-App to assess the risk of falls in PWPD. Methods: In this observational cohort study, we collected a single clinical setting assessment with 100 PWP (1-4 H&Y stage). TechBalance-App consists on a self-report of falls, by the clinical questionnaire and an objective measure collected by Stabilometric variables. Participants completed the TechBalance-App's interview(Risk of falls questionary and Fragility scale). After the interview, patients performed motor tests(MBEST and TUG) while data COM were collected by using a gyroscopic and an accelerometer allocated in a smartphone attached to the patient's body by a belt. The data collected by this smartphone-based digital assessment is processed on a digital platform. The scores of the questionnaires were compared between fallers and non-fallers by the ANOVA test for independent measures and by the ability in discriminate fallers by the Area Under de Curve (AUC) of the ROC curve and traditional classification measures. Results: TechBalance-App use was well acceptable for all participants who completed the assessments (59% man); mean age 68,1. According fragility scale, 67% of patients were in fragile profile. TechBalance-App demonstrated to be feasible to obtain stabilometry parameters, whereas the App generates a score between low (2%), medium (75%), high (16%), and super high (7%) risk of falls. We found a difference between the severity PD stage and the App's scores(p=0.005). In addition, the risk of falls scores were significantly related to corresponding MDS-UPRDS III item 3.12. In addition, the risk of falls scores also showed a significant correlation with MBEST(p=0.005) and TUG(p= 0.003). Our smartphone-based digital assessment results indicate that TechBalance-App provides sensitive fall rates and is a feasible app to screening the risk of falls in PWPD. Further studies should investigate the test-retest reliability, validity, and clinically meaningful in future PD trials.

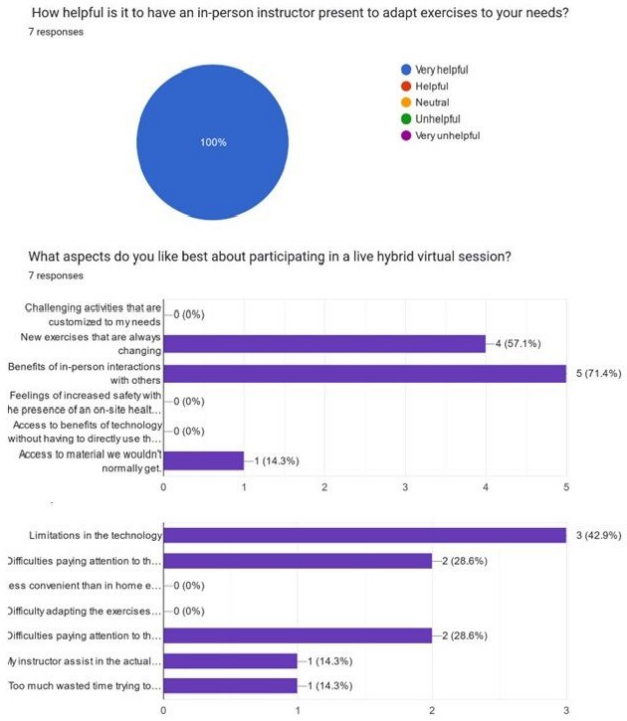
P40.06

Acceptability of a hybrid dual-task exercise program for Parkinson's delivered online to an in-person group, facilitated by an on-site physical therapist

John Dean[1], Josefa Domingos[2], Emily Moncheski[3], Catarina Godinho[4]*
[1] Triad Health AI, Aurora, CO, United States
[2] Donders Institute for Brain, Cognition and Behavior, Center for Medical Neuroscience, Department of Neurology, Center of Expertise for Parkinson and Movement Disorders, Radboud University Medical Center, Nijmegen, Netherlands
[3] Max Capacity PT, Colorado Springs, Colorado, United States
[4] Instituto Universitário Egas Moniz, Centro de Investigação Interdisciplinar Egas Moniz (CiiEM), Egas Moniz School of Health and Science, Almada, Portugal

Background: Online group exercise programs can help people with Parkinson's (PD) access specialized exercise interventions. However, safety, correct performance, and technological difficulties can pose significant challenges. Finding the best model of delivery, with an effective format, has yet to be achieved.
Objective: To evaluate the acceptability of a dual-task cognitive and motor training program for people with PD, delivered online to a small group meeting in person.
Methods: People with PD participated in a weekly in-person small group exercise class that consisted in following an online exercise program ("Dual Task for Parkinson's") that incorporated physical, cognitive, and vocal exercise. The program was facilitated by an on-site physiotherapist who monitored safety and adapted exercises being delivered virtually to individual needs. Patient acceptability (satisfaction, difficulties, and safety) was assessed at 3 months using an anonymous feedback questionnaire emailed to participants. The instructor's feedback was also obtained.
Results: 7 individuals with Parkinson's participated. Participants reported being very satisfied (n=2, 28.6%), satisfied n=2, 28.6%), or neutral (42.9%) regarding the program. Three aspects participants referred to as most liked included: "access to new exercises that are always changing" "benefits of in-person interactions with others", and "it is motivating in a group setting and with an instructor to help you if needed". The aspects less liked included: "limitations in the technology", "some difficulties paying attention to the screen and my therapist at the same time", and "distractions from other participants".
All participants indicated that having an on-site instructor present was "very helpful". Additional comments included: "she pushes us and corrects how we are doing the exercises", "it's good to be monitored, it's helpful guidance, encouragement, and pace-setting", and "guiding us for our personal situation". The instructor reported some challenges with technology, but no severe adverse events

were reported and participants were consistently engaged in the exercises.
Conclusions: Our findings suggest that the hybrid online dual cognitive and motor program was well-received and safe. This innovative delivery model may better assure safety, tailored adaptations, and engagement and may shape future programs.



P40.07

A preliminary feasibility study of online motor assessments of people with Parkinson's disease and related conditions
Menna Eltaras[1], Abdelwahab Elshourbagy[2], Hassan Abdalshafy[3], Samrah Javed[4], Ahmed Sadaney[3], Timothy Harrigan[5], Kelly Mills[6], Manuel Hernandez[7], James Brasic[8]*
[1] Al-Azhar University, Cairo, Egypt
[2] MISR University for Science and Technology, Giza, Egypt
[3] Faculty of Medicine, Cairo University, Giza, Egypt
[4] Jinnah Sindh Medical University, Karachi, Pakistan
[5] Research and Exploratory Development, Applied Physics Laboratory, The Johns Hopkins University, Laurel, United States
[6] Department of Neurology, The Johns Hopkins University School of Medicine, Baltimore, United States
[7] Department of Kinesiology and Community Health, University of Illinois at Urbana-Champaign, Urbana, United States
[8] Section of High Resolution Brain Positron Emission Tomography Imaging, Division of Nuclear Medicine and Molecular Imaging, The Russell H. Morgan Department of Radiology and Radiological Science, The Johns Hopkins University School of Medicine, Baltimore, United States

Background: A protocol for the virtual administration of structured motor assessments of people with Parkinson's disease (PD) is needed when infection risks and travel limitations prevent traditional in-person assessments.
Method: A low-cost quantitative continuous measurement of movements in the extremities (McKay, et al., MethodsX 6 (2019) 169–189 https://doi.org/10.1016/j.mex.2018.12.017) (Figure 1) was administered in person to people with PD (a 76-year-old man and a 64-year-old woman) and to healthy men with typical development (aged 55, 58, and 70 years) by an examiner certified in the Movement Disorder Society-sponsored revision of the Unified Parkinson's Disease Rating Scale (MDS-UPDRS) (Goetz, et al., Mov. Disord. 23 (2008) 2129–2170). Videos of the clinical movement measurements were presented once on a screen-shared monitor to six MDS-UPDRS-certified raters in different locations on three different continents. Independent scores of each task were sent to the moderator directly for tabulation.
Results: Raters agreed on the scores for three or four of the five participants for both literalities of 3.9 Arising from chair for both upper and lower limbs, 3.15 Postural tremor of the right hand, and 3.17 Rest tremor amplitude both with and without counting for both upper and lower limbs. Raters agreed on two participants for both literalities of 3.6 Pronation-supination movements of the hands and 3.15 Postural tremor of the left hand and on one participant for both literalities of 3.4 Finger tapping, 3.5 Hand movements, 3.7 Toe tapping, and 3.8 Leg agility.
Conclusion: Virtual assessment of motor assessment videos presented on the monitor of a coordinator rated by examiners with different monitors in different locations can be accomplished. Agreement for tasks with stationary positions of the extremities was better than for repetitive movements. Future investigations will be enhanced by including more participants with and without PD and more trained raters. Using optimal cameras and monitors will enhance the quality of images presented to raters. Use of a toggle switch to examine individual frames will help rating by visual observation. Colleagues around the world can utilize this virtual protocol to obtain state-of-the-art motor assessments of people with PD and other conditions.

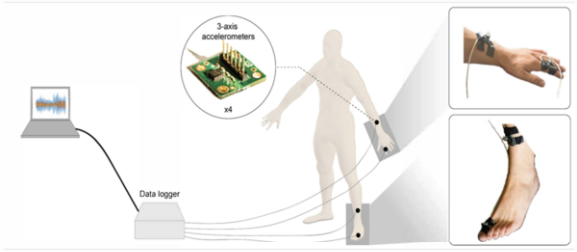


Figure 1. Schematic diagram of procedure to generate output from accelerometers on the extremities to record on a data logger to connect to a laptop computer for conversion to signals for further analysis (McKay, et al. MethodsX 2019).

P40.08

Design and development of a digital therapeutics (DTx) delivering personalized medication optimization for people with Parkinson's disease
Giovanni Gentile[*,1], Maria Teresa Pellecchia[2], Pier Paolo Iagulli[1], Raffaele Aulisio[1], Maria Frediani[1], Silja-Riin Voolma[1], Gerry Chillè[1]*
[1] Newel Health srl, Salerno, Italy
[2] Department of Medicine, Surgery and Dentistry "Scuola Medica Salernitana", Neuroscience Section, University of Salerno, Baronissi, Salerno, Italy

Introduction: Globally, disability and death caused by Parkinson's disease (PD) are increasing faster than for any other neurological disorder. Available treatments help reduce symptoms, but their fluctuating and highly personal nature makes it challenging to identify and adjust treatment plans. The infrequent contact movement disorder specialists have with PD patients, and their lack of access to longitudinal personalized data on symptom experience patients' visits are bottlenecks in treatment management. People

with Parkinson's (PwP) also struggle to track and report to their physician the high variability and frequency of symptoms experienced at home, and which leads to delays and biases in treatment adjustment and personalization.
Objectives: Project Soturi seeks to "democratize" and expand PwP access to healthcare services. Soturi's algorithm aims to optimize levodopa-based treatment with the goal of supporting many different types of low-cost consumer-level wearable devices for the collection and detection of motor symptoms. Remote monitoring devices paired with AI algorithms will thus be powerful tools to aid in the identification of patients with advanced PD who could benefit from treatment modifications and enhanced care.
Methods: This abstract proposes a hybrid project involving community-based co-design activities with patients and clinicians, in-clinic assessment for the validation study of the algorithms, and finally a longitudinal observational study to reflect variability of free-living and improve algorithm efficiency. This trial will apply the IDEAs framework of designing and testing digital health interventions to build a patient-physician-facing prototype of Soturi. Algorithm development will use eXplanable A.I. techniques to explain how the model works, and which are the most important features that drive outcome prediction.
Outcomes: The project will develop a comprehensive digital solution which will contain services for the patients (i.e. medication management, symptoms diary, physical, speech exercises and emotional support) and physicians, including the patients' summaries data; alerts, warning, and insights, displaying meaningful changes in clinical data over the time, and a model for the given medication plan of the individual patient, including estimates of likelihood of OFF symptoms and dyskinesia. Acknowledgements: This project is funded by a grant from The Michael J. Fox Foundation, Agreement ID: MJFF-02271.

P40.09

Moving towards the clinic: Validation of computer vision motor function analysis in clinical-based videos of people with Parkinson's disease

Kathrin Heye[*,1], Renjie Li[1], Quan Bai[2], Rebecca J. St. George[1], Kaylee Rudd[1], Guan Huang[2], Marjan J. Meinders[3], Bastiaan R. Bloem[4], Jane E. Alty[5]*
[1] Wicking Dementia Research and Education Centre, University of Tasmania, Hobart, Tasmania, Australia
[2] Department of Information Technology, University of Tasmania, Hobart, Tasmania, Australia
[3] Department of Neurology, Radboud University Medical Centre, Radboud University, Hobart, Gelderland, Netherlands
[4] Department of Neurology, Radboud University Medical Centre, Radboud University, Nijmegen, Gelderland, Netherlands
[5] Wicking Dementia Research and Education Centre, University of Tasmania, Nijmegen, Hobart, Tasmania, Australia

Background: Current diagnosis and monitoring of Parkinson's Disease (PD) is based on subjective clinical assessments. Objective precise measures of motor function could support clinical acumen. Computer vision (CV) technology is a promising contactless research technique, but evaluation in clinical settings is needed.
Aim: To investigate the performance of CV when analysing clinic-based videos of finger-tapping to (i) distinguish PD from healthy controls (HC), compared to human raters, and to (ii) measure the severity of bradykinesia and (iii) detect ON/OFF medication status.
Methods: Sixty-four videos of people with PD and 96 videos of HC (n=160) were collected in the Netherlands and Australia, using standard cameras in clinical settings. Videos were analysed by CV models (DeepLabCut) to produce speed, amplitude, rhythm and combined bradykinesia measures. All videos were independently rated by three examiners using the MDS-UPDRS and MBRS. Videos of paired recordings (n=20) were classified as conducted in ON or OFF states. CV and modal clinical measures were correlated using Spearman coefficients and classification accuracy for PD/HC status and ON/OFF state measured using Area under ROC curves (AUC).
Results: CV bradykinesia measures correlated well with clinical ratings: 0.740 MDS-UPDRS, 0.715 MBRS speed, 0.714 amplitude and 0.504 rhythm; all $p < 0.001$. CV classified ON/OFF state as accurately as clinical examiners, and discriminated HC from PD with high accuracy (AUC 0.961).
Discussion: We found that CV can provide valid, objective and contactless motor function assessments in real-life clinical videos which holds promise as a new clinical tool, including in remote settings and telemedicine.

P40.10

Wearables for Parkinson's disease monitoring – The kuranos project

Lars Jorgensen[*,1], Manuel Gonzalez Berges[2], Emiliano Piselli[3], Anna Ferrari[4], Samuel Simko[5]*
KURANOS (CERN), Geneva, Switzerland

The motor nature of many Parkinson's symptoms and the ever-better sensors available in newer generations of wearable devices such as smart watches, will make it possible to monitor these symptoms continuously and with far better resolution and with such data available it should be possible to follow the progression with a higher granularity. We expect the improved quality and quantity of these data will lead to new insights and a better understanding of the disease itself and perhaps even help towards finding a cure.
The Kuranos project based at the European Laboratory for Particle Physics (CERN) in Geneva, Switzerland aims to make it possible to get high quality data from several smart watches from different manufacturers and different generations of devices and collect and develop an open and reliable software for analysis of this data leveraging tools and services developed over decades at CERN for analyzing the huge amounts of data generated by e.g. the millions of sensors associated with each of the main experiments at CERNs 27 km circumference Large Hadron Collider (LHC).

P40.11

Data managing for Parkinson's disease monitoring using wearable devices

Lars Jorgensen, Manuel Gonzalez Berges, Emiliano Piselli, Anna Ferrari, Samuel Simko*
KURANOS (CERN), Geneva, Switzerland

The motor nature of many of the symptoms of Parkinson's and the ever-better sensors available in newer generations of wearable devices such as smart phones and smart watches, will make it possible to continuously collect data and with far better resolution than previously possible, both crucial ingredients for analysis using new tools developed for Big Data, such as AI (Artificial Intelligence) and Machine Learning.
However, the sensible nature of most PD data makes data management challenging. Several solutions have been developed in the community to tackle this challenge, for instance by leveraging federation of data.
A long and proven track record of developing, implementing and managing large-scale, data-driven tools, make CERN the ideal place to develop a sustainable framework for data management and orchestration at scale.
The complex nature of Parkinson's disease and the rapid progression of digitalization currently ongoing in the healthcare

sector, make it possible to collect data from many different sources (MRI, wearable devices, patient information) with far better resolution, necessary for analysis involving most recent tools such as AI.
However, the heterogeneous nature of data makes the data consistency and relevance challenging. Indeed, although the larger the amount of data, the better, having a lot of information can sometimes lead to mis-leading results. The selection, homogenization and interpretation of data play a crucial role in the analysis quality and ultimately in the effectiveness of drawing conclusions from the data to help the patient have a better life and perhaps even in helping to find a cure. CERN has championed a number of innovations in health care and has a proven track record in implementing and managing heterogeneous data at large-scale for data-driven tools and aims to extend such tools for society and in particular healthcare applications.

P40.13

Design of theSTEPS trial: A phase II double blind randomized controlled trial evaluating motor-cognitive home training for people with Parkinson's disease

Breiffni Leavy[*,1], Jenny Sedhed Sedhed[1], Elisabet Åkesson[1], Elke Kalbe[2], Erika Franzen[1], Hanna Johansson[1]*
[1] Karolinska Institutet, Stockholm, Sweden
[2] University Hospital of Cologne, Cologne, Germany

Background: Healthcare is rapidly becoming digitalized. This offers to possibility to support people with Parkinson's disease (PD) to manage disease symptoms in the comfort and convenience of their own homes. Although a multitude of eHealth applications are available to support home exercise, few of them are based on scientific evidence and specifically adapted to PD. It is recommended that motor training in PD be complemented with cognitive training aimed at attentional or executive functions. Motor-cognitive exercise conditions appear to positively affect motor function.
Aims: The primary objective of the STEPS (Supported home Training in Everyday life for Parkinson's disease) trial is to evaluate whether a motor-cognitive home exercise program targeting functional strength and exercise capacity can improve walking capacity in PD. We will also investigate whether the intervention will lead to improvements in health-related quality of life, self-reported health, physical activity and motor-cognitive ability.
Method: The STEPS trial is a randomized controlled, double blind intervention study. Following assessment, participants will be randomized to either the intervention (motor-cognitive eHealth training) or to the active control group (individualized paper-based home exercise program). Participants will be blinded, ie. unaware of the hypothesized relative merits of the different group conditions. Training will occur in the home during a 10-week period. At project onset, we recruited a group of end-users − people with PD at varied ages and disease stages – who informed and gave feedback to the research group throughout the design and feasibility stages. This iterative process informed specific decisions regarding intervention content as well as hardware and software features. The intervention also contains cognitive-behavioral components such as, goal setting, goal reflection and digital support, specifically to support people with lower levels of exercise self-efficacy. Data collection: This trial is ongoing. We will include 120 people with PD across a spectrum of functional capacity. The primary outcome measure is walking capacity, captured using the 6-minute walk test.
Implications: This home-based motor-cognitive intervention using eHealth technology is unique in its design. Establishing the efficacy of this intervention will strengthen the evidence base concerning eHealth interventions which enable the self-management of PD symptoms in everyday life.

P40.14

Computer vision, a promising artificial intelligence tool to detect bradykinesia in Parkinson's disease

Alicia Olivares-Gil[*,1], José Miguel Ramírez-Sanz[1], José Luis Garrido-Labrador[1], Álvaro García-Bustillo[2], Álvar Arnaiz-González[1], José Francisco Díez-Pastor[1], Florita Valiñas[3], Marta Allende[3], Maha Jahouh[4], Josefa González-Santos[4], Jerónimo Javier González-Bernal[4], José Trejo-Gabriel-Galán[3], Esther Cubo[3]*
[1] Computer Science Department. Universidad de Burgos, Burgos, Spain
[2] Fundación Burgos por la Investigación de la Salud. Hospital Universitario de Burgos, Burgos, Spain
[3] Neurology Department. Hospital Universitario de Burgos, Burgos, Spain
[4] Health Science Department. Universidad de Burgos, Burgos, Spain

Objective: To analyze the accuracy of assessing bradykinesia in Parkinson's disease (PD) using Computer vision.
Background: PD is a chronic and progressive neurodegenerative disorder characterized by motor and non-motor symptoms. Bradykinesia is one of the cardinal symptoms of PD, and it is characterized by slowness and difficulty initiating voluntary and involuntary movements. Computer Vision is a field of Artificial Intelligence that deals with the ability of computers to interpret images and videos. Detection of PD bradykinesia using computer vision is an open area of research and has been used to extract hand movement characteristics during a finger-tapping test. However, the accuracy of machine learning models has not yet been established in PD.
Methods: Multicenter, cross-sectional, case-control study. Patients diagnosed with PD and age, and gender-matched controls were included. We collected a set of videos of the finger-tapping test (left and right hands) from PD patients and controls. MediaPipe, a computer vision tool, was selected to extrapolate finger positions features in each frame, using complex computed statistics. Feature selection techniques were applied to a set of time-series features extracted from the videos. These features were used to feed various machine-learning models for detecting PD bradykinesia. Then, the best machine learning model was selected based on different evaluation metrics.
Results: 45 patients with PD (56.25%), and 35 controls (43.75%), 41 males (51%%), and 39 females (49%) with a mean age of 69.52 + 9.22 years, and median Hoehn Yahr stage of 2 (1-3) were included. The accuracy of Computer Vision for detecting bradykinesia in PD will be reported.
Conclusions: The diagnosis of PD is based on clinical criteria established by a doctor. By utilizing these techniques, the goal is to develop a non-invasive and accurate method for detecting PD, facilitating an early diagnosis and management of the disease. In addition, computer vision can also assist in tracking the progression of the disease, providing insight into how the disease is evolving, which can help to determine the effectiveness of pharmacological and non-pharmacological interventions.

P40.15

Developing automated video assessment of Parkinson's disease: What happens when the training clinician makes errors?

Kye Won Park[*,1], Mohsen Gholami[2], Tianze Yu[2], Maryam S. Mirian[1], Ravneet Mahal[1], Z. Jane Wang[2], Martin J. McKeown[1]*
[1] Pacific Parkinson Research Centre, University of British Columbia, Vancouver, British Columbia, Canada
[2] Department of Electrical and Computer Engineering, University of British Columbia, Vancouver, British Columbia, Canada

The growth of artificial intelligence/machine learning (AI/ML) algorithms is making the automated assessment of some parts of the Parkinson's Disease (PD) examination (e.g. the motor part of the Unified Parkinson's Disease Rating Scale (UPDRS)) a reality. Most ML algorithms are based on "supervised learning," whereby an algorithm is given many, many examples of videos of PD subjects performing simple motor tasks - such as finger tapping or gait - that have been graded ("labelled") for disease severity. In practice, this typically means that Data Scientists developing the algorithm rely on Movement Disorder Specialists' expert labelling of videos. These labels are then considered "ground truth", and the algorithm tries to mimic this behavior.
Here we consider the case when there may be inconsistencies and/or errors in the labels. One way to approach this would be to recruit a panel of experts to label each video and obtain a consensus label, but this is time-consuming, expensive, laborious and ultimately impractical. Another approach is to employ the approach of "weak supervision," which uses labelling functions, whereby the algorithm breaks the disease severity labelling problem into smaller parts. It first automatically labels each video for different aspects (e.g. for finger tapping: Is there reduced amplitude of movement? Is there slow movement? Is the amplitude of movement decrementing over time?, etc.) The algorithm then learns to weigh these parts appropriately to obtain a robust overall estimate of disease severity.
We consider two situations: evaluation of finger tapping, whereby the labelling functions are essentially pre-defined by prior knowledge (the instructions for UPDRS dictate looking at speed, amplitude, decrement, halts/hesitations), and evaluation of gait, whereby the labelling functions were derived from the data by comparing PD subjects with controls.
We demonstrate that such an approach results in more robust and accurate labelling of videos, ultimately resulting in more accurate models for automatic disease classification.

P40.16

Feasibility of a community-based walking program using autonomous rhythmic auditory stimulation in persons with Parkinson disease

Franchino Porciuncula[*,1], Jenna Zajac[1], James Cavanaugh[2], Colin McGregor[3], Jaimie Girnis[1], Louis Awad[1], Brian Harris[1], Alexander Pantelyat[3], Terry Ellis[1]*
[1] Boston University, Boston, Massachusetts, United States
[2] University of New England, Portland, Maine, United States
[3] Johns Hopkins University School of Medicine, Baltimore, Maryland, United States

Introduction: Declines in walking amount and intensity in persons with Parkinson disease (PD) precipitate a cycle of deconditioning and disability only modestly improved by pharmacological and surgical interventions. Rhythmic Auditory Stimulation (RAS), an effective rehabilitation intervention for improving spatiotemporal parameters in PD, shows promise for increasing walking amount and intensity. However, because RAS primarily has been implemented in supervised clinical and research settings, and has used fixed-tempo cues, its translation to dynamic real-world walking environments is limited. The purpose of this study was to assess the feasibility and proof-of-concept of MR-005, a community-based walking program developed by MedRhythms, Inc. for persons with PD, enhanced with an autonomous RAS-based intervention that utilizes closed-loop music tempo control.
Methods: Twenty-three individuals with mild-to-moderate Parkinson disease (PD) participated in an independent walking program for 4 weeks (5 days/week, 30 minutes/day). MR-005 was delivered though headphones, while a mobile device application utilized real-time step cadence information from foot-worn sensors to adjust music tempo. Feasibility was assessed using adherence metrics, safety and usability. Walking amount (steps) and intensity (moderate intensity minutes) were captured using a step activity monitor, 4 days immediately prior to the program and during first 4 days of the program. Feasibility was analyzed descriptively. Changes in mean daily steps and moderate intensity minutes from pre-training (days 1-4) to during training (days 5-8) were analyzed using paired t-tests.
Results: Participants adhered to the protocol by completing a mean of 17.2 (86.4%) of 20 sessions and exceeding the prescribed session duration by 31.1% (mean = 39.0 minutes). No adverse events were reported. Participants reported the device easy to use (95%) and were confident in their ability to do so (100%). Mean daily walking amount during training (12,661 steps) increased by 3,484 steps compared to pre-training (8,777 steps). Mean daily moderate intensity walking during training (38.19 minutes) increased by 21.44 minutes compared to pre-training (16.75 minutes).
Conclusion: The study demonstrated the feasibility and proof-of-concept of using MR-005, an autonomous RAS-based intervention that utilizes closed-loop music tempo control, for improving amount and intensity of community walking in persons with PD.

P40.17

Real-world effects of autonomous rhythmic auditory stimulation on walking speed modulation in persons with Parkinson disease

Franchino Porciuncula[*,1], Jenna Zajac[1], James Cavanaugh[2], Colin McGregor[3], Jaimie Girnis[1], Louis Awad[1], Brian Harris[1], Alexander Pantelyat[3], Terry Ellis[1]*
[1] Boston University, Boston, MA, United States
[2] University of New England, Portland, ME, United States
[3] Johns Hopkins University School of Medicine, Baltimore, MD, United States

Purpose: Routine walking in the community is an important rehabilitation aim in persons with Parkinson disease (PD). However, PD-mediated deficits in gait automaticity may reduce walking speed and consequently restrict participation in community walking. Rhythmic Auditory Stimulation (RAS) is effective in increasing walking speed through linear modulation of stride length and cadence. While previously studied in controlled experiments, its effectiveness for increasing walking speed in persons with PD walking in real-world settings is unknown. We examined the effects of a novel autonomous intervention using an RAS-based device that delivers music to modulate gait speed in persons with PD in community environments.
Participants: Community-dwelling participants (N=13) with mild-to-moderate PD.
Methods: Secondary analysis from a parent study (NCT04891107) designed to examine the feasibility of using an autonomous device that delivers a musical RAS-based intervention (MedRhythms, USA) as basis for a user-directed community walking program. Participants used the device during 20, 30-minute sessions of walking over 4 weeks. The device delivered music cues with tempos

individualized and dynamically adjusted to each user's performance through sensor-derived closed-loop control. Integrated shoe-worn sensors collected stride-by-stride metrics of speed, stride length, and cadence. Each variable was expressed as within-session change, comparing the middle third of each walking bout to the first minute. Multiple linear regression examined the contributions of changes in cadence and stride length to changes in walking speed.
Results/ Discussion: Out of 20 sessions, participants engaged with the device with faster walking speeds by an average of 0.05 m/s, 17 of which were faster than the starting minute. Modulation of walking speed was achieved by adjusting both stride length and cadence ($R2=0.98$, $p<0.001$). Changes in walking speed were more strongly related to changes in stride length ($B=0.67$) than cadence ($B=0.47$), suggesting preference for adjusting stride length over cadence, which may be a favorable strategy against hypokinesia and shuffling gait.
Conclusion: Real-world use of an autonomous, RAS-based device that utilizes music promotes faster walking in persons with PD, achieved through modulation of stride length and cadence.
Clinical relevance: Study findings support the use of a music-based, closed-loop RAS approach for normalizing gait kinematics in persons with PD during community walking activities.

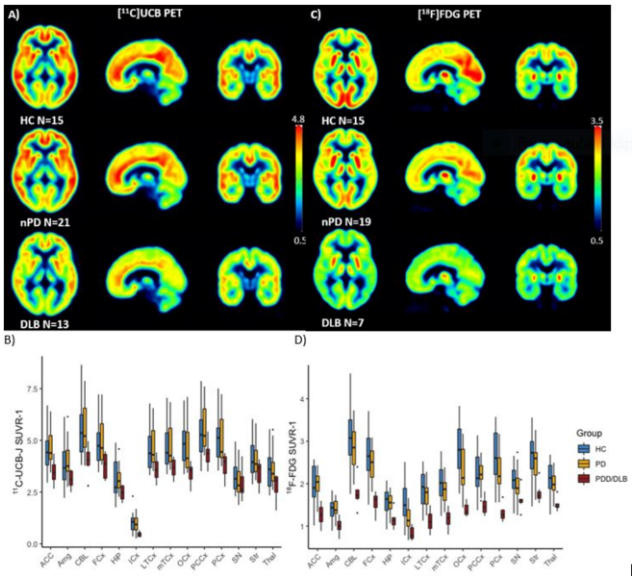
CLINICAL SCIENCE: Neuroimaging

P41.01

Cerebral glucose consumption and synaptic density in patients with Lewy body diseases, as measured with [18F]FDG and [11C]UCB-J PET

Katrine B. Andersen[*,1], Allan K. Hansen[2], Anna Christina Schacht[1], Jacob Horsager[1], David J. Brooks[1], Per Borghammer[1]*
[1] Department of Nuclear Medicine and PET, Aarhus University Hospital, Aarhus N, Denmark
[2] Department of Nuclear Medicine, Aalborg University Hospital, Denmark, Aalborg, Denmark

Background: Collectively, Lewy body diseases (LBD), covers a heterogenous group of neurodegenerative disorders including Parkinson's disease, Parkinson's disease dementia and dementia with Lewy bodies. This patient group exhibit variable degrees of progressive hypometabolism. Generalized synaptic degeneration and restructuring may contribute to this observed hypometabolism. However, the underlying causes remain unsolved.
Objective: The aim was to investigate whether local cortical synaptic loss is proportionally linked to the magnitude of hypometabolism in LBD. We hypothesized a certain overlap in the regional patterns of cortical hypometabolism and cortical synaptic decrease.
Method: We used in vivo PET to quantify cerebral synaptic density and assess cerebral glucose metabolism, as measured with [11C]UCB-J and [18F]FDG PET, respectively. The novel PET tracer [11C]UCB-J binds to the presynaptic vesicle protein SV2A and has been validated as the first universal synaptic density marker in humans. Using the centrum-semiovale as a reference region, we obtained SUVR-1 values for 14 pre-selected brain region-of-interests and calculated the percentage reduction of [11C]UCB-J and [18F]FDG in LBD subjects compared to healthy controls. In addition, between-group comparisons were conducted at voxel-level.
Results: The main findings included 1) regional differences in both synaptic density and glucose consumption in LBD subjects compared to healthy controls, 2) the classical hypometabolism pattern measured with [18F]FDG in LBD patients, and 3) the magnitude of reduced [18F]FDG uptake exceeded the corresponding decline in [11C]UCB-J binding within all cortical brain areas, but comparable reductions were observed in medial temporal regions including hippocampus, amygdala and thalamus.
Conclusion: Here, we investigated the relationship between in vivo glucose uptake and the magnitude of synaptic density. We revealed that whilst several brain regions of synaptic loss overlapped the observed hypometabolism, the magnitude of localized hypometabolism was significantly greater within all cortical brain areas except some medial temporal regions. In brief, this finding suggested a regionally decoupling of synaptic density and metabolism in LBD patients and further suggested that the progressive hypometabolism seen in LBD cannot be fully explained by generalized synaptic degeneration.



P41.02

An interpretable radiomics model of basal ganglia for prediction of dementia conversion in Parkinson's disease

Seok Jong Chung[*,1], Yun Joong Kim[1], Chae Jung Park[1], Yae Won Park[2]*
[1] Yonsei University College of Medicine, Yongin, South Korea
[2] Yonsei University College of Medicine, Seoul, South Korea

Background: Cognitive impairment is common in Parkinson's disease (PD) and severely affects patients' prognosis, and early detection of patients at high risk of dementia conversion is important for establishing treatment strategies.
Objectives: To investigate whether multiparametric MRI radiomics from basal ganglia can improve the prediction of dementia conversion in PD patients when integrated with clinical profiles.
Methods: We included 262 patients with newly diagnosed PD (follow-up >5 years) (168 in training set and 94 in test set). MRI radiomic features (n = 1,284) were extracted from the bilateral caudate and putamen. Two models were developed to predict dementia conversion within 5 years of PD diagnosis: 1) a model based on clinical profiles (age, disease duration, and cognitive composite scores), and 2) a combined model based on the clinical profiles and radiomic features. Their prediction performance and interpretability were studied.
Results: Fifty-one (30.4%) and 24 (25.5%) patients developed dementia in the training and test sets, respectively. Performance of the combined model was superior to that of the clinical model in the

training set (Area under the curves [AUCs] 0.928 vs. 0.894, p = 0.284, Net reclassification index [NRI] = 0.119) and test set (AUCs 0.889 vs. 0.722, p = 0.016, NRI = 0.207). The cognitive composite scores of the frontal/executive function domain contributed most to predicting dementia. Radiomics derived from the caudate were also highly associated with cognitive decline.
Conclusions: Multiparametric MRI radiomics may have an incremental prognostic value when integrated with clinical profiles to predict future cognitive decline in PD.

P41.03

Cingulate island sign is not associated with early dementia conversion in Parkinson's disease
Seok Jong Chung[*,1], Young H. Sohn[2], Su Hong Kim[3], Phil Hyu Lee[2], Yong Jeong[3]*
[1] Yonsei University College of Medicine, Yongin, South Korea
[2] Yonsei University College of Medicine, Seoul, South Korea
[3] Korea Advanced Institute of Science and Technology, Daejeon, South Korea

Objectives: The cingulate island sign (CIS) (i.e., sparing of the posterior cingulate cortex relative to the precuneus and cuneus) is a supportive imaging feature of dementia with Lewy bodies. This study aimed to investigate whether the CIS is associated with early dementia conversion in patients with Parkinson's disease (PD).
Methods: We enrolled 226 patients with newly diagnosed PD and 48 healthy controls who underwent dual-phase 18F-FP-CIT PET scans. Patients with PD were classified into two groups according to the CIS ratio (i.e., the ratio of the regional uptake in the posterior cingulate cortex relative to the precuneus and cuneus) on early-phase 18F-FP-CIT PET images, which reflect regional cerebral perfusion: a PD group with CIS (1 standard deviation above the mean CIS ratio of healthy controls, PD-CIS+; n = 96) and a PD group without CIS (the remaining PD patients, PD-CIS−, n = 130). Subsequently, we compared the risk of dementia conversion within a 5-year time point between the PD groups.
Results: There were no significant differences in age, years of education, and baseline cognitive function between the PD groups. Patients in the PD-CIS+ group had higher Unified PD Rating Scale motor scores and more severely decreased dopamine transporter (DAT) availability in the posterior putamen than those in the PD-CIS− groups. The log-rank test demonstrated that the risk of early dementia conversion did not differ between the PD-CIS+ and PD-CIS− groups (PLog-rank = 0.782). Cox regression analyses also revealed that the risk of dementia conversion in the PD-CIS+ group did not differ from that in the PD-CIS− group (p = 0.941) while adjusting for age at PD onset, sex, the natural logarithm of DAT availability in the posterior putamen, years of education, cognitive status (cognitively normal or impaired) at initial assessment, and total white matter hyperintensity burden.
Conclusions: The results of this study suggest that the presence of CIS on early-phase 18F-FP-CIT PET images is not associated with early dementia conversion in patients with PD.

P41.04

Patterns of regional cerebral hypoperfusion and risk for dementia conversion in early Parkinson's disease
Seok Jong Chung[*,1], Phil Hyu Lee[2], Su Hong Kim[3], Young H. Sohn[2], Yong Jeong[3]*
[1] Yonsei University College of Medicine, Yongin, South Korea
[2] Yonsei University College of Medicine, Seoul, South Korea
[3] Korea Advanced Institute of Science and Technology, Daejeon, South Korea

Objectives: Early-phase images of 18F-FP-CIT PET are known to reflect cerebral perfusion in Parkinson's disease (PD), which is typically coupled to cerebral metabolism and resembles 18F-FDG PET images. This study aimed to investigate whether the patterns of regional uptake on early-phase 18F-FP-CIT PET scans are associated with the risk for dementia conversion in PD.
Methods: We enrolled 397 drug-naïve patients with early-stage PD who underwent dual-phase 18F-FP-CIT PET scans upon initial assessment. Cluster analysis was performed to delineate the PD subtypes according to the patterns of regional uptake on early-phase 18F-FP-CIT PET images. We compared the risk of developing dementia during the follow-up period between the PD subtypes.
Results: Cluster analysis classified patients with PD into three subtypes: subtype 1 (175 patients with relatively preserved cortical uptake), subtype 2 (151 patients with decreased uptake in the frontal, parietal, and temporal regions), and subtype 3 (71 patients with decreased uptake in more extensive cortical regions). Subtype 1 was characterized by a younger age, less severe parkinsonian motor deficits, and better cognitive performance. Subtype 3 was characterized by an older age, more severe parkinsonian motor deficits, and poorer cognitive performance. Subtype 2 was intermediate between subtypes 1 and 3. Cox regression analyses demonstrated that subtypes 2 and 3 had a higher risk for dementia conversion than subtype 1 (p = 0.005 and 0.043, respectively).
Conclusions: These findings suggest that the patterns of regional cerebral perfusion can provide information on cognitive prognosis in patients with early-stage PD.

P41.05

Dancing modifies activations in brain regions associated with movement, mood and reward in people with Parkinson's
Rebecca Barnstaple[1], Judith Bek[*,2], J Royze Simon[1], Rachel Bar[3], Karolina Bearss[1], Katayoun Ghanai[1], Ashkan Karimi[1], Joseph FX DeSouza[1]*
[1] York University, Toronto, ON, Canada
[2] Faculty of Kinesiology and Physical Education, University of Toronto, Toronto, ON, Canada
[3] Canada's National Ballet School, Toronto, ON, Canada

Exercise, music and dance has been shown to improve both nonmotor and motor symptoms in people with Parkinson's (PwP); however, the neural changes underlying these improvements remain unknown. The present study investigated this by tracking behavioural and neural measures in PwP taking dance classes over a period of 8 months. Ten PwP (9 males; age 52-76 years; disease duration 0–17 years) underwent functional MRI while imagining a dance they were learning in the studio, while listening to the corresponding music. A general linear model was used to functionally map brain areas related to imagining the dance. The results show (from strongest to weakest) activation in auditory areas in bilateral superior temporal sulcus, supplementary motor area, premotor area, parietal cortex and cerebellum. To identify brain regions associated with mood, we used an anatomical seed (based on Hamani et al., 2010) in subcallosal cingulate gyrus (SCG) and correlated this with scores on the Geriatric Depression Scale (GDS) completed before and after the dance classes by 7 of the PwP. There was a strong significant positive correlation between change in blood-oxygen-level-dependent (BOLD) signal and average pre-post change in GDS scores ($p<0.025$). To explore effects associated with reward circuitry, we used an anatomical seed based in ventral tegmental area, which showed significant modulation of BOLD signal as a function of learning the dance over time ($p<0.05$). In summary, modulation of neural activity was identified in several brain regions associated with auditory processing, sensorimotor processing, mood, and reward, as a function of learning dance.

These findings suggest the potential to achieve adaptive plasticity through dance in PwP.

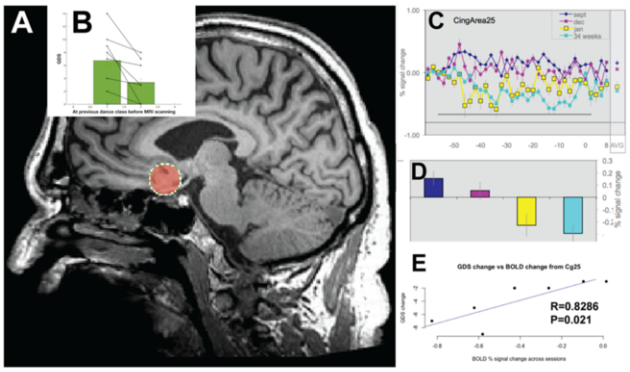


Figure 1: A. Anatomical location of seed in Subcallosal Cingulate Gyrus (SCG) to probe BOLD signals while people with Parkinson's disease visualized learned choreography elicited by music trained in the DfPD class. B. Geriatric Depression Scores (GDS) for this subset of PwPD (p<0.05, paired t-test, n=7 PwPD). C. BOLD signals averaged across PwPD for the music visualization training task during September, December, January and April for all 10 PwPD (28-scans). Data aligned to the end of the one minute of music. Last point is the average plot across the grey bar for the one minute of music visualization. D. Bar graphs showing averaged BOLD signals from SCG with standard error of the mean across PwPD. E. A significant correlation for the change in GDS scores (from Fig B) and BOLD signals reductions (from Fig D) for the seven PwPD who both were scanned in the MRI and completed the GDS questionnaires at the dance studio.

P41.06

Image-guided programming tool for DBS programming used with a multiple-source, constant-current system reduces initial programming time

Jason Aldred[*,1], Theresa Zesiewicz[2], Michael Okun[3], Juan Ramirez-Castaneda[4], Leo Verhagen-Metman[5], Corneliu Luca[6], Ritesh Ramdhani[7], Jennifer Durphy[8], Yarema Bezchlibnyk[2], Jonathan Carlson[9], Kelly Foote[3], Sepehr Sani[10], Alexander Papanastassiou[4], Jonathan Jagid[6], David Weintraub[7], Julie Pilitsis[11], Lilly Chen[12], Roshini Jain[13]*

[1] Selkirk Neurology, Spokane, WA, United States
[2] University of South Florida, Tampa, FL, United States
[3] University of Florida, Gainesville, FL, United States
[4] University of Texas, San Antonio, TX, United States
[5] Northwestern University School of Medicine, Chicago, IL, United States
[6] University of Miami School of Medicine, Miami, FL, United States
[7] Northwell Health, New York CIty, NY, United States
[8] Albany Medical Center, Albany, NY, United States
[9] Inland Neurosurgery and Spine, Spokane, WA, United States
[10] Rush University Medical Center, Chicago, IL, United States
[11] Florida Atlantic University, Boca Raton, FL, United States
[12] Boston Scientific, Valencia, CA, United States
[13] Boston Scientific Neuromodulation, Valencia, CA, United States

Introduction: Optimization of Deep Brain Stimulation (DBS) programming usually consists of a trial-and-error process involving appraisal of various stimulation parameters. Both clinician assessment and patient reporting of clinical benefit are used to define optimal settings. However, this process can be inefficient, lengthy and burdensome. The use of an image-guided programming (IGP) software tool that illustrates DBS lead location within segmented anatomy and volume of tissue activated (VTA) may improve patient-specific efficiency of achieving programming optimization and outcomes. Here, we describe utilization of newly available IGP software for use as a DBS planning tool during initial programming in Parkinson's disease (PD).
Methods: Data from the ongoing prospective, multicenter, registry (NCT02071134) in which novel IGP software (GUIDE XT, Boston Scientific) was utilized and focused on the initial device programming of a multiple source, constant-current DBS System (Vercise, Boston Scientific). The IGP software used pre-op MRI and post-op CT to create patient specific anatomy to enable visualization based programming and to identify the location of the lead relative to anatomical targets. The IGP tool also provides a volume of tissue activated. The time duration to reach effective stimulation settings upon conclusion of initial programming was also collected.
Results: To date, 59 patients have enrolled and 52 have completed an initial programming session. Initial programming of bilateral directional leads (post-implant), where IGP software was utilized to provide settings, lasted a mean of 35.6 ± 4.3 minutes, and 62% of patients completed these sessions in ≤30 minutes.
Conclusions: Shorter and more efficient programming sessions may lead to reduced programming visit time (during the initial programming session) and more patient-specific application of segmented stimulation and improve resource utilization. Thus, this may allow for more rapid achievement of therapeutic and well-tolerated settings than current practice. More data is needed though to determine whether this technique has similar outcomes to more traditional approaches.

P41.07

The effect of nonimpact eccentric lower body exercise on Parkinson's symptoms and substantia nigra structure and function

Senegal Alfred Mabry[*,1], Samantha Moss[2], Jeff Bauer[2], Eve De Rosa[1], Adam Anderson[1]*

[1] Cornell University, Ithaca, New York, United States
[2] SUNY Cortland, Cortland, New York, United States

This study is a collaboration between neuroscientists and exercise scientists to measure how low-impact, eccentric training typically reserved for athletes reduces Parkinson's disease (PD) motor symptoms and influences PD neuroimaging biomarkers. The study is a 12-week intervention with pre-and-post MRI scans. The collaboration expects to replicate findings that this training reduces PD motor and gait symptoms and further demonstrate that this benefit is associated with increased dopamine-associated neuromelanin integrity in the Substantia Nigra (SN) and positive functional connectivity between the SN and cerebellum.
In this study, 40 participants (20 PD, 20 age and sex-matched healthy individuals) will have pre-and-post-training MRI scans and attend 24 training sessions over 12 weeks with 2 training sessions per week. Participants will have physiological and psychosocial cardiovascular disease assessments to control for differences in cardiopulmonary function. Individuals safely balance on the reACT oscillating platform while holding onto support rails, keeping their body in an upright fixed position, similar to mogul skiing, targeting the quadriceps to improve balance, coordination, and stability, The advantages of this training include shorter training time (5 minutes per session), which encourages exercise compliance, and with lower impact loading on major lower body joints.
As PD first causes autonomic nervous system (ANS) disruptions and then progressively worsening motor symptoms, the study will investigate whether training will reduce PD symptoms by engaging the ANS and heart-brain axis to regulate SN structure and function. We hypothesize that SN structure-function changes will be supported by increased ANS vagal nerve activity as measured through increased cardiac coupling with brainstem and midbrain target regions.

P41.08

Microstructural underpinnings of mild behavioral impairment in early-to-mid stage Parkinson's disease

Hannes Almgren[1], Maxime Descoteaux[2], Maryam Ghahremani[1], Zahinoor Ismail[1], Oury Monchi[3]*
[1] University of Calgary, Calgary, Alberta, Canada
[2] University of Sherbrooke, Sherbrooke, Quebec, Canada
[3] Centre de Recherche, Institut Universitaire de Gériatrie de Montréal, Montréal, Québec, Canada

Patients with Parkinson's disease (PD) experience changes in behavior, personality, and cognition. Mild Behavioral Impairment (MBI) is a validated neurobehavioral syndrome that identifies a high-risk group for incident cognitive decline and dementia by leveraging the risk associated with the emergence and persistence of neuropsychiatric symptoms in later life. However, the neurostructural underpinnings of MBI, as well as their differences with mild cognitive impairment (MCI), in PD remain poorly understood. We investigated the neurostructural correlates of MBI and MCI in PD using diffusion-weighted imaging.
Participants included 91 PD patients and 36 healthy controls (HC). 69 PD patients did not have MBI (PD-nonMBI) and 22 patients had MBI (PD-MBI), whereas 53 patients had no MCI (PD-nonMCI) and 38 patients had MCI (PD-MCI). 10 PD patients had both MBI and MCI. We focused on connections from the hippocampus, amygdala, nucleus accumbens, caudate nucleus, and putamen to superior, middle, inferior, and orbito frontal gyri, and connectivity from the hippocampus and amygdala to other subcortical regions. Metrics of white matter integrity included free water (FW), free-water DTI-corrected tissue radial diffusivity (RDt), tissue fractional anisotropy (FAt), and fixel-based apparent fiber density (fixel-AFD). Diffusion-weighted and T1-weighted MRI data were analyzed using TractoFlow. All models for MBI were corrected for MCI status and vice versa.
Results showed that connections between left amygdala and putamen was disrupted in PD-MBI vs. PD-noMBI, as evidenced by reduced fixel-AFD, increased RDt, and reduced FAt. Impaired connectivity with the orbitofrontal gyrus (OFG) was found in PD-MBI vs. HC, as reflected by increased FW for the connections of (1) with left hippocampus, (2) with left nucleus accumbens, (3) with right amygdala, as well as increased RDt for connections between right OFG and amygdala. The microstructural correlates of PD-MCI involved decreased integrity of projections of the hippocampus and caudate nucleus to different frontal cortical regions (Table 1).
Results show that connectivity between regions that are associated with neuropsychiatric symptoms including between amygdala and putamen, and between subcortical limbic regions and OFG, is disrupted in PD-MBI. PD-MCI, however, is related to impaired projections in regions associated with cognition between the caudate nucleus and hippocampus to multiple frontal regions.

Connection		Metric	Statistics		
From:	To:		Effect size[1]	t-value	p-values
Right Hippocampus	Right SFG	Fixel-AFD	β_{stand} = -0.43	t(89) = -2.06	0.04
		RDt	β_{stand} = 0.67	t(89) = 3.32	0.001
		FAt	β_{stand} = -0.57	t(89) = -2.77	0.006
		FW	β_{stand} = 0.50	t(89) = 2.38	0.02
Right hippocampus	Right IFG	FW	β_{stand} = 0.54	t(89) = 2.63	0.01
Right caudate nucleus	Right SFG	Fixel-AFD	β_{stand} = -0.43	t(89) = -2.06	0.04
		RDt	β_{stand} = 0.60	t(89) = 2.90	0.005
		FAt	β_{stand} = -0.61	t(89) = -2.97	0.004
		FW	β_{stand} = 0.49	t(89) = 2.34	0.02
Right caudate nucleus	Right IFG	Fixel-AFD	β_{stand} = -0.46	t(89) = -2.20	0.03
		RDt	β_{stand} = 0.71	t(89) = 3.54	0.0006
		FAt	β_{stand} = -0.61	t(89) = -2.97	0.004
		FW	β_{stand} = 0.57	t(89) = 2.74	0.007
Left caudate nucleus	Left IFG	RDt	β_{stand} = 0.46	t(89) = 2.21	0.03
Right caudate nucleus	Right MFG	RDt	β_{stand} = 0.69	t(89) = 3.41	0.001
		FAt	β_{stand} = -0.66	t(89) = -3.22	0.002
		FW	β_{stand} = 0.56	t(89) = 2.72	0.008
Left Nucleus Accumbens	Left SFG	RDt	β_{stand} = 0.60	t(89) = 2.91	0.005

Table 1. Statistically significant differences between PD-MCI and PD-nonMCI. *Abbreviations:* PD = Parkinson's disease, MCI = mild cognitive impairment, SFG = superior frontal gyrus, IFG = inferior frontal gyrus, MFG = middle frontal gyrus, [1]Positive values indicate higher average values in PD-MCI compared to PD-nonMCI, negative values indicate the opposite.

P41.09

When freezing causes a shutdown! A functional near-infrared spectroscopy study on complex stepping in people with Parkinson's disease

Paulo Pelicioni[1], Stephen Lord[2], Yoshiro Okubo[2], Jasmine Menant[2]*
[1] University of New South Wales, Sydney, Australia
[2] Neuroscience Research Australia, Sydney, Australia

Background and aim: People with Parkinson's disease (PD) who experience freezing of gait (FoG) are at increased risk of falls, particularly in situations relying on anticipatory postural adjustments (e.g., turning). Previous research has shown increased prefrontal cortex activity in people with PD during FoG; however, other cortical areas, such as the supplementary motor area and premotor cortex, involved in movement preparation and sequencing of movement, are understudied. Thus, we investigated cognitive and motor cortical activity during simple and complex stepping tests using fNIRS (functional near-infrared spectroscopy) in people with PD experiencing FoG (PD+FoG) or not (PD-FoG) and healthy older adults. Methods: Fifty-two people with PD (PD+FoG, n=17; PD-FoG, n=35) and 95 healthy older adults participated in the study. All participants performed a simple choice stepping reaction time test (CSRT) and two cognitively-demanding stepping tests (inhibitory CSRT and Stroop stepping task) on a computerised step mat. Cortical activity was determined as relative changes in oxygenated (HbO), and deoxygenated (HbR) haemoglobin concentrations in the prefrontal cortex, supplementary motor area and premotor cortex using fNIRS. The stepping outcomes were: (i) decision time: the time from stimulus onset to foot lift-off; (ii) movement time: the time between lift-off and touchdown onto the correct step panel. Results: Overall, the healthy older adults group had faster decision and movement stepping times than the PD groups ($p<0.05$). Compared with the PD-FoG, the PD+FoG showed slower decision times in all tests ($p<0.05$) but not movement times. There were no between-group differences in cortical activity during the CSRT and inhibitory CSRT; however, in the Stroop Stepping task, the PD+FoG exhibited reduced cortical activity in prefrontal cortex (HbO, p=0.009/ HbR, p=0.003), premotor cortex (HbO, p=0.007/ HbR, p=0.012) and supplementary motor area (HbO, p=0.018/ HbR, p=0.043) compared with the healthy older adults group. Conclusions: People with PD with FoG have a reduced ability to compensate for their motor deficits during a complex stepping test as suggested by reduced cognitive (prefrontal cortex) and motor (premotor cortex and supplementary motor area) cortices activity, a "shutdown" phenomenon. Strategies to overcome this neural inefficiency are

needed for PD+FoG to reduce their risk of falling and improve their quality of life.

P41.10

Neuroinflammation is elevated in people with Parkinson's disease with higher risk of developing dementia: Baseline findings from the NET-PDD (NEuroinflammation and Tau aggregation in Parkinson's Disease Dementia) study

Lennart R B Spindler, Antonina Kouli, Tim D Fryer, Young T Hong, Franklin I Aigbirhio, Simon R White, Maura Malpetti, Marta Camacho, Caroline H Williams-Gray*
University of Cambridge, Cambridge, United Kingdom

Introduction: The development of dementia is a devastating aspect of Parkinson's disease (PD), affecting nearly half of patients within 10 years post-diagnosis. To develop effective therapies to prevent and slow progression to PD dementia, the key mechanisms that determine why some people with PD develop early dementia, while other patients remain cognitively unaffected need to be understood.
Objective: Neuroinflammation/microglial activation and tau protein accumulation have been demonstrated in post-mortem brains donated by people who lived with PD. In other neurodegenerative disorders leading to dementia, both neuroinflammation and tau are strongly linked to cognitive decline. Thus, the aim of our study is to clarify whether these processes mediate dementia risk early-on in the PD disease course. We hypothesised that higher dementia risk patients have greater inflammation and/or tau accumulation, and that degree of neuroinflammation correlates with tau burden.
Method: The NET-PDD study longitudinally assesses forty newly-diagnosed PD patients and twenty age-matched controls, using PET neuroimaging with [11C]PK11195 for microglial activation (indexing neuroinflammation) and [18F]AV1451 for tau. Participants were stratified into two groups at low and high dementia risk based on pentagon copying, semantic fluency, and MAPT H1/H1 genotype. Non-displaceable binding potentials in 46 bilateral brain regions (Hammers' parcellation), were compared between groups (pairwise t-tests), and associations between tracers tested (linear-mixed-effect models).
Results: We found significantly elevated neuroinflammation ([11C]PK11195 binding) in multiple subcortical and cortical regions in the high dementia risk group compared to controls, while in the low-risk group this was limited to two cortical areas. Regional neuroinflammation in most of these regions of interest was associated with worse cognitive performance (ACE-III scores). In contrast, [18F]AV1451 (tau) PET showed increases restricted to subcortical regions where off-target binding is typically seen, and no relationship with cognition.
Finally, we found significant associations between degree of neuroinflammation and tau burden across all brain regions, the strength of which was significantly greater in the high dementia risk PD group.
Conclusion: Significant regional neuroinflammation in early PD might underpin higher risk for PD dementia development, suggesting neuroinflammation as a putative modifiable disease factor to prevent/slow dementia development using immunomodulatory strategies.

P41.11

Pattern of cortical atrophy and its association with motor and cognitive symptoms in Parkinson's disease

Han Soo Yoo[1], Sung Woo Kang[2], Han-Kyeol Kim[1], Chul Hyoung Lyoo[1]*
[1] Gangnam Severance Hospital, Yonsei University College of Medicine, Seoul, South Korea
[2] Yonsei University College of Medicine, Seoul, South Korea

Objective: We aimed to find a characteristic pattern of cortical atrophy in Parkinson's disease (PD) and investigate its association with motor and cognitive dysfunction.
Methods: In this cross-sectional study, we recruited 335 patients with PD who underwent neurologic examination, cognitive evaluation, brain MRI, and dopamine transporter PET. Using principal component (PC) analysis, we determined the expression of the first two PCs (PC1 and PC2) of changes in cortical thickness. We assessed the association of each PC with motor and cognitive symptoms.
Results: PC1 was positively associated with cortical thickness in the inferior parietal, lateral and inferior temporal, primary motor, premotor, and dorsomedial prefrontal cortices as well as supplementary motor area and anterior cingulate cortex, with constituting 68.7% of total variance. PC2 was positively associated with cortical thickness in the anterior and lateral temporal, insular, dorsolateral prefrontal, ventromedial prefrontal, and orbitofrontal cortices, inferior temporo-occipital cortex, and posterior cingulate cortex, with constituting 1.1% of total variance. PC1 expression was negatively associated with UPDRS part III total score, especially bradykinesia and axial subscores, even after controlling for dopamine transporter availability in the putamen. Meanwhile, PC2 expression was positively associated with total K-MMSE score, even after controlling for dopamine transporter availability in the caudate nuclei. Logistic regression analysis showed that PC1 expression was associated with the presence of visual hallucination, while PC2 expression was associated with the presence of dementia.
Conclusions: PD has two patterns of cortical atrophy, one associated with parkinsonian motor symptom and visual hallucination and the other associated with cognitive dysfunction and dementia.

CLINICAL SCIENCE: Prodromal

P42.01

Isolated REM sleep behaviour disorder (prodromal Parkinson's disease) is associated with poor sleep quality in Tasmanian ISLAND sleep study

Samantha Bramich[1], Aidan Bindoff[1], Anna King[1], Alastair Noyce[2], Jane Alty[1]*
[1] University of Tasmania, Hobart, Tasmania, Australia
[2] Queen Mary University of London, London, Tasmania, United Kingdom

Background: Isolated REM sleep behaviour disorder (iRBD) is a prodrome to Parkinson's disease (PD) such that over 60% of people with iRBD (pwRBD) will develop PD within 10 years of diagnosis. Disturbed sleep is frequently observed by bed partners during iRBD dream-enactment episodes but it is unclear whether pwRBD also perceive reduced sleep quality as there have been few studies and results have been inconsistent.
Objective: To investigate the association of poor sleep quality in iRBD. We hypothesise that people with probable iRBD (pwpRBD) will report a reduction in subjective sleep quality, compared to healthy controls.
Methods: Adults aged 50+ years in the Tasmanian ISLAND Sleep Study completed the REM Sleep Behaviour Disorder Single Question Screen (RBD1Q) and the Pittsburgh Sleep Quality Index (PSQI) online. The PSQI includes 7 subscales: duration of sleep, sleep disturbance, sleep latency, day dysfunction due to sleepiness, sleep efficiency, overall sleep quality, and need meds to sleep. Each of these are scored by assigning 0-3 (better-worse) for answers in

all sub-scales, and a total PSQI score is calculated for 'poor quality sleep' on total scores >5.
Results: 2905 participants were recruited (mean (SD) age 64 (7.7) years; 26% male). 273 (9.4%) screened positive for pRBD and 45% of these were male. In the pRBD group, 66% had poor sleep quality compared to 57% in the control group (p= 0.001). Subscale analyses of the PSQI found that pRBD was associated with a greater prevalence of sleep disturbance (67% vs 54%) and daytime dysfunction due to sleepiness (24% vs 11%). There was no difference in sleep duration, sleep latency, or sleep efficiency between pRBD and healthy controls.
Conclusions: We found that people with pRBD report more sleep disturbance, daytime sleepiness and overall poorer sleep quality compared to those without pRBD. This suggests that people with pRBD may be more aware of sleep disturbance than has previously been reported in the literature. It also highlights the importance of enquiring about daytime sleepiness in pRBD as there are potential safety issues around driving and operating machinery.

P42.02

Detecting early symptoms of parkinsonism and isolated REM sleep behaviour disorder in the Tasmanian ISLAND sleep study using a quick online screening questionnaire
Samantha Bramich[1], Aidan Bindoff[1], Anna King[1], Alastair Noyce[2], Jane Alty[1]*
[1] University of Tasmania, Hobart, Tasmania, Australia
[2] Queen Mary University of London, London, Tasmania, United Kingdom

Background: Isolated REM sleep behaviour disorder (iRBD) is often an early symptom of Parkinson's disease (PD), manifesting up to 10 years before a clinical PD diagnosis. People with iRBD demonstrate several objective impairments in olfaction, colour discrimination and motor speed such that these prodromal markers are associated with the highest risk of phenoconversion to PD (or other alpha-synucleinopathies). These changes can be measured objectively in clinical settings, however current tests are expensive and not widely used. There is also little known about whether people with iRBD are aware of subtle motor changes before an overt diagnosis of iRBD or PD is made.
Study objective: To investigate the presence of subjective PD symptoms in probable iRBD (pRBD). We hypothesise that those with pRBD will report greater PD symptomology than healthy controls.
Methods: 2905 participants aged 50+ from the Tasmanian ISLAND Sleep Study completed the REM Sleep Behaviour Disorder Single Question (RBD1Q) and the Michael J Fox Foundation (MJFF) Parkinson's Screening Questionnaire online. Each of the 12 MJFF questions were separately analysed according to yes/no responses. Chi-squared analyses were used to compare the pRBD and control groups.
Results: 273 (9.4%) participants screened positive for pRBD and 45% of these were male. Participants with pRBD reported more symptoms of parkinsonism compared to controls. These included greater feelings of slowness (49% vs 42%, p=0.05) smaller handwriting (12% vs 6%), slurred speech (12% vs 5%), trouble rising from a chair (24% vs 18%) shaking lips, hands or limbs (16% vs 6%), trouble fastening buttons or dressing (14% vs 8%), feelings of stuck feet (7% vs 3%), and trouble with balance (35% vs 26%). There was no difference found between pRBD and healthy controls for feelings of stiffness, feet shuffling, loss of arm swing, or abnormal posture. These findings indicate that people with pRBD experience noticeable changes in motor function, which may be predictive of a future clinical diagnosis. A simple subjective questionnaire could help risk stratify future pRBD cohorts.

P42.03

Parkinson's disease prodromal features and motor symptom progression over five years in the Parkinson's Progression Markers Initiative (PPMI) dataset
*Emily Houston**
The University of Vermont, Burlington, VT, United States

Background: Previous observational and longitudinal studies have found diminished smell and history of REM sleep behavior disorder (RSBD) to be two of the strongest predictors of developing PD. This study aims to examine the relationships between loss of smell, RSBD, and motor symptoms in the Parkinson's Progression Markers Initiative (PPMI) study of untreated, early PD.
Methods: Using a PPMI dataset from 2010 to 2015, the presence of RSBD (yes/no) was compared to the Movement Disorder Society Unified Parkinson's Disease Rating Scale Part III (MDS-UPDRS III) at baseline and Year 5 using a t-test. To examine the relationship between RSBD and motor symptom progression over five years, the change in UPDRS III was calculated using the OFF-medication scores, and a t-test was performed. Loss of smell, measured by the UPSIT, was split into three categories (1=normosmia, 2=hyposmia, 3=anosmia). An Analysis of Variance (ANOVA) allowed for evaluation of the motor scores at baseline, Year 5, and over five years, between each of the UPSIT categories.
Results: At baseline (n=420), 38% of participants with PD reported having RSBD; the mean MDS-UPDRS III scores in the two RSBD groups were similar (yes=20.94, no=20.75; p=0.84). In Year 5, there was a significant difference between the MDS-UPDRS III scores in the RSBD groups (yes=33.18, no=29.42; p=0.02) and 47.6% reported an RSBD (n=229). The change in motor score means from baseline to Year 5 was not significant between the RSBD groups (yes=12.89, no=11.16; p=0.26). Similarly, the MDS-UPDRS III scores within the three olfactory function categories were not different at baseline (p=.15), though they became significantly different at Year 5 (p=0.002). The five-year change in mean MDS-UPDRS III was not significant between groups (p=0.2). The mean change in motor performance from baseline to Year 5 was 11.97 (11.58) in the PD sample.
Interpretations: A history of RSBD and diminished smell do not significantly impact the severity of motor symptoms at baseline or the rate of progression over five years in this group of individuals recently diagnosed with PD. At Year 5, the presence of these early prodromal features could be influencing motor performance in the more severe cases.

P42.04

Grow the prodromal Parkinson's cohort to speed the development of neuroprotective and disease modifying therapies: Five strategies
*Sarah Winter**
Bothell, WA, United States

Synucleinopathies comprise the family of neurodegenerative disorders, namely Parkinson's, DLB, MSA, and pure autonomic failure, characterized by an aggregation of insoluble alpha-synuclein proteins in the neurons. It is now possible to identify patients in the prodromal stages of these diseases through skin biopsy and canine odor detection. Prodromal patients with confirmed synucleinopathy, as research participants and patient advocates, have the potential to speed progress toward neuroprotective and disease modifying therapies. Researchers, policy makers, clinicians, non-profits, and the patient community should concurrently pursue five strategies to grow the prodromal cohort, thereby creating an eager body of research subjects and a groundswell of demand for new therapies. First, it is critical to recognize synucleinopathy in the following

arenas: in the ICD-10 and ICD-11 to promote access to care through billable services; in the National Neurological Conditions Surveillance System to secure research dollars; in longitudinal observational studies such as PPMI and CAM Care in PD in order to contextualize prodromal research responses and conversion times; and in clinical trial registries such as Fox Trial Finder and the Washington PD Registry to build the prodromal research pipeline. Second, providers serving at-risk patients, specifically gastrointestinal specialists (constipation), sleep specialists and general neurologists (RBD), and otolaryngologists and rhinologists (idiopathic hyposmia), require continuing education to ensure they refer patients to accessible diagnostic pathways, such as canine odor detection and skin biopsy. Third, as the Parkinson's staging paradigm broadens to include the prodromal cohort, the AAN and IPMDS should proactively develop standards of care for prodromal patients, to include ethical and decision-making frameworks for early detection; adaptation of the Prodromal PD Calculator for clinical use; prescription of exercise (type, intensity, and duration recommendations); promotion of patient agency in health outcomes; baseline testing; and referral to allied health providers (neuro PT, SLP, and CAM providers for nutritional deficiencies, gut microbiome assessment, lifestyle modification). Fourth, prodromal patients should be connected to research directly from the exam room, to close the gap between clinical practice and research. Fifth, the non-profit community should dedicate staffing to serve the needs of the prodromal cohort, providing patients with supportive communities, education, and advocacy opportunities.

LIVING WITH PARKINSON'S: Public education or awareness programs

P43.01

Parkinson's disease emergency care (PDEC)
*Eric Aquino**
Gray Strong Foundation, Easton, PA, United States

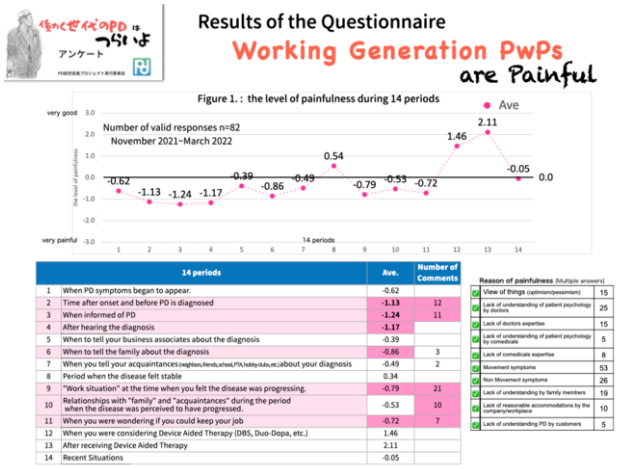
Introduction: Parkinson's disease (PD) is the second most common adult neurological disorder. Healthcare provider training on proper PD protocols is widely available, but not for prehospital providers (PHP). From medications to symptom management, and even simply being able to understand what the patient may be going through, PD requires individual assessment to ensure quality care and outcomes starting in the PHP environment.
Statistics/research: Research demonstrates a gap in training for PD at the PHP level. The Parkinson's Foundation (PF) has established that People with Parkinson's have a higher rate of hospitalization (44 % > than without Parkinson's) and have a longer duration of hospitalization (2-14 days longer than their peers without Parkinson's). In regard to hospital admissions, patients who arrived by ambulance versus non-ambulance had significantly higher admission rates overall (33.7% versus 8.9%, odds ratio, 5.2) and in every triage category. * People with Parkinson's are less likely to be discharged home after hospitalization (on average 62.9% are discharged to either assisted living, nursing care, or a rehabilitation facility). ** These discharges are also more likely to occur via ambulance transport.
Objective: As a PHP with PD, I have a unique opportunity to develop and disseminate a PD emergency care course. This course is designed to improve education for PHP on the complexities of Parkinson's such as medication off times and the assessment pitfalls created. Empowering PHPs to implement improved community healthcare is created by ensuring that all providers are educated and involved throughout the continuum of the care process. This course provides a pathway for PHPs to be integral to facilitating the utilization of the PF's "Aware in Care" kits and partnership with PMD Alliance Certified Parkinson's Disease Care. A prerequisite to the PDEC is the APDA awareness training
Conclusion: Parkinson's medications are as necessary to a Parkinson's patient as insulin is to a diabetic**, or the management of motor symptoms is for a stroke patient. Training exists for both diabetic and stroke patients at the PHP level, but adequate training does not currently exist for PD patients.

P43.02

Subjective evaluation of "painfulness" and its variation factors in working generation PwPs (Parson with Parkinson's)
Yojiro Ashina[1], Yuki Furumoto[2], Junya Ogawa[3], Mikitaka Matsuno[3], Masashi Hiraoka[4], Satoshi Akiyama[5]*
[1] PD's Job Promotion Project, Ageo-city, Saitama, Japan
[2] PD's Job Promotion Project, Hiroshima, Japan
[3] PD's Job Promotion Project, Tokyo, Japan
[4] Hiroshima Bunka Gakuen University, Hiroshima, Japan
[5] Hiroshima International University, Hiroshima, Japan

About PD's Job Promotion Project
PD's Job Promotion Project (PJPP) was launched based on the experience of Mr. Matsuno (founder of PJPP), who had "painfulness" at his workplace.
This paper reports on the results of the survey to the "Working Generation PwPs"
Purpose of the survey:
To clarify the variable factors of "painfulness" of PwPs in the working generation.
Objective1:
To understand the level of "painfulness" at each period of "from the onset to the present" of PwPs in the working generation.
Objective2:
To clarify the factors that influence the level of "painfulness", and to raise the issue with related persons/agencies.
Survey target:
PwPs of working age (20s-60s) nationwide.
Results of the survey:
See Figure 1.
In the process of "from onset to present", the most painful 6 periods out of 14 periods.
The factors contributing to the "painfulness" in the above six periods were, in order of number of responses, as follows.
Movement symptoms/non-movement manifestations (53cases/25 cases)
Lack of understanding of patient psychology by doctors (25 cases)
Lack of understanding by family (19 cases)
Insufficient expertise of doctors (15 cases)
View of things (e.g. optimism) (15 cases)
Lack of reasonable accommodations in company/workplace (10 cases)
Recommendations (issues raised)
In many cases, the way physicians speak to patients at the time of PD definitive diagnosis is hurting them.
In cases where patients go to orthopedics or other hospitals for motor symptoms, many patients suffer for a long time without being referred to neurology.
Weak approach to families by medical care, government, patient community, etc.
Lack of consideration or exclusion orientation by companies (especially superiors and colleagues at work)
Lack of understanding of intractable diseases in society as a whole (lack of understanding of the vulnerable and minorities)
In closing

The PwPs who cooperated with us this time faced the question of looking back on their painful 'past' and provided us with many comments.
On the other hand, the suffering of working-age patients with intractable diseases is a "now" event in many situations.
We have been looking forward to the serious efforts of all concerned.



	14 periods	Ave.	Number of Comments
1	When PD symptoms began to appear.	-0.62	
2	Time after onset and before PD is diagnosed	-1.13	12
3	When informed of PD	-1.24	11
4	After hearing the diagnosis	-1.17	
5	When to tell your business associates about the diagnosis	-0.39	
6	When to tell the family about the diagnosis	-0.86	3
7	When you tell your acquaintances (neighbors,friends,school,PTA,hobby clubs,etc.)about your diagnosis	-0.49	2
8	Period when the disease felt stable	0.34	
9	"Work situation" at the time when you felt the disease was progressing.	-0.79	21
10	Relationships with "family" and "acquaintances" during the period when the disease was perceived to have progressed.	-0.53	10
11	When you were wondering if you could keep your job	-0.72	7
12	When you were considering Device Aided Therapy (DBS, Duo-Dopa, etc.)	1.46	
13	After receiving Device Aided Therapy	2.11	
14	Recent Situations	-0.05	

Reason of painfulness (Multiple answers)	
View of things (optimism/pessimism)	15
Lack of understanding of patient psychology by doctors	25
Lack of doctors expertise	15
Lack of understanding of patient psychology by comedicals	5
Lack of comedicals expertise	8
Movement symptoms	53
Non Movement symptoms	26
Lack of understanding by family members	19
Lack of reasonable accommodations by the company/workplace	10
Lack of understanding PD by customers	5

P43.03

Onda PK: A radio show in Spanish about women and PD
Paqui Ruiz[,1], Sonia Soriano*[,2], Inma García*[,3], Rosa Blázquez*[,4], Sabela Avion*[,5]*
[1] Con P de Párkinson, Tenerife, Spain
[2] Con P de Párkinson, Buñol, Spain
[3] Con P de Párkinson, San Fernando, Spain
[4] Con P de Párkinson, Madrid, Spain
[5] Con P de Párkinson, Long Island City, NY, United States

Con P de Párkinson is a non-profit organization created by and for Spanish-speaking women living with young onset Parkinson's disease (YOPD). We join our voices to share our experiences and to be heard. We want our message to reach health and social services professionals, therapists, researchers and the society as a whole.
We are expert patients willing to share what we have learned with other people living with PD, their families and the society at large. From the virtual world, without borders or time zones, Con P de Párkinson works towards three objectives: to give visibility to Parkinson's disease in general and early onset Parkinson's disease in particular, to promote research that includes a gender perspective, and to improve the quality of life of those affected, their families and those around them.
Onda PK is one of the tools we use to work towards these objectives. Radio Buñol in Spain kindly gives us 60 min of free airtime to interview scientists, healthcare providers, women and men with PD and care partners. Some shows are also available in English. All the shows are available in our YouTube channel (https://www.youtube.com/c/ConPdeParkinson).

P43.04

Maintaining social insertions while facing varying symptoms: Experiences of working-age patients with Parkinson disease
*Myriam Borel**
Observatoire Régional de Santé Bourgogne Franche Comté, Dijon, France

Maintaining social insertions while facing varying symptoms: experiences of working-age patients with Parkinson disease
This qualitative research focuses on how people with Parkinson's disease strive to preserve their social roles in their healthcare pathways and everyday life. This comprehensive approach intends to shed light on the patients' capabilities in their adjustment to symptoms, treatments and their consequences in social life. What kind of resources do they mobilize? What strategies do patients adopt in their various social environments to ensure the continuity of their social life? How do they deal with the progressive loss of their autonomy? The survey will be based on semi-directive interviews with 40 patients under 60 years of age with varied social profiles (age, gender, geographical location, context of (in)activity, symptoms). It is aimed to understand the decision-making process of reorienting their professional life. This research relies on a network of patients' associations in the Burgundy Franche-Comté region, occupational health-care professionals and specialists from the two expert centers in neurodegenerative diseases (Dijon and Besançon University Hospitals).

- Myriam Borel
- Health Observatory, Burgundy and Franche-Comte region

P43.05

"Surely, you are too young"
*Sheenagh Bottrell**
Young@Park peer support group, Melbourne, Victoria, Australia

I was 47 in 2011 when I was diagnosed with Parkinson's Disease (PD), while living in Canberra. At the time, I was employed as a Registered Nurse in a doctor's surgery. When I began to tell people about my diagnosis, the response was often 'surely you are too young'. In time, I came to realise there was a lack of awareness in the community about young/early onset PD, which started me thinking about how I could contribute to raising awareness - this has now become a personal mission. I started by telling my story to medical students at ANU in Canberra. I also became involved with the Shake It Up Foundation, initially through fund raising, and subsequently developing a video that told my story. In 2020 I presented at the National Parkinson's Australia conference, where I highlighted the lack of research into differences of PD in men and women. I was also a member of the Parkinson's Australia Consumer Advisory Committee between 2020-2022. In 2019 my husband and I relocated to Melbourne, where I have become closely involved with the Victorian State Parkinson's peak body - Fight Parkinson's. Since being in Melbourne, I have regularly presented on my PD journey at seminars, undertaken several TV interviews, I run two PD peer support groups, and I am continuously involved in PD fund raising events. In early 2022 I made a podcast for the Australian Primary Health Case Nurses Association, on my experience as a nurse having young onset PD. More recently, I have participated in some PD research through the Michael J Fox foundation in association with Melbourne University, Monash University and The Walter Eliza Hall institute. In 2022 I successfully applied for a Victorian State Government grant to re-established a Young Onset PD Peer Support Group ('Young @ Park'), where we organise events, education, and general discussions to raise awareness of young onset PD. As a result of COVID-19, we also meet via social media, which has expanded our reach across all of

Victoria. I am very proud of my advocacy efforts and plan to continue in a bid to raise awareness across the community.

P43.06

Optimizing hospital care for people with Parkinson's: A new professional education course detailing best practices in inpatient hospitalizations, emergency department visits, and outpatient procedures

Anne Brooks, Lisa Hoffman, Indhira Blackwood*
Parkinson's Foundation, New York, NY, United States

Each year, more than 300,000 Americans living with Parkinson's disease (PD) receive care in the hospital. Data shows that people with PD are at increased risk for hospitalization and, once hospitalized, are more likely to have avoidable complications, worsening PD symptoms, longer stays and poorer outcomes.
To increase health care professionals' understanding of these risks, with support from the CVS Health Foundation, the Parkinson's Foundation created a free accredited three-part course, featuring interprofessional PD experts, detailing best practices in multiple hospital settings.
Care in the Inpatient Setting
For people with PD, inpatient hospitalization can significantly affect morbidity and mortality. Providers can mitigate risk through interprofessional management strategies.
This course reviews:

- The importance of medication timing and type
- How to prepare patients for a safe inpatient experience
- Interprofessional team members' roles in the patient journey from check-in to discharge
- The importance of maintaining mobility during a hospital stay
- PD surgical options, potential complications, and care for people admitted with those complications

Care in the Emergency Department
People with PD present to the emergency department for many reasons (e.g., falls, pneumonia, UTI). Appropriate triage is key to providing optimal care and mitigating risk.
This course reviews:

- The importance of recognizing PD as a relevant co-morbidity and its impact on testing and assessment
- Misunderstandings about the presentation of PD symptoms
- The necessary consultations and the questions each discipline should ask
- The benefits of minimizing stress for people with PD and the significant impact of patient engagement
- Challenges faced during transitions in care and key steps post-discharge

Care in the Outpatient Setting
While outpatient procedures are thought to be much less complex than those that require an overnight hospital stay, for people with PD there are still several safety risks to address.
This course reviews:

- Necessary accommodations for timing of procedures and medications
- Possible side effects of anesthetics
- How processes for common procedures can impact PD symptoms and vice versa
- Interprofessional team members' roles before and after procedures
- The care partner role in preparation and recovery and how to manage everyone's expectations
- The four-step protocol framework for common procedures

P43.07

Development of a patient journey map for people living with Parkinson's disease

Alberto Albanese[,1], Ryan Case[2], Anat Amit[2], Shmuel Ben-Hamo[2]*
[1] IRCCS Humanitas Research Hospital, Milan, Italy
[2] NeuroDerm, Rehovot, Israel

Objective: Develop a Motor Fluctuations Patient Journey Map for people with Parkinson's disease (MFPJM) to describe the holistic patient experience from pre-diagnosis through long-term treatment with a focus on motor fluctuations.
Background: While there have been several surveys addressing the patient perspective of living with Parkinson's disease (PD), most have either focused on medical (treatment) aspects and/or specific treatment issues. There remains a need to understand how motor fluctuations, specifically, are experienced across the disease journey for patients with PD.
Methods: The MFPJM is in development based on in depth surveys with patients and their care-partners (45-minute interviews) and healthcare professionals with experience of treating PD (60-minute interviews). Interviews were conducted with 61 healthcare providers, 40 care-partners, and 33 patients in the UK, Germany, France, and USA.
Results: Qualitative analysis supported 5 stages of the patient journey: onset & awareness, referral & diagnosis, early treatment, living with motor complications, and palliative care. Patients described experiencing subtle (often non-motor) symptoms long before they suspected PD. Across the 4 countries, patients typically started their first treatment (often levodopa monotherapy) immediately following diagnosis. Patients described consistent symptom control for the first few years of treatment. After this 'honeymoon' phase, oral medications typically become less effective, and patients/care-partners recalled noticing a more frequent re-emergence of motor and non-motor symptoms. However, 75% of patients said they were not previously aware of the possibility of motor fluctuations until they developed them. While HCPs aim to minimize OFF time, treatment is centered around the patient's personal tolerance/comfort level with symptoms, side effects, and pill burden. Patients and care-partners described the 'trial-and-error' process of frequently adjusting and optimizing the treatment plan as particularly frustrating. Eventually, as treatment options are no longer effective, patients become dependent on their care-partner or other support services for daily life and seek more advanced treatments.
Conclusions: The MFPJM is in development as a visual aid to enable service providers to identify unmet needs, potential gaps and barriers in service provision, as well as identifying new opportunities for innovation.

P43.08

Exploring public perceptions and awareness of Parkinson's disease: A scoping review of the international literature

Sophie Crooks[*,1], Gillian Carter[2], Christine Brown Wilson[2], Lisa Wynne[3], Gary Mitchell[2]*
[1] Queen's University Belfast, Carrickfergus, United Kingdom
[2] Queen's University Belfast, Belfast, United Kingdom
[3] Parkinson's Association Ireland, Dublin, Ireland

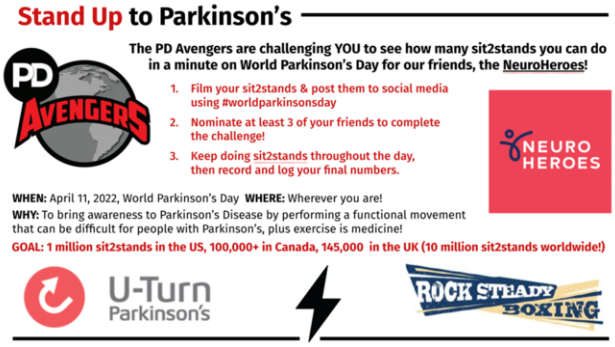
Background: Parkinson's disease (PD) is a common neurological disease affecting around 1% of people above sixty years old. PD is characterised by both motor and non-motor symptoms. As the disease progresses, individuals are likely to lose their independence and autonomy, subsequently affecting their quality of life. People with PD should therefore be supported to live well within their communities but there has been limited research regarding public knowledge about PD.
Aim: The aim of this review is to explore public perceptions and awareness of Parkinson's Disease (PD).
Methods: A scoping review of the literature was conducted following the PRISMA-ScR. Four electronic databases were searched systematically (CINAHL Plus, Medline, PsycINFO and IBSS). The Joanna Briggs Institute Critical Appraisal Tools (JBI) were used to assess the quality of primary studies.
Results: A total of 23 studies were included in the review representing quantitative (N=12) and mixed methods approaches (N=11).. Following narrative synthesis, three themes emerged from the included studies. Theme one was about public knowledge of symptoms, causes and treatments. This theme highlighted a general lack of knowledge and understanding about PD internationally. Theme two related to public attitudes towards PD. This theme highlighted stigma the public often attached to PD and their attitudes towards depression, isolation and loss of independence in people living with PD. The final theme highlighted a significant lack of empirically tested educational resources that could be used to raise public awareness and understanding.
Conclusion: Findings from this novel review have indicated that public awareness of PD is a growing area of interest. To our knowledge, this is the first scoping review on this topic and review findings have indicated that public knowledge and attitudes are variable across the globe. The implications of this are that people with PD are likely to be a marginalised group within their communities, despite this being a common disease of older people. Future research should focus on understanding the public perception from the perspective of people with PD, the development of interventions to promote public knowledge and attitude and further high-quality research to gauge public perceptions of PD internationally.

P43.10

Stand up to Parkinson's: A global awareness campaign for exercise in Parkinson's on WPD 2022

*Laura Douglas**
Neuro Heroes, London, United Kingdom

In 2022 Neuro Heroes hosted a challenge to raise awareness of the vital importance of exercise for people living with Parkinson's. Our physio-led online exercise classes has a community of people with Parkinson's dedicated to exercise and the benefits it brings them. Our STAND UP campaign aimed to empower others to move more too, and take a stand against Parkinson's in solidarity with those living with the condition.
Standing up is a functional strengthening exercise that most of us do many times a day. So, the call to action was for anyone with an association to Parkinson's to complete a collective 145,000 sit to stands over January - one for every person diagnosed with PD in the UK. We offered free events to educate and motivate, and found strength in numbers and collective goodwill, with an 800 strong team smashing the target with a final count of 804,382! We showed the UK Parkinson's community that their therapists, consultants, friends and families were standing up to Parkinson's alongside them.
Exercise helps people with Parkinson's manage symptoms and enjoy a better quality of life, and it may even slow the progression of the disease. After the success of STAND UP UK Neuro Heroes teamed up with organisations around the world like PD Avengers, Rock Steady Boxing, LSVT Global and Parkinson's Africa to further raise awareness of the fact that exercise is medicine, taking on a 24 hour global #SIT2STAND challenge for World Parkinson's Day 2022. People were asked to count through the day or stand up as many times as possible in one minute to add to the total on WPD!
Registrations and counts were collected using Google Forms and collated by Neuro Heroes. The world rallied together accumulating 666,484 sit to stands in just 24 hours! Healthcare teams, charities, exercise groups and individuals from 16 countries used their leg power to make a stand against Parkinson's, spreading the word on social media, sharing videos and photos of sterling efforts, creative ways to stand and tired faces!



P43.11

Raising the voices of women with Parkinson's

Richelle Flanagan[*,1], Kat Hill[2], Sree Sripathy[3]*
[1] My Moves Matter, Dublin, Ireland
[2] Women's Parkinson's Project, Portland, Oregon, United States
[3] Women's Parkinson's Project, San Francisco, California, United States

Three women with young onset Parkinson's (YOPD) from the USA and Ireland met at the WPC in Kyoto (2019). They began a conversation about the void of information about women, especially younger women, with PD. Shortly after their meeting, they began to communicate through social media. This group became a lifeline to another four women with YOPD during the subsequent Covid -19 pandemic. This ongoing dialogue of shared experiences further strengthened that specific needs for women with PD were not being met. We heard women talking about the delay in getting their diagnosis due to clinicians attributing their symptoms to 'hormones' or 'anxiety'. Then, upon diagnosis, the nearly universal dismissal or gaslighting of their lived experience such as the impact of their menstrual cycle on their PD symptoms. It was through this dialogue that the idea was hatched to amplify the voices of these women by creating The Women's Parkinson's Project.
In March 2021 a website and social media accounts were created. Our website showcases the stories and diversity of women with PD from around the world. Through those channels, which have over 3400 followers, we engage with women with PD and the wider

community including researchers, clinicians, therapists & PD organizations where we raise the issues of unmet treatment & research needs of women with PD. To give women another option to access information and connection, we launched a newsletter in March 2022 which now has 350 subscribers.
We have collaborated with other women with PD and advocacy groups worldwide including Con P de Parkinson, Twitchy Woman and PD Avenger's Deutschland. Our post on women with PD on the WPC blog was one of the most read in 2022. We also presented a bi-lingual Spanish and English webinar for the WPC partner webinar series in 2022 on the "Unmet Needs of Women Living with Parkinson's Disease: The Gaps & Controversies" which had 670 registrants.

WOMEN'S PARKINSON'S PROJECT

P43.12

WPC partner series with Womens Parkinson's Project - Unmet needs of women living with Parkinson's disease: The gaps & controversies

Richelle Flanagan[*1], Kat Hill[2], Sree Sripathy[3], Sabela Avion[4]*
[1] My Moves Matter, Dublin, Dublin, Ireland
[2] Women's Parkinson's Project, Portland, Oregon, United States
[3] Women's Parkinson's Project, San Francisco, California, United States
[4] Con P de Parkinson, New York, New York, United States

Aim: To identify gaps in care for women with PD
Methods: World Parkinson Congress (WPC) partner webinar with The Women's Parkinson's Project (WPP) with pre-webinar survey.
Results: The WPC hosted an hour-long bi-lingual English and Spanish webinar which saw 670 registrations of which 303 completed the pre webinar survey. 281 identified as female, 22 male and 1 binary.166 (55%) of those who completed the survey were over 60. 135 (53%) had never taken part in clinical trials.
107 (47%) were unsure if their hormones affected their PD hormones, 26% felt their hormones did affect their symptoms and 27% did not. The key areas of concern included symptom management, hormonal impact on PD, living alone and future care needs. Pre-webinar question themes included hormones, pain management, dyskinesia, fatigue, stress, diet, and DBS.
Conclusion: This WPC/WPP partner webinar and pre-webinar survey demonstrates the need for (1) advice for women under 60 regarding the impact of hormones on their PD (2) the need to address issues for women throughout the lifespan, (3) concerns about future care and (4) the need to ascertain why over 50% of women do not take part in clinical trials.

P43.13

Adapting and replicating a multidisciplinary model of Parkinson's care, rehabilitation and support developed in India to the Kenyan context

Peter Masese[*1], Natasha Fothergill-Misbah[2], Neha Rane[3], Jared Okeno[1], Krupa Ovalekar[3], Hellen Mwithiga[4], Maria Barretto[3]*
[1] Parkinson's Support Group Mombasa, Mombasa, Kenya
[2] Newcastle University, Newcastle upon Tyne, United Kingdom
[3] Parkinson's Disease and Movement Disorder Society India, Mumbai, India
[4] Africa Parkinson's Disease Foundation, Nairobi, Kenya

Introduction: The Parkinson's Disease and Movement Disorder Society (PDMDS) in India has developed and established an evidence-based, community "Multidisciplinary Model of Care" for people with Parkinson's (PwP) and caregivers, delivered through a network of over 70 community-based support group centers across the country. Low- and middle-income countries (LMICs), such as India and Kenya, face similar challenges managing Parkinson's, such as accessing medications and specialists, poor awareness and availability of information, and lack of support.
Objectives: The objective of this pilot project was to test the applicability of the PDMDS model to a different country context, with the hope that the model could be replicated across LMICs globally, while also identifying barriers and alternative methods of implementation.
Methods: The goal of the project was to provide PwP and caregivers with access to knowledge about symptoms, disease management, therapies, and emotional and psychological support. The first stage involved identifying a site, facilitators, and venue in Kenya. Next, the India and Kenya team developed training modules, culturally-specific and translated resource materials, and reporting forms. The facilitators in Kenya received training, identified PwP and caregivers to attend, spread awareness about the program, and initiated the monthly sessions in the local language.

Results: The teams have worked together to successfully adapt and implement the program in Kenya since April 2022. Frequent Zoom meetings facilitated the training and support between the teams in India and Kenya, upskilling the facilitators to deliver new topics during support group sessions. A number of similarities in the country contexts were identified, however, there were also issues which required modifications to the India model. For example, PwPs voiced concerns attending weekly meetings due to travel distances and associated costs, therefore, the sessions were shifted to monthly with longer duration, and a model for home visits is being developed.
Conclusion: The project has consistent attendance at monthly sessions (5-9 individuals), although largely by caregivers rather than PwP. The teams continue to connect with patients living closer to the center to overcome the distance barriers and report on the program outcomes. A final feasibility report outlining the model's applicability is due to be produced and disseminated.

P43.14

APDA trains first responders and fitness professionals to address the unique needs of people with Parkinson's disease
Elvin Yao[1], Allan Bleich[1], Tamara R. DeAngelis[2], Lee Dibble[3], Terry Ellis[2], Robin Kornhaber[1], Merrill R. Landers[4], Cathi A. Thomas[5], Rebecca Gilbert[,6]*
[1] American Parkinson Disease Association, New York, New York, United States
[2] Boston University College of Health & Rehabilitation Sciences: Sargent College, Boston, Massachusetts, United States
[3] Department of Physical Therapy & Athletic Training, University of Utah, Salt Lake City, UT, United States
[4] Department of Integrated Health Sciences, University of Nevada, Las Vegas, Nevada, United States
[5] Department of Neurology at Boston Medical Center and the Boston University Aram V. Chobanian & Edward Avedisian School of Medicine, Boston, Massachusetts, United States
[6] American Parkinson Disease Association, Staten Island, NY, United States

Background: First responders and fitness professionals often work with people with Parkinson's disease (PD) without disease-specific training.
Objective: The American Parkinson Disease Association (APDA) partnered with the Office of Continuing Professional Education (OCPE) at Rutgers, the State University of New Jersey, to develop and provide two free online training courses to educate these key members of the health care community who did not previously have access to PD-specific education, thus enabling them to better serve and care for this population.
Methods: In 2016, the APDA PD Awareness Training for First Responders was created for police officers, fire fighters, and emergency medical service providers to help them recognize the unique symptoms and needs of those with PD. In 2018, the APDA PD Training for Fitness Professionals was developed to help fitness, health, and wellness professionals safely and effectively work with people with PD.
Results: Since its release, 6,802 participants completed the First Responders course. 2,937 were EMTs or paramedics, 1,427 were firefighters, 1,395 were police officers. The results of a post-course survey demonstrated the importance of the training, with 71% responding "definitely" in assessment of the statement: This course helped me understand how to respond to the unique needs of individuals with Parkinson's disease.
Since its release, 4,252 students completed the Fitness Professionals training course. The majority of participants were fitness professionals working with the PD community, but the course was also accessed by physical therapists and occupational therapists. In addition, undergraduate, physical therapy, and occupational therapy students took the course, as well as volunteers in PD-specific programs. Several care partners took the course as well. The results of a post-course survey demonstrated the importance of the training, with 83% responding "definitely" to: I will change the way I approach certain on-the-job interactions as a result of this course. 82% answered "definitely" to: This course helped me understand how to respond to the unique needs of individuals with Parkinson's disease.
Conclusion: Both training courses were heavily accessed by their respective target audiences and met their goals of teaching these communities about the unique needs of people with PD.

P43.15

Eradicating neurophobia through expert patient tutors: The Parkinson's perspective
Gina Hadley, Sally Bromley, Gabriele C. DeLuca*
Nuffield Department of Clinical Neurosciences, University of Oxford, Oxford, United Kingdom

Background: 'Neurophobia' (fear of neural sciences and clinical neurology) is endemic amongst medical students across the globe. Determinants of neurophobia include a poor understanding of neuroanatomy and its relationship to clinical symptoms and signs that people with neurological conditions, such as Parkinson's disease, experience. To eradicate neurophobia, Oxford Medical School invented the concept of 'Expert Patient Tutors' (EPTs)
EPT Programme: EPTs are people with Parkinson's disease and other chronic neurological conditions with symptoms and signs pathognomonic of different patterns of nervous system dysfunction. EPTs share their lived experience to describe the manifestations of such nervous system dysfunction while serving as the vehicle through which students 'observe' and 'feel' how these conditions affect the neurological examination through guided instruction and feedback. Medical students develop an unique opportunity to learn how neuroanatomy and the bedside clinical examination are linked.
Feedback: Students report satisfaction and reward of combating neurophobia and gain a deeper understanding and appreciation of life with a neurological condition.
"The EPT session was perhaps the most useful learning experience I have ever had at medical school. I felt myself become more confident over the session." (Oxford med student)
EPTs report satisfaction with working alongside bright and eager medical students to nurture their development as future doctors.
"We help the doctors of tomorrow gain early hands on experience with real patients, with real complex disease. The assumption is that we inspire them; well, they certainly inspire me." (Parkinson's EPT)
"I am sure that these sessions help the students put a name and a human face to the people who live with these diseases." (Parkinson's EPT)
Students, clinician educators, and EPTs foster meaningful and trusting relationships with one another outside traditional clinical environments through novel teaching and learning styles.
Impact: People with Parkinson's have been integral to the creation, development, and delivery of the EPT programme to eradicate neurophobia one student at a time. In so doing, people with Parkinson's are nurturing the confidence and competence of future doctors to recognise neurological conditions, such as Parkinson's, in the earliest possible stages to make a palpable difference for the better.

P43.16

Global mentor/mentee program for Organizations: A pilot project of allied health education for community volunteers in Africa

Angela Halpern[*,1], Cynthia Fox[1], Hellen Mwithiga[2], Margarita Makoutonina[3], Building Global Alliances Working Group[4]*
[1] LSVT Global, Tucson, United States
[2] Africa Parkinson Disease Foundation, Seattle, United States
[3] ParkiLife Australia, Melbourne, Australia
[4] WPC, NA, United Kingdom

This pilot project is a result of work completed by the WPC Building Global Alliances Group (BGAG). The BGAG recognizes the myriad of barriers that exist for people with Parkinson's (PwP), their families and carers. The aim of the group is to problem solve how our International Parkinson's Community can work together to better share resources and develop global networks that benefit those in low-middle income countries.
An initial survey sent by the BGAG to WPC organizational partners confirmed the inequity of resources globally and the substantial nature of tackling the issue of decreasing this inequity. Due to the vast nature of the concept of "increasing access to resources", the BGAG chose to focus first on a pilot project which could serve as proof of concept in one country/region, then expand broader.
The concept of focus was to develop an organizational support system which connects organizations in low-middle income countries with organizations that have larger structures and greater resources through a mentoring partnership. For this pilot project, we looked internally to the BGAG group for mentor/mentee needs. Africa Parkinson Disease Foundation, represented by a BGAG member, has successfully utilized non-healthcare trained community volunteers to provide basic education about Parkinson's disease to the Parkinson community in Kenya. In consultation with these volunteers, it was identified that they would value education on topics related to voice/speech, movement and swallowing to share with the PwP that they interact with. BGAG members with expertise in these areas provided the training.
The pilot training consisted of pre-recorded learning followed by a virtual live session. Materials were developed using an iterative design for feedback from the volunteers regarding cultural appropriateness; ideal audio/visual format; understandability; and mechanisms to overcome barriers to internet access for delivery of training materials. The effectiveness of the training was measured by completion of knowledge review questions by the volunteers and metrics to evaluate the impact of education provided by the volunteers to PwP and their families/carers over time.
This poster will describe the results of the feedback from the community volunteers and PwP and analyze the potential for replication in other communities.

P43.17

A call to action for community-cased exercise classes: Building a team of healthcare providers, students, and fitness instructors

*Robert Hand**
VCU Health, Henrico, VA, United States

Persons with Parkinson's disease (PwPD) regularly participate in physical therapy (PT) to address individual needs related to strength, balance, mobility, and overall functional abilities related to maintaining a high quality of living. In conjunction with supervised PT sessions, PwPD are prescribed home exercise programs (HEP) and general recommendations for community-based exercise programs, such as Rock Steady Boxing or PWR!Moves classes. However, many regions are lacking these PD-specific exercise programs – not for lack of specialized healthcare professionals. Establishing the bridge between clinical care and community-based exercise is an important and ongoing challenge in our healthcare system.
We present our implementation framework which includes: (1) identifying geographic, financial, and accessibility barriers to participation in existing programs; (2) gathering healthcare providers, local fitness instructors, and PwPD to develop a preliminary program concept; (3) pursuing financial support for pilot program development; (4) partnering with local nursing, physical therapy, occupational therapy, and medical students – especially through existing chapters or organizations (e.g. American Geriatrics Society); (5) developing a schedule with two distinct class levels (twice-weekly per level), and also a fully inclusive Saturday class with the option for care partner participation.
This program, now recognized as a novel 501©3 ("LiftPD"), has successfully provided free exercise classes to over 75 unique PwPD. This is remarkable in that the initial funding which supported the program, through a Parkinson's Foundation Community Grant Award, began during the peak of the COVID pandemic. Quick thinking and adjustments were required to ensure participant safety while continuing to offer classes, as the risks of social isolation and inactivity were especially high during 2020 - 2021. We continue to offer classes with modifications for participant safety and social distancing.
The success of this program is based in reproducible strategies used for recruitment, personalized introduction to exercise training (free one-hour evaluation and sample training session with a LiftPD coach), exercise programming within two distinct classes ("Heroes" and "Warriors"), and ongoing partnership with local healthcare systems and student organizations. Participating in this program has been a first exposure for many students to PwPD, sparking interest in serving this population.

P43.18

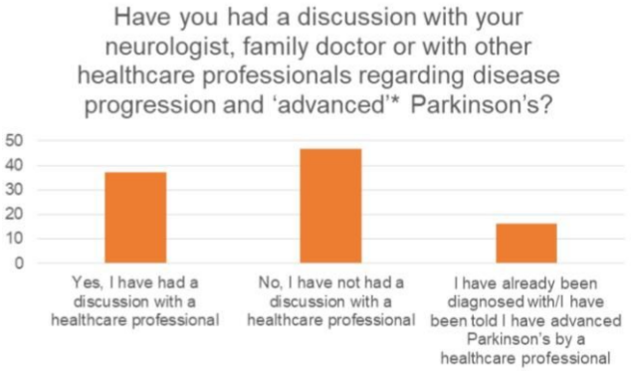
Results from a multi-country survey on advanced Parkinson's treatment knowledge, experience and information

Amelia Hursey, Francesco De Renzis*
Parkinson's Europe, London, United Kingdom

Objective: To understand people with Parkinson's knowledge and perception of their treatment and available options for advanced Parkinson's, and to assess the type and timing of information they receive about available therapies.
Background: In March 2021, Parkinson's Europe launched an online survey to assess people with Parkinson's experience of treatment, their understanding of options that could be considered for advanced Parkinson's, and whether timely and adequate

information about such options was provided by Healthcare Professionals (HCP's).
Methods: The survey questionnaire, developed with input from people with Parkinson's and scientific experts, was published online in eight languages. Participants were asked about their Parkinson's history and experience, satisfaction with treatment, and sources used to receive information about the condition.
Results: Over a 1 year recruitment period, a total of 1,063 participants from 53 countries completed the survey. A high proportion of respondents were taking frequent oral medication doses (63.9% ≥4 times per day), with 66.1% experiencing variations in medication effect. Only 12.8% were receiving Device-Aided Therapies (DATs). Subjects receiving DATs reported higher rates of satisfaction with treatment than those taking only oral therapies. 46.6% of respondents had not had a discussion with any HCP's about advanced Parkinson's treatment options (Figure 1), and many sought information from other sources.
Frequency of visits with HCP's varied significantly in our grouped European regions, but satisfaction relating to the information received about advanced Parkinson's treatments did not.
Conclusions: The survey results suggest that around two-thirds of people with Parkinson's face challenges with oral treatments, and that there are gaps and geographical variations in how information about advanced Parkinson's treatment options are communicated by HCPs to patients. The survey did not ascertain respondents' adherence to individual treatment regimes, an area which requires more research in the future to allow us to understand the full picture of need for escalation from non-oral therapies to DATs.
Disclosures: The survey was supported by, and developed in partnership with, Britannia Pharmaceuticals Ltd.

Figure 1. Frequency of discussions with HCPs about advanced Parkinson's



P43.21

Piece of mind: Parkinson's screening and interactive workshop
Naila Kuhlmann*[,1], Anne McIsaac*[,2], Jeremie Robert*[,3], Alice Masson*[,4], Rebecca Barnstaple*[,5], Louise Campbell*[,2]
1 McGill University, Montreal, Quebec, Canada
2 Montreal, Canada
3 Throw2Catch Circus, Montreal, Canada
4 Madrid, Spain
5 York University, Toronto, Canada

The proposed event is a screening of Piece of Mind, a performance on Parkinson's disease (PD), followed by an interactive workshop led by myself and other members of the Piece of Mind team*. I have submitted a separate abstract concerning the research component of this project.
Piece of Mind: Parkinson's is a multi-media performance co-created by neuroscientific researchers, PwPs, caregivers and artists that aims to unite the lived experience and scientific research of PD on stage. The performance combines circus, dance, music, theatre and testimonials to shine a light on the many invisible aspects of PD; call attention to the problematic communication gap between healthcare professionals and PwPs; and highlight current PD research avenues. The performance is 45 minutes in length and bilingual (English and French) with subtitles. We would be honoured to present 1-2 screening(s) of our performance at the World Parkinson Congress, followed by a short Q&A session and an interactive (30-min) workshop to bring together perspectives from lived experience, scientific research and clinical practice through the arts. Specifically, we would lead an improvisational exercise we developed in the creative process of Piece of Mind, in which pertinent topics (ex. one's relation to the body; the perception of rhythm and time; on-off periods of medication; the role of caregivers) were explored from the angle of lived experience, neuroscientific research, and artistic representation. The activity can be adapted to small or large groups, and works as a round-robin or telephone game in which participants are given 2-3 minutes to share their perspective. We are happy to discuss the specific format of the event to fit the needs and constraints of the WPC.
*The following members of Piece of Mind would co-facilitate the discussion and workshop:
Rebecca Barnstaple - PD researcher and dance facilitator;
Anne McIsaac - PwP and Piece of Mind performer;
Jeremie Robert - circus acrobat and Piece of Mind director;
Lili Saint-Laurent (Alice Masson) - PwP and Piece of Mind participant;
Louise Campbell - musician and participatory music facilitator.

P43.22

Friends of Parkinson's: Involving youth in raising public awareness about Parkinson's disease in India
Deepshikha Mathur, Maria Barretto*
Parkinson's Disease and Movement Disorder Society, Mumbai, Maharashtra, India

Background: To promote public awareness and literacy about Parkinson's disease (PD), the Parkinson's Disease and Movement Disorder Society (PDMDS), involves college students through Friends of Parkinson's-a student volunteer program. PDMDS has identified this active cohort to sensitize the public, using strategies that are attuned to youth interests and ambitions and simultaneously fulfill the organizational aim to raise awareness.
Objectives: The objectives are to involve the younger generation in building sensitized communities and raise awareness about PD among people that students know and interact.

Methods: Volunteers are recruited through awareness programs conducted for college students enrolled in the disciplines of Psychology, Management, Physiotherapy. The Friends of Parkinson's is offered as a community-based volunteering program. Volunteers are provided with a structured program. To understand PD, students get practical experience by involving in support group activities. They are guided through the innovative awareness strategies that are attuned to their interests. These include strategies like awareness programs for their own family and friend, making social media content to post on their own social media account. Other innovative strategies include writing blogs or articles in college journals and fund raising through a perspective of awareness building exercise.
Results: 304 volunteers have enrolled in the friends of Parkinson's program since past 3 years. The volunteering experience is based on these principles: commit, connect, contribute, and continue that have ensured success of the program. This program has resulted in:

1. Raising awareness of PD
2. Capacity building of students to advocate for PD
3. Building sensitivity to the needs of the elderly
4. Increased visibility on social media

The volunteering experience offers the students practical experience, enhancement of skills and recognition for their involvement in a social cause. Volunteer and participant feedback indicate value and sustainability of this program to raise public awareness about PD.

P43.23

The development of a girl scout topic action patch for Parkinson's awareness: T.A.P. – P.D.
Margaret McCormick[*1], Gwyn Vernon*[2]
[1] Towson University, Baltimore, Maryland, United States
[2] University of Pennsylvania, Philadelphia, Pennsylvania, United States

Background: As the pandemic disrupts our engagement with one another, it forces us to reflect and re-evaluate the intersection of health education with community engagement. This intersection draws our attention to the question: How does a community of practice for PD awareness get realized?
Purpose: The aim of this project is to explore how a girl scout patch can influence the design and execution of a project about Parkinson's disease awareness. Girl scouts under the direction of troop leaders can examine and shape the architecture of a topic action project for Parkinson's disease awareness. Scouts can describe insights which arise when implementing the Parkinson's disease awareness badge. During this project, scouts can work together to build a better learning space and enhance their leadership skills which can be used to help others with Parkinson's disease.
Method:
1) Examine evidence- based health information by consulting with nurse experts in the field of Parkinson's disease care.
2) Discuss ways to engage different age levels to raise the level of available health information.
3) Outline age- appropriate activities for the topic action patch which are engaging, fun and informative.
4) Describe which girl scout badge activities help to promote awareness and community engagement about Parkinson's disease.
Discussion: Nurse scholars from the Edmond J Safra Foundation, Visiting Nurse Faculty at the Parkinson's Foundation collaborated with girl scouts of Greater Chicago area to implement the pilot patch program "TAP-PD" during the summer of 2021. Activities ranged from simple to complex such as coloring a picture about things that could result in falls to role playing activities about Parkinson's disease. The results of the girl scout patch program were overwhelmingly positive. Troop leaders felt that "this was the first step to increase awareness about PD for girl scouts who may become our future nurses, doctors, scientists or community health care workers."
As the pandemic re-ignited some of our basic health concerns about community engagement and health education, it also challenged us to look for new solutions. The design of age- specific programs for girl scouts was a valuable way to help increase awareness about Parkinson's disease.

P43.24

Providing authentic learning experiences about Parkinson's disease: Bringing humanity into the classroom-phase II
Margaret McCormick[*1], Gwyn Vernon*[2]
[1] Towson University, Baltimore, Maryland, United States
[2] University of Pennsylvania, Philadelphia, Pennsylvania, United States

Background: Edmond J. Safra Visiting Nurse Faculty implement Parkinson's disease teaching into nursing school curricula in multiple and creative ways. However, it difficult to measure impact on the nursing students on a collective scale. To date, no formal study has been done to evaluate the impact on students learning about Parkinson's disease from V.N.F. scholars.
Purpose: The aim of this multi-state project is to identify patterns and themes from reflective journals from students, faculty and interviewees from four different nursing schools across the United States. Best teaching strategies for educating nursing students about Parkinson's disease will be described. This manuscript will provide information that will help guide nurse educators in their search for evidence-based teaching strategies about Parkinson's disease in multiple educational level settings.
Methods: This project explores a qualitative descriptive study which describes the impact of student learning about Parkinson's disease using an in-class patient interview and reflective journaling method. Qualitative researchers analyze the data collected from reflective journals written by nursing students from four different universities following an in -class meeting with either a patient panel or individual person living with Parkinson's disease. Following the patient visit experience, students wrote a thoughtful consideration of an experience. The qualitative researchers identified patterns within the data. Clear and distinct themes with subthemes were captured from the coded data by both qualitative researchers.
Conclusion/Results: Nursing students from all levels expressed an overall lack of experience with those diagnosed with Parkinson's disease (PD). This lack of clinical exposure and limited lecture time covering PD in the nursing classroom led to more of a generalized "textbook" understanding of PD. However, when classroom lecture was followed by the interview experience with an individual living with PD, students were able to experience "having the lecture come to life" These interview experiences opened the eyes of students to a "new level of humanness that we don't usually get in lecture". The Edmond J. Safra Visiting Nurse Faculty Program (V.N.F.) at the Parkinson's Foundation is producing valuable scholars who benefit nursing education and or patient care while improving classroom teaching about the disease.

P43.25

A Parkinson's manifesto for Europe

Fiona Montague[*,1], *Josefa Domingos*[2], *Amelia Hursey*[1]
[1] Parkinson's Europe, Orpington, Kent, United Kingdom
[2] Radboud University Center, Nijmegen, Netherlands

Background: Parkinson's is one of the fastest growing neurological conditions in the world. Parkinson's Europe (PE) works and campaigns with people with Parkinson's and their families to ensure their voices are heard. PE celebrated its 30th anniversary by launching a Parkinson's Manifesto for Europe - a reflection of the hopes, wishes and ambitions of the European Parkinson's community.
Objective: To collate the wishes and ambitions of the Parkinson's community in Europe and create a guide for those working in health, research and policy of the priorities for people living with Parkinson's.
Methods: We collected data from a variety of sources including desktop research, surveys, social media, e-shots and workshops. Participants were invited to fill in an online survey (SurveyMonkey) with their wishes for the future. The survey comprised of 5 open text and ranking questions and translated into nine languages. Results of the survey framed four workshops held in May and July 2022 attended by people with Parkinson's, caregivers, family members and health professionals.
Results: 913 people from 39 countries responded to the survey. 58% (534) respondents were people with Parkinson's, 35% (317) respondents were caregivers, partners and supporters and 7% (62) were healthcare professionals. The collated 'wishes' were refined to 8 broad themes for the workshops which were attended by 40 members of the Parkinson's community. The workshops resulted in 30 wishes grouped into five key areas: 1) Increasing awareness and understanding of Parkinson's 2) Educating and training all health professionals about Parkinson's 3) Improving diagnosis, treatment and complex care needs for people with Parkinson's 4) Improving the wellbeing and quality of life for people with Parkinson's and caregivers and 5) Strengthening and driving Parkinson's research and innovation. The manifesto was launched on 20 October 2022 and available in nine languages: Czech, Dutch, English, French, German, Italian, Portuguese, Slovenian, and Spanish.
Conclusions: Our results suggest that there are five key priorities that people living with Parkinson's consider important to improving their life. These findings should help to guide and direct those people working in research, health care and policy to ensure their work is aligned to the needs and wishes of the Parkinson's community.

P43.26

What I didn't say – A journey through Parkinson's: An original play about life with Parkinson's, authored and produced by Matthew Moore, Ohio, United States

*Matthew Moore**
Lamp and Light Productions, Hilliard, OH, United States

I have written an original play titled, "What I Didn't Say: A Journey Through Parkinson's" for the purpose of public education and to strengthen the relationships involved with PD, primarily that of neurologist and patient. The script is based on twelve interviews with PD patients, doctors, and care partners. It's a two-person, forty-five minute performance that's adaptable to any setting, and it's always followed by a discussion to let the audience ask questions and to give their perspective of relationship-building in a PD context.
The play premiered in Columbus, Ohio, in September of 2022. It's been performed seven times since then, including a performance at The Ohio State University and for the neurologists of OhioHealth, as part of their academic conference. To date, the play has reached over 1100 viewers, including those attending the live performance and those viewing via livestream.
The post-production discussions have been passionate and practical. For medical professionals, the play has offered a keen reminder to know the whole person, their patient, to whatever extent that is possible. For PD patients and care partners, the play affirms the thoughts and emotions involved in a PD journey. They are not alone. And, the general public has learned what PD is, how it progresses, and the challenges patients and care partners face.
Future goals for the performance include finding an audience with medical professionals in training. How can the play provide provide insight to medical students? Could a series be developed?
Ultimately, the performance harnesses the power of art to make an impact in a way that data and research cannot. Both are critical.
Could the play be performed as part of the conference? I'm happy to answer any questions about that.
Trailer of the performance: https://vimeo.com/788772753
A review of the play by Samantha Elandary, Executive Director of the Parkinson Voice Project
"I'm pleased to support Matthew's efforts in educating the community about PD. The play is AMAZING! It brings to light concerns and feelings often kept quietly inside. By openly sharing these thoughts through theatre, Matthew will help thousands. The play is inspiring and comforting."

P43.27

The Barcelona Parkinson's Ready Program

*Selma Pelaez**
Hospital Clínic de Barcelona, Barcelona, Spain

Parkinson's disease (PD) is a chronic, progressive neurodegenerative disorder commonly affecting the older population but it is increasingly being diagnosed on adults and even on young adults. As worldwide population is ageing rapidly, PD prevalence is expected to double in the next 25 years. Therefore, this situation makes necessary that people should be aware how Parkinson's manifests itself, recognise the cardinal signs and symptoms and help efficiently this increasing amount of sufferers.
As the World Parkinson's Congress (WPC) brings together a huge amount of patients and carers, through the last editions, it was detected the need to train the place where the congress is held in order to make this emplacement a good experience for PD sufferers. Seeing the success of that, the joint collaboration between the WPC, the Catalan Association of Parkinson (CAP), the city of Barcelona, a qualified trainer (a neuro-physiotherapist) and a well-trained PwP advocate, has set the goal of creating a protocol (the

Barcelona Parkinson's ready program) of this process of public education on PD, especially on those bodies who will work closely with PD sufferers during the congress and they may not have knowledge on PD.
Firstly, we pulled all the information from the previous experience of the 5th WPC's Kyoto's team and the counselling from the PwP advocate to create both a general body and specific information for each body of workers: airport staff, hotel staff, police officers, firefighters, taxi drivers and metro and bus drivers.
Aiming to reflect the changes on PD's education, they were sent a short survey related to their confidence levels and awareness on helping PD people before and after the workshops. The trainings were done in person either in Catalan or Spanish, between the World Parkinson's day (April 11th) and July, when the congress takes place. After the workshops, a triptych was given to each attendee with the most relevant concepts and contact details for further information.
In conclusion, the systematization of a public awareness process on PD can help other institutions to educate efficiently their population and make life easier to PD sufferers.

P43.28

A study on social media strategies employed by the PDMDS to create awareness on Parkinson's Disease in India
Neha Rane, Maria Barretto*
Parkinson's Disease and Movement Disorder Society, Mumbai, Maharashtra, India

Background and Objectives: There is a general lack of awareness in society about Parkinson's Disease and its symptoms; which can be one of the factors for people with Parkinson's (Pwps) to face stigma and isolation. For over two decades, the Parkinson's Disease and Movement Disorder Society (PDMDS) has employed various strategies to create awareness about Parkinson's and make a difference in the lives of Pwps and their caregivers. Social media, a recent addition to the awareness initiatives, has been a tool to bridge the geographical gap to enable PDMDS to reach out to PwPs and their caregivers. Through various strategies, PDMDS social media platforms have helped make information about Parkinson's accessible and enabled PDMDS to interact with a wider audience. The PDMDS social media platforms have built an online community for Pwps and their caregivers to further the discourse on PD.
Methods: Social Media Statistics obtained from 4 social media platforms- Youtube, Facebook, Instagram and Twitter were analyzed to gauge the patterns observed in engagement, likes, followers/subscribers, reach and comments. Assessment of new Pwps joining PDMDS support groups which were obtained through social media campaigns. A social media survey form was constructed to further understand the general population's interaction with PDMDS social media platforms, the kind of content they follow PDMDS pages for and the kind of content they would like to see.
Results and Conclusions: Through the statistics and analytics provided by the social media platforms it is observed that social media has been a valuable tool to spread awareness about Parkinson's Disease to reduce stigma and lack of knowledge about the condition and normalize conversation on PD. It was further observed that educational posts and videos such as information on symptoms of PD; and posts depicting stories of people with Parkinson's and their caregivers received the most engagement from the social media users. This study has helped to understand the audience's preferences for Parkinson's related content which will be helpful to plan future strategies and campaigns for social media.

P43.29

Faces of Parkinson's
*Travis Robinson**
Altadena, CA, United States

Faces of Parkinson's
New photographic project by artist Travis Robinson captures the spirit of the PD community
About the project: Through Faces of Parkinson's, the artist aims to capture as many portraits of people with Parkinson's as possible, to celebrate the diversity and humanity of the PD community.
People with PD often learn to hide their face, their tremor, and their symptoms. "Faces of Parkinson's" will educate the public as an ongoing project to showcase the vibrancy and light within these wonderful people.
The process is a unique blend of photography, digital photo manipulation, and laser cutting. The resulting block cut is then rolled with printer's ink and the final image is a unique blend of photography and printmaking that has the sharpness and detail of the former with the texture and depth of the latter. People with Parkinson's have a muted voice in their communities. It is my responsibility as an advocate and an artist to make sure those voices get heard. By doing so I help bring PD into the spot light.
"Travis Robinson's portrait of me illustrates the fact that even with Parkinson's Disease, right now I am alive, and with the support of my community I am living with dignity and an appreciation for life!" – Kurt Rademaekers, Faces of Parkinson's participant.
About the artist: Travis has been using photography to capture and share many aspects of his life. Travis's photographs have been shown at the Brewery Art Walk, Bergamot Art Center, Pasadena City College, and the Joshua Tree Art Gallery as well as in solo shows at the f9 Gallery in Los Angeles. He has participated in PCLA's annual Living Artistically with Parkinson's exhibitions since 2018. He is also a co-host of the I'm Not Dead Yet! Podcast. A podcast about living an extraordinary life, with extraordinary circumstances. Travis was diagnosed with young onset Parkinson's disease in 2014.

P43.30

Parkinson's experience at school: "Viu el Parkinson a l'escola"

Jordi Santandreu Esteve[*,1], *Sofia Malagón Gutiérrez*[2], *Pepa Martín Barceló*[3], *Núria Langa Beltràn*[2], *Paula Artigues Martinez*[4], *Montse Gabaldà Torrente*[5]
[1] @parkinformados, Barcelona, Catalunya, Spain
[2] Viu el Parkinson a l'escola, Barcelona, Spain
[3] Associació Parkinson Terres del Ebre, L'Ametlla de mar, Spain
[4] Universitat de Vic, Manresa, Spain
[5] De bat a bat, Centelles, Spain

Background: Parkinson's disease, despite being the second most prevalent neurodegenerative disease, remains little known by society. Many people associate it with the eldest who tremble.
Objectives: For this reason, a group of people with Parkinson's decided to carry out an awareness campaign at the School that would have a direct impact on children, but also indirectly on their families in order to disseminate knowledge of the disease and raise awareness.
We define the target audience as students in the fifth year of Primary School, that is, around 10 years of age.
Methods: We use an immersive methodology, which allows children to experience some of the symptoms of Parkinson's in first person.
First we make a small introduction, about the nervous system, chronic and neurodegenerative diseases, dopamine, etc.
Then the children are divided into 5 groups and go through five different activities where they experience some of the Parkinson's symptoms: walking problems, communication difficulties, rigidity, motor fluctuations (ON-OFF) and dyskinesias.
After each activity they receive some magnetic letter to the end they form the word Parkinson on a board at the end.
At the end of all the activities, we give them a piece of paper to write down anything they might have learned or felt about the disease.
And lastly we all share our experience, asking questions and encouraging them to share what they have learned with their families.
Results: Along 2021-2022; we visited a total of 7 schools, where we had 11 group sessions for a total of 280 students.
Conclusions: By letting them experience first-hand the effects and symptoms of Parkinson's, we achieve a great emotional impact. While they are participating in the different games, they notice the difficulties that people with Parkinson's suffer in our daily lives and their empathy is awakened.

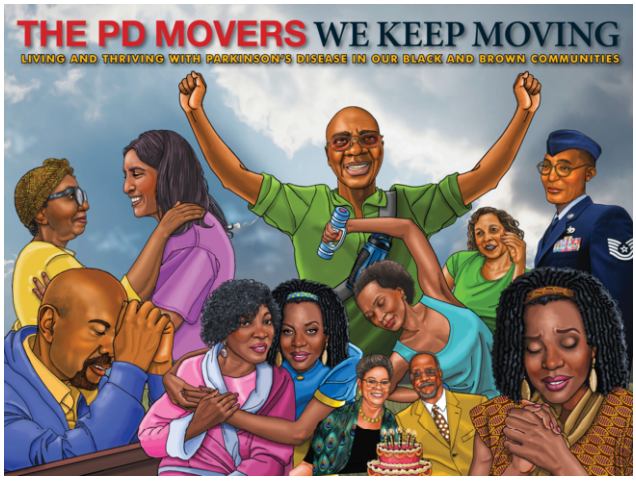
P43.31

Using story to raise awareness, reach and connect African American and black individuals affected by Parkinson's disease

Hiral Shah[*,1], *Denise Coley*[2], *Bernard Coley*[2], *Sandra Coplin*[2], *Elizabeth Delaney*[3], *Victoria Dillard*[2], *Lorraine Haye*[2], *Angela Huckabee*[2], *Richard Huckabee*[2], *Danielle Kipnis*[4], *Michele Lin*[4], *Chelsea Macpherson*[4], *Nia Mensah*[4], *Alissa Pacheco*[4], *Anita Parker*[5], *Terrie Peacher-Ransom*[2], *Randell Pearson*[6], *Don Ransom*[2], *Kermit Smith*[2], *Lori Quinn*[4]
[1] Columbia University Irving Medical Center, New York, NY, United States
[2] PD Movers, New York, NY, United States
[3] Columbia University, New York, NY, United States
[4] Teacher's College, New York, NY, United States
[5] St. Luke A.M.E. Church, New York, NY, United States
[6] Pearson Designs, New York, NY, United States

Background: African American(AA)/Black older adults face numerous barriers to care for Parkinson's disease (PD) and are less likely to have a timely diagnosis. Once diagnosed, they are less likely to receive high-quality care or participate in relevant clinical trials compared to White adults [1, 2]. Furthermore, minorities have increased disability and motor symptoms at the time of presentation [3]. In the AA/Black community, lack of trust in physicians and the healthcare system due to a deep-rooted and powerful history of discrimination and exploitation [4-6] is one significant barrier to accessing care.
Methods: By using a faith-informed and community-based participatory research approach, we partnered with St. Luke African Methodist Episcopal (A.M.E.) Church, trusted gatekeeper in the community, to develop an educational tool that would create heightened awareness of PD, a sense of community, and connection in the AA/Black community. The approach emphasized building trusting relationships and highlighting the community's strength. The result was a compilation of first-person narratives titled, "PD Movers, We Keep Moving." The book utilizes vibrant images that underscore the importance of representation; together

with the narratives, delivers joyful, empowering, and educational messages that are culturally sensitive and engaging.
Results: The book's authentic voices coupled with powerful illustrations address identified barriers such as stigma, fear, and discrimination and have generated high levels of interest and engagement from the AA/Black community. We are sharing the book by word-of-mouth through personal, professional, and spiritual networks. It has been shared at least 500 times in two months.
Conclusion: Educating and empowering AA/Black communities will be an effective method to activate and mobilize individuals and care partners to seek care for Parkinson's disease. In AA/Black communities, it is often the norm to stay quiet about disorders that can lead to mental and physical disabilities. Educational tools such as this book create a shared understanding of one's PD experience and ultimately take steps to close the PD care gap for this vulnerable population. Through this work, we have reached communities of color and empowered them through education, helping break the silence around PD.



P43.32

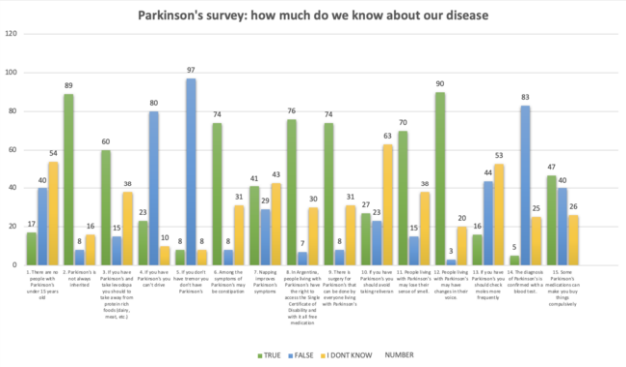
Improving care and reducing professional isolation: Developing a community of practice for occupational therapists treating people with Parkinson's
*Victoria Tull**
Fight Parkinson's, Surrey Hills, Victoria, Australia

Introduction: Occupational therapy is recognized as a key discipline for supporting people with Parkinson's. However, occupational therapists have limited opportunities to access specialist support and training in movement disorders, often practicing in isolation. To address this challenge, an online community of practice for occupational therapists with an interest in Parkinson's was established.
Objective: To improve the experience of people living with Parkinson's when accessing occupational therapy and to reduce practitioner isolation by developing a supportive practice network.
Approach: Occupational therapists were contacted from various movement disorders programs, hospitals, community health, aged care and private providers across metropolitan and regional Victoria, Australia. Those confirming interest in movement disorders and in participating in an online practice community, were electronically invited to the inaugural meeting. To understand practitioner desires and knowledge-gaps, a pre-meeting survey was sent. Survey responses identified learning priorities and established the group's terms of reference and meeting frequency.
Practice implications: 51 Occupational Therapists originally joined the community of practice, with 30 participating in the inaugural online meeting in June 2020. 40 respondents completed the pre-meeting survey which established the key learning priorities, typical caseloads, preferences surrounding meeting frequency and capabilities for future in-person collaborations. The group facilitates regular opportunities for knowledge-exchange and has gained momentum, increasing to over 100 members (current December 2022). The online delivery has transcended geographic and economic barriers, enabling participation from metropolitan and regional areas, and extending to an interdisciplinary offering with other equivalent physiotherapy, speech pathology and nursing communities of practice. Formal evaluation of practitioner and consumer experience is required to validate the informal positive feedback.
Conclusion: The establishment of a Parkinson's-focused community of practice has been favorably received by a broad network of occupational therapists. This forum continues to grow and now collaborates with equivalent communities of practice through interdisciplinary education. Further evaluation and 360-degree feedback will facilitate the group's ongoing evolution and provide insights into consumer experiences.

P43.33

Parkinson's survey: How much do we know about our disease
Lucia Wang[*,1], Lucila Falcone[1], Monica Giuliano[2]*
[1] Parkinson Joven Argentina, Buenos Aires, Argentina
[2] Universidad Nacional del Oeste, Ciudad Autónoma de Buenos Aires, Buenos Aires, Argentina

The purpose of this survey is to determine how much patients and their relatives, caregivers and friends know about Parkinson's, especially about aspects that affect our quality of life.
Methodology: An online survey was carried out with a self-administered questionnaire with sociodemographic data and 15 questions about Parkinson's to answer "True", "False" and "I don't know", in relation to the diagnosis, treatment and self-care of the disease. The sample was non-probabilistic and was collected over the course of 15 days, mainly through the Parkinson Argentina Patient Organization.
The survey was completed by 112 people. All of them lived in Argentina, 40% had been diagnosed Parkinson' disease in average 6 years before the research, 60% were caregivers, relatives or friends of patients. The educational level was high: at least 60% had completed university studies, and barely 16% had an educational level below complete or incomplete secondary education.
Conclusions: Despite the educational level of those who responded the survey there is a lack of knowledge about fundamental issues related to the management of Parkinson's symptoms. For instance, slightly less than 50% of the people surveyed answered that it is false or they do not know that taking levodopa should move away from protein consumption; more than 30% are unaware that taking some medicine (anhydrous metoclopramide hydrochloride) is contraindicated or that people which taking levodopa moles should be controlled frequently (only 14% knew this information).



P43.34

3-part book study of "Ending Parkinson's disease: A prescription for action" Book author: Ray Dorsey, MD, ET, AL
*Jane Rice Williams**
Parkinson's in Motion, London, KY, United States

-part book study by Parkinson's In Motion (PIM), East Kentucky/Appalachian resource group.
Objective: IGNITE OPTIMISM
Spread the truth about PD's prevalence and main cause - environmental toxins, not flawed genetics. If the cause is manmade, it can be corrected!
Reach undiagnosed and undertreated in remote area with no movement disorder specialist, few neurologists; provide hope.
Encourage activism, focus on book's action plan: PACT – Prevent, Act, Care and Treat.
Methods: Library provided books prior to the study. We advertised heavily - social media, newspaper, radio, and civic clubs. Dr. Dorsey participated via Zoom in the last session. Two representatives of the Fox Foundation participated via Zoom and in person. Discussion was prepared to encourage participation. The final session included a sponsored pizza dinner. Financial burden on PIM - $0.00.
Results: Approximately 50 people participated with many attending all 3 sessions. Sign in sheets reflect attendance. Participants were stunned and electrified to learn that the suffering from PD was not their failed genetics but brought on by exposure to toxins that are broadly used in the US but banned in many countries.
PIM has new members as direct result of study.
New active member: 39-year old, diagnosed just hours before the last meeting.
The community has been invigorated including physicians and other providers, far beyond our expectations. Optimism is contagious.
Diagnoses have increased. Donations to PIM increased.
Phase II - This study is the catalyst for dramatic increase in PIM's outreach and strategic plan which includes:
Develop structured plan to implement PACT;
Join with MJFox to introduce legislation at the state level;
5K Run Walk for all;
Develop workout facility with PD specific classes and equipment; and,
Use College interns - 3 college students now work with PIM!
The poster must reflect:
Where we are – ALARMING PD GROWTH RATE
Where we're going - ENDING PD.

LIVING WITH PARKINSON'S: Government advocacy/campaigns/public policy

P44.01

The PD avengers: A patient-led, global alliance demanding change in how the disease is seen and treated, adding urgency to the cause of ending Parkinson's
Larry Gifford[*,1], Tim Hague[2], Soania Mathur, MD[3]*
[1] PD Avengers, Vancouver, British Columbia, Canada
[2] PD Avengers, Winnipeg, Manitoba, Canada
[3] PD Avengers, Toronto, Ontario, Canada

The Global Alliance to End Parkinson's Disease Association, known as, PD Avengers, launched in July 2020 with the audacious goal of ending Parkinson's disease (PD). What inspired this global advocacy group is the book Ending Parkinson's Disease: A Prescription for Action by Michael S. Okun, MD, Bas Bloem, PhD, MD, Ray Dorsey, MD, and Todd Sherer, PhD.
Focusing actions on three pillars – wellness, advocacy, and research – PD Avengers mission is to be a unifying force in the global Parkinson's community. Since its inception, momentum is building and true partnerships are developing as evidenced by growth in numbers. Initially there were 12 founding members. Today, there are more than 6,100 members representing 93 countries, and 115 partner organizations.
At its core, PD Avengers is a movement mobilizing people and organizations behind a shared purpose, ending Parkinson's. As an umbrella organization, this global group is bringing together patients, care partners, friends, organizations, pharma, medical device developers, scientific and medical experts, and others to improve quality of life for those living with this disease.
The PD Avengers works with partner organizations to amplify the voices of the Parkinson's community and is based on the premise "think global, act local". Some examples of the success collaboration has brought include the Fifty Thousand Red Letters campaign asking for banishment of three chemicals that increase risk for PD were sent to the White House in 2021 as a joint effort led by the Ending Parkinson's authors and PD Avengers. In 2022, one of the chemicals the Red Letters targeted was banned for use on food crops and another is under reassessment from the EPA.
With Franklyn Design, the partner organizations imagined, created, and produced "The Spark," for World Parkinson's Day, a new international symbol for PD representing action and urgency. A WHO technical brief and JAMA Neurology article Six Action Steps to Address Global Disparities in Parkinson's Disease: A World Health Organization Priority was co-authored by 32 experts including the President of PD Avengers and 12 members. With each small success, PD Avengers is building towards a future without PD.

P44.02

Anti-antiparkinsonian drug use after diagnosis of Parkinson's disease

Woong-Woo (Woody) Lee[*,1], Beomseok Jeon*[2]
[1] Nowon Eulji Medical Center, Eulji University, Seoul, South Korea
[2] Seoul National University Hospital, Seoul, South Korea

People with Parkinson's disease (PD) suffer from various non-motor manifestations such as constipation, depression, sleep disorder, hallucinations, dementia, etc. These non-motor symptoms influence the quality of life of patients and their caregivers. Decreased gut motility and constipation lead to poor oral intake. Hallucination and dementia are major risk factors for admission to nursing homes. Therefore, physicians treating PD should pay attention to non-motor symptoms, as well as motor symptoms, when adjusting drugs.
There are many drugs to improve non-motor symptoms of PD. Some could interfere with the action of antiparkinsonian drugs (APDs). However, there is a lack of data on the prevalence of these anti-APD use. We investigated the prescription patterns of these drugs to know how many patients were prescribed anti-APDs even after the first diagnosis of PD.
We defined a patient with PD who had ever been diagnosed under the disease code G20 collected from the National Health Insurance database. Exclusion criteria were 1) the code G20 was considered a 'rule-out'; 2) the subject had ever been diagnosed with atypical parkinsonism; 3) a neurologist did not confirm a diagnosis. We investigated the anti-APD use pattern of the 2011 incidence cases for two years.
We found 18317 incidence cases of PD in 2011. Of them, 9784 patients (53.4%) had ever used the anti-APDs for gut motility, such as levosulpiride, metoclopramide, and clebopride. For psychiatric symptoms, the anti-APDs, including risperidone, haloperidol, olanzapine, perphenazine, aripiprazole, etc., were prescribed in 2508 patients (13.7%). Levosulpiride and risperidone were the most used drugs, respectively. Internists and orthopedists prescribed the anti-APDs for gut motility more, while neurologists and psychiatrists prescribed the anti-APDs for psychiatric symptoms more than other doctors.
Many patients with PD had been taking anti-APDs for gut and psychiatric non-motor symptoms even under PD diagnosis. The problem is that these anti-APDs could aggravate PD motor symptoms and result in escalating doses of APDs if there is no prescription information from other departments. Not providing potentially harmful drugs to patients with PD is as essential as prescribing the appropriate APDs. Close cooperation with other departments and repeated education on anti-APDs are required.

P44.03

Assessing access to medications and other health-related barriers for people living with Parkinson's: A pmd alliance policy panel survey

Andrea Merriam[*,1], Greg Chesmore*[2], Maria Cristina Ospina*[3], Jill Farmer*[4], Lori DePorter*[5], Julia Pitcher*[6], Kelly Papesh*[1], Jason Rivera*[1]
[1] PMD Alliance, Tucson, AZ, United States
[2] Gridiron Public Affairs, Madison, WI, United States
[3] Regional Parkinson Center, Phoenix, AZ, United States
[4] Global Neurosciences Institute, Philadelphia, PA, United States
[5] PMD Alliance, York, PA, United States
[6] Michael J Fox Foundation, Washington, DC, United States

Introduction: The recent increase in medical treatment options has offered many people with Parkinson's (PWP) better symptom management and improved quality of life. However, factors including cost, geography, access to specialty care, and health insurance coverage challenge the delivery of these improvements to all PWP. As state and federal public policy decisions influence equal and affordable access, Parkinson and Movement Disorder Alliance (PMD Alliance), a US-based advocacy organization, created the PMD Alliance Policy Panel. This panel of diverse stakeholders includes patients, care partners, clinicians, advocacy organizations, and biopharmaceutical and device companies. Their collaborative effort gathers supporting data for solutions and policy proposals developed around access and affordability, leading to real-world changes for all PWP.
Objective: The Policy Panel created the Assessing Access to Medications for People Living with Parkinson's survey to better understand the PD community and their needs around medication access, cost, and other health-related barriers.
Method: This online survey was distributed by email to (PWP) and their care partners.
Results: According to 345 respondents, most (76%) see a movement disorder specialist, and (78%) have Medicare as their primary insurance coverage, but few (11%) receive any financial assistance for out-of-pocket (OOP) prescription drug costs. Many (89%) take (3) or more total medications, and (44%) take (3) or more PD medications. While (66%) were unaware of the Medicare Part D OOP prescription drug cap beginning in 2025, many (84%) believe lowering prescription drug costs should be a top priority. Ranked in order, the greatest pain points were locating specialists, OOP medication costs, and health insurance premium costs. While (74%) indicated paying for medication is not currently a difficulty, (95%) were not confident their insurance would cover new medications, and (62%) wanted increased efficacy through newer therapies.
Conclusion: While medication costs were not the respondents' greatest concern, barriers exist in accessing treatment options, understanding drug coverages, and the overall burden of healthcare costs. Further assessment is warranted.

P44.04

Networking of NGOs with World Parkinson Coalition: Approach in public health policy evolvement

Shankh Pal, Toshni Roy, Jyothi Kumari*
SFCCP, Meerut, UP, India

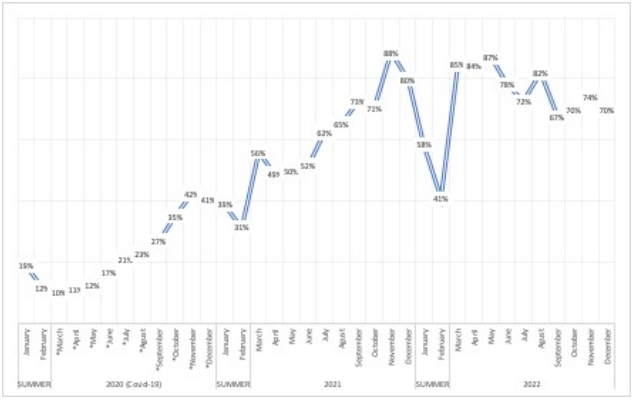
Issues: National-health-registry based data demonstrates subsidized Psychosocial support & treatment-availability are major issues for Parkinson's-sufferers in resource-poor-nations. Hence our Non-Govt-Organisation analysed & started this public health-policy paper recommendation.
Objectives: NGO's close to rural/tribal-communities. Cost of running NGO economical than medical-institution. Medical treatment cost is prohibitive and inaccessible for majority patients in Asia. Govt-Health-Depts need to workout strategy to increase access to care. In resource-poor-setting unaffordable cost leads to poor-therapeutic-compliance therefore high mortality. We develop training program to develop of sound /sustainable Parkinson's-care for rural communities
Methods: No national-program for financial help to Parkinson's patients exists in india. Care programs designed towards rural/tribal population needed. Our NGO since four years offers guidance for Rx-funding, guidance those going to city-centres. This project is unique as we are training NGO health workers to assist patients community in improving access to Rx. Depending on support given by donors we give provide little-financial-assistance for treatment & improve access to governmental hospitals. we started with two towns & intend to offer our services to 16 villages by 2025.
Results: We did face hiccups in mobilising volunteers/resources. This strategy has minimum maintenance-cost & high-acceptability. Forums like WPC-2023 conference must support NGO-activists to

form workgroup with World Parkinson coalition to further develop this concept.
Conclusion: Economical-factors/access to therapy changes out-come of Rx and care. With little training, few resources our community NGO in rural/tribal India formed well knit volunteers-group who is giving free part-time dedicated service. CAM/psychosocial-support improves QOL reducing difficulties faces by resource-poor-southern countries. We urge participants to share views/expertise on this burning-issue at venue to come out with sustainable policy paper for Asian nations.

P44.05

CENPAR: Covid-19
Paola Alicia Riveros Cortés
Cenpar Neurologyc Center Te Parkinson Disease, Providencia Santiago, Santiago, Chile

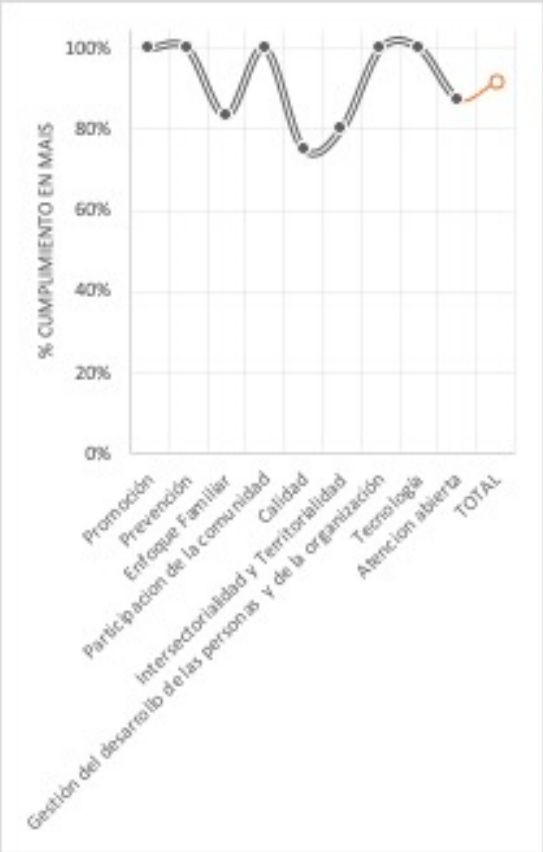
Abstract: In covid-19 pandemic the life of patients with Parkinson's disease changed going from being social individuals who interact with the environment to being people who lived in quarantine for months. CENPAR decreases the request for comprehensive health care in the area of neurology, psychology, neuropsychology, nutrition and rehabilitation.
Introduction: The Covid-19 pandemic wreaked havoc on the survival of people, in health, at work, socially and economically. The health of many patients with Parkinson's disease saw their condition diminish, increasing of signs and symptoms.
Material and method: A retrospective study is carried out and the percentage of monthly care is analyzed from 2020 to 2022 in CENPAR, visualizing the decrease in health care for people with Parkinson's disease during the Covid-19 pandemic. The amounts of care provided in the clinical area, which considers neurology, psychology, neuropsychology and nutrition, were reviewed. The attentions of the integral rehabilitation area are also reviewed.
Result: In 2020 health care due to the drop in appointment requests as a result of the pandemic, giving an average annual care of 22% of the installed capacity in March presenting the least amount of care, patients with 10% and the month of in November the one with the greatest attention with 42%, the majority carried out in person. In December there is a drop in the request for care that ends in February 2021, related to the summer vacation months. In 2021, an average of 60% of the total attentions are presented and in 2022, 72% of the attentions are carried out. During 2020, the care was, from March to July, mainly by telemedicine modality. From August to date, the care is in person, mostly and, to a lesser extent, by telemedicine.
Conclusion: Knowing the abrupt decrease in health care for people with Parkinson's disease allows us to recognize that during the difficult moments of the Covid-19 pandemic, our patients decreased their health benefits, negatively affecting their level of Fragility, increasing the percentage of mortality and comorbidity, being the greatest risk factor.



P44.06

Cenpar and the integral health care model (MAIS)
Paola Alicia Riveros Cortés*
Cenpar Neurologyc Center To Parkinson Disease, Las Condes, Santiago, Chile

Abstract: An evaluation of the development of Health Care Model (MAIS) is carried out at CENPAR, a neurological center specializing in Parkinson's disease, their family members and the community. The evaluation determines that CENPAR performs 92% of the expected compliance in this model, delivers a wellness to the country.
Introduction: CENPAR opens its doors on April 11, 2017 with the aim of improving the quality of life of people with this disease, supporting family caregivers, providing social assistance and preventing early disorders. CENPAR bases its attention on a health care model, MAIS, supported by a Biopsychosocial approach. In Chile the Ministry of Health (MINSAL) developed an instrument that allows evaluating the MAIS, CENPAR to evaluate and certify health care.
Material and method: This study is of a non-experimental design through documentation belonging to the various areas of CENPAR.
Result: CENPAR complies 100% with the promotion of people's health. It also considers a territorial (locations) work plan, such as care education, and intersectoral projects with public (municipalities) and private entities (universities, institutions, foundations);100% compliance in health prevention;100% compliance in health care based on the needs acquired in the participation of the Parkinson's community;100% in compliance with the use of technologies as a means of health promotion, prevention, diagnosis, treatment, rehabilitation;100% compliance in ensuring the development of people;88% compliance in focused care in the open care model, promoting the relationship and transition of people with Parkinson's disease from clinical care to the health care model, reducing the risk of hospitalization;83% compliance in family-focused health care for people with Parkinson's disease;80% in the fulfillment of intersectoral and territorial work with the Government of the Metropolitan Region;75% compliance in quality ensuring access for health care for all people;CENPAR presents 92% compliance with the MAIS in people with Parkinson's disease.
Discussion: CENPAR is an active member in people's health care organized according to the needs of each person served, becoming a benchmark in health care in Latin America.



P44.07

A patient survey: What does the Fahr's community need?
Adam Tate[*,1], Amit Batla*[2]
[1] Fahr Beyond, Melton Mowbray, Leics, United Kingdom
[2] University College London, London, United Kingdom

Fahr's Disease is a Parkinsonism, there are no accurate diagnosis figures but ~200 in the UK, it is estimated that as many as 8,000 people in the UK may have Fahr's. One of the symptoms of Fahr's is the presentation of Parkinson's. Fahr's Disease is characterised by bilateral dense calcification of the brain often involving the Basal Ganglia, Cerebellum, and Cortex; patients often present with Parkinson's features and can involve other neurodegenerative associated symptoms such as psychiatric conditions (Manyam, 2014). Whilst there is a small but growing evidence of the genes associated with disease (Batla, 2017; Gao et al. 2022), there has been a lack of any research into population data about the clinical manifestations, and the clinical need of patients.
Here, we present the findings from a patient survey using JISC Online Surveys was conducted by Fahr Beyond (a patient support charity based in the UK). Respondents were based in the UK, had to identify as a person with Fahr's or the carer of someone with Fahr's, and participated on a voluntary basis.
The findings of the survey have and helped to highlight how 18 patients have been diagnosed and by which type of medical practitioner (this has ranged from a rheumatologist but to most appropriately a neurologist) the perception by patients is that diagnosis should only be made by a neurologist. The results also highlight how patients are currently having their condition managed and by whom, this is contrasted with perceptions of how patients feel the condition should be managed and frequency of ongoing specialist contact. These findings mirror the challenges and priorities in the UK Rare Disease Framework.
The findings of the results have gone on to help clinicians at the National Hospital for Neurology and Neurosurgery establish the UK's first specialist service and the way in which that should operate. Furthermore, the results will help build a case for integrating a more holistic approach to patient care. It allows us to advocate and set out a blue print for minimum diagnostic and care standards with the UK's National Institute for Health and Care Excellence.

LIVING WITH PARKINSON'S: Living well with PD

P45.01

Living well with Parkinson's disease
*Chinyere Rachel Agwu**
Parkinson's Africa, Abuja, Federal Capital Territory, Nigeria

As an African impacted by Parkinson's disease, I understand and have experienced the heavy burden of stigma that is often associated with an illness like PD across different parts of Africa; and the inequities in access to proper healthcare and treatment options across the region.
In my talk, I will share how I live well with Parkinson's amidst the challenges mentioned above focusing on:
a. My journey with Parkinson's;
b. Methods I have adapted and adopted to thrive with the disease;
c. My wins over Parkinson's; and
d. My aspirations.

P45.02

PARK&SUN: An intergenerational discussion
Jean Andresen[*,1], Hannah Nizet*[2], Lily Nizet*[2]
[1] Bellingham, WA, United States
[2] Santa Barbara, CA, United States

How does a person with Parkinson or a caregiver discuss their diagnosis with young grandchildren? Young children ask many, often direct, questions. Many like to draw and color as well. We used their curiosity to create a booklet - the grandchildren, ages 6 and 9 years, asked questions and then made drawings of the answers. The result was a 16 page booklet - PARK&SUN - which as one PD grandparent commented "tells you everything you need to know" about the disease. This concept may serve as a model, not just for PD, but also for any topic that a grandparent needs to talk about with grandchildren.

P45.03

What patients themselves can do to make DBS a success
*Yojiro Ashina**
PJPP Japan, Ageo-city, Saitama, Japan

Deep Brain Electrical Stimulation (DBS) is an effective treatment for Parkinson's disease and I had DBS implantation surgery in 2019.

This paper will address the issue of the gap between what physicians believe is a “good response to the surgery” and what patients feel is “not as good as expected”.
“Patient-centered” is being called for, but “team medicine” efforts are still a ways off in all hospitals.
I approached this issue from the perspective of “what patients themselves can do to make DBS a success.”
In this paper, I would like to propose some of the main factors that create a gap between physicians and patients, and some possible solutions.
The main mismatched factors are

- No shared goals.
- Patients forget about the improved symptoms and complain about the remaining symptoms.
- Lack of knowledge about postoperative care for DBS.

And the measures that patients themselves can take are

- Define success from the patient’s point of view and visualize the results.
- Use videos, illustrations, and quantification to visualize the results.
- Understanding what is needed for DBS post-operative care.

In addition, several “current issues being addressed” or “future issues” will be presented.

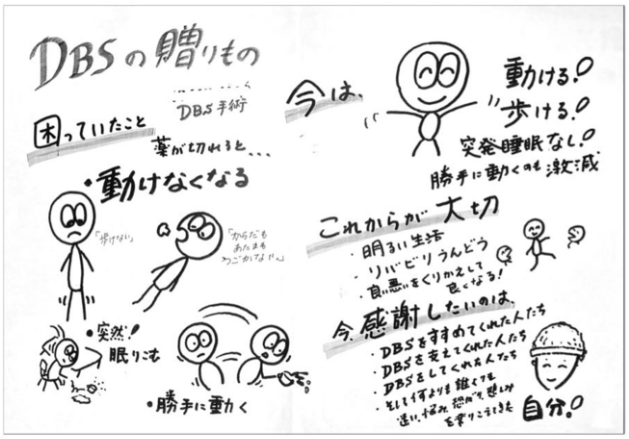


Fig1 An example of visualization, “ GIFTs from DBS ”

P45.05

BC brain wellness program ... Brain wellness beyond all boundaries: From idea to implementation

Elaine Book[*1], Amanda Cammalleri[2], Emily Gerson[2], Katy Chen[2], Alex Barber-Cross[2]*
[1] University of British Columbia, Vancouver, British Columbia, Canada
[2] BC Brain Wellness Program, Vancouver, British Columbia, Canada

As our population ages, there is an increased need for prevention and accessible care. Symptoms of many disorders of ageing can be prevented or mitigated with modification of lifestyle factors. Lifestyle-based research and programs have been emerging as effective adjunct therapies for a variety of neurological conditions. Research indicates positive effects of exercise and movement-based interventions on dementia, PD, MS, stroke, and healthy agers. Recently, creative expression activities such as: mindfulness, art therapy, music, improvisation and gardening have been examined showing positive impacts on brain health and mental well-being. While many lifestyle-based programs involve singular interventions, some more recent therapies have shown the promising results of combining treatments, and have shown the positive impact of multimodal lifestyle interventions on specific populations. We believed that a program which could cater to several neurological conditions and healthy agers alike could mitigate the effect of participants comparing their current state of condition to those who have progressed further along, and could enhance feelings of community, through engagement with others of varying conditions and health qualities. Overall, a lifestyle intervention with a multimodal nature, diverse participant pool, and online accessibility would be ideal for older adults.
The British Columbia Brain Wellness Program (BCBWP), demonstrates the feasibility and effectiveness of an online-program-diverse, multimodal lifestyle intervention. Our program is tailored to individuals with a wide variety of neurological conditions, their care partners, and healthy agers. Through an interconnected three-pillar structure of program delivery, research, and education, we provide programs and classes based on current scientific literature, conduct various research projects on these programs and cycle the research back to improving program delivery as well as dispersing the knowledge in a comprehensible manner to the public and to our participants.
Since opening in October 2019, the BC Brain Wellness Program has had remarkable growth and success. The development history, mission, structure and content of the program as well as highlights from feedback surveys and participant focus groups will be shared, demonstrating the positive impact of our program on participants and encouraging the opportunity for this model of intervention to be replicated in other communities.

P45.06

Everybody has a story: The impact of intergenerational storytelling on wellness

Elaine Book[*1], Rifad Bhuyia[2], Serena Woo[2], Tiffany Chang[2], Julia Handra[2], Jiayi Li[2], Jennifer Lim[2]*
[1] University of British Columbia, Vancouver, British Columbia, Canada
[2] BC Brain Wellness Program, Vancouver, British Columbia, Canada

Rational: The power of connecting with people from different generations is often under-recognized in the world we live in today. Current research supports many positive benefits of intergenerational connections on brain wellness, creativity, and mental and physical health. Storytelling inspires connection and understanding, and can serve to bridge perceived generational gaps while developing a sense of community.
The British Columbia Brain Wellness Program (BWP) leverages the collective power of clinical care, lifestyle programs, education, and research to design a comprehensive and integrated approach to brain wellness for people with chronic brain conditions, care partners and healthy agers. With this mission in mind and recognition of the potential impact on wellness, The Intergenerational Storytelling Project (ISP) was developed, delivered and evaluated, and was subsequently extended to create Intergenerational Conversations.
Method: The development of the ISP was informed by an evidenced-based community building program, students, and seniors. The BWP senior participants were paired university students for an intergenerational story telling experience which resulted in an abridged storybook of the seniors’ life. The 3-month project consisted of orientation sessions, a matching session, multiple student-senior storytelling sessions, and a joint community celebration session. The entire project was delivered online and two standardized measures as well as a qualitative feedback survey were used to determine impact.
Results: Sixteen pairs of students and seniors participated in the project. The student participants were from the Faculties of Arts and

Science with specializations in behavioral neuroscience, science, integrated sciences, cognitive systems and psychology. The seniors, living both urban and rurally, were healthy agers as well as people living with MS, PD, Stroke and TBI. The small cohort encouraged a sense of community and connection among the participants. Evaluations revealed many unanticipated benefits for both the students and the seniors including self-appraised improved mental health, increased self- awareness and new perspectives on life.
Conclusion: The Intergenerational Storytelling Project proved to be an accessible intergenerational experience for university students and seniors with the BC Brain Wellness Program. Benefits were many for all the participants such that the participants requested future ongoing connections, leading to the development of an extension project called Intergenerational Conversations.

P45.07

Live well with Parkinson's through connective dance/movement practices that promote changing flow states: A study by Dr Melanie Brierley, independent dance and health artist and researcher, United Kingdom
*Melanie Brierley**
Conscious Bodies, Carnforth, Cumbria, United Kingdom

This poster presentation (potential hot topic) is based on findings from my PhD (University of Roehampton, 2020) and from my 14 years of experience as a dance/movement artist working with people with Parkinson's in the United Kingdom. Through my PhD research, I explored one to one, co-creative, somatically informed, and home-based dance/movement practice as support to health and the management of everyday life for people with Parkinson's. As a dance/movement and health artist, I recognised that people with Parkinson's experienced changing flow states that altered their movement and thinking. A diminished sense of flow often intensifies the experience of immobility and an experience of bodily-felt disconnection that impacts relationships with other people and a connection to the immediate environment. Through living theory action research, I gathered my shared dancing experiences with 11 people with Parkinson's in their homes to explore how dance/movement positively shifts flow experiences. My research found that connective dance/movement practices enhance the experience of flow in people with Parkinson's. Bodily-felt connections are found in the sensory and aesthetic experience of shared dance/movement, with partners responding positively to the felt sense of dancing together. Connections between dancing partners are made through visual, verbal, and embodied processes, with connective and creative movement practices enhancing body awareness, posture, movement action, feelings of support, movement confidence and improved mood. My research also highlighted the important role of dance/movement in connecting people to everyday objects, spaces, and places as a means of promoting confidence and assurance in the activities of daily living with Parkinson's. Through my research, I created new frameworks of dance/movement practice with people with Parkinson's: One to one practice as Home Performance and Connect and Flow group sessions for the Parkinson's community.

P45.08

4 simple tips for full-time workers with Parkinson's
*Luis Castellanos**
Civil Society, Guatemala, Guatemala

Facing professional life as a data analyst with Parkinson's can be a tricky situation, for the reason that the effects of the disorder might make it difficult to complete tasks that require accurate use of muscles and concentration. Nevertheless, with suitable management and adjustments, numerous people with Parkinson's can continue to work in this area.
Some approaches that may be useful include:
1. Consulting a neurologist to find the most useful medication plan: This can be helpful by regulating the signs of Parkinson's and enabling you to concentrate on your work.
2. Utilizing assistive technology: There are lots of supportive technologies that can help with typing, data entry, and other tasks that require precise use of muscles. Take advantage of speech-to-text software to voice out text in place of typing. Additionally, AI is being utilized in various ways to help people with Parkinson's, providing personalized exercise programs for physical therapy with AI-based tools.
3. Making changes to your work environment: This can comprise of things like altering your working hours or taking regular pauses throughout the day to stretch digits and hands. Utilizing a keyboard with bigger keys or a keyguard can help enhance your typing abilities.
4. Conversing with your supervisor and colleagues about the difficulties of living with Parkinson's and examine any adjustments that may be essential.
It is essential to take care of yourself and your health and to incorporate physical therapy and other activities that contribute to your overall wellbeing and help manage the signs of Parkinson's.

P45.09

Restore your power and control your present with a health education channel you can truly rely on
*Begoña Cirera Perez**
Chabot College, Hayward, CA, United States

It is well accepted by the scientific community that a principal part of our quality of life, longevity and prevention of Parkinson's strongly

depends on our nutritional status. It is also clear that a vast amount of people have a lack of basic nutrition understanding, unsure of what nourishing diets entail, and which health and nutrition information to trust. Additionally, an abundant part of the population believe that they are following correct advice as it pertains to nutrition and health. This is no different for People living with Parkinson's (PwP). PwP and their caregivers are in dire need to understanding the important role nutrition and exercise play as a fundamental part of treating and managing this disease. Proper nutrient intake, omitting foods that can damage overall health status, and basic knowledge of exercise requirements are critical to delaying the progression of Parkinson's symptoms, while improving quality of life.

Today's social media outlets provide an abundance of health and nutrition information that is overwhelmingly incorrect, and potentially harmful to the uninformed consumer. This information is frequently filled with inaccurate recommendations and guidance that could delay improvement of overall well-being, interfere with treatment plans, and accelerate the progression of Parkinson's.

This presentation will highlight a YouTube channel with reliable information you can trust to help manage Parkinson's in impactful ways. With my over 15 years of expertise in the fields of nutrition and health education, and my multilingual upbringing, my YouTube channel offers viewers concise videos in English with accurate subtitles in Spanish, and Catalan. It also provides Closed-Captioning in Chinese, Filipino, Portuguese, Punjabi, and Arabic utilizing built-in translators in YouTube's video editor. The content is science-based, responsible and inclusive, containing nutrition tips, myth debunking, easy recipes, exercise guidance, and basic education in nutrition and health. Anyone with an Internet connection can access the channel and be confident that the information is reliable, with the ability to benefit their general health status. By providing this platform, PwP can reestablish a sense of power to control their present health status to the best of their abilities and reach their full potential even, and especially, after diagnosis.

P45.10

Parkinson Society BC bridges the gap between clinical care and social care: Social prescription initiatives

*Alana Dhillon**
Parkinson Society BC, Vancouver, British Columbia, Canada

People living with Parkinson's Disease (PwP) experience isolation and loneliness resulting in reduced quality of life. Symptoms directly impacting social interaction such as facial masking, difficulty recognizing social cues, and voice dysfunction can coexist with physical and psychological symptoms such as tremor, stiffness, dyskinesia from medication intake, and low mood. All these symptoms can cause social withdrawal because of anxiety around fear of being stigmatized and judged. Despite these social consequences, the gold standard of Parkinson's Disease (PD) care is pharmacological treatment. This bio-medical approach primarily treats physical symptoms without consideration given to social care. By instead utilizing a biopsychosocial approach, to also address the social consequences of PD, Parkinson Society BC (PSBC) aims to bridge the gap between clinical care and social care through social prescription initiative programs designed to improve PwP's quality of life.

Method: Adding to existing PSBC clinical counselling services and 55 support groups, PSBC implemented in person and virtual psychosocial activities around creating community and social interactions. These include drumming, singing, writing classes, exercise groups, book and gardening clubs, mindfulness and improv sessions. These are socially prescribed by PSBC staff, community healthcare professionals, or self-referral.

Results: PSBC's 2021 Community Needs Survey (CNS) indicates that 54.2 % identified mental health and 30.8 % social isolation as primary concerns. In the 2022 CNS this percentage decreased respectively to 35.9 % and 13.5%. This along with testimonials and participant feedback from questionnaire responses over a 3-year period suggests improved quality of life as a primary outcome. Common themes include improved mood, confidence and motivation levels in social engagement, and decreased concern over one's social isolation and mental health. Results indicating improved physical symptoms are inconclusive.

Testimonials:
"Uplifting"
"Sense of belonging"
"Enjoyed new friends"
"Camaraderie"
"Lost feeling of isolation"
"Draws me out..."
"Spurred me to invite friends over"

Discussion: This shows the value of applying holistic PD treatment with inclusion of social prescription initiatives. PSBC continues advancing social care via social prescription to new and existing innovative psychosocial activities. Findings indicate improved quality of life in psychosocial functioning. The positive impact participation has on physical symptoms requires further research.

P45.11

Young Parkies Portugal: Empowered to improve care in young-onset Parkinson's disease

Josefa Domingos[*,1], Maria do Carmo Teixeira Bastos[2], Rui Couto[2], Ana Rita Carneira[2], Ana Leal Cardoso[2], Alexandre Reffóios[2], Susana Magalhães[2], João Massano[3], Tiago Fleming Outeiro[4]*
[1] Radbound University, Lisbon, Portugal
[2] Young Parkies Portugal, Porto, Portugal
[3] Department of Neurology, Centro Hospitalar Universitário São João, Porto, Portugal | Department of Clinical Neurosciences and Mental Health, Faculty of Medicine University of Porto, Porto, Portugal
[4] Department of Experimental Neurodegeneration, Center for Biostructural Imaging of Neurodegeneration, University Medical Center Göttingen, Göttingen, Germany. | Max Planck Institute for Multidisciplinary Sciences, 37075 Göttingen, Germany

Patient organizations play an ever-growing role in modern societies. They provide organized resources for patients and care partners. Yet, there is limited support and resources specifically for people with young-onset Parkinson's Disease (YOPD). These individuals face unique social, professional, and personal challenges. Therefore, accessing a patient organization tailored specifically for YOPD can ensure that the needs of this specific group are better accounted for.

In 2022, Young Parkies Portugal (YPP) was founded to allow people with PD and various stakeholders to join forces to improve care and support those in need. Here, we aim to share our experience of building an association for and with people with YOPD.

We first sought a core multidisciplinary team that could cover important areas of activity of the association. The founding team included people living with PD, a neurologist, a basic science researcher, a physiotherapist, a sociologist, and communication and financial specialists.

We then identified that little was known and available specifically for people with early-onset PD in Portugal, similar to other countries. As such, we created a digital platform (https://www.youngparkiesportugal.org/home/) to provide validated information, gather insight from our members, and deliver care in the Portuguese PD community.

We initiated several online activities through digital platforms – webinars (Parkie Talks), specialized PD exercise classes, yoga, and a psychological support group, where family members are welcome to join, as we believe this is a key element in the field. We created and implemented a yearly 2-day YPP Bootcamp that helps us unite and engage people in person.
We also supported the dissemination of several research studies in Portugal and initiated collaborations with research groups.
Looking ahead, we aim to continue to identify the specific needs of the members through well-defined needs assessments that will help us identify projects to help address each need best. We strongly believe that nonprofit organizations, like YPP, play an essential role in the care and support of people with PD and should be considered partners of care alongside the multidisciplinary team.
We are confident that sharing our experience can inspire and guide the further implementation of similar initiatives in other countries.

P45.12

Walking in a group using urban walking poles to improve physical and mental health

*Sandra Elms**
Newcastle Parkinson's Support Group, Newcastle, NSW, Australia

Introduction: Exercise is vital to living well with Parkinsons. Evidence has shown exercise improves many PD symptoms. Walking is excellent exercise but Parkinson's people may experience problems with balance, gait and falls.
Aim: To observe the benefits of walking in a group using Walking Poles
Such as:-
increased balance and stability
increased posture
reduction of stress, depression
weight management
Objective: To follow the progress of a group of people with PD, walking with Urban Walking Poles. Demonstration of using Poles given by representative of Urban Walking Poles. These Poles mimic the motion of cross country skiing. It uses the arms as well as legs and enables the user to walk faster, more upright and more steadily. The small shuffling steps, typical of many PD sufferers are changed into bigger motions.
Method: A group of people from Newcastle Support Group agree to walk on a regular basis, together, in a park/nature reserve. They all use Urban Walking Poles and walk 2/3 times a week for 30-60 minutes. A questionnaire is given at the start of the program on how they feel physically and mentally and again after walking 2/3 times week for 10 weeks.
The objective is to improve the lives of people with PD by enabling them to improve their health physically and importantly socially. Interacting with others in the fresh air, whilst walking would do just that.
If benefits are seen and felt a more rigorous program could be set up using a qualified physiotherapist to improve validity.

P45.13

Education and exercise support for individuals newly diagnosed with Parkinson disease and their care partners

Alicia Flach[*,1], Reed Handlery[2], Myriam Sollman[3], Travis Gawler[4], Emily Delany[1], Madeline East[1], Rebecca Schmidt[1], Elizabeth Regan[1]*
[1] University of South Carolina, Columbia, SC, United States
[2] Arkansas Colleges of Health Education, Fort Smith, Arkansas, United States
[3] Prisma Health and University of South Carolina School of Medicine, Columbia, SC, United States
[4] Bon Secours Mercy Health, Greenville, SC, United States

Exercise is vital in Parkinson disease (PD) management, but people with Parkinson disease (pwPD) perform 30% less physical activity (PA) than adults without PD. Care partners (CP) are largely inactive but excluded from interventions improving physical health. The purpose of this study was to assess feasibility and preliminary effects of a self-paced education series and 6-months of exercise for pwPD and their CP.
48 newly diagnosed pwPD and CP (pwPD n=27, age: 68 (9); CP n=21, age: 69 (7)) were included. Pre-and post-exercise data was collected for pwPD (n=9) and CP (n=7). PwPD and CP completed pre-recorded education modules on PD, resources, exercise, emotional, cognitive and CP health. They were then provided with a free 6-month of YMCA membership. Feasibility was determined through reach (number enrolled), exercise adherence (number attending ≥2 exercise sessions/week), knowledge acquisition (change in test scores pre to post-program), retention (number continuing YMCA membership post-program), and satisfaction (0-100%). The Starkstein Apathy Scale, International Physical Activity Questionnaire, Self-Efficacy for Exercise Scale, and Social Support for Exercise Survey were used pre- and post-exercise. Additionally, Parkinson Disease Questionnaire-39 and Unified Parkinson Disease Rating Scale Parts 1 and 2 assessed pwPD, and Caregiver Strain Index assessed CP. Means, standard deviations, and effect size (d) were calculated. Reach: Of 74 enrolled (pwPD n=43, CP n=33), 48 (pwPD n=27, CP n=21) completed modules, 36 (pwPD n= 20, CP n=16) completed 6-months' exercise, 16 (pwPD n=9, CP n=7) completed follow-up questionnaires. Exercise adherence: 85% attended ≥2 sessions/week. Knowledge acquisition: Pre- to post-test scores improved 41.7% for pwPD and 35.3% for CP. Retention: 73.3% of pwPD and 58.3% of CP renewed YMCA memberships. Satisfaction: 77% and 73% for pwPD and CP, respectively. PwPD and CP reported a large increase in moderate-to-vigorous PA/week (pwPD: 608 minutes, d=0.89; CP: 222 minutes, d=0.49). PwPD reported a large increase in family support for exercise (d=0.87). Education modules resulted in improved knowledge in pwPD and CP. Participants demonstrated high adherence with community-based exercise and reported increased PA. Increasing education and exercise for newly diagnosed pwPD and CP is feasible and may enhance PA for both parties while increasing social support for pwPD.

P45.14

Evaluating a cross-national multisectoral OPTIM-PARK intervention for people with Parkinson's disease and their family carers in the community: A feasibility study

Ellen Gabrielsen Hjelle[*,1], Tove Lise Nielsen[2], Jacob Callesen[2], Naja Benigna Kruse[2], Louise Buus Vester[2], Line Kildal Bragstad[1], Silje Bjørnsen Haavaag[1], Eline Aas[1], Anita Haahr[2], Maria Victoria Navarta-Sánchez[3], Azucena Pedraz-Marcos[4], Ana Palmar Santos[3], Leire Gutierrez Ambrosio[5], Dorit Kunkel[5], Mari Carmen Portillo[5]*
[1] University of Oslo, Oslo, Norway
[2] VIA University College, Aarhus, Denmark
[3] Universidad Autónoma de Madrid, Madrid, Spain
[4] Unidad de Investigación en Cuidados y Sistemas de Salud, The Carlos III Health Institute (ISCIII), Madrid, Spain
[5] University of Southampton, Southampton, United Kingdom

Introduction: Parkinson's disease (PD) is a common neurological disease worldwide. The prevalence is expected to increase. Living with PD is associated with a number of challenges for the persons affected by the illness and their families. The medical treatment

aims at reducing symptoms. However, there is no medication that can cure or stop the illness.
The overall aim of the OPTIM-PARK-project was to develop and evaluate an intervention to enhance the process of living with PD for persons with PD and their family carers by strengthening the intersectoral collaboration and the optimization of access to and use of community resources and support systems. The new UK MRC framework for developing and evaluating complex interventions was used in the development of the intervention.
Objective: The objective of this specific sub-study of the OPTIM-PARK project is to evaluate the acceptability and feasibility both of the outcome assessments at baseline and at three-month follow up, consider costs involved and analyze the specific content of the intervention through coordinators log data.
Methods: The multisectoral OPTIM-PARK intervention is currently being tested with persons with PD and their caregivers in Denmark, Norway, Spain and the United Kingdom. Participants have been included from March 2022 until September 2022. The intervention is delivered over a 3 month-period and includes consultation with a trained OPTIM-PARK coordinator in the community setting. The last intervention will be finished by the end of January 2023.
In total, 120 (Intervention group=70) persons with PD and 96 (intervention group=58) family carers have been included. The study is designed as a mixed-methods feasibility study and includes evaluation based on quantitative and qualitative data.
Results: The data from the three months quantitative data collection and the qualitative data from the Coordinator's logs are currently being analyzed. The results will be presented at the WPC.
Discussion: It will be discussed which outcome measurements are the most acceptable, feasible and sensitive for a later full trial or implementation study.
Implications of the study results will be discussed in relation to the intervention's potential applicability to enhance the process of living with PD in a community setting.

P45.15

Coordinated care and individualised communication in Parkinson's disease: Four perspectives on the meaningfulness of a cross-sectoral intervention

Anita Haahr[*,1], Louise Vester[2], Line Kildal Bragstad[3], Tove Lise Nielsen[4], Naja Benigna Kruse[4], Ellen Gabrielsen Hjelle[5], Silje Bjørnsen Haavaag[6], M. Victoria Navarta-Sánchez[7], Dorit Kunkel[8], Leire Ambrosio[9], Azucena Pedraz Marcos[10], Ana Palmar-Santos[11], Mari Carmen Portillo[12]*
[1] Research Centre for Health and Welfare Technology, Programme for rehabilitation, VIA University College, Aarhus and Nursing and Healthcare, Department of Public Health, Aarhus University, Aarhus N, Denmark
[2] Research Centre for Health and Welfare Technology, Programme for rehabilitation, VIA University College, Aarhus N, Denmark
[3] Department of Nursing Science and Research Center for Habilitation and Rehabilitation Services and Models (CHARM), University of Oslo and department of Occupational Therapy, Prosthetics and Orthotics, Oslo Metropolitan University, Oslo, Norway, Oslo, Norway
[4] Research Centre for Health and Welfare Technology, Programme for Rehabilitation, VIA University College, Aarhus and Department of Occupational Therapy in Aarhus, VIA University College, Aarhus, Denmark, Aarhus N, Denmark
[5] Department of Nursing Science and Research Center for Habilitation and Rehabilitation Services and Models (CHARM), University of Oslo and department of Occupational Therapy, Prosthetics and Orthotics, Oslo Metropolitan University, Oslo, Norway, Oslo, Norway
[6] Department of Nursing Science, University of Oslo, Oslo, Norway, Oslo, Norway
[7] Nursing Department, Faculty of Medicine, Universidad Autónoma de Madrid, Madrid, Spain, Madrid, Spain
[8] School of Health Sciences, University of Southampton, Southampton, United Kingdom, Southampton, United Kingdom
[9] University of Southampton, School of Health Sciences, Southampton, United Kingdom, Southampton, United Kingdom
[10] Unidad de Investigación en Cuidados y Sistemas de Salud, Nursing and Health Care Research Unit, The Carlos III Health Institute (ISCIII), Madrid, Spain, Madrid, Spain
[11] Nursing Department, Faculty of Medicine, Universidad Autónoma de Madrid, Spain, Madrid, Spain
[12] Health Sciences, University of Southampton, Southampton, United Kingdom, Southampton, United Kingdom

Background: Disease management in Parkinson's disease is known to be complex. Not only for people with Parkinson's disease and their family carers, but also from health care professionals and stakeholders' perspectives.
One challenge is to continuously be knowledgeable of the cross-sectoral and community-based resources available to support better living with Parkinson's disease. Another is to ensure timely support. As availability of resources may also vary from community to community, it challenges professionals as well as patients' and carers in terms of knowing available support systems.
The OPTIM-PARK intervention is currently being evaluated in Denmark, Norway, Spain and UK. The project focuses on optimisation of community resources and systems of support to enhance the process of living with Parkinson's Disease.
This is a mixed method feasibility study involving qualitative interviews, to explore the meaningfulness of establishing an intervention delivered through a community-based coordinator. The presentation will focus on describing how the intervention enhances accessibility, individualised support and use of appropriate resources as it is experienced from the following four perspectives; people with Parkinson's disease, family carers, coordinators, and other health professionals/stakeholders. The aim is to highlight insights that will support the development of integrated care in Parkinson's disease management.
Materials and methods: The qualitative evaluation is based on 80 interviews, dispersed through 20 interviews from each country, covering all four perspectives.
Cross-national thematic analysis of the interviews will take place.
Results: Main results providing insights of how to support everyday life with PD will be presented at the conference
Conclusion: This qualitative evaluation is expected to provide important knowledge of the experience of the intervention, that will inform further development and implementation of the intervention, including organizational aspects to consider.

P45.16

Do you dance? Profile of people participating in dance for Parkinson's in Denmark - before Covid-19

Anita Haahr[*,1], Kristian Winge[2]*
[1] Research Centre for Health and Welfare Technology, Programme for rehabilitation, VIA University College, Aarhus; and Nursing and Healthcare, Department of Public Health, Aarhus University, Aarhus N, Denmark
[2] Department of Neurology, Slagelse hospital, Slagelse, Denmark

Through the last 5 to 10 years dance therapy has become popular as a rehabilitation offer to people with Parkinson's disease, and many studies support that PD dance has a supporting and positive impact on everyday living with Parkinson's disease. This improvement is seen in regard to an improved motor control and also in regard to the psychosocial challenges as part of living with PD.

In 2017, PD dance classes was first offered in Denmark in different areas of the country and since then the number of dance courses has increased, signaling a growing interest among, not only people with Parkinson, but also their partners.
The aim of this study, was to explore and describe the profile of people attending PD dance classes, in terms of understanding who attends PD dance classes and to clarify their motivation to do so.
The study is part of a mixed methods study, also investigation the meaning of attending dance classes with a partner and its impact on everyday life with Parkinson's disease.
Data collection: Participants who attended PD dance classes were invited to fill out an online questionnaire with questions regarding: Age, marital status, duration of illness, medical status, physical activity and music interests using the Barcelona Questionnaire on Music and Enjoyment (BMRQ), and quality of life (PDQ39 score)
In total we collected data from 38 People with parkinson's disease and 26 partners.
Results: Of the 38 people with Parkinson's disease, 20 were men and 18 were women. The people with Parkinson's disease had a mean age of 70.4 years. Their mean age at diagnosis was 63.6 years and mean time since diagnosis was 6.8 years.
Preliminary results show that the participants reported a high level of physical activity, including resistance training, bicycling and walking. Also, data from partners revealed a high level of physical activity.
In regard to music, the analysis shows that people attending dance classes generally also has a higher score on the BMRQ. We are in the process of analysing data and will unfold this further in the presentation.

P45.17

Happiness with Haiku; ZOOM Haiku meeting for PwP
*Nobuko Haneji**
Tokushima, Tokushima-city, Japan

Introduction, Background, and Aims: In 2016, I joined to the himawari haiku association in Tokushima, Japan. In the yearend, I fell down for 18 hours without medication. Fortunately I was rescued and hospitalized. After then I wanted to walk again by myself. In the following haiku, I made me liken to a frozen butterfly.
A frozen butterfly is taking a rest
Believing the time will come to fly
Sooner or later
This haiku won the WPC Kyoto Haiku competition. In 2022, I became one of new coteries of himawari haiku association. At the same time, I joined to the PD Avengers. I was urged to advocate PwP.
Method and summary of work:
1.In March 2022, I set up the New Haiku group "Beginner's Haiku meeting for people with Parkinson's diseases".
2.I transferred to our members the information of the 1st haiku writing workshop in FB group messengers and in LINE group.
3.We used ZOOM Pro to meet. We called each other with nickname.
4.I made haiku writing workshop in March 2022. I explained how to write haiku with seasonal examples. The Haiku meeting was held 7 times in 2022.
5.I used e-mail, LINE, and Messengers for Q & A to support each participant writing haiku.
6.The Haiku meeting procedure follows the example commonly used in ZOOM haiku meeting in Japan. Such as unanimous haiku list is made to vote. Everybody votes for favorite haiku and exchange impressions
7.Haiku meeting, called as Kukai, is interactive and make social activity in the member.
Haiku is recreated by each reader.
8.In the beginning the member was 7 peoples. In the summer of 2022, the member was 10.
Conclusion: We realized that we were not alone. We enjoyed lyricism of haiku. We felt sympathy and understood PD subject in haiku. We look at daily life with more interest and with joy through haiku writing. Participant's feedback made me happy.

P45.18

Caring for the carepartner: Gatekeepers and guardians
Celeste Harris, Kathleen Crist*
Houston Area Parkinson Society, Houston, TX, United States

When an individual receives a Parkinson's diagnosis, their life is not the only one changed: their friends and family are immediately and permanently impacted as well. A carepartner is an individual who is has not been given a Parkinson's disease diagnosis but is still living with and influenced by Parkinson's disease in nearly every aspect of life. Informal, or "family" caregiving is on the rise, with over 50 million adults in the United States caregiving for family members, and Parkinson's carepartners face more expenses and greater financial losses than other familial carepartners dealing with chronic diagnoses.
At Houston Area Parkinson Society (HAPS), we understand that the carepartner is the touchstone for informed decisions regarding client care. A major focus of HAPS' work is with the carepartner: support groups; educational programs; training classes. From diagnosis to death, HAPS social workers have created programs designed for the various paths carepartners might find themselves traversing. 6 dedicated carepartner support groups cover not only the basics of PD caregiving but the intricacies of being an early stage care-partner and the complexities of dealing with the dual dementia/PD diagnosis. A "Friends in Healing" support group, designed specifically for those who are dealing with the loss of their loved one after a Parkinson's diagnosis, provides support even as the path the carepartner is on shifts again.
Through work with the community, including licensed physical therapists providing home wellness visits and carepartner training classes, mind-body wellness classes run by licensed therapists, and access to 2 full-time Parkinson's disease social workers, and a capstone project focusing on occupational therapy interventions for carepartners conducted by a doctoral candidate, HAPS hopes to engage the carepartner through community and empower them with support.

P45.20

PD&ME: Leveraging technology to increase access to wellness and support groups
Rebecca Korduner, Anissa Mitchell*
Parkinson & Movement Disorder Alliance, Tucson, Arizona, United States

Introduction: Community-based support groups and wellness programs offer much-needed resources for the day-to-day management of Parkinson's disease (PD), including education, connection to services, and emotional support that are not part of a typical treatment plan. Accessing this vital information may be challenging especially for those who live in under-resourced communities. While many programs may exist, individuals are often challenged in how to find activities close to them, especially if they are provided by various organizations. Additionally, the Covid-19 pandemic had a negative impact on many services, which in turn, impacted the resilience patients and care partners build through them.

Objective: Parkinson and Movement Disorder Alliance (PMD Alliance), a US-based advocacy organization focusing on connecting people and supporting opportunities for those impacted by PD to learn, and live more fully addresses this challenge through the use of technology with the creation of the PD&ME app.
Method: PD&ME is a smartphone app created to give the user access to support groups, exercise classes, dance, and other therapeutic groups as well as a direct connection to livestream educational programs and the ability to search for movement disorder specialists. The smartphone app uses geolocation services allowing the user to search for programming by location or type, including both in-person and online. The app also provides a ground-up approach connecting individuals within communities and a method to inform of new groups.
Results: The PD&ME app was launched in November 2020. There have been 1,500 downloads with 50% of those total downloads occurring in 2022. The app has a listing of 5,386 total community wellness and support groups listed. 16,000 user sessions occurred in 2022, of those 19% were searches for support groups, 17% utilized the populated feed for activity type, and 14% saved events to their calendar. Users are from all 50 states and 8 countries for the virtual offerings.
Conclusion: Use of technology like the PD&ME app is a convenient tool helping access resources for patients and care partners providing local and international opportunities for education, exercise, and connection. Resources such as this mobile app can help reduce social isolation with potential to improve engagement in vital wellness activities.

P45.21

Sunday mornings with Twitchy Woman: Learn together, play together and thrive together. A response to the pandemic shutdown
*Sharon Krischer**
Twitchy Woman, Beverly Hills, CA, United States

Objective: To create a group using Zoom, for women with Parkinson's Disease to combat the loneliness and isolation of the Pandemic.
Background: Numerous studies have shown that isolation and loneliness are major public health concerns among older adults. This is especially true in the Parkinson's community, according to Indu Subramanian 1 2, Joshua Farahnik 3, Laurie K Mischley in their paper "Synergy of pandemics-social isolation is associated with worsened Parkinson severity and quality of life"*
Program: When the shutdown for the Pandemic was announced in March, 2020, Twitchy Woman (blogger Sharon Krischer) initiated a series Zoom meetings for women with Parkinson's that was to be temporary. We are still meeting over three years later because our meetings have filled a need for women with PD in a non-threatening environment, where they find the camaraderie and support that they need.
Starting with just 9 women on March 22, 2020, Sunday Mornings has continued to meet about twice a month. Over 1000 women have joined us from around the world and we have had over 50 speakers on a variety of topics, with sessions on exercise, women & PD, DBS, drumming, research and more. All programs are chosen with the objective of providing more tools and information specifically for women with PD.
As other needs were identified, volunteers helped create a peer to peer mentorship program for newly diagnosed women, two Zoom chat groups, and scholarships for 15 women to attend the World Parkinson Congress.
Results: A survey sent to all participants shows 97% of those who responded feel that the programs meet their needs as women with PD. Our Peer to Peer Mentoring program has matched over 150 women with mentors. Overall, the program has been very successful in attracting and retaining women with PD who are looking for a place where they can "Learn together, play together and thrive together."
*https://pubmed.ncbi.nlm.nih.gov/33083522/

P45.22

Decades-long fight against PD: A scientist's experience and perspectives
*Prabhakaran Kuniyil**
Hayward, CA, United States

It was almost three decades ago that I was diagnosed with Parkinsons Disease (PD, around the year 1994), and I would like to talk about the various milestones and events in this long and difficult journey. As PD does to everyone, it virtually "hijacked" my life too! I had been an experimental research scientist in the field of Surface Science and was just beginning my career and family life, after completing my PhD.
I have been dealing with this untimely debilitating disease all these years and the fight continues! I realize that several of the Young Onset PD's (YOPD) prefer to leave their jobs upon their diagnosis. The scientific temperament and curiosity played big roles in empowering me with the driving force that was critical to pursue the job. The evolution of ideas derived while playing the dual roles of Science Practitioner and PD Patient was significant. I believe that I have been successful in my fight against PD as I continue to have control of the symptoms and not let PD control me!
I address PD using a comprehensive approach involving Western and Eastern medicines, holistic methods, lifestyle and diet changes. In addition to all these, an intensive exercise protocol customized to the needs of my body was implemented. I will discuss some key features of all these points and highlight the importance of evolving an individualistic strategy different from a generalized methodology, which made it possible to help me achieve my professional goals even after I was diagnosed.
My experience suggests the need to develop a philosophy of medication and the therapeutic strategy based on the specific and customized needs of the individual. I underwent deep brain stimulation (DBS) surgery in 2017. I would like to reach out to the community to state that my relentless efforts helped me build endurance and strength which were essential to make successful resilience.
I want to encourage the newly diagnosed YOPD's to face it with utmost emotional stability and positivity and you can still get productive period and do wonderful things. Diagnosis does not mean the end but simply the beginning of a new chapter.

P45.23

The importance of single peer support relationships for women with Parkinson's
*Susan Lehman, Sharon Krischer**
Twitchy Woman, Beverly Hills, CA, United States

Objective: Women helping other women through their unique transitions with Parkinson's disease.
Background: Since women make up 40% of PwP, research and support focuses gender neutral or on men. Yet, women have unique areas including motherhood, and family caregiving, menstruation cycles and menopause. From these concerns the TwitchyWoman.com (TW) Peer Support Program was created. All participants are volunteers.
Methods: A committee developed a list of concerns for women. A protocol, qualifications and a handbook was created for mentors in

communicating with mentees. Recruitment for mentors are from the TW website and through the TW Sunday morning speaker series. A team interviews potential mentors evaluating their readiness to participate. Mentees apply through the website and are also recommended from healthcare workers. Criteria for matches consist of time zones, age at diagnosis, similar interests and/or background, etc. Never giving medical advice, mentors advise how to create a support team, how to communicate with family and friends and encourage positive behavior for living well with the disease. Mentees and mentors can request a new assignment if either feels the match isn't productive. A supervising team continues to monitor both mentors and mentees.

Results/Outcomes: The program was initially established for newly diagnosed women, it was immediately expanded to include women at other stages of transition with the disease. Though mostly in North American, the program has participants internationally. From November of 2020, to November of 2022 we have matched over 150 women with peers. Mentees report more confidence and empowerment in facing the disease. Mentors report many positive effects mentoring has on their own lives. A weekly zoom support group was formed from the initial program and another group for women living alone. The handbook and other work materials created in TW have been generously shared with other institutions starting their own programs, including the University of Pennsylvania, Jefferson University and several others. The TW program continues to change and grow with our experiences, and as the needs of women are expanded.

Conclusion: Female PwP greatly benefit from other women who have first-hand experience and continue to strive to live well with the disease.

P45.24

Healthcare professionals with Parkinson's: Insights from a support group in the UK National Health Service (NHS)

Claire Lehman[*1], Jonny Acheson[2], Clare Addison[3], Tiny Binu[4], Ed Kirkham[5], Cormac Mehigan[6], Andrew Perkins[7], Garth Ravenhill[4]*

[1] UK National Health Service, Wareham, Dorset, United Kingdom
[2] UK National Health Service, Leicester, United Kingdom
[3] UK National Health Service, Sussex, United Kingdom
[4] UK National Health Service, Norfolk, United Kingdom
[5] UK National Health Service, Suffolk, United Kingdom
[6] UK National Health Service, Co. Limerick, Ireland
[7] UK National Health Service, West Yorkshire, United Kingdom

Introduction: Health care provision in the UK is universal, free to all, provided by the state funded National Health Service (NHS). The NHS is one of the largest employers in the UK.

We have developed the NHS Parkinson's Support group; a group that evolved initially through chance encounter at WPC 2019, and subsequently through word of mouth.

We now number 33 members, aged 35-70, comprising a variety of healthcare professionals:

- Dentists
- Doctors
- Healthcare Managers
- Nurses
- Paramedics
- Pharmacists
- Physiotherapists
- Radiographers

We meet monthly online; and have a WhatsApp group for our weekly question of the week, and ongoing communication.

Purpose: The group evolved initially as a support group primarily to ensure we lived well with Parkinson's. With time our group has expanded its purpose to advocacy in a variety of ways.

Outcomes:

- Positive feedback from members
- Ongoing regular engagement group & meetings
- Developing a repository of tips & insights e.g. research opportunities, DBS
- Advocacy campaigns:
- Awareness raising -World Parkinson's Day video
- Right on time campaign
- Stopping medication charges for PwP

Conclusions: We wished to share this model of support group based not just upon diagnosis but also occupation; there is great value from our shared occupational insight; could this be a model for other professions/organisations/diagnoses to develop their own support groups?

P45.25

A novel peer mentoring support system for persons with Parkinson's disease

Tsao-Wei Liang[1], S. Kenneth Thurman[2], Lance Wilson[*1], Kimberly Stoveld[1]*

[1] Thomas Jefferson University, Philadelphia, PA, United States
[2] Thomas Jefferson University, Voorhees, NJ, United States

Research indicates that peer mentoring approaches can be effective in providing support as well as increasing the well-being of people with various disabilities or health conditions. We developed a novel peer mentoring system to provide an additional support mechanism for persons with Parkinson's (PwP).

The Parkinson's Pals Program was conceived in the fall of 2020 during the height of the COVID-19 pandemic and funded by a grant from the Parkinson Council, Inc. (Philadelphia, PA). The group is based in the Philadelphia metropolitan region and consists of PwP, led by the founder and co-director (K.T), a Neurologist (T.L.), nurse (K.S.), and social worker (L.S.).

Volunteers were selected with a set of core characteristics in mind including strong communication skills, empathy, a history of living well with Parkinson's, and a desire to support the community. Volunteer mentors are further screened and oriented by the project co-director (K.T.). The orientation includes coaching on mentoring processes, privacy issues, difficult conversations, and available resources for people living with Parkinson's. Mentor relationships are highly personalized based on the needs and schedules, but mentors and mentees are encouraged to maintain regular contact with their mentee (at a minimum of once per month). To date, there have been 24 mentees served by ten active mentors. Quarterly meetings and an annual end of year gathering help to ensure that the group remains unified in their approach.

Mentees are typically newly diagnosed individuals but may also have longer standing diagnoses and facing new challenges related to their diagnosis. Potential mentees are either self-referred or referred by their neurologists. The project co-director interviews potential mentees and pairs them with an appropriate mentor. Every attempt is made to match mentors and mentees based on common interests, work experiences, gender, and age.

Preliminary data from the project's first year indicate that both mentors and mentees feel the connections are very beneficial for their well-being. We hope to demonstrate that one-on-one peer support systems fills an important gap in current support systems available for Parkinson's. Future directions include a care partner component, standardization of the mentor-mentee selection and pairing process.

P45.27

HerStory: An opera film showcasing the creative talents of people living with Parkinson's

*Amy Mallett**
Cohere Arts CIC, Woodbridge, Suffolk, United Kingdom

For those living with significant health challenges, the advantages of regular engagement with the arts can be intrinsic to, but also extend beyond the management of symptoms. For example, being part of an artistic collaboration that acknowledges and embraces diversity can not only promote feelings of connectedness but also confidence, motivation and self-esteem [1].
HerStory is an opera film showcasing the creative talents of people living with Parkinsons. The piece, by composer Amy Mallett, incorporates music, libretto, choreography and visual art co-created with 80 members of the UK Parkinson's community. The opera's narrative is inspired by the extraordinary exploits of historical British heroine, Margaret Catchpole, who achieved notoriety when was found guilty of stealing a horse and transported from England to Australia in 1801.
The opera began its journey in an artist residency and workshop performance at Snape Maltings in 2019, after which the cast of community performers expressed their aspirations to use the piece to "show the world what people with Parkinson's can do". During the pandemic, a series of online projects led by performance company Cohere Arts offered a valuable way of keeping cast members connected and active, whilst developing additional material for the opera. In 2022, supported by Arts Council England and partners Britten Pears Arts, English National Opera, Trinity Laban and MuMo Creative, the opera was made into a 30-minute film.
Project evaluations reinforce the well-being potential of engaging with creative activity, and in particular the power of the performative arts to promote positive shifts in identity from 'patient' to 'artist'. Not did participants experience positive impacts on their physical and mental health, but expressed how being part of a performing arts company can offer opportunities for people living with health challenges to redefine themselves by increasing a sense of self-esteem and accomplishment as individuals, whilst promoting social interaction and feelings of connection.
[1] John Steiner (2006); Cohen et al (2006)
[2] Bilby, Caulfield, and Ridley (2013)
[3] Leith (2014); Schiavio et al. (2018)
HerStory Opera Film short promo film:
https://youtu.be/EcC7DAYDCWI

P45.28

Parkinson can't steal my heart, love, thoughts and poetry: Writings by Lili Saint Laurent

*Alice Masson**
Person living with parkinson's, Madrid, Madrid, Spain

For the past 14 years, I am "a young onset parkinsonian person". Ten years ago, I decided to share my emotional journey and experiences with Parkinson's disease through poetry. To do so, I became Lili Saint Laurent (pen name) and created my website - www.filsdeparks.com – related to my daily life with my new "Brain mate", Parkinson. My wish was not to complain or to provide medical information; rather, to investigate Parkinson's from a different perspective, using humor and poetry to cope with it. It may seem surprising, but little by little my daily diary appeased me and offered me a lot of strength and happiness. Moreover, I realized that my poems and writings were also helpful to others—including, but not limited to, fellow patients and caregivers. During all these years, through my writings, I have met a lot of people who are affected by this illness, yet I am still fighting for improving awareness and knowledge on young onset Parkinson's disease. Beside my website, I published a collection of my poems in French (available in Spanish by July 2023), have led writing workshops, produced a performance in Paris based on my poems and writings, and collaborated with the Piece of Mind Collective, which produced a circus and dance performance on Parkinson partially based on my poetry (see poster by [Kuhlmann et al.] at the WPC 2023). In my poster, I would like to share how powerful words are for liberating emotions, and helpful poetry can be for living better with a chronic disease. I will share some of my creative process and a few of my poems in French and Spanish.

Parkinson can't steal my heart

Four years ago,
the 10th of January, you said
'I'll go for it.' Without doubting, nor
hesitating.

Four years ago,
Parkinson was already there,
Without being identified,
Without being called.

Tremor,
Tiredness,
Stiffness,
As new as our love.

But you were here,
With such a beautiful smile,
Optimistic,
With so much love.

One day RMI,
The day after at the City Hall,
But you didn't bend
Truly happy.

Six months later, Parkinson
was detected, we were
already
married
You've
Taken up the
challenge.

In the middle
of the storm, your love protects me
against emptiness and madness, such a
warm feeling.

Love is so important,
I feel so lucky,
I feel so happy,
Thank you so much.

Parkinson is here,
But can't take my heart,
Which is beating for you,
My love forever.

Since the first day I saw you,
I have no doubt,
You are the one
I was waiting for.

Parkinson is nothing
Compared
to
our love
Parkinson is nothing
It has
strengthened
our love.

P45.29

Parkinson's wellness professionals needs assessment

Bradley McDaniels[1], Gabriella Dimotsantos[2], Davis Phinney Foundation[2], National Engagement Advisory Team[3]*
[1] University of North Texas, DENTON, TX, United States
[2] Davis Phinney Foundation, Louisville, CO, United States
[3] Davis Phinney Organization, Louisville, CO, United States

Objective: To identify the needs of wellness professionals who work with people with Parkinson's disease (PD) to better understand the barriers to optimal service provision and to inform the development of solutions.
Background: Community groups are essential outlets for people with PD to become knowledgeable about their disease, learn potential management techniques, participate in group exercise classes, and connect with others who are more like them. Ample literature is available describing the value of participating in

community-based groups for people with PD, but no literature could be found investigating the barriers for those who lead these groups.
Methods: A cross-sectional sample of 270 adults who lead groups serving the needs of people with PD completed surveys to identify challenges faced and areas of unmet need. Descriptive statistics were performed to quantitatively assess the results. Most respondents were 46 to 75 years old (67%), female (81.8%), Caucasian (90.7%), and served people in a suburban setting (50.2%).
Results: The top three groups of respondents were LSVT BIG or LSVT LOUD (24.7%), PD support group (12.7%), and Rock Steady Boxing (12.3%). Respondents disagreed-to-strongly disagreed with the following statements: "I am well connected with my peers in other cities for peer learning and support," (65.5%), and "It's easy to collaborate with other Parkinson's-focused organizations or programs in my community," (58.4%). Results demonstrate that respondents disagreed-to-strongly disagreed that they have access to the tools and support needed to both address the challenges of engaging members who are marginalized or underrepresented (63.1%) and build partnerships with other organizations in the community to reach shared objectives (56.3%). The top three needs reported by respondents were more access to were people with newly diagnosed PD (94.7%), care partners (83.3%), and people with PD (83%).
Conclusion: This is the first study to our knowledge to describe the needs of individuals who lead wellness programs for people with PD in the community. The results of this study can inform the development of new initiatives to help support the efforts of community leaders and improve the delivery of services.

P45.30

Impact of socioeconomic status on severity of symptoms and quality of life in Mexican people living with Parkinson's disease
María Fernanda Medina-Pérez, Diana Paulina Romero-Terán, Andrea García-Hernández, Ana Jimena Hernández-Medrano, Rodolfo Arturo Abundes-Corona, Amin Cervantes-Arriaga, Mayela Rodríguez-Violante*
INNN, Mexico City, Mexico City, Mexico

Introduction: Parkinson's disease (PD) is a disorder characterized by progressive motor and non-motor impairment, being the second most frequent neurodegenerative disease, with economic burden and inequity in care in low- and low-middle income countries. According to INEGI, 76% of the Mexican population belong to the low and medium-low SEL, with a PD prevalence of 82.89 new cases in 100,000. Based on The Michael J. Fox Foundation, $25.4 billion are related to medical costs every year for PwP, which directly affects progression and severity of motor and non-motor symptoms.
Objective: To compare motor, non-motor, QoL, and caregiver burden scales in people living with PD (PwP) according to their socioeconomic levels.
Methods: A retrospective, cross-sectional, observational study was carried out. PwP were divided into three groups according to their SEL: (a) low and medium-low, (b) medium, (c) medium-high and high. Kruskal-Wallis test was used to compare: (i) PD motor dysfunction (Unified Parkinson's Disease Rating Scale [MDS-UPDRS3]); (ii) PD non-motor dysfunction (Non-motor symptoms scale [NMS]); (iii) impact on QoL (39-item Parkinson's Disease Questionnaire index [PDQi]), and (iv) the 22-item Zarit Caregiver Burden Inventory (ZCBI).
Results: 221 Mexican PwP (55.7% males; 63.3±11.9 years old) were included. Distribution among (a), (b) and (c) SEL groups was 63.8%, 18.6%, and 17.6%, respectively. Mean MDS-UPDRS3, MDS-NMS, PDQi, and ZCBI scores were 33.9±16.2, 67.4±52.2, 22.0±12.0, and 25.1±13.0, respectively. The low and medium-low level group had lower score in MDS-NMS compared to the medium level group (mean difference 27.6 points; p=0.015). There was no statistical difference in MDS-UPDRS3, PDQi, and ZCBI (p=0.419, p=0.310, p=0.815). Spearman's test showed very weak correlation between SEL and MDS-NMS total score (r=0.182, p=0.007).
Conclusions: PwP of higher SEL experiment higher non-motor dysfunction. Further analysis is needed to evaluate the impact of inequity in care and socioeconomic status in PwP living in low- and low-middle income countries.

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P45.31

Parkinson's Europe's don't lose sleep over Parkinson's campaign
Tara Nabili, Dominic Graham, Jennifer Stratten, Adrien Moyroud*
Parkinson's Europe, Orpington, United Kingdom

Context: Sleep problems affect almost 90% of people with Parkinson's (PwPs) and can mean PwPs – and their bed partners – are more likely to experience depression and/or stress. It is therefore important for PwPs to develop good sleep habits and to seek help if sleep problems affect their quality of life. This campaign addresses the lack of specific Parkinson's sleep information.
Introduction: Parkinson's Europe's 'Don't Lose Sleep Over Parkinson's' campaign took place in May 2021. It launched with a 60-second motion graphic animation and continued to highlight a variety of content (images, videos and text) to help the Parkinson's community get a better understanding of how to deal with sleep issues.
Overarching objective: Provide and promote enhanced access to sleep resources for PwPs, so they can make a more informed choice on how to improve their sleep.
Planned outcomes:
1) PwPs and their caregivers will understand more about how to improve their sleep, and try new techniques that may benefit them.
Outputs
- Website content on sleep hygiene and ways to address sleep
- Articles and podcast on Parkinson's Life
- Videos from neurologists and PwPs
- Q&A and leaflets on website
- Social media output

2) Wider public recognition of the issue of Parkinson's-related sleep disturbances
Outputs
- 60-second motion graphic video via social media
- Social media output
- Ray Chaudhuri video seminar on sleep (Touch Neurology Website)

3) Healthcare professionals (HCPs) awareness
Outputs
- Ray Chaudhuri's video seminar on sleep (Touch Neurology website)
- Bas Bloem video addressing HCPs (social media)

General summary observations: were these outcomes achieved?
- The campaign was a success and resonated well with PwPs.
- There was a significant increase in engagement and reach both with PwPs and HCPs – over all platforms – regarding sleep

(compared with other topics) – showing that the issue resonated strongly with both audiences.
- Feedback by a large majority revealed the campaign was timely and of interest.
- Images and videos were very popular – and had the highest engagement factor.
- Many national Parkinson's organisations were keen to get involved.

P45.32

'Exchanges': A visual resource to inspire and support deeper conversations in the Parkinson's community

Miratul Muqit[1], Daksha Patel[2], Sarah Patrick[,1], Nur Kockaturk[1], Daniel Saarela[1], Shalini Agarwal[1], Gloria Shi[1], Bill Carton[1], Janet Niven[3], Katrine Wreford[3], Daryl Lawson[3], Ian Keir[3], Sharon Langlands[3], Linda Donegan[3], Anthony Knowles[3], Sandra Knowles[3], Joy Milne[4], Thomas Giddens[5], Paul Davies[1]*
[1] MRC Protein Phosphorylation and Ubiquitylation Unit, Dundee, Scotland, United Kingdom
[2] Freelance, Manchester, United Kingdom
[3] Patient Address, Dundee, Scotland, United Kingdom
[4] University of Manchester, Manchester, United Kingdom
[5] Dundee Law School, Dundee, Scotland, United Kingdom

Interactions between people with Parkinson's (PwP), carers and researchers are often limited to research talks or visits to laboratories. These interactions are hugely beneficial to all involved and improve the understanding of research developments, but the opportunity for deeper conversations – particularly around the complexities and ambiguities of the lived experience of Parkinson's and of the research process itself – can be limited in these settings.
We have developed and co-produced 'Exchanges', an interpretive art card resource with drawings that depict Parkinson's research and symptoms alongside question prompts such as "What does Parkinson's mean to you?" to support deeper conversations between PwP, carers and researchers.
Initial experiences of the art card resource being used by a person with lived experience of Parkinson's and a researcher generated striking levels of engagement, breaking down barriers and prompting deep, quality conversations about Parkinson's. These powerful exchanges were captured on film.
We also discovered that the resource has a wider impact than originally anticipated – it is incredibly successful at prompting discussion of the emotional and physical challenges of Parkinson's between PwP and other PwP or carers too.
Unexpectedly, the resource also supported profound conversations about Parkinson's in a group setting as well as in pairs, with participant feedback advocating future use at conferences, in support groups and clinical settings.
PwPs and researchers will present their experience of 'Exchanges' and why this is a valuable resource, not only to support patient involvement in Parkinson's research, but to support the Parkinson's community as a whole.

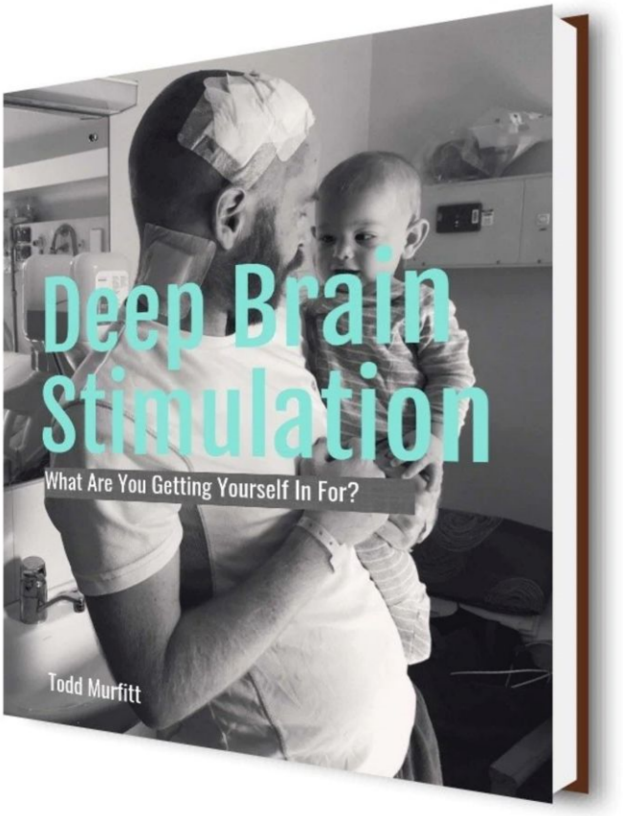
P45.33

Deep brain stimulation – What are you getting yourself in for?

*Todd Murfitt**
Shaky Leadership, Hahndorf, South Australia, Australia

Todd Murfitt is formerly a primary principal in South Australia. Passionate about collaboration and communication, and creating positive learning environments for all students, teachers and leaders.

Diagnosed in 2017 with "Young Onset Parkinson's Disease". Todd's grit to go 'toe to toe' with this challenge; has only strengthened his determination to live a full life; whilst maintaining his burning ambition to impact others positively – which has seen the schools he has led overcome adversity and bring together thriving communities.
Todd's book is designed to give you a glimpse into what you can expect from a personal, emotional account - of a patient. At the end of reading you may not have all the answers – though where this is the case; I hope you will be equipped with the right questions.



P45.34

Eur -up - ian 2023 - A personal endurance event across Europe to raise awareness of YOPD, fundraise for dedicated charity and make long term Europe wide YOPD connections

*Ian O'Brien**
Eurupian, Dungarvan, Waterford, Ireland

Objective: There are many objectives to this challenge:
- To observe the physical challenge for an individual with YOPD to complete such an adventure, moving, hiking, climbing & travelling consistently for 28 days straight!
- Increase awareness of YOPD across Europe through publicity and media coverage.
- Fundraising for a dedicated YOPD focused charity in Ireland called EOPD.ie (Early Onset Parkinson's Disease)

Background: Diagnosed with Young Onset Parkinson's Disease in 2018, aged 38, Ian found hiking to be his go to exercise. Wanting to use this passion along with promoting awareness of YOPD and meeting other YOPD hikers across Europe, Eurupian was born. Ian will visit each of the EU 27 countries and the UK, and will scale their

highest elevation point, all in just 28 days. A race up and down Europe scaling Mount Blanc, Mount Olympus, Ben Nevis to name a few.
Method: Ian's preparation and the complete event will be video documented. The physical challenge of the event will be aided by a support team of companion hikers, drivers and organisers.
The awareness and fundraising has started and will continue until the end of the event on 2nd July 2023 through a website as well as social media pages, TV/Radio and Print interviews and articles.
Result: The measurables will be:
Ian's physical wellbeing, remaining injury free and completing the event
Number of media exposure (print and live)
Social media follower numbers
Successful documentary production highlighting YOPD and showcasing the Eurupian event
No. of people from the YOPD community, in each of the 28 countries, that connect with the event
Funds raised
Conclusions: Ian hopes to finish this adventure safe and healthy, having made new friends in the YOPD network across Europe, inspired others, raised awareness and changed the general public's mindset on how someone with Parkinson's presents.

P45.35

Developing the Parkinson's disease support group network in Massachusetts, USA
Rosemary Owen, Raymond James, Michael T Stevenson, Marie Saint-Hilaire, Cathi A Thomas*
Boston Medical Center/Boston University, Boston, Massachusetts, United States

Background: Individuals with chronic health conditions benefit from participation in a support group. Benefits can include greater connectedness to others, greater access to local resources, and a reported improvement in quality of life and overall wellbeing. Healthcare professionals (including social workers, nurses, and rehabilitation specialists) and lay leaders, who may or may not have PD, facilitate these groups. Currently, the Massachusetts (MA) support group network includes community-based groups, as well as groups for special populations (such as Young Onset and Deep Brain Stimulation).
Objective: To describe a model of support group network development in MA which: 1) Provides appropriate referral for individuals and family members seeking access to a group; 2) Catalyzes the creation of groups in underserved areas; 3) Offers education and guidance to new groups as they develop; and 4) Supplies ongoing training and support to group facilitators.
Methods: At Boston Medical Center, a safety-net hospital with an onsite American Parkinson Disease Association Information & Referral Center, the authors (who are experienced group facilitators) have worked for many years to develop a systemic approach to grow and sustain a PD support group network. Authors provide: 1) Individual consultation to match patients with appropriate groups; 2) Assistance to local senior centers and agencies wanting to create new groups in underserved areas, including rural communities and communities of color; 3) Logistical support (creation of flyers, outreach planning, etc.); and 4) Speaker recommendations. The authors also provide ongoing consultation and education to facilitators through meetings, e-newsletters, virtual sessions, and an annual facilitator conference.
Results: Forty support groups meet regularly in Massachusetts, and 60 facilitators have been educated about supporting people with PD, as well as the resources available to them as group leaders. All participating facilitators are invited to join bimonthly virtual education sessions. Authors work to continue to educate and expand this network.
Conclusion: This model can serve as a guide on how to build and maintain a network of support groups for people with PD, as well as how to provide greater education and resources to group facilitators. Work remains to better serve those in diverse and underserved communities.

P45.36

All in summit: Convening support group and community leaders to connect, learn, collaborate and expand Parkinson's community resources
Clemie Pizzillo[1], Anissa Mitchell[2]*
[1] Parkinson & Movement Disorder Alliance, Dunkirk, AZ, United States
[2] Parkinson & Movement Disorder Alliance, Tucson, AZ, United States

Motivation: Support groups serve a vital role in the overall wellness of the Parkinson's Disease (PD) community. The important contributions from these resources to their communities' knowledge of, adjustment to, and living well with PD has always been impactful. The significance of these impacts was made apparent when the Covid-19 Pandemic underscored the negative effect of social isolation on the Parkinson's community wellness compounded by the loss of 30% of support groups.
Objective: The All IN Summit served as a launchpad to restore, revitalize, and reinvent support group and community leaders to better serve the Parkinson's community.
Method: The All IN Summit, hosted by Parkinson and Movement Disorder Alliance, a US-based advocacy organization, provided a four-day program that offered a variety of interactive workshops, breakout sessions and other activities that included education, exploration, and various perspectives from a variety of community leaders and programs such as dance, improv, and exercise. Participants completed a post-program survey and provided feedback on specific actions they have taken since the Summit to serve the Parkinson's community.
Results: 186 participants attended the ALL IN Summit and 74 post-Summit surveys were completed. The key motivations for participating in the Summit included: learn new ideas to help their local PD support group (74.3%), meet new people and network (64.9%), to be reenergized as a community leader (32.4%) and to become a community leader (12.2%). Attendees of the Summit included existing support group leaders, (34%), PD advocates (15.5%), future leaders (4.9%), and other leaders (23.2%). Outcomes of attending the All IN Summit were that 95.5% of attendees made connections to help them better serve their group or community, 89.2% identified at least one actionable item that will impact how they run or interact with their group or community, 83.8% learned or experienced a new idea or supported something to pursue as a support group or community leader, and 77% felt energized and refreshed in their role as a leader.
Conclusion: The ALL IN summit met the goal of helping to revitalize support groups and underscores the continued need to support the reestablishment of these vital community programs.

P45.37

Art as an avenue for participation in the Spanish-speaking Parkinson's community

Ruby Rendon[*,1], Claudia Martinez[2], Gregory Pearce[1]*
[1] Muhammad Ali Parkinson Center at Barrow Neurological Institute, Phoenix, AZ, United States
[2] Davis Phinney Foundation, Phoenix, AZ, United States

Objective: To provide under-represented Spanish-speaking Parkinson's communities with an avenue for participation at the World Parkinson Congress (WPC) 2023.
Methods: In the last 10 years, the Hispanic outreach program at the Muhammad Ali Parkinson Center at Barrow Neurological Institute has created virtual participative spaces for Hispanics with Parkinson's disease (PD) and their care partners. Its reach goes beyond Phoenix and includes other cities in the USA, Spain, and in various Latin American countries. These communities have responded positively when given the opportunity to participate in collective efforts that give visibility to the Spanish speaking PD community.
The WPC 2023 Parkinson Tulip Project (PTP) will display pictures of community members with tulips. This "international tulip garden" will unite the Parkinson's community at the first WPC to be held in a Spanish speaking country. Unfortunately, many members of our network won't be able to attend due to a variety of barriers. In response, with the help of MAPC art instructor Gregory Pearce, The MAPC and the DPF invited supporters of the Hispanic community to be "Pollinators of Change" for the PTP garden, and support the exchange of ideas, resources, and initiatives to improve the quality of life of PD underserved populations.
The drawing "Pollinators of Change'' has 4 tulips that represent North America, Central America & the Caribbean, South America and Spain. Three pollinators: a bee, a hummingbird, and a butterfly represent people with PD, care partners, and the health care community. The clouds covering the sun, represent the challenges that the PD community still faces. The rainbow in the background symbolizes hope for a better future.
Results: We received a total of ___ (pending) drawings that were used to create this poster, titled "Pollinators of Change." An electronic version of the poster will become an awareness tool and will be shared with all the participants. We include a map of the ___ (pending) participating countries to raise awareness about the large and diverse Spanish-speaking PD community. We hope that more avenues for participation will be created to give this community the opportunity to contribute to the WPC's vision for the future.

P45.38

Podcasting as a way to create a global PD community

*Travis Robinson**
Altadena, CA, United States

Podcasting as a way to form a global PD community:
The issues: PD is an isolating disease to begin with; when added to a global pandemic, many PwPs were suffering from severe social isolation. Many were diagnosed during the pandemic and were unable to find any in-person resources to help them adjust to their new life with PD.
Young Onset PwPs have an even harder time finding peers to relate to. Many are the only ones they know with the disease at their age. Many feel that such a diagnosis at their age is a death sentence.
The experiment: I started a podcast, detailing my personal journey of living with YOPD and invited a care partner of 18 years to be my co-host to explain how a care partner experiences PD and share her story and that of her PwP.
The Results: Our show has been downloaded over 4,200 times in over 32 countries. We've published over 80 episodes, with more than 40 hours of content. Most importantly, we're reaching thousands of listeners around the globe and telling them that they're not alone; That their struggles are understood by someone.
Remarks: Podcasting is a very easy way to reach a global audience. It requires little in the way of equipment, or infrastructure and very little in the way of upfront knowledge or experience in broadcasting. There are thousands of online free resources to guide one through the process of starting their own podcast.
Most importantly it reaches out to people on their terms; a 100% opted in audience, people listen to podcasts when it's convenient to them. Doing their laundry, working out or just sitting alone for a few minutes people invite a podcast into their quiet time. There is no other form of media that can make say the same.
What will your show be about?

P45.40

"Help me card" for off periods

*Jordi Santandreu Esteve**
@parkinformados, Barcelona, Catalunya, Spain

Background: Motor fluctuations can affect people with Parkinson's disease in many different ways, including the inability to walk or speak comprehensibly during an off episode.
The first time I had a very deep OFF while alone, away from home, I realized that I was unable to walk 5 meters to a coffe shop and ask for a chair and a glass of water to take my medication.
After that experience I became afraid to go anywhere alone.
Objectives: So I decided to be prepared for the next time I had an off and couldn't communicate easily.
Methods: I had the idea to make a card to ask for help using predefined messages so that I would only have to indicate if I had any difficulties to communicate, such as: if you can call my caregiver, ask for a taxi, or bring me a glass of water to take my medication.
Results: Over time I have also been incorporating information on the same card about the medication I take and the schedules, medication advice.
The card can be freely downloaded from my blog https://parkinsin.wordpress.com under a creative commons license. And also the same card in Spanish.
The card can be customized before printing or can be printed as is and fill in the gaps later.
You only need a cardstock and a printer where you can print the file on both sides, cut it out and fold it in three parts.

Conclusions: Wearing this help me card in my pocket made me feel ready to do much more things on my own.
An information card, warning, request for help and to facilitate communication all in one. A small card that fits in any wallet, but very full of information.
I hope you don't have to use it, but I always carry it with me, just in case.

P45.41

Parkinson's disease and the use of technology for the management of symptoms: A qualitative study
Richard Walker[*,1], *Francesca Hookway*[2], *Kyle Montague*[3], *Lorelle Dismore*[2]
[1] Northumbria Healthcare NHS Foundation Trust, North Shields, United Kingdom
[2] Northumbria Healthcare NHS Foundation Trust, Newcastle, United Kingdom
[3] Northumbria University, Newcastle, United Kingdom

The approach to monitoring and treating symptoms of Parkinson's Disease (PD) has been revolutionised in recent years due to technology. Wearable sensors have been successfully been used for rehabilitation of neurological conditions. However, current technologies for people with Parkinson's (PwP), are limited to monitoring of symptoms as opposed to management of symptoms and are not readily available. There is an urgent need for more real-world scenarios in which technology can be used for the management of symptom's for PwP's. In order to facilitate this, we need to understand from an individual perspective what PwP's needs are regarding the applications of technologies. This study aimed to explore PwP experiences of the use of technology for symptom management in PD. Nineteen PwP, aged between 60-88 years, participated in a semi-structured telephone/video call interview to explore their experiences of PD symptoms and the use of technology as a way of managing those symptoms. Findings were analysed using Thematic Analysis. Participants described a range of PD symptoms that impacted them physically and psychosocially. Participants rarely used digital technology for the management of symptoms but responded favourably towards its future application. For example, for management of drooling, for setting reminders to take medication, to aid in pacing and to record the symptoms that are occurring and feed this back to consultants. Barriers to using technology included physical symptoms (e.g. hand tremor), lack of concentration and the requirement for a personal approach for the assessment of symptoms. Overall, participants accept the use of digital technology for the management of PD symptoms.

P45.42

The power to give Parkinson's to another
*Lucia Wang**
Parkinson Joven Argentina, Buenos Aires, Argentina

For those of us who live with Parkinson's, especially young people, the news of the diagnosis comes as a shock. And life forces you to rethink, to reinvent yourself and with all the flexibility that your head can tolerate, to think about what we can try to do. The most difficult period is the one in which we make efforts so that what we have is not noticeable. Because that effort is so stressful that it leaves you without dopamine in two minutes. Then the dreaded scene unfailingly happens: you start shaking, you get nervous, your mouth dries up, and you end up confessing your truth with tears in your eyes from anguish and anger. And not only that, on top of that you have to tolerate the look of pity or pity that the others give you back. Even worse is when they start to cry with you. One day I decided to do something different, and I tried to start the meetings saying: "excuse me, I want to make a warning: I have Parkinson's so I can get nervous or need to stop for a while and then we continue. Don't worry because it's normal. Does anyone want to ask me any questions about it? I don't have any problem" ok, let's start the meeting. From that moment on, something magical happened: I relaxed and my symptoms diminished and I left them frozen: in freezing. After that, for a few seconds, the thing turns around: they are the ones who begin to have the symptoms of Parkinson's. I usually make some joke to relax, and in that way, all the feared scenes disappear and although Parkinson's stays with me I no longer have the intention of controlling it. That is one of the biggest challenges: learning to live with this, incorporate it, capitalize it... at least until the scientific community brings us new news, and we can deactivate it once and for ever.

P45.44

Pivoting to a virtual world: How Parkinson Society BC increased impact and reach to the Parkinson's community during the 2020 pandemic and beyond
Jean Blake[*,1], *Alana Dhillon*[*,1], *Shelly Yu*[*,2], *Liz Janze*[1]
[1] Parkinson Society BC, Vancouver, BC, Canada
[2] Parkinson Society BC, Coquitlam, BC, Canada

Introduction: Parkinson Society British Columbia (PSBC) is a non-profit, service-based organization whose mission is to empower the Parkinson's community in British Columbia through providing resources and services to enable self-management, self-reliance, and self-advocacy. Historically, PSBC provided primarily in-person services such as regional and provincial conferences, speech and swallow workshops, counselling, support groups and exercise campaigns. PSBC's online presence was limited to a website with resources on disease management, information on community exercise classes, and recordings of past in-person events. With the 2020 COVID-19 pandemic restrictions on all in-person gatherings, various in-person events and services were cancelled. PSBC problem solved to continue providing essential support services that the Parkinson's community depends on to live well. Although a

hindrance initially, the pandemic provided a unique opportunity to pivot service delivery onto a virtual platform.
Methods: PSBC's solution-focused strategy included identifying communication gaps and assessing implementation challenges linked to virtual programming. A variety of online platforms for educational and support services were explored, and exercise and activity classes, educational presentations, and provincial conferences were held virtually. These were recorded and uploaded to PSBC's public YouTube channel for those unable to attend the live-streamed events. To assist with learning this new technology, technical support via phone or email was offered.
Results: Compared to 2019, PSBC grew in the number of support groups, YouTube subscribers, activity groups, educational webinars, and provincial exercise programs. Expansion into virtual programming led to increased impact and reach by removing financial and geographical barriers associated with in-person events, and improved access to programs and services. These virtual programs continue to run because of their demand and popularity.
Discussion: PSBC was successful in providing continued support to the Parkinson's community in the face of adversity and challenges. Not only has service delivery improved in the long run, but the reallocation of costs also allowed other underfunded programs to thrive. The outcome was a solution-focused strategy of value-added virtual programming that increased accessibility of PSBC services across the province.

LIVING WITH PARKINSON'S: Advancing research: collaborations, capacity building, fundraising, trials, campaigns

P46.01

Including patients and care partners in clinical trial design: The EJS ACT-PD experience
Michèle Bartlett[*,1], Eric Deeson[2], Jodie Forbes[3], Anna Jewell[4], Keith Martin[5], Laurel Miller*[*,6], Kuhan Pushparatnam[3], Dorothy Salathiel[7], Paula Scurfield[3], Carroll Siu*[*,8], Sue Whipps[9], Sheila Wonnacott[10], Kevin McFarthing[11]*
[1] EJS ACT-PD, London, United Kingdom
[2] Expert by experience, Birmingham, United Kingdom
[3] Expert by experience, London, United Kingdom
[4] Expert by experience, Winchester, United Kingdom
[5] Expert by experience, Nottingham, United Kingdom
[6] Expert by experience, Reading, United Kingdom
[7] Expert by experience, Southampton, United Kingdom
[8] Expert by experience, Canterbury, United Kingdom
[9] Expert by experience, Plymouth, United Kingdom
[10] Expert by experience, Portsmouth, United Kingdom
[11] Expert by experience, Oxford, United Kingdom

Objectives: To ensure that people with lived experience of Parkinson's are central to all decisions in the design of a multi-arm, multi-stage (MAMS) clinical trial of therapies for slowing Parkinson's progression.
Background: Many trials fail because they do not recruit enough participants, or too many participants withdraw from the trial. Trials are slow and inefficient. In the Edmond J Safra Accelerating Clinical Trials in Parkinson's Disease (EJS ACT-PD) project we are speeding up the process of how we test therapies for slowing Parkinson's progression, allowing testing of multiple treatments in parallel. People with Parkinson's (PwP) and their care partners (CP) have been involved in all areas of design and decision-making to ensure our trial will be an attractive, positive experience for participants.
Methods: PwPs and CPs joined five working groups (WG) to help design the trial. They form a Patient and Public Involvement and Engagement (PPIE) WG, which is chaired by a PwP. The group uses different methods to support input into trial WG decisions: dedicated time to speak in all WG meetings; post-meeting discussions with WG chairs; use of a Standard Reporting Form for documenting WG decisions, recording questions for the PPIE WG and resolving PPIE concerns. Monthly PPIE forums allow for explanation of difficult topics and give time for PwP/CPs to ask questions. A PwP/CP WhatsApp group creates a safe space for sharing thoughts and ideas.
Results: The PPIE WG has helped shape the EJS ACT-PD trial. Input has impacted trial length, who can take part, what treatments will be tested, and ensuring symptoms that matter to PwP are included in the clinical tests that measure the effects of trial treatments. Trial participants will have the option for in-person or online trial visits, and will be supported by core trial staff. PPIE contributors have created a communications WG and community advice group, including those from ethnic minority and disadvantaged populations. These groups will help EJS ACT-PD reach diverse participants.
Conclusions: Input from PwP and CPs has shaped the decisions of the EJS ACT-PD project, making sure that taking part in the trial will be accessible, easy, and worthwhile.

P46.02

The OPTIM-PARK project: A feasibility study assessing acceptability and feasibility of a cross-national multisectoral intervention for people affected by Parkinson's disease
Line Bragstad[*,1], Tove Lise Nielsen[2], Naja Kruse[2], Ellen Hjelle[1], Anita Haahr[2], Dorit Kunkel[3], Silje Haavaag[1], Louise Vester[2], Victoria Navarta-Sanchez[4], Leire Ambrosio[3], Azuzena Pedraz-Marcos[4], Ana Palmar-Santos[4], Lydia Lopez-Manzanares[5], Fani Carabajal Pendon[5], Beatrice González García[5], Mari Carmen Portillo-Vega[3]*
[1] University of Oslo, Oslo, Norway
[2] VIA University College, Aarhus, Denmark
[3] University of Southampton, Southampton, United Kingdom
[4] The Autonomous University of Madrid, Madrid, Spain
[5] University Hospital La Princesa, Madrid, Spain

Introduction: Due to current demographic issues in Europe and around the world, it is anticipated that the prevalence of Parkinson's disease (PD) will keep rising. Enhancing access to care and services for those with PD is as crucial to improving living conditions for those affected by the disease, as research into its prevention and modification. The OPTIM-PARK intervention was developed to improve the process of living with Parkinson's disease for people with the condition and family carers by enhancing intersectoral collaboration and optimizing access to, and utilization of, local resources and support systems.
Objective: The objective of this study is to report the acceptability and feasibility of the OPTIM-PARK intervention tested in a multi-center, cross-national feasibility study.
Methods: The multisectoral OPTIM-PARK intervention was tested with people with Parkinson's disease (PwPD) and their family carers (FC) in Denmark, Norway, Spain, and the UK. Recruitment of participants occurred between March 2022 and September 2022 and involved 70 PwPD and 58 FC in total. The intervention was delivered over a three-month period and involved consultation with a trained OPTIM-PARK coordinator in a community setting.
The new UK MRC framework for developing and evaluating complex interventions guided the development of the intervention. In this study, the principles of evaluating feasibility studies, including

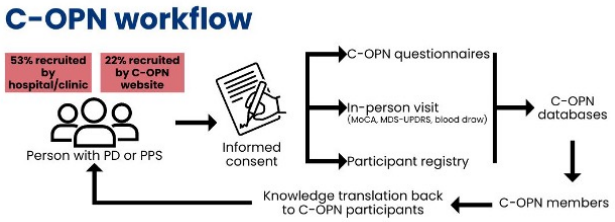
evaluating mechanisms and context as well as the feasibility and acceptability of the intervention implementation, were applied.
The results of this study are based on intervention logs kept by OPTIM-PARK coordinators, acceptability scales completed by PwPD and FC, and feasibility interviews with all three groups in addition to neurologists referring participants to community resources.
Results: At the moment, data collection is drawing to a close, and results will be presented at the WPC. Results will be presented according to feasibility of recruitment and retention of PwPD and FC; sample characteristics; as well as the content, delivery and acceptability of the intervention. We will draw on findings from acceptability scale, field notes and interviews.
Discussion: Implications of the study results will be discussed in relation to the intervention's potential application to enhance the process of living with PD.

P46.03

The Canadian Open Parkinson Network (C-OPN): A multimodal biorepository connecting the Canadian Parkinson's community around the world

Marisa Cressatti[*,1], Catherine Normandeau[2], Clotilde Degroot[3], Iris Kathol[2], A. Jon Stoessl[4], Martin McKeown[4], Janis Miyasaki[5], Richard Camicioli[5], David Grimes[6], Lorraine Kalia[7], Antonio Strafella[7], Penny MacDonald[8], Nicolas Dupré[9], Edward Fon[3], Oury Monchi[10]*
[1] Queen's University, Kingston, Ontario, Canada
[2] University of Calgary, Calgary, Canada
[3] McGill University, Montreal, Canada
[4] University of British Columbia, Vancouver, Canada
[5] University of Alberta, Edmonton, Canada
[6] University of Ottawa, Ottawa, Canada
[7] University of Toronto, Toronto, Canada
[8] University of Western, London, Canada
[9] University of Laval, Quebec, Canada
[10] University of Montreal, Montreal, Canada

Objective: The Canadian Open Parkinson Network (C-OPN) is a pan-Canadian initiative that bridges people, data and resources to accelerate new discoveries in Parkinson's disease (PD) research.
Background: C-OPN aims to operate under the principals of Open Science by facilitating rapid sharing of data and samples with Canadian and international investigators. Ten of Canada's top universities and movement disorders research centres from British Columbia, Alberta, Ontario and Quebec are part of C-OPN.
Methods: The C-OPN database collects de-identified clinical data with comprehensive information about each participant's family history, lifestyle and environment, along with details of their PD symptoms and medications; test results (MoCA, MDS-UPDRS); and a biobank with biomaterials extracted from blood samples (DNA, peripheral blood mononuclear cells and serum). **Results:** To date, the project has enrolled over 1300 participants across Canada, including PD, Parkinson Plus Syndrome and healthy control groups. C-OPN participants exhibit a male:female ratio of 1.7:1 and an average age at diagnosis of 59.8 years. The most reported motor symptoms include tremor (59%), rigidity (50%) and bradykinesia (48%), while the most reported non-motor symptoms include short-term memory loss (48%), anosmia (48%), constipation (44%) and sleep disturbances (24-46%). **Conclusions:** C-OPN resources (data, biosamples, registry for study participant recruitment) are made available to all C-OPN members. By becoming a national or international member, researchers – including principal investigators, graduate students, postdoctoral fellows – clinicians and industry partners can gain access to this wealth of resources from this Canadian PD cohort. Together, C-OPN seeks to support cutting-edge, multi-disciplinary and multi-site PD-related research studies across Canada and around the world. This project has been made possible by Parkinson Canada and Brain Canada through the Canada Brain Research Fund, with the financial support of Health Canada.



P46.04

Parkinson community plays a critical role in new brain health initiaitve

Roseanne Dobkin[1], Maggie McGuire Kuhl[2], Lynell Lemon[3], Christina Destro[2], Caitlin Kelliher[,2], Laura Heathers[4], Michelle Totten[4], Erinn Bryan[3], Craig Stanley[4], Chris Hobbick[4], Bridget McMahon[3], Kim Fabrizio[3], Ken Marek[3]*
[1] RUTGERS RWJMS, Piscataway, NJ, United States
[2] The Michael J. Fox Foundation for Parkinson's Research, New York, NY, United States
[3] Institute for Neurodegenerative Disorders, New Haven, CT, United States
[4] Indiana University, Bloomington, IN, United States

Background: Prevention of Parkinson's requires understanding risk factors and measuring early biological changes to inform the development of therapies that can be used before movement symptoms begin. Studies including the Parkinson's Progression Markers Initiative (PPMI), a landmark study from the Michael J. Fox Foundation, have identified smell loss as an early indicator of potential disease risk. In 2022, PPMI launched an online system to screen the general population for smell loss. The study is using a multi-faceted recruitment strategy, including engaging individual ambassadors from the PD community.
Methods: PPMI's Smell Test (ST) Direct system captures consent and contact information online. The study team mails a smell test; users complete 40 scratch-and-sniff questions and enter answers online. Select individuals with smell loss complete additional screening at a clinical site, with some invited to contribute more data and biosamples over time.
Currently, ST Direct is available to anyone aged 60 and older without a Parkinson's diagnosis in the U.S. or Canada. Spanish and French-Canadian translations and expansion of the system to England are in process. Affiliated programs are screening for smell loss in the Netherlands, Germany, Spain, Austria and Luxembourg. The study aims to enroll 1,200 people with smell loss to follow over time.
Results: The ST Direct website has seen more than 84,000 unique visitors. Over 13,000 consented to take a smell test (92.6% white, 79.3% female), with 580 qualifying for additional screening. Participants learn about Smell Test Direct from varies sources: MJFF emails and events, advertisements in newspapers, and study ambassadors (e.g., people with PD, their friends and family; research participants; other advocates of PD research). Importantly, nearly 3200 individuals have been referred by individual members of the PD community, using a study ambassador toolkit (www.michaeljfox.org/smelltoolkit). Study ambassador efforts have led to approximately 600 new consents, with 50 participants invited for further study.
Conclusions: ST Direct is identifying people with smell loss who can help accelerate prevention efforts. All members of the PD

community have a critical role to play in advancing therapeutic development, by helping to spread the word about a simple scratch and sniff test (https://mysmelltest.org/wpc.).

P46.05

A call to action: Including people with Parkinson's in clinical study design and execution

Anne Donnelly[*,1], Margaret Sheehan*[2]
[1] MJFF Patient Council, Winnetka, IL, United States
[2] MJFF Patien Council, Washington D.C., United States

Preface: We are both people with Parkinson's. We have participated in a number of research studies and have written about the value and challenges of patient involvement in research. We submit this abstract for the World Parkinson's Congress with the thought that the Congress is a great opportunity for researchers, patients and care partners to discuss together the value of standards for engaging patients in research and to debate what those standards might include.

By way of background, in the Short Communication entitled INCLUDING PEOPLE WITH PARKINSON'S DISEASE IN CLINICAL STUDY DESIGN AND EXECUTION: A CALL TO ACTION published in the Journal of Parkinson's Disease (2022, 1359-1363) the authors, including Donnelly and Sheehan, challenge researchers engaged in Parkinson's disease research to purposely address and embrace emerging best practice standards for actively engaging people with Parkinson's in clinical study designs and execution. They delineate the benefits of engaging people with the lived experience of the disease under study, and when and how to do so—emphasizing the value of engaging persons with Parkinson's early in the study and often---as one would with other important team members.

They also discuss the need to identify the variety of barriers which can accompany a person with Parkinson's when contributing to a research effort and the value of identifying ways to remove, minimize or otherwise circumvent these barriers. They offer a listing of more than a dozen common barriers—such as quiet voices, mobility issues, "off time" and offer examples of how to address them -- supply a microphone, include a person's caretaker in the meeting and be thoughtful about the timing of meetings all can help. They present their goal— A CALL TO ACTION, that all Parkinson's researchers regard patient participation in their research as essential for quality outcomes and that a generally accepted set of standards for engaging patients is agreed to.

P46.06

Informing a multi-country Parkinson's research grant in Africa through community engagement and involvement

Jared Okeno[*,1], Natasha Fothergill-Misbah*[2], Richard Walker*[3], Njideka Okubadejo*[4], Tania Park*[5], Omotola Thomas*[5]
[1] Parkinson's Support Group Mombasa, Mombasa, Kenya
[2] Newcastle University, Newcastle upon Tyne, United Kingdom
[3] Northumbria Healthcare NHS Foundation Trust, Newcastle upon Tyne, United Kingdom
[4] University of Lagos, Lagos, Nigeria
[5] Parkinson's Africa, London, United Kingdom

Introduction: Community engagement and involvement (CEI), also known as patient and public involvement (PPI), is crucial in the development of research that is driven by those with lived experience of the condition being researched. We report here on the CEI work being undertaken as part of a multi-country, multi-site grant with the aim of Transforming Parkinson's Care in Africa (TraPCAf), funded by the UK-based National Institute for Health and Care Research (NIHR). The aim of the grant is to provide much needed evidence on the situation of Parkinson's across Africa, from genetics, to pesticide exposures, to the lived experience of stigma.

Objectives: This work has two main objectives. The first objective was to inform the initial research proposal and ensure that all research questions were guided by PwP, their caregivers, and healthcare professionals in-country. The second objective will be to continue the CEI work through the lifecycle of the grant to inform in-country research, dissemination and impact activities.

Methods: The countries involved in this grant include: Egypt, Ethiopia, Ghana, Kenya, Nigeria, South Africa and Tanzania. CEI work is being led by the charity Parkinson's Africa, who will assist in-country research leads throughout the lifecycle of the grant, and beyond. CEI work has, and will continue to involve virtual Zoom meetings to coordinate focus groups and meetings, with workshops planned quarterly in each country.

Results: The initial CEI work carried out by the team was commended by NIHR reviewers on award of the grant, and ensured the aims of the proposed research aligned with need. The team will continue to work closely with CEI teams in multiple capacities. For example, to determine how best to report genetic results back to PwP, or in the development of culturally-specific information packages, public education campaigns, and support groups in each country site.

Conclusion: The CEI work carried out to date by the team has been crucial in ensuring that the research aims align with the needs of those living with Parkinson's, and their caregivers. The team will continue to report on CEI activities and hope that similar initiatives are taken by other researchers working in the field.

P46.07

Transforming Parkinson's Care in Africa (TraPCAf): A newly funded research grant

Natasha Fothergill-Misbah[*,1], Njideka Okubadejo*[2], Catherine Dotchin*[3], Tania Park*[4], Richard Walker*[3]
[1] Newcastle University, Newcastle upon Tyne, United Kingdom
[2] University of Lagos, Lagos, Nigeria
[3] Northumbria Healthcare NHS Foundation Trust, Newcastle upon Tyne, United Kingdom
[4] Parkinson's Africa, London, United Kingdom

The ageing population in Africa is growing faster than any other region in the world, yet country health and social care systems are largely unprepared for the increase in non-communicable and age-related diseases associated with later life. Parkinson's, being one of these diseases, is not seen as a priority by most African countries, despite the evidence to support its prioritisation on account of it being the fastest growing neurological disorder globally with respect to prevalence. This has led to a gap in global health research on Parkinson's and scarcity of evidence from the continent.

The overall aim of the grant, funded by UK-based NIHR, is to transform the landscape of Parkinson's care and treatment in Africa through research in Egypt, Ethiopia, Ghana, Kenya, Nigeria, South Africa and Tanzania. The project's key research questions involve: (1) understanding the burden of Parkinson's in Africa; (2) investigating ways to improve diagnosis rates; (3) providing affordable and sustainable treatment through a clinical trial of Mucuna Pruriens; (4) improving the quality of disease management; (5) establishing genetic and environmental links (e.g., diet, heavy metals and pesticides) to Parkinson's; and (6) understanding the lived experience of people with Parkinson's' (PwP) and their caregivers.

Capacity building and training are crucial components of the grant, with opportunities for knowledge exchange between country sites, and in the UK. The grant will also link with global researchers, such as the GP2 genetics team, as well as the team in the UK investigating the role of metabolome (sweat samples) in diagnosing

Parkinson's. Finally, we will be working closely with Parkinson's Africa to provide support and resources for people with PwP and their caregivers in all sites, including the establishment of local support groups.
The grant began in September 2022 for a period of 4 years. This project is the first of its kind for Parkinson's, involving multiple work packages, fields of research, countries and sites in Africa. The team will continue to report on the project and disseminate findings through multiple channels, with the hope to transform the landscape of Parkinson's care and treatment on the continent.

P46.09

Optimism in the research-based graphic medicine novel "Moving Along": Generating hope for people with Parkinson's and their caregivers through research communication about Parkinson's dance

Lisbeth Frølunde[*,1], Grethe Lundin*[2]
[1] Roskilde University, Roskilde, Denmark
[2] Co-resercher in Danish research project based at Roskilde University, Roskilde, Denmark

Introduction: Moving Along (Frølunde et.al., 2023) is a book for, with, and about people with Parkinson's, which was co-produced as a research-based graphic novel and summary of research results. It contributes to the fields of arts and health, medical humanities, graphic medicine, and narrative medicine with knowledge about what engagement in dance, music and the arts means for people with Parkinson's (e.g., Christensen-Strynø et.al. 2021, Houston, 2019). Dance for people with Parkinson's is spreading, especially due to Dance for PD®.
The main question addressed here is how hope can be shared in solidarity, as exemplified in the characters and narratives in Moving Along. This question brings up the relational, ethical, moral, and practical implications of co-producing a hopeful narrative on illness and the human condition (e.g., Wrigley, 2019).
Objectives: Moving Along is the result of a Danish research project "Dancing with Parkinson's" funded by the VELUX Foundation (2019-2022).
The research project had two overall aims: 1) to generate knowledge about and further dance as a form of person-centered treatment of Parkinson's; and 2) to generate knowledge about the potentials and challenges of participatory research, in which people with lived experience of illness and university researchers co-produce knowledge and research communication.
Methodology: The book's co-production involved 43 co-researchers (people with Parkinson's and caregivers), 7 dance facilitators, 3 researchers, and a creative team. Ethical concerns about anonymity led to creating composite characters in Moving Along through an iterative arts-based process.
The qualitative research methodology ascribes value to personal embodied experiences and interprets meanings in narratives (including poems, songs, dances, etc.) based on a dialogic narrative framework (Frank, 2012). It emphasizes the critical importance of eliciting people's own stories and expressions in order to gain understanding and communicate what Parkinson's dance means (Christensen-Strynø et.al., 2021; in press).
The book's editorial team will be represented by Lisbeth Frølunde (researcher and family caregiver), and Grethe Lundin (co-researcher with Parkinson's).
Outcomes: It was essential for the co-researchers, that the book, through graphic storytelling and humor, generates hope, shows ways of finding new meaning in life (including dance), and raises awareness about life with Parkinson's.

P46.10

A vital piece in a giant jigsaw: A lived experience of participating in an international Parkinson's study

Heather Hunter[*,1], John Vasey[2], Philip Brown[3], Lisa Alcock[4], Walter Maetzler[5], Alice Nieuwboer[6], Pieter Ginis[6], Heiko Gassner[7], Mark Gordon[8], Alison Keogh[9], Anat Mirelman[10], Jeff Hausdorff[10], Clemens Becker[11], Lynn Rochester[4], Alison Yarnall[4]*
[1] The Newcastle upon Tyne hospitals NHS Foundation Trust, Newcastle Upon Tyne, United Kingdom
[2] Mobilise-D Study Participant, Newcastle Upon Tyne, United Kingdom
[3] The Newcastle upon Tyne hospitals NHS Foundation Trust, Newcastle Upon Tyne, Tyne and Wear, United Kingdom
[4] Newcastle University, Newcastle Upon Tyne, United Kingdom
[5] Kiel University, Kiel, Germany
[6] University of Leuven, Leuven, Belgium
[7] University Erlangen-Nürnberg, Erlangen, Germany
[8] Teva Pharmaceuticals Industries Limited, Tel Aviv, Israel
[9] Insight Centre for Data Analytics, University College Dublin, Dublin, Ireland
[10] Tel Aviv Sourasky Medical Center, Tel Aviv, Israel
[11] Robert Bosch Hospital, Stuttgart, Germany

Taking part in a Parkinson's research study may be a daunting prospect for some; however by understanding the participant

experience we aim to demonstrate that it can be an enjoyable and interesting activity.
In order to explore this we will consider the lived experience of taking part in the Mobilise-D study (https://www.mobilise-d.eu/). This is a world-wide consortium of scientists, clinicians and industry partners, based at leading international universities and some of the world's largest pharmaceutical and technical companies. The aims include the identification and validation of low cost, simple, accurate digital mobility outcomes using a wearable sensor. These will be useful in both clinical and research settings to improve patient care. By using valid tools that can detect and measure how well someone walks, including speed, symmetry/efficiency, and endurance, the project aims to target mobility loss.
The Clinical Validation Study uses standardised measures of walking, and looks at a range of assessments including motor and non-motor symptoms, quality of life, frailty, cognition, and functional measures, comparing these to information gathered using wearable sensors.
We will demonstrate some of the measures and technologies used and give people a chance to interact with some of tools. We also include a link to a YouTube video of a research participant talking about his experience of taking part.
By allowing people to explore these measures and discuss them with research staff, we will explain how essential their role is in research studies. We aim to boost people's confidence in research participation and generate new knowledge leading to improved care of patients with Parkinson's.

P46.11

Movement as methodology for individual and collective wellbeing: Overcoming persistent disparities in Parkinson's research and care through dance, qualitative research, and community

Jhia Jackson[*,1], Richard Jackson*[*,2]*
[1] University of California San Francisco, San Francisco, CA, United States
[2] Upper Marlboro, Maryland, United States

The available literature on the incidence of Parkinson's Disease among African Americans and their subsequent experiences highlights the cumulative negative impact of systemic racism, as they continue to be underrepresented in research, diagnosed at a later stage, and face persistent disparities in care. Researchers and practitioners invested in overcoming structural inequities need to be creative, strategic, and empathetic as this population faces challenges within and outside of the healthcare system that directly impact their quality of life. This presentation advocates for the use of qualitative research methods and contemporary dance forms as an innovative methodology for elucidating the experiences of historically marginalized populations, fostering community collaborations, translating research into practice, and expanding the onus of living well with Parkinson's from the individual to the collective. Daddy Matters(2018 - 2021), an interdisciplinary dance work developed and instigated by the authors, serves as a case study for the possibility of movement as methodology to positively engage with diverse stakeholders, including people living with Parkinson's, their family and social networks, clinicians, researchers, and the curious general public. By infusing the choreographic process with autoethnography, structured improvisation, and audience engagement, the authors created a work that invited an intimate perspective on the relationship between race, Parkinson's Disease, and the family unit. This methodology fostered a type of sustainability and adaptability that allowed the work to integrate versatile components including a traditional dance performance, a conference exhibition for healthcare practitioners, an interactive virtual dance exhibition for artists and the general public, and a class series for people living with Parkinson's and their loved ones. Originating in an interview with a family elder and a father-daughter duet, the resulting intergenerational work challenged expectations around what is possible for someone living with Parkinson's Disease, increased access to care and resources, and promoted the development of a knowledgeable, empathetic, and motivated community.

P46.12

Parkinson's with altitude: A case study

Claire Lehman[*,1], Jules Janssen Daalen*[2]
[1] UK National Health Service, Wareham, Dorset, United Kingdom
[2] Radboud University Medical Centre, Nijmegen, Netherlands

Introduction: Anecdotally some individuals have reported that elevated altitude improves PD symptoms; a physician with YOPD aspiring to be Heidi!
The case is a female physician aged 42, diagnosed 2017 aged 37, with tremor dominant right sided Parkinson's Disease. Hoehn & Yahr Scale 1.
Null hypothesis: elevated altitude has no impact upon PD symptoms
Methods: An individual with YOPD went from sea-level to altitude (1000m, 1500m, 2000m) over 8 weeks monitoring PD symptoms daily using a daily diary and validated tools:
PRO-PD score – a validated patient reported outcome measure
CYPD app – ongoing monitoring of tremor using apple watch
Mon4t app –array of tests: mobility, balance tests, tremor.
Menstrual cycle was monitored throughout.
Results: Elevated altitude was associated with improvement in patient reported outcome measure PRO-PD score; this benefit persisted upon return to sea-level for 1 week. Improvement was noted in the following domains:

- Tremor
- Hand function
- Sleep

The participant reported improvement of stiffness and rigidity at all altitudes above 1000m.
Technical issues impeded apple watch monitoring of tremor.
Appraisal of the Mon4t data is ongoing.
Discussion: Despite limitations, n=1, CYPD app issue, impact of menstrual cycle (menses exacerbate PD symptoms), this case study demonstrates that altitude may improve subjective PD symptoms.
Conclusion: Whilst the validity of a single case study is limited, it does contribute to the evidence regarding altitude and Parkinson's.
Regarding potential mechanism of action, this could be hypoxia mediated, although if so, then acclimatisation may reduce the benefit.
Further research is currently in progress.

P46.13

Sparks of experience – Enhancing serendipity – An initiative by PD avengers research committee

*Eirwen Malin**
Parkinson's UK Cymru, Cardiff, United Kingdom

Background: Serendipity was said to play a part in Fleming's discovery of penicillin, in fact it was his curious, alert mind that made sense of the unexpected and created a life saving treatment. In 1969 a woman with PD reported that Amantadine, a prophylactic flu drug affected her PD symptoms, it was redeveloped as a Parkinson's drug. More recently Joy Milne asked about the smell she detected on her husband and now a quick test for PD is close.

We who live with Parkinson's every day (PLP), whether as a person who has been diagnosed or a close associate, feel its twists and turns with a deep knowledge. We notice that, "His symptoms are better in the sunshine", that "My tremor goes away when I'm painting and for a few hours afterwards" and we ask "Why is that?". Disappointingly, often that's the end of a story that may contain the germ of a real revelation, a quirky idea that is a game changer.
Aim: Sparks of Experience is a plan to harvest the curiosity of PLP, enhancing serendipity and identifying novel research.
Method: PD Avengers, a movement led by people with a diagnosis of Parkinson's, and with a large individual and international membership is uniquely positioned to collect what we have called Sparks of Experience.
Beginning with a small group to provide some vernacular examples, we have collected ideas from PLP in their own words. Initial analysis has yielded nearly 50 different "sparks" in 7 different groups. The list is close to saturation point with hardly any new ideas arriving, however, we remain alert
Several members of the PD Avengers research group will be attending WPC2023 and through a variety of interactions including the poster we plan to:-

- Share the list
- Gather some numeric feedback
- Explore whether any of our "Sparks" are already under consideration
- Facilitate action groups of individuals, researchers, medical professionals and funders to take ideas forward
- Potentially collect new ideas

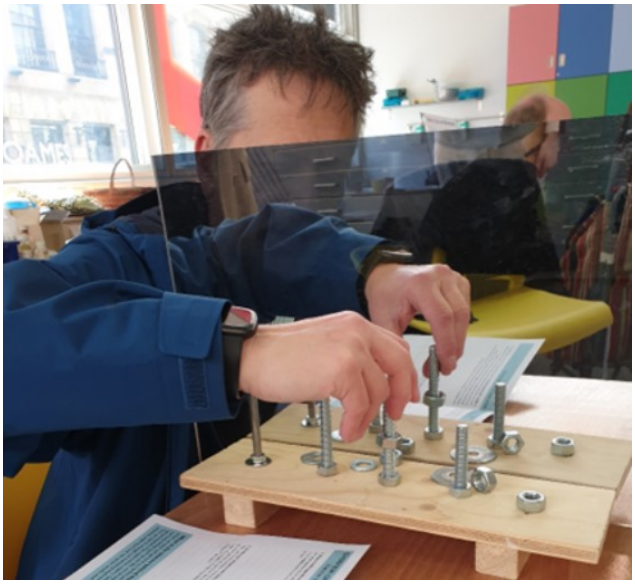
Our poster would be interactive, containing QR codes enabling delegates to affirm experiences, express interest, leave information, contact details etc.
Outcome: Novel research projects on topics identified by PLP explored.

P46.14

Experience in action: Using art-science activities to explore experiences of movement and the body in Parkinson's and autism

Ellen Poliakoff[*,1], *Antony Hall*[1], *Eve Edmonds*[1], *Peter Baimbridge*[2], *Garry Copitch*[3], *Graham Hanks*[4], *Matthew Sullivan*[3], *Emma Gowen*[1]
[1] University of Manchester, Manchester, United Kingdom
[2] University of Manchester, Salford Autism, Manchester, United Kingdom
[3] Expert advisor, Manchester, United Kingdom
[4] Expert advisor, Sheffield, United Kingdom

Introduction: In the ageing autistic population, sensorimotor differences are increasingly recognized, however the causes are not well understood, and little research has been conducted. In contrast, motor symptoms are core to Parkinson's, yet the conditions under which movements may be improved (e.g. cues) and the relationship to bodily perception are not fully understood. Thus, for both autism and Parkinson's it is important to understand bodily experience and how movement is affected under different conditions. Recent research has also emphasised the importance of comparing the two, both of which may be underpinned by the neurotransmitter dopamine. This project used an experiential artistic approach to explore future research questions and methods, as a novel patient and public involvement (PPI) activity.
Methods: In collaboration with artist Antony Hall, members of the Body Eyes and Movement (BEAM) lab delivered drop in art-science sessions at the Manchester Art Gallery. The activities built on Antony's PhD work, in which he took perceptual illusions, many based around the body and movement, out of the laboratory and repurposing them as workshops within an arts context. For example, people performed actions with both hands whilst one hand was hidden behind a mirror. Seven people with Parkinson's and six older autistic adults attended one of the sessions. Activities were trialled with expert advisors, who also advised on the accessibility of the venue and practical aspects of the sessions.
Outcomes and Reflections: Most of the participants enjoyed the sessions, although one queried whether this was art. The activities provoked a context for spontaneous and unexpected conversations between participants and researchers. This led to new insights and ideas for future research; for example, the importance of body position and effects of visual feedback on tremor. However, it was challenging to maintain a balance between providing sufficient instruction, without over-explaining the activities. The sessions also brought new perspective(s) for lab members, as well as new directions for Antony's artistic practice.
Conclusions: Using experiential sessions allowed more informal and exploratory conversations than typical PPI activities such as consultations through focus groups or presentations. This approach is well suited to the early stages of developing ideas and research questions.



P46.15

A patient engagement council for Parkinson's research: Methods of meaningfully incorporating the perspectives of people with Parkinson's into clinical research and decision making

Kate Trenam[*,1], *Karlin Schroeder*[2], *Nikul Bakshi*[3], *Marc van Grieken*[4], *Carol Schulte*[5], *Harold de Wit*[6]
[1] UCB Pharma, Brussels, Belgium
[2] Parkinson's Foundation, New York, New York, United States
[3] Parkinson's UK, London, United Kingdom
[4] Patient Expert, Parkinson's UK, Perth, United Kingdom
[5] Patient Expert, Parkinson's Foundation, New York, New York, United States
[6] Patient Expert, Westerhoven, Netherlands

UCB Pharma, Parkinson's UK and Parkinson's Foundation established a Patient Engagement Council for Parkinson's Research (PECPR). Through this unique and innovative partnership, the council aims to embed patient involvement throughout each step of Parkinson's drug development to improve long-term outcomes for patients. UCB's vision is that all therapeutics

for Parkinson's are developed by a fully integrated and equal partnership between key stakeholders. We report how the PECPR was established and how it is incorporating patient perspectives early in research and development (R&D).
In setting up the PECPR, joint planning meetings were held to align on goals and ways of working, applying the Patient Focused Medicines Development Patient Engagement Quality Guidance (http://patientfocusedmedicine.org/peqg/patient-engagement-quality-guidance.pdf). Three patient experts (people living with Parkinson's, who had the ability to represent the wider Parkinson's community and were interested in R&D), were recruited to the PECPR. The patient engagement experts at Parkinson's UK and Parkinson's Foundation handled recruitment and co-lead the PECPR.
The PECPR was launched in September 2021, where agreement was reached on the vision, mission and objectives. Initial discussions identified which high-value topics to prioritize. The PECPR used the Clinical Trials Transformation Initiative's Prioritization Tool (https://prioritizationtool.ctti-clinicaltrials.org/) to rank topics under: Research, Clinical Development and Real-Life setting, then compare/discuss respective priorities and decide which topics are high value for everyone. Key areas of focus included: developing a patient co-creation process for Target Product Profiles; developing a narrative for the patient community to improve understanding of disease-modifying therapies; and enhancing diversity, equality and inclusion in R&D.
The PECPR reconvened in November 2022, for a reflection meeting to discuss whether initial goals are being met and to determine how the PECPR can be continually enhanced. Some initial learnings from this partnership are: patient experts should be included in all joint planning meetings to align on agendas; and to incorporate more diverse perspectives beyond disease state and geography. These learnings will be useful in informing the PECPR's future work and help build on progress that has already been made with the patient experts, thus helping them achieve their goal of Parkinson's therapeutics developed in a fully integrated partnership with patients.

P46.16

Accelerate research gains and improve service delivery by streamlining the Parkinson's non-governmental organization (NGO) sector in the United States

Sarah Winter[*,1], Melissa Tribelhorn[2]*
[1] Bothell, WA, United States
[2] Seattle, WA, United States

The Parkinson's non-governmental (NGO) sector in the United States provides invaluable benefit to the Parkinson's community in the form of programmatic support and research advancement. The NGO sector is an equalizer for people impacted by Parkinson's: regardless of a patient's insured status or ability to pay, NGOs offer free education, emotional support options, and advocacy opportunities in accessible formats. Additionally, many Parkinson's NGOs actively work to rectify geographic, racial, and gender-based healthcare disparities through dedicated outreach to underrepresented populations. Parkinson's NGOs are a tremendous funding source and a significant driving force for research and biomedical advancements that benefit all people impacted by Parkinson's.
In the U.S., there are several national and a multitude of local and regional NGOs, each delivering valuable services to a segment of the Parkinson's community. The sheer number of Parkinson's organizations, however, creates challenges that impede efficient and effective service delivery and research progress: 1) NGOs can lose sight of their scope and how organization size and service area should dictate the functions they perform; 2) NGOs often work in the same geographic area, causing duplication of services; 3) when multiple organizations work the same geographic area or provide the same services, they generate redundant administrative costs; 4) there is a great deal of confusion for donors and program participants within the Parkinson's community about which organization performs what function; 5) NGOs compete for the same donor dollars and participants, potentially creating an atmosphere of territoriality and self-preservation rather than collaboration.
Some non-profit functions are best served by national organizations, such as research funding, federal advocacy for policy change, international collaboration, accreditation and provision of continuing education for providers, and establishment of health centers for comprehensive Parkinson's care. Conversely, some non-profit functions are best served by local or regional organizations, such as case management, emotional support options, newly diagnosed services, and community-building through in-person or localized virtual events.
Streamlining and merging U.S. Parkinson's NGOs by function and service area would decrease the duplication of services, reduce administrative overhead, provide clarity for donors as they designate their funds, promote collaboration, and ultimately accelerate research gains.

LIVING WITH PARKINSON'S: Other

P47.01

Promoting "custom" Parkinson's medication orders in the hospital improves timely administration

Hooman Azmi[1], Francis Ruzicka[*,2], Lisa Cocoziello[3], Elana Clar[4], Anthony Rocco[3], Florian Thomas[2]*
[1] Hackensack University Medical Center, Hackensack Meridian School of Medicine, NJ Brain and Spine Center, Hackensack, New Jersey, United States
[2] Hackensack University Medical Center, Hackensack Meridian School of Medicine, Hackensack, NJ, United States
[3] Hackensack University Medical Center, Hackensack, NJ, United States
[4] Hackensack University Medical Center, Hackensack Meridian School of Medicine, NJ Brain and Spine Center, Hackensack, NJ, United States

People with Parkinson's disease (PD), and especially those with more advanced stages often rely on complicated medication regimens to maximize ON time without troubling dyskinesias for best quality of life. Patients may be on multiple medications with frequent dosing to this end. Delays in medication can have a significant negative impact on patients with PD. Nowhere else are these delays more pronounced than when a patient with PD is admitted to the hospital. Rigid medication schedules in the hospital, lack of knowledge about PD, and unavailability of all PD medications on hospital formularies have contributed to this crisis. Medications are often missed, omitted, delayed or substituted in hospitals and many times PD patients receive contraindicated medications. These errors have been demonstrated to increase hospital complications such as falls, confusion and dysphagia. The complications in turn result in increased lengths of stay as well as increased mortality.
Using a hospital wide protocol to ensure adherence to a patient's home schedule when ordering PD medications, we have encouraged the use of "custom" timed orders. This type of order is in contrast to the generic hospital default of three times, four time, five times daily, etc orders. From January 1, 2016 to April 30, 2021,

we have noted a significant increase in PD medications being ordered using “custom” timing. During the same time period, we have also observed a significant decrease in PD medication administration delays overall, and in particular when these medications are ordered in a “custom” fashion. While there is much more work to be done, we are encouraged by the trends we have seen in analyzing over 31000 doses of PD medications over a five year time period.

P47.02

A neurologist with PD: What I’ve learnt about being a patient and person with PD

*David Blacker**
Perron Institute, Nedlands, Western Australia, Australia

Background: In November 2018, after 15 years of specialty neurology practice, I received the diagnosis of PD from a colleague. It was not a surprise; I’d had classic symptoms for several years, and an exercise induced foot dystonia for almost a decade. What did surprise me, was the new role as a patient and person with PD (PwP).
Objective: To describe my experience of being a neurologist with PD, focusing on components of the doctor/patient interaction, that might be perceived differently from the two viewpoints. The main objective is to enhance and improve communication.
Methods: I describe my history over about 15 years, from the prodromal phase, to the “end of the honeymoon”. Issues to be presented include;
1. The need for robust, early support around the time of diagnosis.
2. The role of exercise, and my experience, including my work on the Feasibility of Instituting Graduated High intensity Training (FIGHT-PD) study of non-contact boxing.
3. An hypothesis that early, robust psychological support and exercise can modify the course of PD, and initially improve physical and mental health for PwP.
4.The power of sharing my personal story to support PwP at critical times.
5.The challenges of reacting to; “you don’t look like you have PD” and the burden of non-motor symptoms.
6. Coping with progression, depression and career change.
Conclusions: The diagnosis of PD changed the course of my life and career. My hope is that by sharing my experience, some good may come of this.

P47.03

Quebec Parkinson network: a collaborative approach to research in Parkinson’s disease and related disorders

*Sarah Bogard**
McGill University, Montreal, Canada

Intro: Research in Parkinson’s disease is well established through the province of Quebec. However, there is a great challenge in recruiting participants for research projects. Research groups often have difficulty reaching out to participants because they need affiliation to clinicians or community groups. For instance, the main issue is that they often recruit the same participants, which is a problem for diversity in data collection. The QPN was created to tackle this issue, mainly. The main goal of the network was to establish a participant registry, collect data on them and share those data to research groups to facilitate research in PD.
Method: The network has established a collaborative approach between clinicians, researchers and participants to facilitate research. Recruitment of participants was done over ethics approval with movement disorders clinics, patients advocacy groups and newspaper ads. Data collection included demographic, clinical and epidemiological questionnaires, blood draw, neuropsychological assessment (MoCA) and movement disorder evaluation (MDS-UPDRS). Follow ups were completed every 18 months. Biological samples are analyzed and stored in the C-BIGR biobank at the Neuro. Other data collected are stored in the participant registry. Participants answer questionnaires over the phone or in-person, and evaluations are done in-person. They receive a small compensation for their time and commitment.
Results: Since its creation in 2013, we have recruited 1972 participants; 1699 with PD, 273 controls and 35 with RBD for which we have demographic, clinical and epidemiological questionnaires. Biological information for 1040 PD, 132 controls and 35 RBD. MoCA for 425 PD, 60 controls, 3 RBD. Motor evaluation for 355 PD and 10 RBD. With all those data, the network has supported over 120 research projects by either sharing data collected among the network or sharing lists of participants (registry).
Conclusion: Our work is showing its importance and success in the field of research in PD. The collaboration between clinicians, researchers and participants is a useful approach to research groups as the number of supported projects is constantly growing. It promotes open science concept through our participant registry and data sharing platforms. This model could be useful to other network or could serve as a national initiative.

P47.04

Sorting the sock drawer: A performance provocation for changing pan-Parkinson perceptions

*Eirwen Malin**
Parkinson’s UK Cymru, Cardiff, United Kingdom

This abstract is submitted as a proposal for a performance of a storytelling show.
Background: An unexpected diagnosis of Parkinson’s led my GP to suggested 2 week’s leave from work, saying “Go and sort your sock drawer!” In that fortnight I tussled with my sense of self in a life turned upside-down, and in the 9 years since, Sorting the Sock Drawer has become a focus for my Parkinson’s advocacy. Creating, from a bad experience, an entertaining storytelling show has provided a personal tool to educate, raise awareness, provoke thinking and challenge perceptions; informing and inspiring in equal measure.
Aim: To provide a provocation, to the whole Parkinson’s community and beyond, which challenges without confrontation, refreshes thinking, encourages self-management and influences service delivery.
Method: The Society for Storytelling’s, Introduction to Storytelling says the art uses “No script, no props, no cameras, no books. [Just] the magic of ‘Once’ ” (Willison, 2018). The artform drives consideration of personal and/or systemic change. Not tied to a written script, the storyteller can interactively tailor the performance to each audience. Unrestricted by visual images, heterogenous audiences readily identify with characters in the story. On the other hand, entering the story world offers a distance and separation that can depersonalise difficult issues and allow individuals to see themselves differently.
As simple entertainment or active workshop, the content of the show develops through interaction with audiences, life experiences, contact with other advocates and is influenced by developing research and practice in the field.

Result: With audiences as varied as a Dance for Parkinson's class in Brooklyn (2017) and researchers at the UK Dementia Research Institute, Cardiff (2022), Sorting the Sock Drawer has been unfailingly appreciated and responses indicate that it has provoked thought, action and change.
Comments include …
The message will stay with me… Life is different, but not necessarily worse.
… thought provoking, a piece of storytelling that everyone should hear.
I very much enjoyed seeing PD with a new perspective.

P47.05

Medication experiences of people with Parkinson's disease
Sneha Mantri[*,1], Kristin Richards[2], Steven Arcona[3], Rahul Sasane[3]*
[1] Duke University, Durham, NC, United States
[2] University of Texas, Austin, TX, United States
[3] Cerevel Therapeutics, Boston, MA, United States

Purpose: Medication is an important component of the management of Parkinson's disease (PD), yet few studies investigate the factors that inform medication decision-making from the perspective of the person with PD. This study aimed to better understand the medication experiences of people with PD.
Methods: A cross-sectional survey was conducted in 2022 with a US Qualtrics research panel. People diagnosed with PD taking at least one dopaminergic PD medication were invited to complete a survey with multiple choice questions addressing medication utilization, including initiation and daily regimens, as well as side effects. Descriptive statistics were calculated for all variables.
Results: Participants (n = 196) had a mean age of 62.5 years (standard deviation (SD) = 7.6), with mean disease duration of 4.7 years (SD = 4.3). Most were white (68.4%); 15.8% were black and 10.7% were Hispanic or Latino. Forty percent reported advanced PD (self-reported Hoehn & Yahr scale of 3 or greater) and 83.2% said they started taking PD medication at diagnosis. Three in four participants were currently taking levodopa/carbidopa (74.5%) and 58.7% were taking a dopamine agonist. Half (49.5%) took PD medication three or more times a day, 81.7% reported being frustrated with the frequency of their daily PD drug regimen, and 63.8% reported experiencing PD medication side effects. Of those reporting side effects, 63.2% take another medication to treat the side effects. When assessing taking a new PD medication, medication effectiveness and related side effects are the most important medication factors people with PD consider. Regarding experienced side effects, more than 30% of participants reported headache (48.0%), nausea (42.9%), drowsiness (36.7%), vomiting (35.7%), and confusion (30.1%). Other side effects included lightheadedness (26.5%), sudden overwhelming sleepiness (25.0%), abnormal dreams (22.4%), hallucinations (16.8%), and compulsive behaviors (15.8%). One-third (32.7%) of participants reported currently experiencing dyskinesia and 30.1% reported experiencing it in the past. Seventy percent of participants reported experiencing off times.
Conclusion: This study quantified aspects of medication burden in people with PD. Results indicate that many report frustration with medication regimens and substantial side effect burden, highlighting the need for enhanced communication and anticipatory guidance between providers and patients regarding PD medication.

P47.07

APDA Parkinson's Symptom Tracker App, New York, USA
Rosa Pena, Rebecca Gilbert, Eloise Caggiano, Vicky Chan*
American Parkinson Disease Association, Staten Island, New York, United States

Background: Everyone experiences PD differently, and symptoms can vary greatly day to day. The more specific someone can be with their healthcare team about the types of symptoms they care experiencing, the better the doctor (s) can tailor a treatment plan individualized for each person. It can be difficult to remember how certain symptoms have or have not affected each person since their last visit with their health provider. To address this challenge, APDA developed the APDA Symptom Tracker App in May 2019 made possible with sponsorship from Acadia Pharmaceuticals, Inc.
Objective: To describe a specialized mobile application for people with Parkinson's disease, available on Apple ¡OS (Apple Store) and Android (Google Play). The App guides users through a set of questions that allows them to rate how certain motor and non-motor symptoms are affecting them, then creates a simple graph to indicate which symptoms are most impacting their quality of life. This graph is saved in a section, "My Library" and can be emailed to their healthcare provider. A list of suggested follow-up questions is generated for people to review with their doctor about symptoms and concerns they are experiencing. Users can compare results to see if certain symptoms are getting worse and determine which symptoms need to be addressed more urgently.
Methods: An interactive Symptom Tracker was created by working with a medical and scientific communication company, a professional App developer, medical professionals, and feedback from testers. Translation of the App in Spanish was done November 2020 with additional features such as: an interactive medication tracker, helpful notifications and a more comprehensive user profile.
Results: Currently, APDA is working on the next upgrade, APDA Symptom Tracker App 3.0. This update will have expanded functions to enhance the user experience: Appointment reminders, medication time reminders, note section for additional comments, updated medication list and others. There are over 11,500 users of the App.
Conclusion: This App can serve as a tool for users to be more proactive in managing their PD symptoms, connect to resources and improve their quality of life.

Late-Breaking Poster Presentations

BASIC SCIENCE: Etiology, genetics, epidemiology, and toxicants

LBP01.14

The pesticide chlordecone promotes Parkinsonism-like neurodegeneration with tau lesions in midbrain cultures and C. elegans worms

Annie Lannuzel[*,1], Valeria Parrales[2], Patrick P. Michel[2], Aurore Tourville[2], Rita Raisman-Vozari[2], Stéphane Haïk[2], Stéphane Hunot[2], Nicolas Bizat[3]*

[1] Centre Hospitalier Universitaire de la Guadeloupe, Service de Neurologie, Faculté de Médecine de l'Université des Antilles, Centre d'Investigation Clinique (CIC) 1424; Sorbonne Université, Paris Brain Institute - ICM, Inserm, CNRS, Hôpital de la Pitié Salpêtrière, Pointe-à-Pitre ; Paris, France

[2] Sorbonne Université, Paris Brain Institute - ICM, Inserm, CNRS, Hôpital de la Pitié Salpêtrière, 75013 Paris, Paris, France

[3] Faculté de Pharmacie de Paris, Université de Paris Cité, Paris, France

Chlordecone (CLD) is an organochlorine pesticide (OCP) that is currently banned but still contaminates ecosystems in the French Caribbean. Because OCPs are known to increase the risk of Parkinson's disease (PD), we tested whether chronic low-level intoxication with CLD could reproduce certain key characteristics of Parkinsonism-like neurodegeneration. For that, we used culture systems of mouse midbrain dopamine (DA) neurons and glial cells, together with the nematode C. elegans as an in vivo model organism. We established that CLD kills cultured DA neurons in a concentration- and time-dependent manner while exerting no direct proin-flammatory effects on glial cells. DA cell loss was not impacted by the degree of maturation of the culture. The use of fluorogenic probes revealed that CLD neurotoxicity was the consequence of oxidative stress-mediated insults and mitochondrial disturbances. In C. elegans worms, CLD exposure caused a progressive loss of DA neurons associated with locomotor deficits secondary to alterations in food perception. L-DOPA, a molecule used for PD treatment, re-stored these deficits. Cholinergic and serotoninergic neuronal cells were also affected by CLD in C. elegans, although to a lesser extent than DA neurons. Noticeably, CLD also promoted the phosphorylation of the aggregation-prone protein tau (but not of alpha-synuclein) both in midbrain cell cultures and in a transgenic C. elegans strain expressing a human form of tau in neurons. In summary, our data suggest that CLD is more likely to promote atypical forms of parkinson-ism characterized by tau pathology than classical synucleinopathy-associated PD.

LBP01.18

Genome-wide association identifies novel etiological insights associated with Parkinson's disease in African and African admixed populations

Mie Rizig[1], Sara Bandres Ciga[2], Mary Makarious[3], Oluwadamilola Ojo[4], Kristin Levine[5], Olaitan Okunoye[1], Ellen Sidransky[6], Nahid Tayebi[6], Peter Wild Crea[7], BLAAC PD Study Group[8], Nigeria Parkinson's Disease Research Network[9], Cornelis Blauwendraat[10], Henry Houlden[1], John Hardy[11], Andrew Singleton[,12], Njideka Okubadejo[4]*

[1] UCL Queen Square Institute of Neurology, London, United Kingdom

[2] Center for Alzheimer's Disease and Related Dementias (CARD), NIH/NIA, Bethesda, MD, United States

[3] Laboratory of Neurogenetics, NIH, Bethesda, MD, United States

[4] College of Medicine University of Lagos, Idi-araba, Lagos, Nigeria

[5] Center for Alzheimer's and Related Dementias (CARD), NIH/NIA, Bethesda, MD, United States

[6] National Institutes of Health/National Human Genome Research Institute, Bethesda, MD, United States

[7] National Institutes of Health, Bethesda, MD, United States

[8] Study Group, Bethesda, United States

[9] NPDR, Lagos, Nigeria

[10] Laboratory of Neurogenetics, NIH/NIA, Bethesda, MD, United States

[11] UCL Queen Square Institute of Neurology, London, United States

[12] Center for Alzheimer's Disease and Related Dementias (CARD), NIH/NIA, Bethesda, MD, United States

Background: Understanding the genetic and mechanistic basis of disease in ancestrally diverse populations is critical to realizing the global application of precision medicine. The African and African admixed populations offer unique opportunities for studying the genetics of monogenic and complex diseases.

Objective: To provide a genome-wide association study (GWAS)-based insight into the genetics of Parkinson's disease (PD) in Africans and African admixed populations.

Methods: We performed a comprehensive genome-wide assessment of PD in 197,918 individuals (1,488 cases; 196,430 controls) of African and African admixed ancestry, characterizing population-specific risk, differential haplotype structure and admixture, coding and structural genetic variation and polygenic risk profiling.

We identified a novel, common, risk factor for PD and age at onset at the GBA1 locus (risk, rs3115534-G; OR=1.58, SE=±0.07, P=3.44E-09; age at onset, BETA =-2.004, SE =±0.57, P = 0.0005), rare in non-African/African admixed populations. Downstream short- and long-read whole genome sequencing analyses did not reveal any coding or structural variant underlying the GWAS signal. However, we identified that this signal mediates PD risk via expression quantitative trait locus (eQTL) mechanisms. While previously identified GBA1 associated disease risk was via coding mutations, we suggest a novel functional mechanism consistent with a decreasing trend of GBA activity. Given the high population frequency of the underlying signal and the phenotypic characteristics of the homozygous carriers, we hypothesize that this variant does not cause Gaucher disease.

Conclusion: This study identifies a novel African-specific genetic risk factor and points to GBA1 regulation as a major mechanistic basis for PD in African and African admixed populations. This striking result contrasts to previous work in Northern Europeans, both in terms of mechanism and attributable risk. This finding highlights the importance of understanding population-specific genetic risk in complex diseases, a crucial point as the field moves toward target-specific PD clinical trials and while recognizing the need for equitable inclusion of ancestrally diverse groups. This

inclusion represents a valuable step towards insights into novel genetic determinants underlying PD etiology.

LBP01.23

Association of diet with gut microbiome in patients with Parkinson's disease

*Dayoon Kwon, Keren Zhang, Kimberly Paul, Irish Del Rosario, Jonathan Jacobs, Adrienne Keener, Jeff Bronstein, Beate Ritz**
UCLA, Los Angeles, CA, United States

Background: The gut microbiota has been suggested to influence Parkinson's disease (PD) via the gut-brain axis. Here, we examine associations between diet and gut microbiome composition and predicted functional pathways in patients with PD.
Methods: We assessed gut microbiota in fecal samples from 85 PD patients in central California using 16S rRNA gene sequencing. Diet quality was assessed by calculating the Health Eating Index 2015 (HEI-2015) from the Diet History Questionnaire II data. We examined associations of diet quality and nutrients, which we previously identified to differ in PD patients and control subjects, with microbial diversity, composition, taxon abundance, and predicted metagenomic profiles. All models were adjusted for age, sex, race, and sequencing platform.
Results: With higher HEI score and fiber intake, we observed an increase in putative anti-inflammatory butyrate-producing bacteria, such as genera Faecalibacterium and Roseburia, as well as a decrease in putative pro-inflammatory bacteria, such as genera Klebsiella. Associations were in the opposite direction with higher added sugar intake. Predictive metagenomics indicated that bacterial pathways involved in ergothioneine and chlorophyllide biosynthesis contributing antioxidants were enriched with increasing HEI score and fiber intake, whereas pathways involved in allantoin degradation and related to oxidative stress were reduced.
Conclusions: We found that a healthy diet, fiber, and added sugar are associated with gut microbiome composition and its predicted metagenome in PD patients. Diet-driven changes to the gut microbiome may contribute to previously observed associations between certain dietary compounds and PD progression and warrant further investigations of diet-microbiota associations in PD as dietary interventions may contribute to prevention strategies.

LBP01.24

A low-quality diet is associated with Parkinson's disease in central California

*Dayoon Kwon, Aline Folle, Irish Del Rosario, Keren Zhang, Kimberly Paul, Adrienne Keener, Jeff Bronstein, Beate Ritz**
UCLA, Los Angeles, CA, United States

Background: Parkinson's disease (PD) phenotypes may be modifiable by lifestyle factors, including diet. Yet, little is known about the influence of diet on PD.
Methods: We conducted a pilot case-control study that included 96 PD patients and 83 controls (household = 53; community = 30) living in central California who reported their diet during the past month. This allowed us to estimate diet quality by the Healthy Eating Index (HEI)-2015, the Alternate Healthy Eating Index (AHEI)-2010, and the Alternate Mediterranean Diet Score. We assessed associations of diet with PD status using logistic regression and with symptom profiles and medications using linear regression, adjusting for relevant confounders.
Results: Lower healthy diet scores were observed in PD patients compared to controls, with an OR of 0.58 per 9-point increase for the AHEI (95% CI: 0.38, 0.85). This low-quality diet was characterized by high intakes of carbohydrate, trans-fat, total sugars, and added sugars and low intakes of total protein, total fat, monounsaturated fatty acids, fiber, folate, vegetables, fruits, and nuts. PD patients with chronic constipation had a lower HEI score than those without chronic constipation (beta per 9-point: -0.81, 95% CI: -1.47, -0.14). PD patients taking higher doses of dopamine agonists consumed more added sugars and carbohydrate than patients with lower doses.
Conclusions: Our findings suggest that PD patients consume a low-quality diet compared to household and community controls. Dietary modifications may help reduce symptoms and promoting a healthy diet should become a part of routine care and disease management for PD patients.

BASIC SCIENCE: Protein misfolding and handling

LBP03.08

G51D, a rare and aggressive form of Parkinson's disease

*Noelia Pelegrina-Hidalgo**
University of Edinburgh, Edinburgh, United Kingdom

Alpha-synuclein (αSyn) is the major protein implicated in Parkinson's disease (PD) and several other neurodegenerative disorders. During disease progression, αSyn aggregates and forms complex structures known to interfere with neuronal viability. The G51D point mutation of aSyn has been associated with a very aggressive, early-onset form of PD. The aggregation dynamics and propagation of G51D αSyn remain unclear, and so we have developed a rat model in which G51D αSyn is expressed. Following injection with pre-formed fibrils, we have used single-molecule and super-resolution microscopy to visualise the distribution of aggregates in the brain, characterising both the structure and location of the protein below the diffraction-limit of light.
In future studies, we will utilise DNA-PAINT to image multiple targets in the same samples (up to 7). This will allow us to determine which epitopes are exposed in the aggregates, in addition to providing information about which organelles and cell-types they reside in. We will use this information to "finger-print" each protein aggregate. Our results will shed light on the behaviour and structure G51D αSyn takes in the central nervous system to provide a more complete understanding on the development of this rare PD manifestation. Furthermore, our findings will lay framework for the identification of biomarkers for targeted therapies against PD.

LBP03.13

The role of karyopherin abnormalities in the onset and progression of synucleinopathies

Daulet Sharipov[*,1], Erika Bereczki[2], Richard Killick[1], Tibor Hortobagyi[1], Claire Troakes[1], Dag Aarsland[1], Frank Hirth[1]*
[1] King's College London, London, United Kingdom
[2] Karolinska Institutet, Stockholm, Sweden

Parkinson's Disease (PD), Dementia with Lewy Bodies (DLB), and Parkinson's Disease Dementia (PDD) are all characterised by the accumulation and aggregation of alpha-synuclein (aSyn), which are therefore called synucleinopathies. aSyn is an intrinsically disordered protein prone to accumulation via changing its spatial conformation and/or liquid-liquid phase separation (LLPS). Previous studies showed that LLPS is associated with karyopherins, mediating nucleocytoplasmic cargo transport and acting as disaggregases against misfolding proteins. Karyopherin

abnormalities have been implicated in synucleinopathies, but their role in disease formation remains enigmatic.
Here, using a multi-disciplinary approach, we characterised levels and localisation of karyopherin and aSyn in the prefrontal cortex (BA9) of human post-mortem brain tissue of Healthy Controls (HC), Alzheimer's Disease (AD), PD, DLB and PDD. We also used differentiated human SH-SY5Y cells and Drosophila to accumulate aSyn in either wildtype or PD-related mutant A30P and established the levels, localisation, and effect on karyopherins.
Our analyses identified significant alterations in the expression levels of karyopherins in post-mortem BA9 that were not detected in AD nor controls. Further analysis revealed aSyn accumulation and aggregation in the cytoplasm and nucleus and an altered nucleocytoplasmic ratio in post-mortem tissue of the investigated cases versus age-matched controls. Moreover, karyopherins were depleted from the cytoplasm and accumulated in the nucleus in PD, PDD and DLB but not in the control group, with abnormal nuclear colocalisation with aggregated aSyn. New Drosophila models of synucleinopathy demonstrated that accumulating aSyn caused alterations in levels and localisation of karyopherins and progressive motor impairment that was exacerbated by A30P mutant aSyn. In addition, SH-SY5Y cell experiments revealed that accumulating A30P mutant aSyn formed spontaneous intracellular aggregates that sequestered and mislocalised karyopherin. This pathogenic process was accelerated in the presence of prefibrillar aSyn.
Overall, our findings demonstrate the pathological accumulation of nuclear aSyn together with karyopherin alterations in PD, PDD and DLB. Given their functions as nuclear transporter receptors and disaggregases, the observed karyopherin abnormalities suggest a vicious cycle of protein alterations that propagate the pathological aggregation of aSyn in neurodegenerative synucleinopathies.

BASIC SCIENCE: Pathology

LBP05.02

The effect of gut microbiome dysbiosis on tyrosine and cholesterol sex hormone metabolism in Parkinson's disease

Natalia Birch[*1], Nanthini Jayabalan[1], Kerry Roper[2], Helen Woodhouse[2], John O'Sullivan[3], Robert Adam[4], Richard Gordon[5]*
[1] Translational Research Institute, UQ Centre for Clinical Research, Brisbane, QLD, Australia
[2] UQ Centre for Clinical Research, Brisbane, QLD, Australia
[3] UQ Centre for Clinical Research, Royal Brisbane & Women's Hospital, Wesley Medical Research Ltd, Brisbane, QLD, Australia
[4] Translational Neuroscience Laboratory, UQ Centre for Clinical Research, Royal Brisbane & Women's Hospital, Wesley Medical Research Ltd, Brisbane, QLD, Australia
[5] Translational Neuroscience Laboratory, UQ Centre for Clinical Research, Brisbane, QLD, Australia

The progressive loss of dopaminergic nigrostriatal neurons is a primary characteristic of Parkinson's disease (PD), however the implications of this neurodegenerative disease extends beyond the resulting motor symptoms. A change in the gut microbiome and the onset of gastrointestinal dysfunction have arisen as key indicators of PD pathology. Despite this, the link between gut dysbiosis and PD remains largely unknown. This study aimed to perform a comparative analysis of urinary amino acids and metabolites in comparison to altered gut microbiome-associated metabolites in PD. This study analysed 64 urine samples obtained from healthy (n= 31) and PD (n= 33) patients. Samples underwent deproteinisation and analysis by reverse phase (RP)/UPLC-MS/MS methods with positive and negative ion mode electrospray ionization (ESI) and HILIC/UPLC-MS/MS with negative ion mode ESI. Statistical analysis was performed using Welch's two-sample t-test on log transformed data with a significance value of $p < 0.05$. Several metabolites found to be elevated in PD patients, including sex hormone cholesterol metabolites and tyrosine metabolites, also correlated with altered gut microbiome-associated metabolites. This includes dopamine, 3-methoxtyrosine and homovanillate (HVA) tyrosine metabolites which were significantly elevated in PD patients, and directly correlated with increasing levels of p-cresol sulfate. P-cresol sulfate is a known microbiome-associated metabolite found in the large intestine where gut bacteria ferment proteins elevated in PD. This was also observed in sex hormone cholesterol metabolites 21-hydroxypregnenolone disulfate, pregnanediol-3-glucuronie and androsterone glucuronide which also rose proportionally with p-cresol sulfate increases in PD patients. This finding illustrates that the altered gut microbiota in PD is closely linked to both tyrosine metabolism and sex hormone cholesterol metabolism effectively linking the gut-brain axis in neurodegenerative disease. This study illustrates the importance of gut microbiota and its effects on PD, and therefore points towards the importance of further elucidation of this association.

LBP05.06

Spatial transcriptomics identifies molecular signatures of prodromal and advanced alpha-synuclein pathology

Asad Jan[*1], Xiaoying Zhao[1], Poul H. Jensen[2], Yonglun Luo[1], Marina Romero-Ramos[1], Lin Lin[1], Jens R. Nyengaard[3]*
[1] Department of Biomedicine, Aarhus University, Aarhus, Denmark
[2] Danish Research Institute of Translational Neuroscience, Aarhus University, Aarhus, Denmark
[3] Core Center for Molecular Morphology, Department of Clinical Medicine, Aarhus University, Aarhus, Denmark

Spatial transcriptomics has emerged as a powerful approach to interrogate the significance of mRNA transcripts within their histological context. Here, we applied this methodology to investigate the transcriptomic profiles associated with prodromal and advanced stages of alpha-synuclein (aSyn) aggregation in mouse brain. Briefly, we induced aSyn aggregation in vivo by a single intramuscular injection of fibrillar murine aSyn (PFF aSyn) in the hindlimb of 3 months old transgenic mice overexpressing the human mutant A53T aSyn (M83 line; n=4/group; heterozygous). We and others have reported that in this experimental paradigm of peripheral-to-central propagation of aSyn aggregation, there is a prodromal stage whereby the reticular nuclei of brainstem harbor markers of synucleinopathy in the absence of overt motor disability. Subsequently, the mice reach a moribund (end)-stage characterized by hindlimb paralysis and widespread detection of aggregated aSyn in the nervous system along with reactive gliosis (Ref 1-4).
Our differential gene expression analyses (Fig.1, uploaded) reveal remarkably distinct transcript modules in the affected brain regions at the two stages. In the prodromal (non-symptomatic) phase, we observe significant upregulation of pathways involved in the energy metabolism (ie. Oxidative phosphorylation, glucose homeostasis, fatty acid metabolism and cholesterol biogenesis), and protein translation. Intriguingly, there is a dramatic decline in these metabolic pathways at the end-stage (paralysis), with substantial enrichment of inflammatory markers (eg, complement, interferon response). Crucially, we also identified differential expression of unique gene clusters highlighting the effects of pathological aSyn aggregation in the components of white matter, choroid plexus and brain vasculature, which otherwise remain underrepresented features in studies of Parkinson disease (PD) and related disorders. Lastly, data from validation studies involving select candidate markers in PD patient-derived microarrays datasets and immunohistochemical analyses in post-mortem brain specimen will

also be presented. We consider that these findings will have significant implications for obtaining a refined mechanistic understanding concerning the role of aSyn aggregation in neurodegeneration and potentially hold promise for the discovery of surrogate biomarkers in PD and other synucleinopathies.

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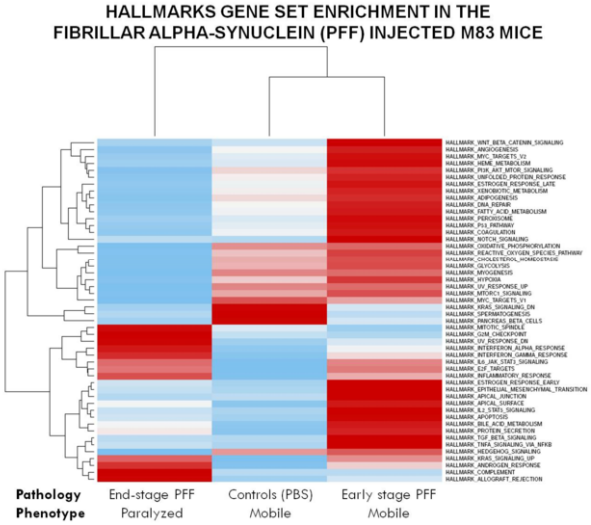


LBP05.13

Exploring LRRK2-Clusterin pathway in astrocytes: implication for a-synuclein clearance and spreading

Alice Filippini[1], Giulia Carini[1], Veronica Mutti[2], Massimo Gennarelli[3], Isabella Russo[,3]*

[1] Unit of Genetics, IRCCS Centro San Giovanni di Dio Fatebenefratelli, Brescia, Italy; Unit of Biology and Genetics, Department of Molecular and Translational Medicine, University of Brescia, Brescia, Italy

[2] Unit of Genetics, IRCCS Centro San Giovanni di Dio Fatebenefratelli, Brescia, Italy

[3] Unit of Biology and Genetics, Department of Molecular and Translational Medicine, University of Brescia, Brescia, Italy; Unit of Genetics, IRCCS Centro San Giovanni di Dio Fatebenefratelli, Brescia, Italy

Accumulating evidence highlights that dysfunction of astrocytes biology might contribute to Parkinson's disease (PD) onset and progression. To this regard, we recently showed that the extracellular clusterin binds to and limits the uptake of a-synuclein fibrils by astrocytes, suggesting that its modulation might control the spreading of a-synuclein. Of relevance, we preliminarily observed that Leucine-rich repeat kinase 2 (LRRK2), a gene linked to genetic and familial PD, regulates clusterin levels. Thus, starting from these premises, here we explore LRRK2-Clusterin pathway in astrocytes to understand whether dysfunctions of this process might contribute to the spreading of a-synuclein species between neurons.

We collected several results showing that LRRK2 controls clusterin levels in astrocytes. Specifically, brain lysates and primary astrocytes from LRRK2 G2019S KI mice exhibit increased levels of clusterin protein compared to their respective wild-type (WT). Accordingly, we found an opposite effect in brain lysates and in primary astrocytes from LRRK2 knock-out (KO) mice in comparison to their respective WT. To gain insights in the molecular mechanism underlying LRRK2-dependent clusterin modulation, we found that LRRK2 controls clusterin at the translation level without affecting the translation-factor 4E-BP pathway. Interestingly, in relation to PD pathology we found that LRRK2 G2019S KI astrocytes, with increased levels of clusterin, exhibited impaired ability to ingest fibrillary a-synuclein. We are now investigating whether dysfunctions of LRRK2 G2019S-clusterin pathway contribute to the spreading of a-synuclein aggregates between neurons.

Future studies will allow us to understand whether the modulation of LRRK2 G2019S-clusterin might improve the ability of astrocytes to clear a-synuclein and thus to attenuate neuron-to-neuron spreading of a-synuclein pathology.

BASIC SCIENCE: Animal and cellular models of Parkinson's disease and Parkinsonisms

LBP06.01

Alpha-synuclein miRNA-based AAV gene therapy leads to target engagement and phenotypic correction in an in vivo rat model of Parkinson's disease

Seyda Acar Broekmans[,1], Rhodé Erbrink[2], Charlotte van Rooijen[2], Lodewijk Toonen[2], Mercedes Valls[2], Astrid Vallès[2]*

[1] uniQure Biopharma BV, Oegstgeest, Netherlands

[2] uniQure Biopharma BV, Amsterdam, Netherlands

Parkinson's disease (PD) is a progressively debilitating neurodegenerative disease with an increasing prevalence with age. Only symptomatic therapies are available which do not tackle the underlying disease mechanism. One of the underlying causes of PD is aggregation of alpha-synuclein protein (α-syn), encoded by the SNCA (Synuclein Alpha) gene. Aggregated α-syn is one of the main components of Lewy Bodies (LBs), a key neuropathological hallmark in PD. Typically, LB pathology originates in brainstem and extends to midbrain and cortical regions with disease progression, in parallel with neurodegeneration of nigro-striatal dopaminergic circuits and other neurotransmitter systems. Our hypothesis for a disease modifying therapy is that lowering α-syn protein levels in relevant brain regions may reduce aggregation and degeneration, ultimately halting disease progression.

We are developing an adeno-associated virus (AAV) gene therapy to deliver SNCA-targeting miRNAs (miSNCAs) engineered to decrease α-syn mRNA and protein levels. We have previously presented data on design and in vitro selection of miSNCA candidates targeting all SNCA splicing variants. Here, we evaluate the potential phenotypic improvement of AAV5-miSNCA in an α-syn rat PD model. Adult rats received AAV1/2 overexpressing human A53T-α-synuclein ipsilaterally in the substantia nigra, at a dose known to cause neurodegeneration and PD-like motor phenotypes. Two weeks after AAV1/2-hA53T-α-synuclein administration, three AAV5-miSNCA candidates were injected in the substantia nigra. All tested AAV5-miSNCA candidates showed correct processing and target engagement at both mRNA and protein levels. Moreover, dopamine metabolite deficiencies and motor deficits in hA53T-α-syn rats were corrected by AAV5-miSNCAs. Additionally, dopaminergic cell loss was rescued in the miSNCA-treated groups as compared to the controls. These results support the potential therapeutic value of α-syn RNAi-based gene therapy for disease modification in PD.

LBP06.02

Combining vectorized antibody and miRNA lowering strategies for synucleinopathies

Seyda Acar Broekmans[*,1], Rhode Erbrink[2], Nikki Timmer[2], Charlotte van Rooijen[2], Sebastian Kieper[2], Verena Hehle[2], Astrid Vallès[2]*
[1] uniQure Biopharma BV, Oegstgeest, Netherlands
[2] uniQure Biopharma BV, Amsterdam, Netherlands

Synucleinopathies are neurodegenerative disorders characterized by aggregation of alpha-synuclein protein (α-Syn), encoded by the SNCA (Synuclein Alpha) gene. The α-Syn aggregates may spread in a prion-like manner, with toxic aggregated forms being transmitted from cell-to-cell as the disease progresses.
We are developing two complementary AAV-based gene therapy approaches targeting α-Syn pathology. First, is an engineered miRNA-based approach, using our miQURE® platform, where we lower SNCA mRNA and α-Syn protein levels. We have previously shown proof-of-concept (PoC) of our SNCA-targeting miQURE approach in relevant preclinical PD models. Second, is our AbQURE™ platform technology for expression and secretion of vectorized, α-Syn targeting antibodies. Finally, we have combined miQURE® and AbQURE™ approaches in our GoQURE™ platform, in which we express a SNCA targeting engineered miRNA and a α-Syn targeting antibody from the same construct. Here, we have established in vitro PoC for AbQURE™ and GoQURE™ platforms for synucleinopathies. Two different antibodies targeting the C-terminal part of α-Syn were successfully expressed in our AbQURE™platform (AbQURE-1 and AbQURE-2). Next, these antibodies were combined with our SNCA-targeting miQURE approach in the GoQURE™ platform (GoQURE-1 and GoQURE-2). Functional antibodies were expressed in the HEK293T and SH-SY5Y cells after transfection with the plasmids carrying either the AbQURE™ or GoQURE™ constructs. Both the cell extracts and the medium of the cells were analyzed for presence of total and functional antibodies using in-house developed MSD assays. Results show that 96% of the antibodies expressed are secreted efficiently into the medium of both HEK293T and SH-SY5Y cells. The AbQURE™constructs were further packaged into AAVs and functional antibodies were successfully expressed from an AAV-AbQURE™ after transduction in SH-SY5Y cells. Moreover, the SNCA-targeting miQURE encoded in the GoQURE™ constructs could also be expressed as well as the α-Syn-antibody.
The present in vitro PoM results show the potential of our GoQURE™ platform to express both a miRNA and an antibody from a single construct, to reduce intracellular α-Syn and target extracellular α-Syn aggregates, and ultimately decrease α-Syn toxicity in synucleinopathies.

LBP06.04

Establishing a Progenitor Cell Bank of iPSC-derived cells poised for neural differentiation for the Parkinson's research community

Michela Ilaria Barbato[*,1], Nicola J. Drummond[1], Yixi Chen[1], Karamjit Singh Dolt[1], Maurice A. Canham[1], Peter Kilbride[2], G. John Morris[2], Andrew Chai[1], Zhijun Wang[1], Tilo Kunath[1]*
[1] University of Edinburgh, Edinburgh, United Kingdom
[2] Cytiva, Cambridge, United Kingdom

Human induced pluripotent stem cells (hiPSCs) can be differentiated into diverse types of cells for disease modelling and cell replacement therapy. Although hiPSCs are widely used, they can be very difficult to reliably differentiate within the same laboratory, and across different laboratories. Furthermore, there are many laboratories with cell culture capabilities, but lack expertise in hiPSC differentiation. This restricts the use of hiPSCs to select laboratories with differentiation expertise.
Our solution to this problem is to differentiate hiPSCs into progenitor cells and cryopreserve them in a state where they are poised for differentiation. Cells are frozen down after passing the early critical stages of the differentiation protocol, and quality-control of the cryopreserved vials is performed before distribution to other labs. We have used alpha-synuclein triplication (AST) iPSC lines to generate an allelic series of isogenic CRISPR-engineered lines with knock-out deletions of the alpha-synuclein gene. These have been differentiated into midbrain dopaminergic (mDA) progenitor cells and cryopreserved. Quality-controlled progenitor cell collections are committed to their dopaminergic differentiation path and are ready to be applied for experimental studies in any laboratory with cell culture facilities. These mDA neural progenitors provide a source of cells for transplantation studies or of mature human dopaminergic neurons for different Parkinson's disease modelling applications.
We have focused efforts on producing mDA progenitor cells that are more than 80% double-positive for LMX1A/EN1 by immunostaining and greater than 90% CORIN-positive by flow cytometry. Upon transplantation, our cryopreserved mDA progenitors have successfully rescued the 6-OHDA lesion rat model of Parkinsion's, and they have been used to model neuroinvasive virus infections. We endeavour to provide the best quality neural progenitors to the academic community and facilitate user-friendly access to differentiated neuronal cells to help accelerate research and collaborations.

LBP06.05

Diverging progression of synucleinopathy in mouse models of Parkinson's disease and multiple system atrophy

Anna Barber Janer[*,1], Eline Vonck[1], Chris Van den Haute[1], Ariel Louwrier[2], Vicky Marie Myhre[2], Jacob Alec McPhail[2], Veerle Baekelandt[1], Wouter Peelaerts[3]*
[1] Laboratory for Neurobiology and Gene Therapy, Department of Neurosciences, KU Leuven, Leuven, Belgium
[2] StressMarq Biosciences Inc., Victoria, Canada
[3] Laboratory of Virology and Gene Therapy, Department of Pharmaceutical Sciences, KU Leuven, Leuven, Belgium

Synucleinopathies are a heterogeneous group of neurodegenerative diseases that include Parkinson's disease (PD) and multiple system atrophy (MSA). The histopathological hallmark of synucleinopathies are insoluble aggregates of the protein alpha-synuclein (αSyn). In PD, these aggregates are mostly found in neurons, termed Lewy Bodies (LBs), whereas in MSA they are enriched in oligodendrocytes, termed glial cytoplasmic inclusions (GCIs). Current transgenic and viral vector-mediated animal models are based on the overexpression of αSyn and recapitulate several key features of synucleinopathies. However, so far it is unclear how the cellular environment might be responsible for the aggregation of conformation-specific assemblies and neuropathology during disease progression. We and others recently discovered that seeding oligodendrogliopathy with αSyn fibrils generates conformationally-restricted and unique fibrillar inclusions in vivo. We now further expand on these findings and investigate the progressive development of synucleinopathy in PD and MSA using recombinant αSyn pre-formed fibrils (PFFs) on a matched host background. To model PD, naïve C57BL/6 mice were injected with mouse PFFs in the striatum. For MSA, naïve C57BL/6 mice were co-injected with mouse PFFs and an adeno-associated viral vector expressing mouse αSyn in oligodendrocytes but not in neurons. Each model developed a distinct phenotype with the MSA model displaying a more aggressive phenotype, pronounced motor

disturbances with neuronal loss, neuroinflammation and brain atrophy. Both models present widespread transmission of αSyn pathology. Seeded aggregation of αSyn with oligodendroglial tropism has synergistic effects on neuropathology. These results suggest that synucleinopathy develops progressively after seeding and that the cellular environment contributes to disease progression. These animal models can be useful to study serial transmission of synucleinopathy and provide a valuable tool for preclinical research of PD and MSA.

LBP06.17

Functional and neuropathological changes induced by injection of distinct alpha-synuclein strains: A pilot study in non-human primates

Audrey Fayard[*,1], Alexis Fenyi[1], Sonia Lavisse[1], Sandra Dovero[2], Luc Bousset[1], Tracy Bellande[1], Sophie Lecourtois[1], Christophe Jouy[1], Martine Guillermier[1], Caroline Jan[1], Pauline Gipchtein[1], Benjamin Dehay[2], Erwan Bezard[2], Ronald Melki[1], Philippe Hantraye[1], Romina Aron Badin[1]*
[1] CEA, Fontenay-aux-Roses, France
[2] Université de Bordeaux, Bordeaux, France

Synucleinopathies like Parkinson's disease (PD), Dementia with Lew body, or Multiple system atrophy (MSA) are characterized by the aggregation of the pre-synaptic protein alpha-synuclein (α-syn). In PD, these pathological forms of α-syn are constituents of large neuronal inclusions called Lewy bodies (LB). Many studies have demonstrated that α-syn aggregates can amplify by recruiting new monomers, spread from cell to cell, and propagate in and outside the brain in a prion-like manner in vitro and in vivo.
α-Syn is a highly dynamic protein. The many conformational states this protein populates allow it theoretically to aggregate into fibrillar assemblies that possess distinct structures and surfaces. These properties could explain the heterogeneity within synucleinopathies.
Recent rodent data demonstrate that the injection of different α-syn fibrillar strains called "fibrils" (FIB) and "ribbons" (RIB) into the rat SN or striatum, lead to a strain-specific propagation of α-syn pathology and pathogenic phenotype.
Here, we bilaterally injected FIB (n=1) and RIB (n=1) α-syn strains in the putamen of NHPs and compared them to patient-derived LB extracts (n=1) as a proof of concept study. The functional impact of the different α-syn inocula on glucose metabolism was assessed longitudinally in vivo for 18 months using [18F]-FDG PET imaging. Post-mortem analysis included TH immunocytochemistry to detect nigrostriatal alterations and quantification of phosphorylated α-syn at Ser 129 and aggregated α-syn to assess seeding propensity of the various α-syn inocula.
In vivo results revealed a decrease in glucose metabolism more pronounced in the RIB-injected animal. Histology showed a decreased number of dopaminergic tyrosine hydroxylase-positive cells in the SN to different extents according to the inoculum used. Biochemistry revealed that α-syn -induced aggregation, phosphorylation, and propagation in different brain regions are strain-specific.
Overall, our findings show that α-syn strains can induce distinct functional alterations and changes in the nigrostriatal pathway that resemble early-stage PD in the NHP.

LBP06.24

Early-life Parkinson's-related behavioural changes in neonatal Lrrk2 knock-in mice

David J Harrison, Fatima M Sheikh, Dayne A Beccano-Kelly*
Cardiff University Dementia Research Institute, Cardiff, United Kingdom

Non-motor signs of Parkinson's (PD) commonly occur before the more-recognised locomotor symptoms that prompt clinical diagnosis. Changes in olfaction and speech are often identified in people with Parkinson's (PwP) prior to diagnosis. These signs are commonly cited by PwP as impacting negatively on daily life. Prodromal manifestation of non-motor signs could be indicative of underlying early neurological pathology and present an opportunity to identify early intervention points to slow disease progression.
Olfaction and aspects of speech are regulated by the basal forebrain cholinergic system and olfactory bulb – brain regions found to be affected in early-stage PD. The same systems are associated with olfaction and vocalisation in mice. The current project uses a Lrrk2 knock-in (KI) mouse PD model to probe changes in these behaviours. These mice carry a G2019S point mutation in the Lrrk2 gene, identified in most common forms of familial and sporadic PD. PwP with LRRK2 G2019S mutations exhibit age of symptom onset and patterns of pathology typical of the majority of PD cases.
Neonatal male and female LRRK2 KI-/+ and wildtype (WT) littermates were assessed between postnatal days two and ten by measuring vocalisation and olfaction using ultrasonic call recordings and homing tests, respectively.
We show that at 2 days old, LRRK2 KI-/+ pups make a greater number of calls and have an increased maximum individual call length when compared to their WT littermates. Female, but not male, LRRK2 KI-/+ mice were unable to locate home-cage bedding by olfactory detection at 10 days old. Further analysis of physiological changes at these ages is ongoing.
These results demonstrate the earliest observed behavioural disruption in a PD model. Furthermore, the data are suggestive of a developmental component to PD, and highlight target areas for early intervention which may alter subsequent disease progression.

LBP06.31

Characterization of the GBA1 E326K mutation in Parkinson's disease progression and its impact on neuroinflammation and α-synucleinopathy

Sangjune Kim[*,1], Sin Ho Kwoen[2], Hye Guk Ryu[1], Hyeonwoo Park[1], Saebom Lee[3], Namshik Kim[4], Han Seok Ko[2]*
[1] Chungbuk National University, Cheongju, South Korea
[2] Johns Hopkins University School of Medicine, Baltimore, Maryland, United States
[3] Korea Advanced Institute of Science and Technology, Daejeon, South Korea
[4] CTX Co., Ltd, Daejeon, South Korea

Mutations in GBA1 gene are recognized as the common genetic risk factor for developing Parkinson's disease (PD). Hetero- and homozygous GBA1 mutations reduce its enzymatic activity, which may lead to lysosomal dysfunction and increased α-synuclein (α-syn) levels. Although most studies focus on the role of GBA1 in promoting synucleinopathy, a prominent pathological change due to GBA1 deficiency could be neuroinflammation. To investigate the molecular mechanism involved in GBA1 deficiency-mediated neuroinflammation, we have developed the GBA1 E326K knock-in (KI) mouse by CRISPR/Cas9 system, which has been identified to confer a risk for PD and dementia with Lewy body (DLB). We found a mild reduction of GBA1 enzymatic activity, accumulation of

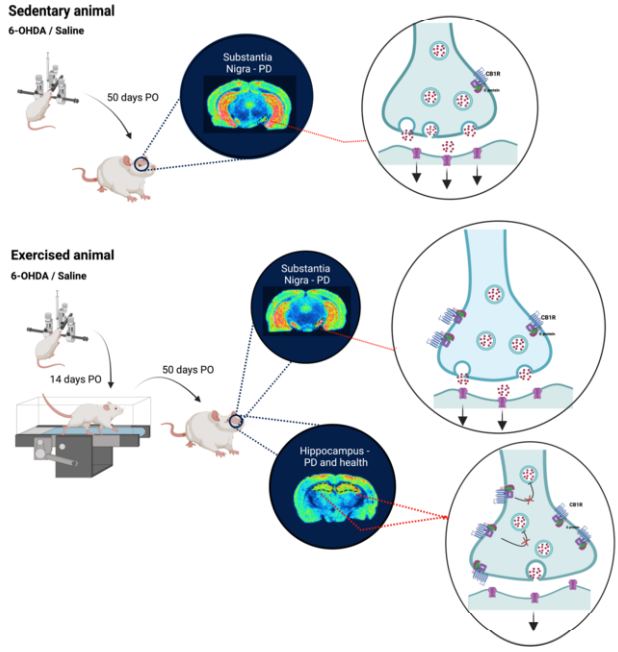
glucosylceramide, and increases of microglia density in the ventral midbrain and hippocampus of 24-month aged GBA1 E326K KI mice. In addition, we also found the higher levels of pro-inflammatory cytokines in primary microglia from GBA1 E326K KI mice by treating pathologic α-syn preformed fibrils (PFF). Moreover, PFF inoculation into the gut of GBA1 E326K KI mice induced a massive deposition of Lewy body in dentate gyrus of hippocampus accompanying with neuroinflammation. This investigation will enhance our understanding of the role of GBA1 E326K mutation plays in neuroinflammation and cell-to-cell transmission of pathological α-syn in the brain, and lead to new therapeutic strategies.

LBP06.46

Treadmill exercise modulates nigral and hippocampal cannabinoid receptor type 1 in the 6-OHDA model of Parkinson's disease

Karina Henrique Binda[1], Anne Marlene Landau[1], Marucia Chacur[2], David J Brooks[3], Caroline Real Gregorio[,1]*
[1] Aarhus University, Aarhus, Denmark
[2] Universidade de Sao Paulo, Sao Paulo, Brazil
[3] University of Newcastle upon Tyne and Aarhus University, New Castle, United Kingdom

Physical exercise is a non-pharmacological tool and has been shown to have the potential to decrease the symptoms of Parkinson's disease (PD) patients but the mechanism is unclear. The endocannabinoid system is altered in PD.
We test the hypothesis that cannabinoid receptor type 1 (CB1R) binding, known to be reduced in PD cases, is normalized by treadmill exercise in the 6-OHDA rat model of PD.
Male rats (n=20) had unilateral striatal injections of 6-OHDA or saline. After 15 days, half were submitted to light treadmill exercise and half remained sedentary (4 groups). The animals were submitted to a mechanical nociceptive threshold test, since pain is a common PD symptom. Autoradiography with [3H]SR141716A, a specific radioligand to CB1R, was performed in postmortem tissue from striatum, substantia nigra (SN) and hippocampus.
There was a 41% decrease of [3H]SR141716A binding in the ipsilateral SN of 6-OHDA-injected sedentary animals (P=0.0018) which was attenuated to 14% by exercise (P=0.43). The CB1R binding in SN also revealed a correlation with nociceptive threshold data (R2=0.48, P=0.0008). No differences were observed in striatum (P=0.8622). A bilateral increase of 30% in hippocampus was observed in both groups of exercised animals (P<0.0001). For each group, 5 animals were included.
Chronic exercise can reduce the detrimental effects of PD on nigral CB1R binding, similar to the reported reduction after dopamine replacement therapy, so should be considered as an adjunct therapy for PD, without side effects in long-term. In addition, treadmill exercise enhances hippocampal CB1R binding in healthy and PD-lesion animals. Future studies are necessary to further investigate the region-specific effects of exercise and the differential findings in healthy vs parkinsonian rats.



LBP06.50

Alpha-synuclein aggregate pathology in the cranial sensorimotor system in a mouse model of Parkinson's disease

Allison Schaser[,1], Brooke Rodgers[1], Vivek Unni[2]*
[1] Purdue University, West Lafayette, IN, United States
[2] Oregon Health & Science University, Portland, OR, United States

Purpose: Voice deficits are common in Parkinson's disease (PD) and significantly impact quality of life. However, despite their impact, there are currently no treatments that target the underlying pathophysiology of PD in the cranial sensorimotor system. The goal of this study was to examine the effect of a potential underlying mechanism responsible for the complex voice deficits that exist in PD, aggregation of the protein alpha-synuclein.
Methods: An alpha-synuclein transgenic mouse model with a fibril seeding approach was used in this study. This model leads to more rapid development of pathology and allows for the study of the propagation of abnormal alpha-synuclein over long distances throughout the cranial sensorimotor system in an efficient and disease-relevant manner. Sixteen transgenic mice and 13 wild-type control mice have initially been analyzed in this preliminary study. Mice of each genotype were assigned to either fibrillar (experimental) or monomeric alpha-synuclein (control) injection into the striatum. Baseline and post-injection acoustic measurements of rodent ultrasonic vocalizations were acquired.
Results: A genotype difference was found at baseline. Transgenic mice called significantly more than wild-type mice prior to injection [t=3.506(27), p = 0.0016], indicating that overexpression of the human A53T mutation alone results in a change in vocal communication. Following injection, at the 2-month post-injection time point, all animals called significantly less than at baseline regardless of their genetic background or type of injection [F(1,25) = 187.8, p = 0.0001]. Analyses of objective vocalization characteristics, later timepoints, and additional mice with injections into the laryngeal musculature is ongoing.

Conclusions: Results depict the development of a mouse model that allows for manipulation of alpha-synuclein within discrete areas of the cranial sensorimotor system and enables the analysis of relevant vocalization behaviors. Results provide a critical foundational understanding of the role of aggregated alpha-synuclein in voice deficits in PD. Future work will continue to refine the mouse model to develop disease-modifying treatments to reduce or eliminate the burden of PD-specific voice disorders.

LBP06.52

Use of in-vitro cell-models and fluorescent protein markers for understanding amyloid-related diseases

Priyanka Swaminathan[*,1], Marikken Sundnes[1], Benedikte Emilie Vindstad[1], Odrun A. Gederaas[1], Mikael Lindgren[1], Therése Klingstedt[2], Ebba Hellstrand[2], Per Hammarström[2], Sofie Nyström[2], K Peter R Nilsson[2], Nathalie Van Den Berge[3]*

[1] Norwegian University of Science and Technology, Trondheim, Norway

[2] Linköping University, Linköping, Sweden

[3] Aarhus University, Aarhus, Denmark

Neurodegenerative disorders are characterized by pathological misfolding of certain proteins into insoluble aggregates known as amyloids, which leads to progressive degeneration of neurons. Build-up of such insoluble amyloid aggregates is known as amyloidosis and is characteristic to many neurodegenerative disorders, including Parkinson's disease (PD) and Alzheimer's disease (AD) or systemic transthyretin amyloidosis and iatrogenic insulin amyloidosis. Emerging evidence suggest that there seems to exist heterogeneity among patients with these disorders. Strikingly, the cellular milieu in which the amyloidogenic protein tends to form aggregates, is also known to influence its molecular architecture, which is linked to protein function and disease representation. Therefore, we aim to use in-vitro cell-models to understand the conformation, and protein-specific amyloid pathology in the cellular milieu. In-vitro models involving cell-lines could provide the physiological microenvironment that is critical in understanding the pathology of each specific molecular conformation of amyloids in relation to the cellular milieu.

Amyloid can be characterized by various protein characterization techniques; however, their precise detection can be very challenging owing to the differences in their intrinsic structures and the cellular environment in which they form aggregates. Here, we aim to use ultra-sensitive luminescent conjugated oligothiophene (LCO) protein aggregate markers that would give distinct spectral information upon binding to various amyloid fibrils, upon exposure of the cell models to various amyloid fibrils. Our primary objective is to assess whether LCO can be used to report on amyloids in in-vitro living systems, secondly, we also aim to investigate the physiological impact of amyloids on basic cellular functions. Here we first demonstrate on how SH-SY5Y and HEK293 cells when exposed to in-vitro TTR amyloid together with the LCO HS336 and a fluorescent congo red derivative, X34 are able to cross the cell membrane. In Figure 1, provisional results are shown with stained amyloids that are within HEK293 and SH-SY5Y together with typical both spectral and time-resolved fluorescence signals.This research approach opens a new gateway to understanding various conformation-specific pathology of amyloids in relation to cellular environment which could be valuable in early, as well as conformation-specific stratification of these amyloid-related disorders, especially when detected in easily accessible tissues or fluids.

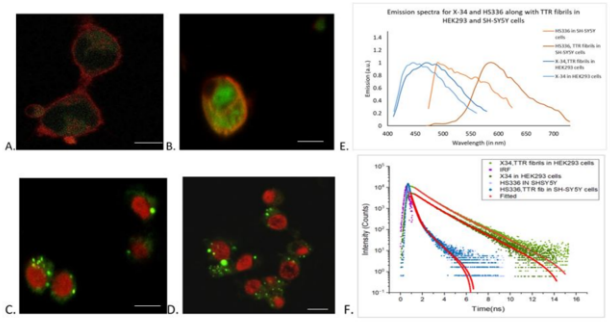


Figure 1: Confocal laser scanning microscope image, emission spectra and time-resolved fluorescent signals for X-34 and HS336 along TTR fibrils in HEK293 and SH-SY5Y cells. A): The red color shows the cell membrane (cell mask red) and the green spots within the cell membrane is the X-34 localization along with B) TTR fibrils in HEK293 cells. Scale bar represents 50µm.C. The red color shows the nucleus (DRAQ5) and the green spots across the cell is the HS336 localization along with D) TTR fibrils in SH-SY5Y cells. Scale bar represents 50µm. E,F : Emission spectra and time-resolved fluorescent day signals for X-34 and HS336 along with TTR fibrils in HEK293 cells and SH-SY5Y cells.

LBP06.53

Vaccination with a modified fungal prion mimicking conformational epitopes on alpha-synuclein fibrils extends survival in mouse models of Parkinson's disease

Verena Pesch[1], Sara Reithofer[1], Liang Ma[1], José Miguel Flores-Fernandez[2], Benedikt Frieg[1], Yannick Busch[1], Pelin Özdüzenciler[1], Gunnar Schröder[1], Holger Wille[2], Erdem Gültekin Tamgüney[*,3]*

[1] Institut für Biologische Informationsprozesse, Strukturbiochemie (IBI-7), Forschungszentrum Jülich GmbH, Jülich, Germany

[2] Department of Biochemistry & Centre for Prions and Protein Folding Diseases, University of Alberta, Edmonton, Alberta, Canada

[3] Heinrich-Heine-Universität Düsseldorf, Düsseldorf, Germany

Aims: Parkinson's disease (PD), dementia with Lewy bodies, and multiple system atrophy are neurodegenerative diseases that are caused by misfolding and aggregation of monomeric and soluble α-synuclein into oligomers and insoluble fibrils that are rich in cross-beta structure, toxic to neurons, and not naturally recognized by the immune system. Here we mutated the fungal protein HET-s to form fibrils that partially mimic α-synuclein fibrils, and vaccinated hemizygous TgM83 mice with them to induce immunity to pathologic α-synuclein species.

Methods: We structurally modified HET-s by mutagenesis to obtain four different fibrils each mimicking a specific conformational surface epitope of α-synuclein fibrils, and used these to immunize hemizygous TgM83 mice. Animals immunized with this quadrivalent vaccine were challenged with synthetic α-synuclein fibrils intracerebrally to model brain-first PD, and intraperitoneally or by injection into the gut wall to model body-first PD. Non-vaccinated mice challenged via the same three routes served as controls.

Results: Vaccination induced immune sera that recognized synthetic alpha-synuclein fibrils and brain homogenates of patients with PD and other synucleinopathies. Vacccination also extended the median survival of intracerebrally challenged mice from 158 to 166 d ($p < 0.05$), of intraperitoneally challenged mice from 223 to 271 d ($p < 0.01$), and of intragastrically challenged mice from 231 to 280 d ($p < 0.05$). Structural analysis by electron cryo-microscopy of the synthetic α-synuclein fibrils used to challenge the mice revealed that the vaccine candidates shared conformational surface epitopes present on the α-synuclein fibrils.

Conclusions: Here we show in mouse models of PD that immunization with a quadrivalent vaccine derived from the fungal protein HET-s has the potential to delay the onset of PD and other synucleinopathies.

LBP06.56

Super high resolution metagenomic identified novel targets associated with pathogenic changes in microbiome composition in a Parkinson's disease mouse model

Connor Wadsworth[*,1], Zizheng Xian[2], Nanthini Jayabalan[2], Kathrein (Kerry) Roper[3], Helen Woodhouse[3], Robert Adam[4], John O'Sullivan[4], Gene Tyson[2], Richard Gordon[2]*
[1] Centre for Microbiome Research, Brisbane, QLD, Australia
[2] Queensland University of Technology, Brisbane, Queensland, Australia
[3] Translational Neuroscience Laboratory, Brisbane, Queensland, Australia
[4] Royal Brisbane and Women's Hospital, Brisbane, Queensland, Australia

Parkinson's disease (PD) is a highly prevalent, progressive neurodegenerative disorder characterised by the selective loss of dopaminergic neurons. Manifesting as a debilitating spectrum of motor and non-motor deficits, the prodromal stage of PD is known to start as early as 20 years prior to the diagnosis of motor symptoms of PD. Recent evidence has strongly supported the role of gastrointestinal dysfunction and alterations in the microbiome as key prodromal features of PD pathology. The accumulation of phenylalanine and tyrosine has been linked with oxidative stress, neurological dysfunction and the progression of neurological diseases. Moreover, emerging evidence suggests that gut microbial metabolites such as phenylalanine are elevated in PD patient bloods and are associated with disease progression. We aimed to investigate and compare the gut microbiome composition in the A53T α-synuclein transgenic line (M83) between the young and aged mice. A high-resolution metagenomic shotgun analysis was performed on the faecal samples (n=8 Tg, n=6 WT) at both time points to investigate the changes in the gut microbiome which could potentially reflect the behavioural or neurological phenotypes. Furthermore, metabolomic analysis was performed on the faecal samples to correlate with the changes observed in the metagenomic analysis of the aged mice. Using liquid-chromatography mass spectrometry, we determined the significant alteration of metabolomic signatures in faecal samples, these were investigated to play a role in PD-related metabolic pathway variations such as phenylalanine, tyrosine and tryptophan biosynthesis. Consistent with these findings, the metagenomic analysis highlighted an altered diversity in the microbiota between WT and Tg mice models with an increase in the BCAA-producing bacterial species and enzymatic pathways. A novel target of the M83 late-stage mouse metagenomic analysis findings, Akkermansia muciniphila lineages show specific enrichment of enzymes associated with phenylalanine and tyrosine biosynthesis and metabolism. Consistent with literature our data confirmed the increase of circulating levels of L-Tyrosine and L-Phenylalanine and metagenomic analysis established key alterations in microbiome composition between the wild type and M83 transgenic mice. This suggests an increased propensity to produce pathogenic microbial metabolites such as L-Tyrosine in the gut of the PD mouse model due to gut dysbiosis which can contribute to PD pathology and progression.

LBP06.59

Development of an alpha-synuclein targeting vectorized antibody strategy: First in vivo proof of mechanism in wild type mice

Seyda Açar Broekmans, Rhode Erbrink, Charlotte van Rooijen, Lukas Schwarz, Meriem Bourajjaj, Kim Wolzak, Verena Hehle, Astrid Vallès*
uniQure Biopharma BV, Amsterdam, Netherlands

Synucleinopathies are neurodegenerative disorders characterized by aggregation of alpha-synuclein protein (α-Syn), encoded by the SNCA (Synuclein Alpha) gene. Alpha-synuclein is expressed in the brain and also peripherally in red blood cells. In the diseased brainα-Syn can form aggregates, which might spread in a prion-like manner, with toxic aggregates spreading as the disease progresses. In this regard, facilitating the clearance of α-Syn aggregates outside of the cell may have therapeutic potential by reducing the spread and slowing or halting disease progression. Hence, passive immunization with α-Syn-targeting antibodies is in focus of many ongoing preclinical and clinical studies. The main challenge of administering α-Syn antibodies peripherally is for them to pass through the blood-brain barrier to perform their function. Additionally, α-Syn antibodies will bind to α-Syn that is abundant in the blood resulting in a sudden decrease in their bioavailability. Lastly, repeated injections is needed for a sustainable antibody therapy, which can lead to anti-drug antibody formation.
We are developing specific α-Syn vectorized antibodies, using our AbQURE™ technology platform, to provide a stable supply of α-Syn antibodies in the brain. Full length α-Syn antibodies AbQURE-1 and AbQURE-2, targeting the C-terminal of α-Syn, were successfully expressed in our AbQURE™ platform, both from a plasmid and from an AAV (AAV-AbQURE-1 and AAV-AbQURE-2). We established proof of mechanism (PoM) in wild type mice after direct brain administration of the vectorized antibodies. In this study, we showed a dose-dependent expression of the antibodies in the brain, using both biochemical and histological methods. Detection of antibodies with in-house developed MSD assays showed functional antibody expression in the striatum. This was confirmed by immunohistochemical methods. No safety concerns were reported in the pathological examination of the Hematoxylin and Eosin (H&E) staining of the treatment groups compared to the negative control group.
Present data demonstrates a safe and efficacious expression of specific α-Syn antibodies using our proprietary AbQURE™ platform. As a follow up, efficacy of anti-α-Syn antibodies to reduce the α-Syn spreading will be evaluated in relevant disease models in the context of therapeutic application to synucleinopathies.
AbQURE is a trademark registered in the European Union and United Kingdom and pending in other jurisdictions.

BASIC SCIENCE: Dopamine, receptors, and other neurotransmitters

LBP08.01

Imaging the noradrenergic system in Parkinson's disease: A [11C]Yohimbine PET and neuromelanin MRI study

Chloé Laurencin[1], Sophie Lancelot[2], Marine Huddlestone[3], Sarah Brosse[4], Inès Merida[5], Nicolas Costes[5], Jérôme Redouté[5], Didier Le Bars[5], Stéphane Thobois[1], Philippe Boulinguez[4], Bénédicte Ballanger[,4]*

[1] Department of Neurology C, Expert Parkinson Centre, Hospices Civils de Lyon, Pierre Wertheimer Neurological Hospital, NS-Park/F-CRIN, Bron, France
[2] Centre de Recherche en Neurosciences de Lyon - Hospices Civils de Lyon - Cermep, Bron, France
[3] Hospices Civils de Lyon, Bron, France
[4] Centre de Recherche en Neurosciences de Lyon, Bron, France
[5] Cermep, Bron, France

Objective: To assess two aspects of the noradrenergic system using multimodal in vivo imaging in a sample of Parkinson's disease (PD) patients and healthy controls (HC): the pigmented cell bodies of the locus coeruleus (LC) with neuromelanin sensitive MRI and the α2-adrenergic receptors (ARs) density with [11C]yohimbine PET [Laurencin et al., 2021].
Background: Degeneration of the noradrenergic system is nowadays considered as a pathological hallmark of PD [Paredes-Rodriguez et al., 2020]. In addition, both antiparkinsonian and neuroprotective properties of the noradrenergic system have been suggested [O'Neill & Harkin, 2018]. Yet, the therapeutic strategies targeting this system in PD are still currently limited as knowledge in the noradrenergic system in vivo are scarce.
Methods: 30 PD patients and 30 HC age- and gender-matched subjects were included. [Table 1]
Results: A reduction in [11C]yohimbine binding in PD patients compared to HC was observed in widespread cortical regions encompassing the parietal lobe, the posterior cingulate cortex (PCC), the temporal and occipital cortex as well as the motor cortices (FWE cluster level, $p<0.05$). In parallel, PD patients showed a reduced signal intensity in LC compared with HC ($p<0.001$). Interestingly, worse performances in executive functioning within the PD group were correlated with a decrease in LC signal intensity (e.g. TMTB-A: r=-0.46), and an increase in [11C]yohimbine binding within specific areas including the right pre- and post-central gyrus and occipital cortex (r=0.38). We also showed that both higher anxiety and depressive symptoms were associated with reduced [11C]yohimbine binding in the left PCC (r=-0.32 and -0.51 respectively) and the right inferior frontal gyrus (r=-0.37 and -0.38 respectively). Finally, the loss of pigmented neurons in the LC was negatively correlated with motor impairments (e.g. UPDRS-III: r=-0.48).
Conclusions: Our results support the existence of substantial PD-related declines in the integrity of the noradrenergic system and highlight its role in the PD pathophysiology. In particular, the decline of LC signal intensity was associated with both executive and motor impairments while the decrease in [11C]yohimbine binding was mainly associated with the magnitude of depressive, anxious and executive symptoms.

Table 1 – Demographics and clinical characteristics of participants

	Healthy controls	Parkinsonian patients	Statistical significance
N (F/M)	30 (12/18)	30 (12/18)	
Age	60.3 (8)	60.1 (7.5)	ns*
Parkinson's disease characteristics			
Disease duration (years)		6.5 (4)	
LEDD (mg/day)		1006 (703)	
Hoehn & Yahr		1.8 (0.4)	
PDQ-39		39.6 (22.1)	
MDS-UPDRS I		8.5 (5.1)	
MDS-UPDRS II		7.1 (4.3)	
MDS-UPDRS III		17.7 (12.3)	
MDS-UPDRS IV		2.3 (3)	
General Cognition			
MOCA	27.9 (1.5)	27.9 (2)	ns§
Memory			
DST-B (working memory)	4.8 (1.4)	4.3 (1.3)	ns§
TFR (episodic memory)	32.1 (5.8)	28.7 (6.6)	**<0.05**§
Executive functioning			
TMTB-A	38.2 (39.8)	65.8 (71.9)	**<0.005**§
Stroop color-word	111.1 (32.7)	128.7 (35.2)	**<0.05**§
Depression			
BDI-II	3 (3.2)	10.5 (6.8)	**<0.001**§
Anxiety			
STAI-A	28.8 (8.5)	34.1 (10.1)	**<0.05**§
STAI-B	29.8 (8.5)	36.8 (9.3)	**<0.01**§

Note. Data are presented as mean (SD). Abbreviations: MoCA, Montreal Cognitive Assessment; MDS-UPDRS, Movement Disorder Society-sponsored revision of the Unified Parkinson's disease Rating Scale; DST-B, Digit Span Test Backward; TFR, Total Free Recall; TMT, Trail Making Test; *Parametric test (Student's t-test); §non-parametric test (Wilcoxon test).

LBP08.08

Pathway dysfunction in dopamine transporter associated parkinsonism and comorbid psychiatric disease

Jamila Lilja, Ulrik Gether, Freja Herborg*
Department of Neuroscience, University of Copenhagen, Copenhagen, Denmark

Dysfunctional dopaminergic neurotransmission is implicated in several pathologies, including movement disorders such as parkinsonism and psychiatric disorders.
More than 25% of patients diagnosed with neurodegenerative disorders display psychiatric comorbidities, suggesting overlapping cellular mechanisms and diseases associated pathways. The dopamine transporter (DAT) is a key regulator of spatiotemporal dopamine signalling by mediating reuptake. Rare disease-associated DAT variants have been shown to cause early-onset parkinsonism, and DAT is implicated in the aetiology of several psychiatric diseases such as ADHD, bipolar disorder, and depression.
Recently, our lab described a patient with atypical dopamine transporter deficiency syndrome who carries two DAT loss of function mutations. The patient is diagnosed with early onset neurodegenerative parkinsonism and ADHD, thus creating an interesting link between parkinsonism and psychiatric disorders. Based on this patient, a novel construct valid mouse model (DAT-I312FxD421N+/+) that replicates the patient's genotype has been established. The DAT-I312FxD421N+/+ mouse model presents with a psychomotor phenotype recapitulating core aspects of parkinsonism and ADHD such as clasping, loss of striatal terminal density, and hyperactivity.
This study revolves around the DAT- I312FxD421N+/+ mouse model and investigates if genetic insults to DAT can trigger parkinsonism disease-associated pathways such as oxidative stress, mitochondrial dysfunction, protein homeostasis, and neuroinflammation. We conducted a qPCR screen targeting pathological pathways and identified interesting changes in the gene expression levels of Park1, Park2, and Gfap in the dorsal striatum of DAT-I312FxD421N+/+. Immunoblotting furthermore suggests an interesting increase of oxidative stress in the midbrain of DAT-I312FxD421N+/+ and a decrease in oxidative stress in the striatum of DAT-I312FxD421N+/+.

BASIC SCIENCE: Neuropharmacology

LBP09.04

A pilot study about the effectiveness of the high-dose donepezil in the cognitive function and neuropsychiatric symptoms in Parkinson disease with cognitive impairment

*Sang Jin Kim**
Department of Neurology, Busan Paik Hospital, Inje University, Busan, South Korea

Background: Donepezil have been known to the symptomatic treatment of Alzheimer's disease (AD), dementia with Lewy bodies (DLB) and Parkinson's disease (PD) with dementia. Donepezil also dose-dependently improved abnormal behavioral and psychological symptoms of dementia in AD and DLB. We analyzed whether 23 mg/day group would be more effective than the donepezil 10 mg/day group for both cognitive functions and neuropsychiatric symptoms in PD with cognitive impairment (CI).
Methods: Ten patients diagnosed as PD by the UK Brain Bank Criteria participated in the study. Cognitive functions of patients were adequate to the criteria for major and minor neurocognitive disorders. Among all patients already taking the donepezil 10 mg/day, 3 patients increased the dosages to 23 mg/day and then maintained them for 24 weeks. Seven of 10 patients continued the dose at 10 mg/day for 24 weeks. The Korean version of mini-mental status examination (K-MMSE), Korean version of Montreal Cognitive Assessment (K-MoCA), and caregiver administered neuropsychiatric inventory (NPI) were examined at the baseline and 24 weeks.
Results: Compared to 23 mg/day group, the donepezil 10 mg/day group showed younger age at onset and longer disease duration at the baseline. K-MMSE and K-MoCA were higher in 10 mg/day group than in 23 mg/day at the baseline. However, K-MMSE and K-MoCA of donepezil 23 mg/day group after 24 weeks were much more improved than those of donepezil 10 mg/day. In eight patients performed the NPI, mood disorders (depression, anxiety, apathy) were frequently appeared at both baseline and 24 weeks, contrast to the psychosis (delusion and hallucination).
Conclusion: Compared to the donepezil 10 mg/day, donepezil 23 mg/day was dose-dependently more effective to the cognitive function in PD. Total scores in NPI showed a worse tendency in 10 mg/day group after 24 weeks, despite a younger age and not severe parkinsonism compared to 23 mg/day group. Because psychosis was frequent in PD with dementia, high rates of mood disorders and low rates of psychosis is associated with the PD-CI in this study.

BASIC SCIENCE: Electrophysiology and functional imaging, optogenetics

LBP10.01

The modulation of subthalamic beta bursts during task execution underlies deep brain stimulation related motor improvement in Parkinson's disease

Manuel Bange[*,1], Gabriel Gonzalez-Escamilla[1], Damian Marc Herz[1], Gerd Tinkhauser[2], Alek Pogosyan[3], Martin Glaser[1], Dumitru Ciolac[1], Christian Dresel[1], Huiling Tan[3], Peter Brown[3], Sergiu Groppa[1]*
[1] University Medical Center of the Johannes Gutenberg-University Mainz, Mainz, Germany
[2] University Hospital and University of Bern, Bern, Switzerland
[3] University of Oxford, Oxford, United Kingdom

Background: Deep brain stimulation of the subthalamic nucleus is an evidence-based effective therapy for people with Parkinson's disease. The stimulation-related modulation of transient, burst-shaped beta oscillations has been suggested to play a considerable role for clinical symptom alleviation. However, if modulations of such bursts relate to an improved execution of voluntary, fine, and prolonged movements like drawing, remains unclear. Therefore, we here investigated subthalamic nucleus beta burst dynamics during spiral drawing in patients undergoing deep brain stimulation surgery.
Methods: We recorded subthalamic nucleus local field potentials in 19 externalized people with Parkinson's disease to investigate the role of beta bursts for spiral drawing. Drawing was performed with and without the application of deep brain stimulation to examine if the modulation of beta bursts improved drawing velocity. A blinded movement disorder specialist assessed the motor part of the Unified Parkinson's disease rating scale (UPDRSIII) to rate clinical impairment. Beta burst amplitude and duration were calculated during rest and task execution.
Results: Despite the reduction of beta band power in the subthalamic nucleus induced by drawing, bursts appeared. Task-related bursts showed reduced amplitude and duration in comparison to bursts at rest. Application of clinically effective, electrical high-frequency stimulation accelerated drawing, and reduced beta burst amplitude both at rest and during task execution. Stimulation-related modulations of burst amplitude correlated with clinical improvement of the drawing hand.
Conclusions: Deep brain stimulation modulates not only bursts that occur during rest but also during task execution. Reductions in burst amplitude might underlie stimulation-related increases in movement speed in people with Parkinson's disease, as manifested in faster drawing and alleviated motor symptoms. Our results suggest that beta bursts occurring during task execution could play an important role for voluntary, precise, and prolonged movements like drawing. Because beta bursts were suggested as a promising biomarker for adaptive deep brain stimulation, task related modulations need to be considered in the development.

COMPREHENSIVE CARE: Caregiving, relationships, respite care, families

LBP12.13

The meaning of caregiving for people with Parkinson's Disease: A hermeneutic study of non-family Muslim caregiver in New Zealand

Martyarini Budi Setyawati[*,1], Bobbi Laing[2], Chistantie Effendy[3], Andrew Lynch[2], John Parson[2]*
[1] School of Nursing, Faculty of Medical and Health Sciences, The University of Auckland, Auckland, New Zealand
[2] The University of Auckland, Auckland, New Zealand
[3] Gadjah Mada Unuversity, Yogyakarta, Indonesia

Muslim caregivers bring their own understanding and perspectives of their role and its meaning. This meaning significantly impacts their capacity to cope with their challenging roles. Understanding their perspectives and how this contributes to developing effective intervention is needed to support their role as informal (unpaid/voluntary) caregivers of people with Parkinson's Disease. The literature on caregiving within the Muslim religion and spiritual context is diffuse, and no systematic explanation or definition within the Muslim community has yet emerged. Thus, this research aims to explore the meaning of caregiving to a person with Parkinson's Disease, which Muslim caregivers voluntarily do. A hermeneutic phenomenological methodology was used in this study. Recruitment

was by snowball sampling, and four voluntary Muslim caregivers who were not blood relatives of PwPD consented to participate. These were all first-generation immigrants to New Zealand. The data was gathered through the in-depth interview before being analysed in an appropriate manner. The result revealed that, firstly, the caregiver interpreted their caregiving activity as an expression of piousness that reflected their religious commitment and hope of God's (Allah) promise of future reward. Secondly, it was seen as an act of humanity demonstrating piety, kindness, and empathy. The meaning that caregiver brought were intertwined with their respective cultural values and belief, which were influenced by their belief system, previous caregiving experiences, personal coping strategies based on their own life event and their encounter and learning from other cultures. These findings highlight the need to fully understand what meaning caregivers bring to their role. Furthermore, enable practical support to be developed for the community so the program would be culturally and spiritually appropriate for people with Parkinson's Disease and their caregiver. Further research is required to understand the meaning of caregiving for Muslim voluntary caregivers who come from various ethnicities and non-immigrant statuses and care for people with Parkinson's Disease.

COMPREHENSIVE CARE: Exercise and physical activity

LBP13.02

Exercise and physical activity promotion after a Parkinson's diagnosis: a UK survey of healthcare professionals

Ledia Alushi[*,1], *Peter Hartley*[2], *Louise Lafortune*[3]
[1] Univeristy of Cambridge, Cambridge, United Kingdom
[2] Department of Physiotherapy, Cambridge University Hospital NHS Foundation Trust, Cambridge, United Kingdom
[3] Cambridge Public Health, Interdisciplinary Research Centre, Cambridge, United Kingdom

Background: Healthcare professionals (HCPs) are pivotal to promoting physical activity (PA) and exercise and to supporting people newly diagnosed with Parkinson's (PwP) become more active. There is, however, limited guidance on what the content of such interventions should be.
Objectives: To explore current practice, perspectives and confidence of HCPs working with PwP around exercise and PA promotion.
Methods: A survey for HCPs working with PwP in the UK was disseminated through social media and professional councils from July 2021-December 2021.
Results: 189 HCPs took part in the survey: 30 doctors, 19 nurses, 137 physiotherapists, two speech and language therapists and one occupational therapist. All nurses, 99% of physiotherapists and 72% of doctors always promote exercise and PA during clinic appointments. However, 52% of doctors and 41% of nurses agree they lack confidence in prescribing exercise to PwP. Although signposting to support groups is identified as one of the seven-core topics in PA promotion, 76% of doctors only sometimes, or rarely, provide this information. Assessing PA levels, barriers to participation, and signposting to support groups are mainly addressed during physiotherapy appointments. Referrals to physiotherapy most frequently occur when PwP experience falls or mobility issues, rather than at the time of diagnosis.
Conclusion: There is agreement within disciplines that PA and exercise education is important for newly diagnosed PwP. The seven-core topics identified by HCPs can inform and guide the design of a discipline-wide framework to aid the development of interventions that systematically and effectively promote PA in newly diagnosed PwP. Future research should also focus on providing practical training for HCPs working with PwP to address some of the barriers identified and enhance PA promotion for PwP.

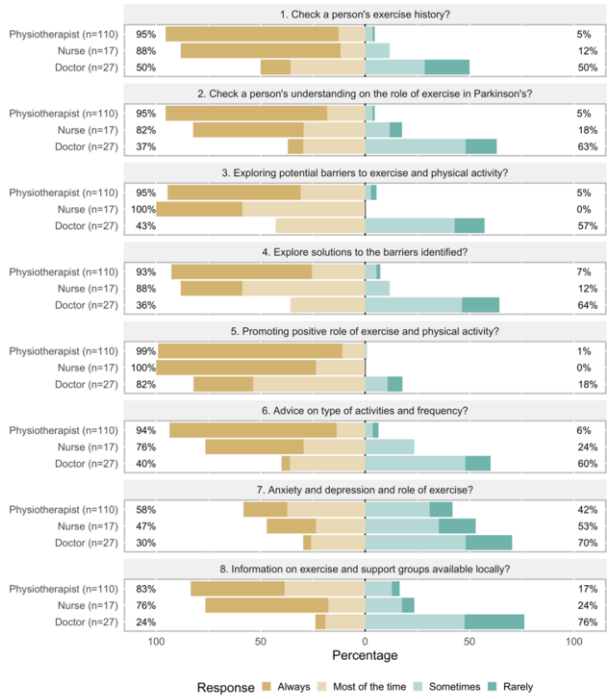


Figure 1: Physical activity promotion during a typical clinic appointment

LBP13.31

Do people with Parkinson's disease in daily life do, what they can do in the clinic? Exploring the "can do, do do" conceptual framework

Sabine Schootemeijer[*,1], *Kirsten de Laat*[2], *Nienke de Vries*[2]
[1] Radboudumc, Nijmegen, Gelderland, Netherlands
[2] Radboud university medical center, Department of Neurology, Center of Expertise for Parkinson & Movement Disorders, Nijmegen, Netherlands

Background: People with Parkinson's disease (PwPD) are less physically active and often have a lower physical capacity than healthy individuals of similar age. We aimed to investigate the association between physical activity and physical capacity in PwPD. Furthermore, we explored a framework applied in people with chronic obstructive pulmonary disease ("can do, do do" framework). Applying this framework may give a better understanding of the nature of the impairments in physical functioning in PwPD.
Methods: We included data from 221 PwPD (Hoehn and Yahr ≤ 3) who took less than 7,000 steps at baseline in the STEPWISE interventional study (NCT04848077). Physical activity (daily step count) was measured with the STEPWISE app over a four-week period. Physical capacity was determined in-clinic with a six-minute walking test (6MWD). We determined the relation between physical activity and physical capacity with linear regression. We classified participants to one of four quadrants based on physical capacity (more or less than 70% of predicted 6MWD) and physical activity (more or less than 5000 steps/day). Clinical characteristics of the

four quadrants ("can't do, don't do", "can't do, do do", "can do, don't do" and "can do, do do") were compared with analyses of variance, Kruskal-Wallis and Chi-square tests.
Results: We found a small, significant relation between physical activity and physical capacity in PwPD (r=0.21, p<0.001). Thirty-three PwPD (14.9%) were classified to the "can't do, don't do", 18 (8.1%) to the "can't do, do do", 100 (45.3%) to the "can do, don't do" and 70 (31.7%) to the "can do, do do" group. Disease duration, medication use, Movement Disorder Society-Unified Parkinson's Disease Rating score (MDS-UPDRS; total score, item II and III), balance, comfortable gait speed and fear of falling differed significantly between the four quadrants.
Conclusions: We showed a weak association between physical activity and physical capacity. Several clinical characteristics differed between the four "can do, do do" quadrants. Insight in these quadrants might aid in the understanding of the level of impairment of the PwPD and inform personalized treatment.

COMPREHENSIVE CARE: Health accessibility/underserved populations

LBP19.02

Transforming Parkinson's disease education & care: Engaging & addressing American Indian & Alaskan Native communities
Somil Bhushan[*1], Peery White[2], Sarah Osborne[1]*
[1] Parkinson's Foundation, New York, NY, United States
[2] Strengthening Native Connections, Norman, OK, United States

Background: The Department of Health and Human Services (HHS) characterizes underserved populations as members of minority populations or individuals who have experienced health disparities, including American Indian and Alaskan Natives (AIAN)1. AIAN populations have endured historical trauma, systemic racism, and a lack of funding and access to health care services. The Parkinson's Foundation established an initiative to understand the needs of AIAN individuals and to improve health education delivery to better address Parkinson's disease (PD). To our knowledge, there are no other nationwide approaches on building AIAN relationships to increase accessibility to PD resources.
Objectives: Objectives involved providing comprehensive educational programs to build understanding of PD, community outreach at tribal health conferences to build relationships with health providers and representatives, and promoting awareness of PD resources from the foundation to increase quality of life for people with PD.
Methods: The Parkinson's Foundation and tribal health consulting firm Strengthening Native Connections created a PSA for PD awareness in April 2022, facilitated through GoodHealth TV across Indian Health Service (IHS) facilities and tribal health clinics. Educational webinar programs were developed as a recurring resource on the topics of understanding PD, hospital safety with PD, and caregiving and PD. Participation in National Indian Health Board served to create a working relationship with health providers and representatives, increasing awareness and accessibility of Parkinson's Foundation educational tools and health care resources such as the "Aware in Care" hospital safety kit.
Results/Outcomes: 56 IHS facilities and tribal health clinics broadcasted the Parkinson's awareness PSA. Live educational webinars throughout 2022-2023 yielded 81 participants who had not previously engaged with the Parkinson's Foundation. Active participation in AIAN health conferences led to connections with 54 individuals across 32 tribes. This corresponded to the shipment of 273 "Aware in Care" kits and 17 educational books in locations where resources had previously not been distributed.
Conclusion: The Parkinson's Foundation and Strengthening Native Connections will continue to build a roadmap to address PD education across AIAN populations and advance health equity for underserved populations.
Citations:
[1] HHS guidance submissions. HHS Guidance Submissions | Guidance Portal. https://www.hhs.gov/guidance/. Accessed March 30, 2023.

LBP19.07

Comprehensive survey data set of women with Parkisnon's by women with Parkinson's
Soania Mathur[1], Kristi Lamonica[2], Kat Hill[3], Helen Matthews[4]
[1] PD Avengers, Ajax, ON, Canada
[2] PD Avengers, Troy, NY, United States
[3] PD Avengers, Portland, OR, United States
[4] Cure Parkinson's, London, United Kingdom

The paucity of research and treatment guidelines for women with Parkinson's has led to suboptimal management of this condition and likely accounts for the poorer health-related quality of life seen in this group. There is some evidence, particularly anecdotally that PD symptoms and medication efficacy vary with the menstrual cycle as well as the hormonal status of women at different points of their lives.
To address the unmet needs of women with Parkinson's disease throughout their changing hormonal life stages, the Women and PD Working Group of the PD Avengers collaborated with the Michael J. Fox Foundation to create a series of surveys Investigating women's health, hormones, menstrual history, and pregnancy. These surveys were deployed in Fox Insight, an online longitudinal health study of people with and without PD.
The questionnaire was disseminated on the Fox Insight online platform with the first questionnaire exploring preventive care that women should receive for optimal health and the impact of this neurodegenerative disease on home, family, occupation and independent living. Data addressing how this disease impacted respondents' perception of themselves was recently published. In the article, "Self-Image in Women with Parkinson's Disease", we found that 62% of women reported a negative internalized stigma.
It is our intention to bring all data to date to the WPC in Barcelona. Other findings include and confirm our hypotheses that women are not being asked questions by their MDS, or neurologists, regarding hormones and menstruation (79%) are reluctant to ask due to fear of being dismissed, lack of time, or lack of knowledge (~50%). We hope that these comprehensive surveys will provide the background information, or data, needed to begin bridging the gaps.
Gender specific medicine can help to inform individualized care and enhance the quality of life of women with Parkinson's disease.

COMPREHENSIVE CARE: Self-management, empowerment, coping strategies

LBP22.01

"It's such a basic instinct to walk, but ..." People with Parkinson's experience using compensation strategies to improve walking

Sheemah Alenezi[*1], Sarah Morgan-Trimmer[1], Sophia Hulbert[2], William Young[1], Victoria A Goodwin[1]*
[1] University of Exeter, Exeter, United Kingdom
[2] Plymouth University, Plymouth, United Kingdom

Background: There is a growing body of research on the use of compensation strategies by people with Parkinson's. However, little is known about what factors may influence the use of these strategies and the challenge of adapting them in everyday life. This study aimed to explore the experiences of people with Parkinson's using compensation strategies to improve their walking.
Methods: Semi-structured online interviews were conducted with people with Parkinson's in the United Kingdom and the United States. Interviews were digitally recorded and transcribed verbatim. Transcripts were coded inductively and analysed thematically.
Results: 11 people with Parkinson's (three female and eight male) participated with a mean age was 64.81 years (SD= 9.83), and the mean duration of Parkinson's was 8.8 years (SD= 3.73). Three themes were developed from the data. The first theme, 'Willing to cope with walking difficulties', reflects how participants created their own strategies to cope with walking difficulties even though they had not received physiotherapy to help their walking. Although participants had the motivation to use compensation strategies, adapting these strategies to daily life situations was not always easy. The second theme, 'Managing higher environmental challenges', discusses the interaction between physical and psychosocial aspects that influenced these strategies and the surrounding environment. Participants perceived it as hindering and impacting their ability to start or carry over using strategies. Although participants had the motivation to use compensation strategies and create them themselves, along with managing walking in challenging environments, there was a varying level of the maximum benefit of compensation strategies that enabled participants to adapt them in daily life. The third theme, 'Adapting in light of perceived support', discusses the ability to adapt compensation strategies related to the received support (i.e. access to physiotherapy).
Conclusion: The varying level of support and motivation, willingness, and aspirations to use compensation strategies impact the participant experience. These findings could help tailor compensation strategies in gait rehabilitation for people with Parkinson's. Further research is needed to understand better the complex interaction between physical and psychosocial aspects to help PwP adapt compensation strategies more effectively in their environment.

COMPREHENSIVE CARE: Multidisciplinary/interdisciplinary teams

LBP23.09

Integrated care for Parkinson's disease: An international practice survey

Jennifer L. McGinley[*1], Jennifer G. Goldman[2], Nabila Dahodwala[3], Laura Brennan[4], Joan Gardner[5], David Grimes[6], Robert Iansek[7], Addie Patterson[8], Norbert Kovacs[9], Ariela Hilel[10], Sotirios Parashos[11], Maria Elisa Piemonte[12], Bastiaan R. Bloem[13], Carsten Eggers[14], Roopa Rajan[15]*
[1] The University of Melbourne, Melbourne, Australia
[2] JPG Enterprises LLC, Medical Division, Chicago, Illinois, United States
[3] Department of Neurology, Perelman School of Medicine, University of Pennsylvania, Philadelphia, Pennsylvania, United States
[4] Genomind, King of Prussia, Pennsylvania, United States
[5] Struthers Parkinson's Center, Park Nicollet Health Services, Golden Valley, United States
[6] Ottawa Hospital, University of Ottawa Brain and Mind Research Institute, Ottawa, Ontario, Canada
[7] Clinical Research Centre for Movement Disorders and Gait, Monash Health, Cheltenham, Australia
[8] Department of Neurology, Norman Fixel Institute for Neurological Diseases, University of Florida Health, Gainesville, Florida, United States
[9] Department of Neurology, University of Pécs, Pécs, Hungary
[10] Movement Disorders Unit, Neurological Institute, Tel-Aviv Medical CenterIsrael, Israel
[11] Struthers Parkinson's Center, Park Nicollet Health Services, Tel-Aviv, Minnesota, United States
[12] University of Sao Paulo, Medical School, Physical Therapy, Speech Therapy and Occupational Therapy Department, Golden Valley, Brazil
[13] Radboud University Medical Centre; Department of Neurology, Sao Paulo, Netherlands
[14] Department of Neurology, University Hospital Marburg; Center for Mind, Brain and Behavior, Universities Gießen & Marburg, Nijmegen, Germany
[15] All India Institute of Medical Sciences, Marburg, New Delhi, India

Background: Access to multidisciplinary integrated care is vital for people with Parkinson's Disease (PD). Although randomised trials and a meta-analysis suggest efficacy of integrated care over usual care, the real-world practices remain unknown.
Objective: We aimed to describe current practices for integrated care for PD worldwide.
Methods: Between November 2020 - December 2020, we conducted a two-stage online survey. A screening survey and detailed care practice survey developed by the Integrated Care Task Force of the International Parkinson's and Movement Disorders Society (MDS) were emailed to MDS members. Integrated care was defined as a movement disorder specialist and ≥ 2 other disciplines and/or extending across care settings.
Results: A screening survey identified 350 centres (Figure 1); 248 (71%) offered integrated PD care. Details of the service were reported by 96 (39%) centres from 41 countries, with the majority from the USA and Europe (60%). In a typical year, 58% treated over 40 people who had been diagnosed with PD within the past six months. Most centres had coordinators (83%) and reported multiple disciplines involved in PD care; the median number in the team was 4 (IQR: 2-6). The most frequently included disciplines (>90%) were neurologists, physician assistant/nurse practitioners, and social workers; with physical therapists, occupational therapists, speech

therapists, clinical psychologist/neuropsychologists, psychiatrists in >70% of teams. Multidisciplinary team meetings were held in the majority of centres (78%), with most meeting at least monthly (66%). Most centres shared care plans with patients and families (66%). Most clinics offered telehealth; 72% offered phone visits and 63% offered video visits. Less than 5% of clinics offered home visits.
Advanced therapies were available in > 80% of centres; deep brain stimulation (68%), levodopa-carbidopa intestinal gel (65%), subcutaneous apomorphine (63%) and apomorphine continuous infusion (38%). Almost all centres (86%) collected information for research or quality of care assessments, with around two-thirds of centres providing feedback to clinicians about adherence to clinical guidelines. Only one third of centres had not reviewed their centre performance data (e.g., patient satisfaction) within the last six months.
Conclusion: This survey highlights current practices in integrated care provided by a group of specialised PD centres worldwide.

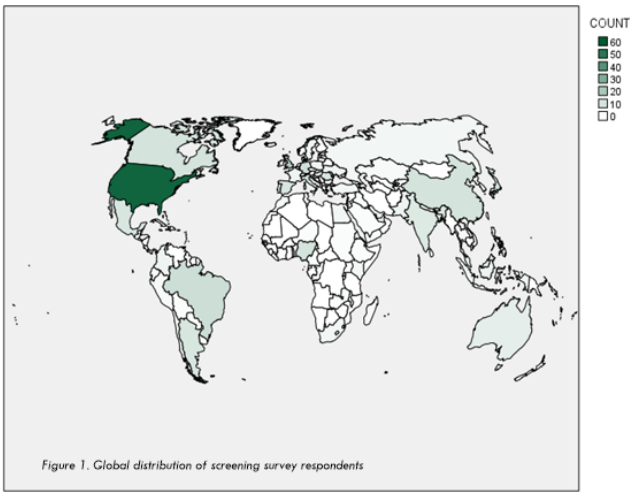


Figure 1. Global distribution of screening survey respondents

COMPREHENSIVE CARE: Digital health, E-health and technology

LBP24.01

Exploring people with Parkinson's disease's experiences of online exercise groups in the UK – a qualitative study
James Alexander[*,1], Caroline Appel[2], Yiota Constantinou[1], Anette Schrag[3]*
[1] St George's University, London, United Kingdom
[2] Central & North West London NHS Foundation Trust, London, United Kingdom
[3] University College London, London, United Kingdom

Background: Online group exercise is popular for people with Parkinson's disease (PwP) with the COVID-19 pandemic creating a step change in online exercise group provision for this population. To improve equity of access to exercise, online exercise classes could form a larger part of future healthcare services. Little is known about the experiences of PwP and how this could inform future online group exercise delivery.
Objective: To explore the experiences of PwP who have utilized online exercise groups in managing their condition.
Methods: A qualitative study utilizing semi-structured interviews and thematic analysis. A purposive sample of PwP who have participated in a live online exercise group.
Results: Five females and four males participated (mean age 69.5 years range 63-78, mean disease duration 9.1 years, range 3 years to 20 years). Analysis revealed four overarching themes: 'Opportunities and challenges to online exercise groups' which related to concepts of adapting to online exercise programmes and how the online format can offer greater access to exercise; 'Role of exercise for Parkinson's disease' which incorporated individuals' rationale for participating in an online exercise group; 'Setup and structure' incorporating the planning and organization of the class; and finally 'Online exercise groups: are they worth it?' which incorporated constructs related to the value of online exercise groups.
Conclusions: Participants found transitioning to online exercise groups manageable allowing for continued self-management of physical activity. Holistic health-related benefits reported included maintenance of physical ability as well as improved mental health and well-being. Participants valued the flexibility that online exercise groups provide but recognized that there may be people who need support to access online groups and that technology issues such as poor internet connection can impede groups from being effective. With the ending of COVID-19 restrictions the integration of both in-person and online exercise groups in a hybrid format may offer greater opportunities for PwP to manage their symptoms through physical activity. Hybrid formats may offer greater equity of access for PwP to manage their condition through physical activity.

LBP24.07

Different speech biomarkers for tremor and motor coordination in Parkinson's disease — Implications for remote disease severity monitoring
Ebru Baykara[*,1], Louisa Schwed[1], Johannes Tröger[1], Nicklas Linz[1], Juan Rafael Orozco-Arroyave[2]*
[1] Ki-elements GmbH, Saarbrücken, Germany
[2] GITA Lab, Universidad de Antioquia, Medellín, Colombia

An essential goal of clinical research on Parkinson's Disease (PD) is to identify patients in the early stages, track disease progression and treatment response while minimising costs and patient burden. Recent studies have demonstrated that speech is one of the areas affected early and consistently by PD pathology. With advancements in speech technology and easy data collection methods, speech has emerged as one of the most promising digital biomarkers for PD.
This research uses audio recordings of a sustained phonation (SP) and a diadochokinetic (DDK) task from the PC-GITA data set. 50 PD and 50 healthy controls (HC) were recorded in a sound-proof laboratory environment (lab set) and another 20 PD and 20 HC in a more real-world environment for validation (real-world set).
We extracted acoustic features using the ki:elements library. We then trained classifiers to differentiate between PD and HC in two scenarios using SP and DDK features and report the best performing classifier. First, the classifiers are trained on the lab set using leave-one-out-cross validation (LOOC) with feature selection limited to 10 features. Next, the same classifier is evaluated additionally in the real-world set.
In the lab set the classifier based on SP could best differentiate PD patients from healthy controls with an AUC of .85. However, in the real-world set the same best-performing classifier performed significantly worse than the DDK classifier (Table 1).
For better understanding, we looked into the clinical characteristics of the correctly classified PD patients from both classifiers in the real-world data set. For the SP classifier, patients had a lower MDS-

UPDRS-III score and shorter time since diagnosis as compared to the DDK classifier.
Our results show that detecting PD remotely with minimal patient burden is feasible. We explored the discriminative capabilities of commonly used speech tasks in PD. The findings indicate that (1) recording environment affects SP features more than DDK features, (2) automatically extracted speech features from SP and DDK measure distinct motor aspects. Moreover, SP features appear to be more sensitive in early stages of the disease, while DDK features are stronger in later stages. Optimizing a feature combination from both tasks can enhance PD detection.

Table 1: Results of the classification experiments. LOOCV = Leave-One-Out-Cross-Validation, ACC = Accuracy, AUC = Area Under Curve, SENS = Sensitivity, SPEC = Specificity.

	LOOCV lab set					Hold out real-world set			
	Model	ACC	AUC	SENS	SPEC	ACC	AUC	SENS	SPEC
Sustained phonation features (SP)	Random forest, 9 features	0.82	0.85	0.82	0.82	0.5	0.44	0.65	0.35
Pa-Ta-Ka features (DDK)	SVM, 3 features	0.64	0.7	0.54	0.74	0.63	0.9	0.25	1.0

LBP24.13

Patient experiences and working alliance in a decentralized, online trial of cognitive behavioral therapy for depression in PD.

Aleksander H. Erga[*,1], Guido Alves[1], Albert Leentjens[2]*
[1] Norwegian Centre for Movement Disorders, Stavanger University Hospital, Stavanger, Norway
[2] Maastricht University Medical Center, Maastricht, Netherlands

Introduction: Depressive symptoms are common in people with Parkinson's disease (PwP). These non-motor symptoms have profound effects on quality of life and activities of daily living of PwP, and contribute to increased caregiver burden. In later years, psychological therapies, like cognitive behavioural therapy (CBT), have showed promising results for across several clinical trials. One of the hallmark benefits of CBT is the possibility to tailor the intervention specifically to the individual PwP, and ensure PwP engagement in the therapy itself. However, despite the documented benefits and cost-efficiency of CBT for neuropsychiatric symptoms in PD, few PwP are offered this line of treatment. The general lack of CBT-therapists within neurological outpatient clinics in general, and in rural areas in particular, is most likely a contributing factor, resulting in differences in available treatment options depending on where the PwP is located. Thus, development of novel, online, evidence based therapeutic strategies is called for.
Method: The ePark-study is an online, randomized, delayed start trial of the effectiveness of eCBT for PwP with depressive symptoms. N=120 PwP with depressive symptoms will be recruited from outpatient clinics and via self-referral in Norway, and randomized into two arms: (A) immediate 10-weeks eCBT with concurrent TAU and (B) a delayed start (14 weeks) of eCBT with TAU alone. PwP will be assessed at baseline before allocation to a specific treatment arm, with follow-up evaluations after 14, 28 and 42 weeks.
Here, we present preliminary data from the N=10 first participants of the trial, with emphasis on participant reported experiences and the establishment of working alliance in an online therapeutic setting. Participant reported experiences was measured using a six item questionnaire, scored on a visual analogue scale anchored with ''not at all'' to ''very much''. The questionnaire is comprised of six question indices: (1) interesting, (2) easy to understand, (3) useful, (4) extent to which the intervention provided novel information, (5) satisfaction, and (6) relevance. Working alliance was measured using the Working Alliance Inventory (WAI), a 12-item questionnaire evaluating the working alliance between participants and the CBT-therapist.
Results: The results will be presented at the congress.

LBP24.26

How can I help you? - Iterative design process of a chatbot for people with Parkinson's

Tessa Femke Peerbolte, Rozanne van Diggelen, Jacqueline Deenen, Pieter van den Haak, Bas Bloem, Nienke de Vries, Sanne van den Berg*
Radboud University Medical Centre, Department of Neurology, Center of Expertise for Parkinsons and Movement Disorders, Nijmegen, Netherlands

Background: The number of people with Parkinson's Disease (PwP) is rising enormously, resulting in a growing demand for healthcare services evoking increased pressure on the healthcare system. Given the increasingly scarce availability of health resources, the ability of PwP to inform themselves independently is crucial. Technology may assist PwP with finding, understanding, and using information to make health-related decisions and actions. Here, we studied the development of a chatbot for PwP to inform themselves independently.
Methods: An iterative human-centered design approach was used to develop a chatbot that fits the information needs and abilities of PwP. We used mixed methods (i.e., focus groups, think-aloud testing, and questionnaires) in three subsequent iterations with PwP (n=15) and carers (n=2). Requirements for the chatbot were identified within a focus group. The first prototype was assessed based on those requirements within another focus group session consisting of the same participants as before. Two consecutive prototypes were developed and tested with two subsamples of 5 end-users that had not been introduced to the chatbot before. Besides qualitative data, we also collected demographics, technological skills, attitudes, and usability (ease of use, perceived satisfaction, effectiveness, relevance, and tone of voice).
Results: Prototype 1 was built based on the results from the focus group. However, during testing, it failed all usability domains. Observed barriers were difficulties with typing and formulating questions. Prototype 2 was re-designed into a guided chatbot requiring users to choose between pre-defined options rather than typing their questions. In addition, prototype 2 directed users to other websites rather than providing information within the chat, with the advantage of integration with other information products and services. Prototype 2 passed all the usability domains.
Conclusions: The iterative design approach we took, helped develop a tool that fits the needs and abilities of a heterogeneous population of people, such as PwP. The results of this study will be used to further optimize the chatbot and design future studies to evaluate (cost-) effectiveness of this innovative tool that aims to improve the capabilities of PwP to inform themselves independently to make health-related decisions and actions.

LBP24.29

Accelerating physical therapy exercise monitoring through digital health technology for people with Parkinson's

Kevin Smaller[1], Bridget Fowler King[1], Kristen Hohl[1], Monica Hendricksen[1], Jillian MacDonald[2], Miriam Rafferty[,3]*
[1] Shirley Ryan AbilityLab, Chicago, IL, United States
[2] Barrow Neurological Institute, Phoenix, AZ, United States
[3] Shirley Ryan AbilityLab; Northwestern University, Chicago, Illinois, United States

While exercise is widely known to delay the progression of Parkinson's Disease symptoms, less than half of people with Parkinson's Disease meet the recommended 150 minutes per

week.1-5 Recent studies have shown that clinicians can use digital health technology (DHT) and behavior change interventions to help people with Parkinson's improve their exercise habits.6,7 This mixed methods study aimed to explore the potential for physical therapy to promote DHT use in patients with early Parkinson's disease who were referred to a low-dose consultative model of physical therapy. The hypothesis was that increasing DHT use would be associated with improving exercise and physical function measures. Eight outpatient physical therapists were educated on DHT use and encouraged to engage with the technology with 33 people with Parkinson's enrolled and 26 individuals completed the study to assess how incorporating DHT into physical therapy sessions and participant's daily life impacted their exercise and physical function. The patients were 64% male with an average age of 65±8 years and average baseline exercise vital sign of 230±139 minutes per week of exercise. After implementation, therapist documentation of aerobic frequency, aerobic intensity, strengthening intensity, and strengthening frequency improved ($p<0.05$). After 6 months, the number of participants that reported using DHT at least 5 days a week went from 34% (n=11) to 67% (n=18). However, this 6-month self-reported increase in DHT use was not sufficient to significantly increase self-reported number of minutes per week of exercise (post: 228±96, p=0.97), 6-Minute Walk Test (pre: 586±92 meters; post: 609.7±76 meters; p=0.06) or estimated VO2 (pre: 20.8±3.8 L/min; post: 20.3±3.1 L/min; p=0.66) in this active sample. Qualitative data suggests differential participant experiences aligned with personal characteristics: those with high comfort and familiarity with DHT were more enthusiastic compared to those with lower technology comfort. These findings suggest that physical therapist education and engagement can positively impact patient-reported use of DHT, but that more research is needed to determine measurable physical or psychosocial benefits of increased DHT use in people with Parkinson's.

COMPREHENSIVE CARE: Rehabilitation sciences (PT, OT, SLP)

LBP25.35

Proprioceptive training for upper limb deficits in people with Parkinson's disease: A systematic review with meta-analyses of randomised controlled trials

Kavinda Malwanage[1], Thusharika Dissanayaka[2], Natalie Allen[3], Serene Paul[,3]*
[1] University of Peradeniya, Kandy, Sri Lanka
[2] Monash University, Frankston, Australia
[3] The University of Sydney, Sydney, NSW, Australia

Introduction: Sensory impairments, including impaired proprioception, are common in people with Parkinson's disease (PD). Proprioceptive training improves somatosensory and sensorimotor function. This systematic review (PROSPERO registration CRD42021270774) aimed to determine the efficacy of proprioceptive training on hand dexterity, upper limb function and quality of life (QoL) in people with PD compared to other active interventions.
Methods: Medline PubMed, Cochrane library, CINAHL, PEDro and Web of Science databases were searched from inception to 16 February 2023. Randomised controlled trials (RCTs) of proprioceptive training conducted among people with idiopathic PD that were peer-reviewed English publications were included. All included studies were assessed for risk of bias and certainty of evidence using the Cochrane risk of bias tool Grading of Recommendations, Assessment, Development and Evaluations (GRADE) framework. Random effects meta-analyses were undertaken when ≥3 pairwise comparisons reported the same outcome.
Results: We retrieved 1332 articles from database searches, of which 32 records were included for full-text screening. Finally, eight RCTs were included in the systematic review, involving 344 people with mild to severe PD (Hoehn and Yahr stages I-IV) and age ranging from 40–83 years. From meta-analyses, there was very low certainty evidence that proprioceptive training improves dominant hand (standard mean difference (SMD) 0.34, 95%CI 0.08 to 0.60, p=0.01, 221 participants, 5 comparisons) and non-dominant hand (SMD 0.36, 95%CI 0.10 to 0.63, p<0.01, 221 participants, 5 comparisons) fine motor dexterity and dominant hand gross manual dexterity (MD 1.8, 95%CI 0.31 to 3.29, p=0.02, 125 participants, 5 comparisons) following 90-180 minutes/day, 2-5 sessions/week for 4-8 weeks of proprioceptive training. There was no evidence of effects on non-dominant hand gross manual dexterity, upper limb function and QoL following proprioceptive training.
Discussion: There were very low certainty evidence that proprioceptive training improves fine motor dexterity and dominant hand gross manual dexterity in the short-term. Future large RCTs should compare proprioceptive training with no intervention and perform comprehensive biomechanical analysis following proprioceptive training to gain a clearer idea of its effects. Further, incorporating longer duration proprioceptive training programs and obtaining frequent follow-up measures are also recommended to investigate the long-lasting effects in people with PD.

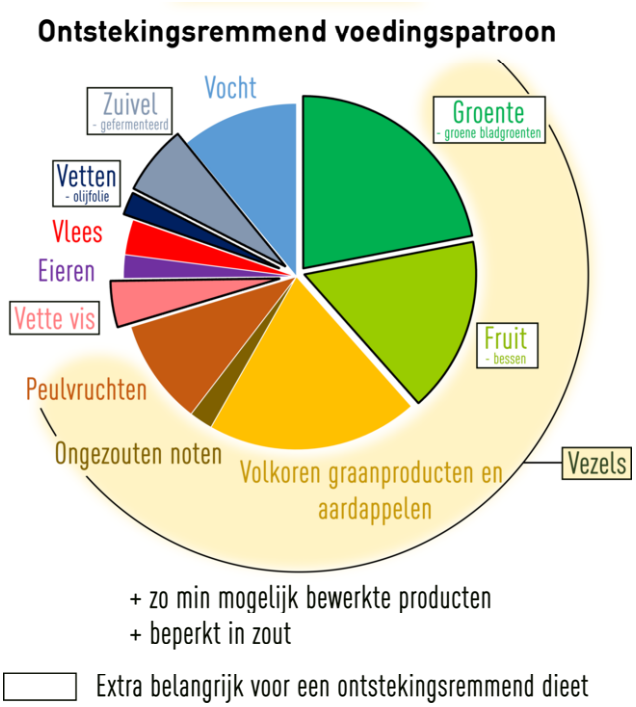
COMPREHENSIVE CARE: Nutrition and gastrointestinal issues

LBP26.07

Food for brain diseases; The development of the Brain Anti-Inflammatory Nutrition (BrAIN) Diet

*Ellen van den Oever**
Punt vor Parkinson, Groningen, Netherlands

Abstract: In several brain diseases, chronic low-grade inflammation plays a role that can be influenced by diet. So far, dietary guidelines for people with a brain disease are lacking. This review presents the current state of evidence regarding the potential effect of various food groups on (I) gut health (including microbial composition), (II) inflammation, and (III) symptoms in common psychiatric disorders (in particular schizophrenic spectrum disorders and bipolar disorder), and the most prevalent neurodegenerative diseases (Alzheimer's disease and Parkinson's disease). Based on this evidence the Brain anti-inflammatory Nutrition (BrAIN) diet was designed. The BrAIN diet contains a minimum of 30 grams of dietary fiber a day from fruits, vegetables, legumes, wheat, and wholegrain products. Furthermore, fatty fish, fermented dairy (such as yoghurt, kefir, and buttermilk), nuts, olive oil, herbs, and spices are recommended. In contrast, red meat, other dairy products, and sugar should be limited. Finally, ultra-processed foods, salt, alcohol, and sweetened beverages should be avoided. This comprehensive review is the first review to synthesize evidence regarding the gut- and immunomodulatory capacity of various food and beverage groups tailored to brain diseases.
Keywords: neurodegenerative diseases; psychiatric disorders; inflammation; gut microbiome; anti-inflammatory diet; food groups.



CLINICAL SCIENCE: Symptoms, signs, features & non-motor manifestations

LBP27.07

Alopecia in females with young onset Parkinson's disease: An exploratory survey

Kelsey Fisher[*,1], Erin Clifford[1], Nicholas Piniella[1], Dr. Rosemary Gallagher[2], Dr. Adena Leder[1]*

[1] New York Institute of Technology College of Osteopathic Medicine, Glen Head, New York, United States
[2] New York Institute of Technology (NYIT) Doctor of Physical Therapy Program, Old Westbury, New York, United States

Objective: To explore the symptoms of females with young onset Parkinson's Disease (YOPD), specifically alopecia, in comparison to females with traditional onset Parkinson's Disease (TOPD).
Background: Females with YOPD (age of diagnosis 21-50 years) display unique physio-psychosocial consequences compared to females with TOPD (age of diagnosis older than 50 years). YOPD progresses at a slower rate and is associated with more levodopa-related motor complications. Alopecia, or a loss of hair, is a rare symptom associated with Parkinson's Disease (PD) reported more often in females. While genetic studies have linked PD and alopecia, case studies implicate PD medications as a proposed cause in TOPD females. Alopecia can lead to anxiety and depression and searching for solutions increases stress. Despite anecdotal evidence, few studies exist that investigate alopecia in YOPD females. Therefore, the purpose of this study is to examine symptoms in YOPD females, with a specific focus on alopecia, compared to females with TOPD.
Methods: Following IRB approval, a custom, online survey investigating PD history, symptoms, and comorbidities was sent to a convenience sample of females with PD. Subjects were recruited from a YOPD female support group, Rock Steady Boxing classes, and the Riland Health Clinic at the New York Institute of Technology.
Results: Surveys were sent to 59 subjects; 33 responded (55.9% response rate) (mean age 52.2y, SD 6.37, 78.8% White). Twenty-six identified as YOPD. The mean age of YOPD diagnosis was 41.9 years. The most common presenting motor symptoms of YOPD females were tremor, poor handwriting, and stiffness. Nine of 26 YOPD females experienced alopecia (34.6%) compared to two of seven (28.6%) TOPD. Two of nine YOPD females (22.2%) stated that they experienced alopecia symptoms prior to PD diagnosis. Eight of nine YOPD females (88.9%) were taking PD medications when alopecia presented, most commonly levodopa (75.0%) [table 1]. Both TOPD subjects were taking levodopa when they experienced alopecia symptoms.
Conclusions: YOPD and TOPD females reported alopecia. Increased awareness of this condition among all females with PD may help guide clinicians during diagnosis, treatment and referral to mental health professionals. Limitations include a homogenous cohort and a small sample size of TOPD females.

Table 1. Reported Medications Associated with Onset of Alopecia

Subject with YOPD and Alopecia	Levodopa	Pramipexole	Amantadine	Rasagiline	Rotigotine Patch	Ropinirole
Respondent 6				X	X	
Respondent 8	X	X	X			
Respondent 9	X		X			
Respondent 13	X		X			
Respondent 17	X			X		
Respondent 18	X					
Respondent 20	X	X				
Respondent 33						X
TOTAL	6	2	3	2	1	1

CLINICAL SCIENCE: Progression & prognosis

LBP28.03

The prevalence of delirium and risk of mortality in hospital inpatients with Parkinson's disease

Florence Gerakios[*,1], Gemma Bate[2], Laura Wright[2], Daniel Davis[3], Blossom CM Stephan[4], Louise Robinson[2], Carol Brayne[5], Linda Barnes[5], Glenn Stebbins[6], John-Paul Taylor[2], David J Burn[7], Louise M Allan[8], Alison J Yarnall[2], Sarah J Richardson[2], Rachael A Lawson[2]*

[1] NHS / Newcastle University, Newcastle upon Tyne, United Kingdom
[2] Newcastle University, Newcastle, United Kingdom
[3] University College London, London, United Kingdom
[4] Nottingham University, Nottingham, United Kingdom
[5] University of Cambridge, Cambridge, United Kingdom
[6] Rush University Medical Center, Chicago, United States
[7] Newcastle University, Newcastke, United Kingdom
[8] University of Exeter, Exeter, United Kingdom

Parkinson's disease (PD) is a risk factor for delirium but reported inpatient prevalence varies widely across the literature and is often underreported. Delirium is a neuropsychiatric syndrome defined by an acute change in attention, level of arousal and cognition. It is associated with detrimental outcomes such as increased mortality,

dementia, and institutionalisation, although to date there are no comprehensive prospective studies in PD. In a prospective study of hospital inpatients, this research aims to report delirium prevalence in PD compared to older adults and examine the association with mortality.
All Participants from the 'Defining Delirium and its Impact in Parkinson's Disease' (DELIRIUM-PD) and the 'Delirium and Cognitive Impact in Dementia' (DECIDE) studies were included. People with PD (DELIRIUM-PD) or older adults from the Cognitive Function and Ageing Study II – Newcastle cohort (DECIDE) admitted to the Newcastle Upon Tyne Hospital Trust were approached to take part. Delirium was classified prospectively using the Diagnostic and Statistical Manual of Mental Disorders – 5th Edition criteria which takes account of observations, standardised testing and collateral history from informants and hospital staff. Date of death was determined by medical note reviews approximately 12 months post hospital discharge.
Participants comprised 121 PD participants and 199 older adult controls. Delirium was identified in 66.9% of PD participants compared to 38.7% of controls (p<.001). Significantly more PD participants with delirium died compared to those without delirium (46.9% vs. 15%, respectively, p<.001). PD participants with delirium had a significantly lower survival probability at approximately 12 months post hospital discharge compared to those without delirium (53.7% vs. 85%, respectively, p<.001) and controls with delirium (71.1%, p=.025). This increased risk of death remained when controlling for age, sex, clinical frailty, and dementia (HR=3.3 [95% CI 1.3-8.6], p=.014).
Delirium is more common in inpatients with PD compared to older adults without PD, with two thirds experiencing a delirium episode in hospital. People with PD who experience a delirium episode have a three times increased risk of mortality within one year of hospital discharge. Further research is essential to understand more about this risk and how to accurately identify, prevent and manage delirium in people with PD.

CLINICAL SCIENCE: Sleep disorders/ fatigue

LBP31.03

Prediction of treatment response and effect on clinical manifestations for Normal Pressure Hydrocephalus of sleep disorders

Ho-Won Lee, Ji-Ye Jeon*
Kyungpook National University Chilgok Hospital, Daegu, South Korea

Background/Aims: Sleep disorder and normal pressure hydrocephalus (NPH) are the issues of growing importance in neurological disorder. Yet, the correlation between the two diseases have not been studied enough. Thus, we discussed the correlation between sleep disorder and clinical features of NPH. **Methods:** Forty patients who visited Kyungpook University Hospital during 2020 and were diagnosed with idiopathic NPH were included in the study. To evaluate sleep disorder (excessive daytime sleepiness, sleep apnea, insomnia, poor sleep quality, morningness - eveningness, REM sleep behavior disorder and restless legs syndrome) and psychiatric problems (depression, anxiety), all patients carried out sleep surveys. To evaluate the severity of dementia and ataxia, all patients completed K-MMSE, K-FAB and UPDRS-motor score before and after CSF drainage. The Pearson's chi-square test, independent student's t-test, Mann-Whitney U test and linear regression analysis were applied to analyze the relationship between the sleep disorders and improvement of symptoms after CSF drainage. **Results:** Of the 40 patients, 21 had poor sleep quality, 8 had insomnia, 11 had daytime sleepiness, 9 to 13 had sleep apnea, 13 were anxious, 27 were depressed. Linear regression analysis showed that the sleep apnea was significantly correlated with cognitive function, and insomnia was correlated with cognitive, motor and frontal lobe functions. Also, patients with severe sleep apnea had a greater recovery of cognitive function after CSF drainage. **Conclusions:** Obstructive sleep apnea (OSA) is deeply related to the clinical symptoms and treatment effectiveness of NPH. Diagnosis and proper treatment of OSA is expected to improve the prognosis of NPH patients.

CLINICAL SCIENCE: Diagnosis (differential, accuracy)

LBP32.04

Which tests? Evaluation of bedside tests to identify delirium in Parkinson's disease

Rachael A Lawson[1], Sarah J Richardson[1], Florence Gerakios[1], Gemma Bate[1], Alison J Yarnall[1], Laura Wright[1], John-Paul Taylor[1], David J Burn[1], Louise M Allan[2], Glenn Stebbins[3]*
[1] Newcastle University, Newcastle upon Tyne, United Kingdom
[2] University of Exeter, Exeter, United Kingdom
[3] Rush University Medical Center, Chicago, United States

Background: Delirium is a serious, acute neuropsychiatric condition associated with fluctuating inattention, altered arousal and impairments of cognition. Delirium commonly occurs in Parkinson's disease (PD) and PD dementia (PDD) but is often missed in hospital due to overlapping clinical phenotypes. The current tools used to assess for delirium have not been validated in PD. Therefore, we aimed to evaluate the diagnostic accuracy of current tools to identify delirium in inpatients with PD.
Methods: People with PD admitted acutely or electively to all hospital wards in Newcastle were invited to take part. Delirium was classified using a standardised assessment based on the Diagnostic and Statistical Manual of Mental Disorders 5th Edition (DSM-5) criteria, comprising objective testing, observations and detailed collateral history (participants' family/carer, hospital staff). Participants were assessed daily for up to five days. We applied the 4 As Test (4AT, score≥4 indicated delirium), Confusion Assessment Method (CAM), the Single Question in Delirium (SQUiD), the Memorial Delirium Assessment Scale (MDAS, score≥13 indicated delirium) and the Delirium Rating Scale (DRS-R-98, score>15 indicated delirium). Measures were evaluated against the gold standard diagnosis (DSM-5 criteria) using Receiver Operating Characteristic area under the curve (AUC); sensitivity, specificity, and accuracy were calculated.
Results: Participants included n=115 people with PD (199 hospital admissions); 66.1% (n=76/115) had delirium. The diagnostic accuracy of tests was good, ranging from 74-89% (AUC=0.764-0.923, p<0.001 for all). The MDAS score had the highest AUC (AUC=0.923, p<0.001, MDAS≥13 sensitivity 78.5%, specificity 89.7%, accuracy 82.9%), followed by the 4AT score (AUC=0.922, p<0.001, score≥4 sensitivity 96.7%, specificity 73.1%, accuracy 87.4%).
Conclusions: Delirium is common in PD, affecting two thirds of participants. Current bedside tests can accurately identify delirium in PD inpatients. Although the MDAS was the most accurate tool, the 4AT may have better clinical utility as a screening tool with higher sensitivity and diagnostic accuracy; it is also quicker to complete and is already in widespread clinical use. However, caution is

recommended as tools did not differentiate between PD features and acute symptoms associated with delirium. A PD specific delirium measure may be helpful for future delirium management and clinical trials.

CLINICAL SCIENCE: Biomarkers and neuroimaging

LBP34.04

Prospective role of PAK6 and 14-3-3γ as biomarkers for Parkinson's disease

Elena Giusto[*,1], Lorenza Maistrello[2], Lucia Iannotta[3], Veronica Giusti[4], Ludovica Iovino[5], Rina Bandopadhyay[6], Angelo Antonini[4], Luigi Bubacco[4], Rita Barresi[2], Nicoletta Plotegher[4], Elisa Greggio[4], Laura Civiero[7]*

[1] San Camillo Hospital IRCCS, Iido-Venezia, Italy
[2] San Camillo Hospital IRCCS, Venice, Italy
[3] Institute of Neurosciences , CNR, Istituto clinico Humanitas, Rozzano (Milan), Italy
[4] University of Padua, Padua, Italy
[5] IRCCS Stella Maris foundation, Pisa, Italy
[6] Reta Lila Weston Institute of Neurological Studies, UCL Queen Square Institute of Neurology, London, WC1N 1PJ, UK, London, United Kingdom
[7] University of Padua and San Camillo Hospital IRCCS, Padua and Venice, Italy

Diagnosis of Parkinson's disease (PD) mainly relies on the clinical examination of patients' motor symptoms, which typically start to appear when a considerable portion of dopaminergic neurons in the substantia nigra pars compacta is lost and nigrostriatal connectivity is irreversibly damaged. This late diagnosis and the consequent delay in the pharmacological treatment may in part explain why neuro-restorative/protective therapies have been failing so far in PD. Here, we aim at exploring whether PAK6 and/or 14-3-3γ can work as novel biomarkers for the diagnosis of PD, since we have previously shown that PAK6 and 14-3-3γ protein interact with and regulate the activity of LRRK2, a kinase associated with both familiar and sporadic forms of the disease. After an initial quantification of PAK6 and 14-3-3γ expression by means of Western blot in post-mortem human brains, we verified the presence of the two proteins in plasma by using quantitative ELISA tests. We analysed samples obtained from 39 healthy subjects, 40 patients with sporadic PD, 50 LRRK2-G2019S non-manifesting carriers and 31 patients with LRRK2-G2019S PD. The amount of PAK6 and 14-3-3γ is significantly different in patients with PD compared to healthy subjects. Moreover, the amount of PAK6 also varies with the presence of the G2019S mutation in the LRRK2 gene, although generalized linear models show a low association between the presence of PD and PAK6.
Altogether, our data suggest that PAK6 and the 14-3-3γ/PAK6 ratio can provide a useful indication to discriminate PD patients from healthy controls and in the future they may contribute to the formulation of a panel of biomarkers for the diagnosis of PD.

LBP34.09

The Synuclein-One study: Detection of cutaneous phosphorylated alpha-synuclein for the diagnosis of the synucleinopathies

Todd Levine[*,1], Christopher Gibbons[2], Jade Stohl[1], Bailey Bellaire[1], Roy Freeman[2]*

[1] CND Life Sciences, Scottsdale, Az, United States
[2] Beth Israel Deaconess Medical Center, Boston, MA, United States

Objectives: The Synuclein-One study is an NIH-funded 31-site, multicenter trial of 425 patients with Parkinson's disease (PD), dementia with Lewy bodies (DLB), multiple system atrophy (MSA), pure autonomic failure (PAF) and healthy controls. The study was designed to describe the sensitivity, specificity, accuracy and precision of cutaneous phosphorylated alpha-synuclein detection in patients with synucleinopathies.
Background: An important unmet need exists for a validated, well-characterized, simple, reproducible marker of synuclein pathology. The number of individuals with neurodegenerative diseases continues to grow and misdiagnosis within and among synuclein and non-synuclein pathologies continues to occur, resulting in incorrect medication choices, iatrogenic complications, poor prognostication and patient frustration.
Methods: After signing informed consent, all participants completed detailed assessments including medical and neurological history review, structured neurological examinations (MDS-UPDRS, Hoehn and Yahr scale), cognitive evaluation (MOCA), RBD questionnaire, orthostatic hypotension signs and questionnaire, MSA red flags and Parkinson's Disease Questionnaire-39. Skin biopsies at the distal leg, distal thigh and posterior cervical sites were performed on all participants. All clinical data were reviewed by a blinded expert consensus panel to confirm the referring diagnosis or move the subject to an 'indeterminate' category. Blinded parallel pathological analysis of the biopsies was performed at CND Life Sciences and Beth Israel Deaconess Medical Center. Phosphorylated alpha-synuclein deposition was quantified by 2 readers at each site, blinded to referring diagnosis and results of the other reader.
Results: As of the preparation of this late breaking abstract, the complete unblinded results have not been fully analyzed. Top line results, reveal >95% sensitivity and >95% specificity for distinguishing synucleinopathies from healthy controls. Final un-blinded results will be presented at the WPC 2023 annual meeting with a focus on test sensitivity and specificity, accuracy and precision. In addition, synucleinopathy subgroup analysis will be performed to define unique pathological characteristics of disease (PD, MSA, DLB or PAF).
Conclusion: The Synuclein-One study is the largest investigation of cutaneous phosphorylated alpha-synuclein detection across all four synucleinopathies. Our results indicate that skin biopsy testing for the accurate evaluation of synucleinopathies will advance the field of neuro-diagnostic testing in neurodegenerative disease.

CLINICAL SCIENCE: Pharmacological therapy

LBP35.01

Discovery and development of a small molecule inhibitor targeting alpha-synuclein pathology

Nadine Ait-Bouziad, Nicolas Dreyfus, Coralie Vallet, Leonida Maliqi, Lorène Aeschbach, Sylvain Pautet, Sebastien Menant, Johannes Brune, Irina Borovko, Alexis Fenyi, Clarisse Schumer, Thomas Jaquier, Nicolas Fournier, Heiko Kroth, Sonia Poli, Andrea Pfeifer, Marie Kosco-Vilbois, Elpida Tsika*
AC Immune, Lausanne, Vaud, Switzerland

Objectives: Synucleinopathies, such as Parkinson's Disease (PD), Parkinson's disease with dementia (PDD) and Multiple System Atrophy (MSA), are characterized by the progressive accumulation of alpha-synuclein (a-syn) inclusions in the brain. Multiple lines of evidence support the connection between a-syn pathology and disease progression, rendering a-syn aggregation a compelling target for altering disease trajectory. The aim of our work is to identify orally bioavailable and brain penetrant small molecules that inhibit the aggregation and intracellular accumulation of pathological a-syn as a treatment for synucleinopathies.
Methods: Our unique proprietary Morphomer® platform contains small molecular weight compounds that are brain penetrant and bind specifically to misfolded proteins, interfering with and preventing the formation of aggregates. Morphomers® were screened and characterized in in vitro pharmacology assays to evaluate their capacity to inhibit a-syn aggregation. These included biochemical approaches to assess a-syn solubility, aggregate size and β-sheet content, and cell-based assays to evaluate the effect of compounds on a-syn aggregate accumulation in cells. Pharmacokinetics, brain exposure and tolerability were evaluated in mice after single and repeated dosing, and efficacy was demonstrated in vivo in an a-syn spreading model based on transgenic mice inoculated with human a-syn preformed fibrils (tg hPFF mice).
Results: Through iterative medicinal chemistry and screening cycles, several chemical Series were identified that prevented aggregation of a-syn in cellular and cell-free models. Compounds also reduced the formation of de novo aggregates in primary neurons treated with brain-derived a-syn aggregates, with nanomolar IC50 values. Selected compounds also demonstrated target engagement on both recombinant and brain-derived a-syn aggregates. An orally bioavailable and brain penetrant compound was progressed in vivo, resulting in significant reduction of a-syn pathology load and spreading in the brains of tg hPFF mice.
Conclusions: Concerted medicinal chemistry efforts and robust in vitro pharmacology screening capabilities led to the discovery of an orally active, CNS penetrant Morphomer® which significantly reduces pathology in an animal model of PD. Further exploration of this Series has led to the identification of more potent compounds which will be further characterized towards the identification of an optimized lead candidate.

LBP35.16

Enhancing lysosomal function and autophagy via TRPML1 as a potential therapeutic strategy for Parkinson's disease

Gabriela Vilema-Enríquez, Matthew Williamson, John Blackwood, Warren Galloway, Geraldine Farjot, James Taylor, Alkmini Kalousi, Nancy Malintan, Jakub Stefaniak, Benjamin Atkinson, Tsz Ting Chow, Catherine Coutts, Zahra Shather, Peter Hamley*
Samsara Therapeutics, Oxford, United Kingdom

Autophagy is a conserved key cellular pathway where cytoplasmic contents are delivered to lysosomes for degradation. Via this method, cells degrade aggregate-prone proteins, damaged mitochondria amongst other organelles, and these functions appear to be linked to several neurodegenerative diseases including Parkinson's disease (PD). An increasing body of evidence points towards defective autophagy as fundamental to both the aetiology and pathogenesis of PD. Furthermore, numerous genetic mutations targeting components of the autophagic machinery or relevant to the autophagy-lysosomal axis have been identified as disease risk factors. Therefore, restoring autophagy and lysosomal function could be key to arresting diseases of misfolded proteins such as PD.
The Lysoseeker® platform developed by Samsara Therapeutics provides a unique autophagy discovery platform based on phenotypic screening. It opens numerous opportunities for first-in-class, disease-modifying molecules. Using our novel platform, we have identified SAM001, a new small molecule targeting the transient receptor potential channel mucolipin 1(TRPML1). TRPML1 is a lysosomal Ca2+ channel whose loss of function leads to neurodegeneration. SAM001 is orally available, central nervous system penetrant and has an excellent pharmacokinetics profile. SAM001 is active in various cell models including dopaminergic neurons. In this midbrain iPSC patient-derived neurons, SAM001 induces TFEB translocation, restores lysosomal function and clears α-synuclein aggregates. Moreover, SAM001 has profound effects in a novel in vitro model of Parkinson's disease, based on intra-nigral α-synuclein toxicity and GBA-linked lysosomal dysfunctions. We observe superior improvements in cellular, and motor function and α-synuclein aggregation readouts compared to Ambroxol.
SAM001 presents all the characteristics to be a new candidate for clinical development in PD and it has the potential to be an excellent pharmacological tool to evaluate autophagy induction in other neurological diseases.

CLINICAL SCIENCE: Surgical therapy, including cell and gene therapy

LBP36.01

Preclinical safety and efficacy of dopamine neuron progenitor cells derived from PD donor induced pluripotent stem cells

Derren Barken[1], Rachel Hills[2], Jim Mossman[1], Ha Tran[1], Ai Zhang[1], Roy Williams[1], Emma Lane[2], Mariah Lelos[2], Xiaokui Zhang[1], Andres Bratt-Leal[,1]*
[1] Aspen Neuroscience, San Diego, California, United States
[2] Cardiff University, Cardiff, Wales, United Kingdom

At the time of diagnosis, it is estimated that a Parkinson's disease (PD) patient has already lost the majority of dopaminergic neurons in the substantia nigra and their projections in the putamen, a major contributing feature to the motor symptoms of the disease. There is a well-established history that replacement of the missing dopamine through transplantation of dopaminergic neurons into the putamen has the potential to improve motor function and reduce Parkinson's medication intake. The technology now exists for ex vivo generation of patient-specific dopaminergic neurons by reprogramming somatic cells into induced pluripotent stem cells (iPSCs) and then further differentiating iPSCs to dopamine neuron progenitor cells (DANPCs) and neurons. Autologous cell therapy has the potential advantage of not requiring immune suppression, which is costly and may not be well tolerated in an elderly population. Towards development of an autologous neuron replacement therapy, Aspen Neuroscience has established the manufacturing process to produce DANPCs from

PD donor iPSCs under GMP conditions, and characterize these cells using a battery of quality control assays. We have generated large reference data sets for developing predictive genomic assays, not only to assess the genome integrity of each lot of cells, but also to predict their ability to form functional dopaminergic neurons. To further validate this approach, DANPCs from multiple PD donors have undergone in vivo assessment. Safety, biodistribution and tumorigencity of the DANPCs were characterized in intact immuno-deficient Rowett nude rats under Good Laboratory Practices (GLP). In a separate study, four lines were tested for efficacy in a 6-OHDA medial forebrain bundle lesion rodent model of PD, and examined histologically to determine survival, phenotype and innervation of the resulting grafts. This presentation describes the results from our preclinical studies that demonstrate the ability to manufacture patient-specific DANPCs which are safe and demonstrate robust efficacy in support of future clinical investigation in PD.

CLINICAL SCIENCE: Clinical trials: Design, outcomes, recruiting, etc.

LBP38.01

Effects of asymmetric vs symmetric dosing of IPX203 during a Phase 3 trial on the occurrence of drug-related adverse events

Robert Hauser[1], Zachary Grieb[2], Ghazal Banisadr[2], Stanley Fisher[2]*
[1] USF Parkinson's Disease and Movement Disorders Center/Parkinson Foundation Center of Excellence, Tampa, United States
[2] Amneal Pharmaceuticals, Bridgewater, NJ, United States

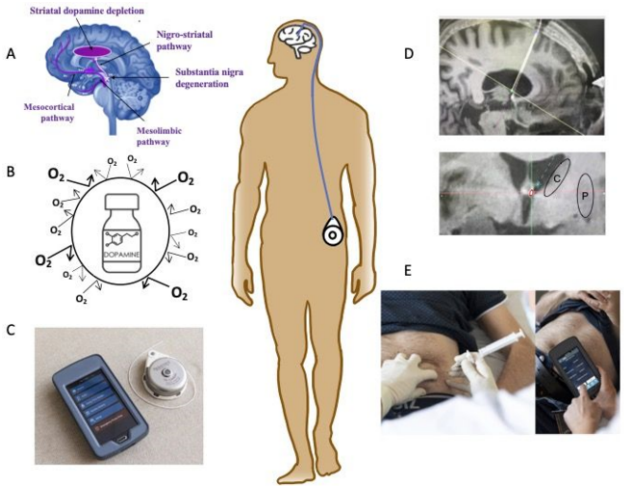
Objective: To analyze the effects of asymmetric vs symmetric dosing of IPX203 on the occurrence of drug-related adverse events (AEs) during a Phase 3 study.
Background: In a Phase 3 study, IPX203, an extended-release oral carbidopa-levodopa (CD-LD) formulation, showed superior efficacy compared to immediate-release (IR) CD-LD in Parkinson's disease patients with motor fluctuations. When examining the prevalence of drug-related AEs during the double-blind treatment period, IPX203-treated patients had a greater incidence of drug-related AEs, including nausea and dyskinesia, compared to IR CD-LD–treated patients. These differences could be related to the dosing frequency restrictions for IPX203 in the study. If the required dosing frequency did not adequately manage motor function for a patient, different individual doses could be increased (ie, asymmetric dosing), which could have resulted in more dopaminergic side effects.
Methods: All patients randomized to the IPX203 treatment arm during the double-blind period were examined for their dosing, overall prevalence of drug-related AEs, and the prevalence of drug-related nausea and dyskinesia.
Results: Two hundred fifty-six patients received IPX203 treatment during the double-blind period. Of those, 90 patients were on asymmetric dosing (35.2%) and 166 patients were on symmetric dosing (64.8%). Forty-two patients had drug-related AEs. Of those, 19 were on asymmetric dosing (21.1% of total asymmetrically dosed patients) and 23 were on symmetric dosing (13.9% of total symmetrically dosed patients); hazard ratio (HR)=1.52. Eight patients had drug-related nausea, of which 4 were on asymmetric dosing (4.4% of total asymmetrically dosed patients) and 4 were on symmetric dosing (2.4% of total symmetrically dosed patients); HR=1.84. Finally, 5 patients had drug-related dyskinesia, of which 2 were on asymmetric dosing (2.2% of total asymmetrically dosed patients) and 3 were on symmetric dosing (1.8% of total symmetrically dosed patients); HR=1.23.
Conclusions: These analyses suggest that asymmetric dosing during the double-blind treatment period may increase the frequency of drug-related AEs, including nausea and dyskinesia, which might be a result of higher individual IPX203 doses to optimize patients' motor responses. In real world practice, where dosing frequency could be adjusted to the patient, drug-related AEs might be comparable to other CD-LD formulations.

LBP38.09

Pharmacological neuromodulation with intracerebroventricular administration of anaerobic dopamine for Parkinson's disease

*David Devos**
University of Lille, INSERM 1171, CHU of Lille, Lille, France

Background: Continuous and circadian compensation of dopamine deficit in the nigro-striatal pathway represents an ideal treatment for Parkinson's disease (PD). The possibility of intracerebroventricular (i.c.v.) administration of dopamine previously failed because of unresolved dopamine oxidation associated with tachyphylaxis. We assessed the feasibility, safety, and clinical outcomes of continuous i.c.v. of anaerobically conserved dopamine (A-dopamine) on motor and non-motor L-dopa related complications (LDRC) in PD patients at the stage of LDRC.
Methods: Continuous and circadian i.c.v. A-dopamine was administered through a telemetry-adjustable intra-abdominal pump delivery system connected to a subcutaneous catheter implanted through the right frontal horn into the third ventricle close to the striatum. After a phase 1 of titration of A-dopamine, PD patients entered a randomised, controlled, open-label cross-over study of 1 month of A-dopamine versus 1 month of optimised oral medical therapy (usual treatment). The first five patients to complete phase I and II were scheduled to be reported to the independent Data Safety Monitoring Board, and are described here. Due to the death of the fifth patient from unrelated community-acquired pneumococcal disease at the end of phase I, a sixth patient was also recruited.
Findings: Administration of i.c.v A-dopamine was safe and induced a dose-dependent improvement in motor handicap and LDRC, with a favourable impact on behaviour. A-dopamine alone induced no dyskinesia.
Interpretation: The results support the clinical feasibility of i.c.v. A-dopamine in PD patients at the stage of LDRC and clinical development of the schedule to demonstrate the risk/benefit balance.



LBP38.11

The Norwegian Parkinson's Registry and Biobank

Eldbjørg Fiske[*,1], Johannes Lange[2], Kenn Freddy Pedersen[3]*
[1] Norwegian Parkinson Registry and Biobank, Stavanger, Norway
[2] Centre for Movement Disorders, Stavanger University Hospital, Stavanger, Norway
[3] Centre for Movement Disorders/Department of Neurology, Stavanger University Hospital, Stavanger, Norway

The Norwegian Parkinson's Registry and Biobank was established in 2016 and startet inclusion of patients with Parkinson's disease and atypical neurodegenerative parkinsonism in December 2018. How many people are living with these disorders in Norway are currently unknown, but estimates from the Norwegian Patient Registry suggest around 10.000 individuals. The main aim of the Norwegian Parkinson's Registry is to ensure quality and uniform diagnostics, treatment and follow-up of the patient group by collecting clinical data, implementing quality offers of treatment and conducting research into causal relationships and disease mechanisms by combining registry data and biobank material. During the first four years of data collection, the Parkinson's Registry has encountered a number of challenges related to coronavirus pandemic and resource scarcity in the health service. Several measures have been implemented to solve these challenges, and we are now starting to see the effect of these measures. By the end of March 2023, around 3000 individuals are enrolled in the registry, and the numbers are rising rapidly. Patient reported Outcome and Experience Measures (PROM/PREM) that include validated questionnaires and patients' perception of their received care are available from more than 60 % of all included patients. More than 80 % have concented to contribute to the biobank. Thus, the Norwegian Parkinson's Registry and Biobank will be an invaluable source for research in the near future.

LBP38.16

A novel technological functional movement Parkinson test. A preliminary study

Marco Gidoni[*,1], Giuseppe Sarcinella[*,2], Milena Guizzetti[3], Marco Esposito[4], Cecilia Gatti[4]
[1] Università degli Studi di Milano, Tecnobody srl, Dalmine, Lombardia, Italy
[2] Associazione Progotan, Lumino, Canton Ticino, Switzerland
[3] Freelances, Brescia, Lombardia, Italy
[4] TecnoBody s.r.l., Dalmine, Lombardia, Italy

Background: Parkinson's disease is a progressive disorder that affects the nervous system and the parts of the body controlled by the nerves. Nowadays, there are some validated scales to evaluate the progress of the pathology of the subjects, but none of them is based on object data independent of the operator performing the tests.
Objective: The purpose of the study is to validate a new type of technological evaluation scale compared the most used Parkinson's ones.
Participants: At present, 13 patients have been included in the study (acquisitions are ongoing). Patients were acquired at "Move Different" near Bergamo and at clinic "Progotan" in Livorno. Exclusion criteria: Hoen&Yahr 4/5; orthopaedic, psychological, social problems; parkinsonism, deep brain stimulation (DBS) patients, visual acuity and impaired problems, or wheelchairs.
Evaluation protocol: Evaluation lasted one and a half hour: first, the specialised physiotherapist administered the Mini-BESTest and UPDRS Part 3, then the technological tests on Tecnobody medical devices. Finally, each patient completed PDQ 39 and ABC Scale by him/herself.
Main Outcome Measure(s): The aim of this research is to correlate validated assessment scales for Parkinson's disease with technological tests. Specifically, on the D-Wall were performed: Chair Stand test that provided the number of repetitions, Foot Up and Go test calculates the time of execution; Different balance tests provide the area in 30"; lastly Limits of Stability indicates the percentage of spatial exploration done compared to the subject's height. For Gait Analysis, on Walker View, the walk ratio was analysed.
Results: Preliminary results of correlations between the validated scales and the technological tests results in Mean R2 = 0.65.
Conclusion: Despite the small number of subjects recruited in the initial phase (13 people with Parkinson's disease), the correlation results show a promising link between the validated scale and technology testing. The next feasible step is to confirm the results of this trend by increasing the study population. The validated scales considered are the most appropriate for analyzing the progression of Parkinson's disease, but they are not specific for assessing individual motor skills. The technological functional movement parkinson's test carried out aimed to assess patients' abilities, in a operator-independent manner.

LBP38.24

Effect of acupuncture stimulation on cognitive reserve in normal aging and neurodegenerative disease: A study design of clinical trial using a functional-near infrared spectroscopy

Dong Hyuk Lee[*,1], Joo-Hee Kim[2]*
[1] College of Korean Medicine, Sangji university, Wonju-si, Gangwon-do, South Korea
[2] College of Korean Medicine, Sangji university, Wonju, Gangwon-do, South Korea

Background: The concept of cognitive reserve (CR) stems from discrepancies between the degree of brain pathology and clinical manifestations. In PD, not only AD, cognitive impairment is up to six times more common than in the healthy populations and is one of the most important non-motor symptoms of PD. Therefore, the concept of CR may also have important implications in PD. Generally, CR has been measured through CR proxy, such as education, occupational complexity, questionnaire, and bilingualism. Meanwhile, acupuncture is one of the most widely used alternative interventions for neurological disorders. The effect of acupuncture therapy has been explored using various neuroimaging methods such as fMRI. In this study, we try to investigate the mechanisms of acupuncture stimulation on cognitive reserve in normal aging and cognitively impaired groups using fNIRS.

Design: A randomized, placebo-controlled trial
Participants: Cognitively unimpaired and cognitively impaired group measured for CRIq (Cognitive Reserve Questionnaire)
Intervention and controls: The study group will receive acupuncture stimulation at the genuine acupoint known to be effective in cognitive decline, and the control group will receive acupuncture stimulation at the sham acupoint.
Modality: resting state fNIRS and task fNIRS (working memory task)
Neuroimaging Methods: We will acquire resting state fNIRS data before and after acupuncture stimulation and also task fNIRS data (corsi block task).
Outcomes: The change of brain activation and connectivity in resting state before and after acupuncture and in working memory task would be investigated. Also, the brain activation between high and low CR groups would be compared. Also the neural substrates correlating with CRIq will be explored.
Discussions: In this study, we aim to identify the mechanism of acupuncture stimulation on CR in neurodegenerative brain disease and to explore the neural substrates of CR.

LBP38.27

Redesigning Parkinson's disease care: rationale, methods and baseline data from the PRIME-UK Parkinson's randomised controlled trial

Katherine Lloyd[*1], Emma Tenison[1], Matthew Smith[1], Rebecca Heath[2], Charlotte McDonald[1], Nicola Giles[1], Alexandru Stan[1], Chloe Thomas[1], Micheál Ó Breasail[1], Yoav Ben-Shlomo[1], Emily J Henderson[3]*
[1] Ageing and Movement Research Group, Population Health Sciences, Bristol Medical School, Bristol, United Kingdom
[2] Royal United Hospitals, Bath, United Kingdom
[3] Ageing and Movement Research Group, Population Health Sciences, Bristol Medical School, Bristol, United Arab Emirates

Background: Current models of Parkinson's disease (PD) care may not account for the complexity and significant heterogeneity in symptoms of PD, which emerge and fluctuate over time, coupled with multi-morbidity and frailty. Individuals' unique phenotype, needs and experience may be overlooked in a system that often lacks continuity, patient-involvement and proactivity. PRIME-Parkinson has been designed to deliver innovative, cohesive, proactive and personalised care, which is responsive to arising problems. The ongoing PRIME randomised controlled trial (RCT) will determine whether PRIME care is able to improve outcomes in people with PD, including those often excluded from RCTs, to enhance their experience of living with parkinsonism.
Methods: This single-centre randomized controlled trial (RCT) recruits adults with parkinsonism from the PRIME cross-sectional study and routine clinical settings. Those lacking capacity are eligible if they have a personal consultee. Participants are randomised to receive either 'usual care' or 'PRIME care', a complex multi-disciplinary individualised care programme. The primary outcome is "goal attainment" measured using the Bangor Goal Setting Interview. Secondary outcomes include other measures of health and wellbeing.
Results: We have consented 125 people (22nd March 2023), with six requiring a personal consultee. The mean age is 75±8 years and 31.5% are female. Participants most commonly have Idiopathic PD (n=96, 88%) spread across all Hoehn and Yahr Stages, with a predominance for stages 2 (n=49, 41.1%) and 3 (n=35, 29.4%). Median disease duration is 5 years (IQR 4-10). Most live in their own homes (n=102, 92.7%) and 20 were consented and assessed at home. We identified 38 participants (30.1%) who were frail (score >4 on the Clinical Frailty Scale). The median MDS Non-Motor Score is 85 (IQR 43-142) and mean UPDRS part III score is 44 (SD 20, range 2-100). The median MoCA score is 24 (IQR 21-27 range 0-30). Participants are taking a mean of 7 medications (SD 4, range 1-15) and 7 (6.4%) use device-aided therapies.
Conclusion: We will describe our experience and challenges to date in delivering this complex intervention to establish if PRIME-Parkinson care supports personal goal attainment and positively impacts health and wellbeing in people with parkinsonism.

LBP38.28

Motor, non-motor, and cognitive trajectories from 4 to 6 years after diagnosis in the AT-HOME PD cohort

Eric Macklin[*1], Jamie Adams[2], Katherine Amodeo[2], Elizabeth Baloga[2], Katherine Callahan[3], Joshua Gottesman[4], Karlo Lizarraga[2], Casey Stevens[2], James Beck[5], Hyun Joo Cho[6], Alberto Espay[7], Codrin Lungu[6], Dan Novak[5], David Oakes[2], Ira Shoulson[2], Ray Dorsey[2], Tanya Simuni[8], Larsson Omberg[9], Michael Schwarzschlid[3], Ruth Schneider[2]*
[1] Harvard Medical School, Boston, MA, United States
[2] Univ of Rochester, Rochester, NY, United States
[3] Massachusetts General Hospital, Boston, MA, United States
[4] Michael J Fox Foundation, New York, NY, United States
[5] Parkinson's Foundation, New York, NY, United States
[6] National Institute of Neurological Disorders and Stroke, Bethesda, MD, United States
[7] Univ of Cincinnati, Cincinnati, OH, United States
[8] Northwestern University, Chicago, IL, United States
[9] Sage Bionetworks, Seattle, WA, United States

Background: Mid-stage Parkinson disease (PD), the interval after initiation of antiparkinsonian medications and before onset of cognitive decline or motor complications, is poorly studied. Characterizing the natural history of PD and evaluating assessment methods are essential to design clinical trials.
Objective: To characterize motor, non-motor, and cognitive trajectories of mid-stage PD patients and compare methods of remote and digital assessment.
Methods: The longitudinal observational study 'Assessing Tele-Health Outcomes in Multiyear Extensions of PD Trials' (AT-HOME PD, NCT03538262) used a fully remote design to characterize motor, non-motor, and cognitive features of former participants of the STEADY-PD III (NCT02168842) and SURE-PD3 (NCT02642393) clinical trials. Participants were assessed over three annual tele-visits (0, 12, and 24 months) using the Movement Disorder Society Unified Parkinson's Disease Rating Scale (MDS-UPDRS), Montreal Cognitive Assessment (MoCA), clinical global impression of severity (CGI-S), and self-report of falls. Motor function was monitored quarterly using a smartphone app (mPower v2.0). MDS-UPDRS Part 2, Non-Motor Symptoms Questionnaire (NMSQ), and the Geriatric Depression Scale (GDS-15) were completed quarterly online (Fox Insight). Change in scores was estimated by mixed model repeated-measures analysis adjusting for sex and disease duration.
Results: At baseline, the 226 participants (median age 66 years, 60% male, median 3.9 years from diagnosis, 93% using antiparkinsonian medications) had moderate motor (mean±SD MDS-UPDRS Part 3 24.9±11.5) and non-motor (MDS-UPDRS Part 1 7.5±4.8) symptoms and were cognitively intact (MoCA 27.9±2.0). The most sensitive measures of progression over 24 months were MDS-UPDRS Parts 1-3 total score (mean±SE 8.9±1.0, effect size [ES] 0.58), smartphone assessments of tapping (improvement by 0.14±0.02, ES 0.51), and NMSQ total score (2.0±0.27, ES 0.50). Sensitivity of clinician-assessed and self-reported measures of motor progression were similar (ES 0.44 and 0.36, respectively). Cognition, mood, and global impression were stable (ES < 0.10). The rate of self-reported falls in the month prior to annual tele-visits doubled from 7.1% to 15.7% of participants.

Conclusions: The MDS-UPDRS Parts 1-3 total score, a common measure of total PD severity, assessed by annual tele-visits, was a feasible and sensitive measure of change in this mid-stage PD cohort. Falls are an increasing risk at this stage.

LBP38.31

NLX-112 has favorable safety, tolerability and efficacy against levodopa-induced dyskinesia (LID) in a randomized, double-blind, placebo-controlled, proof-of-concept Ph2A study

Per Svenningsson[1], Per Odin[2], Filip Berquist[3], Karin Wirdefeldt[1], Dag Nyholm[4], Måns Jergil[5], Christopher Jankosky[6], Mark Varney[6], Fabienne Herbrecht[7], Steven Johnson[7], Adrian Newman-Tancredi[,8]*
[1] Karolinska Institute, Solna, Sweden
[2] Lund University, Lund, Sweden
[3] University of Gothenburg, Gothenburg, Sweden
[4] Uppsala University, Uppsala, Sweden
[5] CTC Clinical Trial Consultants AB, Uppsala, Sweden
[6] Neurolixis, Park Ridge, NJ, United States
[7] Neurolixis, Castres, France
[8] Neurolixis, Castres, Tarn, France

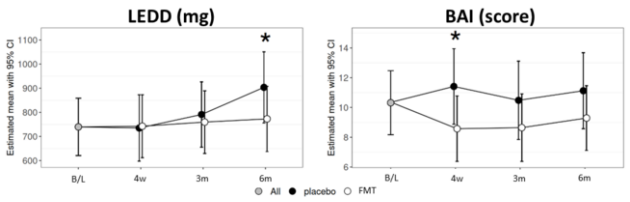
Background: NLX-112, an exceptionally selective, high-efficacy serotonin 5-HT1A receptor biased agonist, shows potent and efficacious anti-dyskinetic properties in rodent, marmoset and macaque models of LID. NLX-112 has previously shown favorable clinical safety and tolerability in trials for other indications.
Methods: PD patients with troublesome LID were randomized to receive NLX-112 or PBO (2:1 ratio) as an adjunct to their regular stable antiparkinsonian medication. Study drug dosing was individually up-titrated over 28 days to a maximum of 2 mg/day (1 mg b.i.d.), kept stable for 14 days and down-titrated over 14 days. Patients received levodopa challenge (150% of usual morning dose) at day 1 (baseline) and at test days 28 and 42. Primary outcome was safety and tolerability; secondary efficacy outcomes included UDysRS as well as other motor and non-motor symptom scales.
Results: 22 patients (15 on NLX-112, 7 on PBO) completed the 8-week treatment according to the protocol. Safety and tolerability, the primary endpoints of the study, were good. No patients withdrew due to adverse events, and there were no serious adverse events in the NLX-112 group. Adverse events were either mild or moderate, and mostly occurred during the 4-week dose up-titration phase. Safety, as assessed by changes in vital signs, ECG or laboratory measures, was good and did not differ between NLX-112 and placebo groups. In motor assessment at day 28, NLX-112 reduced UDysRS total score (parts 1-4) by 4.1 points (p=0.0281) and part 3+4 score (dyskinesia disability) by 1.7 points (n.s.), whereas PBO group changes were not significant (-2.0 and -1.0, respectively). At day 42, a greater reduction of UDysRS scores by NLX-112 was observed: total score was reduced by 6.3 points (p=0.0016) and part 3+4 score by 3.1 (p=0.0038), whereas PBO group changes were not significant (-2.4 and -0.1, respectively). Analysis of other assessment scales is underway and will be presented.
Conclusions: NLX-112 was safe and well tolerated by PD patients with LID; in addition, it significantly reduced LID in an apparently treatment-duration dependent manner. These data will guide the design of phase 2B studies and suggest that NLX-112 could be a promising first-in-class drug candidate for improved treatment of PD.

LBP38.35

Double-blind placebo-controlled multicenter trial of fecal microbiota transplantation in Parkinson's disease

Filip Scheperjans[,1], Reeta Levo[2], Berta Bosch[3], Mitja Lääperi[4], Perttu Lahtinen[5], Rebekka Ortiz[6], Valtteri Kaasinen[7], Reetta Satokari[3], Perttu Arkkila[8]*
[1] Department of Neurology, Helsinki University Hospital and Clinicum, University of Helsinki, Helsinki, Finland
[2] Department of Neurology, Helsinki University Hospital, Helsinki, Finland
[3] Human Microbiome Research Program, Faculty of Medicine, University of Helsinki, Helsinki, Finland
[4] Lääperi Statistical Consulting, Helsinki, Finland
[5] Department of Gastroenterology, Päijät-Häme Central Hospital, Lahti, Finland
[6] Department of Neurology, Tampere University Hospital and University of Tampere, Tampere, Finland
[7] Clinical Neurosciences, University of Turku and Neurocenter, Turku University Hospital, Turku, Finland
[8] Department of Gastroenterology, Helsinki University Hospital and Clinicum, University of Helsinki, Helsinki, Finland

Background: Gut microbiota in PD is linked to disease progression, motor and non-motor symptoms. Fecal microbiota transplantation (FMT) impacts PD pathology and symptoms in preclinical models. Adequately powered and controlled clinical trials assessing safety and efficacy of FMT in PD have not been published.
Methods: 47 dysbiotic PD patients were randomized in a 2:1 ratio to receive either single-dose anaerobically prepared and freeze-stored FMT material from a healthy donor or placebo via colonoscopy. Safety as well as motor and non-motor symptoms were evaluated until 6 months after the intervention. The primary outcome measure was MDS-UPDRS I-III (part III in OFF). Differences between treatment groups over time were analyzed using constrained longitudinal data analysis (cLDA).
Results: 44 patients completed the follow-up. While FMT (n=29) and placebo groups (n=15) were mostly well balanced at baseline, subjects in the FMT group had non-significantly shorter disease duration (5.7 vs. 6.9 years; p=0.88) and higher MDS-UPDRS III (OFF) scores (30 vs. 20; p=0.17).
79 adverse events (AE) were reported for the FMT group and 35 for the placebo group. Most AEs were related to GI dysfunction (16 vs. 1) and anemia (5 vs. 2). All AEs in the placebo group and all but one AE in the FMT group were mild or moderate in severity. The severe AE was "new or worsening anxiety" and was considered unlikely related to the intervention.
There was no significant difference in the primary endpoint or MDS-UPDRS subscores during follow-up. At 6 months, levodopa equivalent daily dose (LEDD) had significantly increased in the placebo group (712mg→902mg) vs. the FMT group (650mg→640mg). The Beck Anxiety Inventory score (BAI) significantly decreased in the FMT vs. placebo group at 4 weeks and remained lower up to 6 months. The timed up and go test (OFF) result slightly but significantly worsened in the FMT (9.9s→10.2s) vs. placebo (9.7s→8.5s) group at 6 months.
Conclusions: The intervention was safe with the potential for mild to moderate GI side-effects. The primary endpoint was not met. FMT significantly improved measures of anxiety. Dopaminergic medication load increased less in the FMT group. Analyses of gut-brain axis target engagement are ongoing.



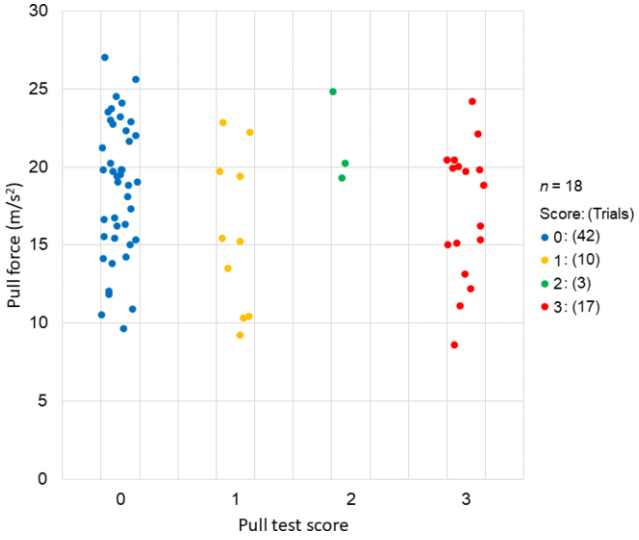
CLINICAL SCIENCE: Rating scales

LBP39.06

Extraction of the pull force from inertial sensors during the pull test in Parkinson's disease: An inter- and intra-rater reliability study

Ryoma Taniuchi[*,1], *Shusaku Kanai*[2], *Amane Hara*[1], *Kazuya Monden*[1], *Hiroaki Nagatani*[1], *Tsuyoshi Torii*[3], *Toshihide Harada*[2]
[1] Department of Rehabilitation, National Hospital Organization Hiroshima-Nishi Medical Center, Hiroshima, Japan
[2] Department of Physical Therapy, Faculty of Health and Welfare, Prefectural University of Hiroshima, Hiroshima, Japan
[3] Department of Neurology, National Hospital Organization Hiroshima-Nishi Medical Center, Hiroshima, Japan

Background: Although the pull test has remained the gold standard to evaluate postural instability in Parkinson's disease (PD), it is unknown whether the variability of the examiner pull force affects the scoring performance. Recent biomechanical analysis of the pull test has shown quantitative data using reproducible mechanically generated pull force. However, efforts have not been made to quantify the pull force clinically generated from the examiner's hand.
Objective: To extract the pull force using inertial sensors and examine the inter- and intra-rater reliability of the pull test in PD.
Methods: Two raters performed the pull test on 18 patients with PD (mean age = 73.2 ± 9.6 years). The pull force was quantified using inertial sensors attached to the examiner's right hand and the patient's lower trunk. In this study, the pull force was calculated as an extracted three-dimensional vector quantity, i.e., resultant acceleration, and it was expressed in meters per second squared (m/s2). The inter- and intra-rater reliability was analyzed using the interclass correlation coefficient (ICC) for the pull force and Cohen's weighted kappa (κw) for the pull test score. Furthermore, Bland-Altman analysis was used to investigate the systematic error.
Results: The pull force for each pull test score group was "0" (18.6 ± 4.4 m/s2), "1" (15.8 ± 5.0 m/s2), "2" (21.4 ± 3.0 m/s2), and "3" (17.2 ± 4.3 m/s2), with no statistically significant differences between groups. The inter- and intra-rater reliability of the pull force was very poor (ICC = 0.002–0.145). The Bland-Altman analysis revealed no systematic error between the pull force at the two test points. In contrast, κw for the pull test scores were in the range of 0.847–0.968 indicating good to excellent inter- and intra-rater reliability.
Conclusions: The pull test score had almost perfect reliability, despite the quantified pull force being variously different both inter- and intra-rater. Our findings may also help show that the pull test is a robust tool to evaluate postural instability in PD and the pull force probably does not affect scoring performance.



CLINICAL SCIENCE: E-health and technology

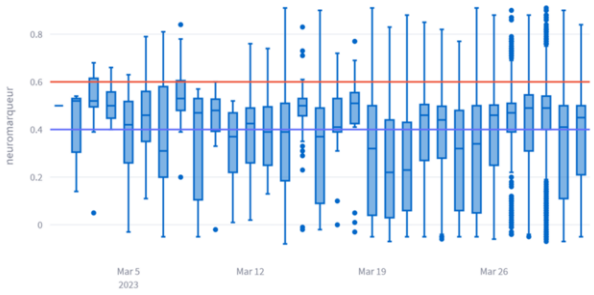
LBP40.05

DigiPark: First results of a medical device based on digital neuromarkers monitoring for better individualized care of patients with Parkinson's disease

Djamchid Dalili[*,1], *Caroline Atlani*[2]
[1] DiamPark, Chaville, IdF, France
[2] DiamPark, Paris, France

Parkinson's Disease is the world's fastest-growing neurological condition, affecting approximately 10 million people worldwide, it is a progressive neurodegenerative disorder that causes a wide range of movement related symptoms as well as non-motor and cognitive symptoms which should be globally captured to get a clear view of the disease progression. DiamPark is a neurotech startup incubated at the Brain Institute in Paris that is focused on developing innovative solutions for capturing, measuring, and analyzing digital biomarkers specific to Parkinson's disease to improve patient care and accelerate the development and assessment of new therapies. DigiPark is a certified medical device embedded in a mobile phone and/or watch-based application that is designed to daily support Parkinson's patients and facilitate consultations with neurologists and other healthcare professionals. The application has been already downloaded by more than 1000 people and has collected millions of anonymous data points that have been used by our scientists to build and consolidate underlying models and algorithms that are protected by patents. The project is divided into two phases to ensure the consistent use of the digital biomarkers in real-life scenarios and clinical research on patients:
1) Validation of our digital biomarkers captured in real life context through our patented specific analysis and models and the proof of the correlation between DigiPark digital biomarkers and UPDRS score.
2) A controlled, multicentric, randomized clinical trial called AWAKENING Study, Clinical and medico-economic evaluation of A neW strategy for monitoring PArKinsonian patiEnts using the DigiPark remote monitorING device, is set to begin in Q3 2023 in France to show the clinical and medico-economic benefit of

DigiPark and its positive impact on decision support and therapeutic adaptation for medical professionals and on patients' quality of life. The visualization of biomarker fluctuations analyzed by DigiPark provides a dynamic, objective and complete view of patients' symptoms and adherence and allows neurologists to better assess the progression of Parkinson's disease and decide optimal treatment adjustments. We present the first data of phase 1 of the project (see figure).

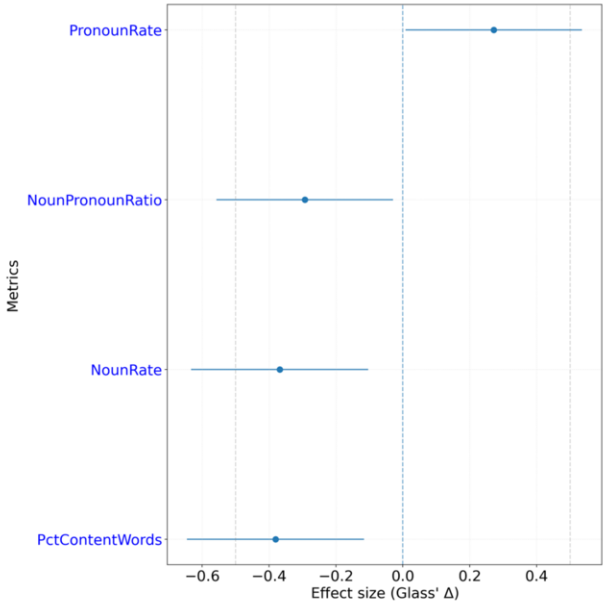


LBP40.12

Lexico-semantic differences between people with PD and healthy controls observed in a story retell task

Hardik Kothare[*1], Andrew Exner[2], Sandy Snyder[2], Jessica Huber[2], Vikram Ramanarayanan[3]*
[1] Modality.AI, Inc., San Francisco, California, United States
[2] Purdue University, West Lafayette, Indiana, United States
[3] Modality.AI, Inc.; University of California, San Francisco, California, United States

People with Parkinson's Disease (pPD), both with and without dementia, exhibit word retrieval difficulties, delayed lexical activation, verbal working memory deficits and impaired lexico-semantic comprehension. The striatum and cortico-striatal circuits have been implicated in these impairments. The progression of dementia in pPD is associated with reduced grammatical ability and information content. Given this, linguistic metrics derived from lexico-semantic tasks show promise of being important biomarkers for PD diagnosis and progression. Here, we present results from an ongoing remote patient monitoring study using the Modality platform (36 pPD, 22 controls; 4 sessions each), a cloud-based multimodal dialogue system which is driven by Tina, a virtual conversational agent. Tina guides participants through a structured interview comprising standard clinical tasks and speech exercises to assess their neurological health. In this work, we focus on a story retell task depicting three different stories of a boy, Bobby, and his mother. All pictures in the story were first described by Tina. Participants were then shown the pictures one more time and were asked to describe what was happening in the picture in their own words. Thus, the task probed the speech production network along with verbal working memory. Participants were presented with only one of the three stories during every session. Lexico-semantic features were computed from transcripts of participant utterances using the spaCy software library. Kruskal-Wallis tests were run to look for differences in the median values of these metrics between pPD and controls. pPD showed a higher pronoun rate and lower noun-to-pronoun ratio, noun rate and content words percentage. The results indicate that as compared to controls, pPD used 'he' and 'they' more than 'Bobby' and 'Bobby and his Mom'. The noun-to-pronoun ratio was also slightly positively correlated with pPD MoCA scores (Spearman's rho = 0.21, p = 0.0158), indicating that more cognitively impaired pPD used more pronouns. A lower percentage of content words is in line with prior work on decreased conciseness of discourse in pPD. Our results suggest that lexico-semantic metrics extracted using a remote monitoring platform have the potential to capture Parkinsonian characteristics relative to healthy controls, and cognitive decline therein.



LIVING WITH PARKINSON'S: Public education or awareness programs

LBP43.09

Support groups are empowering the Parkinson's community

*Lori DePorter**
York, PA, United States

Introduction: The benefits provided by support groups are multifaceted for people with Parkinson's and their caregivers. While providing a safe and judgment-free environment is the foundation of a support group, facilitating camaraderie, education, and advocacy gives participants a sense of empowerment in an otherwise uncontrollable situation.
Method/Materials/Discussion: Informed leaders and facilitators are crucial for a successful program. Education and training with trusted resources, such as the PMD Alliance and The Parkinson's Foundation, provide guidelines to define, develop and implement the program.
As facilitators and co-facilitators of new virtual and in-person groups, we developed programs to be interventions for isolation and the need for more relevant, up-to-date information. Utilizing a format that includes an education segment followed by discussion and activities encourages social interaction while focusing on Living and Learning with Parkinson's.
One vital education topic in Advocacy and Public Policy is the 2023 Congressional reintroduction of the National Plan to End Parkinson's Act, bi-partisan legislation to end Parkinson's Disease. To encourage support of the Act, the MJFF has facilitated discussions between PWP and their US Representatives. Veterans, people with YOPD, and caregivers shared their Parkinson's stories

and gave a face to the nearly ten million people living with Parkinson's worldwide.
Our support group members will become advocates by sharing their stories through handwritten letters to our policymakers. Moreover, they will learn how to utilize available resources to influence future legislation, including banning harmful chemicals such as Paraquat and Trichloroethylene.
Conclusion: Support groups provide social connections that improve the quality of life and tools for PWP to play a role in finding a cure and providing hope for the future.
References:
http://www.house.gov/representatives/find-your-representative
https://www.parkinson.org/understanding-parkinsons/statistics
https://www.michaeljfox.org
https://parkinsonsnewstoday.com/columns/how-to-be-advocate-parkinsons-legislation/

LBP43.19

Increasing Hispanic/Latino participation to provide knowledge, resources, and support through their Promotora/Embajadora de Parkinson around the world
*Adriana Jimenez**
Give for a Smile, Garden Grove, California, United States
Promotores: A. Jimenez, M. DeLeon, A. Corona, K. Garcia, J. A. Gallardo, H. Córdova, N. Vigil, and Ma Fer. López from USA, Arg, Méx, and Perú.
Objective: To outreach Latino PD communities, and their caregivers to deliver information, resources, and create support groups through their international PEDEP program. We provide training to prospective community leaders and to all communities in the world interested in becoming a PEDEP.
BkGround: For the 2nd year, we have organized 3 days virtual IberoAmerican Parkinson's Conference with the participation of over 10 countries and approximately 500 to 700 participants every day, as well as over 10 Parkinson's specialists from all over the world such as Neurosurgeons, Movement Specialists, Phycologists, Nutritionists, Physical Therapists, Professional Physical Trainers and more.
Methods: Twice a year, we provide training to Latino/Hispanic community and leaders from all over the US and the world. To the training we bring advocacy experts to teach leaders how to approach PD communities and their caregivers, doctor specialists bringing topics such as Proper Nutrition, advantages of the early Diagnostic, Genetic Diagnostic, Initial Treatment and New Advancements, the Emotional Intelligence Role, and other topics to explain the different aspect of the PD condition. All these trainings are provided by Spanish-speaking professionals in Spanish to focus on minimizing the language barrier to ultimately provide an easy transition for PEDEP to deliver this information fluently and effectively to PD communities in the US and the world.
Results: Within 5 years and a pandemic, we have hosted 2 in-person events, and 3 virtual events with a total of 1360 virtual attendees, and 150 in-person attendees. The support group meets in the "Un Regalo Para Tí" event where we provide Calligraphic Therapy and Training with M. De Leon's book Living beyond Parkinson's, and a total social media outreach of 825 individuals [table1]. Given the social media impact, there are additional efforts to engage the community through the GFAS_Parkinson Facebook and Instagram pages.
Conclusion: Enrolling and training community leaders makes of this program a unique tool to reach PD communities from all over the world. The PEDEP program has given us the opportunity to reach Hispanic/Latinos.

Event Name	# Registred	# Attended	% AR*	In-Person	Social media
1ra Conferencia de Parkinson In Anaheim	120	80	66.6	80	-
2da Conferencia de Parkinson In Santa Ana College.	150	70	46	70	-
Un Regalo Para Ti	70	70	100	-	40
1st Promotora training session	25	25	100	-	45
1ra Conferencia Iberoamericana de Parkinson	400	300	75	-	150
2nd Promotora training session	80	35	43.75	-	10
2da Conferencia Iberoamericana de Parkinson	1500	800	53.33	-	600
Total	**2345**	**1360**	**455.68**	**150**	**825**

LBP43.20

Parkinson's is not witchcraft: A report by Kabugo Hannington Tamale, Parkinson's Si Buko Uganda, Parkinson's Si Buko USA
Hannington Kabugo Tamale[*,1], Sherryl Klingelhofer*[2]
[1] Parkinson's Si Buko Uganda (Parkinson's is not Witchcraft), Kayunga, Uganda
[2] Parkinsons Si Buko USA, Tillamook, Oregon, United States

PARKINSON'S DISEASE IS NOT WITCHCRAFT
…but in Uganda, it is thought to be so!
Imagine that your family would abandon you, or that you could not hug your grandchildren or you were shunned from society because your condition was contagious. That is a reality faced by people with PD in this country.

LIVING WITH PARKINSON'S: Living well with PD

LBP45.04

Constitution of the Argentinian Parkinson's Network Civil Association - RaPark

Adrián Borches[1], Daniel Merino[2], Andrea Cuellar[3], Natalia Lardieri[3], Beatriz Navarro[,3], María de los Angeles Bacigalupe[4], Fernanda López[3], Graciela Orostizaga*[,5]*

[1] RaPark Red Argentina de Parkinson (Argentinian Parkinson's Network - RaPark), Chascomús, Buenos Aires, Argentina
[2] Red Argentina de Parkinson (Argentinian Parkinson's Network - RaPark), Corrientes, Corrientes, Argentina
[3] Red Argentina de Parkinson (Argentinian Parkinson's Network - RaPark), Buenos Aires, Buenos Aires, Argentina
[4] Red Argentina de Parkinson (Argentinian Parkinson's Network - RaPark), La Plata, Buenos Aires, Argentina
[5] Red Argentina de Parkinson (Argentinian Parkinson's Network - RaPark), San Juan, San Juan, Argentina

The Argentinian Parkinson's Network was born out of the First Online Parkinson Congress held in 2020, which highlighted the need for a federal network that would encompass the entire country and unite all existing associations and support groups to gain a better understanding of the experiences of people with Parkinson's disease (PD), parkinsonism, as well as their families and caregivers. RaPark's objective is to enhance the quality of life of individuals with Parkinson's disease and parkinsonism by advocating for their civil, labor, economic, cultural, health, and overall rights. Additionally, RaPark promotes initiatives that foster a more tolerant and equitable society.
To fulfill this objective, RaPark, as a Civil Association, will undertake the following functions:
1.Serve as a recipient of concerns from the Parkinson's community and their families.
2.Act as an agent for finding mechanisms to address and resolve the issues affected individuals face.
3.Advocate for legislation and regulations that guarantee the full enjoyment of the rights and meet the needs of individuals with PD and their families.
4.Serve as a communication channel for people with PD and parkinsonism, sharing information on scientific, and technological advancements that aim to enhance the quality of life for affected individuals and their families.
5.Raise awareness about the challenges, needs, and demands of the Parkinson's community.
6.Provide support and training for groups throughout the country, even in remote areas and under-resourced settings, for affected individuals, families, and caregivers.
7.Encourage the implementation of activities that promote well-being, health, and social integration.
8.Establish collaborative bonds with international organizations.
Actions taken to date include establishing contact with existing associations, creating and reinforcing new support groups in areas where they did not previously exist, formulating, submitting, and passing laws that benefit people with Parkinson's disease and their families and caregivers, and organizing activities with neurologists specialized in movement disorders and sports activities aimed at raising awareness about PD in society.
We have created this network because we strongly believe that Parkinson's impacts our actions but not our essence and that we have the ability and deserve to live a fulfilling and joyful life.

LBP45.19

Scaling heights: Climbing Mount Kilimanjaro with Parkinson's

*Michael High**
PwP Advocate, Tucson, AZ, United States

Introduction: Climbing Mount Kilimanjaro is a daunting task for anyone, let alone someone with Parkinson's disease. Despite this challenge, I embarked on this journey to prove to myself and others that living with Parkinson's does not have to limit one's ability to achieve remarkable feats. In this presentation, I will discuss my experience climbing Mount Kilimanjaro in January 2023 and the significance it holds for me and others living with Parkinson's.
Methods: To prepare for this climb, I engaged in rigorous physical training and received support from a team of professionals, including a neurologist, an integrative medicine physician, and a physical therapist. During the climb, I used strategies such as pacing, mindfulness, and medication management to manage my Parkinson's symptoms. I will showcase photos of the expedition, including the summit, to demonstrate the accomplishment of achieving such a challenging feat.
Outcomes: Climbing Mount Kilimanjaro not only proved to me that I could still accomplish significant physical, mental, and emotional challenges, but it also provided a platform to raise awareness for Parkinson's research. Through my climb, I inspired others living with Parkinson's to pursue their dreams. The expedition also served as a reminder of the importance of setting high but achievable goals and not letting a Parkinson's diagnosis define one's capabilities.
Conclusion: Climbing Mount Kilimanjaro was a life-changing experience for me and an opportunity to challenge the limitations that Parkinson's can impose. By sharing my experience with a wide audience, I hope to inspire others living with Parkinson's to set their own achievable goals and pursue their passions. I believe that this experience and accomplishment has the potential to change the narrative surrounding Parkinson's and prove that a diagnosis of Parkinson's does not have to be the end of living a fulfilling life.

LBP45.26

SParky Samba - Exploring the benefits of Samba percussion

Eirwen Malin[,1], Emma Lane[2]*
[1] Parkinson's UK Cymru, Cardiff, United Kingdom
[2] Cardiff University, Cardiff, United Kingdom

Background: In late February 2023 the Cardiff Branch of Parkinson's UK (CBPUK) accepted an offer of grant from the Arts Council of Wales(ACW) under their Arts, Health and Wellbeing Lottery fund. SParky Samba is an exploration of how learning percussion samba might affect the symptoms and quality of life of those with a diagnosis of Parkinson's and those around them.
The project is a partnership between CBPUK and Barracwda, a Cardiff based Community Samba band, with Cardiff University supervising the evaluation.
Instigated by a PWP within the Cardiff Parkinson's community and supported by CBUK this is very much a patient initiated and led project.
Assumptions and proposition: Dance for Parkinson's is recognised worldwide as an activity that contributes to living well with Parkinson's. It can be a valuable and enjoyable part of an exercise regime that mitigates movement symptoms and a social experience that encourages engagement and supports mental health. This study is expected to provide further evidence of these benefits. There has been some study of Brazilian Samba dance and Parkinson's, but to our knowledge, no study has evidenced the impact of participating in a Samba percussion band on Parkinson's. Particular features of Samba percussion may provide mechanisms which result in particular beneficial effects on both motor and non-

motor symptoms. The ACW grant allows the first phase of considering these effects and the enhancement of usual learning activities so that they become Parkinson appropriate where necessary.
Activity: Weekly "band practice" will allow the participants to learn Samba percussion, with its complex rhythms and counter rhythms, using different instruments. They will also have the experience of performing, with Barracwda band supporting SParky Samba in the early days.
Evidence collection: An early focus group of participants will shape the focus of semi structured interviews at the end of the project. Where possible participant identified quantifiable measures will be collected e.g. no of falls, incidence of freezing of gait, engagement in further social activity.
The project findings will provide preliminary data to guide the research questions and measures within a larger scale future project.

LBP45.39

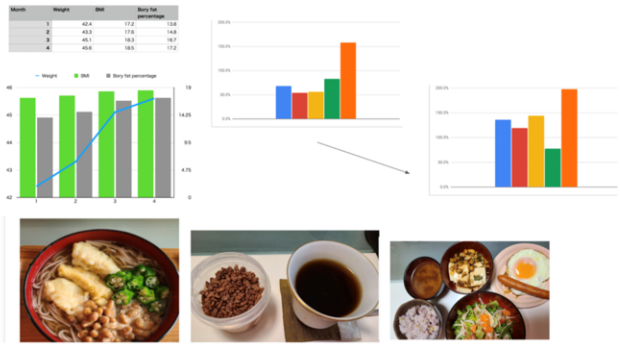
Mime as a therapeutic tool for people with Parkinson's Disease
Barbara Salsberg Mathews, Muhammad Kathia*
Mime Over Mind, Guelph, Ontario, Canada

Background: Exercise is a commonly applied intervention to address gait and clinical symptoms in people with Parkinson's disease (PWP). Significant improvements in gait have been observed when exercising in the presence of external (visual, auditory, and somatosensory) or internal (mental) cues. Moreover, mentally imagining/rehearsing a movement, observing someone else perform it, or performing the movement alongside cues, have all been shown to improve the performance of a motor act in PWP. One way to apply these strategies is through mime practice. Mime is a performance art, where the participant combines mental imagery, and different cueing strategies, to recreate the distinct step-by-step motor sequences of an activity. Studies have shown that adopting a different walking pattern (e.g., an exaggerated arm swing) improves gait initiation, speed, and stride length in PWP. While mime is being used as a therapeutic technique for PWP (e.g., Rob Mermin's Parkinson's Pantomime Project), no formal research to date has investigated mime specifically as a therapeutic approach for PWP. Mime techniques are easy to learn, highly customizable, require no specialized equipment and can be performed anywhere and at any time by an individual or in a group setting. Mime is now emerging as an effective adjunct therapy in PWP (https://parkinsonslife.eu/mime-over-matter-i-aim-to-live-life-fully/).
Aim: To generate significant visibility and awareness of mime as an effective therapeutic strategy in PWP to attract future research in this field.
Method: Lead an awareness campaign through a dedicated website, newspaper articles, televised interviews, and Mime over Mind: Retrain the Brain workshops showcasing the six principles of mime for PWP, i.e., awareness, observation, analysis, visualization, miming, and real-life application. Teach participants the application of the three mime concepts, i.e., freeze/relax, space substance, and point fix, to daily tasks, such as getting dressed and holding a glass. Present descriptive case studies of how mime practice has measurably improved the quality of life for PWP.
Outcomes: To engage and support academic, health and PWP communities to pursue research into using mime as an effective therapeutic tool.

LBP45.43

Utility in nutritional guidance for patients with Parkinson's disease
Misa Yamaguchi[1], Yasunao Baba[2], Makoto Shiraishi[3], Kenji Isahaya[3], Yuri Kintaka[4]*
[1] Nutrition Support Association, Tokyo, Japan
[2] Teikyo University Mizoguchi Hospital, Kawasaki, Kanagawa, Japan
[3] St. Marianna University School of Medicine, Kawasaki, Kanagawa, Japan
[4] Sapporo University of Health Sciences, Sapporo, Hokkaido, Japan

Background: Dietary guidance is necessary in Parkinson's disease to improve levodopa absorption, constipation, and weight loss, and the importance of nutritional therapy through multidisciplinary collaboration is becoming known, but there is no sufficient evidence. So far, I have been engaged in nutritional guidance and education for PD patients by holding seminars regularly as a patient but also as a dietitian.
Objective: From the perspective of a dietitian, we examined the outcomes in patient teaching, focusing on constipation control for Parkinson's disease patients.
Methods: Instruction was given to 25 PD patients. Dietary guidance with photographs and other information was described.
Weight change, food intake, and calories before and after the instruction were checked.
Results: This is presented as one example of improvement. There were no cases of weight gain or weight loss. There were also cases of improvement in constipation.
Conclusion: Nutritional guidance is effective for PD patients even in the early stage of disease onset and in younger patients, and we would like to provide new evidence from the patient's point of view as more cases are accumulated.



LIVING WITH PARKINSON'S: Advancing research: collaborations, capacity building, fundraising, trials, campaigns

LBP46.08

A framework to facilitate access to medicines for people with Parkinson's disease in Africa

Kabugo Hannington[*,1], Soania Mathur[2], Tania Park[3], Kat Hill[4], Nitish Sharma[5], Jared Okeno[6], Natasha Fothergill-Misbah[7]*
[1] Parkinson's Africa, Kampala, Uganda
[2] PD Avengers, Toronto, Canada
[3] Parkinson's Africa, London, United Kingdom
[4] Davis Phinney Foundation, Portland, United States
[5] World Parkinson's Program, Toronto, Canada
[6] Coast Neurology Centre, Mombasa, Kenya
[7] Newcastle University, Newcastle upon Tyne, United Kingdom

Introduction: Levodopa/carbidopa remains the most effective drug treatment for PD. However, people with Parkinson's disease (PwP) in Africa experience challenges with the accessibility, availability and affordability of branded and generic levodopa/carbidopa. Without sustained access to appropriate medication, PwP can experience worsening symptoms, with knock-on effects for the whole family, including stigma and discrimination.
Objectives: The goal of this work is to develop a framework to support a sustainable, long-term supply of zero-cost levodopa/carbidopa to PwP living in Africa who cannot afford PD medication. The shocking consequences of lack of medicines was witnessed in March 2023 during fieldwork in Kenya, driving the urgency of this pilot.
Methods: The Medication Equity Working Group of the PD Avengers will collaborate with partner organizations to develop a pilot proposal primarily supported by 2 organizations. Parkinson's Africa will work in partner countries (initially Kenya and Uganda), establishing need, supporting PwP and facilitating delivery of medications. World Parkinson's Program (WPP) will facilitate the purchase of medicines in-country, utilizing established pharmacy networks and systems. The pilot will have clear guidelines and a review and selection process to register clinically diagnosed PwP in need. The proposed framework will require funding. One option is larger PD charities and organizations assisting in this global effort by allocating a small percentage (1%) of charitable donations they receive towards a medication funding pot centrally held and administered by WPP.
Results: This framework has the potential to support PwP for whom a PD diagnosis has devastating consequences. We hope to establish a sustainable way to fund consistent access to medicines for these individuals, in the hope that more sustainable solutions will be developed, initially expanding ongoing work in Mukono district, Uganda and piloting the project in the coast region of Kenya. Once a successful pilot project is completed, the framework can be modified for other communities in need worldwide.
Conclusion: Ensuring the availability of medicines for PD is a key action of the World Health Organization Parkinson Disease Technical Brief. There is a need for holistic and multi-sectoral engagement to support access to affordable medicines in low- and middle-income countries of the world, such as in Africa.

LIVING WITH PARKINSON'S: Other

LBP47.06

In their own words: Fears of people with Parkinson disease

Sneha Mantri[*,1], Jennifer Purks[2], Daniel Kinel[3], Allison Allen[1], Connie Marras[4]*
[1] Duke University, Durham, NC, United States
[2] Georgetown University, Washington, District of Columbia, United States
[3] University of Rochester, Rochester, NY, United States
[4] University of Toronto, Toronto, ON, Canada

Background: A diagnosis of Parkinson disease (PD) carries substantial psychosocial burden and fear, which may contribute to poor quality of life. However, the range of fears experienced by people with PD is under-reported. The online PD-Patient Report of Problems (PD-PROP), which asks over 25000 participants to list up to 5 "most bothersome problems" and the consequences of experiencing those problems, enables clinicians and researchers to read verbatim reports from people with PD about their most bothersome problems, providing a potential repository of fears.
Design/Methods: The PD-PROP database was queried for terms such as "fear of…" and "afraid of…" After false positives and duplicates were removed, 290 deidentified verbatims from 285 unique individuals were analyzed using the framework method for qualitative research. Domains and subthemes were refined by iterative coding and discussion among the research team. The frequencies of verbatims in each domain and subtheme were quantified.
Results: The most common reported fear was uncertainty around disease progression (n=83/290, 28.6%, sample quotation "This is actually the worst problem with my PD = fear of progression and the future.") Fears of specific non-motor symptoms were also common, including fear of cognitive impairment (n=35, 12.1%). Twenty-eight verbatims (9.7%) expressed fear of becoming a burden on family members, and 27 (9.3%) reported fear of being socially isolated as a result of their PD diagnosis. Some verbatims expressed frustration at the negative framing of PD by the medical community: "I wish we could be told more about people who progress slowly and are able to maintain some semblance of health. I know those people ar [sic] out there!!! It robs me of my ability to have hope.… It would mean so much to me if the PD medical community could be more hopeful."
Conclusions: Fears in PD are wide-ranging and both existential and related to specific symptoms, usually non-motor. Further analysis is needed to understand the demographic, clinical correlates and further impacts of PD fears. The range of fears quantified in the PD-PROP can be used to design educational materials and interventions to lessen the psychosocial burden of PD.

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