

Abstracts of the Third World Parkinson Congress



October 1 – 4, 2013
Montreal, Canada



Hosted and designed by the World Parkinson Coalition Inc., a nonprofit organization based in New York, NY, USA.

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3rd WORLD PARKINSON ABSTRACTS

Pre-Congress Oral Presentations

PCO01

Fundamentals of PD - Introduction

Tom Isaacs

The Cure Parkinson's Trust, London, UK

Objectives: To welcome everyone to the World Parkinson Congress 2013

To provide an overview of the history of WPC and the increasing involvement of people with Parkinson's

To look back at the legacies of previous WPC's and to suggest possible initiatives going forward

To set the tone of the meeting – the importance of having PwP's at the Congress and our role in making the conference a success
"Do's and Don'ts" for WPC 2013

PCO02

Pathology of Parkinson's disease

Dennis W. Dickson

Mayo Clinic, Jacksonville, FL, USA

Objective: To describe pathologic changes in the brain in PD.

Methods: Illustrate pathology in PD from a personal review of over 250 PD brains, as well as a set of over 1000 dementia brains with Lewy body pathology.

Results: The most common pathologic substrate of PD is Lewy body disease. Lewy bodies (LBs) are intraneuronal inclusions composed of α -synuclein. In addition to LBs, abnormal α -synuclein is also found within neuronal processes as Lewy neurites (LNs) and in oligodendroglial inclusions. LNs are widely distributed and are most abundant lesion in most regions. They may also be the earliest alteration in affected neurons and may precede LB formation in perikarya. The vulnerability of select populations of neurons to LBs has been known for many years and includes not only monoaminergic neurons of the substantia nigra, locus ceruleus and raphe nuclei, but also cholinergic neurons of the basal forebrain, as well as neurons in the dorsal motor nucleus of the vagus and the medullary and pontine reticular formation. The hypothalamus and pedunculopontine nuclei are often affected. Spinal cord neurons of the intermediolateral cell column are vulnerable. LBs and LNs are also found in the autonomic ganglia of the gastrointestinal and cardiovascular systems. Neurons in the anterior olfactory nucleus are also vulnerable. Cortical neurons are less often affected in PD, with neurons in the limbic cortices most vulnerable. Braak and co-workers proposed a pathologic staging system for PD that takes these observations into account. In the most advanced stages, LBs are widespread in the cerebral cortex similar to dementia with Lewy bodies (DLB). In contrast to DLB, Alzheimer type pathology is less frequent in PD and PD with dementia (PDD).

PCO03

What causes PD?

Marie-Francoise Chesselet¹

¹Department of Neurology, UCLA, Los Angeles, CA USA

Objective: Our understanding of the causes of Parkinson's disease has progressed very much in the last decade. This presentation will review the current information.

Methods: Both genetic and environmental (epidemiological) studies have contributed to elucidating some of the causes and risk factors of PD.

Results: In most cases, the cause of PD is not known but studies have revealed important factors both from exposure to the environment and from individual genetic make up, that can combine to increase or decrease the risk of developing PD. In addition, in some cases, PD runs into families and many of the genetic factors involved in these familial cases have now been elucidated. Importantly, these have illuminated some general mechanisms of the disease that apply to everyone and may help develop new treatments.

PCO04

Non-motor Features of PD

Ronald F. Pfeiffer

University of Tennessee Health Science Center, USA

Objective: In recent years, recognition has grown that Parkinson's disease (PD) encompasses much more than difficulty with movement. A whole host of features that have little or nothing to do with movement are important, and sometimes dominant, features of PD. Changes in mood, loss of motivation, increased anxiety, difficulty with thinking and memory, excessive fatigue, sleep disturbances, problems with bowel, bladder, and sexual function, excessive sweating, impairment of sense of smell and therefore also taste, changes in some aspects of vision, and a variety of types of pain all are examples of these "nonmotor" features of PD. Although some nonmotor features characteristically appear later in the course of PD, others may occur very early, even before the classic motor features of PD develop and sometimes before PD is even diagnosed. Recognition of the nonmotor aspects of PD is important because they do not always respond to traditional PD treatment measures that typically target dopamine, but may respond to other treatment approaches. The fact that nonmotor features of PD often cause more distress - both for persons with PD and for their family members - makes it especially important that these features are recognized and addressed. In this session, an overview of the nonmotor features of PD will be provided.

PCO05

Medical Therapy

Christopher G. Goetz

Rush University Medical Center, Chicago, IL USA

Parkinson's disease (PD) can be considered as a cellular disease and a biochemical disease. On the one hand, circumscribed cells in the central nervous system begin to die and this process is an ongoing degenerative process; on the other hand, these cells primarily produce the chemical, dopamine, causing a progressing deficit of this chemical and, to a lesser extent, other naturally occurring chemicals, termed neurotransmitters. Existing and evolving medical therapies for PD target both of these processes. To date, no therapy has been documented to preserve brain cells in PD, although many new programs are on-going and are aimed at restoring (neuro-restorative) or preventing (neuroprotection) continued cell degeneration. If successful, these treatments could potentially halt the disease at a very early phase in newly diagnosed patients, stabilize patients in the mid-stage of disease, and potentially prevent the disease from emerging if it can be diagnosed before the typical signs that define the disease emerge (tremor, bradykinesia and rigidity). Most available medical treatments used

for treating PD enhance dopamine function and therefore target the biochemical deficit that results from cell loss. The Movement Disorder Society (MDS) sponsors an Evidence Based Medical Review (EBMR) program to apply a set of standard criteria to compare treatments in different drug categories across four distinct patient applications: use as monotherapy to treat parkinsonism; use as an adjunct to levodopa, the precursor to dopamine and the most widely used drug to treat PD; use in the prevention of motor complications that include involuntary movements, termed dyskinesia and an irregular response to medication, termed motor fluctuations; use in the treatment of dyskinesias and motor fluctuations. A review of the 2011 MDS EBMR document for these four categories of treatment emphasizes the utility of different agents for different problems and allows a focus on those treatments that have been designated as EFFICACIOUS for a given clinical problem. Agents include monoamine oxidase B inhibitors, amantadine, dopamine agonists (pramipexole, ropinirole, rotigotine), and levodopa, prescribed with carbidopa and sometimes with a catechol-O-methyl transferase inhibitor (entacapone or tolcapone). With scientific advances, a number of new agents are being tested to face the challenges of PD and new formulations of older drugs are being developed. These advances are aimed at refining the existing treatments to enhance benefit, reduce side effects, and ultimately improve the quality of life of PD patients and their families.

PCO06

What you can do after you are diagnosed to stay involved

Peter Davison

Person with Young Onset Parkinson's, Bedford, NS, Canada

Objective: This presentation highlights the options and benefits of getting involved and helping at the local and national level with opportunities and needs such as: advocacy, education, fundraising, clinical trials and support groups. Webinars, teleconferences and other community empowering technology will also be showcased as effective tools to keep people informed, encouraged and involved in living well with Parkinson's.

PCO07

Therapeutic options to stay active and involved: Speech and Parkinson's

Bonnie Bereskin

Speech-Language Pathology Clinic, Toronto, ON, Canada

Objective: Speech therapy in Parkinson's is both an art and a science. Communication is one of the most challenging of human behaviors, requiring rapid functioning and coordination of many systems. This talk will review the current understanding of all aspects of communication and its changes throughout the Parkinson journey. Communication includes motor-speech, language, pragmatic and social skills. Parkinson's affects all of these functions. Speech may be quiet and monotonous with indistinct articulation and occasionally, stuttering. Some individuals experience difficulty finding words or following a complicated conversation, in later stages. Others may find a social situation challenging, as a result of slowness in formulating a message and "getting into" a conversation. Current knowledge of all of these changes will be discussed, as they impact the success of therapy and transfer of skills to social settings. The targets of intervention have broadened and include not only the speaker with Parkinson's but the listener, as speech is not a solitary activity. LSVT has proven effectiveness in improving speech and voice loudness in all stages of Parkinson's. With progression of the illness, cognitive and mood changes may make it challenging for some to practice voice

exercises and transfer the louder voice to social settings. As a result, it has been found helpful to involve family members and/or volunteers to support communication. Therapeutic approaches, in addition to LSVT, are beneficial for those with more severe dysarthria.

Discussion: There will be discussion of the resource challenge of providing effective intervention in a neuro-degenerative disorder that spans many years and affects the motor and cognitive systems. A number of creative models of on-going and cost effective approaches will be discussed, such as on-line therapy, cycling of intervention and group treatment.

PCO08

Therapeutic options to stay active and involved: Physical Therapy and Parkinson's

Terry Ellis

Boston University, Boston, USA

In this session, participants will become more informed regarding the benefits of physical therapy and exercise. In addition, participants will gain an appreciation of the role that physical therapy can play in the management of Parkinson's over the course of the disease. The evidence demonstrating the benefits of physical therapy and exercise for persons with Parkinson disease will be summarized and the impact on reducing disability, improving physical function and enhancing quality of life will be reviewed. In addition, the key elements of an exercise program will be explored. The importance of long-term adherence to exercise and adopting an active lifestyle to optimize outcome will also be emphasized. Practical tips to reduce sedentary behaviors and become more active will be shared.

PCO09

Therapeutic options to stay active and involved: Occupational Therapy and Parkinson's

Margarita Makoutonina

ParkLife Australia Pty Ltd, Melbourne, Victoria, Australia

Objective: Despite the benefits of medical and surgical interventions for people with Parkinson's (PwP), patients still develop disability in both the motor and non-motor domains that lead to the likelihood of hospitalisation, a loss of independent living and serious social and economic consequences (Chaudhuri, 2011). Many Occupational Therapists (OTs) lack understanding of the symptoms of Parkinson's disease (PD) and the latest assessment and treatment techniques due to a lack of description of evidence and consensus Occupational Therapy in PD. This presentation will review the OT's vital role within multidisciplinary team (MDT) (lansek et.al., 1995) addressing motor and non-motor symptoms (NMS).

Methods: In this short presentation we will provide a summary of importance of specialist training in PD for OTs and interdisciplinary team work in assisting PwP to stay active and involved; specific guidelines for OT intervention and their relationship with disease severity and duration; implementation of PD specific assessments to address holistic evaluation (Chaudhuri, 2010) thus assisting the OTs in designing of targeted rehabilitation and provision of the best practice in OT for PwP. We will emphasise the importance of: clients to be referred to OT services; self management of the disease by the clients; empowering the patients and families to control and to minimise impairment through taking an active role in the process of both comprehensive assessments and establishing rehabilitation program, considering the functional ability during ON and OFF phenomenon.

Results: Through this presentation we hope to increase awareness and promote OTs as Health Professionals that have expertise in optimising PwP functional performance and engagement in meaningful activities (Bloem et al., 2010) thus delaying the earlier development of disability.

PCO10

Future therapies: Drug treatments

Olivier Rascol

Departments of Clinical Pharmacology and Neurosciences, CIC-9302/INSERM UMR825, Faculty of Medicine Purpan, University UPS of Toulouse III, Toulouse, France

Available antiparkinsonian medications improve the motor symptoms of patients with Parkinson's disease (PD). However, overtime, disability progresses despite the combinations of such medications and three current therapeutic limitations deserve new approaches: Managing "dopa-resistant" motor and non-motor symptoms (speech impairment, abnormal posture, gait and balance problems, autonomic dysfunction, mood and cognitive impairment, sleep problems, pain...), Managing drug-related dopaminergic side effects (psychosis, motor fluctuations, dyskinesias, somnolence, ICD...), Halting or slowing the progression of the disease. Efficacious "disease modifying" medications should prevent the patients from reaching the stages when patients are facing most problems resisting to current therapies. Many candidates are developed. A definite demonstration of such a disease-modifying effect proves difficult, although some pilot encouraging results have been obtained with drugs like rasagiline. Novel symptomatic medications are on development, acting via dopaminergic (new L-dopa formulations, novel COMT inhibitors) or non dopaminergic mechanisms (including agents acting on adenosine A2, glutamate NMDA and mGluR5, serotonergic, noradrenergic alpha-2, histaminergic, cannabinoïds receptors). New delivery systems are also explored such as peripheral transdermal patches, subcutaneous and intraduodenal pumps or direct drug delivery within the brain (pumps, cell- or gene-therapy). Such innovative strategies raise numerous challenges including the refinement of new pathophysiological concepts, the development of more predictive animal models and the improvement of clinical trials designs.

PCO11

What do we face?

Bastiaan R. Bloem

Department of Neurology, Parkinson Centre Nijmegen, Radboud University Nijmegen Medical Centre, Nijmegen, The Netherlands

Parkinson's disease (PD) is a complex disorder with a diverse set of motor and non-motor symptoms (NMS) that are progressively debilitating. Patients may also develop co-morbidities, such as cerebrovascular disease. Traditionally, Parkinson patients are managed by a single medical specialty (neurologist or geriatrician) and are prescribed dopaminergic medication. The drugs can improve some, but not all, motor symptoms, and are generally not effective against NMS. Moreover, efficacy is lost over time, because motor complications limit drug dosage, and psychiatric complications develop. Patient adherence is poor, perhaps because of adverse side effects, difficult drug regimens or perceived lack of efficacy. Non-pharmacological therapies should therefore be considered, in particular multidisciplinary rehabilitation to ensure that patients receive the right treatment at the right time. The rehabilitation team should include medical specialists, Parkinson nurses, allied healthcare specialists, psychologists and dieticians.

Additionally, patients and their caregivers should be included as full team members. Treatment plans should be patient-centered and tailored to the individual's needs, addressing not just disease severity and symptoms but also the associated problems in everyday activities, relationships, employment and independence. Patients should be involved in shared decision making, and prioritize the treatment goals. One example that includes these elements of care is the Dutch ParkinsonNet concept, which consists of a series of regional networks of dedicated professionals specialized in the treatment of PD. A clinical trial involving 700 patients showed that the ParkinsonNet markedly improves the quality of care and allows for considerable cost savings. While the clinical experience with a multidisciplinary rehabilitation approach to managing PD patients has been excellent worldwide, the data to support this approach remains limited. More studies are needed to demonstrate the cost-effectiveness of integrated multidisciplinary care and to find the best organization of care to improve the quality of life for patients, their families and caregivers.

PCO12

How is it addressed? & Overview of available delivery options

Ruth Hagestuen

National Parkinson Foundation
Struthers Parkinson's Center, MN, USA

Objective: Present an overview of care delivery for Parkinson's disease as a dynamic, evolving process. Discuss models and rationale for multidisciplinary / interdisciplinary and / or inter professional patient centered care for person's whose lives are affected by Parkinson's disease throughout the continuum of care. Describe the chronic care model and propose a framework for action based on recommendation of the World Health Organization.

Methods: This presentation will

- lay the groundwork for discussion throughout the day with an overview of how care models for PD have evolved in the recent decade
- include description of currently available PD care delivery options in a variety of settings
- build the case the importance of establishing a PD care environment that offers access to the right information, care and support / wellness options at the right time throughout the continuum of care
- this will be done in the context of acknowledging barriers: educational; financial and healthcare systems.
- examples of successful initiatives and programs which have been established to meet the care needs for Parkinson's will be presented and available evidence for coordinated team and inter professional care will be presented
- outline the framework for action put forth by the World Health Organization as a prototype for delivery of care for chronic illness

Results: Participants will be able to

- Discuss the importance and advantages of patient centered care
 - Identify at least three barriers to accessing optimum care which are often encountered by persons with Parkinson's
 - Describe the core components of an effective inter professional care model
 - Identify two key processes involved in the WHO framework for action

PCO13**What this all means for people with Parkinson's***Alice Templin*

Parkinson Society Ottawa, Ottawa, ON, Canada

At the heart of the discussion about a service delivery model that engages many team members is a unique individual living with Parkinson's. This presentation will explore the perspective of the PwP - the importance of his individuality, his expectations and his role - along with his reaction to a multidisciplinary team, in the development of an effective service delivery model.

First and foremost, the care plan for the PwP must be rooted in a person-centered philosophy of care, one which is sensitive towards the individual expression of the person he is. All clinical interactions and interventions must respect his feelings, needs, values and beliefs. Secondly, each PwP will have his own understandings and expectations regarding his future with PD. The service delivery model faces the challenge of ensuring the alignment of that perspective with facts, realistic hope and the rights of the PwP. Furthermore, the expectation to receive the best treatment possible requires the model to be flexible enough to incorporate new best practices based on the ever-growing body of PD knowledge and the continually changing reality of the world we live in. Finally, the multidisciplinary team approach involves many people. The constant and central role of the PwP needs to work with the changing roles of the other team members. The PwP has a right and a responsibility to be a key member of the team but may not always be able and willing to fulfill that role. The service delivery model should incorporate and foster the leadership role of the PwP while engaging the other team members in a timely, sensitive, effective and efficient manner. The integration of these factors into a service delivery model will ensure that the PwP is receiving the best care possible

PCO14**General practitioner's role***Christiane Lepage*

Montreal University, Montréal, QC, Canada

With the increase prevalence of Parkinson disease, the general practitioner (GP) will be asked to play a important role in PD patients care. Although the current medical literature shows better outcomes for the patient when followed by a neurologist, what is the place for the GP? Would the best model care not be an interdisciplinary team? A team composed by the GP, the neurologist and other healthcare professionals. The GP is often the first one to suspect the diagnosis. He can make the initial assessment and begin a treatment if indicated. He can play an important role in medication's adjustment in association with the neurologist, especially for the patients of remote regions. Besides, the GP is the best placed to make the management of the non-motor symptoms which are quite similar to geriatric problems. He is also well placed to be the conductor of the interdisciplinary team when the patient begins to present a loss of autonomy. However, several difficulties can be raised: in opposition to chronic diseases as diabetes or HBP, the GP often does not feel comfortable with the diagnosis and the management of Parkinson disease. The neurologists sometimes have to substitute themselves for the first line, even to solve problems which do not normally concern them. The difficult access to specialized services and the misunderstanding of specific services for this clientele can limit their use. Suggested solutions: Better training during primary care program and continuing medical education in the management of Parkinson disease. Better communication between GP and neurologists and use of videoconsultation. Diffusion of the available services through the Parkinson societies. Finally, research has to be

made on the impact of services provided by an interdisciplinary team on patients' quality of life.

PCO15**Nurse's role***Lucie Lachance*

McGill University Health Centre, Montreal, QC, Canada

Background: The Canadian guideline for Parkinson Disease recommends that People with suspected PD and untreated should be referred "quickly" to a specialist with expertise in the differential diagnosis of this condition- "quickly" means within 6 weeks, but new referrals in later disease with more complex problems require an appointment in 2 weeks.

Objective: Our goal was to reduce the waiting list from 6 months down to a maximum of 6-8 weeks and. We believe that a rapid access clinic staffed by expert health professionals allow patients seamless care throughout the continuum of their disease. The Rapid Access Parkinson clinic offer each patient the services of a nurse clinician, a highly-trained professional who "coaches" individuals, and their families through the health care system.

Method: This extra clinic day consist of 2 nurses clinicians and one the neurologist. Patients with suspected Parkinson's disease are seen in a timely fashion and have immediate access to the nurse clinician who guide and counsel patients ensuring continuity of care. If need be the nurses clinicians see patients in follow-up in between the MD visits to address emerging and urgent needs. If a patient is admitted to ER, the nurse clinician ensure seamless communication with respect to medication schedules and personalized care.

Results: Already the Rapid Access PD clinic proved to be a better way to function, better triage of our waiting list and the addition of the nurse clinician has already positive feedback in terms of returning telephone calls for anxious patients of caregivers in a timely manner. We are collecting stats and we anticipate other benefits like fewer emergency room visits and more support when in-patient hospital care is required. This program also provide the much needed communication to home care staffs and long-term care facilities.

PCO16**PANEL- Multidisciplinary teams***Ruth A Hagestuen*Struthers Parkinson's Center, Minneapolis, MN
National Parkinson Foundation

Objective: Introduce the individual presenters, and outline theme and logistics of the session.

Methods: Brief speak to the value of joint learning in sessions such as this where we are introduced to service delivery models of care that have developed and are continually evolving in different countries and varying healthcare systems.

Results: Panel will present their care delivery programs and systems. Following the presentation there will be an opportunity for discussion. Participants will be able to identify core themes of all care delivery models and identify unique aspects of each.

PCO17**Israeli Model- Tel Aviv***Nir Giladi*Department of Neurology, Tel Aviv Medical Center, Israel
Sackler School of Medicine, Tel Aviv University, Israel
Sagol School of Neuroscience, Tel-Aviv University Israel

In 1996 we have established the first Parkinson Center in Israel working according to the Interdisciplinary team approach methods. The concept of the Center is that the team members see the patients and the families with Parkinson in the Parkinson Center – the Movement Disorders Unit. Besides 4 neurologists we always have 1-3 specialized Parkinson nurses, a social worker as well as a speech and language pathologist, physiotherapists and sexologist. In addition to the main Parkinson clinic we have opened a special clinic for care givers, a special fall prevention clinic as well as a special clinic for atypical parkinsonism as well as a special service for autonomic dysfunction. In the past year we have realized the importance of the psychiatric aspects involved in PD as well as the results of DBS which justifying a psychiatrist in the team. The addition of a psychiatrist to our team has added a whole new dimension to our center and we are only now realizing the significance and the added value of such a specialized person in our team. Since the recent development in the role of genetics in PD and the fact that in Israel up to a 1/3 of the Ashkenazi patients are genetic cases of PD we have developed over the recent years a genetic counseling service for Families with PD as well as clinical counseling to first degree relatives of PD patients with known mutation, recommending behavioral modification as well as specific interventions to reduce the risk for PD. The Parkinson Center is actively involved in multiple clinical studies as well as more basic research. All researchers as well as the students are participating in a weekly meeting with the clinicians, where exchanges of information as well as new research ideas are brought up. Such weekly meeting is essential for the success of the Center. Since 2005 our center is recognized as a Center of Excellence by the National Parkinson Foundation of Miami USA.

PCO18

Netherlands Model- ParkinsonNet

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The Dutch model to deliver optimal care to all Dutch patients with Parkinson's Disease consists of regional networks of health care professionals (e.g. neurologist, Parkinson nurse, physical therapist, speech therapist, occupational therapist, social worker, etc) who are specialised in the treatment of Parkinson patients, and who work effectively together in a patient-centred approach. We started with this concept in 2004 in our own region (Nijmegen) and other regions followed soon. Currently a ParkinsonNet has been implemented in all of the Netherlands (in total 66 regions, including more than 2.500 specialised healthcare providers who have become members of ParkinsonNet). ParkinsonNet is characterized by adequate and continuous training (to work according to current clinical guidelines) and by certification of all members. In addition, we stimulate collaboration between healthcare providers within regions and provide patients with background information about our members, allowing them to make an informed decision about the treatment that best suits their individual needs. Moreover, we provide feedback to patients about the actual quality of care delivered by our members, both as a service to patients and as a benchmark for professionals (so they can improve their services). More information is presented on our website www.parkinsonnet.info

PCO19

US Model – Struthers Parkinson's Center

Ruth Hagestuen

Struthers Parkinson's Center, Golden Valley, MN

National Parkinson Foundation

Objective: This presentation will provide an overview of the Struthers Parkinson's Center's integrated approach to clinical, educational, research, support, outreach and wellness programs. The Center, established over 30 years ago, is a free-standing facility which is part of the Park Nicollet Health System.

Methods: The SPC integrated system of care is designed to provide access to the right care, information, and support at the right time, over time. The majority of programs which will be presented are team based. The full day assessment clinic, for example, includes physician, nurse, social worker, physical therapy, occupational therapy, speech therapy. Different combinations of the team members are part of the FOCUS program for persons newly diagnosed, the Caregiver Skills-building series, and the DBS educational sessions for patients and families considering Deep Brain Stimulation. The same is true of the regularly scheduled professional education days for nurses, rehabilitation therapists and social workers. Two other unique programs of this Center are (1) the CREATE (Center for Research Education Artistic and Therapeutic Endeavors) program which includes a therapeutic day program, an arts café, and a variety of exercise based wellness and support programs and (2) The Struthers Parkinson's Care Network (SPCN), working with senior residential communities to improve PD awareness, staff education and support services.

Results: Attendees at this session will (1) be able to list at least two unique program initiatives from Struthers Parkinson's Center that can be replicated in other locations, (2) Discuss the role of a Parkinson's Center as a regional hub of specialized care in the U.S. (3) Identify times during the course of living with Parkinson's disease where access to specialized services is most critical.

PCO20

Australian Model- Melbourne

Meg E Morris

La Trobe University, Victoria, Australia

Objective: Parkinson's disease is a chronic and progressive condition that can affect movement, balance, mobility, the ability to perform daily activities, autonomic function, cognition, and psychosocial function. It affects individuals as well as families and caregivers. Each person living with Parkinson's disease is unique and services need to be comprehensive and tailored to individual needs.

Methods: In Melbourne Australia we have led comprehensive inter-professional rehabilitation services to assist people with Parkinson's disease and the significant others in their lives to live well with this condition. Rehabilitation interventions are research led and based on current scientific findings on responses to movement rehabilitation strategies, strength training, cognitive training, and physical activities such as walking, dancing and hydrotherapy. Services are provided in home, community and hospital settings. As well as adopting science informed clinical guidelines, emphasis is placed on teaching health professional how to work effectively and efficiently within a team and how to ensure client centred and family focussed outcomes.

Results: In both young adults and older people with PD, a comprehensive inter-professional team based model of rehabilitation has been found to be effective, feasible and safe. As well as optimising mobility, functional task performance and physical activity, it is argued to reduce care-giver burden by empowering people to be more independent. The aim is to optimise quality and

life and well-being through targeted and effective services provided at the right time by the right person in the right environment.

PCO21

Canadian Model- McGill Movement Disorders Clinic

Anne-Louise Lafontaine

McGill Movement Disorder Clinic, Montreal, QC, Canada

Objective : This presentation will describe a new model for care. The rapid access clinic was established for the diagnosis and early intervention in patients with suspected Parkinson disease. Our goal in establishing this clinic was to reduce the current waiting list from 6-12 months down to a maximum of 6-8 weeks. The clinic would also provide patients access to care in between the scheduled MD visits to deal with important issues as they emerge. The McGill Movement Disorder clinic was established in 2001. The clinic currently follows close to 1000 patients. Because of space and manpower issues, our wait list is 6-12 months for the initial visit and follow up visits are routinely scheduled at 4-6 month intervals. The waiting time to first visit is well outside the window recommended by a recently developed Canadian guideline for Parkinson Disease. The guidelines recommend that People with suspected PD should be referred quickly* and untreated to a specialist with expertise in the differential diagnosis of this condition. (*..should be seen within 6 weeks, but new referrals in later disease with more complex problems require an appointment in 2 weeks).

Method: The Rapid Access Parkinson clinic offers each patient the services of pivot nurses, highly-trained professionals who "coaches" individuals, and their families through the health care system. This model of care has the pivot nurse as the first line contact with patients from first visit and throughout the continuum. Patients will be provided with a telephone number that links them with a pivot nurse for concerns in between visits or for telephone feedback. This program will reduce delays in diagnosis and treatment of Parkinson's disease and will alleviate the anxiety of navigating complex symptoms. Other anticipated benefits include easier access to follow-up care, fewer emergency room visits and more support when in-patient hospital care is required. This program will also provide the much needed communication to CLSCs and long-term care facilities. Pivot nurses and the social worker will see patients in follow-up in between the MD visits to address emerging and urgent needs. When Parkinson patients are admitted to the emergency room or hospital ward, the pivot nurse will ensure seamless communication with respect to medication schedules and personalized care.

Oral Sessions

O1

Propagation of the neurodegenerative process in PD and the Prion-like hypothesis

Virginia Lee

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The accumulation of misfolded proteins is a fundamental pathogenic process in neurodegenerative diseases. These hallmark proteinaceous lesions include extracellular senile plaques comprised of the A β peptide and intracellular neurofibrillary tangles consisted of tau proteins in Alzheimer's disease as well as α -synuclein (α -syn) containing Lewy bodies and Lewy neurites in Parkinson's disease. We hypothesized that templated recruitment of endogenous proteins by misfolded conformers follow by cell-to-cell spreading of the pathology are a common disease mechanism

that account for the progression of these age-related disorders. In both tauopathies and synucleinopathies, we demonstrate that pre-formed fibrils (pffs) generated from recombinant tau or α -syn enters cultured primary neurons as well as transgenic and wildtype mice, promoted recruitment of soluble endogenous proteins into insoluble protein aggregates resembling the pathology in their human counterparts. Pathologic misfolded aggregates propagated along major central nervous system (CNS) pathways to regions far beyond injection sites and appear to follow neuroanatomical interconnectomes. Thus, synthetic α -Syn or tau pffs are wholly sufficient to initiate neurodegenerative disease pathology and transmit disease in primary neurons *in vitro* and in mice *in vivo*. Thus, these data support a prion-like cascade in neurodegenerative disease protein spreading whereby cell-to-cell transmission and propagation of misfolded proteins underlie the CNS proliferation of disease pathology. These findings open up new avenues for understanding the progression of neurodegenerative diseases and for developing novel therapeutics.

O2

Can the interaction between genetics, environment, and behavior be a key determinant of PD expression?

Christine Klein

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The current consensus on the pathogenesis of Parkinson disease (PD) suggests that PD is an etiologically heterogeneous disorder developing from multiple causative/risk factors including genetic predisposition, aging, and environmental exposure. Accordingly, this has led to a multiple-hit model of PD pathogenesis, ultimately resulting in a 'disease map'. Although collectively only explaining about 5% of all cases, causative PD genes are the currently best-studied etiology of the condition and monogenic PD can serve as a human disease model. Among the six unequivocally identified forms causing a clinical picture closely resembling idiopathic PD, three (SNCA, LRRK2, VPS35) follow an autosomal dominant mode of inheritance, whereas three are recessively inherited (Parkin, PINK1, DJ-1). Risk variants in some of these, as well as in other genes - most notably GBA -, can act as susceptibility factors and disease modifiers of 'idiopathic' PD. Importantly, monogenic and 'idiopathic' PD share common pathophysiological mechanisms converging on oxidative modification, impaired protein degradation, and mitochondrial dysfunction. Epigenetics, i.e. heritable changes in gene expression that do not involve coding sequence modifications, is commonly considered the missing link between the genome and the environment. Environmental agents, often present in the context of specific behaviors, such as smoking, have the potential to not only directly damage/protect the developing and mature nervous system but to also impact on genes involved in neurodegeneration by epigenetic means, leading to altered gene expression. Instead of studying individual components of PD pathogenesis, recent attention has increasingly been focused on the interaction and dynamics of these different etiological factors. This has led to the discovery of first significant gene-environment interactions, such as SNCA risk variants and head injury. These observations collectively suggest that a network analysis may be required to disentangle the complex puzzle of genetic, environmental, and behavioral factors in the etiology and expression of PD.

O3

What epidemiological and preclinical studies teach us about inflammation and PD*Etienne C. Hirsch*

Centre de recherche de l'Institut du cerveau et de la moelle épinière, INSERM UMR975, CNRS UMR 7225, UPMC, Hôpital de la Salpêtrière, Paris, France

Both epidemiological and genetic studies support a role of neuroinflammation in the pathophysiology of Parkinson's disease (PD). Indeed, both prospective and retrospective epidemiological studies indicate that the long term use of anti-inflammatory drugs and especially ibuprofen reduces the risk of developing Parkinson's disease. On the other hand genome wide analysis also indicate that one haplotype the immune related gene HLRdr is associated with a higher risk to develop the disease. Furthermore, post mortem studies confirm the involvement of innate as well as adaptive immunity in the affected brain regions in patients with PD. Indeed, activated microglial cells and T lymphocytes have been detected in the substantia nigra of patients concomitantly with an increased expression of pro-inflammatory mediators. Preclinical investigations inflammatory processes are instrumental in neuronal cell death even though they are unlikely to be a primary cause for neuronal loss. Neuroinflammatory processes in PD are rather involved in self-perpetuating deleterious events that lead to protracted neuronal degeneration. In line with this, recent data indicate that glucocorticoid receptors are important in curtailing microglial reactivity, and deregulation in their activity in PD could lead to sustained inflammation-mediated degeneration. Altogether, neuroinflammatory processes might represent a target for neuroprotection in PD.

O4

Developing new treatments founded on the basic science of Parkinson's disease*Patrik Brundin*

Laboratory for Translational Parkinson's Disease Research, Center for Neurodegenerative Science, ¹Van Andel Institute, Grand Rapids, MI, USA, and Neuronal Survival Unit, Wallenberg Neuroscience Center, Lund University, Lund, Sweden

This presentation highlights some challenges facing the translation of findings in the basic science laboratories to clinical therapies for Parkinson's disease (PD). The past three decades have seen a tremendous development of animal-models of PD, primarily along two lines: *First*, researchers have used neurotoxins that are relatively specific for dopamine neurons and/or have mechanisms of action resembling putative pathogenic mechanisms of PD. In animals, these toxins can result in excellent modeling of the transmitter changes occurring in the nigrostriatal pathway, and in motor impairments akin to those observed in PD. The development of new pharmacological treatments to "replace" dopamine has benefitted from toxin-based models. Neurodegeneration in toxin-based animal models, however, is often very rapid lacking the slow, progressive features that are typical of PD. Moreover, these models rarely encompass the non-motor symptoms (e.g. depression, cognitive decline, constipation) that are important sources of morbidity in patients. *Second*, several genetic models have been created based on the numerous mutations that are coupled to rare inherited forms of PD. These models do not always result in neuronal death, but instead recapitulate other neuropathological features of PD (e.g. protein aggregation). Furthermore, these models might not be relevant to the more common sporadic PD. The main challenge today is the need for a therapy that slows PD progression. Such a disease-modifying therapy would revolutionize

the PD treatment. Several experimental treatments have been found to "modify disease", in the toxin-based and genetic PD models. Yet when tested clinically, they have failed. The reasons for failure could be manifold. Possibly, some drugs have a poorer bioavailability or less favorable pharmacokinetics in humans, or simply do not effectively engage the crucial molecular targets in the brain. Another more compelling option is that the animal PD models simply are not relevant to the true disease process in humans, for the reasons briefly mentioned above. It is imperative that better animal models mimicking the slow neurodegeneration seen in PD, with the relevant associated molecular changes, are developed.

The development and testing of new PD therapies cost huge sums of money. Another attractive option for development of novel PD therapies is drug repositioning, i.e. testing drugs that have been proven safe and effective for other disorders. As one of several organizations thinking along these lines, the Cure Parkinson's Trust UK The Linked Clinical Trials Initiative is promoting this approach (1). The advantages are that cost and time delays are reduced dramatically, and issues regarding bioavailability have usually already been addressed. Frequently these drugs are tested with a more open-ended hypothesis as to how they might work in the brain, and not only target the dopamine system. Therefore they might also be found to be effective at treating the important non-motor symptoms.

O5

The Life and Times of James Parkinson*Gerald Stern*

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"English born and bred, an English physician and scientist, forgotten by the English and by the world at large – such is the fate of James Parkinson". LG Rowntree 1912. Thus wrote Parkinson's first biographer. Today, as a consequence of his famous and original essay, ironically, the name of Parkinson is now recognised throughout the world. He was a remarkable man. We remember him not only for his seminal contribution to neurology but also for his benevolent concern for the physical, social and moral welfare of his patients and for his love of honest controversy and freedom of speech. Despite living in dangerous times, he vigorously attacked what appeared to him to be wrong in the society in which he lived and proved himself to be a courageous radical reformer. He had a deep interest in many branches of science, which he pursued with energy and insatiable curiosity. He was a modest, scholarly, astute and original clinician who gained - alas posthumous - fame and global recognition. His story will be briefly recapitulated.

O6

New PD genes and rare variants*Matthew Farrer*

Vancouver, BC, Canada

Parkinson disease (PD) is a multifactorial neurodegenerative disease that was long considered environmental. However, in the past fifteen years a genetic etiology for PD has begun to emerge. This seminar will review results from linkage and next-generation sequencing studies of familial parkinsonism as well as candidate gene and genome-wide association studies of sporadic PD. Many of the genetic findings in these different study designs overlap, providing unequivocal proof. While the altruism of patients, families and their DNA, and the help of their neurologists, made the discoveries possible, seldom are individual pathogenic mutations in specific genes useful for a differential diagnosis or for a patient's

prognosis. Nevertheless the results have enabled the creation of a new generation of genetically-engineered mouse models that are currently providing physiologically-relevant insights into disease pathogenesis. Molecular neuroscience, with these novel targets and tools, now has an opportunity to develop intervention strategies aimed at disease modification (neuroprotection). In parallel, genetic analysis can reciprocally inform patient recruitment into neuroimaging studies and future clinical trials. The genetic revolution has started, not in diagnosis nor personalized medicine, but in our knowledge of the neuronal biology gone awry. In PD, based on only a few years of discovery, a temporal ecology has become apparent whereby deficits in synaptic exo- and endocytosis, endosomal trafficking, lysosomal-autophagy and mitochondrial maintenance increase individual susceptibility. However, most of the phenotypic variance in PD has yet to be explained; for example genetic modifiers are as likely to contribute to age of onset, motor and non-motor symptoms, disease progression and/or a patient's response to medication (trait components) as susceptibility. Knowing an individual's genetic background, the contribution of the environment, epistatic interactions and epigenetic inheritance might also be more readily defined.

O7

Generic Risk factors of sporadic PD

Andrew Singleton

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There has been considerable progress in our understanding of the genetic basis of monogenic, familial forms of Parkinson's disease over the last 15 years. Based on the foundation of this knowledge, and with the use of second generation genetic methods now available, a great deal of progress has also been made in understanding the genetic architecture of the common apparently sporadic forms of Parkinson's disease. Here I will describe the progress that has been made in this regard, starting with a discussion of how candidate gene based analysis initially implicated genetic variability at the gene encoding alpha-synuclein. This will be expanded upon to include lessons learned from deep sequencing of *LRRK2* and from the discovery that *GBA2* mutations are a risk factor for disease. Next I will discuss the application of genome wide association studies, and how these have led to the identification of ~30 genetic risk loci for disease, and more accurate estimates of the heritability of Parkinson's disease. Lastly I will discuss future directions for the genetic dissection of apparently sporadic, genetically complex Parkinson's disease.

O8

Genetics and gene environment interactions

Haydeh Payami

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Objective: During the 20th century, PD was thought to be purely environmental with no genetic component. The turn of the century brought an awakening, and the 21st century unleashed unprecedented progress in the genetics of PD. With more than 20 PD-related genes in hand, it is now time to go full circle, take what we know about environmental factors, and begin building an understanding of which genes interact with which environmental factors. Through the efforts of many scientists we now understand that PD involves interactions between genetic make-up and environmental exposures. Not everyone who is exposed to a neurotoxin will develop neurodegenerative disease. Not everyone

treated with the same drug will experience the same benefit. Our objective is to understand the genetic basis for the individual differences in response to environmental exposures and drugs.

Methods: Gene-environment studies require that several thousands of persons with PD and an equal number without PD are enrolled. They are asked to provide a source of DNA (usually blood) and environmental exposure history (pesticides, smoking, coffee, etc.). DNA is used to determine the genetic make-up of the individuals which can then be correlated with their previous environmental exposures and current disease state. Early studies could only test one or two genes at a time; now, with new technologies, we cast the search across the entire genome.

Results: Our lab is especially interested in environmental factors that can be used for prevention and treatment. To that end, we have conducted genome-wide searches for genes that underlie the population variability in the response to protective effects of nicotine, caffeine, and non-steroidal anti-inflammatory drugs. In this presentation, I will discuss the genes that we have uncovered so far, and the relevance of this knowledge to moving the field forward with regard to development of therapeutics and disease prevention.

O9

Alpha-synuclein conformation and neurodegeneration

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Aberrant alpha-synuclein (AS) is linked to the pathogenesis of Parkinson's Disease and other synucleinopathies. Oligomerization of AS into soluble protofibrils and eventually insoluble fibrils, comprising the building blocks of Lewy Body and Lewy neurites, is thought to underlie its neurotoxic potential. One of the critical factors that determine the propensity of AS to follow this pathway of aggregation is its levels. Excess of AS leads to PD in humans and to abnormal protein deposition and neurodegeneration in experimental animals. Levels of AS are in part regulated by mechanisms of protein degradation. We and others have provided evidence that Wild Type (WT) AS is degraded in part by the lysosomal process of Chaperone-Mediated Autophagy (CMA). PD-associated mutant forms of AS are not degraded by this process, and in fact impede degradation of other CMA substrates. We reasoned that a possible therapeutic avenue against the toxic effects of AS would be induction of CMA, so as to, on the one hand, accelerate AS clearance, and, on the other, attenuate its toxic effects on lysosomes.

To this end, we have expressed the lysosomal transmembrane protein Lamp-2a, the rate-limiting step in the CMA pathway, in SH-SY5Y neuroblastoma cell lines and in cortical neurons. This approach led to significant induction of CMA activity, accelerated clearance of AS and protection against WT AS-mediated neurotoxicity. To extend this approach to the in vivo level, we have examined the impact of Lamp-2a overexpression in the Adeno Associated Virus (rAAV) model of nigral WT AS overexpression. We achieved robust expression of Lamp-2a via nigral stereotaxic injection of the rAAV without any observable toxicity. Significantly, Lamp-2a rAAV co-injection with AS rAAV curtailed nigrostriatal degeneration and attenuated the accumulation of detergent-insoluble and oligomeric AS species. Thus, CMA induction may provide a therapeutic avenue against abnormal AS accumulation and neurotoxicity in synucleinopathies.

O10

Protein misfolding in neurodegenerative disease

Leonard Petrucelli

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Objective: Recent genome wide association studies (GWAS) provide compelling evidence that variants in the tau gene (MAPT) are a major risk factor, second only to risk variants in the gene for α -synuclein (SNCA), for Parkinson's disease (PD). Given that tau and α -synuclein (α -syn) have been shown to promote the fibrillization of one another *in vitro* and *in vivo*, the conversion of soluble tau into oligomeric and fibrillar species may not only cause toxic tau dysfunction, it may also promote the aggregation of α -syn and the formation of pathological α -syn inclusions. As such, blocking filamentous or phosphorylated tau production may have a two-fold benefit: preventing aggregation of tau and α -syn.

Methods: We have previously demonstrated that levels of the enzyme cytosolic histone deacetylase 6 (HDAC6) positively correlate with tau burden, while a decrease in HDAC6 activity or expression promotes tau clearance. Using a variety of approaches, including the generation of a novel tau acetylated antibody as well as *in vitro* and *in vivo* assays, we now know how this may occur. Our new preliminary data reveal loss of HDAC6 activity increases the ratio of tau acetylation to tau phosphorylation, thereby favoring tau clearance and preventing filament formation associated with disease progression.

Results: We have obtained a novel brain penetrant and highly specific HDAC6 inhibitor that we demonstrate simultaneously decreases phosphorylation and increases acetylation at crucial sites on tau, thereby preventing tau aggregation and promoting abnormal tau clearance *in vivo*. These data and future approaches will be discussed in this session.

O11

Link between lysosomal function and neurodegeneration in PD

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The recurrent observation of accumulation and aggregation of mutant proteins such as alpha-synuclein, tau, and a-beta in different neurodegenerative disorders indicates the possibility of a shared pathogenic mechanism. Recent data suggest that elimination of mutant protein accumulation can halt the symptomatic progression and also lead to regression of the disease. The evidence in Parkinson's disease (PD) is most compelling since the clinical and genetic studies point to a clear dosage relationship between alpha-synuclein and disease and subtle alterations in expression level of alpha-synuclein are sufficient to cause a wide spectrum of disease. These findings indicate that if alpha-synuclein can somehow be cleared, the disease can be prevented or even reversed. The clearance of aggregation-prone proteins is largely achieved through the autophagy-lysosomal system. However, one of the main challenges is to identify specific mechanisms and targets involved in the clearance of these proteins in order to develop specific therapeutics. To tackle this challenge, we examined rare disorders caused by mutations in genes involved in lysosomal function that result in neurodegeneration. To this end, we examined a linkage between Gaucher's that is caused by mutations in lysosomal glucocerebrosidase and Parkinson's disease. We found that inactive glucocerebrosidase leads to accumulation of the sphingolipid glucosylceramide in neurons that in turn stabilizes toxic alpha-synuclein oligomers. Interestingly, accumulation of alpha-synuclein interferes with ER to Golgi trafficking of wild-type lysosomal

enzymes which in turn leads to decreased lysosomal activity. These findings suggest that this molecular pathway also applies to patients with idiopathic PD or other synucleinopathies who have a normal glucocerebrosidase gene. The bidirectional effects of alpha-synuclein and glucocerebrosidase forms a positive feedback loop that, after a threshold, leads to self-propagating disease. This study identifies glucocerebrosidase as specific target for therapeutic development in synucleinopathies and highlights the importance of rare diseases for understanding of more common conditions.

O12

Structural imaging for PD: MRI and transcranial sonography (TCS)

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Clinical diagnosis of Parkinson's disease (PD) can be straightforward in classical cases, even though differentiation from other clinical entities such as essential tremor, atypical parkinsonian disorders (APDs) or symptomatic parkinsonism may be challenging especially in the early stages of the disease, when symptoms and signs are often vague. The correct diagnosis of PD is important for prognostic and therapeutic reasons and essential for clinical research. Despite limitations, the different modern magnetic resonance (MR) techniques have undoubtedly added to the differential diagnosis of neurodegenerative parkinsonism. Conventional MRI with visual assessment of T2- and T2-weighted imaging as well as various advanced MRI techniques offer objective measures and may therefore be useful tools in the diagnostic workup of PD and APDs. In clinical practice, conventional MRI is a well-established method for the exclusion of symptomatic parkinsonism due to brain pathologies. Over the past two decades, advances in MR techniques have enabled to quantitatively illustrate abnormalities in the basal ganglia and infratentorial structures in APDs by methods such as volumetric methods, diffusion-tensor imaging, proton magnetic resonance spectroscopy and multimodal imaging. Assessment of the echomorphology of the substantia nigra (SN) with transcranial sonography (TCS) can also be helpful for the diagnosis of PD. Indeed, several independent studies have detected consistently hyperechogenicity in the SN region (SN+) by TCS in about 80-90% of patients with PD, while only 10% of healthy adult controls and patients with APDs and a slightly higher number of patients with ET show this echofeature. Moreover, SN+ has been shown to be related to a number of pre-motor features and risk factors for PD such as RBD and hyposmia and determines a high risk to develop PD in healthy people. This presentation aims to review research findings on the value of MRI techniques and TCS for the early diagnosis of PD.

O13

Neurochemical imaging

Nicola Pavese

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PET and SPECT remain the most useful techniques to assess *in vivo* the neurochemical changes associated with the neurodegenerative process in Parkinson's disease (PD). Both techniques have been used to assess the integrity of the dopaminergic system in idiopathic PD and other Parkinsonisms. [¹⁸F]-dopa PET, [¹¹C]-dihydrotetabenazine (DTBZ) PET and PET and SPECT with a variety of ligands for the dopamine transporter (DAT) are all reliable markers of dopaminergic pre-synaptic function. While [¹⁸F]-dopa PET mainly measures the activity of the aromatic amino acid decarboxylase, providing a marker of dopamine

synthesis and storage, DTBZ PET and DAT SPECT/PET respectively bind to the type-2 vesicular monoamine transporter and dopamine transporter, which are expressed on dendrites and axons of dopaminergic neurons. In general, these three techniques show a similar finding of reduced tracer uptake in the striatum of PD patients indicative of loss of nigrostriatal dopaminergic terminals and are able to differentiate early PD from normal subjects with a sensitivity of around 90%. Several PET and SPECT tracers including [¹¹C]-raclopride and [¹²³I]-IBZM have been used to assess post-synaptic dopaminergic receptor availability in Parkinsonian syndromes. Compared to healthy controls, dopamine receptor binding is generally normal or mildly affected in PD but is significantly reduced in patients with Multiple System Atrophy and Progressive Supranuclear Palsy, suggesting that a degeneration of striatal dopamine receptors occurs in these conditions. [¹¹C]-raclopride PET has also been used to assess fluctuations in synaptic concentrations of dopamine following pharmacological or behavioural challenges. More recently, PET has been used to assess the involvement of non-dopaminergic brain pathways in the pathophysiology of both motor and non-motor symptoms in PD. Neurochemical changes associated with occurrence of dementia, fatigue, sleep disturbances, depression and impulse control disorders in patients with PD begin to be elucidated with potential implications for the treatment of these complications.

O14

Functional connectivity

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Over the past two decades, functional imaging techniques have become commonplace in the study of brain disease. Nevertheless, very few validated analytical methods have been developed specifically to identify and measure systems-level abnormalities in living patients. Network approaches are particularly relevant for translational research in the parkinsonian movement disorders, which often involve stereotyped abnormalities in brain organization. In recent years, network analysis applied mainly to metabolic images acquired in the resting state, has provided a useful means of objectively assessing brain disorders at the network level. By quantifying network activity in individual subjects on a scan-by-scan basis, this technique makes it possible to objectively assess disease progression and the response to treatment on a system-wide basis. To illustrate the utility of network imaging in Parkinson's disease, I will review recent applications of the approach in the assessment of preclinical disease progression, and as an aid to differential diagnosis. I will also discuss novel uses such as predicting cognitive responses to dopaminergic therapy, and the evaluation of placebo effects.

O15

Role of noradrenaline and serotonin systems for the development of non-motor symptoms

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Parkinson's disease (PD) is characterized by the degeneration of dopamine (DA) neurons in the substantia nigra *pars compacta*, and motor symptoms including bradykinesia, rigidity and tremor at rest. These symptoms are exhibited when striatal dopamine level has decreased by around 70%. In addition to motor deficits, PD is also characterized by the non-motor symptoms. However, depletion of DA alone in animal models has failed to simultaneously elicit both

the motor and non-motor deficits of PD, possibly because the disease is a multi-system disorder that features a profound loss in other neurotransmitter systems. Our hypothesis is that additional loss of noradrenaline (NA) and/or serotonin (5-HT) neurons could be involved in the clinical expression of motor as well as in non-motor deficits. Our behavioral data show that NA as well as DA depletion significantly decreased locomotor activity and enhanced the proportion of bursty and irregular STN neurons in the rat. Anxiety-like states required DA depletion plus the depletion of 5-HT or NA. Anhedonia and "depressive-like" behavior emerged only from the combined depletion of all three monoamines, an effect paralleled by an increase in the firing rate and the proportion of bursty and irregular STN neurons. Furthermore, we show that the beneficial effects of L-dopa and STN high frequency stimulation can be limited when NA and 5-HT systems are affected in addition to DA depletion. Our data provide evidence for the exacerbation of behavioral deficits when NA and/or 5-HT depletions are combined with DA depletion, bringing new insight into the combined roles of the three monoamines in PD.

O16

Impact of cholinergic dysfunction on the development of non-motor symptoms

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Objective: Non-motor symptoms are common in PD, are a significant cause of disability, and often do not respond to dopaminergic therapy. Evidence is accumulating that cholinergic system dysfunction is a significant contributor to non-motor morbidity in PD. The cholinergic system is implicated in non-motor functions in PD because of loss of cholinergic basal forebrain (FB) neurons and also secondary to degeneration of degeneration of cholinergic neurons in the pedunculopontine nucleus (PPN). We have used in vivo PET imaging to characterize non-motor correlates of cholinergic denervation in PD.

Methods: [¹¹C]PMP acetylcholinesterase PET imaging and clinical non-motor assessment in PD and control subjects.

Results: We showed previously that cholinergic FB denervation is associated with cognitive decline. These studies have also shown that cholinergic FB degeneration is associated with depressive symptoms in PD, at least in the presence of cognitive impairment. Limbic, in particular hippocampal, cholinergic losses correlate strongly with more severe impairments of odor identification in PD. Olfactory dysfunction in PD may be most marked in subjects at risk of incipient dementia and may reflect the transition of PD toward a stage with more heterogeneous multi-system neurodegenerations. There is significant heterogeneity of cholinergic denervation in PD without dementia with about 1/3 of subjects having FB and about 1/6 PPN denervation. Using [¹¹C]PMP acetylcholinesterase PET, we showed recently that cholinergic denervation, especially of the thalamus, reflecting PPN cholinergic afferent degeneration, is associated with symptoms of REM sleep behavior disorder. These findings may explain why REM sleep behavior disorder is a risk factor for development of dementia in PD. Collectively, these results indicate that cholinopathy has variable presence in PD without dementia and associates with cognitive, olfactory, mood and sleep disturbances. Identification of subjects with PD with cholinopathy provides a non-dopaminergic window of therapeutic opportunity to manage non-motor morbidity and reduce disability in PD.

O17

Role of non-dopaminergic systems in the development of L-DOPA-induced dyskinesias

M. Angela Cenci

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L-DOPA-induced dyskinesias (LID) are abnormal involuntary movements that complicate the dopaminergic pharmacotherapy of Parkinson's disease (PD). The bulk of experimental studies indicate that LID results from the combined effects of a severe nigrostriatal dopamine (DA) lesion and fluctuating presynaptic levels of DA, eliciting abnormal responses in striatal neurons via supersensitive DA receptors. This pathophysiological cascade is both modulated and sustained by several non-dopaminergic neurotransmitters. Hence, much translational research is now focused on developing antidyskinetic treatments that target non-dopaminergic systems, particularly glutamate and serotonin (5-hydroxytryptamine, 5-HT). Dysregulated glutamate transmission and increased stimulation of perisynaptic and extrasynaptic glutamate receptors are attributed an important role in the pathophysiology of LID. Metabotropic glutamate receptor type 5 (mGluR5) is abundantly expressed in striatal neurons, where it shows a predominantly perisynaptic localization. In rodent models of PD, pharmacological antagonism of mGluR5 blunts the supersensitive striatal activation of signaling proteins and gene expression induced by L-DOPA. These molecular effects are paralleled by an attenuated development of dyskinesia during chronic L-DOPA treatment. In the same animal models, mGluR5 antagonism attenuates the severity of already established LID. These experimental results have prompted a rapid clinical development of mGluR5 negative modulators for the treatment of LID, and three Phase-2 clinical trials have recently reported positive results. The serotonin system can drive the expression of dyskinesia by providing an aberrant source of DA release following the administration of L-DOPA. Selective agonists of the serotonin autoreceptors, 5-HT1A and 5-HT1B blunt L-DOPA-induced DA efflux in the brain and attenuate peak-dose dyskinesia. Compounds with agonistic activity at 5-HT1A receptors have been tested in PD patients with mixed results. A future clinical development of this strategy will rely on the generation of suitable 5-HT1A/1B agonist compounds that can reduce dyskinesia without interfering with the antiparkinsonian action of L-DOPA. In conclusion, targeting specific glutamate or serotonin receptor subtypes appears to be a promising approach for the future treatment and prevention of L-DOPA-induced dyskinesia in PD.

O18

Why supporting research is crucial: from government to private funding agencies- IntroductionTodd Sherer¹, Amy Comstock-Rick², Etienne Hirsch³, Remi Quirion⁴, Tom Isaacs⁵¹The Michael J Fox Foundation for Parkinson's Research, NY, USA²Parkinson's Action Network (PAN), Washington DC, USA³Aviesan, French Institute for Neurosciences, Cognitive Sciences, Neurology and Psychiatry, Paris, France⁴McGill University, Montreal, QC, Canada⁵The Cure Parkinson's Trust, London, UK**Objectives**

- To outline the scope of funding opportunities in furthering Parkinson's research
- To identify the sources of funding for different stages in the therapeutic pipeline process
- To illustrate why Parkinson's has suffered from a lack of investment relative to other conditions

- To suggest new sources and methods of funding in the Parkinson's arena and how funding from philanthropic sources can kick-start other investment
- To identify new opportunities and funding models for group discussion

Methods: The panel will provide different perspectives on the issues facing them both as recipients and providers of funding for Parkinson's research. E. Hirsch will look at the need for greater collaboration and cooperation between funding sources so that the most important research is prioritised, as well as the need to have a more coordinated approach to funding research in the entire neurological sector. R. Quirion will discuss specific funding models in Canada and the role that 'Brain Canada' has taken in respect of Alzheimer's. T. Sherer will discuss the role of Foundations in providing needed funding along the drug development pipeline in PD – using some examples from the MJFF portfolio over the past few years. A. Comstock Rick will cover the importance of ensuring US government agencies such as the NIH, FDA and DoD are allocated sufficient funds for research by central government, the role of government in caring for people with Parkinson's, and the role that the Parkinson's advocacy community has in facilitating this. T. Isaacs will provide a personal overview of the barriers that exist to more effectively fund Parkinson's research and possible methods to overcome them.

Results: The presentations will be restricted to 12 minutes each. There will be half an hour for questions, comments and suggestions at the end.

O19

Case presentationsCarolyn M Sue¹, Susan B Bressman²¹Department of Neurology, Royal North Shore Hospital and University of Sydney, Sydney, Australia²Department of Neurology, Beth Israel Medical Center, NY, USA

Parkinson's disease can be caused by mutations in genes that follow both autosomal dominant and autosomal recessive inheritance patterns. Also, genetic risk factors for Parkinson's disease have been identified. We will discuss case presentations to demonstrate the basic principles of Mendelian genetics, the significance of a family history in Parkinson's disease and the genetic contribution to Parkinson's disease.

O20

Overview: sexual challenges in Parkinson's and therapeutic optionsPaul Rabsztyń¹, Gila Bronner²¹Radboud University Nijmegen Medical Centre, Nijmegen, The Netherlands²Sheba Medical Center, Tel Hashomer, Israel

Objective: Motor and nonmotor symptoms in Parkinson's disease (PD) can cause many problems in daily functioning. Intimacy and sexuality can be affected too and have a significant impact on the quality of life of both the patients and partners. Sexuality is an important factor of quality of life, but it plays a minor part in research and patient care. The focus in research and care is primarily aimed at motor symptoms and problems. Although slightly improving, healthcare professionals still find it difficult to discuss sexual life with patients and their partner. Healthcare professionals have a major role in this area. They can proactively address sexual health issues by providing information, by recognizing sexual needs of PD patients and partners and also by referring them to specialists for further treatment. This meeting will discuss changes in sexual

function, in Parkinson's disease, possible sexual and intimate problems experienced by PD patients and partners, the therapeutic options and the role of a multidisciplinary team approach.

Methods: Presentation of PD related sexual problems and the available therapeutic options. The second part of the meeting has an interactive character during which case reports will be discussed with the audience.

Results: Healthcare professionals will increase their awareness of the impact of PD on sexual life and quality of life of both patients and partners. After this meeting healthcare professionals will increase their capability to discuss and cope with sexual aspects of their patients.

O22

Quality of life and comfort in the late stages of Parkinson's disease

Janis Miyasaki, Lisa Mann

University of Toronto, Toronto, ON, Canada

Oregon Health and Science University, Portland, OR, United States

Objective: At the conclusion of this session, participants should be able to: (1) define key late stage Parkinson's disease (PD) symptomatology and treatment problems; (2) identify biopsychosocial issues for patients and caregivers during these stages; (3) discuss treatment options for both psychological and physical comfort during late stage PD; (4) recognize how an interdisciplinary team may contribute to late stage PD patients and caregivers' QOL and comfort.

Methods: Presentation, case study discussion, and panel response to questions by audience.

Results: Participants will achieve a better understanding of quality of life and comfort issues encountered during late stage Parkinson's disease.

O23

Is there a functional defect with mitochondrial in Parkinson's disease?

Miquel Vila^{1,2,3,4}

¹Neurodegenerative Diseases Research Group, Vall d'Hebron Research Institute (VHIR)

²Center for Networked Biomedical Research on Neurodegenerative Diseases (CIBERNED), Barcelona, Spain

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⁴Catalan Institution for Research and Advanced Studies (ICREA), Barcelona, Spain

Mitochondria are highly dynamic organelles with complex structural features that play several important cellular functions, such as the production of energy by oxidative phosphorylation, the regulation of calcium homeostasis, or the control of programmed cell death (PCD). Given its essential role in neuronal viability, alterations in mitochondrial biology can lead to neuron dysfunction and cell death. Defects in mitochondrial respiration have long been implicated in the etiology and pathogenesis of Parkinson's disease (PD). However, the role of mitochondria in PD extends well beyond defective respiration and also involves perturbations in mitochondrial dynamics, leading to alterations in mitochondrial morphology, intracellular trafficking, or quality control. Whether a primary or secondary event, mitochondrial dysfunction holds promise as a potential therapeutic target to halt the progression of dopaminergic neurodegeneration in PD.

O24

Clinical Trials: Present challenges and emerging breakthroughs

Olivier Rascol

Departments of Clinical Pharmacology and Neurosciences, CIC-9302/INSERM UMR825, Faculty of Medicine Purpan, University UPS of Toulouse III, Toulouse, France

The scope of clinical trials in Parkinson's disease (PD) has largely enlarged within the last few years. The objective of new candidates for the treatment of PD is not any more restricted to the improvement of motor symptoms or motor complications, but has also expanded to the treatment of non motor symptoms like depression, pain, cognitive impairment, falls... and to the reductive of the progression over time of symptoms and disability (disease modification). Moreover, the drugs in development for the treatment of PD are not anymore only dopaminergic agents, but include also compounds interfering with non dopamine neurotransmitters, including glutamate, serotonin, noradrenalin, adenosine and others. In this presentation, Professor Rascol will review the main clinical challenges to assess efficacy and safety on motor and non-motor symptoms and disease progression with dopamine and non-dopamine agents.

O25

Practical solutions to driving, early job loss and relationship issues

Peter Fletcher¹

¹Gloucestershire Hospitals NHS Foundation Trust, Cheltenham, UK

Objectives:

Regarding people with Parkinson's disease:

To understand the issues affecting driving. To understand potential employment issues.

To appreciate there may be a variety of ways to maintain family and social relationships under the broad headline banner maintaining independence.

To understand a sense of loss can underpin all of these issues and while expectation may exceed reality, fear may compromise both.

To see all of these issues as major bricks in the wall that is quality of life.

Methods: People with Parkinson's disease (pwp) remain individuals. While the response of each person to its diagnosis and subsequent progression is bespoke, an expectation of loss is common. Its nature will vary in breadth and depth but will not infrequently include the fear of losing one's driving license, a loss of paid work and most pernicious and potentially devastating the loss of relationships. These issues overlap each other and others too. This contribution will explore these major pillars of quality of life.

Conclusions: The breaking bad news paradigm of a little often may give not just an opportunity to temper expectation with reality but in accentuating the positive also find practical solutions to the issues raised. Planning ahead and asking 'what if' questions, in a disease that progresses over many years, lies at the centre of maintaining independence in driving, employment and relationships.

O26

Psychological solutions to dealing with pity, dignity, sense of worth and communication

Diane Cook¹

¹Colorado Neurological Institute, Denver, CO, USA

Parkinson's is characterized as much by psychological and psychosocial challenges as by physical challenges, and psychological solutions are increasingly utilized to assist patients in coping with their disease. These approaches have also shown to be a greater determinant of quality of life in Parkinson's patients than the severity of the disease. The role of attitude and self-efficacy will be explored and their impact on one's ability to address the challenges of a progressive, chronic disease, develop and commit to better health habits, engage in better self-care, and more effectively communicate with and utilize health professionals. Self-efficacy, which evolved from the field of cognitive social theory, is the belief in one's ability to manage one's condition, and is being increasingly recognized as a *tour de force* in fields such as healthcare. Self-efficacy beliefs influence how we feel, think and behave. High self-efficacy is characterized by a positive attitude, proactive approach, high degree of engagement, goal-setting for desired behavior change, confidence in one's ability to manage stressors, problem solving around obstacles, and tenacity and resilience when confronted by adverse conditions. Achieving a degree of control over one's condition can translate into a sense of pride, self-worth, emotional well-being and realistic optimism, which in turn can lessen the effects of apathy, anxiety and depression. The three most effective methods for developing self-efficacy skills will be discussed as well as suggestions for applications in clinical and support group settings.

O27

Physical solutions to coping with pain, motor/non-motor, cognition, mood and behavior

Soania Mathur¹

¹ Designing A Cure Inc., Toronto, ON, Canada

Objective: Parkinson's Disease permeates every aspect of a person's life. Once thought of as primarily a movement disorder, it is now apparent that this illness affects many other systems and that these non-motor symptoms (NMS) are significant and can be debilitating. Along with a diagnosis of Parkinson's, comes potential future disability and quality of life issues. Until there are better drug treatments and better yet, a cure, management must focus on helping patients live more fulfilling and comfortable lives; providing them with physical solutions to cope with some of the less highlighted difficulties seen in Parkinson's Disease such as pain, constipation, sleep disorders, sexual dysfunction, depression, cognitive difficulties and apathy.

Methods: A comprehensive literature review was conducted using standard search engines as well as the comprehensive online medical resource, MD Consult which has access to a wealth of medical journals and publications.

Results: Along with standard medical interventions, pharmacologic or otherwise, there are ways that patients themselves can take an active role in the treatment of their disease. In fact to live well with Parkinson's patients must be active participants in their own management. Studies show that an approach to managing pain, in conjunction with conventional treatment, should include a regular exercise regimen incorporating passive and active exercises and full range of movement. Constipation can be mitigated through high fiber diets, increased fluid intake and again, regular exercise. Sleep disorders benefit from sleep hygiene, regular bedtimes and wake times as well as other physical measures to make the bed itself less restrictive. Nutrition, exercise, stress management techniques and staying involved socially and recreationally help manage mood and behavioral challenges. These as well as many other practical solutions addressing NMS to improve quality of life, will be presented.

O28

Memory and attention issues in Parkinson's disease: clinical characteristics and mechanisms

David Burn

UK

Even in the earliest stages of Parkinson's there may be issues with memory and attention, although these are frequently subtle, and only revealed by detailed neuropsychological testing. With progression, memory issues may become more noticeable although, characteristically, are typically less severe than in Alzheimer's disease. There is on-going uncertainty as to whether memory impairment in Parkinson's relates more to an over-riding executive dysfunction, so impacting upon effective retrieval strategies, rather than retention issues. There is likely to be variability in the underlying pathological basis for the memory impairment (for example, the degree of amyloid pathology in the medial temporal lobe) and, in turn, this leads to clinical heterogeneity. Attentional impairment is a defining aspect of the dementia associated with PD. Typically this can vary from minute to minute. This can be frustrating for the person with PD and also their family, and has a major impact upon activities of daily living. The person may appear to sleep excessively during the day, have sentences that come out jumbled, or appear to stare vacantly into space ("the lights are on but no-one in"). These observations have been shown to predict fluctuating attention quite accurately. The neural basis for impaired attention is not fully established but synaptic dysfunction is likely, given the variability in performance, and cholinergic systems have been implicated. Cholinesterase inhibitors may lead to gratifying improvements in impaired attentiveness, and this has been confirmed using a number of different experimental paradigms. These agents are generally less effective for managing impaired memory in the face of relatively preserved alertness.

O29

Clinical Assessment of Cognition in PD

Connie Marras

Morton and Gloria Shulman Movement Disorders Centre and the Edmond J. Safra Program in Parkinson's Research, Toronto Western Hospital, University of Toronto, ON, Canada

The clinical assessment of cognition in Parkinson's disease aims to identify cognitive impairment relative to normal or decline from an individual's baseline level of cognitive function prior to being affected by Parkinson's disease. These states of impairment have been classified as either Parkinson Disease - Mild Cognitive Impairment (PD-MCI) or Parkinson Disease Dementia (PDD). The latest criteria for each will be discussed, and the instruments or methods to make these determinations will be reviewed. The evidence for the usefulness of cognitive scales for screening or diagnosis of PD - MCI or PDD and for assessing longitudinal change will be reviewed. Finally, there are a number of unmet needs in this area and the next steps for research in this field will be proposed.

O30

Practical management of cognitive deficits in Parkinson's disease: what can occupational therapists offer?

Margarita Makoutonina¹

¹ParkLife Australia Pty Ltd, Melbourne, Victoria, Australia

Objective: Non-motor symptoms (NMS) are identified as a direct cause of reduced quality of life (QoL) in people with Parkinson's (PwP) (Politis et al., 2010). Many of these symptoms and, in particular, cognitive dysfunctions are not responsive to pharmacological management.

A comprehensive care model with multidisciplinary teams (MDT) incorporating medical, rehabilitative and supportive services, is important in preventing the disability amongst PwP (Bloem, 2010). The purpose of our study was to examine the role of Occupational Therapist (OT) within MDT and effect of OT's interventions to optimise cognitive function amongst PwP, thus to prevent the onset of disability and improve QoL.

Method: A cohort of 10 patients with PD was evaluated for cognitive, motor and non-motor domains. The impact of their cognitive impairment on daily functioning was also assessed. The results were compared with 10 controls matched for overall age, gender and education distribution.

The measures undertaken on admission to the outpatient program demonstrated that at least 75% of participants described cognitive difficulties with routine daily activities. Those measures were used for designing the OT specific interventions. The benefits of OT interventions in optimizing cognition, applicability to practice and improvement of QoL amongst PwP were assessed on discharge from the program.

Results: It was concluded that the rehabilitative philosophy and its specific application to the OT interventions, in addition to evidence based approach, enables OT to obtain a bigger picture on cognitive related issues and broadens up spectrum of interventions. Also it was demonstrated that OT's interventions empowers the patients, through education and client centered approach, to take ownership in addressing a variety of cognitive deficits, postpones the earlier development of disability and improves participation in daily activities.

O31

Animal models of hyperdopaminergic behavior in Parkinson's disease

Christelle Baunez
CNRS, Marseille, France

Inactivation of the subthalamic nucleus (STN) is the current strategy for the treatment of Parkinson's Disease. However, using various behavioural tasks assessing non-motor functions such as attention, impulsivity, compulsivity and motivation, we have shown that STN lesion or high frequency stimulation can induce a variety of non-motor deficits that persists in a rat model of Parkinson's Disease. Among these non-motor deficits, are hyperdopaminergic-like behaviours (impulse control disorder, dysfunctional motivation). Interestingly enough, the effects of STN inactivation on impulsive/compulsive behaviour in the rat can be opposite depending on the reward obtained in the task: natural reward (such as food) or drugs of abuse (such as cocaine or heroin) (Baunez et al, 2005, *Nature Neurosci.*; Rouaud et al, 2010, *PNAS*). The presentation will review these different findings and their contribution to the understanding of hyperdopaminergic behaviour observed in Parkinsonism and also the latest model currently developed.

O32

Animal models of sleep disorders in Parkinson's disease

Ingrid Philippens
Biomedical Primate Research Centre (BPRC), Rijswijk, The Netherlands

Objective: Sleep problems are a common phenomenon in most neurological and psychiatric diseases. In Parkinson disease (PD), for instance, sleep problems may be the most common and burdensome non-motor symptoms in addition to the well-described classical motor symptoms. REM sleep behavior disorder (RBD) precedes PD in one-third of patients. Since sleep disturbances generally become apparent in the disease before motor symptoms emerge, they may represent early diagnostic tools and a research tool to investigate early mechanisms in PD and disease modifying strategies. Although classic PD motor signs have been studied for years, it would be ideally that premotor symptomatology, such as sleep, can be distinguished in animal models. We therefore investigated sleep changes in a non-human primate model for idiopathic PD, the 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP) intoxicated marmoset monkey.

Method: Mild parkinsonism was induced in marmosets (3M/2F) over a 2-week period of subchronic MPTP treatment (total dose 7 mg/kg s.c.). Telemetric electroencephalograms (EEGs) and electromyograms (EMGs) for sleep analysis were recorded weekly. Motor activity and hand-eye coordination performance were measured weekly, and clinical signs of parkinsonism were noted each day. Data of sleep parameters, motor function, and parkinsonian signs, before and after MPTP treatment, were compared with control marmosets (1M/3F).

Results: MPTP increased the number of sleep epochs with high-amplitude EMG bouts during REM sleep relative to control monkeys (mean \pm SEM percentage of REM 58.2 \pm 9.3 vs. 29.6 \pm 7.7; $P < 0.05$). Of all sleep parameters measured, RBD-like measures discriminated best between MPTP-treated and control monkeys. On the other hand, functional motor behavior, as measured by hand-eye coordination performance, was not affected by MPTP treatment in the dose used (correct number of hits 23.4 \pm 3.6 vs. control 36.1 \pm 5.9; $P = 0.32$). This REM sleep-specific change, in the absence of profound changes in motor function, suggests that the MPTP marmoset model of PD can be used for studies into the mechanisms of sleep disorders in PD and for validation of early disease modifying treatment in PD.

O33

Animal models of gastrointestinal dysfunction in Parkinson's disease

Marie-Francoise Chesselet¹
¹Department of Neurology, UCLA, Los Angeles, CA, USA

Objective: Gastrointestinal dysfunction is prevalent in Parkinson's disease (PD) and symptoms can precede motor dysfunction by many years. Multiple mechanisms may be involved and these are not well understood. Treatment is imperfect and would benefit from a better understanding of mechanisms. This presentation will review results of studies to model gastrointestinal dysfunction related to PD in rats and mice and what we have learned.

Methods: Various aspects of gastrointestinal dysfunction have been analyzed in a variety of toxin-induced and genetically-based models of PD

Results: Some groups have reproduced aspects of gastrointestinal dysfunction seen in patients with PD in animal models of nigrostriatal dopamine cell loss, suggesting that the loss of dopamine neurons may contribute to these symptoms. However, other studies have shown that early gastrointestinal deficits can be produced in animals many months before any loss of dopamine by overexpressing alpha-synuclein in neurons that innervate the digestive system, indicating that local pathology, as observed in patients with early stages PD, may play a critical role in the gastrointestinal dysfunction. This suggests that treatments that target alpha-synuclein pathology (over-expression, aggregation) and/or its local consequences on gastrointestinal functioning, may

provide better relief for the gastrointestinal symptoms of PD and that some of the genetic models of the disease provide useful tools to test these new treatments pre-clinically.

O34

Optical neural engineering

Antoine Adamantidis¹

¹ McGill University, Douglas Mental Health University Institute, Montréal, QC, Canada

Objective: Recent developments of microbial light-sensitive opsins as a tool to manipulate the activity of neural circuits in the brain have opened new perspectives in systems neuroscience. Optogenetic technology allows to reverse engineer intact neural circuits by directly probing the necessity and sufficiency of cellular and topological circuit characteristics with high-speed optical and cell type-specific perturbations. We implemented *in vivo* optogenetics to probe the modulatory functions of arousal circuits on wakefulness and goal-oriented behaviors.

Methods: We will detail the development of *in vivo* optical neural interface combined with electrophysiological, imaging, and behavioral readout methods.

Results: Using this technology, we established causal link between activation of genetically targeted neural circuits and the modulation of arousal and goal-oriented behaviours. In particular, we showed that activation of dopaminergic neurons in the ventral tegmental area (VTA) facilitates conditioned place preference, as well as the development of positive reinforcement behavior during a food-seeking operant task. We further found that phasic activation of dopaminergic neurons is sufficient to reactivate previously extinguished food-seeking behavior in the absence of external cues. This was also confirmed using a reversal paradigm. Collectively, these data suggest that dopamine is sufficient to assign incentive salience to reward-predicting cues and participates to cognitive processes during reward-seeking and behavioral flexibility.

O35

Regulation of Parkinsonian motor behaviors by optogenetic control of basal ganglia circuitry

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Neural circuits of the basal ganglia are critical for proper motor function. Two parallel basal ganglia pathways have been described, which are proposed to exert opposing influences on motor function. According to this classical model, activation of the direct pathway facilitates movements/actions and activation of the indirect pathway inhibits movements/actions. We directly activated basal ganglia circuitry *in vivo*, using optogenetic control of direct- and indirect-pathway medium spiny projection neurons (MSNs), achieved through Cre-dependent viral expression of channelrhodopsin-2 in the striatum of D1-Cre and D2-Cre BAC transgenic mice. Activation of direct- or indirect-pathway basal ganglia circuits yielded distinct motor behaviors, reminiscent of hyper- or hypo-dopaminergic states. Moreover, in an operant self-stimulation paradigm, direct pathway activation reinforced operant responding, while stimulation of D2-expressing neurons was punishing, demonstrating that direct activation of these circuits is sufficient to modify the probability of performing future actions. Together, these findings provide important insights into the circuit basis of motor and cognitive dysfunction in basal ganglia disease.

O36

Optical interrogation of the dopamine and reward systems: opportunities for understanding Parkinson's

Antonello Bonci

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Objective: The dopaminergic neurons, originating in the ventral tegmental area (VTA) and projecting to forebrain areas, including the amygdala, prefrontal cortex, and nucleus accumbens (NAc) are essential for the manifestation of goal-directed behavior for both natural rewards as well as drugs of abuse, including ethanol. My laboratory has spent the past several years to elucidate the role of plasticity at excitatory synapses in the VTA in physiological and pathological behaviors, such as reward-related learning, motivation and substance abuse.

Methods: Recently, my laboratory has been using a multidisciplinary approach combining electrophysiology, optogenetic and behavioral procedures to better investigate the role of the dopaminergic signaling on substance use disorders.

Results: During my presentation at the World Parkinson Congress, I will show the most recent optogenetic studies from my laboratory focused on the use of optogenetics in understanding the motivational system and highlight the implication for Parkinson's disease.

O37

Overview: What is genetics?

Carolyn M Sue¹, Susan B Bressman²

¹Department of Neurology, Royal North Shore Hospital and University of Sydney, Sydney, Australia

²Department of Neurology, Beth Israel Medical Center, NY, USA

Genetics, or the study of genes (derived from the Greek word for "origin") has revolutionized the clinical approach to many common neurodegenerative diseases, including Parkinson's disease.

Genetic studies provide insights into inheritance patterns of diseases that are passed on from parents to children. Genetic causes of Parkinson's disease were originally discovered using techniques known as genetic linkage and DNA sequencing; methods that allow investigators to locate which regions of the gene are responsible for causing disease. We now know that Parkinson's disease can be caused by mutations in genes that follow both autosomal dominant and autosomal recessive inheritance patterns.

In addition to identifying monogenic forms of Parkinson's disease, newer technologies such as genome-wide association studies (GWAS) and next-generation sequencing (NGS) have further identified genetic risk factors that increase an individual's risk of developing Parkinson's disease and other genes that cause Parkinson's disease. Only a small fraction of patients with Parkinson's disease have monogenic causes. However, clinicians should be aware of related phenotypes to enable genetic counseling to affected families. Furthermore, identification of causative genes and genetic risk factors of Parkinson's disease has provided insights into the molecular mechanisms that lead to the development of commoner forms of Parkinson's disease. We now understand that disturbances in pathways involved in protein clearance and mitochondrial function play a critical role in the degeneration of neurons in Parkinson's disease. We conclude that genetic studies

using new technologies greatly enhance our ability to identify new causes of Parkinson's disease and contribute to our understanding of disease mechanisms that play a role in this disorder.

O38

What we all can learn from each other - international advocacy

Linda Morgan¹, Steve DeWitte², Tom Isaacs³

¹Parkinson's Disease Foundation Research Advocate, PCORI Reviewer, PCORI Prioritization Study Group, Asheville, NC

²Parkinson's Patient Advocate ; President / Keep the Faith LLC; Founder / Parkinson's Young On Set Support Group of CT Inc., New Preston, CT USA

³The Cure Parkinson's Trust, President and Co-founder, London UK

Objective: Traditionally, people with Parkinson's disease (PwP) have participated in research as the *subject* of trials. New treatments and therapies exist because of these volunteers. Theirs is a very important yet undervalued role as statistics show that 1% of individuals with the condition enroll in a trial. 80% of research trials are delayed due to a lack of volunteer participation. This workshop will 1) review considerations of how to become involved in clinical research including the questions to ask 2) review misnomers that may keep PwP's from enrolling 3) describe the need for a greater and unified patient engagement with the design and the outcome measures of trials to accelerate the availability of Parkinson's therapies 4) and suggest a new model for accelerating Parkinson's trials.

Methods: Three individuals with Parkinson's and experience with clinical trials will speak. Between the three of them they have participated in more than 40 trials. S DeWitte will discuss dilemmas with clinical trials; how to find and how to get involved. L Morgan will lead us away from direct trial participation and discuss our emerging roles and influences on the research process and how we can all benefit from that research-patient partnership. Lastly, T Isaacs whose organization has been responsible for funding several clinical trials, will give us an international perspective and suggest a new model for accelerating available new treatments.

O40

Overview: Innovations in neuroscience technologies as they apply to finding target molecules to the point of pre-clinical studies

Howard Federoff, Salim Shah, Habtom Ressom, Linda McArthur
Georgetown University Medical Center, USA

Objective: Parkinson's disease is a movement disorder driven principally by the progressive and slow death of dopaminergic neurons in the pars compacta of the substantia nigra with the concomitant formation of α -synuclein containing intracellular inclusion bodies. There is no unifying mechanism for the disease, and while symptoms may be relieved with drugs that increase dopamine levels or with devices for deep brain stimulation, there is no effective therapy to halt the progression of the disease. Therefore, to develop therapeutics intervention for PD, there is a need to better understand how the risk factors, both genetic and environmental, contribute to the onset and progression of the disease.

Problem: Current efforts in this direction are based on "omics" data acquisition and analysis from patient samples (protein, mRNA, microRNA, lipids, metabolites, DNA methylation sites) and identify effector molecules of therapeutic and/or predictive value. To understand relationship between diverse effector molecules, one approach is to predict biological networks and identify potential

causal relationships- directly or indirectly related to either a known target or a known effect. Building networks and identifying nodes in networks is first step but the significant challenge lies in nodes prioritization according to their role in disease progression.

Results: An effect-centric network validation approach with respect to the genes such as α -synuclein, tau, parkin, and LRRK2 and modulating their expression using combinatorial siRNA approach and monitor their effects on neuronal cell death. Additionally, we propose that the approach to study global gene expression, and building a network that could causatively relate to observed phenotypic effects observed in the disease.

O41

Use of Reiki as a complementary therapy to help those living with Parkinson's disease (PD) and carepartners/caregivers

Angela Robb¹

¹PD Carepartner & Reiki Master, GiveReiki.com

Objective: To share my knowledge as a Parkinson's disease (PD) carepartner/caregiver and Reiki Master about how the use of Reiki as a complementary therapy can benefit those living with Parkinson's disease and their carepartners/caregivers. I will educate the workshop audience about:

- 1) What is Reiki?
- 2) How Reiki can benefit those living with PD and carepartners/caregivers.
- 3) Share my personal anecdotal evidence, articles, and student feedback of the benefits of Reiki.

Methods: I will use a PowerPoint presentation to share this information. I will also provide handouts either via paper or electronically to those who attend the presentation. I will also be available to take questions from the audience about Reiki. I will share my personal experiences as a fourteen year Reiki practitioner and two years as a Reiki Master. I will describe how I've worked with those within the PD community to train them to use Reiki to help themselves. I will also explain that Reiki is not a mono-therapy for PD but part of a PD self-care plan. I will encourage carepartners that Reiki is an excellent practice to cope with being a carepartner, improve carepartner health, and enhance their own self-care plan. I hope to dispel any Reiki myths or mysteries.

Results: To have the workshop attendee to come away with a general understanding of how Reiki can be used to enhance and complement their current self-care strategies. My goal is to encourage attendees to learn more about Reiki, find a practitioner in their area and learn how to use Reiki to help themselves.

O42

Is there a role for gene- and cell-based therapies in the treatment of Parkinson disease?

Stephane Palfi

APHP/Paris University, Créteil, France

Oral dopaminergic treatments have remained the primary standard of care for Parkinson's disease (PD) for the last 40 years. Although highly efficacious in the early stages of disease they are associated with debilitating long term side effects that impact on the quality of life and restrict the longevity of such treatment. The severity of PD, lack of a cure and the limited long term effectiveness of current therapies allow for the consideration of novel therapeutic approaches based on cell and gene therapies. The purpose of the presentation is to describe the current statut of different therapeutic approaches aiming at restoring local and continuous release of dopamine or delivering neurotrophic factors to restore and protect dopaminergic neurons from degeneration.

O43

Sleep, fatigue, and apathy in Parkinson's disease

Nico J Diederich

Department of Neuroscience, Centre Hospitalier de Luxembourg, Luxembourg-City

Reduced sleep quality is among the five most cited complaints in PD patients. Large-scale studies have shown that almost half of all PD patients suffer from sleep problems. *Confusing terminology*. The terms apathy, fatigue, exhaustion and sleepiness are often uncritically interchanged. Apathy or lack of drive may already be encountered at the stage of idiopathic REM sleep behaviour disorder. Apathy is neither synonymous nor necessarily associated with depression. By "fatigue", the patient often expresses exhaustion due to motor and non motor "off"-periods. Paradoxically, sleepiness during the day with non refreshing naps is combined with longer night-time sleep. *Multiple primary or disease-inherent causes*. Neuropathology has convincingly demonstrated that several nuclei in the brainstem regulating sleep/wakefulness are primarily affected by disease propagation, among them nucleus pedunculopontinus, locus coeruleus and Raphé nuclei. PD patients show a reduction of hypocretin neurons in the hypothalamus. Finally, secondary dysfunction of the thalamocortical arousal system has been postulated. *Intertwining of secondary causes*. Exhaustion due to motor impairment and dysautonomia further exacerbates the soporific effects of the medication. This interplay of multiple factors renders identifying the underlying cause complex. *Pragmatic treatment*. Despite this causal complexity of apathy and sleep problems, a scrutinized exploration should nevertheless search for the predominating syndrome. Focused pragmatic therapy mostly relies on established general treatment strategies as randomized controlled trials (RCT) are rare and the Quality standards Subcommittee of the American Academy of Neurology has not given a single level A recommendation. Recently, however, several RCT have shown that long-acting dopaminergic stimulation, while abating nocturnal akinesia, also improves subjective sleep quantity. One RCT suggested treating insomnia in PD with eszopiclone. The use of stimulants during daytime is not supported by RCT. The long-term effect of disease modifying agents on sleepiness is unknown. Thus, evidence based therapeutics remain limited.

O44

Table #1: Speech Pathology & Parkinson's

Lorraine Ramig

University of Colorado-Boulder, National Center for Voice and Speech-Denver, Columbia University-NYC, LSVT Global-Tucson

Speech and voice disorders are key elements in the diagnosis and management of individuals with Parkinson Disease (PD). Nearly 90% of individuals with PD will have these problems with the classic voice symptoms of reduced loudness, monotone and hoarse voice appearing early in the course of the disease, and imprecise articulation and rate problems occurring as the disease progresses. Such symptoms contribute to frustration, embarrassment and social isolation and as such have a negative impact on quality of life. The complex origin of these disorders includes *motor problems* (hypokinesia/bradykinesia reflecting reduced muscle activation and reduced movement scaling), *sensory problems* (resulting in abnormal perception of one's own voice) and *cueing problems* (reflecting deficits in internal/implicit cueing). Historically, speech disorders in PD have been unresponsive to speech or medical treatment. However progress has been made in the treatment of speech in PD. In this session, speech treatment for PD will be described with special emphasis on the Lee Silverman Voice Treatment (LSVT[®] LOUD), an intensive, exercise-based

intervention, which is a PD-specific, neuroplasticity-principled, standardized protocol. The recommendation is made for *early referral* to efficacious speech treatment and continued life-long practice for optimum management of speech and voice disorders in PD. Advances in access to treatment through technology (telemedicine and software) will be discussed.

Financial Disclosure: Research supported in part by NIH-NIDCD R01 DC01150, R21 DC006078, R21 NS043711, Michael J. Fox Foundation, Parkinson Alliance, Davis Phinney Foundation)

O45

Table #2: Physical therapy & Parkinson's: Can it really help?

Terry Ellis

Boston University, Boston, MA, USA

In this roundtable session, participants will become more informed regarding the benefits of physical therapy and exercise. In addition, participants will gain an appreciation of the role that physical therapy can play in the management of Parkinson's over the course of the disease. The evidence demonstrating the benefits of physical therapy and exercise for persons with Parkinson disease will be summarized and the impact on reducing disability, improving physical function and enhancing quality of life will be reviewed. In addition, the key elements of an exercise program will be explored. The importance of long-term adherence to exercise and adopting an active lifestyle to optimize outcome will also be emphasized. Practical tips for integrating increased activity levels in daily life will be shared. This session will also include a discussion of the nature of the treatment provided by physical therapists and the goals of physical therapy intervention. Optimal timing and frequency of physical therapy intervention will also be considered. This session will culminate in a discussion of how to benefit most from physical therapy intervention.

O46

Table #3: Blogging and Parkinson's: How people with Parkinson's can educate and raise awareness via bloggingBob Kuhn¹, Jean Burns²¹ Positively Parkinson's (Blogspot), Canada² www.PDPlan4life.com (website) and PDBLOGGER (WordPress), USA

Objective: Provide both general and detailed information about blogging and how it is being used within the Parkinson's community. Our ultimate goal is to encourage collaboration among bloggers and to create a new group of bloggers who will become founding members of something new: World Parkinson Congress "Blog Partners."

1. Blogspot: Positively Parkinson's Bob Kuhn
2. WordPress: PDBLOGGER Jean Burns
3. Website: www.pdplan4life.com Jean Burn

Methods: We will start by questioning the round-table attendees. It may be that some attendees may be experienced, and others may be totally new to blogging. After initial Q&A, Bob and Jean will decide if they should split the attendees into two groups according to experience, or need, or some other criteria.

We will be prepared to cover the following topics:

Goals

Basic "how to"

Blogspot

WordPress

Collaborating

Tips and Tricks

Statistics – how to increase your readership

Dangers: legal liability

We will provide quick reference (QR) guides on these topics. The QRs will be displayed on laptop or iPad. We will provide links so the attendees can download the documents.

Results: An enthusiastic cadre of Parkinson's bloggers, who will become the founding members of a new group: "WPC Blog-Partners." This will help shrink the Parkinson's community by encouraging greater communication through the Internet. Bloggers will have the additional benefit of living intentionally.

O47

Table #4: What to ask before joining a clinical trial: PwP to PwP

Israel Robledo¹, Jon Stamford²

¹USA

²UK

Objective: To give background information on the research process from the patient perspective and discuss questions to ask before joining a clinical trial that will allow for quality involvement in the process.

Methods: Given the fact that clinical trial participation within the Parkinson's Disease community, reasons to participate in clinical trials will be presented. Beginning with patient safety during the course of a trial, time commitment, what to expect during a trial, being able to stop participation at any point in the trial, and asking about trial results when a trial is completed, to finding about trial outcomes when a trial is cancelled. Participants will be given the opportunity to ask questions about their concerns with clinical trial participation.

Results: Participants will be able to decide if clinical trial participation is right for them based on the information presented during the session.

O48

Table #5: Young Onset Parkinson's: Unique Challenges

Peter Davison

Person with Young Onset Parkinson's, Bedford, NS, Canada

Objective: The purpose of understanding the unique challenges and opportunities facing young onset Parkinson's folks is to improve the effectiveness of outreach, offer appropriate wellness and lifestyle strategies and increase support group attendance. Participants will be invited to share their insights and personal experiences as they learn how to set up sustainable and relevant young onset groups and teleconferences. This session is recommended for young onset participants, support group leaders and organizations who want to improve their outreach to persons with young onset Parkinson's.

O49

Table #6: Psychiatric Changes in Parkinson's disease

Laura Marsh

Michael E. DeBaakey VA Med Center/Baylor College Medicine, Houston, TX, USA

Objective: To describe psychiatric changes in Parkinson's disease (PD) and approaches to their recognition, monitoring, and treatment.

Methods: This Roundtable will begin with an overview of the prevalence of the various psychiatric conditions that can occur in individuals with PD. The general and distinguishing characteristics will be discussed as well as pharmacological and non-pharmacological treatments.

Results: Up to 80% of individuals with PD experience psychiatric changes over the course of their disease. These disturbances include mood and anxiety disorders, psychosis, and behavioral changes such as apathy or impulse control disorders. Often, these have a greater impact on quality of life than motor dysfunction and compound the severity of PD-related motor and cognitive dysfunction. Since effective treatments are available, early recognition and aggressive treatment of psychiatric symptoms is critical to comprehensive management of PD. Accordingly, individuals with PD, their families, and carers should be aware of the potential for psychiatric changes and monitor in an ongoing fashion.

O50

Table #7: Sex & Parkinson's disease

Gila Bronner

Sex Therapy Service, Sexual Medicine Center
Sheba Medical Center Tel-Hashomer, Israel
gilab@netvision.net.il

Objectives: To enable the participants an opportunity to discuss openly sexual issues, evaluate their etiology and learn about adequate solutions.

Methods: A healthy sex life plays an important role in quality of life and the quality of relationships. If one partner in a relationship experiences problems with intimacy, sensuality or sexual activity, it is likely to impact on the sexual enjoyment of the other partner. Consequently, resolving such difficulties can improve sexual satisfaction. People with Parkinson's disease (PD) and their partners have to cope with multi-faceted challenges regarding their sensuality, intimacy and sexuality. Sexual difficulties can be associated with motor and non-motor symptoms of PD, all of which can impact on self-esteem, quality of life, mood and relationships. Sensual perception and intimate communication may be affected by the physical and emotional changes PD may bring, and a less active and enjoyable sex life may result.

Results: This "Meet the expert" session will present the essence of sex therapy and treatment of sexual dysfunctions. The field of sex therapy is relatively new. Many people are unaware of the extensive support and variety of treatments and solutions that they can gain from a sex therapy session. Participants will be able to discuss with the expert most frequent sexual problems in PD (e.g. decreased sexual desire, increased sexual desire (hypersexuality), arousal problems, lack of lubrication, erectile dysfunction, premature ejaculation, difficulties to reach orgasm, sexual pain and sexual dissatisfaction). This session will provide an opportunity to discuss sexual issues openly in a comfortable atmosphere. No personal questions will be asked. On the other hand, those who wish to raise specific questions, will get an opportunity for a professional evaluation and adequate solutions. Such difficulties can place an additional strain on couples who live with PD and a proper intervention can relieve the stress.

O51

The spectrum of non-motor symptoms in PD

K. Ray Chaudhuri

Parkinson Centre of Excellence, London, UK

Non-motor symptoms of Parkinson's disease (NMS) are the leading cause of poor quality of life for both people with Parkinson's and their caregivers. The slowness, stiffness and tremor of Parkinson's disease (PD) are well known, but non-motor symptoms afflict more Parkinson's patients. Though NMS affect every patient, they are under-recognised and under-treated. In a Parkinson's UK survey, members rated symptoms such as sleep disturbance, pain,

constipation, urinary problems and dizziness as more debilitating than their motor symptoms. Hospitalisation from PD is most likely to have been caused by NMS. This loss of independent living has devastating social and economic consequences. Despite the profound and negative effects of NMS, there is a dearth of research into causes and therapies. Treatment remains poor and quality of life progressively deteriorates. The National Institute for Health and Clinical Excellence (NICE) and Parkinson's UK have identified the recognition and treatment NMS across all stages of PD as a key unmet need. Little research explores the cause and progression of common NMS because funders have focused their attentions elsewhere. An integrated and interactive combination of clinical and laboratory-based investigation is required that will focus on the causes and consequences of sleep disturbance, pain and autonomic dysfunction in PD. Using imaging and post-mortem brain tissue to identify the areas of the brain responsible for NMS, we are developing models of the disease that will increase our understanding of the origin of neglected NMS of Parkinson's and provide a test bed for devising effective treatments.

This research promises to increase our understanding of the effects of PD on the brain in order to uncover the underlying causes of NMS. This research will lead to advances in the detection and treatment of NMS, thereby improving the quality of life of millions of people with Parkinson's, both today and in the future. By exploring the practical clinical issues that are the biggest hurdle to the improvement of the symptomatic treatment of PD, we will begin to solve the NMS enigma.

O52

Dementia and psychiatric manifestations in PD

David Burn
UK

Some people with Parkinson's disease (PD) may exhibit early cognitive deficits, increasingly referred to as mild cognitive impairment (PD-MCI), which do not evolve to PD dementia (PDD), or do so over an extended period of time. PD-MCI is common in non-demented PD and includes a spectrum of deficits, ranging from so-called single domain (e.g. non-amnesic) to multiple domain impairments. Overall, non-amnesic, single-domain impairment is the most common PD-MCI subtype encountered. Probably because of improved management of motor problems and secular trends in life expectancy, up to 80% of people with PD may eventually develop dementia. Features commonly associated with PDD include fluctuating levels of attention and visual hallucinations. Anti-psychotic medications have a very limited place at present in the management of PDD. Although drugs like cholinesterase inhibitors can improve several symptoms, this remains an area of major unmet therapeutic need. (Neuro)psychiatric manifestations of PD may precede the diagnosis; so mood disorder, for example, is well documented to predate motor symptoms. During the course of PD psychiatric features may wax and wane, often being under-recognised by both the person with PD and/or their physician. Despite this, psychiatric symptoms frequently have a greater impact upon quality of life than motor features. The spectrum includes depression, anxiety, apathy, fatigue, hallucinations and delusions. They commonly occur together; for example, anxiety and depression frequently co-exist. In contrast to the cognitive aspects, many psychiatric symptoms may be effectively treated, so recognition is important, given the potential impact upon the person and their family. In terms of evidence-base, there have been remarkably few randomized trials of any size evaluating, for example, antidepressants in the context of PD. Non-drug therapies such as cognitive behavioural therapy or exercise should be considered, and also require further evaluation.

O53

Contribution of functional neuroimaging to the understanding of non-motor manifestations of PD

Antonio P. Strafella
University of Toronto, Canada

In the last few years, Non-motor symptoms like cognitive dysfunction and impulse control disorders are increasingly being reported in Parkinson's disease (PD) patients. Given the social implications, these disorders represent a cause of significant distress not only for the patients but mostly their families. To date, the mechanisms underlying cognitive abnormalities and behavioral addictions in PD are poorly understood. Proposed mechanisms include abnormal functioning of nigrostriatal and mesocorticolimbic networks resulting in a dysregulation of dopamine.

O54

The challenge of 'prodromal' Parkinson's disease

Ronald B. Postuma
Montreal General Hospital, McGill University, Canada, Hopital du Sacre Coeur, Universite de Montreal, Canada

Parkinson's disease, like almost all neurodegenerative diseases, does not start suddenly. This implies a period during which subclinical degeneration is present, but has not crossed the threshold to full clinical presentation. In addition, Parkinson's disease has the unique feature of an additional prodromal period that is mostly characterized by non-motor symptoms. This prodromal interval provides an opportunity to detect disease several years before full clinical symptoms, and could eventually lead to neuroprotective therapy to prevent clinical disease.

Recognition of this prodromal period has led to concerted efforts to define prodromal PD, and perhaps even to change the definition of PD. Both population-based studies and at-risk cohorts have been created to assess prodromal disease. The advantages and disadvantages of each will be discussed. These studies have begun to provide clear directions as to how to identify prodromal PD, including the identification of non-motor clinical markers (olfactory loss, REM sleep behavior disorder, color vision loss, autonomic dysfunction, etc) and neuroimaging markers (dopaminergic functional neuroimaging, transcranial ultrasound, etc). Current evidence for the utility of these markers will be summarized, particularly focusing upon their specificity and positive predictive value. Finally, the work of the Movement Disorders Society task force on definition of PD, which includes development of a prodromal PD definition, will be introduced.

O55

Redefining Parkinson's disease: possible approaches to developing new diagnostic criteria

Daniela Berg¹ on behalf of the task for "Definition of Parkinson's disease" of the MDS

¹Department of Neurodegeneration, Hertie-Institute of Clinical Brain Research and German Center for Neurodegenerative Diseases, Tübingen, Germany

Objective: To summarize the various factors that will need to be taken into account in developing new diagnostic categories/criteria.

Methods: In 2011 the Movement Disorders Society established a task force on the definition of Parkinson's disease. Critical issues the group has been working on are:

- A) What is essential for the diagnosis of PD?
- B) How can diagnostic criteria account for subtypes?

C) Can PD be defined before the classic motor features develop?

Results: Several current findings in different fields of PD research seem neither compatible with other fields of research nor with the current gold standard of PD diagnosis. To fill knowledge gaps in an unbiased way a three tiered approach with a clinical, pathology and genetic tier is proposed, which does not commit to insisting on a specific clinical syndrome or a specific pathology and permits incorporation of new information as it becomes available. More specifically approaches will include

(i) for the clinical tier to:

- create models to group subtypes - better characterize non-motor symptoms and develop algorithms for earlier diagnosis

(ii) for the pathology tier to:

- create models that include formation, site and mechanism of alpha-synuclein pathology and account for PD cases without classical Lewy bodies and Lewy bodies in individuals without PD

- recognize way and direction of spreading of pathology

(iii) for the genetic tier to:

- group Mendelian forms into mechanistically homogenous categories by elucidating molecular mechanisms also up- and downstream

- understand how common and medium risk variants can contribute to the differentiation of subgroups of PD patients

Imaging may constitute a bridging element of the pathology, genetic and clinical tier. Here, development of a ligand that permits imaging of brain and extra-cerebral alpha-synuclein in vivo and identification and validation biochemical markers mirroring the pathological process will be essential.

O56

Prototypical and less common hallucinations

Regina Katzenschlager

Department of Neurology, Donauespital / SMZ-Ost, Vienna, Austria

Hallucinations are typically associated with advanced stages of Parkinson's disease (PD) and after 10 years' disease duration, they have been found in 60% of PD patients. However, a minority of patients develop hallucinations on their first antiparkinsonian treatment and the presence of dementia is not strictly required for the formation of hallucinations. Once they do occur, however, the risk of subsequent dementia is considerably increased.

The most common form of hallucinations in PD is visual. Patients may initially have the feeling of a person's presence in the room, or they may perceive inanimate objects as animals or persons, movements where there are none, or changes in patterns or colour. These visual misperceptions may precede frank hallucinations, which do not have a basis in reality, but hallucinations may occur without prior illusions. Visual hallucinations are typically well-formed, often involve persons or animals and often consist of repetitive scenes. Non-visual hallucinations rarely occur in isolation and are usually associated with advanced PD. Patient with marked visual hallucinations may have auditory or, less commonly, tactile hallucinations as well, for example, they may hear their imaginary visitors speak and may then interact with them. Initially, patients often retain at least partial insight into the nature of their misperceptions but this tends to get lost over time. Mild and moderate forms of hallucinations may go almost unnoticed by the care-givers as patients are not always bothered by them or do not mention them due to embarrassment. Nevertheless, hallucinations have a clear tendency to progress over time, they are an important indicator of possible future dementia and their presence guides the choice of antiparkinsonian drugs. They may lead to delusions, which usually have a dramatic impact on the patients' and care-givers' quality of life. For all these reasons, hallucinations should be routinely enquired about.

O57

Where is the nucleus hallucinatorius and how it gets stimulated?

Nico J Diederich

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Approximately one third of PD patients suffer from hallucinations. The breadth of the phenomenology is remarkable, ranging from illusions, minor hallucinations of passage or presence, to vivid scenery, multisensory hallucinations and full-blown secondary paranoid psychosis. After a phase of pseudo-benign hallucinations, there is usually intractable progression over the years. Unimodal models of pathogenesis have focused on levodopa psychosis, sleep/wake dysregulation and visual impairment, among others. While there is fruitful clinical applicability of these models, none has succeeded in identifying a single nucleus or network responsible for hallucinations in PD. In contrast, theoretically conceptualized models embracing multiple domains, such as the Perception and Attention Deficit model (PAD) and the Activation-Input-Modulation model (AIM) by Hobson have been largely confirmed by recent clinical and neuroimaging data. Indeed patients with hallucinations demonstrate simultaneous impairments in several domains, especially in terms of sustained attention and complex visual processing. Within the hypothesis of default network dysfunction several nodes of breakdown have also been posited. It is thus no surprise that diffusion tensor imaging, successfully applied in schizophrenia, is a new strategy to be applied in PD hallucinations. To date, reduced fractional anisotropy in parieto-occipital white matter tracts has been documented along with neuropathological demonstration of multiple areas with high burden of Lewy bodies, such as the amygdala and the cholinergic neocortical areas of the temporal lobe. Other areas within attention loops and primary and secondary visual pathways remain to be examined in detail, in the quest for the Holy Grail of one "nucleus hallucinatorius".

O58

Mitochondrial quality control: a matter of life and death for neurons

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Objective: Mitochondrial dysfunction has been increasingly implicated in the development of neurodegenerative diseases, including Parkinson's disease. There are 3 established mechanisms that regulate mitochondrial quality control pathways, including the action of mitochondrial proteases, retrotranslocation of substrates for degradation in the proteasome, and the entire removal of organelles through mitochondrial autophagy, or mitophagy. At least two distinct Parkinson's disease genes coding Parkin and PINK1 are required for mitophagy, suggesting that mitochondrial quality control is interrupted in patients with PD. I will describe a fourth pathway in mitochondrial quality control, which is the removal of selected, damaged mitochondrial content through a vesicular transport route.

Methods: The experiments presented will include imaging and biochemical approaches to establish the generation, content and fate of mitochondrial derived vesicles (MDVs). Using siRNA and other molecular biology approaches we address the functional contribution of PD and other genes in these pathways.

Results: The data outline a novel pathway for mitochondrial quality control, and identify new functions for PD genes in the generation of MDVs.

O59

Mechanisms of mitophagy in Parkinson's diseaseCharleen T. Chu¹, Hülya Bayır^{2,3} and Valerian E. Kagan³¹Department of Pathology, Pittsburgh, PA, USA²Department of Critical Care Medicine, Pittsburgh, PA, USA³Department of Environmental and Occupational Health, University of Pittsburgh, Pittsburgh, PA, USA

Objective: Dysregulation of mitochondrial autophagy has been implicated in sporadic and familial Parkinson's disease. A key feature of mitophagy regulation is the ability to selectively recognize damaged mitochondria for autophagic degradation. These studies were designed to elucidate the nature of "eat-me" signals expressed by damaged mitochondria in neurons.

Methods: As decreased complex I activity may contribute to Parkinsonian neurodegeneration, we utilized low-dose treatments with rotenone or other parkinsonian toxins to induce mitophagy in primary cortical neurons and SH-SY5Y cells. A combination of fluorescent imaging, immunocytochemistry, mass spectrometry, site directed mutagenesis and computational methods were used to study changes in mitochondrial surface phospholipid composition and potential interactions with the autophagy protein microtubule-associated protein 1 light chain 3 (LC3). In some studies, the expression of PTEN-induced kinase 1 (PINK1) was manipulated to determine its functional relationship to mitophagy pathways stimulated by complex I inhibitors.

Results: Our data indicate that multiple mitophagy-inducing injuries trigger the externalization of cardiolipin, which targets damaged mitochondria into autophagosomes by direct binding to LC3. Unlike HeLa cells, which can tolerate complete clearance of mitochondria, we found that elevated levels of mitophagy cause dendrite retraction in toxin and dominant genetic models of PD. Residues of LC3 that are involved in binding cardiolipin are located adjacent to a phosphorylation site that we previously identified. Mimicking LC3 phosphorylation reduced mitophagy and protected against dendrite retraction. These data suggest that a proper balance of mitophagy activators and brakes are essential for maintaining neuron health.

O60

Mitochondrial remodeling in the control of apoptosisLuca Scorrano^{1,2}¹University of Padova, Padua, Italy²Dulbecco-Telethon Institute, Venetian Institute of Molecular Medicine, Padua, Italy

Objective: Mitochondrial ultrastructural and morphological changes have been implied in the control of several physiological and pathological changes, including the progression of apoptosis. However, the precise role of mitochondrial dynamics in the response to reversible and irreversible cellular damage is not completely understood. Our data indicate that the shape of mitochondria dictates function of the organelle and therefore complex tissue responses, opening the possibility for treatment of pathological conditions where mitochondrial dysfunction plays a crucial role.

Methods: Today we will present our recent data obtained in genetic models of ablation and up-regulation of the key mitochondrial shaping proteins Optic atrophy 1 (Opa1) and mitofusin in *D. melanogaster* and in the mouse. The *in vivo* experiments of tissue damage by inducing atrophy, apoptosis or ischemia/reperfusion indicate that the master cristae biogenetic regulator Opa1 can prevent multiple forms of tissue damage by controlling mitochondrial cytochrome c release and metabolic efficiency. On the other hand, the interplay between mitochondria and the endoplasmic reticulum

is highlighted by the ablation of the multifunctional mitofusin of the fruitfly, that results in the development of ER stress that contributes to the lethality of the phenotype.

Results: Our data indicate that the shape of mitochondria dictates function of the organelle and therefore complex tissue responses, opening the possibility for treatment of pathological conditions where mitochondrial dysfunction plays a crucial role.

O61

Why and how people with Parkinson's need empowerment - Finding your own nicheFulvio Capitanio¹¹Unidos contra el Parkinson, Barcelona, Catalonia, Spain

Objective: What is patient empowerment?

Patient empowerment is simply a process to help people gain control, which includes people taking the initiative, solving problems, and making decisions, and can be applied to different settings in health and social care, and self-management.

This is only a definition of patient empowerment.

The questions now are: Do PwP really need to be empowered, and how?

Methods: Since we were child we were constantly learning and preparing ourselves to live an adult productive life as part of the mechanism that runs our society.

We developed a set of skills, we acquired and enriched a tool box perfectly designed to commit our tasks. Unfortunately nobody prepared us to face a breakthrough event like the diagnosis of Parkinson's disease. We need to adjust our skills, to learn different ways to use the tools we already have, to acquire new abilities and to renew our toolbox.

Results: The benefit of empowered patients is particularly true for chronic diseases, the treatment or management of which have been moved gradually from the doctor's office or hospital to the patient's day-to-day life. While this gain in independence is a blessing for affected patients and can dramatically increase their quality of life, it also means that patients need to take a more active role in the management of their condition, from lifestyle changes to the use of medical devices and implementation of therapy adjustments following discussion with their doctor or nurse.

O62

Evidence-based self-management practicesPatrick McGowan¹¹University of Victoria, Victoria, BC, Canada

Over the last 30 years there has been a growing perception that people experiencing chronic health conditions are capable and should participate in managing their health, and the notion of "patient as the passive recipient of care" is not appropriate. The aging population, increasing prevalence of chronic conditions, burgeoning costs of providing health care, and focus on quality of life have further accentuated this perception. Chronic disease management has emerged as a viable paradigm of care and patient activation and self-management support are integral components in this model. With the acknowledgement that persons with chronic conditions mainly manage on their own, patient education began including behavioral change interventions, competency in problem-solving and "empowerment" enhancing strategies. Self-management programming focussing on skill and confidence development emerged and became popular across the spectrum of health conditions. This presentation will provide an overview of the emergence of self-management programming and the theoretical and research studies conducted over the past decade. Self-management support strategies provided by health professionals

during clinical care represent another viable mechanism of developing informed and activated patients and will be described. A case will be made that self-management as a strategy to create and enhance patient empowerment is essential with Parkinson's disease.

O63**Introduction: Overview of genetic testing**

Oksana Suchowersky

University of Alberta, Edmonton, Canada

Since 1997, it has been recognized that approximately 10% of patients with Parkinson disease (PD) have a family history of this condition. With the advent of genome sequencing, eight genes have now been identified that are associated with PD, the 2 most common being *LRRK2* and *parkin*. It is now possible to perform genetic testing for mutations in these genes, thus confirming a specific diagnosis. It is also possible to identify asymptomatic individuals who carry these mutations and may develop symptoms in the future (presymptomatic testing). This type of testing has limitations. For example, a negative gene test does not rule out a diagnosis of PD, or mean that the condition is not hereditary. Alternatively, having the gene does not mean the person will get PD. The physician arranging for genetic testing needs to be knowledgeable, as many different genes may cause a similar clinical picture (phenotype), or the same genetic mutation may cause different phenotypes. In addition to the limitations of the genetic testing itself, it is important to recognize the ethical, legal, and psychosocial implications. Secondly, the testing is currently quite expensive. It is also important to realize that in over 90% of individuals, even with a family history, a specific causative gene cannot be identified. In this workshop, the pros and cons, as well as limitations of genetic testing for PD will be discussed.

O64**Introduction: Overview of sleep, sleepiness and fatigue in PD**

Joseph H. Friedman

Brown University, RI, USA

Sleep disorders affect 90% of PD patients in some populations. Fatigue has a consistent prevalence of about 50% in all reports from a variety of cultures. While sleepiness and fatigue are often thought of as a single problem, they are quite different, although often seen together. Fatigue refers to a sense of severe lack of energy. Napping does not help, and, paradoxically, exercise does. Fatigue is an early symptom of PD, often developing in the "pre-motor" phase and is unrelated to motor dysfunction. This talk will stress the difference between fatigue and sleepiness, and treatment recommendations will be made although evidence to support treatment is scant. Excessive daytime sleepiness (EDS) is often the result of poor quality sleep at night, but may be due to an increased need for sleep in some PD patients who develop a narcolepsy-type of disorder as a result of changes in the hypothalamus. PD patients may have difficulty falling asleep, staying asleep, returning to sleep once awake, or awakening too early. Pain, daytime naps, difficulty getting comfortable, overactive bladder, depression, nightmares, tremor, medication side effects and a variety of other problems may complicate sleep. Approaches to dealing with the manifold problems will be discussed, but no medication has been proven to improve sleep in PD.

O65**Panel discussion Tricks of the trade: clever strategies to improve mobility**

*Graziano Mariella*¹

¹European Parkinsons' disease Association, Esch-sur-Alzette, Luxembourg

Objective: To motivate people from the audience to share their own strategies to overcome their daily mobility obstacles.

Methods: Through interactive discussions and using illustrations, like video clips from the Coping strategies Tips and Tricks multilingual website www.epda.eu.com/en/resources/coping-strategies-tips-and-tricks/ and tricks examples brought by the public, people will be able to share and understand strategies developed by themselves.

Results: Willing participants will have their tips and tricks captured on video (those who agree to sign a waiver provided onsite) which will be added to the EPDA Coping Strategies - Tips and Tricks website.

O66**Introduction: Overview of Strategies for Improving Mobility**

*Terry Ellis*¹, *Mariella Graziano*², *Samyra Keus*³, *Pamela Quinn*⁴

¹Boston University, Boston, USA

²Board Member of the European Parkinson Association, London, UK

³Radboud University Nijmegen Medical Centre, Nijmegen, The Netherlands

⁴Brooklyn Parkinson Group, Brooklyn, NY, USA

Persons with Parkinson disease often find it challenging to navigate effectively in the home and community environments. Many describe difficulty maneuvering through doorways, over thresholds and in small spaces. Movement can be difficult to initiate, is typically small in amplitude, slow and less automatic. Some may experience freezing where the feet feel glued to the floor. With a deficiency in dopamine, the basal ganglia no longer act as an internal cueing mechanism contributing to the loss of automaticity and movement regulation. However, various forms of external cueing have been used effectively to help improve mobility by bypassing the basal ganglia circuitry. Auditory cues are typically rhythmic and be generated by a metronome or embedded into music. Persons with Parkinson disease are able to "entrain" or synchronize their movements to the music resulting in a faster, more fluid movements. Visual cues in the form of lines on the floor have been shown to improve stride length and walking speed. Laser lines projected on the floor provide a visual cue to step over - helping persons with Parkinson disease to initiate walking or to overcome a freezing episode. Strategies involving consciously paying more attention to walking are known to be effective in improving upright posture, arm swing and step length for example. Other forms of cueing, such as verbal and tactile cues, can also be helpful in improving daily mobility. This session will explore the use of clever cueing strategies to facilitate mobility in the form of live demonstrations and video case studies. In addition, this session will include a discussion of the mechanisms thought to underlie the effectiveness of cueing strategies in persons with Parkinson disease.

O67**Advances in the genetics of Parkinson's disease**

*Nicolas Dupré*²

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In families with a non-mendelian form of Parkinson's disease (PD), first-degree relatives of an affected individual are between 2.7 and 3.5 times more likely to develop PD than individuals without a family history of PD. Their cumulative lifetime risk of developing PD is between 3% and 7%. Individuals with onset before age 20 years are considered to have juvenile-onset PD, those with onset before age 50 years are classified as having early-onset PD, and those with onset after age 50 years are considered to have late-onset PD. The genetic cause of some forms of mostly juvenile and early-onset PD has been identified. Even if most cases of PD are thought to result from the effects of multiple genes as well as environmental risk factors, PD can be inherited in an autosomal dominant or autosomal recessive manner. Several disease genes have been implicated. Mutations in three genes, SNCA (PARK1), UCHL1 (PARK5), and LRRK2 (PARK8) result in autosomal dominant PD. Mutations in three genes, PARK2 (encoding for parkin), PARK7 (PARK7), and PINK1 (PARK6), result in autosomal recessive PD. Molecular genetic testing is clinically available for PARK2, PINK1, PARK7, SNCA, and LRRK2. Once results are available, genetic counseling of affected individuals and their family members must be done on a family-by-family basis.

O68

The experimental models of Parkinson's disease: Are they useful?

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Objective: De nombreux modèles de la maladie de Parkinson ont été développés par les chercheurs pour comprendre ses mécanismes et tester de nouveaux traitements. Beaucoup de controverses ont émergé à ce sujet. Le but de cette présentation est de présenter les modèles utilisés aujourd'hui et de clarifier leur limites et avantages, et d'expliquer comment ils contribuent à nos efforts pour développer de nouveaux traitements.

O69

Drug Induced Parkinsonism

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Parkinsonism is a serious complication of many drugs. Most prominent are the dopamine receptor blocking agents (DRBA) including antipsychotics and antiemetics. The frequency in treated patients is ~50% in the elderly and up to 60% in schizophrenics depending on several risk factors. Drug-induced parkinsonism (DIP) makes up 10-20% of parkinsonism patients seen in movement disorders clinics. Clinically, DIP can be indistinguishable from Parkinson's Disease (PD), with unilateral or bilateral onset and akinetic-rigid or tremor predominant forms. Differentiating clinical features in DIP include the subacute onset, rapid progression, and co-occurrence of tardive dyskinesia. Older woman are at greatest risk for developing DIP. DIP is serious because of its potential chronicity, disability, morbidity, admissions to nursing homes and mortality. Atypical antipsychotics (AA) have largely replaced typical neuroleptics and are frequently used to treat the elderly. Recent studies have suggested that AA do not decrease the risk of DIP. DIP is under-recognized as patients are either diagnosed with PD or not diagnosed at all. Large population studies based on Medicare and Medicaid record reviews demonstrated that patients treated with neuroleptics were 2-5 times more likely to be diagnosed with PD and treated with anti-PD medications as those not exposed. Over 70% maintain the inciting agents. One way to detect this

difference would be to stop the DRBA but reversal can take a year. The development of ¹²³I-FP-CIT SPECT imaging has changed that problem being normal in DIP but abnormal when the drug worsened already present PD or hastened its development. To treat DIP the first step besides recognition is the removal of DRBA or switching to a less potent one. The role of anti-PD agents is unclear. Other non-neuroleptic drugs are important causes of DIP including: Valproate (5%), tetrabenazine (4-15%), amiodarone, cyclosporine, lithium, and SSRI's.

O70

PD or progressive supranuclear palsy

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The early and accurate diagnosis of progressive supranuclear palsy (PSP) and Parkinson's disease (PD) is at times challenging. There are no biological markers that could help diagnose these disorders. However, differentiating them early is crucial as their prognosis and management differs. PSP is the most common atypical parkinsonian disorder. It is a 4-repeat tauopathy, usually presenting in the sixties with various phenotypes. The most common and classical PSP phenotype should be easy to differentiate from PD as it is characterized by features would be very unusual in early PD. PSP classically presents with progressive postural instability and falls, non-levodopa responsive axial parkinsonism, difficulties with vertical ocular movements, early dysarthria, dysphagia and executive dysfunction. However, there are other PSP phenotypes that pose major challenges. PSP patients may present with a progressive asymmetric parkinsonism benefiting from levodopa therapy, PSP-parkinsonism, or with freezing of gait, PSP-akinesia and freezing of gait. Early suspicion and search for tell-tell signs help the clinician differentiate PSP from PD.

O71

PD or Multiple system atrophy

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Multiple system atrophy (MSA) and Parkinson's disease (PD) are both degenerative diseases of the basal ganglia. MSA is a progressive disease associated with autonomic features. Diagnosis can only be made with certainty with pathological confirmation showing characteristic glial cytoplasmic inclusions in a variety of regions of the brain (basal ganglia and cerebellum, spinal cord). As MSA carries a worse prognosis than PD it is important to try to distinguish them. MSA is divided into MSA-P (Parkinsonism) and MSA-C (Cerebellar) reflecting the prominent initial symptom. MSA-P can sometimes be difficult to distinguish from PD as there are many overlapping features. PD may have features that were formerly thought to be found only in MSA, such as significant autonomic involvement. Both diseases are treated with levodopa, although with MSA-P there may be greater need to treat the orthostatic hypotension with medications. Levodopa responsiveness and motor fluctuations can be seen in cases of MSA-P. Also, it is now recognized that there are examples of MSA-P which are benign and of long duration. There are some well described "red flags" to distinguish MSA-P from PD including orofacial dystonia, cold hands and feet, myoclonic (jerky) tremor, camptocormia (extreme forward flexion of spine), disproportionate antecollis (neck flexion), severe dysphonia (impaired voice) and sighing. Autonomic testing, anal sphincter EMG, neuroimaging including MRI, PET and SPECT can

be supportive. The imaging characteristics will be discussed in further detail. There are distinct differences in prognoses between these disorders, with MSA-P being more rapidly progressive and more challenging to manage. Therefore, it is important for the clinician to distinguish and diagnose the patient with MSA-P.

O72

The placebo effect: how it complicates clinical trial results

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When a clinical trial of a new medication or surgery is conducted for patients with Parkinson's disease (PD), researchers are trying to test whether the new treatment improves a specific element of the disease or overall disability. The testing program necessarily involves more visits to the study center, more attention by the study staff, and more focus by the patient, family, and raters on the possibility of change in the PD. All of these latter issues can positively affect patients and changes induced by study participation independently of the actual new treatment being studied are collectively known as "placebo-associated improvements". Because these effects can be striking specifically in PD, almost all important studies of new treatments are "placebo-controlled", meaning that patients are randomly assigned to receive the study intervention or an inert treatment (empty pills or sham-surgery) so that neither the patient nor the raters know to which group a given patient is assigned. In this way, both groups experience whatever placebo-associated improvements occur, and an added benefit documented in the study treatment group can be safely ascribed to that specific intervention. Prior studies have indicated that placebo-associated improvements are quite marked, but varied, in PD studies. In an evaluation of 11 clinical trials, covering mild, moderate and advanced PD subjects and both medication and surgical interventions, an overall placebo-associated improvement occurred in 16% of patients and reached as high as 50% in surgical interventions. In this analysis, the primary criterion for determining "placebo-associated improvement" was a 50% improvement in objective ratings of PD impairment using the internationally recognized scale known as the UPDRS that measures tremor, bradykinesia, rigidity, gait and balance. Whereas from a clinical management perspective, clinicians and patients are happy to see improvement from any cause, placebo-associated improvements pose a very significant challenge to clinical trials. If the placebo effect is strong, the challenge increases to document a benefit from the study intervention. Further, because the frequency of placebo response is varied, it is difficult to estimate this effect for a given study beforehand. Many studies of seemingly effective treatments for PD have failed and been abandoned, not because the treatment group failed to improve, but because the placebo-treated group improved too, making the difference between placebo treatment and new intervention treatment statistically equivalent. The particular sensitivity of PD to placebo effects is likely due in large part to the activation of dopamine that occurs when the human brain responds to novelty, expectation, and risk. Enrollment in clinical trials naturally activates all of these behaviors. Scientists cannot reduce novelty or risk, because they are implicit to the experience of a clinical trial, but potentially expectation is controllable. The aim of a clinical study is to test a new intervention, and ideally, raters and patients who participate are those who are ready to rate whatever they see or experience. Their role is accurate reporting. They cannot help from hoping for improvement, as they wish to establish new treatments for PD; however, they may be able to discipline themselves against expectation and to concentrate on accurate reporting whether there is improvement, decline or no change. Paradigms to test this type of control can be implemented, and

efforts have been developed to try to reduce expectation in programs.

O73

Slowing clinical progression in PD - Can it be proven in clinical trials?

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No drug has yet been established to have a neuroprotective effect in PD. Several clinical trials of putative neuroprotective agents have shown positive results, but it could not be determined with certainty if the benefit was due to neuroprotection because of potentially confounding pharmacologic or regulatory effects of the study agent. In an attempt to separate an early symptomatic from a disease modifying effect, the delayed washout and delayed start studies have been proposed. Both are two period studies that rely on change from baseline in UPDRS score. In the first period of each of these studies, patients are randomized to active treatment (early start) or placebo. In the second period of the delayed washout study, the active intervention is stopped and patients in both treatment groups receive placebo. If the early start group maintains a benefit in comparison to placebo at the end of the second period, this is consistent with the treatment having a disease-modifying effect. This design, however has ethical and practical issues. In the second period of the randomized start design, patients in the placebo group are placed on the active intervention (delayed start) while those in the early start group are maintained on their original treatment. If at the end of the trial the early start group continues to show a benefit in comparison to the delayed start group, even though both groups are on the same treatment, this suggests that the treatment has slowed the rate of clinical deterioration. Such studies are complex and difficult to carry out. Another approach is the long-term simple study, where subjects are randomized to active treatment or placebo, and then followed for a prolonged period of time in which the physician can manage the patient in any way they deem to be appropriate. The outcome measure capture factors related to the development of cumulative disability. A combination of the delayed start and long term simple studies offers assessments of mechanism and clinical significance, and provides a roadmap for the development of a neuroprotective drug. Adaptive design is another approach that can be of great value. Here, unannounced but predetermined interim analyses examine data accumulated during the course of the trial without compromising the blind or the integrity and validity of the study. Such an approach can permit early termination of a study for adverse events or futility, examination of large numbers of doses with rejection of those doses that are futile, re-estimation of sample size, and early planning and streamlining of next phase studies. These approaches can substantially reduce the cost and time of the development program for a putative neuroprotective drug.

O74

Infusion therapies and other non-oral routes of drug delivery

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Chronic pulsatile oral administration of dopaminergic drugs, particularly levodopa, contributes to the development of motor fluctuations and dyskinesia in Parkinson's disease (PD). Motor complications also represent a significant burden for patients and

their caregivers and are an important cost driver in overall PD management. Infusion and transdermal delivery of dopaminergic drugs (levodopa and dopamine agonists) helps providing continuous receptor stimulation that in turn would minimize motor fluctuations and improve dyskinesias in advanced patients. The following options are available: rotigotine patch, apomorphine subcutaneous infusion and levodopa-carbidopa intestinal gel (LCIG). Rotigotine is a dopamine agonist that has shown its effectiveness at all PD stages and may be particularly helpful in patients with specific non-motor symptoms like sleep and mood disturbances as well as in presence of permanent or transient gastrointestinal problems (thanks to its transdermal delivery). Continuous subcutaneous infusion of apomorphine has shown benefit in advanced patients. Apomorphine exerts its anti-parkinsonian effect by direct stimulation of striatal postsynaptic dopamine D1 and D2. Alternative routes of apomorphine delivery such intranasal or inhaled are under development. Finally, LCIG treatment was recently shown to not only reduce off time and extend on time but also to have a beneficial effect on troublesome dyskinesia. LCIG was also shown to have effect on non-motor symptoms. The rationale for favoring a continuous dopaminergic delivery instead of pulsatile regimen regards primarily the avoidance of peaks and troughs in plasma. Such therapeutic strategy may improve quality of life and decrease patient disability likely resulting in economic benefits because of reduced costs for medical care, physician visits and hospitalization.

O75

Delivering therapeutic genes into the brain - a future way of drug delivery?

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The brain is an highly heterogeneous structure divided in many interacting circuits involved in complex behavioral tasks. These neuronal networks are composed by neuronal populations expressing receptors and neurotransmitters that can be involved in either motor, associative or limbic territories. Thus, systemic drug administration may induced adverse reactions due to a diffusion of its action behong the therapeutic target stressing the need to develop local delivery methods. Gene transfer technology is one of the most advance delivery method capable of locally delivering protein of therapeutic interest to highly specialized subpopulation of neurons. The presentation will give an overview of the gene transfer technology dedicated for brain diseases as well as methods to surgically administered viral vectors.

O76

Pathological evidence for axonopathy in Parkinson's disease

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Objective: To review the role of axonal pathology in PD.
Methods: Overview of the neuropathologic literature on axonal pathology in PD, as well as personal experience from evaluating over 1000 brains with Lewy body pathology, including over 250 with PD.

Results: While neuronal perikaryal inclusions composed of α -synuclein (referred to as Lewy bodies) are the histologic hallmark of Parkinson's disease and related α -synucleinopathies, including dementia with Lewy bodies, much evidence suggests that the greatest disease burden in PD is in neuritic processes that are axonal in origin or in presynaptic axonal terminals. Inclusions with morphologic characteristics of Lewy bodies are also detected in axons (so-called intraneuritic Lewy bodies) in certain vulnerable

brain regions, notably the dorsal motor nucleus of the vagus and the basal nucleus of Meynert. Lewy neurites, lesions that are not visible with routine histologic methods, were first described with ubiquitin immunohistochemistry in the hippocampus and amygdala, but with the advent of α -synuclein immunohistochemistry, it became clear that they were widespread and a fundamental characteristic of PD and not only a feature of advanced disease, but also one of the earliest neuronal alterations. Another pervasive but subtle pathology is accumulation of abnormal conformers of α -synuclein in axonal termini at the synapse. In addition to these α -synuclein-immunoreactive lesions, there is evidence to suggest that nigrostriatal dopaminergic degeneration in PD may have its origin in the distal axonal termini analogous to a dying back process. While there may be α -synuclein pathology in dopaminergic cell bodies in the substantia nigra, the central dying back axonopathy in the striatum does not seem to be associated with striatal α -synuclein pathology. In contrast, in advanced disease, the striatum in PD and related α -synucleinopathies has extensive neuritic pathology that increases with disease duration.

O77

Evidence for synaptic dysfunction in Parkinson's disease

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Objective: α -Synuclein (α -Syn) is an abundant, soluble presynaptic protein that is broadly expressed in brain. Point mutations, duplication and triplication of the α -Syn gene have been shown to cause Parkinson disease, yet its physiological functions remain unknown. The objective of this study is to investigate the normal synaptic functions of α -Syn and its role in Parkinson's disease.
Methods: We generated $\alpha\beta\gamma$ -Synuclein knockout ($\alpha\beta\gamma$ -Syn^{-/-}) mice that lack all murine synucleins. These mice are viable but have a shorter lifespan than wildtype controls. The overall brain architecture and morphology of neurons in young $\alpha\beta\gamma$ -Syn^{-/-} mice appears normal but the size of synapses is decreased. We carried out an unbiased proteomic screen to identify proteins that are changed in $\alpha\beta\gamma$ -Syn^{-/-} synapses and observed increases in the levels of select membrane curvature sensing/generating proteins. These proteomic data suggest that α -Syn participates in the exo- or endocytic steps of the synaptic vesicle cycle—two steps that require membrane bending. To directly determine the roles of α -Syn in the synaptic vesicle cycle, we have used vGlut-pHluorin imaging as well as slice electrophysiology.

Results: Our data suggest that α -Syn regulates the kinetics of the endocytic step in the synaptic vesicle cycle and the deficits in this function could contribute to the initiation of Parkinson's disease.

O78

Alterations in axonal transport in Parkinson's disease

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Intracellular aggregates of α -synuclein known as Lewy bodies (LB) or Lewy filaments (LF) are a pathological hallmark of Parkinson's disease (PD). Further, point mutations in α -synuclein are linked to some familial Parkinson's (fPD) cases, but no consensus explanation has emerged to elucidate the roles α -synucleins play in PD pathogenesis. Recombinant α -synucleins were used to evaluate changes in axonal transport associated with both fPD mutant α -

synucleins and LF made from wild type (WT) α -synucleins in a cell-based model of synucleinopathy. Mutant α -synucleins (A30P and A53T) activated specific isoforms of a neuronal protein kinase C (PKC) leading to increased dynein-based retrograde transport, reduced kinesin-based anterograde transport and failure of neurotransmission. The net effect of these changes in fast axonal transport is a reduction in synaptic vesicles and other components needed for the continued function of the presynaptic terminal, leading to failure of neurotransmission in affected neurons and an associated loss of adequate neurotrophin supplies. Pathogenic forms of α -synucleins or LB/LF alter regulatory pathways critical for maintaining the normal balance between anterograde and retrograde transport in dopaminergic neurons. Altered trafficking of organelles in axonal transport affects trophic interactions and synaptic function, leading to synaptic loss and eventual neuronal death.

O79**Introduction: Overview of care models and options**

Elaine Book

Pacific Parkinson's Research Centre
University of British Columbia, Canada

Considering residential care for a loved one can be an emotional process as well as challenging as one navigates the health care system. A variety of options exist offering varying levels of care and often with complicated processes for accessing the services. This workshop will address some of the issues in deciding when it is time to plan for facility care, considerations to think about when choosing a care facility and what options are available. The panelists each representing Canada, USA, Australia, India and the Netherlands will present an international perspective on care models and how Parkinson's concerns are addressed. The discussion will identify some of the challenges and successful approaches used to meet the needs of PD patients and their families.

O80**Case presentation: Care models in the Netherlands**

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The situation in Dutch nursing homes for patients with Parkinson's disease is highly variable and, unfortunately, often not optimal. In many Dutch nursing homes, patients with Parkinson's disease are not treated optimally. We recently performed a research project aiming to examine the clinical characteristics, motor impairments, and drug treatments of nursing home residents with Parkinson's disease. Based on this study we concluded that PD in nursing home residents is characterized by severe motor impairment and a high proportion of daily "off" time. Non-motor symptoms were very common, and quality of life was poor, largely due to non-motor symptoms. In addition, 20% of diagnoses within the parkinsonian spectrum were inaccurate. Almost 9% of residents had inadvertently received a diagnosis of parkinsonism. Interviews with patients, informal caregivers and healthcare workers revealed that PD care in Dutch nursing homes is suboptimal. Three core areas for improvement were identified, including a need for greater attention to psychosocial problems, a need for improved PD-specific knowledge among nursing home staff, and a need for better

collaboration with hospital staff trained in movement disorders. These findings underscore the need for improved management of PD in nursing homes, but also the need to avoid admission altogether by enabling patients to remain in their homes. ParkinsonNet (www.parkinsonnet.nl) has started a healthcare innovation project aimed to reach these targets.

O81**Case presentation: Care models in the USA**

Ruth Hagestuen

Struthers Parkinson's Center, Golden Valley, MN, USA
National Parkinson Foundation

Objective: This presentation will provide an overview of the Struthers Parkinson's Center's integrated approach to clinical, educational, research, support, outreach and wellness programs. The Center, established over 30 years ago, is a free-standing facility which is part of the Park Nicollet Health System.

Methods: The SPC integrated system of care is designed to provide access to the right care, information, and support at the right time, over time. The majority of programs which will be presented are team based. The full day assessment clinic, for example, includes physician, nurse, social worker, physical therapy, occupational therapy, speech therapy. Different combinations of the team members are part of the FOCUS program for persons newly diagnosed, the Caregiver Skills-building series, and the DBS educational sessions for patients and families considering Deep Brain Stimulation. The same is true of the regularly scheduled professional education days for nurses, rehabilitation therapists and social workers. Two other unique programs of this Center are (1) the CREATE (Center for Research Education Artistic and Therapeutic Endeavors) program which includes a therapeutic day program, an arts café, and a variety of exercise based wellness and support programs and (2) The Struthers Parkinson's Care Network (SPCN), working with senior residential communities to improve PD awareness, staff education and support services.

Results: Attendees at this session will (1) be able to list at least two unique program initiatives from Struthers Parkinson's Center that can be replicated in other locations, (2) Discuss the role of a Parkinson's Center as a regional hub of specialized care in the U.S.

O82**Overview**

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Experimental animal models of Parkinson's disease are characterized in a variety of ways including the "animal" used (e.g. invertebrates, rodents, nonhuman primates) and the "disease" producing mechanism (e.g., neurotoxins, transgenic models of Parkinson-related mutations, overexpression of alpha synuclein using viral vectors, direct brain injections of fibrillar synuclein). Features of these models that are generally considered in evaluating their utility include behavioral manifestations, whether or not the model demonstrates progression over time, nature and involvement of dopaminergic neurons of the substantia nigra, additional non-nigral involvement, nature of the underlying neuropathological features (including synuclein aggregation/Lewy body formation), and the presence of various pathogenic features (e.g., mitochondrial dysfunction, neuroinflammation, abnormalities of proteolytic pathways, cell-to-cell spread of pathology, etc.). These

models can be used for a variety of purposes depending on the underlying neuropathological/neurochemical disturbances including the assessment of possible pathogenic factors underlying the disease, evaluation of putative neuroprotective or disease modifying therapies, and the study of novel symptomatic therapies for both the disease and the complications of its treatment. In this workshop the panelists will discuss the advantages and disadvantages of available experimental models particularly emphasizing their utility in predicting outcomes of various forms of treatment.

O83

Introduction: Insights into Complementary Therapies

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³PD Carepartner & Reiki Master, GiveReiki.com

Objective: To provide an overview of complementary and alternative therapies and their use in Parkinson's disease.

Background: Complementary and Alternative therapies (CAM) are traditionally defined as therapies outside of the realm of traditional medicine. These therapies are playing a greater role in the self-care of people with Parkinson's disease to improve symptoms, influence disease, improve personal wellbeing and enhance innate natural healing abilities. The field is broad and difficult to define as the boundaries between what represents traditional medicine and CAM therapies are blurred. This workshop will begin with a discussion of healing based therapies, contribution to health and wellbeing and the philosophical differences that often separate these modalities from traditional medical treatment. A brief overview of CAM therapies and their role in categorical review of CAM therapies to include: Natural Products, Manipulation and Body Therapy, Mind-Body Medicine, Energy Medicine, and Health Systems. Panelists Angela Rob and Dr. Louis Tan will share their insights on the role of CAM and the potential use for people with Parkinson's disease. An exploration of possible mechanism of action(s), safety considerations and practical guidance for use will be offered given the limited controlled research results to date.

O84

Overview: How do we know dance helps people with Parkinson's?

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³Mark Morris Dance Group, Brooklyn, NY, USA

⁴The Parkinson's Dance Project, Montréal, QC, Canada

Objective: This workshop has three main objectives: 1) to review the scientific literature supporting the use of dance in the management of Parkinson disease (PD), 2) to discuss various dance approaches (e.g. merengue, improvisation, modern dance, ballet and tango) tailored specifically for people with PD, and 3) provide examples of how dance programs for people with PD can be implemented in community settings.

Methods: Through individual presentations we will summarize the evidence to date regarding the benefits of different dance approaches for people with PD. A comprehensive bibliography of literature regarding dance for people with PD will be provided to participants. Participant input will be encouraged during the panel discussion which will provide multimedia demonstrations of

successful ongoing dance programs for people with PD. **Results:** Over the past several years there is growing evidence that dance is beneficial for people with PD. Specific benefits include reduction of PD symptom severity, enhanced balance and walking, and improved quality of life. Workshop participants will come away from the session with a broad overview of the literature on dance for PD, knowledge of the different forms of dance that have been employed, and specific recommendations and guidelines for implementing community-based dance programs for people with PD.

O88

The problem of the accumulation of toxic proteins and the significance of the quality control mechanisms in Parkinson's disease

Edward A. Fon

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Même si les causes de la maladie de Parkinson (MP) demeurent inconnues, l'identification de plusieurs gènes responsables de formes héréditaires de la MP a permis des percées importantes et prometteuses. Plusieurs de ces gènes semblent agir à l'intérieur des neurones pour maintenir le bon fonctionnement cellulaire en éliminant les protéines mal repliées ou désuètes. Ce travail de dégradation est particulièrement important pour maintenir un équilibre à l'intérieur des neurones et empêcher l'accumulation des déchets qui pourraient être toxiques. Mon programme de recherche se penche sur parkin, un gène qui est intimement impliqué dans la voie ubiquitin-protéasome, le principal système cellulaire de dégradation des protéines. Le but de cette conférence est de présenter un aperçu des découvertes récentes concernant parkin ainsi que plusieurs gènes apparentés.

O89

Non-motor manifestations of Parkinson's disease

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La maladie de Parkinson (MP) est surtout connue pour ses manifestations motrices toutefois, les symptômes non moteurs (SNM) occupent une place importante. Parfois ils vont précéder les manifestations motrices sinon ils vont inévitablement apparaître avec la progression de la maladie. Dans les stades plus avancés de la maladie ils peuvent même dominer le tableau clinique et interférer significativement avec la qualité de vie. Malheureusement ces symptômes non moteurs sont souvent mal appréciés tant par le patient que par son médecin traitant. Dans cette présentation, nous nous attarderons plus longuement aux symptômes non moteurs de la MP et surtout, nous aborderons les traitements non pharmacologiques et pharmacologiques de ceux-ci.

O90

Table #2: Effective Fundraising models for PwP founded non-profit organizations: How to survive

Fulvio Capitanio¹, Tom Isaacs²

¹Unidos contra el Parkinson, Barcelona, Catalonia, Spain

²The Cure Parkinson's Trust, London, UK

Objective: To provide information about how to start, run and maintain a 'not for profit' organisation to help improve the quality of life of people with Parkinson's whether this be through enhancing psychological or physical wellbeing. To illustrate the different types of non-profit organisation and the resources required to establish, expand and retain their effectiveness over time. To suggest fundraising ideas, give examples of successful fundraising campaigns and to reveal some tricks of the trade to ensure the best results. To have an interactive discussion with those present, to answer questions and share experiences.

Methods: Tom Isaacs has lived with Parkinson's for 18 years and is President and Co-founder of The Cure Parkinson's Trust which was set up in 2005. Since that time the organisation has invested over \$5 million (Canadian) into research projects around the world. The organisation has been responsible for some major advances in the Parkinson's arena and has also funded and facilitated several clinical trials which have all shown the promise of delaying or reversing the disease process. Fulvio Capitanio (Spain) is an economist and ITC manager. He was diagnosed with Parkinson's in 2007. In January of 2008, with a group of PD friends he met over the Internet, he started an online organization called "Unidos contra el Parkinson" (together against Parkinson's disease) at <http://portal.unidoscontraelparkinson.com>. Since October 2009 UCP coordinated the group's International Meetings in Spain. In March 2010 UCP edited a comic "Through the eyes of a child" to help parents to explain PD to their children. In April 2010 started the project "Run 4 PD", a worldwide yearly event involving about 100 cities from different countries.

Results: At this round table session, Tom will share his fundraising experiences and will pass on valuable insights into which income generation schemes work and which don't. There will be some amusing anecdotes among these. Fulvio will be happy to share his experience starting a network community organization, building and promoting events using the "Zero Budget" model.

O92

Table #3: Non-motor Symptoms & PD

Ronald F. Pfeiffer

University of Tennessee Health Science Center, USA

In recent years, recognition has grown that Parkinson's disease (PD) encompasses much more than difficulty with movement. A whole host of features that have little or nothing to do with movement are important, and sometimes dominant, features of PD. Changes in mood, loss of motivation, increased anxiety, difficulty with thinking and memory, excessive fatigue, sleep disturbances, problems with bowel, bladder, and sexual function, excessive sweating, impairment of sense of smell and therefore also taste, changes in some aspects of vision, and a variety of types of pain all are examples of these "nonmotor" features of PD. Although some nonmotor features characteristically appear later in the course of PD, others may occur very early, even before the classic motor features of PD develop and sometimes before PD is even diagnosed. Recognition of the nonmotor aspects of PD is important because they do not always respond to traditional PD treatment measures that typically target dopamine, but may respond to other treatment approaches. The fact that nonmotor features of PD often cause more distress - both for persons with PD and for their family members - makes it especially important that these features are recognized and addressed. This session will be open to questions and discussion of any and all of these nonmotor features of PD.

O93

Table #4: Genetic Testing & PD: What questions you should be asking

Susan Bressman

Beth Israel Medical Center, NY, USA

Over the last 15 years we have learned that mutations in several different genes cause Parkinson's disease (PD); other genetic changes may greatly or moderately increase the chances of developing PD and are not fully determinative. Testing for some of these mutations is now available either through a request by a physician or through "direct to consumer" testing. Although testing has yet to be widely and routinely adopted, increasingly individuals are becoming interested in knowing their "gene status" or in understanding the potential advantages and disadvantages of testing. In this roundtable we will review questions or issues people often need to consider when contemplating genetic testing for PD. Examples of such questions include: How likely am I to be positive for the gene being tested? What is the cost? Do I need a background understanding of genetics in order to interpret results? Will knowing the results affect my current treatment? Will results influence other life decisions? Will results affect my insurance? My job? Can a test result have implications regarding the genetic status of my relatives? It is hoped that by considering these questions participants will have a better understanding of the testing process and feel more comfortable about personal decision making in regard to genetic testing.

O94

Table #5: Parkinson's disease and cancer

Rivka Inzelberg¹

¹ The Sagol Neuroscience Center, Department of Neurology, Sheba Medical Center, Tel Hashomer and Tel Aviv University, Israel.

Objective: To discuss the particular relationship between Parkinson's disease (PD) and skin and non-skin cancers.

Methods: There is evidence based on well-designed epidemiological studies for unusual cancer rates in PD patients as compared to the general population. These findings will be reviewed and discussed.

Results: PD patients are at significantly low risk for most cancers as compared to the general population. This risk reduction cannot be attributed to the recognized low incidence of smoking in patients with PD, since not only smoking-related cancers but also non-smoking related ones are less common in PD. While the risk for most cancers appears to be relatively low in patients with PD, breast cancer and melanomas occur more frequently in the PD population as compared to controls. These peculiar patterns of cancer rates in PD might be related to the involvement of common genes in both diseases. Recently, increased risk for non-skin cancers has been reported in *LRRK2* related PD. Furthermore, genes involved in familial forms of PD appear to be abnormally expressed in cancers. Cell survival signals may differ due to mutated genes and represent two opposite extremes such as cell proliferation in cancer and cell death in PD. Unraveling the link between PD and cancer may open a therapeutic window for both diseases.

O95

Table #6: Staying engaged and raising children after a Parkinson's diagnosis

Soania Mathur¹, Sharon Daborn²

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² Australia

When a parent is diagnosed with any chronic illness, it undoubtedly affects the whole family unit in many ways. Of utmost concern are the children and their ability to cope with having a parent with a progressive illness. Likewise, parents that are struggling with their diagnosis often have trouble dealing with the idea that their parental role may now have to adjust given the change in their health. It becomes challenging from a physical point of view to manage some of the practical aspects of parenting as well as an emotional one as the uncertainty of functioning day to day can lead to feelings of frustration and guilt. Although initially overwhelmed by their unexpected diagnoses, Mathur and Daborn made it their mission to ensure that they provided their young children with the coping skills necessary to deal with this challenge and to find new parenting strategies to help themselves and other parents remain effective caregivers for their families. In their experience key elements to navigate this process were to first to prioritize their own self care, adapt and accept the sometimes inevitable changes that need to be made to their parenting techniques and create a positive family environment through truthful dialogue, education and optimism. Through their own personal experiences of raising young children as well as the perspectives that they have received from other parents with Parkinson's Disease and allied health professionals, Daborn and Mathur will present methods they have found helpful in staying engaged and inspired as parents as well as ways to help children feel empowered despite this family challenge. They will discuss how parents can continue to create happy, productive family environments after a diagnosis of Parkinson's Disease.

O96

Table #7: Parkinson's disease and women

Claire Henchcliffe¹, Sara Riggare²

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Objective: Parkinson's disease (PD) affects over a million women worldwide, and women comprise over 40% of those with young onset PD. In addition to differences in reproductive and social roles, growing data now indicates gender-specific differences in PD itself, in treatment effects, and disparity in access to specialty care. This Roundtable will provide a focused discussion group addressing issues affecting women with PD.

Methods: This focused discussion group, including people with PD and members of the medical and scientific community, will review current knowledge of how Parkinson's disease affects women, and examine issues specific to women with PD. Importantly we will share experiences of women with PD, and of those involved in their lives and their medical care. Using this knowledge, we will enhance our understanding of the specific needs of women with PD, and of what pathways of further action are needed.

Results: It is well known that PD manifests differently in women than men, for example women are more commonly affected by certain non-motor symptoms such as depression, and are more likely to develop medication-associated dyskinesias. Moreover, a number of PD risk factors are differently associated in women and men, and genetic burden may also differ. Despite this, the majority of PD study participants are men. There is also very little research into issues affecting women with PD specifically, such as child bearing, sexual function, or effects of menopause.

Conclusion: In striving to provide the most appropriate individual care, it is imperative that we better understand gender differences in PD. Approaches to provide improved neurological care and empowering women with PD will need to consider reproductive issues, caregiver roles, and facilitating better specialty healthcare access. Moreover, a better understanding of fundamental differences in PD between women and men needs to be addressed by targeted clinical data collection.

O97

Table #8: Flying solo - living alone with Parkinson's

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Living single with Parkinson's disease presents challenges that require careful planning in the immediate and for the future. Many people with Parkinson's live alone and are quite successful. In order to accomplish this, adjustments in the home environment and activities of daily living may be needed to increase safety, and improve quality of life. This session will provide an opportunity for attendees to share common concerns and challenges of living alone at home with Parkinson's on a daily basis. A guided discussion will be facilitated by a person who lives at home alone and a specialized RN. The discussion will focus on strategies to modify and equip the home, build a support system to deal with motor and non-motor symptoms, and identify important human and financial resources.

F – freedom **L** – listen **Y** – yahoo **I** – independence **N** – network **G** – goal setting
S – smile **O** – openly **L** – laugh **O** – often

O99

Table #9: Service dogs and Parkinson's: Everything you need to know

Carolyn Weaver and Renee Le Verrier

Living with a mobility service dog can redefine living with Parkinson's. The fear of falling or getting stuck becomes less overwhelming with a canine companion because specialized training teaches the dog to assist with symptoms such as slow or uneven walking, instability, freezing and getting in and out of chairs. In this roundtable discussion, Carolyn and Renee share their stories of increased confidence, independence, social connectedness, and dog food bills. This interactive forum presents information on the steps before, during and after applying for a service dog with question-and-answer opportunities throughout. In addition, the session includes video clips and demonstrations on the benefits as well as the corresponding responsibilities of this medicine-free, surgery-free option to improved well-being. Carolyn Weaver of Michigan has been living with PD for thirteen years and with her service dog, Selma, for two [will be 2-1/2 years come the October mtg]. Renee Le Verrier of Massachusetts has been living with PD for ten years and with her service dog, Sir Thomas, for six months [will be one year come the Oct mtg.] Read about life with a service dog on Renee's blog:

http://www.limyoga.com/service_dog_parkinsons/

O100

Cell and gene-based technologies for restorative and neuroprotective therapies

Roger A Barker

Cambridge Centre for Brain Repair, Department of Clinical Neuroscience, University of Cambridge, UK

The ability to more effectively rescue the brain from the pathology of Parkinson's Disease (PD) has long been sought. One particular area that has been the subject of several clinical trials involves trying to restore the dopaminergic nigrostriatal pathway back to normal using either cell transplants or gene therapies.

In the case of cell therapies this has largely involved implanting the dopaminergic neurons from the developing midbrain (ventral mesencephalon- VM) of aborted fetuses. Other cell types have been trialled but none have the pre-clinical data to support their use in the way that VM tissue does. Even then, these VM transplants have produced mixed results in terms of clinical benefits and side effects and in this talk I will attempt to summarise the trials that have used these cells and explain why the results have been so variable. This will lead on to a description of the new FP7 funded EU study of VM transplants in patients with PD (TRANSEURO), which also serves to provide a framework for future stem cell based therapies for PD. In terms of gene therapies these have involved two main strategies. One involves trying to rescue the nigrostriatal pathway using growth factors (i.e. Neurturin), whilst the other involves trying to correct some of the pharmacological abnormalities within the basal ganglia. This latter approach embraces attempts to better deliver striatal dopamine as well as increase the inhibition outflow of the subthalamic nucleus. These trials have yet to show the benefits of some of the cell based approaches but nevertheless still offer hope for selective groups of patients with PD. I will conclude by discussing the challenges that trials with these agents engender which if not properly addressed could undermine this whole therapeutic area.

O101

Exercise, diet, and other lifestyle activities as treatments for Parkinson disease

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Many patients with Parkinson's disease become progressively incapacitated, not only because of the well-known motor symptoms but also because of a wide variety of non-motor symptoms. Drug treatment and brain surgery are important cornerstones of the treatment program but evidence is growing to support the effectiveness of various additional treatment options. Accumulating evidence suggests that patients with PD might benefit from physical activity and exercise in a number of ways, ranging from general improvements in health to disease-specific effects and, potentially, disease-modifying effects (although this is thus far only suggested by animal data). So the time might be ripe to regard exercise as a real intervention – much like a drug – for people with Parkinson's Disease. Notwithstanding the positive effects of exercise, many patients adopt a sedentary lifestyle because of their motor (e.g. gait disturbances) and non-motor (e.g. apathy) limitations. Identifying ways to induce a sustained behavioral change, using specifically tailored programs that address potential barriers such as depression, apathy and postural instability, may lead to an improved quality of life in individuals with PD. Another frequently mentioned treatment option includes the use of special diets, to counter malnutrition, to avoid interference with medication, and (again) to possibly modify the course of the disease. Unfortunately, scientific evidence to support a specific diet for these purposes is still lacking. In this presentation I will review the existing evidence supporting the use of lifestyle activities in the treatment of Parkinson's Disease. In addition I will give an overview of effective strategies to change lifestyle. This overview will clearly show that changing a lifestyle is for everyone, with or without Parkinson's Disease, one of the most difficult things to do.

O102

Living Positively After a Diagnosis of Parkinson's

Rich Clifford

I was diagnosed with early onset Parkinson Disease in 1994 at the age of 42. I was an Astronaut with two space shuttle missions already completed. I was aware of the progressive and degenerative path the disease follows but, I was not ready to quit flying into earth orbit. NASA managers responsible for crew selection and certification were fully behind my desire to continue in the cue for another space mission. With the exception of the NASA leadership I kept my condition as a secret for 17 years. I was assigned to a third space shuttle mission and I performed a space walk during the mission in March 1996. This was very rewarding. I told myself to "Live life to the fullest extent possible". My message to those with Parkinson Disease is you can do anything you want to do - maybe not as well as you use to perform. I still play golf. My game is not as good as it was years ago but I enjoy the game. My friends enjoy playing with me and the exercise is good therapy. The disease has progressed as expected. I no longer fly privately and I do miss the exhilaration of precise flying. I still live life's adventures to the fullest. I encourage those with Parkinson Disease to be well informed of current research and the multitude of varied therapy options. Any program that improves the quality of your life should be explored. Exploration is fun and beneficial. Stories from my space shuttle missions will be interjected at appropriate places for emphasis. The theme of the presentation is "Life is Good - Make the most of your opportunities."

O103

Living Positively After a Diagnosis of Parkinson's

Soania Mathur¹

¹Designing A Cure Inc., Toronto, ON, Canada

Dr. Soania Mathur was diagnosed with Young Onset Parkinson's Disease at the age of 27 at the start of her medical career and just as she and her husband were starting a family. This diagnosis was met with denial, fear and secrecy, a battle that lasted almost a decade - a time during which thoughts of disability and a focus on all that she was losing, consumed her. Now 15 years later Dr. Mathur has found herself on a more positive path - one of patient education and advocacy, inspiring patients to live well with this challenge while advocating for better treatments and that much needed cure. Embracing her diagnosis was not an easy process but through personal reflection and struggle, she began to recognize that although Parkinson's Disease was part of her future for now, her life experience would ultimately depend on how she confronted her illness. That the power to choose to tackle this disease with a positive outlook and hope, was truly hers. In her words "At some point you have to abandon your fear of the future in order to begin living your present." She encourages others to recognize that they are so much more than their disease and that they too can take back some measure of control in what appears to be an uncontrollable situation. She stresses that living positively after a diagnosis of Parkinson's Disease includes many factors that go beyond conventional multidisciplinary care and begin with a fundamental paradigm shift and recognition of true personal power. Also critical to this process and integral to coping with any chronic illness is education, stress reduction, a strong support network, proactivity and making crucial lifestyle changes that, combined with conventional treatments, improve disease management and experience.

O104

What is new about the link between Gaucher and ParkinsonismRoy Alcalay²

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The link between Gaucher disease (GD), glucocerebrosidase (*GBA*) mutations and Parkinson's disease (PD) has been established in multiple genetic epidemiology studies. GD is the most common lysosomal storage disease in the world and the most common genetic disease among Ashkenazi Jews. Individuals affected by the benign form of the disease, Type-1, inherit two *GBA* mutations (autosomal recessive) and produce insufficient amounts of the enzyme, glucocerebrosidase. Consequently, lipid-substrates accumulate in the cells of the bone marrow, spleen, and liver and can lead to hepatosplenomegaly or bone disease. Both Type-1 GD patients and carriers of a single *GBA* mutation are at an increased risk for PD. Large studies conducted at GD Centers estimate the risk for PD in GD patients at 9-12% by age 80 compared to 1-1.5% among non-carriers. The estimated risk for PD in heterozygote carriers varies from 6.8% at age 75 among *GBA* carriers with no family history of PD to 29.7% at age 80 among those with a first degree family history of PD. The PD characteristics of carriers are often similar to idiopathic PD, but carriers may also present with atypical features including more rapid motor progression. Cognitive impairment is more common among carriers than non-carriers, and autopsy studies suggest *GBA* mutations are more common in autopsies of patients with PD and Lewy Body Dementia compared to autopsies of controls or patients with Alzheimer's disease. Given the pathological similarities between *GBA* mutation carriers and non-carriers, further understanding of the link between *GBA* mutations and PD may shed light on the pathological mechanism of PD in general. It is possible that low enzymatic activity of glucocerebrosidase is important in mediating this association. Considering the risk of PD among GD patients and heterozygote carriers is comparable, it is likely the mechanism underlying the PD-GD association is more complex.

O105

Exploring mechanisms that underlie the link between mutations in the Gaucher disease gene and synucleinopathy riskMichael G. Schlossmacher^{1,2}, Priyanka Singh^{1,2}, S. Pablo Sardi³, Lamya S. Shihabuddin³, Steffany Bennett⁴, Julianna J. Tomlinson¹¹Program in Neuroscience, Ottawa Hospital Research Institute, Ottawa, ON, Canada²Department of Cellular & Molecular Medicine, and ⁴Department of Microbiology, Biochemistry and Immunology, University of Ottawa, Ottawa, ON, Canada³Genzyme-Sanofi Corporation, Framingham, MA, USA

Introduction: The molecular mechanisms that underlie the risk association between mutations in the acid beta-glucosidase-1 (*GBA1*) gene, Parkinson disease and dementia with Lewy body disease remain elusive. The two disorders are characterized by misprocessing of neuronal alpha-synuclein. *GBA1*-mediated activity within lysosomes promotes the degradation of specific glycolipid substrates, glucosylceramide and glucosylsphingosine. Reduction in *GBA1*'s normal enzyme activity below 20% leads to variable organ dysfunction and results in Gaucher disease. Several scenarios have been considered to explain the strong risk association between the expression of one (or two) mutant *GBA1* alleles and synucleinopathy risk.

Methods: To better understand the molecular cascade that links *GBA1* mutations to alpha-synuclein accumulation, we pursued 3 experimental avenues: 1.) the exploration of over-expressing *GBA1* mutants in neural cell cultures and their effects on enzyme activity

as well as alpha-synuclein steady-states; 2.) the analysis of already available mouse models of mutant *Gba1* expression to monitor the effects on endogenous alpha-synuclein; and 3.) the generation of bigenic animals to examine the interaction between murine *Gba1* knock-in mutations (D409V) and multiple copies of human alpha-synuclein-encoding transgenes that carry a mutation (A53T). We refer to the latter as "SYNeRGY mice".

Results: We observed that the expression of mutant *GBA1* variants promoted a dose-dependent rise in total alpha-synuclein; however, these mutants did not lower the activity of endogenous, wild-type *GBA1* enzyme, thereby excluding a dominant-negative effect. We found that in bona fide Gaucher cells and mouse brain, activity of *GBA1* at less than 20% did not immediately elevate the concentration of total alpha-synuclein, but rather led to global lysosomal impairment. Finally, the expression of *Gba1* D409V mutants in SYNeRGY mice elevated the concentration of total human alpha-synuclein to ~120% throughout the neuroaxis when compared with alpha-synuclein transgenic mice that express wild-type *Gba1* alleles.

Conclusion: Our collective results suggest that *GBA1* mutants increase the steady-state of alpha-synuclein in cells and in vivo. Furthermore, likely more than one mechanism is responsible for the association: 1) a gain-of-toxic function by mutant *GBA1* that impairs alpha-synuclein degradation; 2) a partial loss-of-*GBA1*-mediated enzymatic function in neurons leading to an indirect rise in alpha-synuclein; or 3) a combination of both. Finally, the interaction between mutant *Gba1* and human alpha-synuclein was confirmed in mouse brain.

O106

How the understanding of Gaucher could lead to new therapies for Parkinson's

S. Pablo Sardi

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Introduction: Biallelic mutations in the glucocerebrosidase gene (*GBA1*) cause Gaucher disease (GD), the most prevalent lysosomal storage disease. Routine administration of glucocerebrosidase has been shown to be effective in treating hematological, skeletal, and visceral disease manifestations. However, the recombinant enzyme is unable to traverse the blood-brain barrier to address the increasingly recognized CNS manifestations. Monoallelic mutations in *GBA1* have been recognized as the most common genetic risk factor for developing synucleinopathies, including Parkinson's disease (PD) and dementia with Lewy bodies. In addition, PD patients with or without *GBA1* mutations exhibit lower enzymatic levels of glucocerebrosidase in the CNS.

Objective: To probe the link between glucocerebrosidase and alpha-synuclein and shed light into putative therapeutic approaches for Gaucher-related PD.

Methods: We evaluated the presence of synucleinopathy features in mouse models of Gaucher disease as well as the existence of Gaucher characteristics in alpha-synuclein transgenic mice. In addition, we evaluated the efficacy of glucocerebrosidase augmentation in the CNS of these animal models.

Results: We found that a mouse model of Gaucher disease (*Gba1*^{D409V/D409V}) exhibits characteristics of synucleinopathies, including progressive accumulation of proteinase K-resistant alpha-synuclein/ubiquitin aggregates in hippocampal neurons and a coincident memory deficit. Glucocerebrosidase augmentation in the CNS of symptomatic *Gba1*^{D409V/D409V} mice reduced the levels of ubiquitin/alpha-synuclein aggregates. Importantly, hippocampal expression of glucocerebrosidase in *Gba1*^{D409V/D409V} mice also reversed their cognitive impairment when examined using the novel object recognition test. Correspondingly, overexpression of glucocerebrosidase in the CNS of A53T alpha-synuclein mice

reduced the levels of soluble alpha-synuclein, suggesting that increasing this glycosidase activity can restore alpha-synuclein processing and modulate the progression of synucleinopathies.

Conclusion: The data support the contention that mutations in *GBA1* can cause Parkinson disease-like alpha-synuclein pathology, and that increasing glucocerebrosidase activity in the CNS represents a potential therapeutic strategy for *GBA1*-related and non-*GBA1*-associated synucleinopathies.

O107

Use of human ES and iPS cells for cell replacement in Parkinson's disease

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Objective: Parkinson's Disease (PD) is a particularly interesting target for stem cell based therapy. The central pathology is confined to a small group of neurons in the midbrain, the nigral dopamine (DA) neurons and their projection to the striatum. Transplants of DA neurons could be used to restore DA neurotransmission in the striatum, substitute for the lost neurons, and bring back normal motor behavior. Proof-of-principle that this can work has been obtained in trials where fetal DA neuroblasts, have been transplanted to the putamen in patients with advanced PD. Despite these encouraging results, work with human fetal tissue presents a number of ethical and logistical problems and therefore does not represent a realistic therapeutic option in the future. Further progress in this field is critically dependent on the development of a bankable and renewable source of transplantable DA neurons.

Methods: We have developed a method to generate human neural progenitors and neurons from human embryonic stem cells (hESCs), which recapitulates human fetal brain development. By addition of a small molecule to activate canonical WNT signalling, we induced rapid and efficient dose-dependent specification of regionally defined neural progenitors ranging from telencephalic forebrain to posterior hindbrain fates. In parallel, we also develop cell reprogramming as an alternative source of neurons. We have found that the neural conversion genes (*Mash1*, *Brn2a*, *Myt1l*) can convert human fibroblasts into induced neurons (iNs). When combined with DA fate determinants, functional DA neurons can be obtained with this technique.

Results: The DA neurons obtained via our protocol closely resembled their fetal counterparts, making them useful as a model system for studies of human fetal brain development and also for developing transplantable therapeutic cells.

O108

Role of Sonic hedgehog in maintaining striatal homeostasis

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Objective: Non-neurotransmitter mediated cellular signaling is thought to play critical roles in the maintenance of neuronal circuits in the healthy and diseased brain but mechanistic details remain unclear. We investigated the relevance of neurotrophic and growth factor signaling in the mature basal ganglia for the structural and functional integrity of nigro-striatal neuronal circuitry.

Methods: Utilizing gene expression tracer and conditional gene ablation strategies targeting Sonic Hedgehog (Shh) expression in the nigro striatal pathway we produced an unanticipated genetic model of progressive neuronal dysfunction and -degeneration reminiscent of Parkinson's disease.

Results: The interruption of a non-cell autonomous mode of Shh signaling originating from dopaminergic neurons causes progressive, adult-onset degeneration of dopaminergic, cholinergic, and fast spiking GABAergic neurons of the mesostriatal circuit, imbalance of cholinergic and dopaminergic neurotransmission, and motor deficits. Variable Shh signaling results in graded inhibition of muscarinic auto-receptor- and GDNF- expression in the striatum. Reciprocally, graded signals that emanate from striatal cholinergic neurons and engage the canonical GDNF receptor Ret inhibit Shh expression in dopaminergic neurons. Our work reveals a novel mechanism for neuronal subtype specific and reciprocal communication that is essential for neurochemical and structural homeostasis in the nigrostriatal circuit. These results provide integrative insights into non cell-autonomous processes likely to play in neurodegenerative conditions such as Parkinson's disease, Parkinson's disease with fronto temporal dementia and related conditions.

O109

Nurr1 as a therapeutic target for neuroprotection and disease modification in PD

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The transcription factor Nurr 1 is an orphan nuclear receptor that is known to be a key regulator of the survival and maintenance of dopamine neurons during embryonic development. Recently, however, it has been recognized that this gene regulator may play an important role also in adult dopamine neurons, and as a mediator of the degenerative changes seen in Parkinson's disease (PD). Rare cases of familial PD have been associated point mutations in the Nurr1 gene, and recent observations in brains from PD patients have shown that the expression of Nurr1 is greatly reduced in affected dopamine neurons. These data suggest that reduced cellular levels of Nurr1 may be associated with increased vulnerability and impaired function in the nigro-striatal dopaminergic system. Studies in mice and rats have provided further support for this idea, showing that reduced Nurr1 expression, induced either by deletion of the Nurr 1 gene or by overexpression of the disease-causing protein alpha-synuclein, leads to a PD-like state characterized by impaired dopamine neurotransmission and loss of responsiveness to trophic factors like GDNF. These observations suggest that reduced Nurr1 expression, induced by increased cellular levels of alpha-synuclein, is a key element in the induction of dopamine neuron dysfunction seen in early stages of the disease, and that loss of Nurr1 function may lead to increased vulnerability of the affected dopamine neurons and thus contribute to the progression of the disease. Together, the clinical and experimental data point to Nurr 1 as key player in the pathogenesis of PD and

identifies Nurr 1 an interesting novel therapeutic target for disease intervention in PD.

O110

Maladaptive plasticity in L-DOPA-induced dyskinesia: emerging role of serotonin transmission and other presynaptic factors

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The development of L-DOPA-induced dyskinesia (LID) in Parkinson's disease (PD) is attributed to maladaptive neuroplasticity resulting from the combined effects of dopamine (DA) denervation and dopaminergic drug treatment. Once LID has developed, it becomes difficult to reduce or reverse, and it can also be elicited by strong emotions or stress. Studies of striatal gene expression in animal models of LID have shown upregulation of genes involved in synaptic and neuritic plasticity, extracellular matrix remodeling, endothelial and cellular proliferation. By reviewing these studies, this lecture will first highlight the complex plastic adaptations associated with LID, which clearly affect cells, processes, and circuits in the brain at many different levels. Thereafter, the lecture will zoom in on the role of serotonin transmission and other presynaptic factors. Serotonin neurons express enzymes that mediate conversion of L-DOPA to DA and storage of DA in synaptic vesicles, but they lack high-affinity DA reuptake capacity and DA autoreceptors. Hence, they cannot sense and autoregulate a possible, aberrant DA release. In the 6-OHDA-lesion rat model of PD, L-DOPA-derived peak DA efflux in the striatum is reduced by 60-80% upon either chemical lesion of the serotonin innervation or treatment with agonists of the serotonin autoreceptors, 5-HT_{1A/1B}. Moreover, chronic treatment with L-DOPA has a growth-promoting effect on serotonin axon terminals, an effect that may further contribute to the presynaptic dysregulation of DA release associated with LID. In addition to these mechanisms, recent studies are highlighting the role of cortical serotonin receptors, 5-HT_{1A} in the presynaptic regulation of glutamate release both locally and in the target areas of corticofugal projections. In the rat, the increased striatal glutamate efflux accompanying the expression of LID is attenuated by 5-HT_{1A} selective agonists, which also improve dyskinesia. These and other studies warrant further investigations on the role of anatomically distinct populations of 5-HT_{1A} and 5-HT_{1B} receptors in the pathophysiology and treatment of LID.

O111

Pre- and post-synaptic molecular mechanism underlying L-DOPA-induced dyskinesia as possible new pharmacological targets

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Objective: Levodopa induced dyskinesia (LID) has been recognized since the introduction of levodopa for the management of Parkinson's disease (PD) and continues to be one of the most clinically challenging factors in long term management of patients with PD. Most patients develop LID within ten years of PD onset. Various risk factors including disease demographics, pharmacological and possibly genetic causes might play a role. The

pathophysiology of established LID is however now better known and the potential armamentarium to address and manage LID has significantly increased in the last decade.

Methods: Seminar is based upon exhaustive literature search through PubMed and based upon original data collected by presenter's laboratory.

Results: This seminar describes the molecular mechanisms implicated in the emergence and manifestation of LID. Particular emphasis is given to the role played in this condition by abnormalities in signal transduction at the level of the medium spiny neurons of the striatum, which are the principal target of L-DOPA. Recent evidence pointing to pre-synaptic dysregulation is also discussed.

O112

Multiple dopamine-dependent synaptic mechanisms underlying dyskinesia in animal models

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It has been suggested that the impairment in activity-dependent modifications in synaptic efficacy, such as long-term depression (LTD) and long-term potentiation (LTP), could account for the onset and progression of motor symptoms of Parkinson's disease (PD). Understanding of these maladaptive forms of plasticity has mostly come from the electrophysiological, molecular and behavioural analyses of experimental animal models of PD. In PD condition, a host of cellular and synaptic changes occur in the striatum in response to the massive loss of dopamine innervation. Chronic L-DOPA therapy restores physiological synaptic plasticity and behaviour in parkinsonian treated animals, but most of them, similarly to patients, exhibit reduction in the efficacy of the drug and disabling abnormal involuntary movements (AIMs) defined in their complex as L-DOPA-induced dyskinesia. In those animals experiencing AIMs, synaptic plasticity is altered and is paralleled by modifications in the postsynaptic compartment. In particular, dysfunctions in trafficking and subunit composition of NMDA receptors (NMDARs) on striatal efferent neurons result from chronic non-physiological dopaminergic stimulation and contribute to the pathogenesis of dyskinesias.

O113

Myopathy causing camptocormia in idiopathic Parkinson's disease

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Objectives: Some patients with idiopathic Parkinson's disease develop severe unfixed bent forward posture, a symptom called camptocormia or head drop. The cause is a matter of debate. Controversial concepts include dystonia of abdominal wall muscles versus isolated myopathy of the deep thoracic and cervical extensor muscles.

Methods: We studied 17 patients Parkinson's disease and camptocormia or head drop clinically and electrophysiologically and obtained muscle biopsy specimens from deep back extensor muscles after IRB approval. Back extensor muscle obtained during back surgery served as age-matched controls (n=6). We performed histological and immunohistochemical analysis. Further, stable

isotope labeling by amino acids (SILAC)-based LC-MS/MS proteomics was performed on eight muscles obtained from camptocormia-patients and four controls.

Results: Our results demonstrate that deep extensor muscles from camptocormia patients exhibit myopathic features. Inflammation, mitochondrial damage or neurogenic atrophy were only occasionally associated with camptocormia or head drop. Aggregates of desmin positive and dystrophin positive material were also identified. Proteome analysis revealed altered expression of a high number of proteins in camptocormia muscle.

Conclusion: The results point towards a primary myopathic cause of camptocormia in Parkinson's disease.

O114

Camptocormia: pathogenesis, classification, and response to therapy

Joseph Jankovic

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James Parkinson in his 1817 "Essay on the Shaking Palsy" drew attention to "a propensity to bend the trunk forward" as one of the classic signs of Parkinson's disease (PD). Postural deformities involving the neck and trunk, such as the "head drop", "bent spine", "pisa sign", and "camptocormia" (extreme truncal flexion), have been receiving growing attention and have been subjected to several recent reviews (Jankovic, 2010; Doherty et al, 2011). Camptocormia is characterized by severe, often 90 degree or even greater flexion of the trunk, that may be present in a sitting position and typically increases during walking and resolves in supine position or when patient achieves an erect posture while performing the "climbing on the wall" maneuver. Camptocormia may be a feature of axial dystonia but is also often associated with PD and other parkinsonian disorders. No factors have been identified that reliably predict which patients with PD will develop this deformity, although it appears to be more common in patients with more severe, postural-instability-gait-difficulty (PIGD) form of PD. The pathogenesis of this disabling PD feature is not well understood, but the two most frequently proposed mechanisms include dystonia-rigidity or extensor truncal myopathy. Although these and other hypotheses have been debated for some time, many experts agree that the deformities associated with PD are somehow related to dysfunction of the basal ganglia resulting in axial dystonia and rigidity, which leads to truncal flexion and other abnormal postures (such as striatal hand and foot deformities) with secondary muscle atrophy, inflammation, fibrosis and other non-specific changes. Additional support for dystonia, rather than myopathy, as the primary mechanism of camptocormia and the head drop syndrome associated with PD, is provided by the finding of muscle contraction associated with these abnormal postures and that the abnormal posture often improves during certain maneuvers (sensory tricks), such as wearing a backpack (Gerton et al. 2010). Furthermore, botulinum toxin when injected into the rectus abdominus and paraspinal muscles, and deep brain stimulation can at least transiently improve the abnormal posture in some patients.

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O115

Dropped head syndrome in Parkinson's disease

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Objective: Dropped head syndrome (DHS), characterized by forward neck flexion is a common occurrence in neuromuscular disorders, but it is also known to occur in approximately 5.8% of patients with Parkinson's disease (PD). I update current knowledge of DHS in PD.

Method: Using PubMed, English publications were reviewed on antecollis or dropped head associated with PD.

Results: One of the main causes of DHS in PD is antecollis. Patients with PD and DHS typically show little or no muscle weakness and instead display disproportionately increased tone of the neck extensor muscles. In fact, bulging of the neck extensor muscles, with a hard wooden feel on palpation, is a useful indicator of antecollis in PD. Antecollis in PD was more often found in patients whose prominent parkinsonian signs were rigidity and akinesia. Myopathy of the neck extensor muscles also has been reported in PD to induce DHS. Majority of myopathic changes in muscle biopsy specimen or EMG study, however, could be induced secondarily to a chronic dystonic posture. In some cases, dopaminergic medications, especially dopamine agonists, reportedly aggravate antecollis, while improving symptoms in other patients. The mechanism by which it induces these paradoxical effects requires further investigation. Once elucidated, these findings will help us understand the underlying event leading to antecollis and assist in the development of new therapeutic approaches for the treatment of DHS in PD. Besides dopaminergic medication, several authors have reported on the efficacy of botulinum toxin or lidocaine injection for the treatment of DHS. Intensive physiotherapy and deep brain stimulation (DBS) might also be beneficial, even though there is insufficient evidence to justify the use of DBS to solely treat antecollis. Lastly, use of a soft neck brace can help elevate the chin, and thus improve the patient's visual field and reduce discomfort.

O116

Overview: Deep brain stimulation

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Objective: To review the most important information for patients and families regarding deep brain stimulation (DBS) therapy for Parkinson's disease.

Background: The field of DBS therapy for Parkinson's disease has been changing rapidly. Recently many prospective randomized DBS trials have been published, and also there have been many advances in both technology and management. In this session we will aim to review the most important advances in the field, and we will present several illustrative cases to emphasize best management strategies. The session will cover patient selection, brain target selection, interdisciplinary DBS management teams, and troubleshooting DBS problems. Additionally, the session will briefly cover new and emerging technologies.

O117

Overview: Aging and PD

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Aging is the best-documented primary risk factor for Parkinson's disease (PD). This workshop will examine the connections between aging and PD. We will highlight evidence of selective neuronal vulnerabilities in aging and PD and the relevance of models of normal aging to PD.

Selective Vulnerability.

One feature of PD is that subpopulations of midbrain dopamine (DA) neurons are more vulnerable to degeneration than those immediately adjacent to them. We exploited this regional variation to test the hypothesis that if aging is related to PD at a cellular level, markers with known associations to PD would accumulate in the vulnerable DA cell population with advancing age. We conducted this study with tissue from nonhuman primates ranging in age from 9-30 years. We found that all markers associated with PD that we examined were increased in PD-related vulnerable DA neurons during normal aging – markers of oxidative stress, dysfunction of degradation of abnormal proteins, and inflammation. In other studies, evidence indicates that neurons with the greatest vulnerability in PD have high mitochondrial oxidant stress in healthy animals. We have data now from vulnerable DA neurons and other neurons at risk in PD indicating they have very high mitochondrial oxidant stress levels. Genetic mutations associated with PD (e.g., *DJ-1* deletion) or intracellular alpha-synuclein inclusions increase mitochondrial oxidant stress, providing a means of explaining the effects of genetic alterations associated with increased risk.

Aging as a Model of PD.

Modeling PD is problematic. We know that aging is a primary risk factor for PD. Yet aging is seldom incorporated in models of PD for preclinical testing of experimental therapeutics. Whenever it is, results are clearly different than in young subjects. The majority of clinical testing involves elderly individuals and has yielded inconclusive results. Is aging the best test platform for testing therapeutics for PD?

O118

Overview: Pain in PD

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Pain is a common symptom in Parkinson's disease and accounts for substantial morbidity in up to 80% of patients. Despite contributing to disease-related discomfort and disability, pain in PD is frequently overlooked and undertreated in clinical practice. Converging evidence from recent neurophysiology and neuropathology studies has led to an improved understanding of the neuroanatomical and electrophysiological substrate of pain in PD. Although the underlying neurophysiology remains unclear, there is increasing understanding of the role of the basal ganglia in somatosensory processing as well as involvement of additional brainstem structures and non-dopaminergic pathways. Categorizing painful symptoms based on their clinical description into musculoskeletal, dystonic, radicular/peripheral neuropathic and central pain categories provides a useful framework for management. The precise breakdown of painful symptoms into each category varies between studies but it would appear that most pain in PD is related to a musculoskeletal cause or painful dystonia. Pain in PD is often cyclical and should be evaluated in relation to motor symptoms and dopaminergic therapy: musculoskeletal pain associated with rigidity and immobility benefits from addition of dopaminergic agents; dystonia related to levodopa therapy responds to medication adjustment. For intractable pain, a multi-disciplinary approach is recommended: physical therapy, liaison with pain management and consultations to rheumatologic, orthopedic and neurosurgical services should be considered.

O119

Overview: Models of care on speech for people with Parkinson's

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The ability to be understood by others, intelligible communication, is one of the primary goals of speech and language therapy. Individuals with Parkinson disease and other parkinsonism related conditions (e.g., PSP, MSA) may face substantial challenges in being understood by others. Effective and intelligible communication depends on a variety of factors including the severity of speech impairment (e.g., voice loudness, clarity of speech sounds, intonation). Further, changes in language and cognition (e.g., finding words, formulating thoughts, understanding others) can also affect communication in PD. Environmental factors, sensory impairments (e.g., hearing and vision), and also listener variables contribute to the complexity of communication in PD. This complex interaction highlights the need to address communication from the perspective of the individual with the communication impairment and also the perspective of the communication partner. Today there are a myriad of treatments available for individuals with communication impairments in PD and related disorders. These include exercise treatments based in theories of neuroscience, treatment approaches focused on enhancing everyday participation in communication activities, and technologies to support communication. In this session an overview of current models of speech treatment in PD will be presented to enhance understanding of the complexity of communication, provide a survey of the most recent science relative to communication challenges in PD and related disorders, and to enhance knowledge of options available for treating communication changes associated with PD and related disorders.

O120

Is there a link between Parkinson's disease and the Gaucher metabolic disorder?

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Contexte: La maladie de Gaucher est une maladie génétique rare caractérisée par une déficience de l'enzyme glucocérébrosidase lysosomale (GBA) conduisant à l'accumulation de lipide dans les cellules. Dans les familles des gens souffrants de la maladie de Gaucher, on note une augmentation de l'incidence de la maladie de Parkinson (PD). D'ailleurs, une étude multicentrique a démontré une fréquence plus élevée de mutations dans le gène *GBA* chez les patients parkinsoniens par rapport aux individus sains contrôles. Le principal objectif de notre étude était d'évaluer l'implication éventuelle des mutations du gène *GBA* dans une cohorte canadienne-française PD.

Méthodes: Nous avons procédé au reséquençage du gène *GBA* dans une cohorte de 213 patients canadiens-français avec un diagnostic clair PD et 190 contrôles sains, d'âges similaires. Les

amorces ont permis l'amplification des 11 exons codants du gène *GBA* préférentiellement à son pseudogène.

Résultats: Des mutations hétérozygotes ont été retrouvées chez 10,8% des patients PD comparativement à 5,8% chez les contrôles. Cette étude nous indique de l'implication probable du gène *GBA* dans la maladie de Parkinson dans la population canadienne-française.

O121

Freezing: Underlying mechanisms and the role of cueing

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Objective: To summarize the evidence on the origins of freezing of gait (FOG) and highlight the contribution of cueing in preventing FOG in Parkinson's disease (PD).

Methods: Literature review and experimental pre-post cueing studies during turning. We compared groups of age- and disease-matched freezers and non-freezers during straight-line gait and turning using 3D Vicon technology off medication.

Results: FOG may be related to 5 hypotheses. The first is that there is a specific spatiotemporal deficit of stepping which brings on freezing. The second is that there is a deficit of internal generation of gait, especially when adaptations are required. A third motor hypothesis is that the coupling between postural control and step generation is deficient, probably also related to an incomplete weight shift to the supporting leg. A fourth is that FOG is brought on by executive dysfunction. Finally, the fifth hypothesis states that FOG is due to reduced visuospatial perception.

Cueing has the potential to regulate the stepping deficit and aid the generation of movement through the provision of discrete (visual or auditory) external information as a motor trigger or target. Neuroimaging studies indicate that fronto-parietal and dorsal neural networks are less active in FOG, networks which are thought to be activated by cueing. Our gait lab studies and other work show that cueing can reduce the severity of FOG and the number of episodes but cannot convert freezers to non-freezers. Cues remain effective during obstacle crossing and dual tasking up to an extent. Cues do not correct postural control, yet are effective in reducing FOG. Hence, the effects of cues confirm the first and second motor hypotheses. Impaired cognitive function would predict that applying cues to daily life and in a variety of situations is hampered in patients with FOG, which needs to be addressed in rehabilitation.

O122

Why do persons with PD fall? Does treatment help to reduce falling?

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This presentation will review a system's framework for understanding how postural disorders in Parkinson's disease result in falls. All six postural systems involved in controlling postural control can be affected by Parkinson's disease: 1) The musculoskeletal system is impaired by flexed postural alignment, position of the body CoM near limits of stability, and axial rigidity; 2) The postural limits of stability are reduced and verticality perception may be abnormal; 3) Automatic postural responses to external perturbations are slow and weak, but not late and show inflexible strategies with changes in conditions; 4) Anticipatory postural adjustments are reduced and do not scale; 5) Sensory orientation is affected by poor kinesthesia with compensatory visual dependence; and 6) Postural stability during gait is affected by trunk stiffness, increased double support time, reduced foot clearance, lack of arm

swing, and variable timing. In addition, both posture and gait require more attention than in subjects without Parkinson's disease. Early in the disease, postural control is primarily affected by bradykinesia and rigidity that can be reduced with levodopa. However, later in the disease nondopaminergic postural problems, such as inflexible changes in strategy and poor kinesthesia may be added. Levodopa and Deep Brain Stimulation have been shown to worsen some postural disorders but improve others, but not always in the same manner. In contrast, many studies have shown that exercise or physical therapy can improve balance and gait and reduce falls in people with Parkinson's disease. However, the best exercise approach and dose of exercise to improve mobility and prevent falls is uncertain. Recently, integrative exercise approaches that include agility training with cognitive challenges, such as Tai Chi, Tango dancing and an Agility Boot Camp have shown to be particularly effective in improving mobility and preventing falls.

O123

The benefits of exercise in reducing falling in PD

Victoria Goodwin¹

¹University of Exeter, UK

Background: Despite the extensive evidence, particularly for exercise-based programmes, for preventing falls amongst the general population there has been comparatively little research evaluating effective interventions for people with Parkinson's. Studies have identified a number of risk factors for falling that may be amenable to exercise such as freezing, impaired balance and gait, lower limb muscle weakness and fear of falling.

Current evidence: To date, the evidence for the effectiveness of exercise-based interventions to reduce both the number of people with Parkinson's who fall and the number of falls remains uncertain. However, the trends are encouraging and there are a number of large randomised controlled trials and economic evaluations underway in Europe and Australia that will provide a clearer understanding of what may be effective and cost-effective management strategies that can be implemented into clinical practice in the future.

This presentation will provide:

- A rationale for the potential benefits of exercise to prevent falls among those with Parkinson's;
- An update of the existing evidence;
- An overview of ongoing research.

O124

What are biomarkers and why do we need them?

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Biomarkers are measurable and quantifiable biological features which can be used to assess a disease condition and enable the development of therapeutics. Biomarkers can be used to identify those at risk for developing a disease, to assess the severity and rate of change of the disorder, or to assess the response to therapy. A wide variety of different technologies can be employed, ranging from simple biochemical measurements to complex imaging modalities. Biomarkers may be discovered through rationale, disease-based strategies or may be found through open-ended empiric approaches. There are a number of biomarkers which have been accepted in common clinical practice. Examples include tumor markers such as the prostate specific antigen, and markers of cardiac injury such as serum troponin levels. Biomarkers are also employed in neurological disorders and have played a key enabling role in the development of new therapies; an example is the use of

MRI imaging to assess disease activity and severity in multiple sclerosis. In Parkinson disease, the most pressing need is for a biomarker to assess the rate of disease progression. This would be a critical tool in the search for neuroprotective therapies, but at the present time no marker with sufficient reliability has been identified. Several strategies are being pursued but there are substantial challenges to be overcome, particularly the validation of potential markers in human disease populations.

O125

Update on unbiased methodologies to identify biomarkers

Howard Federoff, Massimo Fiandaca, Amrita Cheema, Yuriy Gusev and Subha Madhavan

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Objective: Detecting Parkinson's disease (PD) at the earliest stage possible holds the greatest promise for evaluating interventions that may modify natural history. This talk will review unbiased methods that are used to detect and stage PD including research methods that may be useful in preclinical diagnosis.

Problem: PD is proposed to be initiated outside of the midbrain and may possibly be a systemic disease. Efforts to identify preclinical PD need to consider the Braak staging and the confluence of epidemiological data implicating relatively soft symptoms and signs that antedate the classical presentation of PD most typically involving motor features. The Braak staging commends consideration of Stage 1 with involvement of the dorsal motor nucleus of IX/X, anterior olfactory nucleus and enteric nervous system. The clinical observations of hyposmia, constipation, and dysautonomia may be correlated with the proposed Stage 1 pathologies.

Results: A brief description of methods to assess GI, cardiovascular and smell are described along with the application in the evaluation of patients at-risk and those presenting with possible PD. A summary of these methods will be discussed. In addition, new and robust peripheral methods relying in the informational molecules harbored by circulating blood cells, plasma and CSF will be discussed using new data to explore the potential clinical utility of these methods. Overall, we will review the methods that are used to identify and validate biomarkers in an effort to detect preclinical PD. We will illustrate the use of multimodal data integration to strengthen biomarker utility.

O126

Emerging biomarkers

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Objective: To examine the most recent molecular, genetic, and imaging biomarkers for Parkinson's disease (PD), and to critically evaluate their potential for diagnosis, measuring disease progression, and defining response to treatment.

Methods: Survey of recent peer-reviewed publications including fluid-based and neuroimaging markers.

Results: Hypothesis-driven studies have identified specific proteins, transcripts, and metabolites that alone or in combination are associated with PD. Recent studies have highlighted alpha-synuclein, DJ-1, markers of oxidative stress, and markers of inflammation. While none of these are yet validated, coordinated efforts including BioFIND and the Parkinson's Progression Markers Initiative (PPMI) are underway to facilitate marker discovery and validation. Sophisticated imaging techniques are also proving promising. The ¹²³I-ioflupane ligand with single photon emission computed tomography is approved as an aid to diagnosis. Other

ligands targeting nigrostriatal pathway integrity, for example the vesicular monoamine transporter (VMAT), may also prove useful but at present are only available in the research community. Moreover, whether these will accurately measure neurodegeneration remains to be determined. Ultrasound provides valuable information on the substantia nigra, and is under intensive investigation, but is not yet in use in clinical practice. MRI measures of fractional anisotropy, arterial spin labeling, and diffusion tensor imaging are of great interest, and magnetic resonance spectroscopy provides distinct neurochemical profiles that associate with PD. Ligands that target other processes, such as amyloid deposition, or integrity of the acetylcholinergic system, are predicted to provide complementary information but are early in development in PD.

Conclusion: With rapidly evolving technology, multiple candidates are presenting as putative PD biomarkers. Most likely a battery of complementary markers will be required, and one marker will not suit all needs. Despite progress in developing diagnostic markers, there remains a critical need for progression and treatment response markers, and for markers of endophenotypes to aid in personalizing therapeutic strategies.

O127

Drug development challenges - Pharmaceutical industry perspective

Bernard Ravina

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There are numerous challenges in developing new therapeutics for Parkinson's disease. Dopamine replacement therapies and interventions, such as deep brain stimulation, that are based on basal ganglia physiology have been successful. However, efforts to develop agents that modify the disease course and slow progression have not been fruitful. This presentation will focus on process of drug development, from bench to bedside, and the challenges of developing disease modifying interventions, which can be broadly grouped in three categories: preclinical research including target validation and animal models; biomarker development to assess target engagement and downstream effects; and clinical trial design and clinical measurement. Each of these categories contributes to risk and attrition in the drug development process. The emphasis of this presentation will be on the roles of biomarkers and clinical trials.

O128

Recognizing the subtypes and assessing severity of dyskinesia and the clinical impact

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Objective: After the introduction of high dose levodopa oral therapy in the 1960s, levodopa has been established and remained as the gold-standard in the medical treatment of Parkinson's disease (PD). Long-term treatment with levodopa, however, is associated with the development of motor fluctuations and drug-induced dyskinesias, which cause significant disability to patients and represent a huge challenge to clinicians.

Methods: This presentation will review the various spectrum of motor fluctuations and dyskinesia and the assessment of their severity as well as impact on the health related quality of life of patients.

Results: Motor fluctuations and drug-induced dyskinesias are common and important problems for advanced PD patients. Careful history of present illness and examination are the first step in

identifying these complications and can elicit useful patterns of symptoms and phenomenology. The duration, frequency, intensity, time factors to "on" or "off" period, anatomical distribution, patient perceptions, functional disability, and objective impairment are the major dimensions of subtype classification of motor complications. In clinical practice, motor fluctuations are commonly measured by patients' home diaries or obtained from unified PD rating scale (UPDRS) part IV responses. More objective evaluation tools, such as actigraphs, portable video monitoring units, or patient-worn compact motion sensor devices (using accelerometers and gyroscopes) can be used in conjunction with the conventional procedures. Several clinical scales which are proposed for the assessment of drug-induced dyskinesia in PD will be discussed and practical applications will be suggested. Early detection and prompt management of motor fluctuation and dyskinesia are crucial to the ongoing care of the PD patients with advanced disease.

O129

Current management of LID - medical and surgical

Jose A. Obeso

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Objective: Sample language for WPC abstract objective. To review the pharmacological tools and the surgical options to treat levodopa-induced dyskinesias in Parkinson's disease.

Methods: Sample language for WPC abstract methods. Literature search of clinical trials using anti-dyskinetic drugs and the effect of surgery (DBS and ablative surgery). Personal experience in the management of patients with severe LID.

Results: Sample language for WPC abstract results. The most efficacious anti-dyskinetic treatment is surgery of the globus pallidus pars interna. Deep Brain Stimulation has the advantage of a bilateral effect when LIDs are generalized or have a predominant axial distribution. Pallidotomy is reserved when an unilateral effect is sufficient. There is no single drug available which have an anti-dyskinetic effect that parallels the one of surgery. Duodenal levodopa administration or subcutaneous apomorphine delivery can substantially ameliorate LIDs.

Conclusions. Patients with severe LID require first, careful adjustment of levodopa and other dopaminergic drugs. A trial with Amantadine is worth pursuing but with relatively limited value. Continuous dopaminergic stimulation may provide significant improvement. When highly disabling, LIDs are best controlled with surgery.

O130

Future Management of LID: What's in the pipeline?

Susan Fox

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Objective: to review potential therapies for treatment of levodopa-induced dyskinesia (LID)

Method: Preclinical studies and RCTs published in the past 2-3 years investigating treatment options for LID will be reviewed.

Results: Options for managing LID include agents that a) reverse parkinsonism, without inducing dyskinesia as well as b) therapies that directly reduce dyskinesia. Preclinical studies have been performed using a range of strategies, including non-dopaminergic drugs and novel agents that target second messenger systems that are implicated in the pathophysiology of LID. Clinical studies involving a range of pharmacological targets including glutamate antagonists; serotonin and adrenoceptor antagonists, that have progressed to phase II/III studies, will be presented.

O131

Introduction: Overview of the research process and advances in communication between researchers and participants

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This workshop will present an overview of research in Parkinson's disease, but will focus on clinical trials including the following areas: identification of research need, study design, funding, research team, recruitment, trial participation and participant protection. There will be discussion of the collaborative nature of the process that will highlight organizations, resources and tools that offer information, education and support at various stages, such as the Fox Trial Finder, a Parkinson's clinical trial matching tool. The emphasis will be on why it is important to engage people with Parkinson's and care partners in the research process and how they can play a role at different points in that process, such as clinical trial participation, providing input into study design, or serving on an Institutional Review Board. Discussion will also cover how people with Parkinson's and care partners can prepare to take leadership roles in educating and promoting participation by others through programs such as the Parkinson's Disease Foundation's Parkinson's Advocates in Research Program (PAIR). The important partnership between trial participant and researcher will be explored, as well as ways to strengthen and expand that relationship through improved communication and collaboration. The benefits of this collaboration to both patient and researcher will be emphasized. The panel will share personal stories that promote deeper understanding of the significance and broad implications of personal involvement in the research process.

O132

Overview: depression, apathy, and anxiety in Parkinson's disease

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²Robert Wood Johnson Medical School, Piscataway, NJ, USA

Objective: To recognize the everyday presentations of depression, apathy, and anxiety in Parkinson's disease (PD), including the behavioral changes that can occur in each type of affective disturbance, how to distinguish psychiatric disturbances from non-clinical emotional changes, and their treatments using non-medication and medication-based therapies.

Methods: The clinical features and treatment of depressive, apathy, and anxiety disturbances in PD, with an aim towards increasing early recognition and treatment of clinically significant mood disturbances. Details of behavioral treatments of depression, apathy, and anxiety will be described along with the role of coping with everyday stressors. The impact of stigma on obtaining psychiatric treatment will also be reviewed.

Results: Depressive, apathetic, and anxiety disturbances involve emotional, cognitive, and physical features that can overlap with features of PD. Awareness of their distinguishing features and course helps with early identification and monitoring response to treatments, which include medications and psychotherapies. Effective treatments are identified for depressive disorders and there is ongoing research on treatments for apathy and anxiety. Once mood disorders are effectively treated, there remains a role for effective coping strategies to address the challenges of PD. In

addition, stigma about seeking psychiatric care remains a major barrier to care to effective treatment.

O133

Dyskinesias: Mechanism and treatment

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Objective: Les dyskinésies dopa-induites sont une conséquence invalidante du remplacement de la dopamine par la levodopa. Les quinze dernières années ont vu les connaissances de leur physiopathologie progresser à grand pas, autorisant maintenant l'espoir de développer des stratégies thérapeutiques efficaces. Cette présentation a pour objectif de présenter l'état de l'art des connaissances sur les causes de ces dyskinésies ainsi que sur les solutions thérapeutiques prometteuses en cours de développement préclinique et clinique.

Methods: Le séminaire est basé sur une revue exhaustive de la littérature utilisant le moteur de recherche PubMed.

Results: Les avancées conceptuelles dans la genèse de modèles expérimentaux heuristiques seront mises en avant ainsi que les cibles thérapeutiques potentielles que sont les agonistes des récepteurs à la sérotonine 5-HT_{1A} et 1B, les antagonistes ou modulateurs allostériques du récepteur mGluR5, le contrôle de la voie des MAPKs ou encore la diminution de la disponibilité des récepteurs dopaminergiques, notamment de type D1. Nous terminerons avec les dernières études cliniques testant ces hypothèses.

O134

Parkinson's disease is much more than a disease of dopamine

Etienne C. Hirsch

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La maladie de Parkinson est caractérisée par une lente et progressive des neurones dopaminergiques associée à la présence de corps de Lewy contenant de l' α -synucleïne. Les symptômes qui sont la conséquence de cette dégénérescence à savoir : akinésie, rigidité et tremblement sont relativement bien corrigés par des traitements dopaminergiques qui restaurent la neurotransmission altérée. Toutefois, avec l'évolution de la maladie d'autres symptômes qui ne répondent pas aux traitements dopaminergiques apparaissent. Ceux incluent la détérioration intellectuelle, l'altération de l'odorat (anosmie), les troubles de la parole (dysarthrie), la douleur, la constipation, les troubles de l'humeur et l'apathie ainsi que dans des stades avancés de la maladie les troubles de l'équilibre et les chutes. Ce dernier symptôme est particulièrement préoccupant car associé à la détérioration intellectuelle il réduit l'espérance de vie des malades. Il constitue aussi un problème en termes d'économie de la santé car il multiplie par trois le coût de prise en charge. Récemment, plusieurs analyses en IRM fonctionnelle ont montré que la marche implique une structure du tronc cérébral appelé le noyau pedunculopontin. Postmortem une diminution du nombre de neurones cholinergiques a été mise en évidence chez les parkinsoniens chuteurs mais pas chez ceux qui

ne chutent pas. Enfin, la lésion de ces neurones chez l'animal provoque des troubles de la marche et de l'équilibre.

L'analyse des corrélations entre la mort des neurones non-dopaminergiques, les dépôts d' α -synucleïne dans ces neurones et les symptômes ouvre la voie vers l'identification de nouvelles cibles thérapeutiques pharmacologiques ou par chirurgie fonctionnelle pour la maladie de Parkinson.

O135

Table #1: How can occupational therapists help manage memory challenges?

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Objective: Non-motor symptoms (NMS) represent the biggest challenge faced by those working with the Parkinson's disease (PD) community and are the primary determinants of quality of life (Chaudhuri, 2011). Many of these symptoms are not responsive to dopaminergic therapy (Crossiers et al., 2010) or resistant to surgery (Bloem et al., 2009). Cognitive dysfunction in PD contributes to disability, caregiver strain, and diminished quality of life (Calleo et al., 2012). Many health professionals lack expertise, understanding of the symptoms and complexities of PD, or the latest assessment and treatment techniques in their own discipline (Hagestuen et al., 2010).

Methods: This roundtable discussion will outline the vital role of the Occupational Therapist (OT) in managing memory challenges using the rehabilitative philosophy. The emphasis will be on the OT's interventions that enable the patient and family to address a variety of cognitive problems, improve cognitive skills (Calleo et al., 2012), thus encouraging participation in activities of daily living. Specific considerations for effective interventions to overcome cognitive challenges will be discussed. An example of a 9 week cognitive education program used for patients and caregivers will be presented.

Results: This roundtable crosstalk will provide a hands-on practical approach in assisting PwP to overcome cognitive challenges. The intended outcome of this roundtable discussion is to:

- empower patients through information sharing and provide them with practical tips that are proactive and preventative in nature to help manage the memory challenges thus assisting them to stay active and involved
- advance effectiveness of OT services in assessing and making recommendations on how to promote participation and quality of life amongst PwP

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Table #2: Motor fluctuations and dyskinesias

Joseph Jankovic

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Motor fluctuations in patients with Parkinson's disease (PD), such as wearing-off and on-off effects, and dyskinesias are related to a variety of factors, including duration and dosage of levodopa, age at onset, stress, sleep, food intake, and other pharmacokinetic and pharmacodynamic mechanisms. The majority of patients, particularly those with young onset of PD, experience these levodopa-related adverse effects after a few years of treatment. Assessment of these motor complications is difficult because of the marked clinical variability between and within patients. Daily diaries and various scales have been used in clinical trials designed to

assess the effects of various pharmacological and surgical interventions on motor fluctuations and dyskinesias. The most common type of dyskinesia, called "peak-dose dyskinesia", usually consists of stereotypical choreic or ballistic movements involving the head, trunk, and limbs, and occasionally, the respiratory muscles (Mehanna and Jankovic, 2010). Dystonia is also typically seen in patients with diphasic dyskinesia and wearing-off effect and may contribute to pain often associated with PD (Ha and Jankovic, 2012). Proper recognition of the full spectrum of clinical phenomenology of levodopa-related motor complications is essential for their treatment and prevention. Therapeutic approach to the treatment of these levodopa-related complications must be individualized, although some general guidelines for medical and surgical interventions have been proposed (Jankovic and Poewe, 2012). Novel therapeutic strategies include novel deliveries of levodopa and dopamine agonists (IPX066, XP21279, Duodopa intestinal gel), adenosine A2A antagonists (tozadenant), and other experimental approaches, such as, MAO and glutamate release inhibitors (safinamide), AMPA antagonists (perampanel), mGluR5 antagonists (ADX48621), and others (Poewe et al, 2012).

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Table #3: Speech and PD

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The ability to be understood by others, intelligible communication, is one of the primary goals of speech and language therapy. Individuals with Parkinson disease and other parkinsonism related conditions (e.g., PSP, MSA) may face substantial challenges in being understood by others. Effective and intelligible communication depends on a variety of factors including the severity of speech impairment (e.g., voice loudness, clarity of speech sounds, intonation). Further, changes in language and cognition (e.g., finding words, formulating thoughts, understanding others) can also affect communication in PD. Other factors that contribute to the success of being understood by others include the listener's familiarity with the person speaking, the familiarity of the topic being discussed, sensory impairments (e.g., hearing or vision loss), speaking rate, and the degree of background noise or distraction. Collectively, the interaction of these factors underscores the complexity of communication in PD. Furthermore, this complex interaction in PD and parkinsonism related conditions highlights the need to address communication from the perspective of the individual with the communication impairment and also the perspective of the communication partner. Recent advances in neuroscience have substantially increased our knowledge of and treatment options for communication disorders in Parkinson disease including exercise based programs and technology solutions. These advances build on 20 years of proven efficacy in treating speech disorders in PD using systematic exercise programs such as LSVT LOUD. New advances in telemedicine enable increased access to communication therapies including LSVT LOUD and conversation support strategies. In this session attendees will gain an understanding of the complexity of communication, understand the most recent science relative to communication challenges in PD and related disorders, and learn about proven interventions for treating communication changes associated with PD and related

disorders. Case study illustrations and group discussions will be used to explore these issues in detail.

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Table #4: Nonmotor Symptoms & PD

K. Ray Chaudhuri

Parkinson Centre of Excellence, London, UK

Non-motor symptoms of Parkinson's disease (NMS) are the leading cause of poor quality of life for both people with Parkinson's and their caregivers. The slowness, stiffness and tremor of Parkinson's disease (PD) are well known, but non-motor symptoms afflict more Parkinson's patients. Though NMS affect every patient, they are under-recognised and under-treated. In a Parkinson's UK survey, members rated symptoms such as sleep disturbance, pain, constipation, urinary problems and dizziness as more debilitating than their motor symptoms. Hospitalisation from PD is most likely to have been caused by NMS. This loss of independent living has devastating social and economic consequences. Despite the profound and negative effects of NMS, there is a dearth of research into causes and therapies. Treatment remains poor and quality of life progressively deteriorates. The National Institute for Health and Clinical Excellence (NICE) and Parkinson's UK have identified the recognition and treatment NMS across all stages of PD as a key unmet need. Little research explores the cause and progression of common NMS because funders have focused their attentions elsewhere. An integrated and interactive combination of clinical and laboratory-based investigation is required that will focus on the causes and consequences of sleep disturbance, pain and autonomic dysfunction in PD. Using imaging and post-mortem brain tissue to identify the areas of the brain responsible for NMS, we are developing models of the disease that will increase our understanding of the origin of neglected NMS of Parkinson's and provide a test bed for devising effective treatments. This research promises to increase our understanding of the effects of PD on the brain in order to uncover the underlying causes of NMS. This research will lead to advances in the detection and treatment of NMS, thereby improving the quality of life of millions of people with Parkinson's, both today and in the future. By exploring the practical clinical issues that are the biggest hurdle to the improvement of the symptomatic treatment of PD, we will begin to solve the NMS enigma.

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Table #5: Issues specific to Adolescents of Parents with Parkinson's disease

Elaine Book

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Parkinson's disease (PD) is a family affair and as a result, everyone in the family is affected by the disease. As a parent of children/adolescents/young adults or as a professional working with families with PD, it is important to consider how PD specifically impacts children and family life. There is a great deal of research in the area of parental illness and its impact on children. However, the specific area of parental PD and its affect on children is ripe for further understanding as well as for the development of support and resources. This roundtable session will plan to address issues related to disclosure of diagnosis, how, what and when to share information and strategies to manage the impact on daily life for children. There will be opportunity to gain insight into common emotions and reactions of younger family members and to discuss options for support. The session will also provide a venue to

explore and generate ideas for the future development of resources critical to meeting the needs of children/adolescents/young adults of parents with Parkinson's disease.

O140

Table #6: What are animal models and why are they important in PD research? What are the challenges in using them?

Marie-Francoise Chesselet¹

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Objective: Advances in understanding the mechanisms of Parkinson's disease (PD) to develop better treatments require modeling the disorder in animals. Animal studies are also critical to test the safety and efficacy of drugs before administering them to humans in clinical trials. This round table will discuss the many attempts to model PD and how they can be used to advance our quest for a cure.

Methods: Various aspects of PD have been modeled using toxins or genetic manipulations in different animals.

Results: Animal models remain indispensable for PD research. They are developed based on scientific principles and submitted to rigorous oversight. Choices of animal models for specific purposes are dictated by our advancing scientific knowledge but need to recognize the advantages and limitations of each model. Patients play an essential role in educating the public about the need for the responsible use of animals in PD research.

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Table #7: Parkinson's disease and cancer

Rivka Inzelberg¹

¹The Sagol Neuroscience Center, Department of Neurology, Sheba Medical Center, Tel Hashomer and Tel Aviv University, Israel

Objective: To discuss the particular relationship between Parkinson's disease (PD) and skin and non-skin cancers.

Methods: There is evidence based on well-designed epidemiological studies for unusual cancer rates in PD patients as compared to the general population. These findings will be reviewed and discussed.

Results: PD patients are at significantly low risk for most cancers as compared to the general population. This risk reduction cannot be attributed to the recognized low incidence of smoking in patients with PD, since not only smoking-related cancers but also non-smoking related ones are less common in PD. While the risk for most cancers appears to be relatively low in patients with PD, breast cancer and melanomas occur more frequently in the PD population as compared to controls. These peculiar patterns of cancer rates in PD might be related to the involvement of common genes in both diseases. Recently, increased risk for non-skin cancers has been reported in *LRRK2* related PD. Furthermore, genes involved in familial forms of PD appear to be abnormally expressed in cancers. Cell survival signals may differ due to mutated genes and represent two opposite extremes such as cell proliferation in cancer and cell death in PD. Unraveling the link between PD and cancer may open a therapeutic window for both diseases.

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Table #8: Open Discussion on Parkinson's disease

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This is an open discussion on topics of broad interest to the Parkinson community. Discussion will be guided by the interests of the attendees, but suggested areas might include: (i) What is needed in treatment? (ii) How can we improve models of care? (iii) What areas should research focus on? (iv) What is the role of the WPC with respect to the Parkinson community and other Parkinson organizations?

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Table #9: Deep Brain Stimulation

Michael S. Okun

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There have been many new developments in the field of deep brain stimulation (DBS) for Parkinson's disease. In this meet the expert forum, we will cover important changes in the field from a patient perspective, and we will do so in an open style question and answer format. Potential topics include patient selection, interdisciplinary teams, the operative procedure, target choice, programming, medication management, and troubleshooting. We will also potentially cover questions on emerging research.

Poster Presentations

BASIC SCIENCE: ETIOLOGY, GENETICS, EPIDEMIOLOGY, AND TOXICANTS

PO1.01

Calmodulin regulation of L-type calcium channels in SNc DA neuron culture

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Objective: Motor symptoms are the first clinical manifestation of Parkinson's disease (PD) and are primarily linked to degeneration and death of dopamine (DA) neurons in the substantia nigra pars compacta (SNc). Over the past decade, there has been an intense effort to uncover why SNc DA neurons in particular are susceptible in PD. There is growing evidence that a high cytosolic calcium (Ca^{2+}) load leads to mitochondrial stress and high levels of reactive oxygen species (ROS) in these cells; making them particularly susceptible to genetic and environmental factors associated with PD. The high Ca^{2+} load is primarily a consequence of Ca^{2+} influx through voltage-gated L-type Ca^{2+} channels (the $Ca_v1.3$ subtype) during continuous autonomous pacing. Yet, a complete understanding of the role of endogenous $Ca_v1.3$ channels in PD pathophysiology and their potential as a target in PD therapy is hindered by limited understanding of their biophysical properties, modulation by other proteins, and their precise role in action potential (AP) generation and pacing rate.

Method: Here we have developed long term SNc DA neuron cultures from juvenile mice to explore endogenous $Ca_v1.3$ channels. This system permits in-depth electrophysiological interrogation of $Ca_v1.3$ channel function, as well as genetic manipulation to explore channel-protein interactions and modulation.

Results: With this approach we provide the first evidence for a powerful form of Ca-dependent feedback inhibition of endogenous $Ca_v1.3$ channels mediated through the Ca sensing protein calmodulin (CaM). Furthermore, by over-expressing dominant-

negative mutant CaM through viral infection, we provide compelling evidence for the contribution of CaM regulation of endogenous Ca_v1.3 and small-conductance potassium (SK) channels to action-potential shape and pacing rate. Results such as these furnish new insights into the role that L-type Ca²⁺ channels play in mediating Ca²⁺ dynamics within SNc neurons, and the potential therapeutic benefit entailed by manipulating Ca²⁺ influx through these channels.

P01.02

Analysis of Gene Expression in Peripheral Blood of Patients with Parkinson's Disease

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Objective: To date a number of genes is known to be involved in pathogenesis of Parkinson's disease (PD). However, causes and mechanisms of progression of PD are not sufficiently clarified. In order to identify new genes involved in the pathogenesis of PD, we carried out an expression analysis of candidate genes, which may be involved in the pathogenesis of PD.

Methods: At the first stage of our work we performed a bioinformatics analysis and selected 8 candidate genes on the basis of their possible roles in the pathogenesis of PD. Studies of gene expression (*ZNF746*, *ALDH1A1*, *PINK1*, *PARK7*, *PDHB*, *PGC1-A*, *ATP13A2*, *LRRK2*) were carried out in two groups: newly diagnosed PD patients and patients with different neurological disorders as a control.

At the second stage, we carried out a whole transcriptome analysis in the peripheral blood of untreated PD patients by using HT-12-V4 Expression BeadChip (Illumina Comp.).

Results: Expression analysis of 8 candidate PD genes revealed no statistically significant differences of expression of these genes between patients with PD and the control group. At the second stage seven new metabolic processes, which may be involved in the PD pathogenesis, were revealed. Subsequently we plan to conduct further investigations of chosen metabolic processes from the whole transcriptome analysis for selection of possible candidate genes which may be involved in the pathogenesis of PD. Also we will continue to carry out expression analysis of 8 candidate genes and new selected genes in formed groups of the patients and control groups, and we plan to increase groups of patients and form additional comparison groups.

P01.03

Acute and Sub-acute oral toxicity study of L-dopa and Hyoscine hydrobromide in combination in rodents

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Objective: The present investigation was carried out to evaluate the safety of a combination of L-Dopa (a known Antiparkinson Drug) and Hyoscine hydrobromide (which is employed for treatment of Parkinsonism in Homoeopathic System of medicine) by determining its potential toxicity after acute and sub-acute administration in rats.

Methods: The acute and sub-acute oral toxicity of combination of L-dopa and Hyoscine hydrobromide was investigated according to OECD Guideline 423 and 407 respectively. In acute toxicity study,

combination of L-dopa and Hyoscine hydrobromide was administered at 5 times the upper limit of Therapeutic dose of each drug which is 1200 mg per day for L-Dopa and 0.75 mg per day for Hyoscine Hydrobromide for adult human being and which was converted to required dose for Wistar rats (3 males and 3 females). In sub-acute toxicity study, the dosing was done in combination at 3 levels, first at lower level of the aforesaid therapeutic dose, second at twice the upper limit of therapeutic dose and third at 5 times the upper limit of therapeutic dose. Animals were divided in to 6 groups of 6 Animals each (3 males and 3 females) for 28 days study. Hematological, biochemical and histological analyses and other parameters were recorded.

Results: The combination of L-dopa and Hyoscine hydrobromide at 5 times the upper therapeutic dose produced no treatment-related signs of toxicity or mortality in any of the animals tested during 14 days of the study. In the repeated dose 28-day oral toxicity study, there was no significant difference in any of the assigned parameters between the control and all treatment groups. No significant change has been noticed in reversal group. It is established that the combination therapy is safe at 5 times the upper limit of therapeutics dose of each drug.

P01.04

Case report with a novel homozygous PARK2 gene mutation in early onset Parkinson's disease

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Objective: To report a case of a 38-year old Turkish patient first diagnosed with Parkinson's disease (PD) with a novel homozygous PARK2 gene mutation.

Case report: A 38-year old patient of Turkish descent presented with progressive slowness and stiffness of movement accompanied with fatigue and cognitive impairment.

Neurological examinations revealed symptoms of PD with brady- and hypokinesia and rigidity of the body predominantly on the right side with mild action tremor and postural instability. Dystonia as a frequent symptom with parkin-linked parkinsonism could not be found. Neuropsychological examination showed mild cognitive deficits concerning attention, concentration and delayed memory. The patient showed a good response to levodopa therapy.

MRI of the brain was normal, Dopamine transporter imaging (DaTSCAN) demonstrated a reduced uptake of [123I]FP-CIT in both putamen with an asymmetrical pattern.

Genetic examinations of the patient's DNA revealed a novel homozygous duplication of the exons 7, 8 and 9 and intronic regions 6 and 9 within the PARK2 gene. DNA analysis of the parents confirmed the mutation in a heterozygous state in both parents.

Conclusion: Mutations in the parkin (PARK2) gene are known to cause autosomal recessive inherited Parkinson disease (PD) and are associated with early disease manifestation.

This case report illustrates a patient with early onset Parkinson's disease revealing a novel homozygous genetic mutation in the PARK2 gene, which to our knowledge has not been previously reported. Functional studies in fibroblasts or differentiated stem cell lines might help to further understand the role of the PARK2 protein in PD pathogenesis.

P01.05**Dietary administration of paraquat for 13 weeks does not result in a loss of dopaminergic neurons in the *substantia nigra* of mice**

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Objective: The *i.p.* administration of high doses of paraquat to C57BL/6J male mice has been reported to cause a reduction in the number of dopaminergic neurons in the *substantia nigra pars compacta* (SNpc). These studies have been cited as providing biological plausibility for the limited epidemiological evidence of an association between paraquat exposure and Parkinson's disease. The *i.p.* mouse model is not relevant to humans. Dietary administration is used as a surrogate for the technically difficult, but occupationally relevant, dermal and inhalation exposure of operators. Therefore, we have conducted a 13-week dietary study in C57BL/6J mice to evaluate the potential neurotoxicity of paraquat.

Methods: Brains were examined for evidence of dopaminergic neuronal cell loss using stereology, changes in striatal neurochemistry and pathological changes using stains to detect neuronal cell damage and glial cell activation. Dietary concentrations of 10 & 50 ppm paraquat dichloride were used; achieved doses were 2.4 & 14.1 and 3.7 & 21.5 mg (paraquat ion)/kg/day for males and females, respectively. MPTP (4 x 10 mg/kg *i.p.* at 2 hr intervals) was administered to a separate group 7 days prior to the end of the dietary study, serving as a positive control.

Results: Paraquat did not result in a reduction in the number of tyrosine hydroxylase positive (TH+) dopaminergic neurons in the SNpc, did not alter the concentration of striatal dopamine or its metabolites and did not cause neuronal cell damage or glial activation. With MPTP, the numbers of TH+ neurons in the SNpc and striatal dopamine were reduced and pathological changes indicative of neuronal damage and cell death were observed. These results bring into question the human relevance of previous studies using *i.p.* administration of paraquat.

P01.06**AD GWAS top hits and risk of Parkinson's disease in Korean population**

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Objective: Alzheimer's disease (AD) and Parkinson's disease (PD) have overlapping clinical and pathological features, suggesting a

common pathway for these two neurodegenerative disorders. Here we investigated the association of both AD GWAS top hits with PD susceptibility.

Methods: We selected nine single nucleotide polymorphisms (SNPs) in the five genes (*ABCA7*, *APOE*, *CLU*, *CR1*, and *PICALM*) based on results of the recent GWAS on AD and all selected genes were listed in the AlzGene top 10 results (<http://www.alzgene.org>) and genotyped in 1,108 PD cases and 1,208 controls. Cases and controls are all ethnic Koreans.

Results: None of the AD GWAS top hits showed a statistically significant association with PD susceptibility. The SNP rs677909 in the *PICALM* gene that previously had a significant association with AD in Korean population showed no association with PD. The SNP rs7412 in the *APOE* gene that reproducibly associated with AD worldwide showed no association with PD susceptibility.

Conclusions: Our results show no significant associations of AD GWAS top hits with PD susceptibility in Korean population. Although AD and PD may have overlapping clinical and pathological features, two disorders may have distinct genetic risk factors for the disease susceptibility.

P01.07**Enabling research through informatics: a researcher turned patient's point of view**

Sue Dubman

Patient and Bioinformatics Professional in Sanofi's R&D Organization

Objective: Translating biomedical research into safe and effective treatments remains a slow, expensive, and failure-prone endeavor. Informatics is an essential and powerful way to enable science, reduce costs and speed new treatments to market. Yet biopharmaceutical companies have been extremely slow to adopt these innovations; instead they often continue to use tools and processes that were invented 20+ years ago. The objective of this presentation is to provide one researcher turned patient's view of how we might streamline and accelerate clinical and translational research by enabling them with new, innovative informatics capabilities.

Methods: Now a patient but having worked almost my entire life in the biopharmaceutical industry as well as in government health care research organizations, I know we can do much better. Suggestions on how to address and remove the social, organizational, and cultural barriers to innovations enabled by informatics will be discussed. In addition, examples of informatics innovations from other therapeutic areas that could be applied to Parkinson's research will be reviewed.

Results: There are so many opportunities to streamline and accelerate the whole clinical development process with Informatics. In presenting some examples from other therapeutic areas, my hoped for outcome is that some of these new, innovative approaches will be adopted by Parkinson's researchers. Time is a patient's most precious commodity. Patients can't wait 15+ years for new treatments. This is a call to action to ensure informatics-enablement is considered from the start of every investment in research, to develop an informatics strategic roadmap that supports the needs of research, to create an informatics manifesto that includes principles to ensure success for informatics-enabled research and to ensure that informatics investments support new paradigms as opposed to automating yesterday's practices.

P01.08

Transcriptome analysis in MPTP mouse models of early stages of Parkinson's disease

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Objective: To date, etiopathogenesis of early stages of Parkinson's disease (PD) remains largely obscure. One of the main approaches to the study of this problem is the investigation of the transcriptome changes in PD. In connection with the above we analyzed transcriptome alterations in MPTP mouse models of pre-symptomatic and early symptomatic stages of PD.

Methods: As part of this objective we extracted total RNA from substantia nigra and striatum of mice with pre-symptomatic and early symptomatic stages of PD. Further, we analyzed levels of transcripts using the MouseRef-8 v2.0 Expression BeadChip Kit (Illumina) and Genome Studio (Illumina). Next we conducted a bioinformatic analysis using DAVID Bioinformatics Resources. After selection of seven transcripts we performed additional analysis of relative expression of these genes in substantia nigra, striatum, and frontal cortex of mice with pre-symptomatic and early symptomatic stages of PD using reverse transcription reaction and real-time PCR.

Results: As a result of the experimental and bioinformatics analysis, we selected 60 genes, which may be involved in the pathogenesis of PD. These genes take part in neurosynaptic signal transmission, endo- and exocytosis, protein transport, protein catabolism (including ubiquitin-mediated). Thus, we selected *Drd2*, *C1b2*, *Cplx2*, *Exoc4*, *SncA*, *Epsn2*, and *Ntrk2* genes from the 60 previously described for more detailed analysis. Our results will help to build a complete picture of all molecular and genetic processes, involved in the etiopathogenesis of the disease, in the future and will help to understand mechanisms of functioning of individual neurons and the whole nervous system better. These data also will allow us to select transcriptomic markers for development of a panel of biomarkers for diagnosis of PD on early stages.

P01.09

LRRK2 Expression in Innate Immune Cells during Microbe-Induced Inflammation of Nervous System Structures

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Objective: The mechanisms by which altered LRRK2 genotypes are linked to the risk of parkinsonism and Crohn's disease, and possibly leprosy, remain unanswered. We recently demonstrated robust LRRK2 expression in monocytes and macrophages, we have now focused to characterize LRRK2 in granulocytes.

Methods: We have used FACS analysis to determine LRRK2 expression in organs from adult mice monocytes, granulocytes and dendritic cells. We visualized LRRK2 expression in human organs and mice using immunohistochemistry and immunofluorescence. Also, we have determined cytokine profile of WT mice vs. PD-linked R1441C knock-in mice in various inflammatory paradigms using ELISA and multiplex assays.

Results: Here we report that human lymph nodes, spleen and distal ileum contain numerous LRRK2-expressing macrophages and granulocytes. In LRRK2-deficient mice and PD-linked R1441C knock-in animals versus wild-type cells (Tong et al., PNAS 2010, 2011), LRRK2 did not detectably regulate the release of select cytokines in stimulated macrophages. However, the gene was strongly expressed in activated leukocytes during acute and chronic infections of neural structures. Also, We found that LRRK2-positive leukocytes were overrepresented among infiltrating, myeloperoxidase-reactive granulocytes and CD68-positive macrophages in diseases such as viral encephalitis, idiopathic radiculitis, neuropathy of the skin due to *M. leprae* infection, terminal ileitis and abscess formation. In post mortem midbrain sections from patients with sporadic and genetic variants of Parkinson disease, we detected LRRK2-reactivity mostly in intravascular leukocytes including in areas of dopamine cell loss. This finding is consistent with the known distribution of *LRRK2* mRNA in mammalian brain (Galter et al. Ann Neurol 2006).

P01.10

COMT × DRD4 epistasis impacts cognitive flexibility during the Trail Making Test

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Objective: Dopaminergic neuromodulation of prefrontal inhibition/excitation has been linked to mediating between neural states favoring stable (e.g., working memory) or flexible (e.g., set shifting) representations and behavior. Moreover, polymorphisms in dopaminergic genes such as catechol-O-methyltransferase (*COMT*) degrading dopamine, and the inhibitory dopamine receptor D4 (*DRD4*), as well as their epistatic interaction, have been shown to impact neurobehavioral stability/flexibility.

Methods: As part of the TREND study (Tübingen evaluation of Risk factors for Early detection of NeuroDegeneration) cognitive flexibility was measured by the Trail Making Test (TMT) in elderly, neurodegeneratively healthy subjects. We genotyped for *COMT* (Val158Met, rs4680) and *DRD4* (-521C/T, rs1800955) polymorphisms in 637 subjects and analyzed genetic main and epistatic effects on TMT performance.

Results: *COMT* and *DRD4* genotypes showed no main effects, but a significant gene-gene interaction. At intermediate *COMT*-dependent dopamine levels (*COMT* Val/Met) TMT performance was impacted by *DRD4* genotype. Here, subjects with relatively decreased D4 function (*DRD4* T-allele carriers) showed 14.2 % lower cognitive flexibility (7.2 s slower, TMT B-A) compared to subjects with relatively increased D4 function (C/C homozygotes). In line with previous electrophysiological and behavioral findings, increased neural/cognitive stability at intermediate dopamine levels

might be accompanied with the risk of overly decreased flexibility, if inhibitory D4 receptor function is reduced.

An independent replication sample (n~450) is currently analyzed, and further analyses of *COMT* × *DRD4* epistasis on cognitive flexibility (n~1100) will also include analyses of allele-dose effects and *DRD4* 48bp-VNTR data.

P01.11

PARK18 SNP is Associated with Differential Expression of Major Histocompatibility Complex II genes in Healthy Controls and Parkinson's Disease Patients

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Objective: A single nucleotide polymorphism (SNP) in the first intron of the HLA-DRA gene termed *PARK18* was shown to be associated with a higher risk of Parkinson's disease (PD) in a genome-wide association study. Individuals homozygous for the rs3120882 G SNP (*PARK18GG*) have a 1.7 fold higher risk ($p=5 \times 10^{-8}$) for PD than individuals homozygous for the A allele (*PARK18AA*). HLA-DRA is located in the major histocompatibility complex II (MHCII) locus that encodes proteins that present antigens on the surface of immune cells to activate adaptive immunity. We tested whether *PARK18GG* versus *PARK18AA* carriers (+/- PD) displayed differences in MHCII expression.

Methods: We used flow cytometry and real-time PCR to measure MHCII expression under resting or stimulated conditions in human B cells and monocytes.

Results: We found clear differences in expression of HLA-DR and DQ in peripheral blood cells of individuals related to *PARK18GG* and/or disease status. Monocytes from PD patients with the risk allele also responded differently in MHCII expression after stimulation. Preliminary results suggest the existence of regulatory activity associated with *PARK18* at the MHCII locus. These results may provide evidence for a novel, pathogenic mechanism involving adaptive immunity for PD as well as be used as a disease biomarker. *PARK18GG* is associated with altered expression of immune molecules and thus, provides clues about the role of adaptive immunity in PD pathogenesis and progression.

P01.12

SCA 8 mimicking excellent levodopa responsive Parkinson disease and amyotrophic lateral sclerosis

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Objective: Spinocerebellar ataxia type 8 (SCA8) is an inherited neurodegenerative disorder caused by the expansion of untranslated CTA and CTG triplet repeats on 13q21. The

phenomenology of SCA8 is relatively varied when compared to the other types of SCAs and its spectrum is not well established.

Methods: We describe two newly detected families with the nonataxic phenotype of SCA8 with unusual clinical manifestations such as levodopa responsive parkinsonism and amyotrophic lateral sclerosis. Nonataxic phenotypes of SCA 8 and its possible pathogenic mechanisms which have been described in the literature is also reviewed and critically examined.

Results: Family A expressed excellent levodopa responsive parkinsonism as an initial manifestation and developed mild cerebellar ataxia, and additional movement including dystonic gait and unusual oscillatory movement of trunk during the disease course. The proband of family B presented as a probable ALS with cerebellar atrophy on brain MRI, positive family history in his brother with typical cerebellar ataxia and genetic confirmation for SCA 8. The phenotype of SCA 8 was categorized into following 3 groups; 1) typical ataxia predominant syndrome including scanning dysarthria, oculomotor dysfunction, limb and gait ataxia, 2) atypical movement predominant syndrome 3) incidental detection of CTG repeat expansion in various neurodegenerative disorders.

Conclusions: Our finding support that the unusual nonataxic phenotypes could be caused by a mutation of the SCA8 locus which might affect neurons other than the cerebellum.

P01.13

Role of *MAPT* variation in Parkinsonian disorders

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Objective: Rare variants in the microtubule associated protein tau gene (*MAPT*) cause tau dysfunction leading to neurodegeneration. Additionally, a common non-recombining *MAPT* haplotype (*MAPT* H1) has been shown to increase the risk of both Parkinson's disease and progressive supranuclear palsy. Preliminary sub-haplotype analyses suggest that different genetic variants on the *MAPT* H1 haplotype associate with each of these Parkinsonian disorders. To date it remains unclear which variant(s) at the *MAPT* locus is (are) responsible for the risk and what is the underlying pathomechanism of disease. The objective of this study is to identify causal variants for Parkinson's disease and progressive supranuclear palsy within the *MAPT* region using next generation sequencing technologies.

Methods and Results: We captured the entire *MAPT* gene and 10kb on each side, a 154kb genomic region that was sequenced in 300 patients with Parkinson's disease, 300 patients with progressive supranuclear palsy and 300 controls using a pooling strategy (10 DNA samples/pool). We used the Haloplex system and designed 4248 amplicons for a total coverage of 96.3%. We selected: (a) common variants tagging each of the *MAPT* sub-haplotypes (frequencies >5%); and (b) rare variants most likely to be functionally relevant. Common and rare genetic variants identified will be genotyped in an independent case-control series (747 progressive supranuclear palsy patients vs 727 controls; Parkinson's disease: 692 clinically diagnosed patients vs 689 controls). We will use linear regression analyses to study all variants with a minor allele frequency (MAF) ≥1%. A collapsed marker approach will assess joint effects of variants with MAF<1%. We will perform follow-up association studies in additional independent series. We will present results using the latest sequencing and genotyping technologies to comprehensively define the *MAPT* locus associated with Parkinson's disease and progressive supranuclear palsy and thus identify novel targets for both neuroprotective and symptomatic therapies.

P01.14

Exome sequencing of Norwegian families with PD reveals novel gene mutations

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Objective: Approximately 14% of patients with Parkinson disease (PD) have a family history of parkinsonism. In larger, multi-incident families, pathogenic mutations/genes have now been identified using traditional linkage and contemporary exome sequencing methods. We report a clinical and comparative genetic study of Norwegian families.

Methods: Four Norwegian families (pedigree structure of 3-5 generations, 93 individuals, of whom 22 have parkinsonism) were invited; 17 affected (mean age-of-onset 62.8±4.9SD, range=55-75 years) and 10 unaffected members participated in the study. Late-onset, asymmetric, levodopa-responsive PD appears to segregate in an autosomal dominant fashion. Three affected members from each pedigree, screened negative for known genetic mutations using a proprietary diagnostic panel^a, were exome-sequenced on an Illumina HiSeq platform. Genome alignment, annotation and pairwise bioinformatic comparisons of affected family members were performed. Coding variants observed at <1% frequency were validated by Sanger sequencing in all family members and matched control subjects. Mutations segregating with PD but not observed in controls were genotyped in 3112 subjects (1613 patients) of Scandinavian origin. Subsequently, mutations were genotyped in multi-ethnic GEO-PD^b samples using Sequenom and TaqMan technologies. Additional exonic sequencing was performed in candidate genes.

Results: One mutation in each family was ultimately found to segregate with PD in four genes (*NOVA2*, *PABPC1L*, *RPE65* and *OR56B4*). Each mutation was highly conserved through evolution, and those substitutions were predicted to have deleterious consequences on protein function. Mutations in *PABPC1L* and *RPE65* were observed in additional unrelated patients but not control subjects. The functions of the encoded proteins are not well characterized but are involved in RNA splicing in developing neurons, translation, retinal regeneration and olfaction. In conclusion, pair-wise exome-sequencing is an efficient method to identify novel gene mutations in familial PD that enhances traditional linkage efforts in disease gene mapping.

^a see abstract by Lin, Evans *et al.*

^b see www.geopd.org

P01.15

The effects of previous cigarette smoking on olfaction in Parkinson's patients

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Objective: Smokers have a lower risk for Parkinson's disease (PD) than nonsmokers. Olfactory dysfunction is a non-motor symptom in Parkinson's patients that may precede motor symptom onset by years. We therefore examined the hypothesis that among PD patients, smokers may have better olfaction than nonsmokers.

Methods: Smoking history was obtained from 76 PD subjects (23 ever smokers, 53 nonsmokers) and 67 healthy control subjects (16 ever smokers, 51 nonsmokers). Olfactory function was assessed using the standardized 40 item University of Pennsylvania Smell Identification Test (UPSIT). Comparisons between groups and subgroups were performed using two-way analysis of covariance with correction for multiple comparisons.

Results: PD patients and controls showed different patterns of association between smoking and olfaction. Among PD patients, ever smokers had a better olfactory function than never smokers (UPSIT score 24.4 vs. 20.3, P=0.046). Among controls, no difference was observed between ever smokers and never smokers (UPSIT score 32.5 vs. 33.9, P=1.000).

Discussion/Interpretation: These data suggest that previous smoking may be protective against PD-related olfactory dysfunction. Further studies are needed to investigate the mechanism underlying this observation.

P01.16

Investigation of PD brain DNA for SNCA (alpha-synuclein) mutations, and cellular study of the recently reported H50Q

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Objective: To investigate PD brain DNA for somatic SNCA mutations, and establish and study cell lines overexpressing the H50Q mutation we recently reported. Misfolding of alpha-synuclein (SNCA) appears crucial to the PD pathogenesis, yet mutations in the gene are very rare. The possibility of sporadic cases being due to somatic mutations in early embryogenesis, which might be restricted to the neuroectoderm and undetectable in peripheral lymphocyte DNA, has not been formally investigated. We recently detected a novel missense change (c.150T>G, p.H50Q) in DNA from the cerebellum and substantia nigra of one apparently sporadic, late onset, typical PD case, and demonstrated an effect on co-ordination of copper (Proukakis *et al.*, *Neurology* 2013). To investigate the possibility of a somatic origin of H50Q, as no relatives or other DNA sources were available, we sought indirect evidence of mosaicism by analysis of phase in relation to a nearby intronic polymorphism, but none was found. H50Q has now been reported in another case (Appel-Cresswell *et al.*, *Movement Disorders* 2013), and appears to be a pathogenic rare germline variant.

Methods: We analysed 457 PD brain DNA samples (from more than one region in 25 cases) using High Resolution Melting (HRM) analysis, which has higher sensitivity than sequencing for low level mosaicism. Serial dilution confirmed HRM could detect 1-5% level of H50Q/ A53T. We introduced the H50Q mutation in a plasmid encoding HA-tagged SNCA, transfected neuroblastoma cells, selected and characterized expressing clones, and treated them with copper added as Cu(II) to the medium.

Results: No evidence of exonic somatic mutations was seen, but other types of mutation (eg CNV) could not be excluded. We did not detect any evidence of oligomers or aggregates in response to Cu(II), or differential toxicity of Cu(II) to wild type and H50Q overexpressing cells. Further work is ongoing.

P01.17

Revisiting Smoking and Parkinson's: Marker, Cause or Effect?

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Objective: Almost all epidemiologic studies conducted on this found a negative association between smoking and Parkinson's disease (PD). However, it is not known whether this is due to neuroprotection by smoking or nicotine or a common cause resulting in the avoidance or ability to quit smoking and in PD. This distinction is important because smoking may either provide important leads for the prevention of PD or simply be a marker of insidious PD onset or risk. Here we examine the role of difficulty to quit smoking and of nicotine replacement in PD.

Method: We studied 1,808 patients with medical record confirmed PD diagnosed between 1996 and 2009 and 1,876 randomly selected Danish population controls matched on sex and birth year in Denmark. Information on lifelong smoking habits was collected in telephone interviews. We conducted logistic regression analyses adjusting for matching factors and confounders.

Results: Among former smokers, the risk of developing PD was 43% higher (95% CI=1.00-2.05) in participants who said it was "easy to quit" smoking compared to "extremely difficult". The strongest inverse associations with PD were observed for smokers who used nicotine substitutes in order to quit: odds ratio (OR)=0.47, 95% CI=0.27-0.81 for former smokers and OR=0.15; 95% CI=0.06-0.34 for current smokers using nicotine substitutes compared to nonsmokers. Nicotine substitute usage was strongly positively associated with quitting difficulty and duration of smoking, perhaps indicating that the insidious onset of PD influences the ability to quit smoking. Our findings are compatible with there being an unidentified strong risk factor for PD that prevents smoking, facilitates quitting of smoking, and prevents the need to use nicotine.

P01.18

Household organophosphorus pesticide use and Parkinson's disease

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Objective: Household pesticide use is widespread in the United States. Since the 1970s, organophosphorus chemicals (OPs) have been common active ingredients in these products. Parkinson's disease (PD) has been linked to pesticide exposures but little is known about the contributions of chronic exposures to household pesticides. Here we investigate whether long-term use of household pesticides, especially those containing OPs, increases the odds of PD.

Methods: In a population based case-control study, we assessed frequency of household pesticide use for 357 cases and 807 controls relying on the California Department of Pesticide Regulation product label database to identify ingredients in reported household pesticide products and the Pesticide Action Network pesticide database of chemical ingredients. Using logistic regression we estimated the effects of household pesticide use.

Results: Frequent use of any household pesticide increased the odds of PD by 47% [odds ratio (OR) =1.47 (95% confidence interval (CI): 1.13, 1.92)]; frequent use of products containing OPs increased the odds of PD more strongly by 71% [OR=1.71 (95% CI: 1.21, 2.41)] and frequent organothiophosphate use almost doubled the odds of PD. Sensitivity analyses showed that estimated effects were independent of other pesticide exposures (ambient and occupational) and the largest odds ratios were estimated for frequent OP users who were carriers of the 192QQ paraoxonase genetic variant related to slower detoxification of OPs. We provide evidence that household use of OP pesticides is associated with an increased risk of developing PD.

Previously presented subset of findings in a poster at: The 2013 Parkinson's Action Network Forum on Monday, February 25th, 2013

P01.19

NOS genes and PD: Marginal associations and gene environment interactions with pesticides

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Objective: Nitric oxide (NO) produced by nitric oxide synthase (NOS) enzymes is a potent pro-oxidant that can damage dopaminergic neurons. Thus, the NOS genes are candidates for Parkinson's disease (PD). Organophosphates (OPs) are widely used agricultural and household pesticides that can induce oxidative stress and have been previously associated with PD. We investigated the contribution of genetic variation in the NOS genes to PD risk alone and in combination with OP pesticide exposure.

Methods: In 357 incident PD cases and 495 population controls from Central California, we investigated 10 single nucleotide polymorphisms (SNPs) under a dominant genetic model for association with PD; and considered gene-environment interactions for *NOS1* rs2682826 with self-reported household OP use and computer-modeled ambient OP exposure.

Results: Replicating previous findings, we estimate 1.6-2 fold increases in PD risk for variant allele carriers of *NOS1* rs1047735, *NOS2* rs1060826 and *NOS2* rs2255929. Additionally, we replicate the interaction between *NOS1* rs2682826 and any household pesticide use (Odds ratio (OR)=1.81, 95% Confidence Interval (CI)=1.02-3.24). When we limit to subjects reporting household OP pesticide use, we estimate a stronger interaction (OR=2.63, 95% CI=1.23-5.63). Specifically, there was no effect of the genetic variant in subjects unexposed to household OPs, yet when a subject was exposed to OPs the variant T allele was associated with an increased risk of PD beyond that observed for the CC genotype (OR_{CC+OP} =1.09, 95% CI=0.65-1.82 vs. OR_{CT/TT+OP}=2.37, 95% CI=1.34-4.18). We also found risk increases for high ambient OP exposure (OR_{CC+OP} =2.09, 95% CI=1.18-3.71 vs. OR_{CT/TT+OP}=3.35, 95% CI=1.79-6.30). Results did not change when we mutually adjusted for household pesticide use, ambient exposures and occupational exposures to pesticides. Our findings support *NOS1* and *NOS2* as risk factors for PD and *NOS1* rs2682826 as a modifier of OP associations with PD.

P01.20**Exploring the impact of Parkinson disease (PD) susceptibility loci in older persons without PD**

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Objective: Recent studies have identified a number of loci significantly associated with PD; however, little is known about the impact of these alleles on disease related clinical and pathologic outcomes in elders without a PD diagnosis. We therefore investigated if PD susceptibility loci are associated with PD endophenotypes, including parkinsonian motor signs, Lewy body pathology, and substantia nigra neuronal loss in older individuals.

Methods: We studied 1,698 subjects (mean age=78) from the Religious Orders Study and Rush Memory and Aging Project with longitudinal clinical evaluations, and a nested neuropathologic cohort including 789 brains. Genotypes were available for 19 single nucleotide polymorphisms previously associated with PD susceptibility from published genome-wide scans. The primary outcomes included a clinical summary measure of parkinsonism, based on a modified motor unified Parkinson's disease scale, and the presence of Lewy bodies or neuronal loss within the midbrain substantia nigra at autopsy. Linear or logistic regression analyses were adjusted for subject age and gender.

Results: PD risk alleles at the *MAPT* ($p=6 \times 10^{-4}$), *CCDC62* ($p=0.004$), and *MED13* ($p=0.006$) loci were associated with parkinsonian signs, even after excluding subjects with clinical diagnosis of PD. In secondary analyses, *MAPT* and *CCDC62* were predominantly associated with bradykinesia, whereas *MED13* and another risk allele, *SREBF* were associated with gait impairment. Surprisingly, none of the PD susceptibility loci were associated with Lewy body pathology; however, *LRRK2* ($p=0.01$), *MED13* ($p=0.03$), and nominally *BST1* ($p=0.05$) were related to nigral neuronal loss. Besides their established link to PD susceptibility, our results support a broader role for several risk loci on the development of mild parkinsonian motor signs and associated motor disability in older persons.

P01.21**The complex interaction of LRRK2 with the cytoskeleton**

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Objective: The interaction of LRRK2 with microtubules has pathogenic relevance, since mutations in *PARK8* segregating with Parkinson's disease reduce neurite outgrowth and cause an accumulation of hyperphosphorylated tau. In turn, defective post-translational modifications of tubulin and microtubule-associated proteins alter the dynamic instability of microtubules. The overall effect is aberrant axonal transport, synaptic dysfunction and axonal degeneration. The aims of this study were to identify the determinants of the association between LRRK2 and microtubules and the subcellular distribution of LRRK2 at the cytoskeleton.

Methods: The LRRK2-microtubule association was investigated using yeast two-hybrid, quantitative yeast two-hybrid and co-immunoprecipitation. LRRK2 distribution at the cytoskeleton was determined using confocal microscopy.

Results: The interaction between LRRK2 and tubulin is specific to β -tubulin isoforms TUBB, TUBB4 and TUBB6, and is conferred by the LRRK2 Roc GTPase domain and β -tubulin C-termini. It is

dependent on guanidine nucleotide binding and is disrupted by both the pathogenic *PARK8* mutation R1441G and artificial mutations mimicking Roc autophosphorylation. The interaction requires Lys-362 and Ala-364 and is blocked in β -tubulin isoforms expressing serine at these positions. Endogenous LRRK2 is expressed in growth cones of dopaminergic neuronal cell lines. Overexpression of the LRRK2 wild-type and G2019S mutation influences growth cone parameters and posttranslational modifications of cytoskeleton-associated proteins. These results demonstrate the specificity of the LRRK2-tubulin interaction and suggest phosphorylation of β -tubulin isoforms at Ser-362 and Ser-364 could hinder LRRK2-tubulin interactions. We propose that reciprocal mutations affecting the C-terminal β -tubulin residues could disrupt LRRK2 interaction without compromising microtubule integration. In addition, we suggest an effect of overexpression of LRRK2 wild-type and the familial G2019S mutant on growth cone function and microtubule stability.

P01.22**Identification of LRRK2 G2019S modifiers of disease penetrance**

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Objective: LRRK2 p.G2019S is a major risk factor for parkinsonism with a frequency >30% in North African Arab-Berber patients. The estimated age-associated penetrance of p.G2019S at 50 years is 30%, rising to 80% by age 70. However, some carriers develop early-onset (<45 years) parkinsonism and some elderly carriers remain asymptomatic. We hypothesize that genetic factors influence phenoconversion of p.G2019S carriers from an asymptomatic to motorically-affected state.

Methods: To identify genetic modifiers of age of onset (AAO) we performed whole-genome sequencing (WGS) in seven LRRK2 p.G2019S carriers with early-onset of disease (AAO 34.9 SD \pm 7.2 years, range 22-42) and seven elder asymptomatic carriers (age 77 SD \pm 6.9 years, range 68-90) from Tunisia. In addition, we also performed whole-exome analysis on four patients with early-onset (AAO 42.5 SD \pm 1.9 years) and five with late-onset of disease (AAO 84 SD \pm 4.2 years). We used locus-based logistic regression methods to prioritize genes and variants for validation. Sanger sequencing and subsequent SNP genotyping in 580 Tunisian cases and 480 controls was used for replication. Gene-environment interactions for smoking and caffeine intake were also explored with this data. Survival curves were plotted for each genotyped variant.

Results: WGS identified ~11 million variant per person, including 287 coding changes which are differentially represented in early-onset and asymptomatic groups. Four variants in *TMTC4* ($p=0.0478$), *LOC149134* ($p=0.0197$), *CENPQ* (0.0492) and *CYFIP1* (0.0292) were observed at significantly different frequencies between early-onset patients and asymptomatic carriers. Smoking ($p=0.08$) and caffeine intake ($p=0.33$) appear to have no effect on AAO.

Conclusions: Despite the ethnic, genetic and environmental homogeneity in this population, the AAO of disease for p.G2019S carriers spans over 60 years. WGS have identified four variants which appear to modulate AAO and may provide novel therapeutic strategies to delay the onset of disease.

P01.23

Movement disorders in EthiopiaDawit K. Worku¹¹Addis Ababa University, Department of Neurology, Addis Ababa, Ethiopia

Background: In this country of 80-million plus people, there is a shortage of physicians - only 15 neurologists serve the entire country and most are concentrated in the capital city - making it difficult for all who need care to see a neurologist.

Methods: A review of journals was done on papers: movement disorders in Ethiopia available until the end of June, 2011 at main Library of Addis Ababa University, School of Medicine, Department of Neurology.

Results: There is little information on the frequency of movement disorders seen by physicians in the continent of Africa. In one retrospective study in a university-based neurology clinic in Addis Ababa, Ethiopia, over 1 year period a total of 15.1% of the neurological patients were seen for movement disorders. Of these, most were for Parkinsonism (47.7%), followed by ataxia (16.5%), dystonia (8.3%), essential tremor (8.3%), chorea (7.3%), and miscellaneous (11.9%). Data on Parkinson's disease in sub-Saharan Africa is limited but it appears that the age-adjusted prevalence may be a little lower than other parts of the world. The likely explanation for this is a lack of diagnosis, and therefore treatment, leading to early fatality. Diagnostic evaluations are limited, but treatment is available, although expensive. In spite of the limitations, patients with movement disorders require and seek care in Ethiopia in proportions comparable to developed nations.

Conclusions: There are no adequate prevalence studies to conclude with figures. The magnitude of the disease prevalence needs to be studied with further research to reach for those desperate patients. In a county where patients with movement disorder highly stigmatize the problem even become worse. These findings underline the need for adequate training in movement disorders for physicians and neurologists, and community education in Ethiopia.

BASIC SCIENCE: CELL DEATH, NEUROPROTECTION AND TROPHIC FACTORS

P02.01

Neuroprotective properties of oleuropein against 6-hydroxydopamine-induced cytotoxicity in neuronal PC12 cellsImène Achour¹, Manon Legrand¹, Anne-Marie Arel-Dubeau¹, Everaldo Attard² and M-G. Martinoli¹¹Cellular Neurobiology, Dept. of Medical Biology, Université du Québec à Trois-Rivières, Québec, Canada²Institute of Earth Systems, University of Malta, Msida, Malta

Objective: Oleuropein (Ole) is a phenolic compound found in the olive leaf from *Olea europaea*, it is believed to have various pharmacological benefits, including antioxidant and anticarcinogenic properties. The aim of this study was to investigate whether Ole may protect neuronal cells against degeneration in a cellular model of Parkinson's disease (PD), neuronal PC12 cells exposed to the potent neurotoxin 6-hydroxydopamine (6-OHDA).

Methods: cytotoxicity assays, DNA fragmentation apoptosis assay as well as epifluorescent dyes and immunofluorescence by

autophagy-specific proteins have been used in 6-OHDA- treated versus normal cells.

Results: Cytotoxicity assays showed that the administration of Ole prior to the oxidative insult prevents cell death induced by 6-OHDA. Furthermore, the results obtained by measuring specific apoptotic DNA fragmentation, demonstrate that Ole significantly decreases apoptosis. Currently, a growing body of evidence shows that autophagy plays a key role in the pathogenesis of PD. Indeed, we observed autophagic vacuoles in the cytoplasm of neuronal cells treated with Ole and we identified them by labeling with acridine orange, Cyto-ID and by measuring LC3 expression, a reliable marker for monitoring autophagy-related processes, including autophagic cell death. Altogether, the results obtained suggest that Ole has interesting neuroprotective properties which might be related to the increased number of autophagic vacuoles. Other studies are in progress to better define the role of Ole in apoptosis and autophagy.

P02.02

The phytosterol Cucurbitacin E exerts neuroprotective and pro-autophagic effects in an "in vitro" model for Parkinson's disease.Anne-Marie Arel-Dubeau¹, Fanny Longpré¹, Everaldo Attard², Maria-Grazia Martinoli¹¹Cellular neurobiology, Department of Medical Biology, Université du Québec à Trois-Rivières²Institute of Earth Systems, University of Malta, Msida, Malta

Objective: Neuroprotective therapies are currently investigated because of their potential to reduce the incidence of neurodegenerative disorders such as Parkinson's disease (PD). As such, natural molecules such as polyphenols and phytosterols are studied as neuroprotective strategies to preserve cells from a variety of toxic effects often linked to PD neurodegeneration, oxidative stress, mitochondrial dysfunction, protein aggregation and formation of intracellular inclusions. In this study, we have analyzed the neuroprotective potential of Cucurbitacin E (CuE), a triterpene phytosterol extracted from the Cucurbitaceae *Ecballium elaterium*, on an *in vitro* model of PD.

Methods: Our experimental paradigm uses nerve growth factor (NGF)-differentiated PC12 cells treated with 1-methyl-4-phenylpyridinium (MPP+), a well known neurotoxin provoking a PD-like syndrome. To evaluate the neuroprotective effects of CuE, we administered this natural molecule to neuronal PC12 cells prior and during MPP+ exposure. We measured the cytoprotective effect of CuE by cytotoxicity and apoptosis assays. The antioxidant potential of CuE has also been analyzed using the intracellular ROS production and the superoxide anion content of the dopaminergic neurons. Then, epifluorescent dyes and immunofluorescence by autophagy-specific proteins have been used to observe autophagosome amounts in treated versus normal cells.

Results: While CuE proved to be an effective neuroprotective molecule, as measured by cytotoxicity and the expression of apoptotic parameters, it failed to present antioxidant effects, leading our researches towards new cellular pathways of CuE activities. Indeed, we studied whether CuE may modulate autophagy, a complex organelle- and protein-degradation and recycling pathway. We can conclude that CuE is a pro-autophagic compound and its implication in the autophagy cascade may be accounted for its neuroprotective properties.

P02.03

Neuroprotective treatment with PPAR-gamma agonist modulates microglia phenotype in the MPTP model of Parkinson disease

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Objective: A dysregulated cytokines production by microglia is a pathological event in Parkinson's disease (PD) neuropathology, conferring a neurotoxic phenotype to these cells. In the chronic MPTP/probenecid (MPTPp) model of nigrostriatal degeneration, we sought if stimulation of PPAR-gamma modulates microglia phenotype, since PPAR-gamma is highly expressed in CNS immune cells, and receptor agonists, such as rosiglitazone, mediate neuroprotection in PD models (Carta et al, 2011).

Methods: Mice received 10 MPTPp injections over 5 weeks. As previously shown, rosiglitazone (10 mg/kg i.p.) arrested the dopaminergic degeneration when administered late in the treatment, starting after the 7th neurotoxin injection. To evaluate microglia phenotype, the colocalization of pro- and anti-inflammatory cytokines with CD11b-positive microglia was measured.

Results: In vehicle-treated mice, microglia expressed low levels of the pro-inflammatory cytokine TNF-alpha and of the anti-inflammatory cytokine TGF-beta. Across the chronic MPTPp treatment microglia progressively acquired a highly activated morphology. The percentage of microglia expressing high levels of TNF-alpha progressively increased, as measured after 0 (6.83%), 1, 3, 7, 10 (23.94%) neurotoxin injections. In contrast, the percentage of microglia expressing high levels of TGF-beta initially increased, as shown by measures after 0 (17.54%) and 3 (34.97%) MPTPp injections, to be reverted to control levels after 10 (18.56%) injections, indicating that MPTPp treatment directed microglia activation toward a pro-inflammatory phenotype. Rosiglitazone administration in the late part of neurotoxin treatment did not counteract microglia activation as indicated by morphological analysis, however it reduced TNF-alpha production, reverting to control levels the percentage of microglia highly expressing this cytokine (11.15%). Moreover, rosiglitazone induced an overproduction of TGF-beta, increasing the percentage of microglia expressing high levels of this cytokine (44.44%), suggesting that rosiglitazone induced a switching in microglia phenotype from pro-inflammatory to anti-inflammatory. Driving microglia activation toward a beneficial phenotype may arrest the "microgliosis" and underlie the neuroprotective activity of PPAR-gamma agonists.

P02.04

Measurement of plasma cytokines suggests T helper type 2 dominated T cell dysregulation in Parkinson's disease.

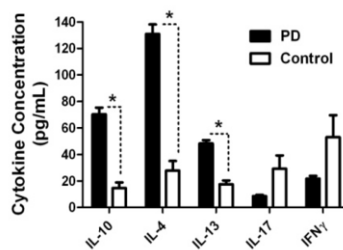
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Objective: The specific role of CD4+ or "helper" T cells in the course of Parkinson's disease (PD) is unclear. It has been hypothesized that pro-inflammatory cytokines secreted by T cells, including IL-17 and IFN-gamma, are associated with progression of PD. The presence of specific T helper (Th) cytokine signals in the blood may indicate systemic imbalance of T cell responses that contributes to PD pathology. We questioned whether the Th-associated cytokines secreted in the blood of PD patients would differ significantly from those measured in age-matched controls.

Methods: Plasma samples were collected from PD patients and age matched controls every 6 months over the course of 2 years. Cytokine levels (pg/ml) were determined using a Millipore Multiplex MAP human cytokine/chemokine panel and analyzed with a BioPlex 100 (BioRad). Unknowns were extrapolated using standard curves generated from manufacturer-supplied standards. Mean +/- SD of cytokine concentrations were compared between PD and control and significance determined via Student's t test with Welch's correction.

Results: Surprisingly, secretion of inflammation-associated IL-17 was lower in PD patients than control, as was secretion of IFN-gamma, which is the hallmark of Th1 response. In contrast, plasma isolated from PD patients contained significantly greater IL-4 and IL-13 (p < 0.001), which are linked to Th2 response. The significant increase in IL-10 expression (which directly down-regulates Th1 response) in PD patients also indicated an overall shift towards Th2 response. Importantly, cytokine levels did not significantly change in patients over the course of the study, suggesting that a stable, Th2-skewed, systemic T cell response is maintained in PD.



P02.05

Lmx1a and Lmx1b regulate survival of midbrain dopamine neurons

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Objective: During embryonic development, a combination of transcription factors specifies neural fate and promotes differentiation by inducing distinct gene expression profiles. Lmx1a and Lmx1b are transcription factors expressed by dopaminergic progenitors and their expression persists in mature dopaminergic neurons. However, the role of these factors in mature dopaminergic neurons remains unknown and the objective of this study is to define it.

Methods: Conditional mutant mice were used for the inactivation of Lmx1a and Lmx1b specifically in postmitotic midbrain dopamine neurons without affecting the specification or the proliferation of dopaminergic progenitors. In order to elucidate the mechanisms by which Lmx1a and Lmx1b influence the maintenance of dopaminergic circuits, the gene expression profile of Lmx1a and Lmx1b mutants was analyzed.

Results: The results suggest that Lmx1a and Lmx1b are required to maintain mature dopaminergic neurons. Inactivation of Lmx1a and Lmx1b causes progressive degeneration of dopaminergic neurons, preferentially affecting the SNpc. Reduced dopaminergic axons innervating the dorsal striatum and the onset of motor problems were observed. The study of gene expression profiles of Lmx1a and Lmx1b mutants suggests that these factors regulate genes from complexes I, III and V of the mitochondrial respiratory chain. These results show that the maintenance of dopaminergic systems is underpinned by the continued action of Lmx1a and Lmx1b beyond the stages of development process. Lmx1a and Lmx1b could prove to be master regulators coordinating and regulating mitochondrial biogenesis and signaling cascades to meet the specific energy

needs of neurons. Considering that mitochondrial dysfunction is involved in Parkinson's disease, these findings could lead to the identification of therapeutic targets to prevent the degeneration of dopaminergic neurons in patients suffering from the disease.

P02.06

Determination of the neuroprotective effects of SIRT3 in Parkinson's disease.

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Objective: SIRT3 is a NAD-dependent deacetylase localized in the mitochondria where it deacetylates mitochondrial proteins resulting in enhanced ATP production and decreased reactive oxygen species (ROS) levels. This globally enhances mitochondrial health. In Parkinson's disease (PD) mitochondrial dysfunction is central to the pathogenic process. Therefore, we hypothesized that SIRT3 may have a neuroprotective role in PD. The aim of this study was to utilize *in vivo* and *in vitro* models to test this hypothesis, and to determine the mechanisms underlying the neuroprotective effects of SIRT3.

Methods: Endogenous SIRT3 levels were assessed in a rat model of PD by Western blot three weeks following infection with mutant (A53T) human α -synuclein. The neuroprotective effect of ectopic over-expression of SIRT3 in this rat model of PD was also determined. Rats were infused with recombinant adeno-associated viruses expressing SIRT3-myc or α -synuclein in the substantia nigra. Three and six weeks following infection, behavioural deficits were assessed using the cylinder test. To investigate the mechanism underlying SIRT3-induced neuroprotection, a catecholaminergic cell line (SH-SY5Y) stably overexpressing SIRT3-myc was used as a cellular model of PD. They were exposed to two agents to induce neurotoxicity, dopamine (65 μ M) and rotenone (30nM). Cellular toxicity and ROS production were assessed using propidium iodide and DCF-FA respectively.

Results: We found that SIRT3 levels were elevated in the early stages of parkinsonian pathology in the α -synuclein rat model of PD. In parkinsonian rats, overexpressing SIRT3 in the substantia nigra reverses behavioural abnormalities. Overexpression of SIRT3 resulted in a decrease in cellular toxicity after exposure to dopamine and rotenone (35 and 36% respectively). Overexpression of SIRT3 also decreased ROS production by 29% after dopamine exposure and 50% after rotenone-induced toxicity.

Conclusion: These results suggest that SIRT3 is neuroprotective in a rat model of PD. These neuroprotective effects are likely due to decreasing ROS production.

P02.07

Nuclear Receptors Agonists as Neuroprotective Agents in Parkinson's disease Alleviation

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Objective: Parkinson's disease (PD) is the second prevalence neurodegenerative disorder characterizing by tremor, rigidity, dyskinesia and dementia. The main pathology of this disease underlying selective degeneration of dopaminergic neurons in the substantia nigra (SN). Orphan nuclear receptors such as PPAR γ and Nurr1 have important roles in many cardinal pathways in cells. Previous studies confirmed PPAR γ agonists' protective effects in neurological disorder such as PD. Nurr1 as an important transcription factor which has a critical role in stem cells differentiation into dopaminergic neurons can be focused as a potential target to ameliorate PD symptoms.

Methods: In this study we used PC12 as an *in vitro* model of PD. These cells were treated with various concentration of MPP+, it caused the death of PC12 cells in a time- and dose-dependent manner. GW1929 (PPAR γ agonist) and 6-mercaptopurine (Nurr1 agonist) act as neuroprotective agents in this experiment and we analyze their influence on TH, Ferritin Light Chain, Nurr1 and Ephrin A1 expressions. In addition we tested ROS level and Mitochondrial Membrane Potential (MMP) by flow cytometry.

Results: We found that Nurr1 agonist beyond its neuroprotective feature can increase ferritin light chain expression which important in iron metabolism. In addition PPAR γ agonist combination with Nurr1 agonist has impressive effect on Ephrin A1 expression that has a critical role in dopaminergic neurogenesis. Present study suggests that Nurr1 agonist might be a new compound to alleviate PD patients' symptoms by controlling various pathways in neurons.

P02.08

IRX4204 as a novel disease-modifying therapeutic agent in Parkinson's disease

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Objective: IRX4204 is a second-generation retinoid X receptor (RXR) agonist currently being tested for prostate cancer treatment with an excellent safety record. Nurr1-RXR heterodimer selective agonists have been actively pursued as a potential pharmacological target for Parkinson's disease (PD) due to their neuroprotective effects in models of PD. The objective of our study is to evaluate the effects of IRX4204 as a potential novel therapeutic in PD neuropathology.

Methods: Primary rat mesencephalic cultures were used study the role of IRX4204 on Nurr1-mediated neuroprotection. The 6-hydroxydopamine (6OHDA) induced rat model of PD was used to examine the potential neuroprotective role IRX4204 on PD pathology. Nuclear magnetic resonance (NMR) and photo-induced cross-linking of unmodified protein (PICUP) were used to evaluate the role IRX4204 on prevention of α -synuclein binding and oligomerization.

Results: We found IRX4204 can selectively promote dimerization of the nuclear factor Nurr1-RXR at nM concentration *in vitro* and can promote expression of neurotrophic factors for the survival and maintenance of nigral dopaminergic (DA) neurons in a dose-dependent manner *in vivo*. This evidence is consistent with a significant attenuation of PD-type motor impairments following 6-OHDA lesions in response to IRX4204. Using a combination of NMR spectroscopy and PICUP assays, we found that IRX4204 shifts and prevents oligomerization of α -synuclein. Our data suggest that IRX4204 may benefit PD by providing neuroprotective support for DA neurons and by protecting DA neurons from α -synuclein neurotoxicity. We hypothesize that IRX4204 may neuroprotect DA neurons through Nurr1 mediated neuroprotective mechanisms intracellularly and possibly at more advanced PD-like states through inhibition of α -synuclein oligomerization.

P02.09

Novel low heparin affinity neurturin variants with disease modifying effect in a rat model of Parkinson's disease

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Objective. Neurturin is a neurotrophic factor with therapeutic potential in Parkinson's disease. One of the main problems with parenchymal neurturin injections has been the inadequate distribution of the protein. Therefore, we have developed novel, biologically active neurturin variants with improved spreading in the brain.

Methods. Mutations were introduced to the putative heparin binding site of neurturin and the variants were produced in mammalian cells. The biological activity of the variants was tested with RET phosphorylation assay and the spreading capacity by injecting 5µg of variants into rat striatum. To assess the disease modifying effects, 5µg of the proteins were injected into striatum two weeks after 6-OHDA (4x7µg). The behavioral effects were evaluated by amphetamine-induced rotations. The histological effects were analysed by quantification of TH-positive fibers and cell somas.

Results. Neurturin variants with reduced heparin binding capacity showed improved spreading in tissue. Neurturin variant N4 reduced significantly the rotational behavior. The histological analyses showed both neurturin variants N2 and N4 to protect the dopaminergic neurons in substantia nigra from degeneration. In addition, the N4 variant was efficient in protecting the striatal TH-positive neurites. These results together suggest that especially the novel neurturin variant N4 has an increased potential to protect the dopaminergic nigrostriatal pathway from degeneration in Parkinson's disease.

P02.10

Resveratrol protects dopaminergic cells against high glucose-induced oxidative stress and apoptosis: role of glucose-regulated protein 75

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Objective: Resveratrol (RESV), a natural polyphenolic compound, has long been acknowledged to have cardioprotective, anticarcinogenic and anti-inflammatory actions. RESV holds antioxidant properties reducing the formation of reactive oxygen species (ROS) which lead to oxidative stress and apoptotic death of dopaminergic (DAergic) neurons, a hallmark of Parkinson's disease (PD). Recent literature has recognized hyperglycemia as a cause of oxidative stress reported to be harmful for the nervous system. In this context, our study aimed: a) to evaluate the effect of RESV against high glucose-induced oxidative stress in DAergic cells b) to study the anti-apoptotic properties of RESV on DAergic cells in a high-glucose condition, and c) to investigate the role of glucose-regulated protein 75 (GRP75), a marker of mitochondrial homeostasis known to be depleted in post-mortem PD patient brains, in mediating the beneficial actions of RESV.

Methods: Differentiated PC12 cells were treated with low-glucose medium (1 g/L) or high-glucose medium (4.5 g/L) for 96 hours. For

the last 24 hours, PC12 cells were administered RESV at a concentration of 0.1 µM. Mitochondrial superoxide anion was measured to assess oxidative stress while the apoptotic cascade was investigated using DNA fragmentation assays, Western blotting and immunofluorescence measurements.

Results: Our results showed that RESV protects DAergic neurons against high glucose-induced oxidative stress by diminishing levels of superoxide anion. Then, RESV reduced high glucose-induced apoptosis in DAergic cells by modulating DNA fragmentation and the expression of apoptotic markers such as Bax, Bcl-2, p53, cleaved caspase-3 and cleaved PARP-1. Moreover, RESV rescued expression levels of GRP75 which were significantly decreased by high-glucose treatment. GRP75 is known to bind and sequester pro-apoptotic p53 in the cytosol, preventing its translocation to the nucleus. Altogether, our data evoke a correlation between hyperglycemia and neurodegeneration, which provides new insight on the high occurrence of PD in diabetic patients.

P02.11

Fasudil administration elevates striatal dopamine and protects against alpha synuclein mediated toxicity

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Objective: No treatments exist to slow nigrostriatal degeneration in Parkinson's disease (PD). Repurposing of drugs with known safety profiles in humans can accelerate clinical trials and discovery of effective treatments. The present experiments were conducted to determine whether fasudil, an orally available Rho-kinase (ROCK) inhibitor with a favorable safety profile in humans, could be successfully repurposed as a neuroprotective agent for PD.

Methods: We conducted preclinical studies in cell culture and in vivo rat models of alpha-synuclein mediated toxicity. Fasudil was orally administered in chow (10 or 25 mg/kg/day), rats were assayed for a number of outcome measures including levels of striatal monoamines, levodopa-induced dyskinesias, and number of surviving nigral DA neurons following intranigral injection of recombinant adeno-associated virus expressing human wild-type alpha-synuclein (rAAV α-syn).

Results: Fasudil and other ROCK inhibitors provide neuroprotection from α-syn mediated toxicity in H4 cell cultures. Oral administration of fasudil to rats: 1) significantly increased fasudil and hydroxyfasudil levels in plasma and brain, specifically in the substantia nigra (SN), in a dose-dependent manner, 2) resulted in no overall impact on heart rate and arterial pressure, 3) significantly increased (doubled) DA and DA metabolites in the striatum, 4) did not exacerbate existing levodopa-induced dyskinesias, and 5) provided significant neuroprotection from rAAV α-syn mediated toxicity. Specifically, rAAV α-syn injected rats fed control chow exhibited a 70% reduction in tyrosine hydroxylase immunoreactive (THir) neurons in the SN pars compacta (SNpc) eight weeks after vector injection. In contrast, rats fed 25 mg/kg/day fasudil chow (high dose) exhibited only a 40% reduction in THir neurons. Counterstaining with cresyl violet verified that high dose fasudil provided true neuroprotection of SNpc dopamine neurons. To our knowledge this is the first orally available compound to provide neuroprotection in the AAV α-syn PD model and suggests that fasudil holds great potential for the treatment of PD.

P02.12

Activin A is neuroprotective in the 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP) mouse model of Parkinson's disease

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Objective: There still remains a pressing need to identify therapeutic targets that effectively protect against the dopaminergic degeneration that is characteristic of Parkinson's disease (PD). Growth factors have been demonstrated to promote survival, differentiation and maintenance of neuronal cells within the central nervous system and as such, are promising disease-modifying targets. Activin A, a member of the transforming growth factor- β superfamily, has significant neuroprotective effects against the Parkinsonian toxin 6-OHDA *in vitro*. In addition, activin A has been shown to possess potent anti-inflammatory effects in an acute brain injury model. The aim of this study was to investigate if activin A was neuroprotective in an *in vivo* model of PD.

Methods: 12 week old male C57BL/6 mice were implanted subcutaneously with osmotic micro-pumps, filled with recombinant activin A (24ng/ μ l) or vehicle control, and connected to an infusion cannula in the right lateral ventricle (AP -0.26mm, ML -1.0mm). The following day mice were administered MPTP subcutaneously (4 x 20mg/kg, 2 h interval). Tissue was harvested 7d later and analyzed for dopaminergic neurons, total neurons, astrocytic and microglial populations by immunolabelling for tyrosine hydroxylase (TH), NeuN, GFAP, and Iba1, respectively, and quantified in the substantia nigra pars compacta via stereology. Quantification of striatal dopamine transporter expression was performed by measuring binding of [3H]-mazindol.

Results: MPTP-injected animals that received activin A had significantly higher numbers of TH and NeuN-positive cells compared to animals receiving vehicle. Treatment of MPTP-injected animals with activin A significantly protected striatal dopamine terminals as measured by increased [3H]-mazindol binding. Stereological analysis revealed a significant decrease in GFAP and Iba1-positive cells in the substantia nigra in activin A-treated animals following MPTP compared to controls. Our study suggests that activin A is neuroprotective in the MPTP mouse model, indicating its potential as a novel therapeutic target in the treatment of PD.

P02.13

Enhancement of ATF4 and parkin function as a neuroprotective strategy for Parkinson disease

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Objective: The lack of disease-modifying treatments is a critical unmet need in the treatment of Parkinson disease (PD). Our group recently identified a novel neuroprotective pathway in PD models: activation of the transcription factor ATF4 maintains parkin levels in response to PD-mimetic stressors. In this study, we show that multiple neuroprotective interventions require ATF4-parkin signaling for their beneficial effects, thus further validating the therapeutic potential of enhancing ATF4-parkin function.

Methods: Differentiated PC12 cells or primary ventral midbrain cultures were pretreated with the different protective regimens, then exposed to the PD-mimetic stressors 6-hydroxydopamine (6-OHDA) or 1-methyl-4-phenylpyridinium (MPP+). Silencing of ATF4 or parkin was achieved by lentiviral infection with specific shRNA constructs.

Survival was assessed by counting viable nuclei. Analysis of protein expression was performed by Western blotting of total cell lysates. Analysis of mRNA expression was performed by real-time quantitative PCR.

Results: We assessed two different approaches to activating ATF4 function. First, cells were exposed to sub-lethal doses of thapsigargin in order to activate the ER stress response. Indeed, this preconditioning regimen led to a greater increase in ATF4, mitigated the reduction in parkin, and also protected PC12 cells against 6-OHDA-induced cell death. ATF4 is necessary for this protection, as silencing ATF4 abolished the protective effect of the preconditioning treatment. Second, we used guanabenz, an FDA-approved drug that inhibits the GADD34-PP1 complex, leading to enhanced translation of ATF4. Guanabenz attenuated 6-OHDA-induced cell death in both PC12 cells and primary ventral midbrain dopaminergic neurons. Guanabenz leads to an increase in ATF4 and parkin levels; if either one of these is silenced, then the protective effect of guanabenz is lost. In sum, these data support ATF4-parkin as potential neuroprotective targets. Furthermore, we identify a specific drug for further evaluation as a disease-modifying treatment for PD.

P02.14

Neuroprotective effects of blueberry anthocyanins in Parkinson's disease models

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Objective: Parkinson's disease (PD) is characterized by a loss of dopaminergic neurons in the *substantia nigra*. Epidemiological evidence suggests that the consumption of dietary polyphenols reduces the risk of neurodegeneration. We hypothesize that a blueberry (BB) extract rich in anthocyanins may be neuroprotective in PD models. Our goal is to assess if a BB extract can rescue dopaminergic cell death triggered by PD-related insults and to identify the underlying mechanisms of neuroprotection.

Methods: We tested a BB extract in a dopaminergic cell viability assay. Primary midbrain cultures obtained from E17 rat embryos were exposed to PD-related insults including rotenone, paraquat and virus encoding mutant alpha-synuclein (A53T α Syn) in the presence and absence of the extract. Dopaminergic cell viability and neurite length and number were assessed by immunocytochemical analysis. We also determined the effect of the BB extract on expression levels of DJ-1, a redox-sensitive chaperone protein implicated in PD, by Western blot analysis. In addition, we tested the effect of the extract on the transcriptional activity of Nrf2 (nuclear factor erythroid 2-related factor 2), a transcription factor that regulates the expression of antioxidant enzymes, using an adenoviral reporter construct encoding the EGFP gene downstream of the heme oxygenase promoter.

Results: The BB extract was found to alleviate dopaminergic cell death and neurite loss in primary midbrain cultures exposed to rotenone, paraquat and A53T α Syn. Preliminary results suggest that the extract induces an increase in the transcriptional activity of astrocytic Nrf2 and up-regulates DJ-1. Current efforts are aimed at determining whether Nrf2 and DJ-1 up-regulation are necessary and/or sufficient for the neuroprotective effects of BB anthocyanins in PD models. Ultimately these studies may yield valuable insight

into neuroprotective strategies to decrease the risk of PD or slow disease progression.

P02.15

Effect of a co-administration of neurotrophic factors CDNF and GDNF in a 6-OHDA model of Parkinson's disease in rats

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Parkinson's disease (PD) is a neurodegenerative disease associated with a progressive loss of dopaminergic neurons of the substantia nigra (SN) and accumulation of intracellular inclusions containing α -synuclein. Current therapies of PD do not stop the progression of the disease and their efficacy wanes over time. Neurotrophic factors (NTF) are naturally occurring proteins promoting survival and differentiation of neurons and maintenance of neuronal contacts. CDNF (cerebral dopamine neurotrophic factor) and GDNF (glial cell line-derived neurotrophic factor) have shown neurorestorative activity in the unilateral 6-hydroxydopamine (6-OHDA) lesion model of PD in rats when administered individually.

Objective: Study the effect of a low dose of CDNF alone or in combination with a low dose of GDNF in a unilateral 6-OHDA lesion model in rats.

Methods: CDNF was given with or without GDNF into the striatum four weeks after a unilateral intra-striatal injection of 6-OHDA (20 μ g). Amphetamine-induced (2.5 mg/kg, i.p.) rotational behavior was measured every two weeks for 3 months. Tyrosine hydroxylase (TH)-positive cells from SN pars compacta and striatal TH-positive fiber density were analyzed at 12 weeks post lesion.

Results: CDNF (1-10 μ g) and GDNF (1-10 μ g) alone had robust neurorestorative effect in the 6-OHDA model of PD but one specific dose combination had an additive effect: CDNF (2.5 μ g) and GDNF (1 μ g) co-administration led to stronger trophic effects relative to the injection of either NTF alone at the same dose. Our results indicate, for the first time, that a co-administration of two NTFs with different mechanism of action, i.e. CDNF and GDNF, shows stronger trophic and functional effects than either NTF alone. The results may have clinical implications in the future use of NTFs in therapy of PD.

P02.16

Lewy body fractions from patients with Parkinson's disease initiate α -synuclein-dependent neurodegeneration in mice and non-human primates

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Objective: Mounting evidence indicate that neuropathological α -synuclein lesions may self-propagate and spread progressively throughout the brain of Parkinson's disease (PD) patients by a cell-to-cell transmission mechanism, thereby contributing to the extension and progression of the disease process. While synthetic α -synuclein fibrils can lead to α -synuclein pathology in mouse brain, the physiopathological significance of disease-associated, Lewy body (LB)-linked human α -synuclein is unknown.

Methods: Here, we stereotactically inoculated α -synuclein-containing LB fractions derived from nigral post-mortem PD samples into the substantia nigra or striatum of wild-type mice and non-human primates (NHP).

Results: In mice, a single LB nigral injection resulted in progressive nigrostriatal neurodegeneration starting at striatal dopaminergic terminals. At the onset of LB-induced denervation, endogenous murine α -synuclein adopted a pathological conformation and accumulated within nigral neurons. LB-induced pathogenic effects required both human α -synuclein present in LB fractions and host expression of α -synuclein. In NHP, striatal or nigral LB injections caused nigrostriatal degeneration and accumulation of pathological α -synuclein in anatomically interconnected regions. Our study unravels a pathogenic prion-like species-barrier crossing effect of human-derived pathological α -synuclein.

BASIC SCIENCE: PROTEIN MISFOLDING AND HANDLING

P03.01

Administration of L-tyrosine with levodopa prevents insertion of levodopa into proteins and could be neuroprotective in Parkinson's disease

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Objective: The 20 'protein' amino acids (AA) account for less than 2% of all AA in nature. Most 'non-protein' AA are made by plants and can be used to defend against predation. Canavanine, from jack bean, kills larvae by replacing arginine in the peptide chain and is lethal to rats. L-DOPA (levodopa), from mucuna plants, also kills larvae¹. LDOPA replaces L-tyrosine in protein synthesis². Proteins containing incorporated LDOPA are present in brain and plasma of L-DOPA-treated patients^{3,4} and induce apoptosis in human neurons *in vitro*⁵. Here we test the ability of L-tyrosine to prevent LDOPA incorporation into proteins *in vivo*.

Methods: Rats (n=22) were administered L-dopa (6.5mg/kg) and benserazide (1.5mg/kg), IP, twice daily with or without L-tyrosine (100 mg/kg). After sacrifice (21 days), proteins were extracted from the motor cortex (MC), substantia nigra (SN) and striatum (CPu) and levels of DOPA-containing proteins measured by HPLC.

Results: At sacrifice there was a 2-fold increase in tyrosine levels in the brain regions examined but no difference in levels of DOPA and dopamine. Levels of DOPA in hydrolyzed proteins increased 5 fold in the CPu of DOPA-treated rats but were unchanged in SN and MC. Co-administration with L-tyrosine reduced DOPA levels in CPu proteins by 60% (p<0.01).

Discussion: The question as to whether levodopa produces long-term toxicity in PD patients remains unresolved. Mischarging of tRNA^{Tyr} with L-DOPA and incorporation into neuronal cell proteins is a mechanism of L-DOPA toxicity that has been overlooked⁴. L-tyrosine is protective *in vitro*⁴ and in the present study we demonstrate that after a relatively short exposure to L-DOPA,

proteins containing incorporated L-DOPA are detectable in the rat brain and incorporation can be significantly reduced with L-tyrosine.

P03.02

Modulation of alpha-synuclein protein folding by a marine-sourced extract

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Objective: Protein misfolding has increasingly recognized causative roles in several human neurological diseases. Alpha-synuclein is a protein involved in the regulation of several neuronal synaptic functions. When misfolded and aggregated into an amyloid form, it has been implicated in neuronal dysfunction and degeneration in Parkinson's disease and related disorders. Marine species, notably those exposed to extreme or fluctuating conditions, offer new understanding of cellular protein folding challenges as well as novel opportunities to address them. Therefore, preventive and therapeutic options are being sought from our cold oceans to limit amyloid formation in alpha-synuclein. The goal of this project was to evaluate the effects of several marine species-derived extracts from the Bay of Fundy, Canada, on the fold stability of alpha-synuclein.

Methods: Marine samples were collected and aqueous extracts were prepared from them. The effects of the extracts on protein fold stability were measured using a standard thermofluor melting point assay. The identified active extract was fractionated and the fractions were assessed using the same method. The active extract and fractions thereof were then analyzed for modulation of amyloid formation in alpha-synuclein using a standard thioflavin T assay, which was confirmed by fibril determination using transmission electron microscopy. Additionally, effects of the active extract and its fractions on the secondary structure of alpha-synuclein were examined.

Results: Activities that increased and decreased the alpha-synuclein fold stability were identified within a single extract. Components with these contrasting activities were separated both by acetone precipitation and by size fractionation, providing insight into the distinct sources of these activities. The effects on amyloid formation and protein structure were also assessed. Compounds identified in this way may lead to novel marine-sourced products that directly address the protein misfolding that appears to be causative in Parkinson's disease.

P03.03

Protein misfolding cyclic amplification (PMCA) as an alpha-synuclein anti-aggregation drug-screening tool

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Objectives: The hallmark of Parkinson's disease is the presence of intraneuronal inclusions known as Lewy bodies. Their main component is a misfolded isoform of an otherwise normal protein called alpha-synuclein. The spread of the aggregated alpha-

synuclein in the brain is related to the progression of the disease. Inhibiting alpha-synuclein aggregation could halt the spread and therefore slow or even arrest the disease progress.

Formation of alpha-synuclein filaments can be reproduced *in vitro* using recombinant protein, but the filament growth is very slow and so unsuitable for high throughput anti-aggregation drug screening. To overcome this obstacle we have investigated whether the protein misfolding cyclic amplification (PMCA) technique, used for fast amplification of prion protein aggregates, could be adapted for growing alpha-synuclein aggregates. Furthermore we explored the application of the alpha synuclein PMCA for drug screening.

Methods: During PMCA, recombinant alpha-synuclein was subjected to cycles of sonication and incubation and the growth of fibrils was monitored by enhanced Thioflavin T fluorescence. Circular dichroism, electron microscopy, native and SDS-PAGE gels and enzymatic digestions were used to demonstrate alpha-synuclein aggregate formation. A panel of drugs was studied to evaluate the sensitivity of the system for alpha-synuclein anti-aggregating drug screening.

Results: Our results indicate that PMCA can be used to form stable alpha-synuclein fibrils. We have characterized the newly generated material as authentic alpha-synuclein filamentous aggregates using several biophysical and biochemical methods. We have also demonstrated that anti-aggregating drugs can selectively inhibit PMCA fibril formation of alpha-synuclein.

Conclusions: Our results show that alpha-synuclein PMCA is a fast and reproducible system that could be used as high throughput screening for alpha-synuclein anti-aggregating compounds. Therefore this system is relevant for identifying therapeutic compounds for Parkinson's disease and other alpha-synucleinopathies.

P03.04

The association between Gaucher disease and Parkinson disease: from Human to *Drosophila*

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Gaucher disease, an autosomal recessive disease, results from mutations in the *GBA1* gene, encoding the lysosomal enzyme acid β glucocerebrosidase (GCase). Mutant GCase variants undergo ERAD, the degree of which is a major determinant of disease severity. The presence of mutant molecules in the ER induces ER stress and the unfolded protein response (UPR). Previous publications noted UPR in GD derived skin fibroblasts. We have extended these studies to show that UPR exists in GD derived skin fibroblasts, manifested by upregulation of the expression of the transcription factor CHOP and the chaperone BiP (Grp78), phosphorylation of eIF2 α and cytoplasmic splicing of the transcription factor Xbp1. UPR exists also in skin fibroblasts that derived from carriers of GD mutations. We assume that ERAD of mutant GCase and UPR are a major determinant in the development of Parkinson disease among GD patients and carriers of GD mutations. To confirm this assumption we developed *Drosophila* models for carriers of GD mutations. There are two *GBA1* homologs in *Drosophila*, designated CG31414 and CG31148, both encoding proteins showing ~31% identity and ~49% similarity to the human GCase. There are two *Drosophila* lines available, each with a transposable element insertion (a minos insertion) in one of

the fly GCCase orthologs, expected to result in a truncated protein. We tested UPR in double heterozygous flies, as a model for carriers of GD mutations. Our results showed activation of the UPR machinery in the heterozygous flies as tested by *Hsc70* (the fly BiP ortholog) activation, Xbp1 splicing and phosphorylation of eIF2 α . We also established fly lines expressing the human N370S and the L444P mutations. Both lines portrayed UPR and climbing difficulties, reminiscent of Parkinson disease. Our results strongly indicate that UPR is a determinant in the development of Parkinson disease among GD patients and carriers of GD mutations. To summarize, the *Drosophila* model is the first animal model in which expression of mutant GBA1 allele in a heterozygous state leads to development of Parkinsonian signs.

P03.05

Smoking and Parkinson's disease: nicotine binds to alpha-synuclein and causes large conformational changes which may prevent it from misfolding.

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Objective: -Synuclein (AS) is an intrinsically disordered protein of 140 amino acids which is abundant in dopaminergic neurons. Misfolding and aggregation of AS leads to the formation of intracellular Lewy Bodies which are the hallmark of Parkinson's disease and related dementias. The binding of dopamine and nicotine to AS was investigated by nanopore analysis.

Methods: In this technique single AS molecules are interrogated electronically as they interact with an α -hemolysin pore. The electronic signal is very sensitive to the structure and conformation of the protein and, thus, if a drug causes a conformational change it can be readily detected.

Results: Wild type AS adopts an extended conformation which can pass through the pore whereas the A30P mutant AS (found in familial PD) is mostly folded or aggregated. Upon binding dopamine the mutant protein unfolds and can now pass through the pore. There are independent binding sites for dopamine in both the N- and C-terminus of the protein which was confirmed by ¹H-¹⁵N-HSQC NMR. Wild type AS also binds nicotine but the conformation is different from that of the dopamine-AS complex. With the A30P mutant, nicotine again prevents aggregation but the conformation of the complex is different from that of the wild type complex. These results demonstrate a new methodology for studying drugs binding to AS which may prove useful for developing therapeutic solutions for PD. It is also of interest that epidemiological studies have shown that PD is less prevalent in smokers and our results provide a direct link between nicotine binding and the conformation of AS.

P03.06

14-3-3 chaperone protein modulates alpha-synuclein aggregation and toxicity

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Objective: Idiopathic and familial Parkinson's disease (PD) is associated with the neuronal accumulation of fibrillar forms of alpha-synuclein (aS) into proteinaceous aggregates called Lewy Bodies. A connection between PD and the 14-3-3 chaperone proteins was recently proposed: some 14-3-3 isoforms have been found in Lewy bodies and 14-3-3 η isoform interacts with aS. The goal of our work was the characterization of the effect of 14-3-3 η on aS aggregation *in vitro* and in cells.

Methods: Nuclear magnetic resonance (NMR), fluorescence spectroscopy techniques, atomic force microscopy (AFM) and transmission electron microscopy (TEM) were used to characterize the interaction between aS and 14-3-3 η *in vitro*. Cellular assays were used to study the effects of 14-3-3 η overexpression on aS aggregation and toxicity in cell systems.

Results: aS aggregation kinetics performed *in vitro* showed that aS and 14-3-3 η interact during the aggregation process. 14-3-3 η does not bind monomeric aS and is not able to disaggregate amyloid fibrils. Instead, it associates with aS aggregation intermediates to yield aggregation products that are morphologically different from canonical fibrils. Quantitative AFM and TEM analyses of aS aggregation products in the presence of 14-3-3 η revealed that: (i) 14-3-3 η leads to curved aggregates with smaller diameter than aS fibrils; (ii) 14-3-3 η is included within these curved objects; (iii) 14-3-3 η partially interferes with the elongation of preformed fibrillar seeds due to aS monomers addition in solution. The chaperone was found trapped within these growing fibrils, overwhelmed by the aggregating aS. In cell system, overexpression of 14-3-3 η is protective against aS-induced toxicity, unless massive aggregation is triggered by exogenous aS fibrillar seeds, which likely sequester and inactivate 14-3-3 η . Based on these findings, we propose that 14-3-3 η counteracts aS fibrillization process by inhibiting the early phases of aggregation, thus providing a new avenue for PD therapeutics.

P03.07

Mutations in LRRK2 potentiate age-related impairment of autophagic flux

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Objective: Aging and autophagy play an important roles in the pathophysiology of Parkinson's disease (PD). However, little is known about how genes linked to PD affect autophagy in the context of aging. The objective of this study is to characterize autophagic flux over the life-span, and to determine how LRRK2 and α -synuclein modify autophagy during aging.

Methods: We created an optical reporter for autophagic flux in *C. elegans* dopamine neurons using the dopamine transporter promoter to drive expression of Igg-1::mCherry (Igg-1 is the *C. elegans* homolog of LC3). Driving expression the dopamine transporter promoter allowed us to selectively visualize autophagy in dopamine neurons. This reporter line was then crossed with nematodes lines expressing WT, G2019S, R1441C and km-17 (deletion) LRRK2 lines, and autophagy followed over the lifespan. Autophagic flux was also investigated in triple crosses, expressing Igg-1::mCherry, LRRK2 and WT α -synuclein.

Results: The nematodes exhibited a progressive age-related decrease of autophagic flux upon finishing their reproductive period. WT LRRK2 increased autophagic flux in young nematodes, while mutant LRRK2 (G2019S and R1441C) inhibited autophagy. Introducing α -synuclein increased autophagy in young adult nematodes, even when G2019S LRRK2 was co-expressed.

During aging, both mutant LRRK2 and α -synuclein inhibited autophagy and increased dopaminergic degeneration. Co-expressing the two proteins produce a synergistic inhibition of autophagy, a corresponding accumulation of insoluble, oligomeric α -synuclein and synergistic increases degeneration of DA neurons. In addition, although WT LRRK2 improves autophagy throughout the lifespan when expressed in absence of α -synuclein, co-expressing α -synuclein with WT LRRK2 lead to an age dependent inhibition of autophagy, and a synergistic increase in degeneration of DA neurons. These data suggest that LRRK2 and α -synuclein modulate autophagy through interacting pathways that lead to age-related synergistic effects, and provide the first evidence that WT LRRK2 can directly contribute to degeneration associated with α -synuclein.

P03.08

Effect of membranes on alpha synuclein aggregation and neurotoxicity in Parkinson's disease

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Objective: Oligomerization of the presynaptic protein alpha-synuclein (aSyn) is a critical factor in the onset of both genetic and sporadic Parkinson's disease (PD). Although aSyn associates with phospholipid membranes to modulating neurotransmission, aberrant interactions of aSyn with membranes may promote its conversion to neurotoxic aggregates. Therefore, elucidation of this interaction is critical to determinate pathogenicity of aSyn in PD. The goal of this project is to analyze aSyn-membrane interactions to increase our understanding of aSyn induced toxicity. We hypothesize that reduced membrane interaction between the central hydrophobic region of aSyn and cellular membranes promotes aggregation of the protein.

Method: We generated a series of aSyn variants with familial genetic mutations or substitutions that are predicted to affect aSyn-membrane interactions. The association of these variants with synthetic phospholipid vesicles or isolated intracellular organelles has been examined by circular dichroism (CD) and solution NMR HSQC to determine secondary structure, affinity, and residue-specific interactions upon binding of the protein to membranes. Aggregation was examined by gradient ultracentrifugation and western blotting. Lastly, neurotoxicity was characterized by adenoviral-mediated expression in a primary midbrain culture model of PD.

Results: We identified several aSyn variants which display both increased and decreased membrane interaction. We observed little correlation between membrane affinity, aggregation propensity and neurotoxicity. From this we hypothesize that the conformation of membrane-bound aSyn (rather than the protein's membrane affinity per se) is critical for formation of toxic aggregates at the membrane surface. We have established a powerful NMR method to analyze residue-specific interactions of different aSyn variants with membranes to confirm this hypothesis. The data from these studies will reveal whether reduced binding in the central hydrophobic region correlates with aggregation and the observed neurotoxicity. These results will set the stage for novel therapeutic strategies to reduce aSyn aggregation through stabilization of the membrane bound state.

BASIC SCIENCE: MITOCHONDRIA, OXIDATIVE, STRESS, INFLAMMATION AND PATHOGENESIS

P04.01

Neuroprotective effects of ATP13A2 and DJ-1 in Parkinson's disease models

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Objective: Parkinson's disease (PD) involves a loss of dopaminergic neurons from the *substantia nigra* and a buildup of Lewy bodies enriched with fibrillar forms of the presynaptic protein α -synuclein (aSyn). Two proteins implicated in familial PD are ATP13A2, a lysosomal ATPase, and DJ-1, a protein with antioxidant and chaperone activities. Although there is evidence of functional overlap between these two proteins, the mechanistic details are poorly understood. The objective of this study is to elucidate cellular protective mechanisms of ATP13A2 and DJ-1 in neurons exposed to PD-related stresses, including aSyn-encoding virus and methamphetamine (METH), a drug that disrupts autophagy in dopaminergic neuronal cells. We hypothesize that a loss of function of either protein triggers defects in autophagy coupled with an accumulation of dysfunctional mitochondria.

Methods: Rat midbrain cultures were transduced with aSyn adenovirus and ATP13A2- or DJ-1-shRNA lentivirus. Cells were stained with primary antibodies that recognize tyrosine hydroxylase (TH), a dopaminergic neuronal marker, and microtubule-associated protein 2 (MAP2), a general neuronal marker. Ratio of viable dopaminergic neurons to total neurons was calculated, and neurite lengths were measured by confocal microscopy. SH-SY5Y cells stably expressing a tandem LC3 construct (GFP-RFP-LC3) were transduced with virus encoding LacZ or ATP13A2 and scored for green and red puncta, a measure of autophagic flux.

Results: Knocking down ATP13A2 resulted in a buildup of aSyn, whereas ATP13A2 over-expression reduced the accumulation of autophagosomes. In addition, human wild-type DJ-1 protected against METH toxicity and induced the phosphorylation of Akt, a protein kinase involved in modulating autophagy. Current efforts are focused on assessing whether over-expression of WT DJ-1 rescues lysosomal and mitochondrial deficits in ATP13A2 knockdown cells and vice versa. The results of these studies will provide insight into cellular mechanisms underlying the neuroprotective functions of ATP13A2 and DJ-1 and suggest new strategies to slow PD pathogenesis.

P04.02

DJ-1 loss-of-function affects adult neurogenesis in rodent brain

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Objective: Loss-of-function mutations in DJ-1 lead to autosomal recessive early-onset Parkinson's disease (PD). On the other hand, impaired adult neurogenesis has been involved in the pathogenesis of PD. Here we aimed to study the role of DJ-1 in the neurogenic process in adult mouse brain.

Methods: We developed bicistronic lentiviral vectors (LVs) encoding a short hairpin RNA (shRNA) sequence against DJ-1 or a control shRNA, with eGFP as reporter. We performed stereotactic injections of LVs in the subventricular zone (SVZ) of 2 months old C57BL6 mice. In addition, primary cultures of adult neural progenitors from the mouse SVZ were established. Proliferation was measured using BrdU and Ki67. Mitochondrial membrane potential and superoxide production was measured using TMRM and Mitosox red.

Results: To study the effect of DJ-1 knock-down on adult neural stem cells *in vivo*, we injected shDJ-1 or control LVs in the SVZ of adult mice. eGFP allowed to follow the fate, morphology and number of newly generated neurons. At 2 weeks post-injection we observed a reduced proliferative activity of adult neural progenitors in the SVZ. Furthermore, the number of newborn neurons in the olfactory bulb (OB) was significantly diminished at 1 and 4 months post-injection, without apparent effects on neuronal morphology. In order to further elucidate the mechanism-of-action, we transduced primary cultures of adult neuronal progenitors from mouse SVZ with shDJ-1 or control LVs. Knock-down of DJ-1 resulted in impaired proliferation, size and renewal capacity of the neurospheres. In addition we observed a reduced mitochondrial membrane potential and enhanced mitochondrial superoxide production in the knock-down condition compared to control.

In conclusion, our data suggest that DJ-1 is involved in the generation of new neurons in the adult OB. This impairment of adult neurogenesis may shed a new light on the role of DJ-1 loss-of-function in PD.

P04.03

Antioxidant activity of superoxide dismutases protect dopaminergic neurons against degeneration

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Objective: To date, the cause of the preferential death of nigrostriatal dopaminergic neurons in Parkinson's disease (PD) remains poorly understood. Although PD is considered a multifactorial disorder, experimental evidences suggest that oxidative stress play a central role in the pathogenesis of the disease. In the present study, we investigated the potential protective role of superoxide dismutases (SODs) against oxidative stress conditions in human in human dopaminergic neuroblastoma cells.

Methods: Stable SH-SY5Y cell lines overexpressing either cytosolic (SOD1) or mitochondrial (SOD2) superoxide dismutases were produced and used to evaluate the cellular response to the herbicide paraquat and to disulfiram, an aldehyde dehydrogenase inhibitor which is responsible for DOPAL accumulation in cytosol. After treatment, cell viability was assessed by colorimetric assays and apoptotic response was measured using fluorescence activated cell sorting.

Results: Our data showed that paraquat decreased the viability of wild type cells in a dose-dependent manner. While SOD1 overexpressing cells behaved as control, the overexpression of SOD2 protected cells against the oxidative insult induced by paraquat. Our results suggest that paraquat toxicity is due to production of superoxide radicals at mitochondrial level. A completely different behavior was observed after exposure to disulfiram: cell viability was significantly recovered only in SOD1 overexpressing cells, in agreement with the mechanism of action of disulfiram, which interferes with the metabolism of dopamine, at cytosolic level. In conclusion, our results emphasize the antioxidant protective effect due to SODs, ultimately also with respect to PD-related damages.

P04.04

The role of intramolecular interactions in parkin activation *in vivo*

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Objective: Recent work from our group characterizing the full-length structure of parkin, an E3 ubiquitin ligase implicated in early-onset heritable forms of Parkinson's

Disease, has offered clues as to the intramolecular interactions underlying its basal autoinhibition and activation in response to mitochondrial damage. We sought to examine parkin's ability to translocate to the mitochondrial surface and ubiquitinate substrates *in vivo* to better understand parkin activation in the context of a model pathway for neuroprotective mitochondrial quality control.

Methods: Targeted point mutagenesis was utilized to produce an array of eGFP-fused parkin mutant DNA vectors. HeLa cells were transfected with eGFP parkin constructs and subjected to treatment with the protonophore CCCP at various time points in order to induce mitochondrial depolarization. Subcellular localization of parkin was examined by confocal microscopy and immunofluorescence. Cells were assayed for mitophagy after 24 hours as a downstream readout of parkin enzymatic function.

Results: Analysis revealed abnormalities in parkin recruitment to the mitochondria when interactions within the protein were disrupted by the introduced mutations. Of interest, the S65A mutant in the ubiquitin-like domain (Ubl) shows markedly slower kinetics of mitochondrial recruitment, suggesting that the polarity and/or ability to phosphorylate this residue is necessary to maintain efficiency in parkin translocation. In addition, the PD mutation R275W within the RING1 domain shows a similar phenotype. A common theme arising from our experiments is that the enzymatic activity of parkin as a ubiquitin ligase is intimately tied to its ability to translocate to the mitochondria and carry out its adaptive function, as evidenced by the complete recruitment defect of the active site mutation C431S.

P04.05

Functional compensation of the motor deficits after dopaminergic nigrostriatal system degeneration DIGE analysis of mitochondrial membranes proteins in relation to early Parkinson's disease

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Objectives: First movement disorder signs of Parkinson's disease (PD) are observed after the irreversible loss of almost 70% of neurons in substantia nigra (SN). This proves existence of potent compensatory mechanisms, preventing appearance of the symptoms at the earlier, preclinical stages of disease. Some data indicate that survived neurons increase their activity in order to compensate for the degeneration, so their energy demand is probably higher, therefore the functional adaptation of mitochondria is especially interesting in this aspect.

Methods: We have prepared rat model of selective nigrostriatal dopaminergic system degeneration by injection of 6-OHDA into medial forebrain bundle.

Results: Three days after the operation behavioral analysis revealed decreased locomotor activity in lesioned rats comparing to sham operated controls. Interestingly, 4 weeks post lesion all motor deficits disappeared even though histological verification showed progressing decrease in number of dopaminergic cells in SN by 16% and 41% after 4 days and 4 weeks post lesion, respectively. The dopamine levels decreased first in the striatum by 50% already after 3 days and remained low, while in SN its level dropped by 37% only after 4 weeks. Using solubilised crude mitochondrial membranes fraction from SN we performed differential gel electrophoresis (DIGE) in 2D-BN/SDS gels and identified 23 proteins with significant changes in expression between groups. 7 proteins showed significant changes between lesioned and lesion-compensated groups of animals. The above results indicate involvement of mitochondria in the spontaneous process of functional compensation of dopaminergic system-driven movement disorder.

Acknowledgements: The study was supported by the Statutory Funds of the Institute of Pharmacology, PAS, Kraków, Poland, DAAD scholarship to KK and funding from the Technische Universität Darmstadt.

P04.06

Neuroprotective mechanisms of the Parkinson's disease-related protein DJ-1

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Objective: Dysfunction of the neuroprotective protein DJ-1 has been associated with familial and sporadic cases of PD. Recently we showed that human wild-type DJ-1 protects against different PD stresses via induction of different pro-survival mechanisms. We hypothesize that this behavior may be due to the fact that differences in the subcellular localization of DJ-1 result in the activation of different neuroprotective responses. Methamphetamine (METH), a widely abused drug, can trigger preferential toxicity to dopaminergic neurons by increasing cytosolic dopamine levels leading to formation of dopamine quinone adducts, ultimately generating ROS. Our goal is to characterize DJ-1-mediated protective pathways activated against METH neurotoxicity.

Methods: Rat primary midbrain cultures transduced with adenoviruses encoding WT DJ-1 or the localization mutants MLS- and NLS-DJ-1 (targeting mitochondria and the nucleus, respectively) were incubated in the absence or presence of METH. The cultures were immunostained for tyrosine hydroxylase (TH) and microtubule associated protein 2 (MAP2), and dopaminergic neurite lengths were measured via confocal microscopy. Levels of the autophagosome marker LC3-II and endogenous DJ-1 were determined in METH-treated versus untreated neuronal cells via Western blotting. Flow cytometry analysis was used to study effects of DJ-1 on Nrf-2-mediated transcription.

Results: We found that DJ-1 over-expression protected against neurite loss triggered by METH in primary midbrain cultures, and DJ-1 was up-regulated in METH-treated SH-SY5Y cells. METH induced an increase in autophagic flux in N27 cells, and this effect was potentiated in cells over-expressing DJ-1. Preliminary data also suggest that DJ-1 activates pro-survival pathways including Akt phosphorylation and Nrf-2-mediated transcription in METH-treated cultures. Collectively these data suggest that DJ-1 mitigates METH-induced neurite loss by activating a range of neuroprotective responses. Current efforts are focused on exploring whether DJ-1

must be expressed in glia and/or neurons to alleviate toxicity elicited by METH and other PD-related insults.

P04.07

Membrane recruitment and activity of LRRK2 is important for innate immune cell activation

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Mutations in leucine-rich repeat kinase 2 (LRRK2) are the most common genetic cause of Parkinson's disease, but recent evidence indicates LRRK2 also plays a significant role in monocyte immune cell function. Previously, we demonstrated that membrane-associated LRRK2 dimers are likely the more physiologically relevant subcellular population of LRRK2, but the cellular conditions by which endogenous dimers form, resulting in LRRK2 activation, remain unknown. Here, we show that activation of macrophage or microglial cell lines results in LRRK2 phosphorylation, dimerization and membrane recruitment, which then coincides with iNOS expression and nitrate production. This activation also results in localization to a novel membrane compartment distinct from the location of LRRK2 at rest. Disruption of LRRK2 kinase activity reduces iNOS expression and abolishes phagocytic activity in a macrophage cell line. A parallel analysis of primary human macrophages revealed numerous changes in LRRK2 biochemistry, including a similar membrane recruitment following Toll-like receptor (TLR) activation, as observed in cell lines. This work shows, for the first time, that acute changes in dimerization and membrane localization of endogenous LRRK2 can be linked to a cellular role in monocyte immune cells.

P04.08

Examining the functional interaction of the m-AAA protease AFG3L2 with PINK1

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Objective: PTEN induced putative kinase 1 (PINK1) is known to be endogenously processed first by mitochondrial processing peptidase (MPP) and by presenilin-associated rhomboid-like protease (PARL). However, following the stages of mitochondrial import and cleavage, the basal function of PINK1 and its processed forms are currently not well understood. This study attempts to better understand PINK1 function by characterizing its interaction with a novel protein interactor mitochondrial m-AAA protease AFG3L2.

Methods: In this study, we assessed PINK1 and AFG3L2 protein levels in various tissues and the interaction of PINK1 with AFG3L2. Using an AFG3L2 knockout mouse model, the effect of AFG3L2 loss upon PINK1 processing and protein levels in murine neuronal and fibroblast cell models were examined. Via immunocytochemistry, we observed mitochondrial morphology in AFG3L2 deficient fibroblasts after PINK1 overexpression and assessed Parkin translocation in AFG3L2 deficient cortical neuronal cultures.

Results: Interestingly, with similar protein levels of PINK1 and AFG3L2 found in all tissues analyzed, knockout of AFG3L2 shows decreased processed PINK1 isoforms and total PINK1 levels in mouse embryonic fibroblasts and cortical neuronal cultures

examined. Decreased processed PINK1 was also confirmed in human cell line HeLa cells with siRNA mediated AFG3L2 knockdown. In fibroblasts examined, the fragmented mitochondrial phenotype observed with AFG3L2 deficiency could not be rescued by full-length PINK1 over-expression. However increased translocation of Parkin, known to be associated with clearance of damaged mitochondria, was observed in stressed AFG3L2 deficient primary cortical neuronal cultures. Taken together, these results suggest that AFG3L2 is involved in PINK1 processing and may play a role in the regulation of PINK1 mediated mitochondrial clearance. Work is currently underway to identify AFG3L2 mediated cleavage products of PINK1. Results obtained from these and other experiments will also be presented.

P04.09

Inhibition of NADPH oxidase by Apocyanin alternatively prevents microglia induced neuroinflammation in Lipopolysaccharide induced Parkinson's disease model

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Objective: Recent studies have revealed an essential role for neuroinflammation that is initiated by microglial and infiltrated peripheral immune cells and their toxic products (cytokines, chemokines etc) in pathogenesis of Parkinson's disease. Lipopolysaccharide, a bacterial endotoxin is the most extensively utilized glial activator for the induction of inflammatory dnergic neurodegeneration.

Method: To establish the neuroprotective efficacy of apocyanin a NADPH oxidase inhibitor in inflammation driven animal model of PD. LPS at a dose of (5ug/5ul PBS) injected stereotaxically into the Substantia Nigra of rat brain was utilised for the establishment of PD model. Apocyanin was administered at a dose of 10mg/kg b.wt for a period of 21 days.

Results: LPS injection leads to microglial activation and hence increased level of pro-inflammatory cytokines and activation of NADPH oxidase complex leading to excessive superoxide anion production which combines with NO to form OONO- and other ROS/RNS species which further results in neurotransmitter dopamine loss and behavioural impairment. Apocyanin significantly lowered the production of superoxide anions which was further supported by decreased NADPH oxidase activity and suppressed expression of various NADPH subunits gp91(phox), p47(phox). It significantly decreased microglial activation and suppressed mRNA expression of various proinflammatory cytokines (TNF- α , IL-1 α , β , IFN- γ , IL-6), NO/iNOS in mid brain region hence, prevented neurotransmitter dopamine loss and resulted behavioural impairment. Histopathological studies also indicated the neuroprotective efficacy of apocyanin in PD. Since apocyanin treatment attenuated ROS production which alternatively leads to decreased cytokine production and iNOS in response to LPS further strengthened the notion that Phox-derived ROS are crucial for proinflammatory gene expression in glial cells. Thus, its supplementation can prove to be beneficial for curing PD.

P04.10

Paraquat and diquat induced-toxicity in PC12 cells is mediated through the generation of intracellular reactive oxygen species and dysregulation of redox regulated pathways

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Objective: Recent epidemiological and toxicological studies have shown that environmental factors especially, pesticides such as paraquat (PQ) and diquat (DQ) represent one of the primary classes of neurotoxic agents associated with PD. The objective of our study was to investigate the toxic effects of PQ/DQ mixture and elucidate the mechanisms involved in their toxicity in rat dopaminergic PC12 cell line.

Methods: Cell survival in PC12 cells was measured by XTT, LDH and Resazurin assays. Intracellular reactive oxygen species (ROS) and superoxide levels were measured by using the fluorescent dyes 2', 7'-dichlorofluorescein-diacetate (DCF-DA) and MitoSox red respectively. Levels of different redox-regulated proteins were measured by western blot analysis.

Results: Our results show that a treatment with PQ/DQ mixture (80.0 μ M/60.0 μ M)-induced approximately 50% cell death in PC12 cells. Besides, PQ/DQ mixture also generated intracellular ROS and increased mitochondrial superoxide levels. PQ/DQ treatment activated the Akt, glycogen synthase kinase 3beta (GSK3beta), nuclear factor E2-related factor2 (Nrf2) pathway however their activation could not prevent the down regulation of glutamylcysteine synthetase (-GCS), thioredoxin1 (Trx1), and tyrosine hydroxylase (TH) indicating that other redox-regulated transcription factors may also be involved in their regulation. PQ/DQ-treatment also induced the expression of heat shock protein70 (HSP70) and 90 (HSP90). Thus, our findings demonstrate that PQ/DQ-induced toxicity in dopaminergic cells is mediated through generation of oxidative stress and dysregulation of various cellular redox pathways and their modulation with antioxidants could have a therapeutic application in the treatment of PD.

P04.11

Mutant LRRK2 expression induces calcium dysregulation and dendritic mitophagy

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Objective: Parkinson's disease (PD) is the second most prevalent neurodegenerative disease. The most common known genetic cause of PD is mutation of the gene for leucine-rich repeat kinase 2 (LRRK2). Expression of the PD-associated G2019S and R1441C LRRK2 mutants has been shown to cause neurite shortening, though the mechanism of injury has not been delineated. Because disruptions in normal mitochondrial function and dynamics have been linked to PD pathophysiology and LRRK2 has been shown to partially localize to mitochondria, we investigated whether mutant LRRK2 expression disrupts mitochondrial homeostasis.

Methods: Mouse cortical neurons, or differentiated SH-SY5Y cells were transfected with eGFPc-1, COX8-GFP or GFP-LC3, and wild type or mutant LRRK2-HA constructs. Cells were incubated in Fura2-AM and imaged to analyze calcium handling. Mitochondrial content and number of autophagosomes were quantified. In some experiments, autophagy levels and mitochondrial content were measured following treatment with a calcium chelator or voltage gated calcium channel inhibitors. Mitochondrial trafficking was analyzed by measuring the mobile fraction and anterograde/retrograde velocity of dendritic mitochondria.

Results: We found a selective loss of dendritic mitochondrial content that could be prevented by inhibiting autophagy. This

dendritic mitophagy preceded dendrite shortening in neurons expressing mutant LRRK2. There were no significant effects on mitochondrial transport kinetics. Mitochondrial dysfunction, in the form of disrupted calcium handling occurred upstream of mitophagy and dendrite retraction. In further support of a possible primary role for mitochondrial dysfunction in LRRK2-mediated pathogenesis, overexpression of the mitochondrial PD-linked kinase PTEN-induced kinase 1 (PINK1) prevented LRRK2-induced pathology. Modulation of intracellular calcium levels prevented mutant LRRK2 mediated mitophagy and dendrite retraction. These data suggest that maintenance of calcium homeostasis may be an effective therapeutic intervention for PD, and studies to further delineate the neuroprotective or "mitoprotective" role of PINK1 are underway.

BASIC SCIENCE: PATHOLOGY

P05.01

Striatal pathology in Parkinson's disease and dementia with Lewy bodies is associated with small α -synuclein aggregates

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Objective: A common feature of neurodegenerative disorders such as Parkinson's disease (PD) or dementia with Lewy bodies (DLB) is the deposition of misfolded proteins present in the brain. One of these proteins, the cytosolic protein α -synuclein, appears in the form of aggregates in Lewy bodies, a hallmark of PD and DLB. It was recently shown that large amounts of small α -synuclein aggregates outside of Lewy bodies are located at presynaptic terminals in DLB cases, leading to the hypothesis that these small aggregates cause neurodegeneration in DLB. In the present study, we investigated in more detail the significance of small aggregates of α -synuclein for the pathogenesis of neurodegenerative diseases. To test the possibility that striatal α -synuclein pathology is caused by these aggregates, we analyzed the accumulation of misfolded α -synuclein in brain tissue from the caudate nucleus from PD and DLB patients and compared them with other brain regions.

Methods: The appearance and amount of α -synuclein aggregates were determined in different subcellular fractions of brain homogenates using the previously established protein aggregate filtration (PAF) assay. The different brain samples were further analyzed with paraffin-embedded tissue (PET) blots.

Results: We were able to show striatal pathology in PD as well as DLB cases due to the detection of small α -synuclein aggregates in the caudate nucleus. Based on these results we propose that this particular α -synuclein pathology in the basal ganglia may contribute to the clinical features observed in these diseases. Furthermore, we detected in all other analyzed brain samples much higher amounts of small α -synuclein aggregates than Lewy bodies, confirming that these small aggregates play an important role in the pathological mechanism of PD and DLB.

P05.02

High Cortical LB burden and A β pathology in Lewy Body Dementia and Parkinson's disease Dementia

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Objectives: We studied a large sample of patients-donors to the Parkinson's UK Brain Bank, with Lewy Body dementia (LBD), Parkinson's disease Dementia (PDD) and Parkinson's disease without clinical evidence of dementia (PDnD) to evaluate the neuropathologic substrates of dementia in LBD and PDD. Clinical, neuropathological and genetic data were utilised to assess the respective roles of Lewy body pathology, A β burden and tau load, as well as of the MAPT and APOE genotypes on the development of dementia in LBD and PDD.

Methods: 122 cases (56 PDD, 17 DLB and 49 PDND) with a neuropathological diagnosis of Parkinson's disease and reliable clinical information on dementia status were included in the analysis. We carried out topographical and semi-quantitative assessment of cortical and striatal LB, A β plaques and tau-positive neuropil threads. APOE genotype and MAPT haplotype status were determined.

Results: DLB cases had a significantly higher LB burden in parietal and temporal cortex compared to PDD; DLB cases were also characterized by a higher cortical and striatal A β plaque burden compared to PDD. Higher cortical loads of both LB and A β plaques were associated with a faster progression to dementia. Cortical LB body burden was the only independent neuropathological determinant of dementia in multivariate analysis. Total cortical A β plaque burden was an independent predictor of a shorter latency to dementia from onset of motor symptoms. APOE E4 carrier status was strongly correlated with a higher cortical LB burden. The presence of high cortical LB burden is the key neuropathological substrate of dementia in DLB and PDD. Similarly, cortical A β plaques are associated with a faster progression to dementia from the onset of motor symptoms, with a gradient of severity parallel to the one we see in LB, differentiating LBD from PDD and these forms from PD without dementia.

BASIC SCIENCE: ANIMAL AND CELLULAR MODELS OF PARKINSONISMS

P06.01

Effects of deep brain stimulation on impulsive choice and action in a rat model of early Parkinson's disease

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Objective: Deep brain stimulation (DBS) is effective for the motor symptoms of Parkinson's disease (PD), but has been associated with increased impulsivity. A critical question is whether the impulse control problems result from the treatment per se, or from interactions with the underlying PD neuropathology and/or concomitant dopamine replacement therapy. Here we utilized intact and PD-like rats trained to perform a rat gambling task (rGT), which models two distinct facets of impulsive behaviour, impulsive choice (rGT choice distribution among four holes with different reinforcement schedules), and impulsive action (rGT premature responding).

Methods: After initial rGT training, rats (n=45) underwent bilateral stereotaxic surgeries: 6-OHDA/vehicle microinfusions into the dorsolateral caudate putamen (dLCPu), as well as electrode implantation into the subthalamic (STN) or entopeduncular (EPN) nuclei. Animals were then retested for 14 days, with EPN- or STN-DBS (100µA, 90µs, 130Hz) administered daily for 2 hours prior to rGT testing to separate animal cohorts.

Results: Chronic EPN- or STN-DBS had no effect on rGT choice behaviour, suggesting that stimulation does not seem to disrupt the ability to identify and avoid high-risk options, on its own or in a PD-like background. Moreover, EPN-DBS did not affect, whereas STN-DBS tended to decrease, rGT premature responding in both intact and dopamine-lesioned animals ($p > 0.05$).

Significance: While we previously demonstrated that STN-DBS at lower intensities (12.5 µA) significantly increased rGT premature responding in intact animals, stimulation at 100µA failed to produce the same impulse control deficit, and in fact, tended to improve rats' ability to withhold premature responses. Our work suggests that DBS is not intrinsically associated with increases in impulsivity in normal or PD-like rats, and the effects of high-frequency stimulation on impulse control might be amplitude-dependent. Future studies systematically evaluating chronic stimulation with various current intensities would help establish the link between DBS and impulsivity.

Funding Source: L.A. is the recipient of a Studentship from the Ontario Problem Gambling Research Centre.

P06.02

Identification of cis- and trans-regulatory elements and signaling pathways in parkin gene expression — A genomic fugu parkin model

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Objective: Wild-type human Parkin protein confers several protective effects to prevent cell damage and neuronal death. Therefore, increasing the expression of Parkin might be helpful in preventing or treating Parkinson disease (PD). To date, the most promising signaling mechanism is mediated through ATF4 function [Bouman et al., 2011]. The overall goal of this study is to identify regulatory elements and signaling pathways involved in the up-regulation of Parkin gene expression at the PARK2 locus.

Methods: Identifying cis- and trans-regulatory elements of the human Parkin gene has been problematic because of its large size

(~1.4 Mb; the second largest human gene). We took advantage of the previously identified orthologue of PARK2 in fugu fish (fugu parkin), which is highly similar to human Parkin in genomic organization, tissue expression and protein function, and considerably smaller (~4.5 Kb) [Yu et al., 2005].

Results: We successfully cloned genomic fugu parkin tagged with a reporter (firefly luciferase or eGFP). A strong repressor element was detected in the -820 bp to -311 bp region of the 5'-flanking region of fugu parkin. We also determined that intron 1 was essential for reporter gene activation. Accordingly, a 310 bp-long 5' flanking region encompassing the putative promoter (with the repressor removed) and containing intron 1 effectively facilitated the transcription of fugu parkin. Moreover, we generated several hybrid constructs in which human PARK2 5'-flanking sequences of various lengths were cloned upstream of the start codon of fugu parkin's genomic DNA. These permitted the identification of previously unrecognized signature response elements and a specific transcription factor-linked signaling pathway, which is independent upon ATF4, that led to the expression of our reporter constructs. The relevance of this pathway in PARK2 activation under select stress conditions was confirmed for endogenous Parkin in neural (SH-SY5Y) and non-neural (CHO) cell cultures.

P06.03

Molecular mechanisms of neurodegeneration in the *En1*^{+/-} mouse model of Parkinson's disease

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Background and Objective: Most rodent models of Parkinson's disease (PD) fail to replicate the slow degeneration of midbrain dopamine (DA) neurons. Mice with a heterozygous deletion of the gene encoding engrailed (*En*) 1 were recently found to exhibit a phenotype with some features resembling PD. These *En1*^{+/-} mice display slow degeneration of substantia nigra DA neurons starting a few weeks after birth (with ventral tegmental area DA neurons only mildly affected), striatal DA depletion, and motor dysfunction. In the present study, we investigated the molecular mechanisms of neurodegeneration in the *En1*^{+/-} mice.

Methods: Dopaminergic nigrostriatal degeneration was assessed by tyrosine hydroxylase immunohistochemistry and stereological method. HPLC analysis was used to measure DA levels in the striatum. We also used amperometric techniques to monitor DA release and reuptake in axonal terminals in the striatum.

Results: We found that nigral DA neurons in *En1*^{+/-} mice exhibit synaptic terminal dysfunction and degenerate retrogradely. Thus, we identified that some of the axons of the degenerating nigrostriatal DA neurons in *En1*^{+/-} are swollen in the striatum as early as post-natal day 15, preceding the death of the neurons. We also observed a mild, but significant, reduction in striatal DA levels and a loss of nigral DA cell bodies at 8 weeks of age. Interestingly, we monitored a dramatic (>90%) decrease in potassium-evoked DA release and DA reuptake in synaptic terminals in the most dorsal striatum of *En1*^{+/-} mice at 16 weeks of age, whereas in the ventral striatum the same parameters were unchanged compared to control mice.

Conclusion: Taken together, our observations suggest that in *En1*^{+/-} mice a specific subset of nigral neurons innervating the most

dorsal parts of the striatum exhibits dysfunctional terminals and axonal swelling starting during the first two months of age and die after a few additional weeks.

P06.04

The group II p21-activated kinases as therapeutic targets in LRRK2-related Parkinson's disease

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Several missense mutations in *LRRK2* (coding for the protein Leucine Rich Repeat Kinase 2) are associated with a familial form of Parkinson's disease similar to the sporadic syndrome. Despite intense efforts, information on the physiological and pathological function(s) of LRRK2 is incomplete. Because LRRK2 mutations lead to neuronal cell death in a kinase-dependent manner, LRRK2 kinase activity is an attractive pharmacological target for PD. However, current knowledge of the physiological role of LRRK2 kinase suggests that it controls several functions, not all linked to disease. Of note, LRRK2-kinase inhibitors induce a decrease of LRRK2 basal phosphorylation at a cluster of serines (Ser910, 935, 955 and 973), which regulates 14-3-3 binding and LRRK2 cytoplasmic localization. Interestingly, phosphorylation at these sites is disrupted in the context of several Parkinson's disease associated mutations (R1441G/C, Y1699C, and I2020T) as well as the binding with 14-3-3. To gain insights into LRRK2 function, we performed a proteoarray screen for LRRK2 specific binding partners and identified p21-activated kinase 6 (PAK6) as a robust interactor. In the nervous system, PAKs are abundantly expressed and have been implicated in diverse cellular functions including neurite and synapse formation. Subsequent validation of LRRK2:PAK6 interaction with biochemical and imaging techniques demonstrated that: (i) LRRK2 efficiently interacts with group II PAKs at the actin cytoskeleton; (ii) PAKs induce LRRK2 de-phosphorylation at Ser910 and Ser935 in a kinase dependent manner; (iii) PAKs-dependent LRRK2 de-phosphorylation induces LRRK2 cellular relocalization. We are currently evaluating how PAK6 activity impacts mutant-LRRK2 mediated neurotoxicity. Given the role of Ser910-935 phosphorylation in LRRK2 pathological function and the observed effect of the Group II PAKs, inhibition of this class of kinases has the potential to specifically target pathological LRRK2 function, thus providing a new avenue for PD therapeutics.

P06.05

A reverse engineered Parkinson's disease gene regulatory network identifies RGS2 as a direct modulator of LRRK2 activity

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Objective: To elucidate the gene regulatory networks linked to *LRRK2*, and identify key proteins regulating *LRRK2* function.

Methods: Systems biology algorithms were applied to reverse-engineer a genome-wide *LRRK2*-centered regulatory network based on transcriptomes obtained from human Parkinson's disease (PD) brain and blood cells. Our *in silico* network identified approximately 600 genes whose expression levels are highly coordinated with those of *LRRK2*. To determine the extent to which these genes modify the function of *LRRK2 in vivo*, we performed an RNAi high-throughput screen on *C. elegans* expressing wild type human *LRRK2* in a pan-neuronal manner. 280 (40%) of our systems biology-predicted interactors were found to modify *LRRK2*-mediated dopamine (DA) neuron survival.

Results: We focused particularly on *RGS2* (regulator of G-protein signaling 2) because it exhibited co-regulation with a number of PD-linked genes, including *LRRK2*, *Parkin*, *PINK1* and *DJ-1*. We observed that *RGS2* and *LRRK2* interact *in vitro* in mammalian cells and *in vivo* in human striatum. *RGS2* was found to stimulate the GTP hydrolysis activity of *LRRK2* whilst inhibiting its kinase activity. *RGS2* expression in primary cortical neurons rescued the neurite shortening phenotype induced by the PD-associated mutant G2019S *LRRK2*. Finally, we observed that protein levels of *RGS2* were significantly decreased in striata from subjects with *LRRK2*-associated and sporadic PD. Taken together, these results point to a role of *RGS2* as a direct regulator of *LRRK2* GTPase activity and associated neuronal toxicity.

P06.06

Altered Alpha Synuclein degradation and augmentation of Parkinson disease phenotype in a transgenic mouse model

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Objective: The involvement of the protein α -Synuclein (*Snc*) in the pathogenesis of Parkinson's disease (PD) has been well documented. Heterozygous carriers of Gaucher disease mutations, who are otherwise healthy, have an increased risk for PD. Since mutations in the gene encoding for the Glucocerebrosidase (*Gba*) enzyme are known to reduce degradation of some proteins in the lysosome, it has been suggested that reduced *Snc* degradation might facilitate its accumulation and aggregation. In this study we investigated the half-life of *Snc* in neurons. We also asked how it might be affected by a Gaucher mutation, and what impact that would have *in vivo* in a PD mouse model.

Methods: We used cultured primary cortical neurons generated from mice expressing wildtype mouse *Snc*, wildtype human *Snc* or A53T *Snc*, in a background of either wildtype *Gba* or heterozygosity for the p.L444P *Gba* mutation. We also tested these double transgenic mice for behavioral and biochemical PD related phenotypes.

Results: We found that *Snc* is very stable, with a $t_{1/2}$ = ~60 hours for both the wildtype and A53T human protein in culture, while the mouse protein had an even greater $t_{1/2}$ of ~140 hours. Heterozygosity for the Gaucher mutation reduced *Gba* activity by ~40%, reduced *Snc* degradation and triggered accumulation of the protein in culture. This mutation also prompted the augmentation of motor and gastrointestinal deficits found in the A53T mouse model of PD, albeit only when mice reached an advanced age. This study demonstrates that heterozygosity for mutations in *Gba* interferes with *Snc* degradation and contributes to accumulation of the

protein. We have created a mouse model for the interaction between *GBA* mutations and synucleinopathies, thereby strengthening the *Gba* enzyme as a potential therapeutic target for PD.

P06.07

Investigating the impact of α Synuclein overexpression in human neurons with a novel viral system

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Objective: α Synuclein (α Syn) plays a critical role in the pathogenesis of Parkinson's disease (PD). It is implicated in both familial and sporadic forms of the disease. Duplication and triplication of the α Syn gene, *SNCA*, causes autosomal dominant, early-onset PD, with triplication patients exhibiting a more aggressive course of the disease. This indicates that levels of α Syn impact directly on disease pathogenesis. α Syn is a natively unfolded protein that adopts an α -helical structure when bound to lipid membranes. However, under pathological conditions it aggregates into reportedly toxic small oligomers and insoluble fibrillar structures that are stabilized by β -sheet-like interactions. In this study, we have generated a novel α Syn viral delivery system to investigate the impact of α Syn overexpression in PD-relevant human neurons.

Methods: We exploited a modified baculovirus system (BacMam 2.0) that can efficiently overexpress proteins in human post-mitotic cells. We used the BacMam virus to deliver a polycistronic transgene encoding mitochondrially-targeted emerald-GFP (emGFP) and human α Syn in the same cell. Using different viral doses we infected the neuroblastoma cell line, SH-SY5Y, and assessed emGFP expression by FACS and α Syn expression by immunostaining. We will investigate aggregates formation, and α Syn post-translational modifications. Impact on mitochondrial function will be assessed including measurements of mitochondrial respiration, ATP production, membrane potential, dynamic movement as well as fusion and fission. The aforementioned investigations will also be carried out using forebrain glutamatergic and midbrain dopaminergic neurons derived from induced pluripotent stem cells (iPSCs) from a PD patient carrying a triplication of *SNCA*, and an allelic series of transgenic human embryonic stem cell (hESC) lines overexpressing varying levels of α Syn.

Results: The BacMam system allows efficient (97%) transduction of differentiated SH-SY5Y human dopaminergic neuroblastoma cells, and a dose-dependent level of overexpression was achieved using different titers of the virus with no apparent cytotoxic effect.

P06.08

Synergistic effects of mGluR5 antagonism and 5-HT1A/1B agonism in a rat model of L-DOPA-induced dyskinesia

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Objective: L-DOPA-induced dyskinesia (LID) in Parkinson's disease is driven by both pre- and postsynaptic alterations in dopamine (DA) transmission, and it is modulated by several non-dopaminergic transmitters. Emerging pharmacological strategies for the treatment of LID include negative modulation mGluR5 and positive modulation of serotonin autoreceptors 5-HT1A/1B. These strategies are assumed to act through different mechanisms, and to be associated with different profiles of untoward effects. We set out

to determine whether the two strategies in combination may provide synergistic therapeutic benefits.

Methods: The study was performed in 6-OHDA-lesioned rats chronically treated with either L-DOPA or the D1 receptor agonist, SKF38393 in order to induce abnormal involuntary movements (AIM). Rats with stable AIM scores received challenge doses of either the mGluR5 antagonist, MTEP (2.5 and 5 mg/kg), or the 5-HT1A/1B agonists 8-OH-DPAT/CP94253 (0.035/0.75 and 0.05/1.0 mg/kg). The two categories of drugs were given either alone or in combination.

Results: In agreement with previous studies, 5 mg/kg MTEP and 0.05/1.0 mg/kg 8-OH-DPAT/CP94253 significantly reduced L-DOPA-induced AIM scores (reduction of peak AIM scores by 37% and 34 % respectively). The two treatments in combination achieved a greater effect than each treatment alone (- 66%). Moreover, a significant attenuation of L-DOPA-induced AIM scores was achieved when combining doses of MTEP (2.5 mg/kg) and 8-OH-DPAT/CP94253 (0.035/0.75 mg/kg) that did not have a significant effect if given alone. Neither combination treatment had a negative impact on the improvement produced by L-DOPA in tests of forelimb akinesia (cylinder test) or global motor dexterity (rotarod test). SKF38393-induced AIM scores were reduced by 5 mg/kg MTEP (- 56%) but not by 0.05/1.0 mg/kg 8-OH-DPAT/CP94253.

These results indicate that combining negative modulators of mGluR5 with positive modulators of 5-HT1A/1B receptors may achieve synergistic antidyskinetic effects without interfering with the antiakinetin effects of L-DOPA.

P06.09

Positive allosteric modulators of mGluR4 can synergize with L-DOPA in alleviating motor abnormalities in a rodent model of Parkinson's disease

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Objective: Metabotropic glutamate receptor type 4 (mGluR4) is a potential therapeutic target for treating motor symptoms in Parkinson's disease. This receptor is expressed selectively in the output structures of the indirect pathway where it has a presynaptic location and negatively regulates both GABA and glutamate release. Considerable effort has gone into the discovery of positive allosteric modulators of mGluR4, that can enhance the effects of the receptor once its endogenous ligand (glutamate) is bound to the receptor active site. It is only recently that selective ligands for mGluR4, have become available and very few of these compounds are systemically active. One of these compounds, ADX88178 has been shown to reverse haloperidol-induced catalepsy in intact rats, and to potentiate the effect of L-DOPA on measures of forelimb use in rats with 6-OHDA lesions, without exacerbating L-DOPA-induced dyskinesia (Le Poul E., et al., J Pharmacol Exp Ther 2012, 343(1):167-77).

Methods: In the present study, we investigated whether ADX88178 co-administered with low doses of L-DOPA (that do not induce dyskinesia) can achieve comparable therapeutic effects to a high dose of L-DOPA. ADX88178 was given alone or in combination with sub-threshold doses of L-DOPA in rats with unilateral 6-OHDA lesions of the medial forebrain bundle (MFB). Animals were assessed on two different behavioural tests: drug-induced rotation and overall motor performance on the rotarod.

Results: We found that ADX88178 (30 mg/kg, p.o.) potentiated the effect of the low dose of L-DOPA on peak rotational activity. In the rotarod test the combination treatment was the only treatment that

induced a significant increase in motor performance (40% above baseline). The use of mGluR4 modulators is receiving increased attention as an approach to treat Parkinson's disease. These data further validate the potential of mGluR4 PAM for the treatment of motor symptoms of Parkinson's disease.

P06.10

Evaluation of anti-parkinson activity of methanolic extract of *Hyoscyamus Niger* seeds in stereotaxically induced rotenone rat model

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Objective: To evaluate anti-parkinson potential of methanolic extract of *Hyoscyamus Niger* seeds (MHN) in stereotaxically induced rotenone rat model of Parkinson's disease.

Methods: In the present study we have evaluated anti-parkinson potential of methanolic extract of *H. niger* seeds in stereotaxically induced rotenone rat model of parkinson's. Air dried authenticated *H. niger* seeds were extracted using methanol and were characterized by HPLC-UV and LCMS. Extract showed presence of L-dopa with significant inhibition in DPPH, ABTS assay and monoamine oxidase activity. Rotenone was injected unilateral in substantia nigra pars compacta (SNpc) to induce Parkinson. Male Wistar rats were pretreated with MHN (125, 250, 500 mg/kg body weight p.o.) twice daily for 7 days and after the induction for 21 days. Three weeks after rotenone infusion, rats were tested for neurobehavioral (actophotometer, rotarod and Morris water maze test) activity, estimation of lipid peroxidation (TBARS), glutathione content, and activity of antioxidant enzymes like glutathione peroxidase [GPx], glutathione reductase [GR], catalase [CAT], and superoxide dismutase [SOD]. The standard antiparkinson drug used was L-dopa.

Results: The methanolic extract of *H. niger* seed shows considerable anti-parkinson activity by attenuated motor disabilities (actophotometer, rotarod and Morris water maze test) and increased level of antioxidants in the different group of treatment.

P06.11

Human cathepsin D does not enhance synucleinase activity in wild-type and SNCA-transgenic mice

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Background: Parkinson's disease (PD) is characterized by Lewy inclusion formation and cell loss. Alpha-Synuclein (SNCA) is the main constituent of Lewy bodies and its prefibrillar aggregation is thought to promote neurotoxicity. Three laboratories including ours recently demonstrated that over-expression of human cathepsin D (CTSD) cDNA in dopaminergic cells promotes the degradation of excess SNCA. This result identified in CTSD a potential target to lower SNCA.

Objectives and Methods: To determine whether an increase in CTSD activity promotes lysosomal 'synucleinase' activity *in vivo*, we generated *hCTSD*-transgenic (tg) mice. We furthermore generated *hCTSD*/*SNCA* double-transgenic mice to observe whether *hCTSD* over-expression reduces synucleinopathy in *SNCA* tg mice. There, we used two different models, i.e., "line D" of Masliah et al.

(Science, 2000) and a PAC1-SNCA A53T line of Kuo et al. (Hum Mol Genet, 2010).

Results: We confirmed the generation of *hCTSD* over-expressing animals by Southern, Northern and Western blotting, as well as immunohistochemistry. A CTSD activity assay revealed a 27% and 31% increase in single tg mice between the ages of 9 and 18 months. Unexpectedly, Western blots and sensitive ELISA analyses for SNCA levels in brain lysates did not show any difference between single tg mice and controls at the age of 9 and 18 months. We also performed quantification of SNCA by ELISA and Western blotting using lysosomal fractions of whole brains from double transgenic mice at the age of 6 months. Despite the 1.9 x fold enhancement of the enzymatically active CTSD form, we failed to detect any significant SNCA (and total Tau) differences in lysosomal fractions from tg versus control mice.

Conclusions: In contrast to our hypothesis, a 30% increase in neuronal CTSD activity did not lower the total concentration of mouse or human SNCA *in vivo*.

P06.12

Investigating the process of axonal degeneration in the striatal 6-hydroxydopamine lesion model of Parkinson's disease

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Objective: The 6-hydroxydopamine (6-OHDA) lesion is the classic model of Parkinson's disease (PD) in experimental animals. Functioning as a specific neurotoxin for dopamine (DA) neurons, 6-OHDA causes intracellular oxidative stress, and leads to axonal degeneration and neuron death. This pattern of neurodegeneration has been shown to be a primary aspect of the etiology of PD. To better understand this process, we are using this lesion model to investigate the progression of retrograde axonal degeneration.

Methods: To do this, striatal axons were visualized independent of the phenotypic marker for DA neurons (tyrosine hydroxylase (TH)) with green fluorescent protein (GFP) delivered with recombinant adeno-associated virus (rAAV). The cells of the substantia nigra pars compacta (SNpc) were transfected via intracranial injection. GFP transfected rats were given unilateral injections of 6-OHDA in the striatum to initiate axonal degeneration, to mimic the progression seen in human PD. Animals were sacrificed in a time course of 1, 3, and 7 days to allow for analysis of the rate and extent of the axonal degeneration throughout the striatum.

Results: Sagittal tissue sections will be analysed with respect to the density of axonal fibers in the striatum as well as number of remaining neurons in the SNpc expressing and not expressing TH. The results of this study will hopefully lead to the ability to use this classic 6-OHDA lesion model of PD as a new model of axonal degeneration. By using an early time course and possibly lower doses of 6-OHDA, the factors of synaptic degeneration and retrograde axon retraction will be studied before neuron death occurs. These findings would be very valuable to the study of PD as it is believed that the early loss of axonal DA synapses is the first symptomatic event of PD progression.

P06.13

Longitudinal in vivo imaging in a novel model of Parkinson's disease in minipig

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Objective: The ubiquitin proteasome system is the main intracellular pathway for protein degradation and its dysfunction has been implicated in the pathophysiology of Parkinson's disease (PD). Direct intracerebral injection of proteasome inhibitors can provide a progressive model of parkinsonism. Here we translate this approach to an animal model, with a large brain and the ability to express complex behaviors, and investigate the longitudinal effects of chronic exposure to a proteasome inhibitor on monoaminergic projections using *in vivo* imaging.

Methods: Four female Göttingen minipigs were implanted in the cisterna magna with a catheter connected to a subcutaneous titanium injection port. After recovery, we performed positron emission tomography at baseline (after saline injections through the access port) with C-11 labeled dihydrotetrabenazine (DTBZ, a vesicular monoamine transporter type 2 tracer) and yohimbine (a selective alpha2 adrenoceptor tracer). Pigs received multiple doses of 20 or 50 micrograms of the proteasome inhibitor lactacystin dissolved in saline through the access port, and were imaged over a one-year period. Data were analyzed using standard Logan graphical analysis to determine the binding potential of DTBZ and the volume of distribution of yohimbine.

Results: Mild initial symptoms including bradykinesia, freezing, and weakness of hindlimbs, progressed over time. Striatal DTBZ binding decreased on average by 35% after 4-6 injections of the proteasome inhibitor, and remained decreased by 26% after one year. Yohimbine volume of distribution was increased early, by 15-25%, in various cortical and thalamic brain regions after the 3rd lactacystin injection, and remained increased by 30-40% after one year. Decreased striatal binding of DTBZ is consistent with previous studies in human PD and animal models. Increased yohimbine volume of distribution suggests early noradrenergic deficits consistent with recent hypotheses that noradrenergic cell loss occurs early in PD.

P06.14

Functional LRRK2 genetic interaction screen in *Drosophila*

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Objective: Using the UAS-GAL4 over-expression system we previously published a LRRK2 PD model in *D. melanogaster*. This fly showed loss of DA neurons and locomotor deficits when human (h) LRRK2 mutants were expressed under a DA promoter.

Additionally, a damaged eye phenotype was observed upon expression of hLRRK2 in the compound eye under the GMR promoter (Venderova *et al.*, HMG 2009). We elucidated putative hLRRK2 genetic interactors by conducting a functional suppressor/enhancer screen *in vivo*.

Methods: We genetically crossed commercially available genomic deficiency lines with the GMR-hLRRK2 fly. This allows us to screen for potential LRRK2 interactors, which modify the LRRK2 eye phenotype by suppression/enhancement. These preliminary interactors are then examined for phenotypic modification under a DA promoter.

Results: We have elucidated specific genetic interactors implicating LRRK2 in, amongst others, immune function, vesicular trafficking, cell cycle, mitochondrial function, and cell signaling pathways. Our screen has elucidated LRRK2 genetic pathways that may be key to understanding LRRK2 biology and therefore PD pathogenesis.

Financial Disclosure: Funding was provided by MJFF, CIHR, PSC and PRC.

P06.15

Intrastratial injection of pre-formed α -synuclein fibrils initiates the formation of Lewy body-like intracellular inclusions and nigrostriatal degeneration in naïve rats

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Objective: Previous studies have demonstrated that injections of fibrillar forms of alpha-synuclein (α -syn) into the mouse striatum can induce Parkinson's-like Lewy pathology in anatomically interconnected regions and ultimately results in significant neurodegeneration of the nigrostriatal system. The aim of this study was to evaluate whether intrastratial injection of exogenous pre-formed α -syn fibrils (PFFs) into naïve rats would result in similar Lewy body (LB)-like intracellular inclusions and neurodegeneration. The establishment and characterization of a rat model of α -syn PFF-induced toxicity would provide a valuable research tool for the therapeutic development

Methods: Thirty-six male *Sprague Dawley* rats received unilateral intrastratial injections of either monomeric or PFF mouse α -syn in one or two sites (8 μ g total). Rats were sacrificed at 30, 60 or 180 days post injection to assess the temporal progression of α -syn pathology. Animals were subjected to monthly behavioral tests to determine temporal course of motor disability. Upon sacrifice, brains were processed for immunohistochemistry and levels of striatal dopamine and metabolites.

Results: At 30 and 60 days post-injection, α -syn PFF rats and not monomeric α -syn controls, exhibited hyper-phosphorylated α -syn intraneuronal accumulations (i.e., diffuse Lewy neurite (LN)- and LB-like inclusions) in several areas interconnected with the striatum, most prominently in the frontal and piriform cortices, the amygdala, and substantia nigra. Furthermore, α -syn pathology in PFF-rats colocalized with ubiquitin, indicating that they share common properties with LBs/LNs. At the 60-day time point, a slight reduction of tyrosine hydroxylase immunoreactive neurons in the ipsilateral substantia nigra was observed. Ongoing quantitative assessment will determine the magnitude of nigrostriatal degeneration; however, behavioral results do not indicate significant deficits at this time point. Our results thus far, parallel findings in wild-type mice in which α -syn PFFs are sufficient to seed the pathological conversion of endogenous α -syn and induce a progressive, neurodegenerative model of α -synucleinopathy in rats.

Financial Disclosure: Supported by the Morris K. Udall Center of Excellence for Parkinson's disease Research at Michigan State University (TJC).

P06.16

LRRK2 interacts and phosphorylates Synapsin I: implication for synaptic vesicle trafficking

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Objective: We recently showed that neuronal electrophysiological properties and synaptic vesicular trafficking are modulated by the presence of LRRK2 at pre-synaptic bouton; moreover, we reported that LRRK2, through its WD40 domain, pulls down from mouse brain lysate different pre-synaptic proteins including Synapsin I a phosphoprotein associated with synaptic vesicles (SVs) and involved in the neurotransmitter release. In this regard, the aim of our study was to validate the interaction between LRRK2 and synapsin I, to investigate the physiological function of this interaction and to understand how LRRK2 pathogenic mutations might affect and alter the synaptic transmission.

Methods: LRRK2 and Synapsin I interaction was investigated by co-immunoprecipitation from rat cortical synaptosomes and highly pure SVs. Phosphorylation assay was performed with purified bovine synapsin I and recombinant 3xFlag LRRK2 wild type, G2019S pathogenic mutant and K1906M kinase-dead constructs.

Results: We demonstrated that LRRK2 co-localizes with synapsin I and actin filaments on SVs fraction and highly pure SVs thus confirming that LRRK2 efficiently interacts with vesicular protein complex at pre-synaptic site. Moreover, *in vitro* kinase assay revealed that LRRK2 phosphorylates synapsin I a and b and a chemical cleavage at cysteine residues showed that LRRK2 phosphorylation occurs on the C-terminus of synapsin Ia and b. We are now investigating the physiological function of LRRK2 phosphorylation on synapsin I to understand whether LRRK2 modulates synapsin I binding to SVs or actin filaments and thus controls the dynamics between vesicle pools at pre-synaptic site.

P06.17

Effect of vinpocetine a PDE-1 inhibitor on MPTP-induced experimental Parkinson's disease in rats

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Objective: Up regulation in phosphodiesterase 1 (PDE1) expression and decreased levels of cyclic nucleotides (cAMP and cGMP) have been reported in Parkinson's disease. The present study was designed to investigate the effect of vinpocetine a PDE1 inhibitor on MPTP- induced experimental Parkinson's disease in rats.

Methods: To produce stable motor deficit, 1-methyl-4-phenyl-1, 2, 3, 6-tetrahydropyridine (MPTP) was repeatedly administered intranigally (bilaterally) at an interval of one week (day 1, 7 and 14). Following development of stable motor deficit, which was observed after third infusion of MPTP (day 14) in rats, the animals were treated with vinpocetine at different doses (5, 10 and 20mg/kg) from day 15-28. Motor deficit in MPTP treated rats was assessed by grip strength, narrow beam walk and by spontaneous locomotor activity in rats. Oxidative burden was assessed by measuring the levels of

malondialdehyde, nitrite, protein carbonylation and glutathione in striatal brain homogenate. Striatal dopamine levels (DA) was also measured by HPLC analysis. Further, MPTP-induced neurotoxicity was also checked histologically in nigral regions.

Results: Intranigral administration of MPTP produce significant stable motor deficit, increased markers of oxidative-nitrosative stress and decreased levels of striatal dopamine. Chronic administration of vinpocetine (for 14 days) significantly and dose dependently improved motor behavior, attenuated oxidative-nitrosative stress and restored striatal dopamine levels in MPTP treated rats. The current study supports the potential role of PDE-1 in mediating neurodegenerative changes associated with PD and PDE1 inhibition may prove to be useful therapeutic strategy in the treatment of neurodegenerative disorders associated with motor disabilities.

P06.18

Parkinsonian features in aging GFAP.HMOX1 transgenic mice overexpressing human HO-1 in the astroglial compartment

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Objective: To determine whether mid-to-late life overexpression of glial heme oxygenase-1 (HO-1), a stress protein induced in the Parkinson disease (PD) substantia nigra, recapitulates neurochemical, neuropathological and behavioural features of the disease in an animal model.

Methods: Motoric behaviour, basal ganglia neurotransmitter levels and neuropathological markers were ascertained in conditional GFAP.HMOX1 transgenic mice expressing human HO-1 (*HMOX1*) in the astrocytic compartment from 8.5 to 19 months of age.

Results: *HMOX1* expression was documented in astrocytes, ependymocytes and tanycytes. Relative to wild-type controls, the GFAP.HMOX1 mice exhibited impaired motor coordination (rotarod test), striatal dopamine deficiency and augmented substantia nigra GABA concentrations (HPLC-EC), pathological brain iron deposition (DAB-Perls stain), increased neuronal and glial MnSOD protein (mitochondrial OS marker; IHC), and increased ubiquitin staining in astrocytes and tyrosine hydroxylase-positive (dopaminergic) neurons (IHC). Impaired motor performance did not occur in transgenic mice overexpressing glial HMOX1 between 1.5 and 12 months of age, attesting to the important role of brain aging in this model.

Conclusions: Corroborating and extending our earlier *in vitro* findings to the intact brain, over-expression of astrocytic *HMOX1* in mice between 8.5 and 19 months of age promotes several behavioural, neurochemical and neuropathological features of idiopathic PD. Curtailment of glial HO-1 hyperactivity by pharmacological or other means may afford neuroprotection in PD and other aging-related neurodegenerative disorders.

P06.19

Gene expression changes induced by long-term subthalamic nucleus deep brain stimulation in rats

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Objective: The use of deep brain stimulation (DBS) as a neurosurgical intervention for Parkinson's disease (PD) has outpaced our understanding of its effects on basal ganglia circuitry. We have demonstrated in a rat model of subthalamic nucleus (STN) DBS that stimulation induces the upregulation of brain derived neurotrophic factor (BDNF) mRNA in the substantia nigra (SN) and increases BDNF protein in the primary motor cortex (M1) however a comprehensive gene expression analysis of the impact of STN-DBS had yet to be conducted. The present experiments were conducted to elucidate the impact of STN-DBS on gene expression within the rat SN and M1 cortex.

Methods: 6-hydroxydopamine (6-OHDA) lesioned and unlesioned rats were implanted unilaterally with electrodes in the STN. Half the rats received continuous stimulation for 2 weeks; the other half were unstimulated. SN and M1 were collected for comprehensive gene expression analysis using the Affymetrix Rat Genome 1.0 ST Array. Data were analyzed using ArrayStar 5.0 to identify fold differences in gene expression followed by qPCR confirmation. Pathway analysis using Ingenuity Pathway Analysis software was conducted.

Results: Gene expression analysis revealed that STN-DBS induced a >1.5 fold change in 66 genes in the SN of lesioned rats (11 genes upregulated and 55 genes downregulated). Pathway analysis indicated decreased expression of genes involved in ERK1/2 signaling and nicotinic acetylcholine receptors whereas increased expression of some trophic factor genes was identified. In the M1 cortex of lesioned rats a >1.5 fold change in expression was observed in a total of 52 genes in response to STN-DBS, with the majority of these genes downregulated (48 out of 52). Ongoing direct comparisons to unlesioned rats will provide further insight into effects of STN-DBS-mediated gene expression changes in rats with intact nigrostriatal circuitry. These results will provide important insight into the long-term consequences of STN-DBS.

P06.20

Distinct patterns of gene expression in the striatum of dyskinetic versus non-dyskinetic responders to levodopa priming in the 6-hydroxydopamine lesioned rat

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Objective: Levodopa-induced dyskinesias (LIDs) are a frequent side effect of symptomatic therapy for Parkinson's disease (PD). The 6-hydroxydopamine (6OHDA) rat model of parkinsonism provides the most commonly used animal model of PD and LIDs. It provides insight into the compensatory changes that occur in the basal ganglia in response to DA neuron degeneration and chronic levodopa treatment. We previously characterized gene expression changes in tissue collected from striatum and substantia nigra (SN) of 6OHDA, vehicle treated, or naive rats at 1, 2, 4, 6 and 16 weeks post-lesion. In the current study, we overlaid post-lesion levodopa administration to examine whether LIDs result in differential gene expression in striatum.

Methods: Male Sprague Dawley rats were sham or 6-OHDA lesioned and treated chronically with levodopa (12.5 mg/kg daily) or vehicle. After priming, approximately 80% of lesioned rats developed LIDs (responders) whereas 20% did not (non-responders). Lesions were confirmed by HPLC. Striatal tissue from 'responders' and 'non-responders' was microdissected. Comprehensive gene expression analysis using the Affymetrix Rat Gene 1.0ST array was conducted followed by analysis using Arraystar 5 (DNASTar) to detect significant differences in gene expression.

Results: The average LID severity score for 'non-responders' was 0.33±0.14 (mean ±SEM) with DA depletion of 97.3%±0.97; the average LID severity score for 'responders' was 16.14±0.49 with DA

depletion of 98.4%±0.29. Using a cutoff of >1.5 and a t-test with the Benjamini-Hochberg FDR correction, 35 genes significant at the 95% confidence interval. Of these 35 genes, 34 were upregulated. Genes associated with LIDs included those with influence on neuronal differentiation, axonal guidance, neuronal excitability, MAP kinase and ERK pathway activation, and several genes associated with neuroendocrine function. Comprehensive gene expression data from the 6OHDA model when overlaid with levodopa priming for dyskinesias provides new interventional targets and a solid foundation for better understanding mechanistic underpinnings of dyskinesias.

Financial Disclosure: Supported by Michigan State University Morris K. Udall Center of Excellence in Parkinson's disease Research (P50-NS058830).

P06.21

SYNerGY mice: modeling GBA1 dysfunction and human synucleinopathy risk

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Objective: We have created a new animal model of genetic susceptibility to dementia, parkinsonism and related SNCA-driven neurodegenerative diseases: the SYNerGY mouse

(Synucleinopathy related to Gaucher disease and Lewy body dementia). These mice carry three distinct susceptibility traits at two loci (SNCA, GBA1); both of which are independently and equally linked to dementia and parkinsonism.

Methods: The SYNerGY mouse was created by crossing PAC-hSNCA^{A53T} mice [Kuo et al., 2010] with Gba1^{D409V} knock-in mice [Xu et al., 2003] resulting in a mouse that combines (1) human SNCA burden (gene dosage; n=4) with (2) SNCA^{A53T} point mutation, on an murine Snca null background; and (3) Gba1^{D409V} knock-in mutations. Our characterization of these mice is guided by histological, biochemical and behavioural analysis of the parental strains as well as human disease pathology.

Results: We have published that homozygous mutations in the murine Gba1^{D409V} gene lead to accumulation of endogenous Snca protein in the hippocampus determined using both biochemical (ELISA) and histological methods [Cullen et al., 2011] and memory deficits that can be ameliorated by delivery of wild-type GBA1 into the CNS [Sardi et al., 2011]. PAC-hSNCA^{A53T} mice develop SNCA allele dosage- and age-dependent synaptic changes in the same region of the hippocampus and in the cerebellum. By crossing these two strains, we hypothesized that SYNerGY mice would develop stronger, and possibly earlier onset of synucleinopathy-type changes. Indeed, preliminary histological analyses of brains from young SYNerGY mice revealed evidence of SNCA rise in both the hippocampus and cerebellum. A first SYNerGY mouse cohort has been generated, and we are now beginning the detailed characterization of SNCA metabolism and glycosphingolipid turnover in their CNS and are performing relevant behavioural studies.

Conclusion: The SYNerGY mouse represents the first bigenic mouse model to examine pathophysiological events involved in human dementia with Lewy bodies and Parkinson disease.

P06.22

Further characterization of a novel, environmentally induced progressive rodent model of Parkinson's disease

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Objective: Chronic exposure to dietary phytosterol glucosides has been found to be neurotoxic. When fed to rats, β -sitosterol β -D-glucoside (BSSG) triggers the **progressive** development of neurological deficits, with behavioural and cellular features that closely approximate those observed in Parkinson's patients. Clinical signs and histopathology continue to develop for several months following cessation of exposure to the neurotoxic insult. Here, we further characterize the progressive nature of this model, its non-motor features, and response to levodopa administration.

Methods: Adult male Sprague Dawley rats received daily feedings of either plain flour pellets or BSSG-containing flour pellets (3 mg) for 16 weeks. Animals were monitored for locomotor activity, coordination, olfaction, and cognitive function beginning immediately following cessation of toxin exposure and continuing throughout the duration of the study. Animals were sacrificed at 4, 6, 8, and 10 months following initial toxin exposure. Tissues were assayed by immunohistochemistry for the loss of dopaminergic neurons, appearance of inflammatory cytokines, and abnormal protein aggregates.

Results: Chronic exposure to BSSG resulted in the progressive loss of dopaminergic neurons of the substantia nigra. At approximately 4 months following initiation of BSSG exposure, animals displayed the early emergence of an olfactory deficit, in the absence of significant dopaminergic nigral cell loss or locomotor deficits. Locomotor deficits developed gradually over time and were reversed by levodopa treatment. Cognitive impairment was observed in the form of spatial working memory deficits, as assessed by the radial arm maze. In addition to the progressive loss of TH⁺ cells in the substantia nigra, the appearance of insoluble intracellular α -synuclein aggregates was also observed. The slowly progressive nature of this model, together with its *construct, face* and *predictive* validity, make it ideal for the screening of potential neuroprotective therapies for the treatment of Parkinson's disease.

P06.23

PET imaging of rats that express the LRRK2 G2019S mutation: initial findings

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Objective: To study transgenic rats that express the Parkinson's disease (PD)-related, mutated form of LRRK2. Positron emission tomography (PET) is used, enabling comparison of pathophysiology between species. Imaging is complemented by behavioural testing to determine if the rodents recapitulate the pathogenesis of PD and if neurological abnormalities are progressive.

Methods: Transgenic LRRK2 G2019S (BAC) rats (n=5) aged 1 year, together with non-transgenic littermate controls (n=3), were imaged using [¹¹C]methylphenidate PET. Nine month old rats (n=4 transgenic, n=4 controls) were also imaged. The radiotracer binds to the dopamine transporter (DAT), with relative striatal DAT density

quantified by the tracer's binding potential (BP_{ND}). Behavioural testing was performed at 7-8 months (n=11-18 per group). Tests included the accelerating rotarod (time on the rod), ledge-beam (time to traverse the beam) and drag test (steps per meter when dragged backwards at constant speed, repeated on 4 consecutive days). Statistical analysis of group differences was performed using appropriate ANOVA and post-hoc tests.

Results: One year old transgenic rats had the lowest BP_{ND} , 15 % lower than age-matched controls (p<0.05). No other group differences in BP_{ND} were found. Behavioural testing demonstrated various deficits; transgenic rats spent 26 % less time on the rotarod, took 80 % longer traversing the ledge beam, and took 22 % fewer steps on day 1 of the drag test (all p<0.05). On days 2-4 of drag testing, the reduction in the number of steps was no longer significant. If additional cohorts display reductions in DAT at 1 year, the rodent model mirrors PD in an essential manner.

P06.24

LRRK2 G2019S knock in Mice display progressive alterations in Dopamine release and metabolism

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Objective: Mutations in the kinase leucine rich repeat kinase 2 (LRRK2) are the leading cause of genetic Parkinsonism. The most common mutation, G2019S has been shown to exert its toxic effects via enhanced kinase activity. To assess the effects of this mutation in mice we created gene-targeted knock-in mice that express the G2019S mutation within their own genome.

Methods: Mutant littermate heterozygous, homozygous and wild-type mice were studied up to 20 months of age. Our analysis included extensive characterization of the dopaminergic system, using *in vivo* microdialysis to measure striatal extracellular release of dopamine and dopamine metabolites 3, 4-dihydroxyphenylacetic acid and homovanillic acid in conscious freely-moving animals, total monoamine axonal neurochemistry in striatal lysates and stereological dopaminergic counts. A complete behavioral battery involved motor (rotarod, gait, locomotor in open field) and cognitive testing (novel object, elevated plus maze, water maze, fear condition). Biochemical analysis encompassed kinase activity assays and quantification of protein levels of LRRK2 and phospho-LRRK2 with progressing age. Neuropathological analysis with various Parkinson's Disease immunohistochemical markers was also performed in aged mice.

Results: G2019S mice are viable, fertile and have normal bodyweights and lifespans. As predicted, the G2019S mice have elevated kinase activity, with 2-fold activity in heterozygous mice and 4-fold activity in homozygous mice. At 6 months of age, the dopaminergic system was intact in G2019S mice. However by 12 months of age, a reduction both basal and amphetamine-evoked extracellular dopamine release was observed, along with significant changes in the dopamine:metabolite turnover ratios, though no significant reduction was observed in dopamine neuronal number even by 20 months of age. No behavioral alterations were detected in G2019S mice and no major neuropathological alterations were observed, although levels of non-phosphorylated axonal tau were reduced in aged G2019S mice.

Our data suggest that less dopamine is available for release at the nerve terminal in G2019S mice and the increased biochemical turnover ratios suggest a compensatory mechanism to increase firing. Remarkably these changes are apparent with just one copy of the mutant allele. Analogous neurochemical findings have been

observed in other PD models and in imaging studies of early stage PD and asymptomatic LRRK2 carriers. Our model may represent a progressive preclinical model of LRRK2-PD that will be useful for mechanistic studies to gain further insights in early LRRK2 dysfunction.

P06.25

Neuronal characterization of mesenchymal dog stem cells into dopaminergic neurons

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Objectives: Stem cells are undifferentiated cells that possess the ability to differentiate into several cell types. There are various types of stem cells, but our experiments are focused on the use of mesenchymal stem cells, found mainly in adipose tissue. They may differentiate into several mesenchymal tissues such as fibroblasts, bones, tendons and ligaments. The aims of our study were 1) to establish a method of differentiation of canine stem cells towards a neuronal phenotype 2) to achieve the differentiation of canine neuronal cells into dopaminergic (DAergic) neurons and 3) to develop a neuroprotective strategy to rescue DAergic neurons from oxidative stress damages characteristic of Parkinson's disease (PD) degeneration.

Methods: In order to establish the typical morphological properties and neuronal phenotype of DMSC-ad cells, differentiation was induced by a specific medium for 4 days. Western blotting and immunofluorescence measurements were used to confirm the differentiation.

Results: Our characterization results show a neural character by increased expression of neuronal markers such as the three subunits of neurofilament, β -3-tubulin, NeuN and GFAP. In addition, we also detect the expression of tyrosine hydroxylase (TH) and dopamine transporter (DAT). However, these DAergic markers do not appear to be modulated following treatment with differentiation medium. Our analysis demonstrates that the neuronal character of our canine mesenchymal stem cells is properly established and other experiments are in progress to successfully induce the dopaminergic nature of these stem cells.

BASIC SCIENCE: BRAIN PHYSIOLOGY AND CIRCUITRY

P07.01

Sample entropy of GPi neurons dependence on the level of alertness in 6OHDA rats

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Background: The analysis of neuronal data obtained during functional neurosurgery from alert human patients with Parkinson's disease, raised the question to what extent the increase in the entropy of single parkinsonian Basal ganglia (BG) neurons depends on the level of consciousness and to what on the disease itself.

Objective: To assess the dependency of sample entropy on the level of alertness in healthy and parkinsonian rats.

Methods: Thirty-six adult Sprague-Dawley rats were assigned randomly to two groups: control and 6OHDA-lesioned animals. Between 21 and 28 days after the lesion procedure, animals underwent the cylinder test and went through stereotactic surgery with the objective of registering spontaneous activity of the medial Globus Pallidum (GPi). Animals were placed in an ad-hoc built restraining device that did not allow any spontaneous movements during the whole recording time. The eyes of the animals were covered; all recordings were obtained in conditions of environmental silence. The alertness level was characterized periodically with a standardized non-painful stimulus.

Results: We recorded the activity of 38 single GPi neurons during the awakening process in relaxed, head-restrained, control and 6OHDA-lesioned rats. The sample entropy increased in the 6OHDA group with an increasing level of alertness, but it was reduced in the control group. With increasing levels of alertness, single neurons changed their behavior adaptively, showing that the measured characteristics should be considered as emergent properties of the state of the neural system rather than static, intrinsic electrophysiological properties of GPi neurons. We interpret the increment observed in the level of entropy of parkinsonian neurons as the inability of dopamine-depleted Basal Ganglia to handle increased levels of input associated with higher levels of alertness. Our results emphasize that an extrapolation from data obtained under anesthesia to the wake subject or animal is bound to lead to incorrect results.

P07.02

Rewire dopaminergic neurons: involvement of the transcription factors Lmx1a and Lmx1b

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Objective: Degeneration of midbrain dopaminergic neurons (mDA) is the principal cause of Parkinson's disease. Graft of dopaminergic neurons newly generated from stem cells represents a promising therapeutic avenue. However, a major factor limiting success in transplantation studies is the inappropriate re-innervation of the grafted neurons. It is thus primordial to identify factors regulating axon projection and connectivity of mDA neurons. We recently discovered that transcription factors Lmx1a and Lmx1b were essential for mDA progenitor specification, proliferation and differentiation. In this new study we investigate the role of Lmx1a, Lmx1b and their downstream target PlexinC1 in postmitotic mDA neurons.

Methods: Conditional mutant mice were used for the specific inactivation of Lmx1a and Lmx1b in postmitotic midbrain dopamine neurons. Analysis of axon projections in mutant mice was done using both immunohistochemistry on brain sections and using optical projection tomography. To study the role of PlexinC1 in mDA neurons development, we performed in vitro experiments and examine the response of dopaminergic growth cones to PlexinC1 ligand Sema7a.

Results: Analysis of dopaminergic axon projections of Lmx1a/b double conditional mutant mice reveals a striking axon guidance defect and confirms the essential role of Lmx1a/b in the establishment of dopaminergic circuit formation. We also identified PlexinC1 as a target gene regulated by these transcription factors. Our in vitro experiments show that Sema7a and PlexinC1 regulate mDA axon development and these effects are mediated by Src family kinases. At the light of our data, we propose a novel model to

explain the segregation of the nigrostriatal and mesolimbic pathways. Data generated here will shed a new light on mechanisms that regulate dopamine neuron connectivity and will certainly help in the effort to understand the molecular factors contributing to the efficiency of cell replacement therapies in Parkinson's disease.

P07.03

Quantitative assessment and ultrastructural features of the cholinergic innervation of the globus pallidus in squirrel monkeys

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Objective: The primate basal ganglia are heterogeneously innervated by cholinergic (ACh) varicose fibers arising mainly from the pedunculopontine tegmental nucleus located in the brainstem. The aim of this light and electron microscopic study is to characterize and compare the ACh innervation of the internal (GPi) and external (GPe) globus pallidus of squirrel monkeys (*Samiri sciureus*).

Methods: Serial sections immunostained with a choline acetyltransferase (ChAT) antibody were analyzed by means of stringent stereological procedures at light and electron microscopic levels.

Results: Light microscopy analysis reveals ChAT+ axons seen to emerge from PPN neurons and course mainly in the central portion of the mesopontine tegmentum. Rostrally, this bundle splits into ventromedial and dorsolateral fascicles that arborize in basal ganglia and thalamic nuclei, respectively. In the pallidum, several thick fibers are oriented dorsolaterally and give rise to thinner varicose fibers. Unbiased counts of ChAT+ axon varicosities reveal that total density of innervation is similar in GPi ($0.24 \pm 0.03 \times 10^6$ axon varicosities / mm³) and GPe ($0.49 \pm 0.11 \times 10^6$), with an anteroposterior decreasing gradient in both pallidal segments. Neuronal counts on Nissl-stained adjacent sections indicate that GPi and GPe neurons are similarly innervated by ChAT+ axon varicosities, with an anteroposterior decreasing gradient observed in the GPi only. At the electron microscopic level, ChAT+ axon varicosities are comparable in size and shape in GPi and GPe. Less than 20% of ChAT+ axon varicosities establish a synaptic contact, indicating that synaptic as well as diffuse cholinergic transmission occur in both pallidal segments. No axo-axonic contacts were visualized suggesting that presynaptic ACh modulation of pallidal afferents is largely exerted through diffuse neurotransmission. Altogether, these morphological data underline the strategic position of brainstem cholinergic afferents in the functional organization of the basal ganglia in both normal and pathological conditions, such as in Parkinson's disease.

P07.04

Distribution of the vesicular glutamate transporter in serotonin projections arising from the dorsal raphe nucleus: A single-axon study in rats.

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Objective: Serotonin ascending projections are believed to play a significant role in non-motor symptoms of Parkinson's disease. Being able to store and release dopamine following L-Dopa

administration, these projections are considered as an important presynaptic determinant of L-Dopa-induced dyskinesia. Serotonin neurons giving rise to ascending projections are located in the dorsal raphe nucleus (DRN) and are known to contain the vesicular glutamate transporter 3 (VGlut3) indicating that, in addition to serotonin and dopamine, they are able to release glutamate in their target sites. This study aimed at providing the first detailed description of single-axon projections arising from DRN neurons, including distribution of VGlut3 within their axons.

Methods: We used electrophysiological guidance to microiontophoretically label neurons of the rat DRN with an anterograde tracer. Somatodendritic and axonal arborizations were reconstructed individually and entirely from serial sagittal sections using a computerized image analysis system. High-resolution images acquired with a confocal microscope were used to characterize the distribution of VGlut3 protein in BDA-injected axons.

Results: DRN neurons were easily recognizable by their highly regular (2-3 Hz) spontaneous firing patterns. They have a medium size cell body (15-20 µm) from which emerge 3-5 primary dendrites, mainly oriented along the anteroposterior axis. The DRN neurons are endowed with a highly collateralized axon and display different axon morphology depending on target sites. Typically, the axon leaves the DRN by piercing its anterior aspect, arches rostroventrally and crosses the midbrain tegmentum to course caudorostrally in the medial forebrain bundle where many axon collaterals are emitted. The proportion of axon varicosities that contain the Vglut3 varies depending on target sites. Our data support the existence of a complex trafficking mechanism of VGlut3 protein within the highly collateralized axon of DRN neurons. We hypothesize that this feature might play a significant role in maladaptive plasticity involved in L-Dopa-induced dyskinesia.

P07.05

Role of postural instability in freezing of gait in Parkinson's disease

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Objective Postural and gait deficits in Parkinson's Disease (PD) have mixed responses to dopaminergic medication (meds). Meds improves mobility but increases risks for falls (Nantel et al.,2012). Gait speed and stride length are generally responsive to meds while gait variability is not. This suggests a regulation by different neural pathways (Rochester et al.,2012) and possibly some shared pathophysiologic mechanisms as freezers have larger gait variability and higher risk for falls (Nantel et al.,2012, Plotnik et al.,2005). The aims of this study were to: 1) to determine the contribution of the dopaminergic pathways on gait variability, 2) measure postural stability and determine its relationships with FOG and gait variability.

Methods We measured postural stability, FOG, stepping in place (SIP) variability in 30 PD subjects (15 freezers/15 non-freezers) and 14 healthy controls using static posturography and the SIP (Nantel et al., 2011), which consists of alternative stepping on force platforms. Clinical evaluation: UPDRS-III and FOG-questionnaire (FOG-Q). Gait and UPDRS-III were performed off/on meds and posturography off-meds only.

Results Four freezers out of 15 froze on-meds. On/off-meds, freezers had larger asymmetry than controls and non-freezers ($P < 0.01$). Freezers had shorter stride duration compared to both groups off-meds only as they improved on-meds ($P < 0.01$) while cycle asymmetry/rhythmicity did not. CoP displacement/velocity in both directions were higher in freezers versus controls ($P < 0.01$) and correlated with on-meds asymmetry (medial-lateral: $R = 0.46$, $R = 0.45$; $P < 0.05$). Asymmetry correlated with CoP displacement

(anterior-posterior: $R=0.44$; $P<0.05$). UPDRS-III was significantly higher in freezers on/off meds ($P<0.02$) and improved with meds in both groups ($P<0.01$). Improvement of FOG occurrence on meds but not of gait asymmetry/arrhythmicity suggests that both dopaminergic and non-dopaminergic networks could contribute to FOG. The greater postural instability in freezers and the correlations between CoPs and both FOG-Q and asymmetry suggest that postural instability could play a role in the mechanisms of FOG.

P07.06

Regional changes in cortical neuronal density with idiopathic Parkinson's syndrome

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Objective: It has been hypothesized that cortical thinning in neurodegenerative diseases such as Idiopathic Parkinson's syndrome (IPS) might be associated with a change in neuronal density. The aim of this study was to determine whether changes in neuronal density are present in IPS subjects.

Methods: Fifteen subjects with IPS (mean age: 60 years [range 42-75]) and 9 healthy controls (mean age: 60 years [range 49-70]) underwent PET with 18-F-FMZ on a high-resolution brain scanner (CTI/Siemens HRRT) and volumetric T1 MR imaging (Siemens TRIO). Binding Potential (BPND) of GABA-A receptors was calculated with parametric voxel-by-voxel Logan plots (relative to white matter activity in the oval center). Images were corrected for partial volume effects (PVE) using simulated PET images derived from gray matter segmentation of the T1 MRI (e.g., Collins, et al., 1994). Regional PVE corrected GABA-A BPND were obtained from right and left hemisphere and from bilateral primary motor (M1) and premotor cortex (PMC).

Results: In control subjects, BPND was increased on the left side for both M1 (Left 7.8 [SE 0.9] vs. Right 7.4 [SE 0.9], $p<0.01$) and PMC (Left 8.1 [SE 1.0] vs. Right 7.6 [SE 0.9], $p<0.01$) but was similar in the left and right hemispheres (Left 7.8 [SE 1.1] vs. Right 7.7 [SE 1.0], $p=0.91$). In IPS subjects, there was a significant increase in neuronal density on the left hemisphere (Left 10.7 [SE 1.4] vs. Right 10.3 [SE 1.4], $p<0.01$), irrespective of the most affected side. In addition, the neuronal density in IPS subjects was significantly increased in PMC areas as compared to M1 and hemisphere (PMC 10.2 [SE 1.2] > M1 10.9 [SE 1.2], $p<0.01$ and > hemisphere 10.4 [SE 1.0], $p<0.05$). These findings may indicate a differential susceptibility of motor regions to the neurodegenerative process underlying IPS.

P07.07

Striatal interneurons expressing choline acetyltransferase or calretinin in normal and 6-OHDA-lesioned mice.

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Objective: The striatum is the largest and major integrative component of the basal ganglia. Composed of a multitude of projection neurons, it also comprises a smaller number of interneurons that play a crucial role in its functional organization. This study provides a detailed description of the distribution and chemical phenotype of two subpopulations of striatal interneurons encountered in the mice striatum, under both normal and parkinsonian (PD) conditions.

Methods: Striatal sections immunostained for ChAT, CR, NeuN, VAcHt and VGlut3 were scanned by means of a high-resolution confocal imaging system. The data were analyzed with stringent stereological quantitative procedures, whereas the optical density of striatal VGlut3 immunoreactivity in normal and 6-hydroxy-dopamine (6-OHDA)-lesioned mice was estimated with the help of a Li-Cor scanner.

Results: In the striatum of normal mouse, ChAT+ neurons are much more abundant and widely distributed than CR+ neurons. The large (18-22 μ m), multipolar, ChAT+ interneurons are distributed according to a rostrocaudal decreasing gradient. All ChAT+ striatal interneurons express VGlut3, but some of the numerous ChAT+ axon varicosities that pervade the striatum are devoid of VGlut3 immunostaining. None of the ChAT+ striatal interneurons express CR, in contrast to the situation in human and non-human primates. Two types of CR+ interneurons were detected in the mouse striatum. First, there are small (5-15 μ m), round and intensely fluorescent cells that abound particularly in the area of the subventricular zone and the subcallosal streak. These immature-looking cells are NeuN- and display a unique, markedly varicose and moderately arborized process that extends far within the striatal neuropil. Second, a smaller number of ovoid (15-20 μ m) and less intensely immunoreactive CR+ neurons occurred throughout the striatum. The comparison between normal and 6-OHDA-lesioned mice revealed no significant changes in striatal VGlut3 immunoreactivity, whereas the number of CR+ interneurons appears significantly decreased in the denervated striatum.

P07.08

BDNF and dopamine D3 receptor agonist potentiate each other and promote substantial motor recovery in the rat model of Parkinson's disease

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Background: Parkinson's disease (PD) is produced by progressive degeneration of dopaminergic neurons. The successful use of the preferential D3R agonist (Pramipexole) in PD has been validated in several clinical trials (Hubble, 1995; Shannon, 1997). Pramipexole is useful as monotherapy for up to 4-6 years (CALM-PD, 2009). This reduction in the efficacy of pramipexole after several years of treatment could be due to the fact that expression D3R gene is progressively decreased as Parkinson's disease progresses (Levesque, 1995; Ryoo, 1998; Joyce, 2004), becoming dopaminergic D3R activation monotherapy less effective (Joyce, 2002). BDNF has been implicated in several functions of dopaminergic neurons and the control of normal expression of D3R (Guillin, et al; 2001; Sokoloff, et al; 2002). However, it has been shown that BDNF is low in PD (Howells, 2000).

Objective: We investigated whether the combined treatment of BDNF and dopamine D3R agonist (7-OH-DPAT) could potentiate each other and restore the motor behavior of the 6-OHDA rat Parkinson model.

Methods: Local non-viral BDNF gene transfection into the substantia nigra (Alvarez- Maya, 2001) and i.p. application of 7-OH DPAT by osmotic pumps during 18 weeks.

Results: The combined treatment of BDNF and 7-OH-DPAT can potentiate each other, producing significant recovery from the motor deficit and neuronal degeneration caused by the 6-OHDA, evidenced by improvement of fine coordination during gait, gross coordination and equilibrium on rotarod and disappearance of rigidity. All these motor improvements were accompanied by an increment of TH+ neurons, increase in number of TH+ neurons reinnervating the striatum and recovery of dendritic spines of medium spiny neurons.

P07.09

Using eye movements to differentiate subclinical and clinical types of Parkinsonism

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Objective: Patients with idiopathic REM behavior disorder (iRBD) have a variable prognosis and are at high risk for the development of Multisystem Atrophy (MSA) or Parkinson's disease (PD). Differential diagnosis of MSA and PD in early stages has proven difficult with standard clinical measures alone. Our primary goal was to evaluate the usefulness of reflexive and voluntary eye movement tasks to differentiate types of preclinical and clinical Parkinsonism.

Methods: Individuals with iRBD (n=8), MSA (n=8), PD (n=11), as well as control subjects (n=12) performed prosaccade (PS) and antisaccade (AS) eye movement tasks. Latency and error rates of horizontal and vertical saccades were measured with an infrared eye tracker. The University of Pennsylvania Smell Identification Test (UPSIT) was used for olfactory performance.

Results: As expected, the MSA group performed significantly better than PD on the UPSIT. MSA and PD groups showed significantly higher error rates than controls on AS task, while MSA also showed significantly longer PS latencies than controls. The iRBD group was divided into two groups based on a median split of UPSIT score. The iRBD group with higher olfactory scores showed significantly higher AS error rates than iRBD patients with lower olfactory scores, consistent with an earlier onset of frontal degeneration and disinhibition in MSA. iRBD patients with higher olfactory scores also showed shorter latencies on the PS task, indicating preclinical degeneration may result in shorter PS latency that will secondarily show marked slowing as the disease progresses. Thus, performance on eye movement tasks in conjunction with standard clinical measures may prove useful as early markers of disease onset and course.

BASIC SCIENCE: DOPAMINE, RECEPTORS AND OTHER NEUROTRANSMITTERS

P08.01

Blockade of cannabinoid CB₁ receptors attenuates behavioral and biochemical changes following repeated MPTP assault to nigral neurons in rats

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Objective: Parkinson's disease is a movement disorder that occurs due to dopaminergic dysfunction in brain, especially in substantia nigra pars compacta (SNpc). Recently, the controversial role of cannabinoid receptors was reported in the pathophysiology of PD. In the present study, we have investigated the possible role of cannabinoid CB₁ receptor modulation following repeated intranigral administration of MPTP (1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine).

Methods: Repeated intranigral (day 1, 7, 14) administration of MPTP was done to produce stable motor deficits in rats. Noladin ether a putative endocannabinoid, AM 251, a CB₁ receptor antagonist were administered alone or in combination chronically (14-28 days) in MPTP treated rats. Behaviorally, grip strength, spontaneous locomotor activity and narrow beam walk tests were used to access motor behaviors. Biochemically, oxidative stress and pro-inflammatory cytokine levels (TNF- α and IL-1 β) were determined in striatal and cortical brain homogenates.

Results: Following third (day 14) intranigral administration of MPTP, rats produced stable motor deficit and elevation in oxidative stress markers and cytokine levels (day 28). AM 251 significantly attenuated elevated levels of cytokines, oxidative stress and improved motor behavior in MPTP treated rats. On the contrary, noladin enhanced MPTP-mediated neurotoxicity, which was significantly attenuated by AM 251 pre-treatment. The above results indicating that chronic activation of CB₁ receptors may play a significant role in the development of MPTP-induced motor deficit in rats and suggest CB₁ receptor blockade would be beneficial in restoring motor functions in PD.

P08.02

Mechanisms of activation of dopamine D₁ receptors by rotigotine: a route to novel Parkinson's disease drugs

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Objective: Neupro[®] (Rotigotine) is a dopamine agonist used as symptomatic therapy of Parkinson's disease (PD). Although most clinically approved agonists target dopamine D₂-like receptors, activation of D₁ receptors by high-intrinsic activity agonists has been shown to have efficacy in PD equal to levodopa. D₂ agonists as monotherapy are far less efficacious. Among the approved dopamine agonists that do not have to be given intravenously, the D₂-selective drug rotigotine is unique in that it has high D₁ intrinsic activity. Unlike the available selective full D₁ agonists (e.g., dihydroxidine or SKF81259), rotigotine does not contain the catechol moiety that is known to cause rapid metabolism and poor bioavailability. Thus, understanding the molecular mechanisms by which rotigotine activates the D₁ receptor may provide leads to novel D₁ agonists.

Methods: Both wild-type and mutant human D₁ receptors were expressed in HEK-293 cells. The mutations were made in highly conserved transmembrane 5 serines (S5.42¹⁹⁸A, S5.43¹⁹⁹A, and S5.46²⁰²A), as well as transmembrane 6 aromatic amino acids (F6.51²⁸⁶A and F6.52²⁸⁹A) that have been shown to be critical for agonist interaction and receptor activation.

Results: S5.42¹⁹⁸A and S5.43¹⁹⁹A mutations greatly decreased the affinity and receptor activation mediated by rotigotine, whereas S5.46²⁰²A mutation did not cause any significant change. This suggests that hydrogen bond formation occurs between the hydroxyl group of rotigotine and S5.42¹⁹⁸ and/or S5.43¹⁹⁹, but not S5.46²⁰². Similarly, the F6.51²⁸⁶A mutation decreased the affinity of rotigotine to a far greater extent than F6.52²⁸⁹A suggesting that

hydrophobic interactions with F6.51²⁸⁸ are particularly important. These receptor-ligand interaction data produced a basic model of the possible docking pose of rotigotine that provides insight into a new scaffold for non-catechol D₁ receptor agonists with the high D₁ intrinsic activity of rotigotine, but with greater D₁:D₂ selectivity.

P08.03

P11 gene therapy for Parkinson's disease motor dysfunction and L-Dopa induced dyskinesias

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Objective: P11 is a scaffold protein involved in the membrane localization of receptors. Recent studies showed that P11 knockout mice have altered dorsal striatal dopamine responsiveness in the 6-OHDA mouse model of Parkinson's disease (PD). We investigated the relationship between dopamine signaling and striatal p11 in both normal and 6-OHDA unilateral lesioned mice.

Methods: We generated an AAV vector to block production of murine p11 and stereotactically injected the AAV.sip11 into the dorsal striatum, which is the area that receives dopamine produced in the substantia nigra and is lost in PD.

Results: Inhibition of striatal p11 significantly improved spontaneous motor function in both normal and 6-OHDA mice. In 6-OHDA mice, blocking p11 on the "lesioned" side significantly reduced the rotations that these mice develop in response to D1 and D2 receptor specific agonists and L-Dopa. This indicates that the animals are less-sensitive to the dopamine-like drugs following blockade of p11 in the striatum on the side in which the normal dopamine-producing cells were destroyed. Furthermore, we expanded these findings by studying the relationship between L-Dopa-induced dyskinesias and p11 expression. L-Dopa is the most commonly used drug in the treatment of PD; however chronic use of L-Dopa often leads to a variety of complications, including dyskinesias. We have scored the dyskinesias over 3 weeks of L-Dopa treatment and observed that inhibiting striatal p11 expression significantly reduced the dyskinesias by 50% when compared to control mice. Taken together our results demonstrate that loss of P11 in the dorsal striatum reduces dopamine responsiveness through a mechanism that modifies dopamine receptors activity. Furthermore, we show that normal striatal p11 levels are necessary for full expression of L-Dopa-induced dyskinesias. This also suggests that blocking striatal p11 actions may be a potential therapeutic target to improve striatal function and treat dyskinesias following chronic dopaminergic drug therapy.

P08.04

Dopamine inhibits protein L-isoaspartyl methyltransferase at both protein and gene levels in SH-SY5Y cells

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Objective: Parkinson's disease (PD) is a chronic and progressive neurological disorder that is characterized by the loss of dopaminergic neurons in the substantia nigra. Dopamine, via the oxidative stress that it generates in the cytosol, could contribute to

the selective loss of neurons observed in PD. Protein L-isoaspartyl methyltransferase (PIMT) is an enzyme, with antiapoptotic properties, that repairs L-isoaspartyl-containing proteins. PIMT expression has been shown to decrease with age. Together, these observations prompted us to investigate whether dopamine can regulate PIMT expression in SH-SY5Y neuroblastoma cells. **Methods:** Protein expression was monitored by Western blotting whereas gene promoter activity was measured using dual luciferase assay. Truncated and mutated versions of the PCMT1 gene promoter were synthesized by PCR to identify the regions that are sensitive to dopamine action. Cell viability was measured via the MTT assay and reactive oxygen species (ROS) production was measured via a fluorescent probe.

Results: Cells treated with dopamine showed a PIMT down-regulation at both protein and gene levels. The same down-regulation of PIMT protein was caused by the electron transport chain inhibitor, rotenone, which was accompanied, in both cases, by an increase in cell death and ROS production. PIMT dopamine-associated down-regulation was blocked by N-acetyl cysteine pre-treatment resulting in a decrease in cell death and ROS levels.

PCMT1 promoter mapping experiments allowed the identifying of a 55 bp-long dopaminesensitive region. The inhibition of PCMT1 transcription was mediated by dopamine-induced ROS. In addition, H₂O₂ inhibited in a dose-dependent manner the transcriptional activity of PCMT1 promoter. Therefore, PIMT could be a target of choice during neuronal cell death observed in PD. This would be mediated by the ROS generated from cytosolic dopamine that reduces the PCMT1 gene promoter activity and the PIMT protein stability.

PC08.05

Striatal pre-enkephalin overexpression improves motor symptoms and neuronal insults in the MPTP mouse model of Parkinson's disease

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In Parkinson's disease (PD), the nigrostriatal lesion is associated with an upregulation of opioid peptide pre-enkephalin (pENK) in striatopallidal neurons. Our previous results using the MPTP parkinsonian monkeys suggested that increased expression of pENK is a compensatory response to alleviate PD motor symptoms. However, the exact function of this increase is still unknown.

Objective: To determine the functional role of striatal pENK in motor behavior, and to define whether striatal pENK may have a protective effect against the neurotoxin insults in the MPTP mouse model of PD.

Methods: Viral vector gene transfer was used to overexpress striatal pENK before dopamine depletion by MPTP (i.p.). Various methodologies were carried out to assess motor behavior, the site of injection, the level of pENK mRNA, the integrity of nigrostriatal dopaminergic terminals, and the number of dopaminergic neurons in the substantia nigra compacta (SNc).

Results: Our results show that mice overexpressing pENK displayed higher locomotor activity compared to control groups. This effect was significantly and positively correlated with pENK mRNA expression in the striatum. Moreover, overexpression of striatal pENK improved the impairment of associative learning task induced by neurotoxin MPTP. Higher density of striatal tyrosine hydroxylase (TH) positive fibers was also detected in mice with pENK overexpression in different regions of the striatum compared to control groups. In addition, the number of TH positive neurons in

SNc of MPTP-treated mice with striatal pENK overexpression was higher than mice treated with MPTP alone.

Conclusion: These results provide evidence that upregulation of striatal pENK can be involved in the delay of the appearance of PD motor symptoms, and may also have protective effect against the MPTP insults at nigrostriatal dopaminergic nerve terminals.

Acknowledgment: This work was supported by Parkinson's Society of Canada.

P08.06

Differential morphological changes of D₂ versus D₁-expressing striatal neurons in a transgenic mice model of Parkinson's disease

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Objective: Parkinson's disease involves a progressive loss of substantia nigra pars compacta neurons resulting in a decrease of striatal dopaminergic innervation. Such denervation is known to differentially affect striatal projection neurons expressing dopaminergic receptors of the D₁ type and which are involved in the direct pathway, compared to those expressing the D₂ type at the origin of the indirect pathway. The specific consequences of such denervation on fine dendritic processes being poorly known, we attempted to characterize morphological changes of three different types of striatal projection neurons: the D₁+, the D₂+ and the D₁+/D₂+ medium spiny neurons, after dopaminergic denervation.

Methods: We used double transgenic BAC mice *Drd1a-tdTomato/Drd2-EGFP* allowing the identification of the direct and indirect striatal projection neurons based on their dopamine receptor content. Striatal dopaminergic denervation was induced by unilateral injections of 6-hydroxydopamine in the medial forebrain bundle. Cylinder test and immunohistochemistry staining of tyrosine hydroxylase and dopamine transporter confirmed the extent of the lesion. Single-cell intraneuronal injections of Lucifer yellow combined to immunohistochemistry were applied to the D₁+, D₂+ and the D₁+/D₂+ striatal neurons. Detailed morphometric analyses of dendritic trees and spines as well as their glutamatergic afferents were performed on high-resolution images acquired from a confocal imaging system.

Results: Our results indicate that dopaminergic denervation causes a decrease in dendritic length and dendritic spines density that is more pronounced in the D₂+ neurons of the indirect pathway. Preliminary data indicate that a reorganization of the corticostriatal projections also contribute to the neuroplastic changes observed. Our data provide direct evidence for selective morphological alterations of the D₂+ striatopallidal neurons involved in the indirect pathway following dopaminergic denervation of the striatum that characterizes Parkinson's disease.

P08.07

The effect of noradrenaline depletion on motor impairment and dopamine cell loss in a rat model of Parkinson's disease

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Objective: Parkinson's disease (PD) has been mainly known as a neurodegenerative disease with loss of dopaminergic (DA) neurons in the substantia nigra. However, studies of post mortem PD brains

have shown that not only DA neurons but also the noradrenergic (NA) neurons in the locus coeruleus degenerate, and that the NA neurodegeneration may be as profound, and also precedes degeneration of the midbrain DA neurons. The early involvement of the NA system is also in line with the caudal-to-rostral disease progression predicted by the model proposed by Braak et al. Hence, we have investigated the effect of NA depletion on motor deficits and DA cell loss in a rat PD model.

Methods: To generate two lesion paradigms, rats were injected with a dopamine toxin, 6-OHDA in striatum and/or a NA toxin, DBH-saporin in lateral ventricles. Animals have been tested in a battery of behavioural tests to check the degree of motor impairment. Perfused tissues were then subjected to immunohistochemistry to assess the amount of degeneration in striatal DA fiber and nigral DA neurons.

Results: In three motor tests (cylinder, amphetamine-induced rotation, and corridor tests) there was no significant difference in motor deficit between groups. However, the DA- and NA-lesioned animals showed more severe motor deficits than the DA-lesioned animals in stepping, staircase, and rotarod tests. Post mortem analysis revealed that NA depletion did not affect the degree of DA loss in striatum and substantia nigra determined by optical densitometry with tyrosine hydroxylase staining and stereological cell estimation with vesicular monoamine transporter staining, respectively. These results suggest that Parkinsonian-like motor symptoms could be worsened by NA degeneration and it is not due to more profound DA cell degeneration upon NA removal but maybe by dysregulated DA cell function.

BASIC SCIENCE: NEUROPHARMACOLOGY

P09.01

Neuroprotection and neurorescue properties of Sitagliptin in 6-hydroxydopamine rodent model of Parkinson's disease

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Objective: Type 2 diabetes (T2D) is one of the major risk factors associated with Parkinson's disease (PD). Pharmacological agents, such as glucagon-like peptide-1 (GLP-1) which ameliorates T2D, have become valuable candidates as disease modifying agents in the treatment of PD. In addition, endogenous GLP-1 possesses neuroprotective properties in PD. GLP-1 can be increased by inhibiting dipeptidyl peptidase-4 (DPP-4). The present study examines the efficacy of Sitagliptin, a DPP-4 inhibitor in a 6-hydroxydopamine (6-OHDA) induced rat model of PD.

Methods: Three weeks following induction of PD by intracerebral administration of 6-OHDA, animals were orally administered with Sitagliptin (5, 10 and 20 mg/kg) for 30 days. The effect of the DPP-4 inhibitor on brain GLP-1 and dopamine levels, oxidative stress, and behavioral tests were evaluated.

Results: The results reveal an attenuation of oxidative stress, improved brain GLP-1 and dopamine levels following treatment. This remarkable therapeutic effect of Sitagliptin mediated through DPP-4 inhibition demonstrates a unique mechanism for protecting

dopaminergic neurons by increasing GLP-1 levels and reverses the key deficits and pathology observed in PD.

P09.02

The influence of pramipexole and imipramine on behavioral and biochemical parameters in animal model of pre-clinical stage of PD and comorbid depression

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Objective: The motor dysfunction in Parkinson's disease (PD) is frequently preceded by comorbid depression. Dysfunction of monoaminergic systems could be its underlying cause. Recent studies have suggested that the administration of mixed dopamine D2/D3 receptor agonist - pramipexole may reduce both motor symptoms and depression in PD. The aim of study was to compare the influence of classic antidepressant - imipramine and pramipexole on the "depressive-like" behavior and monoaminergic systems parameters of rats with moderate lesion of the nigrostriatal system.

Methods: Male Wistar rats were stereotactically injected, bilaterally, with 6-OHDA (15 µg/2.5 µl) into the ventral striatum (vSTR). Imipramine was injected *i.p.* (10 mg/kg) once a day and pramipexole *s.c.* (1 mg/kg) twice a day, both for 14 days. On the 15th day after the surgery the locomotor activity test and forced swimming test (FST) were performed. The lesion extent was analyzed by HPLC and tissue content of monoamines and their metabolites and immunohistochemically. Also autoradiographic binding of ligands to dopaminergic and noradrenergic transporters were analyzed.

Results: The lesion of vSTR did not influence the locomotor activity of rats but increased immobility and swimming and decreased climbing in FST, suggesting depressive-like changes, not induced by motor disturbances. All the above disturbances observed in FST were decreased by pramipexole. Imipramine increased only climbing, but had no influence on immobility in lesioned rats. Pramipexole and imipramine had no influence on dopamine levels in lesioned rats. Pramipexole increased levels of DA metabolites in striatum and n.accumbens and increased the turnover of dopamine both in control and lesioned rats.

These results indicate that moderate, presymptomatic dopaminergic lesion may induce "depressive-like" symptoms which are reversed by dopamine agonist but not by a classic antidepressant.

Acknowledgements: Study supported by "DeMeTer" (POIG.01.01.02-12-004/09-00), co-financed by EU from European Regional Development Fund, part of the Operational Programme "Innovative Economy 2007-2013".

P09.03

The effect of a chronic treatment with MPEP, an mGlu5 receptor antagonist, on brain basal ganglia D1/D2 receptors, preproenkephalin/preprodynorphin mRNA levels and ERK/Akt signaling pathways in de novo parkinsonian monkeys

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Objective: The objective of this study was to investigate the long-term effect of the prototypal metabotropic glutamate 5 (mGlu5) receptor antagonist 2-methyl-6-(phenylethynyl)pyridine (MPEP) with L-3,4-dihydroxyphenylalanine (L-DOPA) on dopamine (DA) receptors, preproenkephalin (PPE), preprodynorphin (PPD), ERK and Akt signaling in monkeys lesioned with 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP).

Methods: MPTP monkeys were treated for one month with L-DOPA and developed dyskinesias while those treated with L-DOPA and MPEP (10 mg/kg) developed significantly less L-DOPA-induced dyskinesias (LID). Normal control and saline-treated MPTP monkeys were also included for biochemical analysis.

Results: [³H]SCH-23390 specific binding to striatal D1 receptors was decreased in all MPTP monkeys compared to controls and no difference was observed between saline, L-DOPA and L-DOPA+MPEP-treated monkeys. Striatal D1 receptor mRNA levels remained unchanged for all experimental groups and did not correlate with D1 receptor specific binding. [³H]raclopride specific binding to striatal D2 receptors was increased in saline and L-DOPA+MPEP-treated monkeys as compared to control and L-DOPA-treated monkeys, no difference between the latter groups was observed. The same pattern of changes as [³H]raclopride specific binding was observed for striatal D2 receptor mRNA levels with a positive correlation between these measures. Following L-DOPA treatment, PPE and PPD mRNA levels and the relative levels of phosphorylated ERK1/2 and phosphorylated Akt/GSK3 increased in the striatum of L-DOPA-treated monkeys compared to control, saline and L-DOPA+MPEP groups. By contrast, in the latter experiments, no change in the L-DOPA+MPEP group compared to control and saline-treated monkeys in the striatum was observed and there were positive correlations between these measures and mean dyskinesia scores of the MPTP monkeys. A chronic treatment with MPEP reduced the development of LID and was associated with a normalization of striatal D2 receptors, PPE/PPD mRNA levels and ERK/Akt signaling, while D1 receptors remained unchanged.

P09.04

A novel mGlu5 receptor antagonist, LY2300979, restores motor function and normalises abnormal beta oscillations observed in animal models of Parkinson's disease

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Objective: Metabotropic glutamate receptor 5 (mGlu5) are G-protein coupled receptors that are highly localized in limbic, basal ganglia and cortical brain regions. It has been reported that mGlu5 receptors may play a critical role in motor dysfunction in (Parkinson's disease) PD and the expression of mGlu5 is increased in both rat and monkey PD models that exhibit L-DOPA-induced dyskinesias (LIDs). In addition mGlu5 antagonists such MPEP and MTEP reduces the severity of these LIDs and attenuate the biochemical and molecular changes associated with dyskinesia.

Methods: We profiled a novel mGlu5 antagonist, 5-[2-(1H-pyrazol-4-yl)ethynyl]pyridine-3-carbonitrile or LY2300979, *in vitro* and *in vivo*. We then went on to study the efficacy of the compound in a range of models of Parkinson's disease in mice and rats.

Results: *In vitro* data indicated that LY2300979 had good selectivity and functional negative allosteric activity for mGlu5 rat and human receptor sub-types. LY2300979 exhibited good CNS penetration and displaced MPEPy (ED₅₀ = 2.3 mg/kg in mice and 1.4 mg/kg in

rat) and ABP688 (ED₅₀ 2.2 mg/kg in rat) binding in the rodent brain following oral administration. In addition, receptor occupancy and pharmacokinetic data indicated that the compound provided pharmacologically-relevant levels of target engagement for 6-8hr post-dosing. Confirmed using sleep EEG, in which an increase in NREM sleep and a reduction of REM sleep persisted for 8-10hr. In symptomatic models of PD, LY2300979 increased habituated locomotor activity and reversed reserpine-induced akinesia in mice. Synchronized oscillatory neuronal activity in the beta frequency range has been observed in the basal ganglia of PD patients and is thought to mediate the initiation of bradykinesia. LY2300979 (10 and 30 mg/kg) normalised the 6-OHDA induced-increases in beta oscillations in rats. In summary, these data indicate that LY2300979 has broad pharmacological activity across a range of preclinical models of PD.

P09.05

GCSF improves behavioral and motor coordination, monoamine levels and associates depression in 6-OHDA induced experimental model of Parkinson's disease (PD)

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Objective: Experimental evidenced suggested role of oxidants levels, behavioral (motor) deficit, locomotion and loss of dopaminergic neurons in SNc in Parkinson's disease. In our recent work we have seen the neuroprotective and neurogenesis effect of GCSF in an *in vivo* model of Alzheimer's disease. In the present study, we have aimed to elucidate the neuroprotective role in Parkinson's disease, 2nd most common neurodegenerative disease. Published literature showed unilateral intrastratial 6-hydroxydopamine (6-OHDA) administration produces motor decline and depressive-like behaviors which resembles Parkinson's disease.

Methods: In a parallel designed experimental model, animals were divided into seven groups. After selectively insult with 6-OHDA (12µg in 4µl) in substantial nigra par compacta (SNc) rats were treated with the GCSF, carbidopa/levodopa and their combinations. Neuroprotection and improvement in neuroamines were assessed with battery of behavioral tests, biochemical and ROS levels. All results were selectively correlated with histopathological finding of the study.

Results: 6-OHDA significantly induced motor loss and Parkinson's like behavior in rats. The muscle coordination, exploratory and rotation behaviors were improved significantly in the GCSF alone and in combination with the L-DOPA/carbidopa (p<0.05). Muscle rigidity was significantly corrected in the adhesive tests (p<0.05) and ROS levels were significantly declined in GCSF treated rats (p<0.05). FST observation suggested that depression associated with the PD was also found to be ameliorated in FST exposed rats. GCSF improved neuroprotection and increased monoamine levels at the SNc. The important finding of the study, GCSF also ameliorated depression like behavior associated with Parkinson's disease.

Conclusion: Hence, the present study concluded that GCSF not only improved Parkinson's like behavior and monoamines level in SNc but also co-morbid depression.

BASIC SCIENCE: ELECTROPHYSIOLOGY & FUNCTIONAL IMAGING, OPTOGENETICS

P10.01

A functional magnetic resonance imaging approach towards understanding the circuit-level effects of deep brain stimulation

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Objective: To evaluate, on a whole-brain scale, the neural circuitry modulated by deep brain stimulation (DBS) at the subthalamic nucleus (STN) and internal globus pallidus (GPi) in a rat model.

Methods: The present study employed blood-oxygen-level-dependent (BOLD) and cerebral blood volume (CBV) functional magnetic resonance imaging (fMRI) to evaluate the global modulatory effects of deep brain stimulation at the STN or GPi. Anesthetized rats were implanted with 2-channel tungsten microwire electrodes and stimulated at a range of frequencies (10-400Hz) during fMRI acquisition with a 9.4 Tesla system. An iron oxide contrast agent (MION, 30 mg/kg) was administered intravenously for CBV measurements.

Results: Robust, frequency dependent positive BOLD activation was observed in the ipsilateral motor, somatosensory, and cingulate cortices during stimulation at either the STN or GPi. Interestingly, these cortical responses were maximal at high frequencies (100-130Hz) known to be therapeutic for Parkinson's Disease. Contralateral negative BOLD responses were additionally observed during DBS at the GPi, and occurred diffusely throughout cortex and subcortical areas. This negative response peaked at 40Hz, suggesting recruitment of a functionally distinct circuit- possibly off-target stimulation of the neighboring internal capsule. Further analysis of DBS circuit modulation using the more sensitive CBV readout at the STN target revealed additional areas of DBS effects, including discrete sites of thalamic activation and striatal responses both ipsi- and contralateral to the stimulation site. Future experiments will confirm and extend these findings using a parkinsonian rat model. This study introduced a novel imaging methodology for studying DBS effects in animal models. The combination of DBS with fMRI would permit examination of DBS circuits and has potential to ultimately address a prevailing question in DBS therapy, namely, how DBS modulates neural activity in different brain regions to achieve symptom alleviation.

P10.02

Brain networks involved in dance: a model mechanism for examining plasticity during dance therapy.

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Objective: Our research program examines the neural mechanisms of dance, with a future goal to then examine dance in Parkinson's disease (Earhart 2009). Although the neural mechanisms of dance have been examined, these mechanisms have not been probed

during learning of a novel dance routine in expert, normal and in abnormal brains. Thus, our long term goals are to examine the plasticity that occurs during learning. To this date we have begun examining this in experts and normal controls.

Method: Ten dancers were scanned over 8 months as they learned a choreographed. Eleven controls included both dancers and non-dancers. Dancers were scanned up to 4 times.

Results: Using task based random effects GLMs while the subjects visualized their dance during fMRI scans, we found supplementary motor cortex (SMA), auditory, premotor and parietal cortices activated with an increasing pattern up to 7 weeks of learning/performing. This was followed by a decrease at 8 months (n=5). We will contrast these functional findings with structural diffusion tensor imaging (DTI) scans at three different times during learning (1, 7 and 32 weeks), using SMA and auditory regions of interest to probe for structural changes. Additionally, we found that the basal ganglia (caudate) activated after the 7th week up to 34 weeks. This suggests that while experts visualize a learned dance, their cortical network of activation decreases once the dance is learned, while basal ganglia activation remains activated. This procedure would be possible for PD patients since the whole scanning sequence lasts 12 minutes.

P10.03

Quantitative evaluation of hypokinesia in Parkinson disease using sensor gloves

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Objective: To evaluate the utility of sensor gloves on quantitative evaluation of bradykinesia on Parkinson's Disease.

Methods: The authors carried out a study of type cases and controls, organized in two groups: 13 patients with clinical diagnosis of idiopathic PD in "on" state and 24 controls, to which were carried out a registration of the "finger tapping" movement using sensor gloves (5DT-14Ultra) the analysis of the amplitude was calculated through the power spectra derived from a Fourier Transform (FFT). Also we examine the relationship between glove data obtained, the clinical scale employed (UPDRS) and the early and late components of the premotor potential.

Results: The authors observed that patients presented a smaller speed in the execution of the movements, demonstrated to reach their maximum amplitude at smaller movement frequency (1,5-2Hz) than controls (3,5-4Hz), as well as, a significant decrease of the amplitude of movement toward the frequencies of movement =3Hz. The most favorable values in the clinical scale employed were in connection with broader movements toward the high frequencies (=3.5Hz). Our study demonstrated a relationship between amplitude of movement and the area of the earlier and later components of the premotor potential. A bigger area associated to a broader movement.

Conclusion: The authors conclude that sensor gloves are a useful device as quantitative complement of the clinical evaluation in the patients with PD.

P10.04

Pre- and post-synaptic dopaminergic dysfunction in multiple system atrophy: combined [¹⁸F]FP-CIT and [¹⁸F]FDG-PET study

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Objective: To investigate the integrity of presynaptic nigral and postsynaptic striatal dopaminergic systems in MSA patients, especially in relation to the presence of parkinsonism

Methods: We studied 26 patients who were diagnosed with probable or possible MSA based on the second consensus statement on the diagnosis of MSA and underwent both [¹⁸F]FP-CIT PET and [¹⁸F]FDG PET. The PET images were analyzed with 12 striatal subregional volume-of-interest templates (bilateral ventral striatum, anterior and posterior caudate, anterior, posterior and ventral putamen). The PET results of study subjects were compared with the results of age-matched normal controls.

Results: Of 26 MSA patients, eight patients had no parkinsonism. Between MSA patients with parkinsonism and those without parkinsonism, there were no significant differences in age at onset, age at study, sex, disease duration, and global disability scale. Seven (87.5%) MSA patients without parkinsonism, and all MSA patients with parkinsonism revealed decreased striatal binding value in the [¹⁸F]FP-CIT PET. In five (62.5%) MSA patients without parkinsonism and 14 (77.8%) MSA patients with parkinsonism showed decreased striatal glucose metabolism in [¹⁸F]FDG PET. The dissociation between [¹⁸F]FP-CIT PET and [¹⁸F]FDG PET were considered in 11 MSA patients with parkinsonism and 6 MSA patients without parkinsonism. In quantitative analyses, the binding values of [¹⁸F]FP-CIT PET and [¹⁸F]FDG PET are correlated in the caudate region ($r = 0.504$, $p = 0.009$), but not correlated in the putamen region.

Conclusions: High prevalence of subclinical dopaminergic denervation in MSA without parkinsonism could suggest that the evaluation of dopaminergic system using PET scans might be useful in differential diagnosis of cerebellar ataxia. The dissociation between presynaptic and postsynaptic dopaminergic denervation in MSA patients suggest the presence of presynaptic type parkinsonism in MSA. Further research is needed to find out levodopa responsiveness according to the dissociation of presynaptic and postsynaptic dopaminergic denervation.

P10.05

Changes in resting state EEG following motor performance in PD.

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Objective: We have recently found that the spontaneous resting-state EEG of normal subjects shows frequency specific changes after a forty-minute visual task. As they are confined to the areas involved in the task, these changes or traces likely reflect use-

dependent plasticity. Here, we determined whether patients with PD, a disease associated with abnormal plasticity, show similar frequency-specific changes in the resting state EEG after a forty-minute motor task as normal controls.

Methods: Twenty-three patients with PD (stage 2 and 3) and 20 age-matched controls performed a forty-minute reaching motor task with their right dominant hand. High-density EEG was recorded in the eyes-open resting state (3 minutes) before (RS1) and after (RS2) the motor task. We performed spectral analysis to identify individual alpha peak (IAP) value; we aligned each individual power spectrum on the peak. With permutation t-tests within each group, we identified local changes. As task-related power changes were spread across the entire scalp, average scalp power in different frequency bands was then submitted to a mixed-model ANOVA with Time (RS1, RS2) and Group (PD, Controls) as main factors.

Results: Confirming previous results, IAP of patients was significantly lower (9.0 ± 1.1 Hz) than controls (9.8 ± 1.0 Hz, $p=0.01$). Moreover, after the forty-minute motor task, IAP decreased further in PD (-0.2 ± 0.4 Hz, $p=0.04$) but not in controls ($+0.1 \pm 0.6$ Hz, $p=0.50$). After the task, comparison of power on the whole scalp showed widespread increases in alpha and beta bands in both groups, without significant changes for theta and gamma. Average Alpha power increased significantly after task in patients ($p=0.0001$) but not in controls ($p=0.63$). Instead, Beta power showed a similar significant post-task increase in both groups ($p<0.03$). These results indicate that motor performance induced power increases in both groups, but only PD shows also involvement of lower frequencies, a possible sign of abnormal plasticity.

P10.06

Increase of Intra-motor-network connectivity in Parkinson's disease patients – an fMRI study with graph theory approach –

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Objective: Over-activation in the motor cortex has been reported in animal models of Parkinson's disease (PD), and PD patients, during resting state and tasks. We hypothesized that the connections within the motor network increases in PD, and investigated this hypothesis.

Methods: Fourteen healthy volunteers and twelve PD patients performed a series of finger movement tasks, involving self-initiated (SI), externally triggered (ET) and control finger movements while being scanned with functional MRI. Fifty-eight regions of interest (ROIs) were selected in areas where task-related significant activation occurred in the HV group, and divided into two categories, the motor related areas (MTR) and the others (VisInt). Using a specified connection number (388 connections corresponding to 23.5% of all the connections), between ROIs, counting from the strongest connection, we counted the number of ROIs within the intra-MTR, intra-VisInt, and between MTR-VisInt networks, respectively. Using simple t-test, each number was compared between the HV and PD. Correlational rate was calculated between the number of the intra-MTR and the UPDRS motor score. Significance level was set at $p < 0.05$.

Results: The number of intra-MTR connection was significantly greater in the PD than in the HV group ($p = 0.027$). The other numbers were not significantly different between groups. The number of the intra-MTR was negatively correlated to the UPDRS motor scores ($r = -0.80$, $p = 0.002$). We speculate that the increase of the intra-MTR connectivity might be related to the motor dysfunction in PD, which is more prominent for demanding tasks, but that might be compensatory for relatively simple movement.

P10.07

Disease and sex-related differences in daily electromyography influence functional performance in Parkinson's disease

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Electromyography (EMG) recordings made bilaterally may reveal important information about asymmetric muscle activation patterns associated with reduced functional performance in Parkinson's disease (PD). Also, sex-differences in muscle activation patterns would contribute to understanding underlying causes of differential functional decline between males and females with PD.

Objective: Quantify daily muscle quiescence through EMG gap analysis and examine handgrip-strength in PD-females ($n=13$) and PD-males ($n=10$) (Hoehn/Yahr= 2.1 ± 0.7) compared with age-matched controls. Hypothesis: muscle quiescence will be less in PD compared with controls and fewer EMG gaps will be observed in PD-females compared with PD-males. The more-affected PD side will demonstrate fewer EMG gaps and greater weakness relative to less-affected.

Methods: Bilateral daily EMG was recorded (7-hours) and normalized to maximal voluntary exertions (MVE). EMG gap was defined as $<1\%$ amplitude of MVE for >0.1 sec and characterized as number, duration and time occupied by gaps. Handgrip-strength was evaluated with a dynamometer. Three-way repeated-measures ANOVA examined differences in gap characteristics and strength.

Results: Percentage of time leg muscles were quiescent was less in PD compared with controls as a result of shorter EMG gaps ($p<0.04$), suggesting greater burst activity in PD. Fewer periods of muscle quiescence in PD-females compared with PD-males ($p=0.004$) suggests that female muscles have less opportunity to rest and recover, and indicates greater muscle activity necessary to execute daily activities. PD-females were weaker than PD-males ($p=0.00$) for handgrip-strength. Fewer gaps were observed on more-affected PD side ($p=0.01$) and decreased grip strength in more-affected hand ($p=0.04$). Handgrip weakness in PD compared to controls ($p=0.04$) likely results from peripheral changes and slowed onset of voluntary contractions. Bilateral quantification of daily muscle quiescence provides insight into the underlying neuromuscular contribution to declines in functional performance, reflecting central and peripheral changes that may explain differences in muscle weakness, in males and females with PD.

P10.08

Altered striatal spiny neuron activity as a therapeutic target in Parkinson's disease

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Objective: The loss of striatal dopaminergic modulation in Parkinson's disease (PD) presumably leads to changes in firing rate and patterns of striatal output neurons (medium spiny neurons, MSNs). The status of the MSN activity has not yet been described in PD, and thus, we examined the parameters of the MSN firing in patients undergoing DBS surgery.

Methods: We analyzed striatal data obtained during electrophysiologic mapping for DBS treatment in PD patients, along with dystonia and essential tremor (ET) patients for comparison. Strict criteria were applied for MSN classification.

Results: The mean firing rate of MSNs was significantly higher in PD (32 ± 9 Hz) than dystonia (9.5 ± 4 Hz) and ET (< 3 Hz). In PD, a larger fraction of striatal neurons also exhibited burst activity. These findings are aligned with previous data from parkinsonian monkeys (Liang et al., 2008), challenging the classic functional model of PD. The role of glutamatergic hyperactivity in these striatal changes suggests that manipulating the glutamate signaling is critical for improved responses to dopamine replacement. The less increased frequencies in dystonia highlight the relevance of specifically high MSN activity to PD, but also suggest that there may be grounds for the frequently alluded Dystonia-PD continuum. The very low firing rates in ET resemble MSN activity in normal monkeys, suggesting a parallel with normal humans. These findings demonstrate profound alterations of the MSN discharge in patients with PD, and point to the importance of investigating its molecular basis to develop function-restorative therapies.

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P10.09

Restoration of normal striatal dopamine responses with NMDA receptor blockade

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Objective: Dopaminergic innervation of medium spiny neurons (MSN) of the striatum is essential for normal motor behavior. However, in patients with idiopathic Parkinson's disease (PD), long-term levodopa replacement therapy is associated with debilitating motor complications such as involuntary choreodystonic movements (levodopa-induced dyskinesias, LID). In non-human primate models of advanced parkinsonism with chronic levodopa therapy, MSNs are profoundly hyperactive and often exhibit reversal of levodopa-induced firing rate changes ("inversions") that is highly correlated with the onset of LID (Liang et al., 2008). It was hypothesized that baseline hyperactivity mediated by hyperglutamatergic tone may lead to these abnormal inversions, and play ultimately a primary role in the mechanisms of LID.

Methods: The electrophysiological effects of striatal NMDAR antagonism were studied in three awake, behaving, parkinsonian rhesus monkeys. Local microinjections of the competitive NMDAR antagonist LY235959 were performed at the site of extracellular recordings in the striatum in monkeys receiving systemic levodopa administration (s.c.) during the recording session. Behavioral effects of the antagonist were evaluated in tests of systemic co-administration with levodopa.

Results: We found that local microinjection of the vehicle (artificial CSF) alone had no effect on firing rates and did not alter the pathological MSN responses to systemic levodopa. However, reduction of baseline activity via local microinjections of LY235959 completely abolished the abnormal inversion response of MSNs to systemic levodopa. The local effects of the NMDAR antagonist correlated with its antidyskinetic effects with systemic injections. These findings have profound implications for elucidating the pathophysiological mechanisms underlying LID, and may contribute to developing new pharmacological agents to alleviate dyskinesias in advanced PD.

BASIC SCIENCE: PREVENTION, NEUROPROTECTION, NEUROPLASTICITY

P11.01

Dose-dependent therapeutic effects of FK506 on dopaminergic neurodegeneration and neuroinflammation in a viral vector-based α -synuclein rat model for Parkinson's disease

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Objective: Testing of new therapeutic strategies for Parkinson's disease (PD) is currently hampered by the lack of a robust and reproducible animal model that displays the hallmark features of PD. In this study we aimed to develop a viral vector-mediated rat model based on α -synuclein, presenting reproducible nigrostriatal pathology and behavioral deficits in a short time period. Next, we used this optimized PD rat model to study the therapeutic effect of the immunophilin ligand FK506 *in vivo*.

Methods: An adeno-associated viral vector serotype 2/7 encoding A53T mutant α -synuclein was stereotactically injected into the substantia nigra of adult Wistar rats and the effect was determined by histology, biochemical analysis, non-invasive imaging, microdialysis and behavioural analysis. FK506 was administered at different doses by daily tail vein injection

Results: Overexpression of (A53T) α -synuclein in rat substantia nigra resulted in extensive and reproducible nigrostriatal pathology and behavioral deficits in a 4 weeks time period. Progressive dopaminergic dysfunction was corroborated by histopathological and biochemical analysis, motor behavior and *in vivo* microdialysis. L-dopa was found to revert the behavioral phenotype. Non-invasive PET and MR imaging allowed longitudinal monitoring of neurodegeneration, highlighting the translational value of this model. In addition, insoluble α -synuclein aggregates were formed in this model. Treatment with FK506 for four weeks significantly increased the survival rate of dopaminergic neurons in a dose-dependent way. No reduction in α -synuclein aggregation was apparent in this time window but FK506 significantly lowered the infiltration of cytotoxic T cells and the number of microglia/macrophages. In conclusion, the anti-inflammatory properties of FK506 prevent neurodegeneration in this α -synuclein-based PD model, pointing to a causal role of neuroinflammation in the pathogenesis of PD.

P11.02

Neuroprotective effect of plasmalogen precursor analogs, PPI-1011 and PPI-1025, in MPTP mice

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Objective: This study investigated a new neuroprotective mechanism: membrane plasmalogen augmentation. This strategy is a promising neuroprotective mechanism because of the roles plasmalogens play in membrane structure mediated functions such as vesicular release of neurotransmitters and membrane protein activity, free radical scavenging, and as a storage of depot of neuroprotective polyunsaturated fatty acids (docosahexaenoic acid (DHA)).

Methods: Male mice were treated for 10 days with daily oral administration of either the DHA-plasmalogen precursor PPI-1011 (10, 50 or 200 mg/kg) or the linoleic acid-plasmalogen precursor PPI-1025 (10, 50 or 200 mg/kg). On day 5 the mice received 4 injections of MPTP (6.5mg/kg). The mice were sacrificed on Day 11 and striatal biogenic amine concentrations were measured by high performance liquid chromatography with electrochemical detection.

Results: PPI-1011 (10 and 50 mg/kg) and PPI-1025 (10 mg/kg) completely prevented the decrease of dopamine concentration induced by MPTP, the PPI-1025 prevention at 50 mg/kg was partial and no effect was observed at 200 mg/kg for either compound. PPI-1011 and PPI-1025 at 10 and 50 mg/kg prevented the MPTP induced decrease of DOPAC and HVA concentrations. All doses of PPI-1011 as well as PPI-1025 at 200 mg/kg maintained serotonin concentrations at control values. MPTP had no effect on 5-HIAA concentrations whereas mice treated with PPI-1011 or PPI-1025 (all doses) had increased concentrations of 5-HIAA. All groups showed an increase in 5-HIAA/serotonin ratios but this augmentation was greater in PPI-1011 (10 and 50 mg/kg) and PPI-1025 (50 mg/kg) treated mice than MPTP and vehicle groups. In conclusion, the neuroprotective effect of plasmalogen precursor analogs appears to have a bell-curve dose-dependency in that the effect was reduced at the higher doses tested. The equal activity of linoleic (PPI-1025) and DHA (PPI-1011) plasmalogen precursors indicates that the observed neuroprotection is principally due to the plasmalogen backbone and not DHA.

P11.03

Transient silencing of RXR β retinoid receptor enhanced neuronal differentiation by retinoic acid in SH-SY5Y cells

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Objective: Retinoic Acid (RA) is a potent inducer of catecholaminergic differentiation in vitro. Classically, it is known that RA effects at cellular level are dependent on gene transcription mediated by retinoid receptors, which are subdivided in to RAR and RXR. Recently, nongenomic mechanisms (not dependent on RAR/RXR-mediated gene transcription) have been proposed to play an important role in biological actions by RA by influencing post-translational processes, such as protein phosphorylation, tubulin acetylation, actin polymerization, synaptic transmission and redox signaling. However, there is no data on the role of nongenomic mechanisms in RA-induced neuronal differentiation. Therefore, we studied the effect of retinoid receptor silencing in a well-

characterized model of in vitro neuronal differentiation with RA (human SH-SY5Y neuroblastoma-derived cells).

Methods: We used an approach of transient protein silencing with small interfering RNA (siRNA). Cells transfected with siRNA for the receptor isoform RXR β were subjected to neuronal differentiation by RA. To confirm the status of retinoid receptor inhibition, we will perform western blot and qRT-PCR analysis. Neuronal differentiation was evaluated by contrast-phase microscopy (neurite extension and ramification) and by using confocal microscopy and western blot analyses to detect neuronal biochemical markers, such as neuronal-specific enolase, beta-III tubulin and tyrosine hydroxylase.

Results: After 5 to 10 days of RA-induced neuronal differentiation, RXR β -silenced cells presented increased tyrosine hydroxylase and beta-III tubulin content. Neurite extension and ramification was also enhanced compared to control cells, as observed by contrast phase microscopy and confocal analysis with beta-III tubulin staining. These results suggest that effects of RA during neuronal differentiation may involve nongenomic actions able to modulate post-translational events. The comprehension of such mechanisms may be applied to improve cell replacement-based therapies for Parkinson's disease.

P11.04

The bioavailable plasmalogen precursor PPI-1011 reduces levodopa-induced dyskinesias in parkinsonian monkeys: comparison with docosahexaenoic acid (DHA)

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Objectives: A majority of Parkinson disease (PD) patients develop abnormal involuntary movements called dyskinesias after 5-10 years of levodopa (L-DOPA) treatment that are difficult to manage. No drug is yet available for dyskinesias, aside from a modest benefit with amantadine in some PD patients. Hence, alternative drugs are needed that may alleviate dyskinesias. We reported that docosahexaenoic acid (DHA, omega-3) has antidyskinetic activity in the 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP) monkey model of PD. This experiment tested a new target for dyskinesias, plasmalogens, because of their roles in membrane structure mediated functions such as vesicular release of neurotransmitters and membrane protein activity, free radical scavenging, and as a storage depot of polyunsaturated fatty acids such as DHA.

Methods: MPTP-lesioned monkeys received L-DOPA to induce dyskinesias. First we measured the behavioral motor effect of a daily treatment for 10 days with DHA (100 mg/kg) and the DHA-plasmalogen precursor PPI-1011 (50 mg/kg) as compared to their plasma DHA and plasmalogen concentrations. Then, we investigated the dose-response (10, 25 and 50 mg/kg) behavioral effect of PPI-1011.

Results: PPI-1011 and DHA reduced levodopa-induced dyskinesias (LID) while maintaining the antiparkinsonian activity of L-DOPA. The PPI-1011 reduction of LID was observed at the earliest time point behavioral measure that is 2 days after PPI-1011 administration whereas the DHA effect was later at 10 days. DHA treatment led to increased plasma levels of DHA; these levels were higher than those obtained with PPI-1011. Next, we confirmed the effect of 50 mg/kg PPI-1011 to reduce LID and also at 10 and 25 mg/kg, the extent of the effect being similar with these doses but occurring earlier in the 10 days of treatment at high doses. **In conclusion,** PPI-1011 has antidyskinetic activity in MPTP monkeys that could be due in part but not only to its production of DHA.

P11.05

Nigrostriatal expression and modulation of the Sigma-1 receptor in experimental parkinsonism

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Objective: Sigma-1 receptor (Sig-1R) is a chaperone protein widely distributed in the mammalian brain, peripheral neurons and visceral organs. Several studies suggested its implication in aging and many human diseases, but its possible role in Parkinson's disease has not yet been reported. In this study we examine the nigrostriatal expression and modulation of Sigma-1 receptor in experimental parkinsonism.

Methods: 6-OHDA intrastratial lesions were performed in rats and Sigma-1 receptor nigrostriatal immunoreactivity was observed at different time points post surgery. The time-course of Sig-1R expression was confirmed in mice sustaining intrastratial 6-OHDA lesions.

Results: Sig-1R immunopositive cells were found in the striatum and in the substantia nigra of both intact and 6-OHDA lesioned animals. However, neurotoxic lesions caused a massive and widespread upregulation of Sigma-1 receptor in the entire striatum on the side ipsilateral to the 6-OHDA injection at 2 and 7 days post surgery. Its expression decreased at longer time points (14 and 28 days), being restricted to the dopamine-denervated subregions of the striatum. Cells immunopositive for Sig-1 receptor in the striatum showed mainly glial morphology. Changes in Sig-1R expression also occurred in the substantia nigra, although with a different temporal pattern and cellular morphology. These results show that Sigma-1 receptor is expressed in the nigrostriatal system and becomes upregulated after neurotoxic lesion, as possible part of a compensatory response to damage. The effects of Sigma-1 receptor ligands are currently being investigated in 6-OHDA lesioned mice and will be presented at the meeting.

P11.06

A novel thiazolidinedione protects dopamine neurons in culture and in a preclinical model of Parkinson's disease

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Objective: Mitochondrial impairment is suggested to play a central role in Parkinson's disease (PD) pathogenesis. It is hoped that therapies that improve mitochondrial function might retard PD progression. The mitochondrial target of thiazolidinedione insulin sensitizers (mTOT) is a complex of pyruvate carrier proteins that is located in the mitochondrial membrane. Modulation of mTOT improves mitochondrial oxidative metabolism (Colca et al. 2013) and changes nutrient-sensing pathways such as the AMP-activated protein kinase. Furthermore, this modulation mitigates over-activation of the mammalian target of rapamycin (mTOR) pathways. We hypothesize that a specific modulator of mTOT (MSDC-0160) can protect dopaminergic neurons in models of PD.

Methods: We assessed the neuroprotective properties of MSDC-0160 (micromolar concentrations) in a human dopaminergic cell line (LUHMES cells) and cultured primary mouse midbrain mesencephalic neurons in the presence of MPP⁺. We quantified neurite length and numbers of surviving tyrosine hydroxylase-positive neurons. In parallel, we examined the effects of MSDC-0160 *in vivo* in a sub-acute MPTP mouse model of PD. We pretreated mice with MSDC-0160 via oral gavage before giving them MPTP. After 5 days of MPTP treatment we assessed motor function and 7 days following MPTP treatment we sacrificed the mice and stereologically counted the number of TH-immunoreactive neurons.

Results: We found that MSDC-0160 treatment attenuated MPP⁺-induced loss of TH positive dopaminergic neurons and terminals in LUHMES cells and primary midbrain cultures. Moreover, treatment with MSDC-0160 improved locomotor activity and protected nigrostriatal dopaminergic neurons in the subacute MPTP mouse PD model. Taken together, we demonstrate significant neuroprotective effects of MSDC-0160 in cell culture and an established pre-clinical animal model of PD. MSDC-0160 is a safe compound already approved for clinical evaluation (type-2 diabetes and Alzheimer's disease) and based on our results MSDC-0160 might be a candidate drug for clinical trials aimed at modifying the course of PD.

P11.07

Unilateral 6-OHDA lesion and Dopa administration in Nur77 knockout rats reveal an important role of this transcription factor in Parkinson's disease and its treatment

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Objective: Nur77 (Nr4a1) is a transcription factor of the nuclear receptor family that is associated with neuroadaptation pathways triggered by perturbation of dopamine (DA) neurotransmission. We have previously shown that DA denervation and repeated L-Dopa treatment modulate Nur77 mRNA expression patterns in the striatum. However, the exact role of this transcription factor in Parkinson's disease (PD) and L-Dopa treatment is still unknown. In the present study, we investigated the role of Nur77 in a newly developed rat knockout model (FHH-Nr4a1^{m1M^{co}wi}, nonsense mutation, Y130stop).

Methods: We performed unilateral 6-hydroxydopamine (6-OHDA) lesions in wild type and Nur77 knockout rats. Daily L-Dopa treatments (6.25 mg/kg, benserazide 15 mg/kg) were maintained for 21 days. Circling behavior and Abnormal Involuntary Movement (AIM) scores were measured five times. We also evaluated the effect of striatal Nur77 overexpression using an adeno-associated viral construct in this PD model. In addition, we quantified the effect of the neurotoxin on DA cells using stereology (TH immunoreactivity).

Results: Nur77 knockout rats showed a dramatic reduction in both L-Dopa-induced circling and AIM scores. On the other hand, Nur77 striatal overexpression tended to increase these behavioral measures. Moreover, the effect of 6-OHDA injections on TH immunoreactivity was reduced in Nur77 knockout, compared to wild type rats. Thus, these results suggest that Nur77 plays an important role in L-Dopa-induced dyskinesia as well as in DA cell loss in this PD model. Supported by the Michael J. Fox Foundation (MJFF) for Parkinson's disease.

P11.08

Selective knockout of the vesicular GABA transporter (VGAT) in the motor cortex completely protects against MPTP-induced lesioning in mice

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Objective: Alterations in activity of the motor cortex (MC) in patients with Parkinson's disease (PD) provides a new potential therapy. Recent studies suggest that rTMS or direct targeting/stimulation of the MC of PD patients can provide motoric improvement.

Methods: To examine physiological effects of possible MC activation and neuroprotection in PD, we infused unilaterally an AAV-Cre-GFP vector into the motor cortex of *Vgatflox/flox* mice to prevent the translation of the vesicular GABA transporter (VGAT). Mice (C57Bl/6J) were subjected to 4 weeks of a progressive dose of 1-methyl-2-phenyl-1,2,3,6-tetrahydropyridine (MPTP), 5 d/wk injected i.p. at doses of 8, 16, 24, and 32 mg/kg/d, or vehicle (Goldberg, et al, 2011). One week after the last dose of MPTP, the dorsolateral striatum (STR) and substantia nigra pars compacta (SNpc) were processed for light microscopic immunohistochemistry (IHC).

Results: Analysis of the optical density of tyrosine hydroxylase-immunoreactive (TH-ir) nerve terminals in the STR showed a 79% reduction in the C57 mice after MPTP lesioning when compared to the vehicle group ($p < 0.001$) that was completely prevented by the AAV-Cre-GFP infusion ($p > 0.19$). This protection was bilateral within the CPU. The average number of TH-ir cells/section within the SNpc demonstrated that the 59% loss of TH-ir cells in C57 mice compared to control animals was completely prevented in the floxed mice. The TH-ir neuronal protection was also bilateral. Cytochrome oxidase histochemical analysis of the central substantia nigra pars reticulata demonstrated a surprising decrease in optical density after MPTP insult in wild type mice (60%, $p < 0.01$) that is partially protected by the loss of VGAT expression in the MC (36%, $p < 0.001$). These data suggest a novel therapy for PD, with unilateral inhibition of the GABAergic interneurons within the MC resulting in bilateral protection against the loss of both TH-ir terminals and neurons following progressive MPTP administration.

P11.09

GM1 ganglioside as a disease modifying agent for Parkinson's disease: Clinical and neuroimaging findings

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Objective: A single center, double-blind, delayed start study was conducted to examine possible symptomatic and disease-modifying effects of GM1 ganglioside in Parkinson's disease (PD). As part of this study, some subjects were studied longitudinally with [¹¹C]Methylphenidate ([¹¹C]MP) positron emission tomography (PET) to evaluate effects of GM1 treatment on striatal dopamine terminals.

Methods: Seventy-seven subjects with PD were randomly assigned to receive GM1 for 120 weeks (early-start) or placebo for 24 weeks followed by GM1 for 96 weeks (delayed-start). Seventeen subjects who received standard-of-care were followed for comparative information about disease progression. Primary outcome was change from baseline Unified Parkinson's Disease Rating Scale

(UPDRS) motor scores. PET studies were performed on 32 subjects (14 early-start, 18 delayed-start, 11 standard-of-care). Ten striatal regions-of-interest were defined on MRI: left/right anterior and posterior caudate; left/right anterior and posterior putamen; left/right ventral striatum. Mixed effects linear regression simultaneously modeled signal for all 10 regions. Within the mixed effects model, changes in signal were estimated and groups were compared using appropriate linear contrasts.

Results: At week 24, the early-start group significantly improved in UPDRS motor scores vs. a significant worsening in the delayed-start group. PET results showed increased signal in 7 of 10 regions in the early-start group vs. baseline and decreased signal in all regions in the delayed-start group. At 1 yr., [¹¹C]MP binding was significantly preserved in several striatal regions in the early-start group vs. the standard-of-care group with the greatest difference observed in the posterior putamen, the region with the most severe loss of [¹¹C]MP binding in PD.

Conclusions: GM1 use for 24 weeks was superior to placebo for improving motor symptoms and extended GM1 use resulted in lower than expected symptom progression. PET results support the possibility that GM1 may preserve striatal dopamine terminals and may even stimulate a sprouting response.

P11.10

Performance of movement in hemiparkinsonian rats influences the modifications induced by dopamine agonists in striatal efferent dynorphinergic neurons

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We have previously shown that movement performance induced by dopamine agonist drugs in hemiparkinsonian rats unilaterally lesioned with 6-hydroxydopamine (6-OHDA), governs the occurrence of a sensitized motor response to a subsequent dopaminergic challenge (priming model). In the present study, we examined the influence of movement performance (rotational behavior) on the molecular events induced by priming in the striatum. To this end, unilaterally 6-OHDA-lesioned rats were primed with apomorphine (0.2 mg/kg) in immobilized or freely moving conditions (priming induction) and 3 days later the D1 receptor agonist SKF 38393 was administered (priming expression). Evaluation of striatal mRNA for enkephalin and dynorphin, markers of the indirect and direct striatonigral pathways, and of GAD67 showed an increase in dynorphin in primed SKF 38393-treated rats, no matter whether immobilized or freely moving during priming induction, whilst enkephalin and GAD67 did not show any changes. In contrast, evaluation of mRNA for the early gene *zif-268* in the striatum showed a generalized increase after administration of SKF 38393, in both primed and unprimed rats. However, examination of *zif-268* mRNA at the single-cell level, showed that only dynorphin(+) neurons of primed not immobilized rats displayed a significantly higher number of *zif-268*-positive silver grains in response to the SKF 38393 challenge. This selective activation of *zif-268* in dynorphinergic striatonigral efferent neurons demonstrates that movement performance in response to dopaminergic drug administration under conditions of dopamine denervation is critical for the emergence of neurochemical modifications in selected striatal efferent neurons. Furthermore, these results may provide information on the first initial molecular events taking place in the complex processes that lead to dyskinetic movements in Parkinson's disease.

CLINICAL SCIENCES: SYMPTOMS, SIGNS, FEATURES, & NON-MOTOR MANIFESTATIONS

P12.01

Profile of Parkinson's disease patients presenting at the Calabar neurology clinic

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Introduction: Calabar is a coastal city in the Niger delta region of Southern Nigeria, with a population of about 400, 000. The Movement disorders arm of the Neurology clinic in Calabar was established about one year ago. We have enrolled about 21 new cases so far.

Objective: To determine the profile of newly registered patients in our clinic.

Method: Basic demographic data and clinical features were obtained with a structured questionnaire.

Results: Twenty-one new cases were registered of which 7(33.3%) were females and 14 (66.3%) were males. Average patient age was 60 years, while mean age at onset of motor symptoms was 56.6 years. 10 patients had diabetes mellitus as co-morbidity, while 9 had coexisting hypertension.

Only 17 (81%) had a correct diagnosis from the referring Physician. The interval between onset of motor symptoms and presentation at the clinic ranged between one week and 3 years. 95.5% of the patients had rigidity, while only 33.3% had postural instability. A family history of PD was found in only 2 (9.5%) of the patients.

The patient distribution on the Modified Hoehn and Yahr staging was as follows: stage 1=14.3%; stage 1.5=19%; stage 2=33.3%; stage 2.5=14.3%; stage 3=14.3% and stage 4=4.8%. The initial limb affected was right upper limb in 19 (90.5%) and left upper limb in 2 (9.5%) of the patients.

Conclusion: Very few new cases were registered over the one year period, of which majority presented several months after the onset of motor symptoms.

P12.02

Applause sign in clinically overlapping diseases: a case of TDP-43 proteinopathy

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Objective: To report a case of Corticobasal syndrome with TDP-43 proteinopathy and positive applause sign.

Background: The 'Applause sign' was initially considered specific for Progressive Supranuclear Palsy but its specificity was questioned after it was also documented in clinically diagnosed patients with Parkinson's disease, Corticobasal syndrome, Multisystem Atrophy and Alzheimer disease. The debate regarding the specificity of the 'Applause sign', however, is based on clinical rather than definite pathological diagnosis.

Methods: We describe the clinical and autopsy findings of a patient with Corticobasal syndrome with TDP-43 proteinopathy.

Results: A 64-year-old right-handed woman developed slowness of speech and intermittent curling of her right toes. Within a year she had right arm clumsiness and an alien hand. Two years after the onset of her first symptoms, examination revealed slow speech output, dementia, hyperreflexia, significant right-sided rigidity and

bradykinesia, dystonic posturing of her right hand and circumduction of her right leg while walking. When asked to imitate the three-clap applause, she clapped continuously. Brain MRI revealed left frontoparietal atrophy. She was diagnosed with Corticobasal syndrome. Her condition slowly progressed and she died at age 69. Her autopsy revealed asymmetric cortical and subcortical atrophy, worse on the left. Cortical and white matter intracellular inclusions stained positively for TDP-43, staining for tau and alpha-synuclein was negative

Conclusions: This case suggests that in debating the utility of the applause sign to differentiate between clinically overlapping syndromes, the pathological, rather than clinical diagnosis should be used.

Financial Disclosure: David Arkadir is supported by a fellowship award in movement disorders from the Parkinson's Disease Foundation.

P12.03

Postural instability and history of falls in Parkinson's disease: correlation with the pull test score

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Objective: To evaluate the correlation of postural instability as measured using the pull test (PT) and the history of falls as rated by item 13 of the UPDRS.

Methods: Were assessed 314 patients with a clinical diagnosis of PD. Mean age 65.4(29-94) years with mean disease duration 8.65(1-33) years. History of falls was considered positive if the item 13 of the UPDRS was scored >0, frequent fallers were those with a score ranging from 2 (occasional falls, less than once daily) to 4 (more than one daily fall).

Results: Of all patients, 158 (50.4%) had a normal response to the PT; 67 (21.4%) had a score of 1; 55 (17.6%) had a score of 2; 22 (7%) had a score of 3; and 11 (3.5%) had a score of 4. Among those with a score of 0 in the PT, 22 (13.9%) had a history of falls with only 3 (1.9%) having frequent falls. For patients with a score of 1 in the PT, 34 (50%) reported falls with 9 (13.4%) having a score >1 for item 13 of the UPDRS. Forty-seven of the 55 patients (85.4%) with a score of 2 in the PT reported falls, with 29 (52.7%) of them considered frequent. All 22 subjects with a score of 3 in the PT reported falls, frequent for most of them (2;90.1%). Among the 11 subjects scored as 4 in the PT, 10 reported daily falls (scores 3 or 4 in item 13 of the UPDRS).

Conclusions: The PT scores showed a good correlation with scores of the item 13 of the UPDRS meaning that this parameter of postural instability is a good predictor of falls in PD.

P12.04

Relationship between motor laterality and nonmotor symptoms in Parkinson's disease patients

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Objective: To evaluate the predominant laterality of motor symptoms and its relationship with non-motor symptoms in patients with Parkinson's disease (PD).

Methods: A transversal study was undertaken, including 53 patients diagnosed with PD. The presence of non-motor symptoms was determined by applying the Non-Motor Symptoms Scale (NMSS),

Hamilton Anxiety and Depression Scale (HADS) and Parkinson's disease Sleep Scale (PDSS). Right PD (RPD) and Left PD (LPD) was defined based on the motor signs on the SCOPA-motor scale and complaints reported by the patient. T-test, Mann-Whitney and Chi-squared tests were used for comparison, and Spearman's rank correlation coefficient was used for analysis of correlation.

Results: 25 RPD and 28 LPD were enrolled on this study. For the entire sample, the most prevalent symptom present in 42 patients was nocturia. There were statistically significant differences between the PD groups in relation to NMSS sleep-fatigue score (RPD: 6.96±5.41 points; LPD: 12.32±11.27 points, $p=0.035$), PDSS total score (RPD: 105.12±27.55 points; LPD: 86.28±36.91 points, $p=0.046$) and PDSS subitems on overall quality of night's sleep (RPD: 7.40±3.20 points; LPD: 5.50±3.58 points, $p=0.031$) and sleep onset (RPD: 8.04±3.46 points; LPD: 5.42±4.40 points, $p=0.017$). There were no significant differences between LPD and RPD with respect to gender, Hoehn and Yahr Staging, SCOPA-motor, age at diagnosis and/or onset of the symptoms, duration of the disease, HADS, NMSS total, and values of NMSS for other domains. An inverse correlation was found between mean PDSS total score and motor and non-motor aspects of the PD: SCOPA-motor score, HADS score, NMSS total and domains scores.

P12.05

Marked Increase in Risk for Parkinson's Disease with Olfactory Dysfunction in LRRK2 G2385R Carriers

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Objective: To investigate the characteristics of olfaction in Chinese Parkinson's disease (PD) patients and healthy controls with or without LRRK2 G2385R variant, and further evaluate the role of olfactory dysfunction in predicting risk for PD.

Methods: PD patients were recruited from the Center of Movement Disorders of Xuanwu Hospital of Capital Medical University, and healthy controls were enrolled from the Beijing Longitudinal Study on Aging (BLSA) cohort. Subjects had LRRK2 genotype information and agreed to give informed consent were enrolled in this study. "Five odors olfactory detection arrays" was applied for olfactory function.

Results: One hundred and twenty-two subjects were enrolled in this study, with 22 LRRK2 G2385R carriers (LRRK2-PD) and 24 non-carriers (iPD) in PD patients, and 38 LRRK2 G2385R carriers and 38 non-carriers were healthy controls. PD group had significantly higher scores in olfaction detection (OD) and olfaction identification (OI) as compared to the control group (OD: 1.58±1.12 vs 1.00±1.22, $p=0.005$; OI: 2.59±0.59 vs 2.44±0.65, $p=0.017$), especially in subjects who were younger than 70 years old (≤ 70 y: OD 1.52±1.16 vs 0.52±1.10, $p=0.009$; OI 2.59±0.50 vs 2.04±0.69, $p=0.002$; >70 y: OD 1.66±1.10 vs 1.24±1.21, $p=0.261$; OI 2.59±0.72 vs 2.64±0.53, $p=0.778$). OI scores for the individual odors of banana and mint were significantly higher in PD group than controls (banana: 2.80±0.93 vs 2.27±1.18, $p=0.002$; mint: 2.91±0.78 vs 2.42±1.00, $p=0.001$). Subjects with severe hyposmia (the olfaction test score >2) had increased risk for PD, compared with the ones with normal or mild hyposmia (84.8% vs 75%, $p=0.017$, OR=4.19, 95% CI 1.29-13.57, adjusted for age and gender). When the individuals with severe hyposmia were LRRK2 G2385R risk variant carriers, the risk for PD significantly increased (90.9% vs 65.8%, $p=0.004$, OR=39.07, 95% CI 3.24-471.46, adjusted for age and gender).

P12.06

Individual and joint prevalence of three non-motor symptoms in the US general population

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Backgrounds: Non-motor symptoms are common among patients of Parkinson's disease (PD), and some may precede the clinical diagnosis of PD by years. The presence of multiple non-motor symptoms in the same individual may indicate a high risk of developing PD. Understanding the background prevalence of these symptoms in the general population will facilitate research of PD non-motor symptoms.

Methods: Using data from the US National Health and Nutrition Examination Surveys 2005-2008, we examined the individual and joint prevalence of daytime sleepiness, infrequent bowel movement, and depression among 10,468 participants ages 20-85 years.

Results: These symptoms were relatively uncommon in the general population, and prevalence differs by gender. Importantly, few participants had ≥ 2 symptoms: 1.3% at ages 20-29, 1.0% at 30-39, 1.2% at 40-49, 3.6% at 50-59, 1.6% at 60-69, 1.1% at 70-79, and 1.2% at 80 or older among men; among women, the percentages were 3.1%, 5.3%, 5.7%, 4.1%, 3.0%, 2.3%, and 1.2% respectively. Further analyses showed that depression was correlated with both infrequent bowel movement and daytime sleepiness, but the latter two were mutually independent. These symptoms were each associated with the use of anti-Parkinsonian medication. The age- and gender- adjusted odds ratio (OR) and 95% confidence interval (CI) were 3.0 (1.5-6.2) for depression, 2.1 (1.1-3.8) for infrequent bowel movement, and 2.0 (1.0-4.1) for daytime sleepiness. Comparing to individuals without any symptoms, the ORs were 1.7 (0.8-3.2) for the presence of one symptom and 4.6 (1.8-11.7) for the presence of ≥ 2 symptoms. In conclusion, this study showed that nonmotor symptoms were uncommon in the general population, and they were associated with anti-Parkinsonian drug use.

P12.07

Cognitive influence on swallowing function in patients with Parkinson's disease

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Objectives: Both dysphagia and cognitive dysfunction are common in Parkinson's disease (PD). Although the possibility that cognitive decline may contribute to dysphagia in PD patients has been raised, the association between cognition and swallowing functions has not been studied well. We evaluated cognitive influence on swallowing function by using detailed neuropsychological profiles and video fluoroscopic swallowing studies as objective measurement.

Methods: We prospectively enrolled 56 non-demented PD patients. All participants received selective neuropsychological tests covering general mental status, visuospatial function, attention, language and related functions, learning and memory function and frontal executive function. Video fluoroscopic swallowing studies were also performed, and the Modified Barium Swallow Impairment Profile, a

validated and reliable scoring system, was applied to quantify the nature of the physiologic swallowing impairment.

Results: During the oral phase, hold position/tongue control, bolus preparation/mastication and bolus transport/lingual motion were significantly associated with general mental status, learning and memory domains and frontal/executive functions with varying degree. Aspiration is associated with attention tested by digit symbol test. Correlation analysis between motor subsets and swallowing components revealed that oral residue of oral phase, epiglottic movement and tongue base retraction of pharyngeal phase are associated with different motor subsets.

Conclusions: Our findings suggest that cognitive dysfunction, especially attention, memory and executive function, is mainly involved in the oral phase of swallowing, in PD patients. Furthermore, we supposed that as the severe motor symptoms progress, swallowing dysfunction will be influenced in the pharyngeal phase as well as oral phase.

P12.08

Concurrent arm swing-stepping (CASS) test for dual task-related movement incoordination and hesitation in Parkinson's disease

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Objective: Parkinson's disease (PD) patients frequently show gait and balance impairments while simultaneously performing parallel tasks under sustained and divided attention. In this study we have developed a simple dual task by asking patients to perform concurrent arm swing and on-the-spot stepping (CASS). Our initial aim was to examine whether CASS can reveal deficits in movement initiation and coordination, and whether the detected deficits were associated with self-assessment of fall risk.

Methods: The study included a total of thirty-three PD patients (mean age: 66.6 years, SD 9.5; mean disease duration: 8.1 years, SD 5.9) who were first instructed to swing their arms and then to initiate the secondary task of leg stepping. We defined a lack of arm-leg coordination as arm swing and leg stepping occurring on the ipsilateral, instead of the contralateral side. Gait hesitations were scored as follows: no-hesitation (0 sec), slight hesitation (<5 sec), and large hesitation/freezing (>5 sec). The Falls Efficacy Scale-International (FES-I) was used to assess fall-related self-efficacy.

Results: We found 78.8% patients showed some degree of deficits in coordination across three trials, whereas gait hesitation and/or freezing occurred significantly less (36.4%; $p < 0.01$). Furthermore, multilevel regression analysis controlled for age, gender, and disease duration revealed that CASS-related hesitation/freezing, but not coordination, was a significant predictor of FES-I score ($p < 0.01$), with R^2 increasing by 33.3% after adding the hesitation variable but not the coordination variable (2.0%; $p > 0.05$). Our results indicate that CASS can be used as a simple clinical test to reveal dual task-related movement incoordination, gait hesitation and/or freezing, as well as their relationship with self-reported functional efficacy in PD patients.

Acknowledgments: CIHR, Parkinson Alberta Society, and Dr. Sarah Furtado and the Movement Disorders Clinic-Alberta Health Services.

P12.09

Antipsychotic efficacy and motor tolerability in a phase III placebo-controlled study of pimavanserin in patients with Parkinson's disease psychosis (ACP-103-020)

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Objective: Parkinson's disease psychosis (PDP) is frequent, distressing and a leading cause of institutionalization. It also complicates PD management and has been linked to increased morbidity, incident dementia and mortality. Current antipsychotics lack efficacy and/or have considerable tolerability and safety concerns. Pimavanserin, a selective non-dopaminergic 5-HT_{2A} receptor antagonist, has shown antipsychotic effects and good tolerability in previous Phase III trials, but a robust placebo effect precluded statistical separation. A Phase III outpatient study, optimized to reduce placebo response, was conducted to assess the efficacy and safety of pimavanserin in PDP.

Methods: Following 2-weeks screening, in which brief (non-pharmacological) psychosocial therapy adapted for PD (BPST-PD) was offered, 199 non-demented patients with moderate to severe psychosis (and on stable PD medication) were randomized to once-daily oral doses of 40mg pimavanserin or placebo (1:1) for 6 weeks.

Results: Pimavanserin met the primary endpoint using SAPS-PD (a PD-adapted version of the Scale for Assessment of Positive Symptoms, assessed by independent raters): -5.79 PIM vs -2.73 PBO change from Baseline at Day 43 (LSM difference=-3.06; $p=0.001$). These results were supported by highly significant improvement in the secondary efficacy measure, CGI-Improvement (LSM difference -0.67; $p=0.001$), which was assessed by site investigators blinded to the SAPS-PD. Additionally, clinical benefits were observed in all exploratory efficacy measures with significant improvements in nighttime sleep, daytime wakefulness, and caregiver burden. Consistent with previous studies, pimavanserin met the key secondary endpoint for noninferiority to placebo on motor function (using UPDRS II+III) and was otherwise safe and well tolerated. The most common AEs were UTI (11.7% PBO, 13.5% PIM) and falls (8.5% PBO, 10.6% PIM). The only serious AEs that occurred in more than one patient were UTI (1-PBO, 3-PIM) and psychotic disorder (0-PBO, 2-PIM). These data suggest that pimavanserin is effective, safe and well-tolerated for PDP. Utility in other neuropsychiatric disorders remains to be explored.

P12.10

Role of inflammation in the origin of fatigue syndrome in Parkinson's disease

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Fatigue syndrome (FS) is an overwhelming sense of tiredness, lack of energy and feeling of exhaustion. The prevalence of fatigue in Parkinson's disease (PD) ranges from 35% to 60%. Research on the nature and treatment of fatigue has been challenging. The role of inflammation in the origin of FS is being debated.

Objective: examine peripheral biomarkers of inflammation in relation to FS in patients with PD.

Methods: We included 20 PD patients with FS. Mean age was 64.5±6.5. Mean disease duration was 5.9±4.04. Mean Hoehn&Yahr stage was 2.6±0.5. Fatigue was defined as score>3.3 on the Parkinson Fatigue Scale (PFS). C-reactive protein (CRP) and tumor necrosis factor- α (TNF α) were used as biomarkers of inflammation in peripheral blood.

Results: Mean CRP level was 1.54±1.04. Mean TNF α was 6.72±0.83. None of the 20 patients showed pathological level of these biomarkers in blood.

Conclusion: We didn't find link between FS severity and level of CRP and TNF α in peripheral blood. This fact can imply that other than inflammation factors contribute to FS severity, or role of inflammation is subtler and other biomarkers should be detected.

P12.11

Evaluation of impaired integration of proprioception and motor information in Parkinson's disease using extremity drift in the absence of visual input

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Objective: Parkinson Disease (PD) is associated with widespread dysfunction of central and peripheral nervous system, with basal ganglial and cortical impairment. We evaluated if extremity drift resulting from a "failure" to integrate proprioceptive and motor information can be reliably used to distinguish subjects with PD from controls.

Methods: The degree of extremity drift was measured in 11 PD patients, 8 Essential Tremor (ET) patients, and 11 healthy control individuals. All subjects were seated, asked to extend their arms in front of them at their shoulder width, pointing their index fingers towards two targets (one target for each finger), and close their eyes. They were asked to continue pointing to the targets without visual input for next 15 seconds while their movements of tip of their index fingers were measured using a DynaSight 3-D optical radar system. Three trials were performed, data were low-pass filtered to exclude tremor-induced movements, and average displacement of index fingers in the mediolateral and upward and downward directions were obtained across subjects in each group.

Results: PD patients on the average exhibited a net downward displacement of 3.0 ± 2.4 cm from their original starting position compared to 0.1 ± 1.1 cm and 1.5 ± 1.9 cm downward displacements exhibited by control and ET subjects, respectively. The difference in the displacement between PD patients and controls was statistically significant at $p < 0.05$. In the mediolateral direction, PD patients showed a medial displacement of 0.2 ± 1.2 cm whereas control and ET individuals showed a lateral displacement of 0.02 ± 0.7 cm and 0.7 ± 1.3 cm, respectively. These results suggest that extremity drift in the absence of visual input can be useful in investigating impairments involving proprioception and sensory motor integration in people with PD.

P12.12

A case of vascular hemiparkinsonism responding to levodopa

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Background: Vascular parkinsonism is known to be less responsive to levodopa when compared to its response in idiopathic Parkinson's disease. There have been few reports of patients with a focal vascular lesion in the striatonigral pathway that have induced a levodopa responsive parkinsonism.

Case: The case involved an 8-year-old male who presented with a left hemiparkinsonism that was related to an arteriovenous malformation that ruptured in the right substantia nigra. Symptoms of resting tremor and marked rigidity occurred a few months after the hemorrhage. The patient was unable to move his left arm due to the rigidity and weakness. Levodopa was introduced which resulted in a significant reduction in the resting tremor. From the initial dose of levodopa the patient experienced peak dose effect with decreased rigidity enabling him to move his arm despite some weakness.

Conclusion: This case reinforces the theory that striatonigral lesions are more susceptible to respond to levodopa treatment than diffuse vascular lesions.

P12.13

Quantitative and clinical measurements of bradykinesia in advanced Parkinson's disease. Are they related?

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Background: Bradykinesia is usually assessed using clinical rating scales. In some circumstances, a laboratory assessment of bradykinesia using tools of higher resolution is required. One task often used for the evaluation of bradykinesia is a rapid alternating movement (RAM) of the hand. However, the relationship between clinical scores of bradykinesia and the properties of a RAM task assessed quantitatively has yet to be determined.

Objective: Identify which of the commonly used properties of a RAM task are related to a clinical score of bradykinesia and assess the strength of this relationship.

Methods: Nineteen patients with idiopathic Parkinson's disease were tested ON and OFF medication. They performed three trials of the RAM task and were assessed clinically using the Unified Parkinson's Disease Rating Scale in each condition and with each hand.

Results: A statistically significant correlation was observed between the clinical score of bradykinesia and two of the properties of the RAM task; namely mean and maximal velocity.

Conclusion: These results indicate that a RAM task does provide a measure of bradykinesia but it is only moderately correlated to a clinical rating of this motor symptom. We propose that the results from the RAM task represent a measure of "core bradykinesia" while a clinical evaluation represents a composite score of bradykinesia, movement amplitude and motor coordination.

P12.14

Are sensory-perceptual deficits responsive to dopaminergic replacement therapy?

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Objective: Although dopaminergic replacement therapy is believed to improve sensory processing in PD, while delayed perceptual speed is thought to be caused by a predominately cholinergic deficit, it is unclear whether sensory-perceptual deficits are a result of *corrupt* sensory processing, or a *delay in* updating perceived feedback during movement. The current study investigated whether sensory-perceptual deficits were influenced by dopaminergic medication while manipulating visual flow speed in virtual reality. If sensory-perceptual deficits were a result of *delayed* updating of perceived feedback, slowing visual flow speed might improve perceptual judgments. Alternatively, if *corrupt* sensory processing underlies sensory-perceptual deficits dopaminergic medication might be expected to improve perceptual judgments.

Methods: 14 PD were tested in the ON (~1hr after taking L-dopa) and OFF state (after 12hr withdrawal). Participants estimated the distance of a remembered target by walking to the location that the target formerly occupied. This task was completed in VR in order to manipulate the visual flow speed in 3 conditions: 1)Baseline: visual flow speed was equal to participants' real-time movement speed; 2)SLOW: visual flow speed was reduced by 50% of participants' real-time movement speed; 3)FAST: visual flow speed was increased by 30% of participants' real-time movement speed.

Results: Dopaminergic medication did not significantly influence judgment error, however PD performed significantly worse in the FAST condition compared to Baseline and SLOW. Interestingly, judgment errors were less variable in the SLOW condition and similar in accuracy to that of Baseline. Additionally, a significant interaction between medication state and condition revealed that PD-ON had higher step times during Baseline and FAST conditions compared to PD-OFF, however did not differ during the SLOW condition. Since judgment error did not improve with dopaminergic treatment, and slowing visual flow reduced the variability in judgment error, these findings suggest that delayed perceptual processing might contribute to sensory-perceptual deficits.

P12.15

Comparison of OnabotulinumtoxinA injections targeting submandibular versus parotid glands in the treatment of sialorrhea for patients with Parkinson's disease

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Objective: Most studies investigating BoNT-A injections for the treatment of sialorrhea in Parkinson's disease (PD) report on parotid gland injections. This study aims to compare between submandibular and parotid glands as targets for BoNT-A injections for the treatment of sialorrhea in PD.

Methods: Patients with PD and sialorrhea of a score of at least 3 or 4 on the UPDRS 6 were recruited. By means of a within-subject design, patients were randomized to receive either parotid or submandibular gland injections and the reverse 3 months later. Comparisons between submandibular to parotid gland injections were made in the resting and in the stimulated state. Objective measures and subjective scales and questionnaires were administered. The Wilcoxon signed-rank test was performed to compare parotid vs. submandibular within group differences. Exploratory analysis to seek significant differences between pre- and post-injections for each gland was performed. P values were calculated at the 0.05 significance level in 2-tailed tests. We need 13 patients to reach a power of 0.90 with an alpha level of 0.05.

Results: Five PD patients have completed the study at this point. The means and standard deviations for the parotid and submandibular injections in both the resting and stimulated conditions during baseline (pre-injection) visits and the one 1-month post-injection visits are shown in Table 1. Our primary analysis reveal no significant difference while exploratory analysis suggest

that parotid injections may have a greater effect on objective measures of drooling, that of weight and volume while both the parotid group and the submandibular groups show a treatment effect on subjective drooling as measured by the EDQ.

P12.16

Dental health of patients and carepartners in Parkinson's disease

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Objective: To compare the dental health of PD patients with their carepartners. Previous studies indicate that dental health in PD is worse than controls, despite similar dental health care.

Methods: Surveys were sent to 1,499 PD patients seen at our center in the last 2 years. A carepartner (CP) survey was included. Questions included: Rate your dental health, with 0 being poor and 10 being excellent (rating); When were you last at the dentist office (last visit); Was it a routine or an urgent, unplanned visit (routine); How often do you brush your teeth (mouth care); Do you have dry mouth (dry mouth); Do you have too much saliva (excess saliva). T-test and chi-square was conducted using Minitab® 16, statistical significance was set at p<.05.

Results: To date, 620 patient (41.3%) and 393 spouse surveys have been received (age: 72.2±9.2 years; 60.1% male). Survey results indicate that average rating of dental health was 6.9±2.0 for patients versus 7.8±1.7 for CP (p<.001). There was no significant difference in last visit and routine between patients and CP. There was a significant difference in frequency of mouth care with 71.3% of patient's brushing at least twice a day compared to 80.9% of CP (p=.002). Dry mouth was experienced by 40.4% of patients and 15.9% of CP (p<.001). Excess saliva was experienced by 41.7% of patients and 2.3% of CP (p<.001). Interestingly, 15.0% of patients and 0.5% of CP experienced both dry mouth and excess saliva (p<.001). Despite similar dental visits, home dental care is significantly less frequent for PD patients as compared to their spouses. Further, PD patients are more likely to experience dry mouth, too much saliva, and the combination of dry mouth and too much saliva.

P12.17

Dental health in Parkinson's disease

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Objective: To determine the impact of PD symptomatology on dental health in PD. Previous studies indicate that dental health in PD worsens with disease severity. PD symptomatology may play a role.

Methods: Surveys were sent to 1,499 PD patients seen at our center in the last 2 years. Questions included: Since your diagnosis of PD, do you have more problems with your teeth and gums (dental health); Do your PD symptoms affect your ability to do mouth and teeth care (PD symptoms); Rate your dental health, with 0 being poor and 10 being excellent (Rating); Do you have dry mouth (dry mouth); Do you have too much saliva (excess saliva). UPDRS-II (ADL) score within the last year was calculated. Pearson correlation was conducted using Minitab® 16, statistical significance was set at p<.05.

Results: To date, 620 surveys (41.3%) have been received (age: 72.2±9.2 years; 60.1% male). Survey results indicate that 24.8% felt that dental health was more of a problem since the PD diagnosis; 33.8% felt that their PD symptoms affected their ability to do mouth and teeth care. The average rating of dental health was 6.9±2.1. Dry mouth was experienced by 40.3% and 41.3% had excess saliva. 15.6% experienced both dry mouth and excess saliva. ADL scores were available on 89.8%, average score was 12.2±7.1 (range 0-41). As ADL scores increased, ratings of dental health worsened (Pearson CC= -0.372, p<.001). PD symptoms affect the oral health of PD patients.

P12.18

Prevalence and impact of Parkinson's disease symptoms: A patient survey across the range of disease severity

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Objective: To obtain an understanding of the complexity and heterogeneity of Parkinson's disease (PD) and PD patient's perception of their symptoms.

Methods: In April 2012, Impax Laboratories developed a patient survey on presence and perceived impact of symptoms of PD. Disease severity was estimated as mild, moderate, or severe, using an algorithm that incorporated cardinal symptoms, sidedness, independent functioning, and participant's impression of physician-perceived symptom severity.

Results: Participants comprised 50 with mild, 50 with moderate, and 50 with severe PD. Of these, 13% had been diagnosed within 1 year previously, 36% within 4 years, and 32% within 10 years. 87 participants not working full-time said PD hindered their ability to work. Symptom prevalence, types, and perceived burden varied with disease severity. Most common were slowness of movement (81% overall, 56% mild, 88% moderate, and 100% severe), tremors/shaking (78% overall) and muscle stiffness (77% overall). Overall, tremors/shaking (23%), loss of balance (12%) and cognitive challenges (9%) were the most bothersome symptoms. On average, symptoms were deemed to be uncontrolled 4.4 h/day (3.8h mild, 3.3h moderate, and 8h severe). Largely, participants hoped their medicine's desired effect could improve walking (56% overall, 42% mild, 58% of the moderate, and 68% severe), and every group ranked physical mobility and independent self-care as the highest and second highest concerns, respectively. The mild group collectively ranked hobbies/interests (20%) and independent self-care (20%) high. The moderate group ranked physical mobility (42%) and independent self-care (36%) nearly equivalently. In the severe group, desire for physical mobility (60%) was paramount. The top challenge of living with PD was fear of disease progression (55% overall). Expenditure of great effort (38%) was also listed by moderate and severe groups.

Conclusion: Patients with PD report substantial symptom burden that varies by stage of the disease, and unmet medical need persists.

P12.19

The prevalence and severity of non-motor symptoms in patients with Parkinson's disease in Korea

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Background and Purpose: Non-motor symptoms (NMS) are common in Parkinson's disease (PD) and can be the primary cause

of disability in many PD patients. The aim of the study is to assess the prevalence and severity of NMS in Korean PD patients according to the clinical status and motor subtypes.

Subjects and Methods: Patients with PD and normal controls have been evaluated in the neurology department of 37 hospitals throughout Korea. The subjects were assessed using the battery of standard assessment measures, HY Stage, UPDRS, MMSE, MoCA, frontal lobe assessment battery, NPI, BDI, BAI, Parkinson Fatigue Scale and PDSS. Prevalence and severity of NMS were determined through Non-Motor Symptoms Scale (NMSS). We analyzed 323 PD patients and 94 normal subjects. We classified PD patients according to their clinical status as de novo, early and advanced PD patient. We also divided the PD patients in akinetic-rigid (AR), tremor dominant (TD) and intermediate according to motor symptoms.

Results: The prevalence of NMS and total NMSS score were significant higher in PD patients compared to controls. The most common domains of NMSS in PD patients were as followings: sleep/fatigue (82.0%), mood/cognition (79.3%), attention/memory (77.4%), urinary function (73.7%). However, the domains more related to PD are perceptual/hallucination, gastrointestinal and miscellaneous. AR type of PD patients had more NMSS scores than TD type. (60.0 vs 37.6, p=0.035, respectively). Gastrointestinal function was more prevalent and severe in AR type.

Conclusions: Non-motor symptoms are common in Korean PD patients. However, NMSs with higher prevalence in PD do not more relate to PD. The domains of NMSS with higher scores are different depending on motor subtype.

P12.20

Frequency and risk factors for falls in Parkinson's disease

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Aim. Falls are common in Parkinson's disease (PD) and can be an important source of disability because of fractures. Our goal is to evaluate the frequency of falls in a population of PD patients and to determine the features associated with its development.

Patients and Methods. A retrospective study of falls in 107 consecutive patients with PD (48 men/59 women) followed-up in a neurologic consultation in Salamanca, Spain. The mean age of PD patients was 77,2 ± 8,3 years (age at onset 65,6 ± 11,5 years and mean duration of PD 10,7 ± 4,8 years) and Hoehn & Yahr Staging median: 3[1-5]. Falls were defined as any report of falls on the UPDRS (Falling>0). We assessed the frequency of falls overall and by age. The relationship between potentially related variables and the probability of falling was assessed using statistical analysis.

Results. Forty-six patients (44%) (26 men/20 women) reported at least one fall since the onset of PD, and 30 of these patients were recurrent fallers (68% of patients with falls). Falls led to fractures in 9 patients (22.5% of fallers). Freezers experienced falls more frequently than non-freezers (88.1% vs 11.9%, OR=4.429, IC95%:1.874-10.466, p<0.001). Also disease duration, UPDRS (part III) score, Hoehn and Yahr staging, Schwab and England activities of daily living, motor fluctuations, Mini-Mental State Examination and neuroleptic use were associated with subsequent fall risk. No differences were observed between fallers and non-fallers in other drug treatments, age at onset of PD, initial predominant motor signs (tremor or akinesia-rigidity subtypes), dyskinesias and symptoms of orthostatic hypotension and cerebrovascular disease.

Conclusions. Falls are frequent and are associated with impaired quality of life. This symptom change in function of the PD stage. New investigations are required to better evaluate this important problem.

P12.21

Severe echolalia, palilalia and palipraxia in a patient with Progressive Supranuclear Palsy syndrome

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Background: Speech disturbances in parkinsonian syndromes may cause severe disability affecting a patient's QOL. Palilalia and echolalia are repetitive speech phenomena. We present an unusual case with disabling, severe repetitive speech and motor difficulties.

Case presentation: 58y/o woman was well until 3yrs ago when she developed word and phrase repetitions. These became severe, and she was unable to stop the repetitions, thereby losing her ability to continue with her desired speech. Initially, this responded to levodopa. A year later, she developed ocular motor abnormalities and severe generalized slowness, losing her independency. No relevant family history. Her exam revealed staring expression, no blinking, procerus sign, slow horizontal ocular movements, hypometric saccades, and visual grasping. When she tried to talk, she repeated the first words and kept repeating them (palilalia). Occasionally, the repetitions developed after several words were successfully spoken, blocking her speech forward. The repetitions would continue until she broke in with a statement. Similarly, she repeated non-stop words that she spoke to her (echolalia). Motor examination: moderate bradykinesia/rigidity throughout. Writing: repetitions of letters and then blocked, unable to finish the task. Feet and both arms went into a continuous repetitive tremor-like pattern that stopped on command (palipraxia). She arose and walked slowly on command, but she arose rapidly spontaneously after an unrelated command. Pull test was positive. Applause Test was "non-stop" positive.

Discussion: Repetitive disturbances have been associated with frontal lobe alterations. Our patient has severe repetitive symptoms in the context of PSP-like syndrome, which is well known to be related with frontal dysfunction. The Applause Sign, common in PSP, can be considered a mild manifestation of a repetitive motor phenomenon.

P12.22

Gender differences in non-motor symptoms in early, drug naïve Parkinson's disease

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Objective: Gender differences in brain structure and function may lead to differences in the clinical expression of neurological diseases, including Parkinson's disease (PD). Few studies reported gender-related differences in the burden of non-motor symptoms (NMS) in treated PD patients, and this matter has not been previously explored in drug-naïve patients. In consideration of this, we assessed gender differences in NMS frequency in a large sample of early, drug-naïve PD patients compared with age-matched healthy controls.

Methods: Two hundred early, drug-naïve PD patients and sixty age-matched healthy controls were included in the study. Frequency of NMS was evaluated by means of NMS Questionnaire. The

difference in gender distribution of NMS was evaluated with the X² exact test; multiple comparisons were corrected with Benjamini-Hockberg method.

Results: Male PD patients complained of problems having sex and taste/smelling difficulties significantly more frequently than female PD patients. Furthermore, men with PD complained more frequently of dribbling, sadness/blues, loss of interest, anxiety, acting during dreams, and taste/smelling difficulties as compared to healthy control men, while female PD patients reported more frequently loss of interest and anxiety as compared with healthy control women.

This study shows specific sex-related patterns of NMS in drug-naïve PD. In contrast with previous data, female PD patients did not present higher prevalence of mood symptoms as compared to male PD patients. Comparison with healthy controls showed that some NMS classically present in premotor and early stage of disease (i.e. acting during dreams, taste/smelling difficulties) are more frequent in male than in female patients.

P12.23

Low awareness of non-motor features of Parkinson's disease among doctors in a tertiary institution in Nigeria: a cross-sectional survey

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Objectives: To assess awareness of non-motor symptoms of Parkinson's disease (PD) among non-neurologists.

Methods: This cross-sectional study took place at the University of Port Harcourt Teaching Hospital, Nigeria between March and April 2013. Eighty-six doctors mostly residents were administered questionnaires to complete. Apart from basic demographic data, they were also asked to provide information on their awareness of both motor and non-motor features of Parkinson's disease, and also knowledge of various drugs used in the treatment of Parkinson's disease. Completed questionnaires were collated and relevant data extracted and analyzed.

Results: Out of 86 doctors surveyed, 3(3.5%) did not return their questionnaires. Of the 83 respondents, 25.3% were interns, 54.2% residents, 19.3% senior residents and 1.2% consultants. Hundred percent of the respondents admitted to be aware of motor features of Parkinson's disease whereas 71.1% were ignorant of non-motor features of Parkinson's disease. Awareness of non-motor symptoms amongst respondents is very low.

P12.24

Highlighting the significance of pain in screening and managing Parkinson's disease

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Introduction: Pain is a common problem faced by PD patients. Despite its impact and disabling effects pain is still frequently overlooked. In this study we analyze current peer reviewed literature for the prevalence and types of pain in PD, correlation of pain to depression and quality of life, reporting to physician, and the use of analgesics. The objective of this study was to review current

literature about the various aspects of pain in Parkinson's disease (PD).

Methods: By using key words of PD, prevalence of pain, quality of life and depression in relation to pain in Parkinson's we searched the pubmed database. Twenty-seven articles pertaining to pain in PD were found. After a careful further review of the articles eighteen were selected for our meta-analysis.

Results: A total of 15693 patients were studied in these articles. The average prevalence rate was 59%. Five types of pain were noticed: dystonia, akathisia, musculoskeletal problems, nerve or root pain, and primary or central pain. Patients with more severe pain had increased depression and lower quality of life. There were no significant gender differences. Analgesics were used less frequently by PD patients despite poor pain management. In conclusion, pain is an important symptom of PD and therefore should be screened and adequately managed in every follow up visit.

P12.25

Effects of pain on functional outcome in Parkinson's disease and healthy controls

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Introduction: Pain can be substantially detrimental to one's daily activities due to its ability to inflict the individual by both physical and psychological means. Despite significant prevalence, pain has not been well-studied among Parkinson's disease patients. It is possible that pain contributes to debilitation in patients, in addition to the difficulties that are normally prevalent as a result of the disease. The current study compares the severity of deficiencies in functional outcomes of patients and healthy controls who attribute such deficiencies to existing pain.

Methods: Self-report questionnaires on several aspects relating to pain were administered for 127 Parkinson's disease patients and an equivalent number of healthy controls. The subjects were not individually matched, but the two groups were matched overall to have equivalent gender distribution and near-equivalent mean age, and are also expected to have similar lifestyles (given that controls in most cases were caregivers of PD patients). The 90 patients and 76 controls who reported having any pain were invited to complete the Brief Pain Inventory (BPI) and the Pain Disability Index (PDI). Scores from these were used to assess deficiencies in various aspects of functional outcome, compared across the two groups. Further, different data collected on various aspects of pain (severity, location, duration, etc.) were analyzed for their potential predictive effects on the various functional disruptions.

Results: Comparison between the groups for measures of functional outcome indicated that Parkinson's disease patients experience substantial debilitation on a majority of the relevant items in the BPI and PDI. In conclusion, the results indicate that Parkinson's disease patients who experience pain tend to have increased functional deficits compared to a similar group of healthy controls. Pain is implicated as the cause of these deficiencies by both groups.

P12.26

Factors affecting pain in Parkinson's disease

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Objective: To study the associations between various factors and pain in a Parkinson's disease (PD) patient population.

Methods: This study investigated 121 PD patients, of which 80 reported to have pain in at least one area of the body. Exclusion criteria included patients suffering from external causes of pain, such as trauma and patients with cognitive impairment whose accounts may not have been reliable. Further inquiry determined the etiology of pain, as well as aggravating and alleviating factors. The efficacies of pharmacological or non-pharmacological therapies were assessed through additional questioning. Individuals were also asked whether their pain was unintentionally affected by other measures, such as prescribed PD medications.

Results: Multiple linear regression analysis with a Wald test value of 4.070 ($p = 0.044$) demonstrated a statistically significant relationship between the administration of analgesics in patients with high reported pain and their pain relief. However, patients who experienced moderate pain did not exhibit any statistically significant levels of pain relief with the use of analgesics (Wald = 2.097, $p = 0.148$). Similarly, non-pharmacological therapies, PD medicine, and comorbidities showed no statistically significant correlations with pain relief.

P12.27

Factors contributing to variations in visual hallucinations experienced within Parkinson's disease patient populations.

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Objective: To examine the potential effects of patient age, Parkinson's disease (PD) duration, dementia duration, visual hallucination (VH) duration, and Hoehn and Yahr (H&Y) stage progression on the experience of hallucinations within a PD patient population.

Methods: This retrospective study investigated 42 PD patients aged 63 to 95 who reported having VH. All individuals were diagnosed with idiopathic PD and were regularly followed every three to six months at a community-based Parkinson's disease and movement disorders centre between 2005 and 2011. VH were diagnosed and rated by the clinic neurologist using the VH component of the Parkinson's Psychosis Rating Scale (PPRS).

Results: Of the 45 patients with VH that were initially assessed, three were removed for experiencing VH for reasons other than PD. Among the inclusion group, multiple linear regression analysis demonstrated a statistically significant relationship between the duration of PD and the occurrence of threatening VH ($p = 0.004$). Specifically, there was a significant relationship between the

duration of PD before VH and threatening VH ($p = 0.001$), as well as the duration of dementia before VH and threatening VH ($p = 0.003$). There were no significant correlations found between the duration of dementia and the duration of VH with recorded parameters of VH experience or with patient age and H&Y stage progression with the recorded parameters of VH experience.

P12.28

Sleep disturbances in a Senegalese patients series with Parkinson's disease in Fann Teaching Hospital

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Objective - Sleep disorders are common in Parkinson's disease (PD). They are the consequence of both neurodegenerative process and neurochemical changes, but also of drug intake. Despite its high incidence, they are not included in the routine clinical examinations. Our aim was to assess sleep disorders among PD patients followed-up in a hospital center in Dakar.

Patients and Methods - The study enrolled 26 consecutive patients who fulfilled criteria for idiopathic PD in the neurological department of Fann Teaching Hospital. They were tested with standardized scales: unified PD rating scale (UPDRS) and Hoehn and Yahr staging scale (HY scale). Parkinson's disease sleep scale (PDSS) was applied for the assessment of sleep problems.

Results - There were 54% of male and 46% of female. Correlations were found between PDSS score, HY stage and the mean duration of disease, but not between PDSS score and UPDRS. There was no difference in PDSS scores regarding gender and age. Analyzing each item in the PDSS scale, the lowest score was obtained for item 8 (nocturia). We did not find any difference in PDSS score between the patients under dopamine-agonist and those under L-dopa. In conclusion, patients in advanced stages of the disease and worse motility are more likely to have sleep problems. This could lead practitioners to take sleep disorders into account while following-up PD patients.

P12.29

Non-motor clinical staging using the non-motor symptoms scale and motor correlation in an UK cohort of Parkinson's

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Objective: We recently described a novel grading system of people with Parkinson's (PwP) using the non motor symptoms scale (NMSS) and assessing NMS burden (NMSB staging), the stages ranging from no NMS (stage 0) to severe burden of NMS (NMSS > 71, stage 4).¹ In this unselected UK cohort of 517 cases, we provide a clinical categorization of cases after allocating each case to the NMSB staging system.

Methods: Retrospective and prospective data on 517 cases have been collected in the UK for the validation studies of NMSS as well as an ongoing NMS natural history study. All cases were staged as per NMSB and clinical association with motor staging (Hoehn and Yahr) and other parameters were assessed.

Results: Only 1 of 517 patients (0.19%) reported no NMS (NMSB stage 0). 154 (30%) were at stage 2 moderate level of NMS and had a mean age of 68± 12yrs with a median HY stage of 2, a relatively mild motor stage. However, 23% had severe NMSB stage while HY score was moderate at a median of 2, while 21% had very severe NMSB stage with HY score median of 2.5, not be considered as advanced Parkinson's from the motor perspective. Amongst the NMSB stages 3 and 4, several NMS dominant endophenotypes were recognised (sleep dominant, fatigue dominant for example) from a clinical perspective.

Conclusions: This study outlines the importance of including NMS assessments, now formalized by the NMSB staging as part of a clinical process to implement holistic care of the multi-morbid PwP.

Reference: Chaudhuri KR,¹ Rojo JM,² Schapira AHV³, Brooks DJ,⁴ Stocchi F, Odin P et al. A proposal for a comprehensive gradation of Parkinson's disease severity combining motor and non-motor assessments: meeting the unmet need. PLOS One. February 2013 | Volume 8 | Issue 2 | e57221

P12.30

Movement festination of repetitive movements on the more and less affected side in patients with Parkinson's disease

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Objective: Patients with Parkinson's disease (PD) demonstrate movement festination (increase in rate, decrease in amplitude, accompanied by hesitations) during repetitive finger movements. Movement festination is not in most cases improved with dopaminergic medication or STN-DBS, suggesting that it may not be associated with changes in basal ganglia function. Typically the presentation of motor symptoms in PD is asymmetric correlating with asymmetric degeneration of dopaminergic neurons in the basal ganglia. It remains unknown if festination of repetitive finger movements shows asymmetry between sides. The purpose of this study was to compare the performance of repetitive finger movements between the clinically defined more and less affected side in persons with PD. We hypothesized there would be significant difference in clinical measures between sides, but no difference in movement festination between both sides.

Methods: Thirty-eight participants with idiopathic PD completed a repetitive finger movement task "on" medication. Clinical evaluation scores were collected to determine the most affected side. Movement rate and peak-to-peak amplitude were obtained. For both measures, a repeated measures ANOVA was used to compare differences between sides and across tone rates. A paired t-test was conducted for the clinical evaluation measure.

Results: Clinical evaluation confirmed the more affected side ($p < 0.001$). Movement festination was revealed in both hands ($p < 0.001$). Movement amplitude ($p = 0.57$) and movement rate ($p = 0.06$) did not differ between sides. These results demonstrate that festination of repetitive finger movements was evident on both sides, even though participants demonstrated a clinically more affected side.

Conclusion: This study supports the notion that movement festination in patients with PD may be due to changes in other motor control processes, possibly outside the basal ganglia. Further study of movement festination in other repetitive movements and investigation of potential treatment is needed.

P12.31

Examination of non-motor symptoms in early-stage Parkinson's disease

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Objective: Parkinson's disease (PD) is currently diagnosed on the basis of the presentation of various motor symptoms. However, non-motor symptoms, such as olfactory deficits or sleep disturbance, may be present years prior to the emergence of motor impairment. Our previous work showed that newly diagnosed PD patients exhibit alterations to olfactory regions of the brain, leading us to speculate that non-motor symptoms, and the associated neurological changes, may precede the onset of motor symptoms, and that this may provide a novel tool for the earlier diagnosis of PD. Preliminary analyses of an ongoing study examining the relationship between PD and the presence of non-motor symptoms are presented here.

Results: Comparisons between healthy controls (n = 10; 8 males) and individuals with early-stage PD without REM behaviour disorder (n = 8; 3 males; i.e., Hoehn and Yahr <= 2; diagnosed within an average of 4.6 months of initial testing) were conducted. PD patients were found to rate their sense of smell to be poorer than controls, and in line with this, exhibited significantly greater impairment on the University of Pennsylvania Smell Inventory Test (control M = 34.6; PD M = 24.7, out of 40). Those with PD were more likely to be on sleep medication, although no significant changes were found to specific aspects of sleep or daytime sleepiness. Diffusion tensor imaging MRI (i.e., 1.5T) demonstrated visible alterations in the direction of diffusion within the substantia nigra of PD patients; however, further examination of non-motor regions is still required. Continuation of our analyses will focus on whether the combination of olfactory, sleep, cognitive, and DTI testing will allow for the specific and sensitive detection of early-stage (premotor) PD.

P12.32

The impairment of metaphor comprehension in Parkinson's disease: the role of polysemy

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Objective: Metaphor comprehension seems particularly affected in Parkinson's disease (PD), and this impairment has been attributed to executive dysfunctions (e.g., working memory and inhibition deficits). However, so far, no study was conducted to measure the influence of different type of metaphors on metaphor comprehension in PD. Polysemy (the property of a word to have multiple related meanings) may influence metaphor comprehension processing. In PD, inhibition and mental flexibility impairments may lead to difficulties to switch between the literal and figurative meanings in order to understand polysemous metaphors (such as *These spies are foxes*). By comparison, understanding a non-polysemous metaphor (such as *These dancers are swans*) does not require switching between concepts, so that this type of metaphors might be preserved. The main goal of this study was to investigate the role of polysemy in metaphor comprehension in PD, considering its high reliance on executive functions. We expected that only polysemous metaphor comprehension would be impaired in PD individuals.

Methods: Twenty individuals with idiopathic PD and twenty healthy controls (HC) were evaluated with an experimental metaphor comprehension task (including non-polysemous and polysemous metaphors) and a neuropsychological battery of tests for executive functions (inhibition, mental flexibility and working memory).

Results: As expected, a slowing in polysemous metaphor comprehension was observed in PD compared to HC, an impairment significantly correlated with the executive deficit observed in the PD group. Interestingly, PD participants made more comprehension errors than the HC group in both types of metaphor. Our findings indicate that, in PD, polysemy influence the processing time of metaphors, but do not impact their comprehension.

P12.33

A comparative study of LRRK2 G2019S parkinsonism and idiopathic Parkinson's disease in Tunisia

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Objective: One third of Tunisian Parkinson's disease (PD) patients may be attributed to a LRRK2 G2019S mutation. Clinical data and blood samples were recruited from 580 patients; 360 with idiopathic PD, 220 with LRRK2 G2019S. In the present study we provide the age-associated cumulative-incidence (penetrance). We describe and compare disease onset and clinical symptoms among homozygous and heterozygous LRRK2 G2019S patients compared with idiopathic PD.

Method: Regression was performed for autonomic (SCOPA-AUT), cognitive, motor, psychiatric, sensory and sleep assessments. Survival analysis techniques were used to estimate the penetrance in sporadic cases and familial carriers.

Results: No differences were observed between LRRK2 G2019S heterozygotes and homozygotes, hence these genotypes were combined. With the exception of cognitive testing, the scales applied were sensitive to dysfunction in motor and non-motor domains. Motor assessments and sensory assessments between idiopathic PD and LRRK2 Parkinsonism were comparable. However, LRRK2 G2019S had fewer problems with REM sleep disorder (16% vs.

29%, $p < 0.001$) and gastrointestinal dysfunction (0.64 vs. 0.74, $p < 0.04$). The age-associated cumulative incidence (penetrance) of parkinsonism for *LRRK2* G2019S carriers was 30% at age 50 increasing to 80% at age 70. While the cumulative of male *LRRK2* carriers is comparable to idiopathic PD, female carriers become affected 5 years earlier, and within families the same trend was observed.

Conclusions: Findings from *LRRK2* parkinsonism may be generalized to idiopathic PD. Future studies might include a retrospective questionnaire of first symptoms and signs, as well as a smaller, longitudinal effort of *LRRK2* families with kinetic analysis of normal movement.

P12.34

Postprandial and orthostatic hypotension in patients with de novo Parkinson's disease

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Objective: To examine the correlation between postprandial hypotension (PPH) and orthostatic hypotension (OH) in patients with de novo Parkinson's disease (PD).

Methods: Twenty-eight patients never treated with anti-Parkinson drugs were enrolled in this study. PPH was examined via a 75-g oral glucose tolerance test. Systolic blood pressure (SBP) was initially measured after 20 min of rest in the supine position, and then the subjects drank 75 g of glucose water. Thereafter, the SBP was measured every 10 min for the next 120 min.

Plasma norepinephrine (NE) concentrations were initially measured after the 20 min of rest, and after the subjects drank the glucose water, NE concentrations were measured again every 30 min for the next 120 min.

Differences in the NE concentrations between each blood collection time and that measured after the 20 min of rest (Δ NE_{PPH}) were calculated. OH was examined by head-up tilt-table test. SBP was measured after the 20 min of rest and every 1 min after tilting. NE concentrations were measured after the 20 min of rest and after 10 min in the tilted position, and the difference in NE concentrations between the two positions (Δ NE_{OH}) was calculated. PPH and OH were defined as a decrease in systolic BP of 20 mmHg or more after completion of glucose ingestion and in a tilted position, respectively.

Results: PPH was observed in 15 (53.5%) of 28 patients. The severities of PPH and OH correlated significantly, and they also correlated significantly with NE concentrations measured after 20 min of rest. Δ NE_{OH} correlated significantly with the severity of OH but Δ NE_{PPH} did not correlate with that of PPH. The correlation between PPH and OH in de novo PD was therefore attributed to blunted sympathetic nerve activity.

P12.35

Characterization of freezing of gait in Parkinson's patients utilizing wearable foot pressure sensors

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Objective: Freezing of gait (FoG) is a debilitating symptom of Parkinson's disease associated with disease duration and severity. Patients who experience FoG report their feet being stuck to the

ground during walking despite having intention to walk. Freezing of gait is a major risk factor for falls in PD patients, but currently rehabilitation and treatment for patients with freezing is limited. Our aim is to characterize freezing episodes kinematically to aid in the development of rehabilitation processes.

Methods: Patients with FoG were identified by a movement disorders specialist. Five tasks were used to elicit FoG in patients, including Timed-up-and-go (TuG), TuG while performing serial subtractions, TuG with 90 degree turns, surprise 90 degree turns, as well as 360 turns. Episodes were recorded in video and identified in kinematic data through MatLab. Freezing episodes were defined from the point where patients stopped moving up until patient initiates/reinitiates gait. Mean CoP values for each foot were compared within each FoG episode.

Results: Of 20 Patients participated, six patients with a total of 145 episodes were recorded. Back and forth (BF) movement in Center of Pressure (CoP) decreased in amplitude during FoG episodes across all patients. Absolute differences in mean CoP between the feet for the beginning or whole duration of freezing episodes were significantly different than zero ($t(136)=14.14$, $t(136)=13.90$, $p < .001$ respectively). Overall, foot pressure sensor technology and CoP analysis is a viable tool for characterizing FoG episodes. Difference in mean CoP suggests an asymmetric posture in FoG, despite resemblance to standing. This characterization could be used to differentiate FoG from simple standing. This asymmetry is a necessary precondition for step generation and freeze breaking. The results could be potentially useful in rehabilitation or suggestion of strategies breaking freeze.

P12.36

The effects of dopaminergic drugs on speech in individuals with Parkinson's disease

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Objective: The purpose of this study was to examine the effects of dopaminergic medications on speech in individuals with Parkinson's disease.

Methods: Eleven patients with Parkinson's disease were enrolled in the study. Patients were, on average, 63.5 years old and had been diagnosed for 13.3 years. United Parkinson's Disease Rating Scale (UPDRS) scores ranged from 24-57 (mean=43) off medication; and from 9-34 (mean=20) on medication. Average Mini Mental Status Exam (MMSE) score was 27.8. Patients produced a monologue on a topic of their choice and read a short passage and single sentences. Cognitive testing was completed on medication for all patients.

Results: Patients produced significantly shorter utterances when on medication, as compared to off. There were no significant differences in sound pressure level (a measure of vocal intensity/loudness) and no change in the number, duration, or grammatical location of silent pauses. UPDRS scores off medicine were significantly correlated with the production of shorter utterances and more silent pauses. Six patients were categorized as primarily having difficulty with postural instability and gait, four patients were categorized as intermediate, the most classic form of Parkinson's disease, and one was categorized as tremor dominant. Examination of speech measures in the two larger groups demonstrated lower sound pressure level, more abnormal speech rate (faster and slower), more breaths at locations unrelated to syntax, more speech revisions, and more filled pauses ("um" for example) in the postural instability and gait group as compared to the intermediate group.

Results/Conclusions: Dopaminergic medications have a slight negative effect on speech by reducing utterance length. Disease severity, as indexed by the UPDRS off medication score, has a much greater effect on speech impairments. Patients who show primary difficulty with postural stability and gait also show greater speech impairments than those patients who have more classic Parkinson's disease symptoms.

CLINICAL SCIENCES: PROGRESSION & PROGNOSIS

P13.01

Investigating motor symptom progression in the more-affected versus less-affected side in Parkinson's disease

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Objectives: Currently, it is unclear whether disease progression in Parkinson's disease (PD) differs between the more-affected side compared to less-affected side. The objectives of the current study were to investigate the change in motor symptoms in the more-affected and less-affected sides after one year, and to evaluate the asymmetry between the two sides after one year.

Methods: 70 patients with PD (M:42; F:28; Age: 67.6±8.1) were evaluated twice (one year separating the assessments) using symptom subsets of Unified Parkinson's Disease Rating Scale motor score evaluation (UPDRS III). The subsets included resting tremor, action tremor, rigidity and voluntary motor control. Participants were evaluated while 'on' their Parkinsonian medication. Wilcoxon signed-rank test was used to evaluate the differences between the initial assessment and the one-year assessment for the two sides (alpha = .0125).

Results: Overall, significant deterioration was observed in the less-affected side after one year in resting tremor (p=.009), voluntary movement (p<.001) and rigidity (trend, p=.013). No changes were observed in the more-affected side after one year. Despite the worsening in the less-affected side, the more-affected side remained more impaired than the less-affected side at both assessments in all subsets (p<.0125). Additionally, asymmetry between the two sides decreased significantly in the action (p=.02) and resting tremor subsets (p=.02) after one year. There was also a significant increase in the daily dose of dopaminergic medication after one year (p<.001).

Conclusions: Separating the UPDRS III into subsections identified progression in the less-affected side but not in the more-affected side. Although the increased dopaminergic medication may have masked the progression in the more-affected side, disease progression was still evident in the less-affected side. These results suggest that clinicians and future research trials should consider evaluating the two sides of the body independently – according to the side-affected – when monitoring disease progression in patients with PD.

P13.02

Clinical Outcomes in patients with Parkinson disease treated with an MAO-B inhibitor

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Purpose: To assess differences in clinical outcomes between patients with Parkinson disease (PD) treated or not treated with an MAO-B inhibitor.

Methods: Demographic, treatment, and clinical outcome data were collected retrospectively from medical records of patients with PD treated at a single clinic of movement disorders. Patients in the MAO-B inhibitor group were included only if duration of rasagiline or selegiline therapy was for at least a year. Patients were excluded if: 1) less than one year on current or previous MAO-B inhibitor therapy; 2) not currently on any of type of PD medication; 3) incomplete/missing information for controlled variables (i.e., age, gender, months since diagnosis, and levodopa equivalent dose). A Wilcoxon test to compare age, months since diagnosis and average levodopa equivalent dose (LED) between the two treatment groups and a chi-square test to compare gender bias, and proportion of patients prescribed amantadine, levodopa, pramipexole, ropinirole, and deep brain stimulation were performed. Multivariate logistic regression was performed to calculate the odds ratio (OR) of Non-MAO-B treatment versus MAO-B inhibitor treatment. Controlled variables (age, gender, months since diagnosis, and levodopa equivalent dose) were included to improve the model.

Results: Charts of 423 patients were reviewed and 287 were included for analysis. Baseline demographics were similar amongst both groups with the exception of greater use of levodopa and less use of ropinirole in the Non-MAO-B group. The mean LED was similar among groups. The occurrence of dementia, dyskinesias, falls/unstable gait, freezing gait, and hallucinations were lower in the MAO-B inhibitor group. The reduced occurrence of dyskinesia in the MAO-B inhibitor group was statistically significant (OR=1.874; p=0.0426).

	MAO-B Inhibitors:	Non-MAO-B Inhibitors	Odds Ratio	p-value
Hallucinations	28.28% (56/198)	29.55% (26/88)	0.95	n/a
Falls/Unstable Gait	46.73% (93/199)	57.95% (51/88)	1.35	0.266
Freezing Gait	23.74% (47/198)	32.95% (29/88)	1.42	0.239
Dementia	25.76% (51/198)	34.09% (30/88)	1.37	0.272
Dyskinesia	25.00% (49/196)	41.38% (36/87)	1.87	0.043

Conclusions: This retrospective analysis suggests MAO-B inhibitors may reduce the risk of dyskinesia (OR = 1.87) in patients who take them for at least one year.

P13.03

Rapid disease progression in adult-onset Mitochondrial Membrane Protein associated neurodegeneration

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Objective: To report genetic findings of two families with Mitochondrial Protein-Associated Neurodegeneration.

Background: MPAN is a recently described NBIA syndrome caused by C19orf12 mutations and shows significant phenotypic heterogeneity.

Methods: Three patients and 4 healthy individuals from two families were included for genetic study. SNP genotyping was performed using the HumanOmniExpressExome bead-chip that contains 700,000 genome-wide markers plus additional 240,000 putative functional exonic variants. The entire coding region and intron-exon boundaries of C19orf12 were PCR amplified in all available DNA samples. All purified PCR products were then sequenced. The resulting sequencing reactions were resolved on an ABI3130 genetic analyser and analysed using Sequencher 5.0 software.

Results: Three patients from two families with rapidly progressive extrapyramidal syndrome and decreased signal intensities in g.pallidus and s.nigra were included. Homozygosity mapping through genome-wide SNP genotyping was performed. We identified a single homozygous segment common to all three affected individuals. This homozygous segment of 2Mb and located on chromosome 19q12. This disease-associated locus containing 613 consecutive SNPs in length only comprised eight different genes, including the C19orf12 gene. Direct sequencing of the entire coding region of C19orf12 identified a disease segregating p.Thr11Met mutation.

Conclusions: In conclusion, we present three new NBIA cases with C19orf12 mutations that presented with an adult-onset form without optic abnormalities, and, in 2 cases, with a rapidly progressive extrapyramidal and pyramidal disorder.

P13.04

Distribution of Clinical subtypes in Parkinson's disease associated with Dysphagia: Comparison of de novo drug naive stages with advanced stages.

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Objective: Prevalence of Clinical subtypes in Parkinson's disease associated with swallowing impairment measured by videofluoroscopy, clinical examination and scoring in stages 1-4 (Hoehn & Yahr).

Methods: Clinical Examination, videofluoroscopy and scoring by UPDRS I to V, ESS, BDI and PDNMS Questionnaire. We divided into Akinetic Rigid type (AR), Tremordominant type (TD) or Mixed type (M). Frequency of swallowing disturbances determined by videofluoroscopy and rating scales were expressed in terms of number, standard deviation.

Results: 57 PD patients, 17 de novo drug naïve PD in stage 1 to 2, n= 34 in stage 3 and n= 6 in stage 4 of Hoehn & Yahr. Videofluoroscopy detected swallowing disturbances in n=6 (35%) of de novo PD, almost in pharyngeal phase, thereby in 3 cases AR and 3 cases M. The corresponding frequencies in stage 3 H & Y were n= 14 (41%), AR 9 and M 5; and in stage 4 H & Y n=5 (83%), AR 4 and M1, respectively. TD subtype in stage I, II or III was not affected. With PDNMS and ESS higher than 10 pts, we observed a small association of AR and M with item constipation and fatigue. In contrast, regarding clinical swallowing disturbances measured by self rating scales, we found a lower prevalence of 17% PDNMS question 3 in de novo, 29% in stage 3 and 67% in stage 4 H & Y.

Our data demonstrate early occurrence of dysphagia, detected by videofluoroscopy in Parkinson's disease. We found a preference of the clinical subtype AR more frequent than M within all stages. This pattern was already observed in the early and drug naive stages of Parkinson's disease with de novo diagnosis.

P13.05

Motor, cognitive and affective characteristics of new-fallers compared to non-fallers in an incident cohort of Parkinson's disease

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Objective: To compare motor, cognitive or affective characteristics in people with Parkinson's disease (PD) who transition from being a non-faller to a faller and those who remain non-fallers.

Methods: We measured prospectively falls in 70 people with PD with no history of previous falls (self-report) for 12 months. In this study, we used the term new fallers to identify those people who transitioned from no history of falls to their first fall. A faller was defined as someone who experienced two or more falls over 1 year of prospective monitoring. We compared the motor, cognitive and affective characteristics from baseline assessment between new fallers and non-fallers using Mann-Whitney U tests.

Results: 13 participants transitioned to become new fallers (mean (SD) age 69.0 years (9.0) years) whilst 57 remained non-fallers (67.1 yr (9.4)). Participants who became new fallers walked more slowly than non-fallers with a slower and more variable step time, slower sit-to-stand, increased PIGD (Postural Instability and Gait Disorder) score and poorer executive function (One Touch Stockings) (Table 1). Balance and depression scores did not discriminate new fallers from non-fallers.

Table 1 Baseline description of new fallers compared to non-fallers.

Variable	PD non fallers (n=57)		PD new fallers (n=13)		p
	Mean	SD	Mean	SD	
PIGD score	2.70	1.75	3.95	1.65	.022
Sit to stand (s)	12.5	3.6	15.0	3.1	.026
OTS mean latency (ms)	19,191	11,030	25,829	11,877	.016
Global Depression Scale	2.11	2.07	2.69	2.18	.329
Total Fatigue (MFI)	43.7	16.7	48	14.1	.277
Ambulation and Balance Confidence Scale	88.1	16.7	85.0	11.6	.083
Walking speed m.s ⁻¹	1.17	.20	1.02	.19	.022
Step time (ms)	548	43	588	66	.021
Stance time variability (ms)	21.0	8.8	26.3	10.2	.031

P13.06

Gait predicts decline in attention over 18 months in an incident cohort of Parkinson's disease

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Objective: To examine whether gait characteristics measured at baseline can predict cognitive decline over 18 months in an incident cohort of Parkinson's disease (PD).

Methods: Fifty-eight people with idiopathic PD (mean (SD) age 67.4 (10.6) years) participating in the ICICLE-GAIT study were assessed for age, sex, disease severity, gait and cognition within four months of diagnosis and 18 months after the baseline assessment. Gait speed was collected using a 7m instrumented GAITrite mat whilst walking for 2 minutes at their preferred pace. Power of Attention (PoA) was assessed using the Cognitive Drug Research (CDR) computerised assessment system. Loess regression was used to identify the nature of the relationship between gait and change in attention at 18 months. Segmented linear regression was then used to test if baseline gait speed predicted change in cognition for those who walked faster and slower than 1m.s⁻¹ at baseline.

Results: Thirty-one males and 21 females, with average (SD) MDS-UPDRS III scores of 10.6 (9.8) participated in the study. There was a non-linear relationship between gait speed and change in attention, with a slower gait speed predicting cognitive decline for slow (<1m.s⁻¹, n = 18) but not fast walkers (1.0 1m.s⁻¹, n = 40). A second model showed that gait speed remained an independent predictor of cognitive decline for the slow walking group even after controlling for baseline attention (Fig 1). Age, sex and disease severity did not correlate with change in attention and were not included in the model.

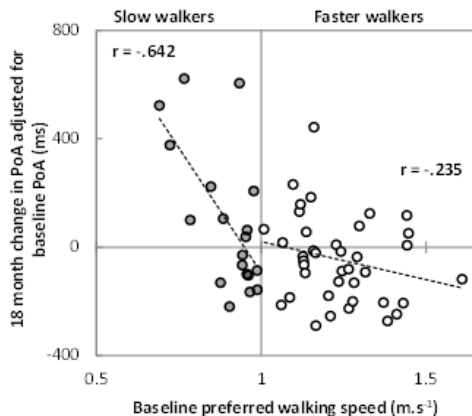


Fig 1: Scatter plot for gait speed and baseline attention correlated with change in attention scores

P13.07

The SURE-PD trial: Safety, tolerability and urate-elevating efficacy of inosine in Parkinson disease

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Background: Convergent biological, epidemiological and clinical data have identified urate elevation as a candidate strategy for

slowing disability progression in Parkinson disease (PD). In contrast to urate, its metabolic precursor inosine has shown favorable oral bioavailability.

Objective: To assess the safety, tolerability, urate-elevating efficacy and other effects of oral inosine in early PD, and thereby determine whether and how to conduct a subsequent phase 3 disease modification trial.

Methods: The 'Safety of URate Elevation in PD' (SURE-PD) study, a randomized, double-blind, placebo-controlled, dose-ranging trial of oral inosine, enrolled subjects with early PD and serum urate <6.0 mg/dL. They were randomized to three treatment arms: placebo or inosine dosed to elevate serum urate – either mildly (to 6.1-7.0 mg/dL) or moderately (to 7.1-8.0 mg/dL). Subjects were followed up to 24 months on study drug plus 1 washout month, with visits every 3 months to assess adverse events (AEs), tolerability and urate concentration in serum and (once after 12 weeks) in CSF, along with multiple secondary outcome measures.

Results: Seventy-five subjects (mean age 62; 55% women) enrolled at 16 clinical sites, with median follow-up of 1.6 years. Serious AEs (17) including infrequent cardiovascular events occurred at the same or lower rates in the inosine groups relative to placebo. Although no subject developed gout, 3 (1 in the mild urate elevation group and 2 in the moderate group) developed kidney stones. 95% of subjects tolerated treatment at 6 months (significantly above the preset 30% futility boundary for intolerability). Serum urate rose by 2.3 and 3.0 mg/dL in the respective inosine groups (p<0.001 for each vs placebo), and CSF urate was greater in inosine groups (p=0.006 and <0.001, respectively).

Conclusion: Inosine was safe, tolerable, and effective in raising serum and CSF urate levels. The findings support advancing to phase 3 development of inosine for PD.

Funding: The Michael J. Fox Foundation

CLINICAL SCIENCES: BEHAVIORAL DISORDERS

P14.01

Impulse Control Disorders in young-onset patients with Parkinson's disease: cross-sectional study unveiling associated factors

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Objective: The aim of our cross-sectional study was to describe the frequency and associated factors of ICD in young-onset PD patients in two specialized movement disorders centers in the Czech Republic (Prague and Brno).

Methods: We have examined 34 young-onset PD patients- PD group (age 47.0 (35.0; 63.0) years, onset of PD 35.0 (28.0; 40.0) years; average duration 10.5 (4.0; 25.0) years; UPDRS 13.5 (7.0;

27.0) and 34 age and sex- matched healthy control subjects- control group. Used questionnaires: South Oaks Gambling Screen for pathological gambling and modified Minnesota Impulse Disorders Interview for other types of pathological behaviour. For detection for any neuropsychological symptoms as possible associated factors, questionnaires for depression (Montgomery-Asberg Depression Rating Scale), anxiety (Hamilton Anxiety Rating Scale), psychopathology (The Symptom Checklist 90; SCL-90) and Personality Style and Disorder Inventory were introduced to both groups.

Results: We have found significantly higher prevalence of pathological gambling in PD group (3 PD patients (8.8%) / no control subject) and higher prevalence of hypersexuality (2 patients-5.9% / no control) when compared to the control group. 6 PD patients (17.6%) had a history of overusing of medication. Symptoms of any ICD were more frequent in PD group (8 patients (23.5%) / 4 controls (11.76%). We have observed following factors associated with occurrence of any ICD in PD group: anxiety, depression, personal typology and use of antidepressants. We have not found any association related to the PD duration, actual stage of PD or antiparkinsonian medication intake.

Discussion: We can confirm increased incidence of ICD (especially pathological gambling and hypersexuality) in young-onset PD patients. Other associated factors have to be carefully detected and followed.

Acknowledgement: Supported by unrestricted grant from Novartis. MB, TG and KC were supported by the project "CEITEC - Central European Institute of Technology" (CZ.1.05/1.1.00/02.0068) from European Regional Development Fund.

P14.02

Effect of Parkinson's disease on proprioceptive control of reaching movements and postural stability limits

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Objective: The aim of this study was to assess how medicated (ON, n=6) and non-medicated (OFF, n=9) patients with mild to moderate Parkinson's disease (PD) use proprioception to control three-dimensional (3D) reaching movements and postural stability limits, compared to healthy volunteers of similar age.

Methods: In the reaching task, subjects performed 3D reaching movements in two conditions in which the target location and hand positions were defined by either vision or proprioception. The positions of the tip of the index finger and arm segments were recorded using a NDI motion analysis system. In the postural task, subjects stood on an AMTI force plate with bare feet at comfortable stance width and arms crossed on the chest. Subjects were instructed to lean as far as possible in four directions (forward, backward, rightward and leftward) without lifting their feet or flexing their hips and to maintain this maximal position for 10 sec. Subjects were tested in vision and no vision-proprioceptive conditions. Accuracy of reaching movements and center of pressure (COP) displacements during the stabilization phase of leaning movements were analyzed.

Results: PD patients in the ON state displayed a higher average level of 3D reaching errors than control subjects (n=10) only when proprioceptive signals were used to define target and hand positions

(ANOVA, group by condition interaction, $p < 0.05$). In contrast, PD patients showed an overall smaller average level of stability limits than healthy subjects (n=6) in both visual and proprioceptive conditions. This difference was larger in OFF state patients, particularly along the mediolateral axis (ANOVA, group by axis interaction, $p < 0.05$).

Conclusion: These preliminary findings suggest that the proprioceptive guidance of reaching and posture are differentially affected by PD and dopaminergic medication. An ongoing study in our laboratory assesses whether a proprioception-based training program improves the proprioceptive control of reaching and stability limits.

P14.03

Postural instability and future falls in Parkinson's disease: contribution of increased tremor

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Objective: Postural instability leading to falls is a major health and injury problem for people with Parkinson's disease (PD). This study sought to objectively assess relationships between tremor, postural instability and falls.

Methods: 63 PD (67 ± 8.1 yrs) and 39 age- and gender-matched controls (68.1 ± 9.3 yrs) independently living in the community. Bilateral resting and postural tremor was recorded from the hand and index finger segments of each arm using light-weight uniaxial accelerometers. Postural motion in the anterior-posterior (AP) and medio-lateral (ML) directions were recorded from a force plate (100Hz). PD participants were assessed while optimally medicated. Participants completed monthly falls calendars over 12 months. Tremor and postural motion data were analysed by calculating root mean square (RMS) and approximate entropy (ApEn).

Results: 69% of PD and 46% of older people fell over 12 months. PD fallers had longer disease duration, greater dopamine agonist medication use and had worse measures of activities of daily living (UPDRS II, Schwab & England) and Freezing of Gait than PD non-fallers. PD participants had 4-7 Hz peak in resting and postural tremor whereas older people's tremor contained peaks between 2-4 Hz and 8-12 Hz. Both resting and postural tremor RMS and ApEn were greater for PD fallers than non-fallers. For the older group there were no differences in tremor RMS or ApEn between fallers and non-fallers. PD fallers and older fallers had greater ML postural sway than non-fallers. Compared to non-fallers, ML postural sway was more regular for PD fallers whereas anterior-posterior postural sway was more irregular for older fallers.

P14.04

Influence of impulse control disorders on the quality of life among cognitively-intact Parkinson's disease patients living in the Tomsk region, Russia

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Background: Non-motor features of Parkinson's disease (PD) patients are frequent and prevalent which impair the patients quality

of life. Among impulse control disorder (ICD) the behavioral dysfunction causes the greatest impact on quality of life. Unknown whether how prevalent ICD are among PD patients in the Tomsk region.

Objective: To determine the prevalence of ICD and its correlation with life quality among cognitively-intact patients with PD seen at the Movement Disorders Center of "Siberian Medical University".

Methods and materials: 73 Tomsk patients fulfilling the UK Parkinson's Disease Society Brain

Bank Clinical Diagnostic Criteria for PD were included in the study. Demographic data were obtained including: age, sex, onset of disease, disease duration and medication intake. The Mini

Mental State Examination (MMSE) was done to exclude significant cognitive impairment. The Questionnaire for Impulsive-Compulsive Disorders in Parkinson's Disease-Rating Scale (QUIPRS) was administered to quantify ICD. The degree of ICD was correlated with the quality of life instrument, Short form health survey (SF-36); and the functional and motor severity using the Unified Parkinson's Disease Rating Scales (UPDRS).

Results: Our cohort of patients had a mean: age of 62.4±8.6 years, and disease duration of 7.2±4.6 years. Out of the 73 patients, 33 (45.2%) probably had ICD based on the QUIP-RS. ICD greatly impacts scores on SF-36.

Conclusions: The prevalence of ICD among this Tomsk region cohort of patients is 45.2% which is higher than commonly reported worldwide. The presence of ICD significantly correlated with poorer quality of life.

P14.05

The relation between obsessive-compulsive behaviors and *PARKIN* genotype

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Background: Mutations in *PARKIN* are a known genetic risk factor for early onset Parkinson's disease (EOPD). We have shown that people without PD who harbor two *PARKIN* mutations (compound heterozygotes) have a higher risk of depression than those without mutations, possibly representing a pre-motor feature of future PD. Other psychiatric symptoms, like obsessive compulsive behaviors, are also seen in PD but the genetic contribution to these symptoms is not well characterized. We investigated the role of *PARKIN* mutations in obsessive compulsive symptoms among those with EOPD and their relatives.

Methods: We collected psychiatric information using the Schedule of Compulsions and Obsessions Patient Inventory (SCOPI), Patient Health Questionnaire and Beck Depression Inventory II on 104 probands with (n=49) and without (n=55) *PARKIN* mutations. We also evaluated 169 genotyped unaffected family members of patients with *PARKIN*-associated EOPD (6 with two *PARKIN* mutations (3 of whom belong to the same family), 83 with one mutation and 80 without (wild-type)). We compared SCOPI performance of persons with EOPD to their family members. We then assessed for predictors of higher scores (outcome) among people with PD using linear regression models adjusted for demographics, disease characteristics and *PARKIN* mutation status. Among family members, we tested whether *PARKIN* mutation status was associated with a higher SCOPI score.

Results: There was no significant difference in SCOPI scores between people with PD and their family members (p=0.419). Among people with PD, higher BDI scores (p=0.035), and wild type *PARKIN* mutation status (0.019) were associated with higher SCOPI

total score. Gender, age, education, disease duration, presence of anxiety, and motor severity were not. Among unaffected relatives of *PARKIN*-associated EOPD, compound heterozygotes (who are at high risk of PD) scored higher than either heterozygotes or non-carriers on SCOP1 total ($p=0.01$) and on the combination of subscales most representative of obsessive compulsive behaviors (obsessive checking, obsessive cleanliness and compulsive rituals) ($p=0.005$).

Conclusions: People with EOPD are not more likely to demonstrate obsessive-compulsive behavior than their family members. However, family members who are compound heterozygote *PARKIN* carriers (i.e. with a high genetic risk for PD) score higher on scales of obsessions and compulsions. Long term follow up is required to assess whether these are pre-motor signs of PD in *PARKIN* carriers.

CLINICAL SCIENCES: COGNITION/ MOOD/ MEMORY

P15.01

Personality and Depression: Factors that influence reported quality of life among PD Patients

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Objective: Previous work has cited both personality factors, mainly neuroticism and conscientiousness, and depression as major factors affecting the functioning of patients with Parkinson's disease (PD). We were interested in understanding the contribution of each of these to reported quality of life (QoL), an outcome measure incorporated into many clinical studies.

Methods: 97 PD patients, under the age of 66 and without dementia completed the NEO Five Factor Inventory (NEO-FFI) of personality, the Parkinson's Disease Quality of Life Questionnaire (PDQL) and the Beck Depression Inventory. Patients were clinically assessed for motor function using the Unified Parkinson's Disease Rating Scale (UPDRS) - III and evaluated for the presence of depression with the Hamilton Depression Rating Scale (HDRS). Stepwise regression models were constructed to examine the contribution of neuroticism, conscientiousness, depression symptomatology and motor function (UPDRS-III) to scores on the four subscales of the PDQL (parkinson symptoms, systemic symptoms, emotional function, social function). Age, education, and symptom years were also included but were non-significant and were dropped from the models.

Results: The sample was two-thirds male, with an average of 16 years of education and an average of 6 years since the onset of PD symptoms. The overall PDQL score was significantly associated with scores on the Beck Depression Inventory ($F=7.41$, $p<.01$). The four PDQL factors however, had differing predictors. The Parkinson's Factor was related to the UPDRS III and Neuroticism ($F=20.19$, $p<.001$); the Systemic Factor was related to the Beck ($F=31.312$, $p<.001$); the Social Factor was related to the Beck and the UPDRS III ($F=43.625$, $p<.001$); and the Emotional Factor was predicted by Neuroticism and Conscientiousness ($F=26.916$, $p<.001$). In interpreting patient responses on the PDQL it is important to understand whether they reflect aspects of PD, i.e. motor impairment and depression, which are amenable to treatment, or whether they reflect personality traits.

P15.02

Impact of Parkinson's disease on social role function: Multifaceted disability

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Objective: Much of the focus on understanding and characterizing the disability that accompanies Parkinson's disease (PD) has focused on the impact of motor impairments on activities of daily living that are required for maintaining independence in the home and accomplishing self care. However, the impact of PD on the maintenance of social roles and social integration has received little attention. This study undertook to examine changes in social roles in this disease and the factors related to this disability.

Methods: 101 PD patients, under the age of 66 and without dementia were enrolled in the study. Participants were assessed for motor function using the Unified Parkinson's Disease Rating Scale (UPDRS) - III Motor Scale, Groove Pegboard and Finger Tapping task. They also were administered several cognitive tests (Hopkins Verbal Learning, Brief Test of Attention, Verbal Fluency, Trails, Ravens) and were evaluated for the presence of depression with the Hamilton Depression Rating Scale (HDRS). In addition they were administered the Social Adjustment Scale, which examines functioning for six different roles. Regression models (SPSS) were constructed for each of the 6 roles as well as overall social functioning.

Results: Overall social functioning was predicted by depressive symptomatology, decreased verbal fluency and decreased fine motor skills, $R^2 .52$ ($F=22.88$, $p<.001$). Work, ($R^2.268$, $F=10.96$, $p<.001$) leisure ($R^2.364$, $F=17.17$, $p<.001$) and extended family roles ($R^2.260$, $F=10.34$, $P,.001$) were related to depression and decreased cognitive performance. The parental role was the only role related solely to motor function, the UPDRS III ($R^2 .086$, $F=5.71$, $p<.02$). The family unit role was predicted by depression and fine motor control ($R^2.249$, $F=9.96$, $p<.001$). Only the marital role failed to be predicted by any of the assessments. Psychiatric and cognitive impairments, rather than motor dysfunction, are the major factors affecting the ability of PD patients to maintain their social roles.

P15.03

A new paradigm in neuropsychological assessment: Motor Imagery. A pilot Study with Parkinson's disease patients

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Objective: To evaluate the motor imagery through mental chronometry paradigm in patients with Parkinson's disease (PDp). Motor Imagery (MI) is the ability to create mental images or representations of a motor act in the absence of the actual execution of the movement. It can be evaluated through the mental chronometry paradigm, which measures the time it takes the patient to mentally imagine performing movements and then compare it with the time for the motor execution. The MI has been poorly evaluated in PDp. One previous study reported IM conservation in these patients.

Methods: 20 PDp who participated in the "Dance Therapy Program using Argentine Tango" were recruited. Average age: 66.11 (SD = 5.9); male: 60%; H&Y: II-III; average disease duration: 6.3 years; MOCA: 26,8 (20-30). The MI was assessed through the Box and Block test where the participant must transfer 20 blocks from side to side of a box during the real implementation phase and during the imaginary phase. The time spent in each stage was recorded.

Results: The average time execution phase was 37.15 seconds (SD = 11.9) and the average time in the MI phase was 32.17 (SD = 10.5). This difference was not statistically significant ($p > 0.05$). The time in both phases was positively associated: $r = .47$, $p < 0.05$, which could indicate that depend on common processes. Patients spend similar time for imagining and for executing the task. This may reflect an appropriate temporal consistency, showing that patients adapt their imagination to reality. It would suggest that patients may benefit from rehabilitation strategies that require the use of MI. These results are consistent with previous studies.

P15.05

Interactions between cognition, depression and L-Dopa in Parkinson's disease

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Objective: It has been reported that 50% to 70% of patients with Parkinson's disease (PD) will experience depressive symptoms during their disease and it is also well established that cognitive deficits exist even at the early stages of PD. These non-motor symptoms are thought to be the most predictive of the quality of life in those patients. However, there is a lack of consensus regarding the nature and interactions between neuropsychological dysfunction and depression in PD and the effect of L-dopa on depression is controversial.

Methods: 44 PD participants at stages I and II Hoehn and Yahr were recruited with 20 healthy matched volunteers. They underwent a comprehensive neuropsychological evaluation and also filled the Beck Depression Inventory scale II (BDI). The neuropsychological battery included tests of executive, visuo-spatial and mnemonic, and language functions. The BDI items were divided into 3 different parts: mood, cognition and somatic

Results: Patients were divided in two groups: with and without depressive symptoms. There were significantly more PD patients with cognitive deficits in the depressed group compared to the non-depressed one. Furthermore, amongst cognitively affected patients, depressed ones exhibited significantly more impairments on mnemonic and executive functions than non-depressed ones. We have found correlations with L-Dopa and neuropsychological functions (some mnemonic and executive measures worsen as L-Dopa dosage increase) but not with dopamine agonists. An increasing number of studies have reported early PD patients with significant mnemonic deficits and not just executive ones. Our results show that these latter impairments may be more common in PD patients with depression. Furthermore, our study indicates that the dose of L-Dopa may interact with depressive symptoms and that it might have an incidence when determining the global therapeutic approach.

P15.06

Relationships between motor, cognitive and psychological outcomes following bilateral subthalamic nucleus deep brain stimulation (STN-DBS) in patients with Parkinson's disease

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Objective: Motor improvements associated with bilateral STN-DBS in patients with PD have been documented at the group level, but the degree of symptom relief varies greatly in individual patients. Similarly, cognitive and psychological outcomes have been heterogeneous in these patients. The aim of this study is to examine whether motor, cognitive and psychological outcomes of the STN-DBS surgery are related.

Methods: We analyzed the results of 17 patients (10 men, 7 women, with a mean age 61 years) who underwent bilateral STN-DBS to relieve the symptoms of PD. All of the patients were tested before and after the surgery (mean follow-up interval 16.5 months). Their motor outcomes were measured as pre-post differences off-medication from the motor examination (part 3) of the Unified Parkinson's Disease Rating Scale. We analyzed their cognitive outcomes using standardized pre-post change scores from 24 neuropsychological measures, grouped into 8 cognitive domains (reasoning, short-term memory, information processing speed, verbal episodic memory, nonverbal episodic memory, language, visuospatial and executive functions). Psychological outcomes were measured as pre-post differences in depression (Beck Depression Inventory-II) and anxiety (Beck Anxiety Inventory).

Results: As expected, we found significant motor improvements following DBS-STN. Cognitive decline was noted in the fronto-executive and speed of information processing domains, while the symptoms of anxiety improved. In general, motor changes were not related with cognitive and psychological outcomes. Only marginally significant correlations were found between motor changes with visuospatial functions and short-term memory, and with the symptoms of anxiety. The reduction of the symptoms of depression was associated with short-term and verbal episodic memory improvements.

Conclusion: Patients showed the expected declines in cognition as well as the improvements in anxiety following the STN-DBS, but these changes were not prominently associated with motor outcomes. Nevertheless, post-surgical relief from depression was associated with some cognitive benefits.

P15.07

The impact of treatment response to cognitive-behavioral therapy on different clusters of depressive symptoms in Parkinson's disease

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Objective: Parkinson's disease (PD) is frequently complicated by depression and there is limited controlled research that can inform the management of this disabling psychiatric comorbidity. A National Institutes of Health-sponsored randomized controlled trial (RCT) of Cognitive-Behavioral Therapy (CBT) plus clinical management, versus clinical management only, for the treatment of depression in PD (dPD) was recently conducted. The goals of the current study are to describe the impact of treatment response to CBT on different clusters of depressive symptoms in PD and to explore the extent to which stabilized antidepressant use throughout the trial moderated specific symptom change.

Methods: Eighty depressed people with PD participated in this RCT. CBT was provided for 10 weeks and incorporated behavioral activation, cognitive restructuring, sleep hygiene, anxiety management, and caregiver psychoeducation. Treatment response was defined a priori as a rating of depression "much improved" or "very much improved" on the Clinical Global Impression-Improvement Scale, or a reduction of at least 50% from baseline in

the Hamilton Rating Scale for Depression (HAM-D) total score. HAM-D and Beck Depression Inventory subscales (BDI), which reflect the heterogeneity of depressive symptoms in PD, were the focus of this study.

Results: CBT response was associated with significant improvements in core mood (Cohen's $d = 3.28$), sleep (Cohen's $d = .58$), anxiety (Cohen's $d = 1.17$), and somatic symptoms (Cohen's $d = .77$) as assessed by the HAM-D, and negative attitudes toward self (Cohen's $d = 1.74$), performance impairment (Cohen's $d = 1.60$), and somatic symptoms (Cohen's $d = .83$), as measured by the BDI. Stabilized antidepressant use moderated the impact of CBT response on symptom change for somatic complaints only (HAM-D and BDI). In conclusion, CBT has the potential to improve a diverse array of depressive symptoms in PD. Combination treatment (CBT plus antidepressants) may help to optimize the management of somatic complaints associated with dPD.

P15.08

Apnea-hypopnea index and supine apnea-hypopnea index could be indicators for severity of cognition impairment in Parkinson's disease: Retrospective pilot study

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Objective: Sleep disturbance and cognitive impairments are frequent in Parkinson's disease (PD) and important non-motor symptom in PD. Some studies shows high prevalence of obstructive sleep disorder (OSD) in PD and correlation with severity of PD. It has been assumed that sleep apnea syndrome(SAS) may have negative impact on sleep quality and affect memory performances of PD patients. Although, Obstructive sleep apnea is a recognized cause of cognitive dysfunction. Yet, the relationship between cognition impairments and sleep-disordered sleeping in Parkinson with mild cognition impairment (MCI) and dementia was not studied before.

To assess the relationship between cognition impairments and obstructive sleep disorder in cognitively impaired Parkinson's disease patients.

Methods: Twenty patients with PD with cognitive impairments (9 patients with neuropsychologic-confirmed mild cognitive impairment(MCI) and 11 patients with neuropsychologic-confirmed dementia) were recruited from Inha polysomnography registry and underwent full night polysomnography (PSG).

Results: In baseline study, body mass index (BMI) was higher in PD with dementia(PD-D) group (24.6 Vs. 21.7, $p = 0.007$) Among the parameters studied apnea-hypopnea index(AHI), supine AHI and supine and non-supine AHI ratio were statistically different between PD-D with PD with MCI(PD-MCI) groups.

P15.09

Mild Cognitive Impairment in Parkinson's disease is linked with extensive cortical thinning during longitudinal analysis

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Objective: We performed a longitudinal study in patients with Parkinson's disease (PD) with and without mild cognitive impairment (MCI) at the beginning of the study and tested whether cortical thickness in the MCI group would reveal significantly more changes over time than the non-MCI patients.

Methods: We included 33 non-demented PD patients at the early stages of the disease who were studied twice 20 months apart. On each session (Time 1 and Time 2) they participated in an MRI investigation and a comprehensive neuropsychological assessment. Based on the Time 1 neuropsychological assessment, patients were divided in two groups: MCI positive and MCI negative. The construction of cortical surface was based on MPRAGE 3T images, using FreeSurfer 5.1 image analysis suite. Images underwent a standard pre-processing and analyzing procedure according with FreeSurfer longitudinal stream. (Reuter et al. 2010). Misclassification of tissue types was corrected by minimal manual adjustment. Cortical thickness was computed as the shortest distance between the grey/white boundary and gray/cerebrospinal fluid boundary at each vertex on the tessellated surface (Fischl et al. 2000). Analysis of longitudinal data was performed using the linear mixed effects model included in FreeSurfer (Bernal-Rusiel et al. 2013).

Results: The intergroup analysis revealed increased cortical thinning in PD-MCI compared with PD non-MCI in the right supplementary motor area (SMA), ventral premotor cortex, left middle temporal gyrus, supramarginal gyrus and lingual cortex. The intragroup results showed bigger clusters of cortical thinning in PD-MCI in occipital lobe and premotor cortex bilaterally, as well as right SMA, middle temporal gyrus and precuneus cortex. On the other hand, the PD non-MCI group exhibited smaller clusters in the right occipital cortex, supramarginal gyrus and superior temporal gyrus. Our results suggest that the early presence of MCI in PD patients is indicative of faster neural degradation.

P15.10

Subthalamic Nucleus deep brain stimulation and impulsivity : dissociating impulse expression and suppression in Parkinson's disease patients

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Objective: although deep brain stimulation (DBS) of the subthalamic nucleus (STN) tremendously alleviates the motor symptoms of Parkinson's disease (PD), growing evidence suggests that DBS also induces motor impulsivity. Impulsive actions constitute a major source of errors in daily life. They entail (i) capture of the motor system by an action impulse, which is an urge to act and (ii) a lack of suppression of that impulse to prevent an overt error. Most experimental studies fail to dissociate between the effects of STN DBS on impulse capture and on the ability to keep

that fast impulse in check. We propose a novel psychophysiological approach based on electromyographic (EMG) analyses to decipher the effects of STN DBS on the expression and suppression of erroneous impulses.

Methods: we used a reaction time (RT) protocol, the Simon task that elicits prepotent response tendencies. We analyzed performance and EMG activity of sixteen PD patients on and off STN DBS and on and off dopaminergic medication in a full factorial design.

Results: we provide the first direct evidence that STN DBS on the one hand increases the occurrence of erroneous response impulses and on the other hand impairs the proficiency to suppress impulse driven errors. Dopaminergic medication specifically impairs impulse suppression.

Discussion: STN DBS increases impulsivity both by enhancing the excitability of cortical motor structures and by reducing the efficiency of the indirect pathway that links the striatum to the globus pallidus interna to the globus pallidus externa via the STN. Dopaminergic medication may reduce the inhibitory influence of the STN through its action on the indirect pathway of the basal ganglia.

P15.11

Initial Results of a Clinical Trial comparing a Neurocognitive Intervention to Supportive Therapy in Individuals with Parkinson's disease

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Objective: Parkinson's disease (PD) is now conceptualized as a whole body neurodegenerative disease with neurocognitive symptoms that gradually develop and progressively compromise individuals' activity levels, quality of life (QOL), and independence. No neurocognitive interventions have been tailored to the needs of individuals with PD despite the prevalence of neuropsychiatric and neurocognitive symptoms in PD. This trial aimed to adapt empirically supported memory and problem solving techniques for use in a PD population.

Methods: This ongoing, randomized controlled trial (RCT) seeks to evaluate the feasibility and preliminary effectiveness of a novel neurocognitive intervention, which incorporates memory enhancement and problem solving strategies, compared to nondirective supportive therapy in individuals with PD and Mild Cognitive Impairment ($N=11$) and their support persons ($N=6$). Individual outcomes include neuropsychological tests of attention, processing speed, memory, and executive functioning, and self-reported mood symptoms and QOL, given at baseline, immediate follow-up, and 6-month follow-up visits.

Results: Preliminary findings from the immediate follow up showed trends for improved short-term memory among participants receiving the neurocognitive intervention. Attention, processing speed, and mental flexibility appeared relatively stable for both groups. Mood and QOL ratings did not appear to significantly alter in either group, but overall depression ratings were mild in both groups and QOL ratings were generally positive. Apathy ratings of participants in the neurocognitive intervention condition appeared to markedly decline following completion of the trial. Ongoing enrollment of additional participants and evaluation of outcomes at a 6-month follow-up will reveal whether these benefits are consistent in a larger sample and whether they are maintained over time. These initial results suggest that targeting memory and problem solving skills may be effective in counteracting aspects of neuropsychiatric and neurocognitive symptoms experienced by individuals with PD.

P15.12

Does rTMS enhance memory retention in Parkinson's disease (PD)?

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Objective: In patients with PD, skill retention is poorer than in normal age-matched controls, despite a generally preserved acquisition rate. It has been shown that, in normal subjects, treatment with repetitive transcranial magnetic stimulation (rTMS) at 5Hz may induce phenomena of long-term potentiation at the cortical level. Here we verified whether a 5Hz rTMS treatment enhances retention of a visuo-motor skill in a group of patients with PD.

Methods: Eighteen right-handed patients with PD (Hoehn & Yahr stage: 2-3) and twelve age-matched right-handed normal controls were tested one week apart in two separate sessions (rTMS and sham), each encompassing two consecutive days. In both sessions, on day 1, subjects learned to adapt their movements to a progressive 60° rotation of the visual display (counterclockwise rotation in one session, clockwise rotation in the other) and, immediately after the task, either real or sham 5Hz rTMS was applied over the right posterior parietal cortex (P6, 10-20 EEG system); on day 2, retention was tested. Acquisition and retention indices were evaluated by computing directional errors of the movement trajectories. The effect of treatment was assessed with repeated-measures ANOVA and post-hoc tests with correction for multiple comparisons.

Results: On day 1, controls and patients (in both sham and rTMS sessions) adapted their movements to the rotated display in a similar manner ($p>0.05$). On day 2, the mean retention index in normal subjects was significantly different from that of the PD patients in the sham session ($p<0.001$), but not from that of the TMS session ($p>0.3$). On average, there was a significant difference between the retention indices in the sham and rTMS sessions ($p<0.05$), although this effect was not uniform across patients. These data, first, confirm that, in PD, retention is decreased and, then, suggest that rTMS applied after learning might enhance retention.

P15.13

Working memory and facial expression recognition in Parkinson's disease individuals

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Objective: Parkinson's disease (PD) is associated with cognitive and also with emotional impairments. Nonetheless, it remains controversial the precise nature of emotional recognition problems. Specifically, while some results point to particular and distinctive emotional and cognitive disabilities in PD; others indicate that emotional problems may be secondary to (a consequence of) some cognitive-executive deficits implicated in recognition tasks (e.g., in working memory). The present study aims to discern whether emotional facial expression recognition abilities in PD are related to working memory abilities.

Method: we compare the performance of 50 PD patients and 49 healthy controls in four recognition tasks by means of an N-Back procedure. In short, task consisted of identify similarity or difference to the previous shown (1-Back) either of (1) an emotional facial expressions, (2) gender of the face, (3) nonsense syllables, and (4) spatial locations of squares inside a matrix.

Results: the PD group performed worse than healthy individuals in the emotional facial expression and in the spatial location tasks. Moreover, statistical contrast for single effects showed that differences between groups were significantly larger for facial expression than for the spatial location task. Taking together these results, we conclude that working memory seems to be partially altered in PD, in particular when it is required to operate with visuospatial material. Nevertheless, higher differences in the emotional task suggest an additional and specific difficulty in emotional facial expression recognition in PD. These set of results indicate the difficulty to clearly differentiate emotional and cognitive problems in PD. However, it also opens the possibility to design cognitive rehabilitation programs including emotional facial expressions as stimuli. It may be a way to work together and improve executive and emotional problems with very relevant and common stimuli in everyday situations, as facial expressions.

P15.14

Dance and cognitive functioning in Parkinson's disease

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Objective: Parkinson's disease (PD) is commonly accompanied by reduced health related quality of life (HRQoL) and cognitive decline which decreases participation in activities of daily living. Moreover, worsened motor abilities exacerbate dual tasking performance such as walking while performing another task e.g. talking. Unfortunately, pharmacotherapies and other treatment methods employed in PD fail to address the cognitive impairment exhibited in this population. A growing body of evidence associates dance with increased HRQoL in PD and ameliorated motor function. Additionally the relation between HRQoL and cognition in PD has also been described. However, to date it has not been investigated whether dance can ameliorate cognition in PD.

Methods: Six PD participants took part over a 10 week period in 90 minute dance for PD classes once a week; three of them were described as single case studies. A battery of cognitive tests was applied at the baseline, after dance intervention and in a 1 month follow up.

Results: Dance intervention ameliorated various aspects of functioning of X, Y and Z. X significantly improved on scales of HRQoL, balance and balance confidence, subtracting accuracy and walking distance in dual task condition between 1st vs 2nd testing sessions. Y significantly improved in walking distance in single (1st vs 2nd) and dual task (1st vs 2nd, 1st vs 3rd) condition and on balance confidence (1st vs 2nd). Z significantly improved on measures of visual attention and executive function (1st vs 2nd); moreover, his HRQoL significantly increased by 19.5% and balance confidence increased by 37% (1st vs 2nd, 1st vs 3rd).

P15.15

Double-blind, placebo-controlled trial of donepezil for dementia or mild cognitive impairment in Parkinson disease

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Objective: Measure the effects of donepezil on cognitive and motor function in Parkinson disease patients with either mild cognitive impairment (MCI) or dementia.

Methods: Subjects were classified as MCI based on Mini Mental Status Exam (MMSE) score of at least 26 and a Clinical Dementia Rating of 0.5. Subjects with MMSE of 25 or less were included in the dementia portion of the study. Both groups were randomized to placebo or donepezil 5mg daily for 12 weeks and evaluated at baseline, 6 weeks and 12 weeks. The primary cognitive outcome was the ADAS-Cog in the demented group and the cognitive battery utilized the TEST/RETEST study in the MCI group. Evaluations for all subjects also included MMSE, Unified Parkinson's Disease Rating Scale (UPDRS), Neuropsychiatric Inventory and clinical global impression of improvement. PD medication doses were held constant during the study. Scores were used in a two way repeated measures analysis of variance for statistical analysis.

Results: A total of 28 subjects were enrolled (13 demented, 15 MCI). No significant changes were observed in MMSE, UPDRS total, UPDRS motor or UPDRS tremor subscores in either group. No significant changes were observed in the ADAS-Cog in the demented group. Donepezil was well tolerated.

Conclusions: Donepezil was well tolerated but did not result in significant improvements in cognition in PD patients with dementia or MCI.

P15.16

Exercise for the mind: Investigating the effects of exercise on cognition in Parkinson's disease

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Objective: The overall objective of this systematic review was to accumulate evidence for the effects of exercise on cognition in patients with Parkinson's disease (PD). The rationale for conducting this systematic review was to provide guidance on the potential for exercise to benefit cognitive deficits in PD.

Methods: This systematic review was completed according to the Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) statement. Original research articles were included if the primary intervention was exercise and the primary outcome was a behavioral or neurobiological marker of cognitive function.

Results: Searching electronic databases yielded 272 records. One hundred and fourteen full-text records were assessed for eligibility. Eight original clinical research articles were included in the systematic review. All eight studies showed that exercise improved cognitive function, although the neurobiological mechanisms have not yet been determined. Three studies examined the effects of exercise on cognition specifically related to tasks of executive function. Improvements in cognitive function were shown using the Montreal Cognitive Assessment, as well on tests of reaction time and transfer of learning. Improvements in executive function were demonstrated on tasks such as the Wisconsin Card Sorting Test, Trail-Making Tests, tests of verbal fluency, working memory and spatial memory. Exercise may additionally decrease levels of serum homocysteine, a marker linked to cerebral vascular disease and cortical-hippocampal injury.

Conclusions: Exercise can be an effective treatment to improve cognitive function. The evidence from clinical studies suggests that a more intensive aerobic exercise program combined with strength and balance training may promote greater cognitive gains. However, low-intensity exercise also showed benefits. Patients should use these findings as further rationale to be as physically active as possible. Health care providers and policy makers should

encourage aerobic exercise with resistance training to the maximum tolerated intensity as part of the routine management of PD.

P15.17

The effects of rivastigmine therapy in Parkinson's disease dementia: A clinical, neuropsychological and electrophysiological study

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Objective: In this study, we evaluated positive effects of rivastigmine therapy on cognition in Parkinson's disease dementia (PDD) by means of behavioral inventory and neuropsychological tests and P300. In addition, we investigated the patients clinically and electrophysiologically using UPDRS, movement related cortical potentials (MRCP) and reaction time (RT) to show whether there are any negative effects of rivastigmin on motor function.

Methods: Ten non-demented idiopathic PD patients and 9 PDD patients were included the study. PDD patients were assessed by a neuropsychological test battery (MMSE, Rey auditory verbal learning test, Wechsler memory scale III visual memory subtest, trail test A-B and Luria drawing, digit span, similarities and category fluency test) which evaluate attention, memory and executive function and also electrophysiological tests (P300, MRCP and RT) before rivastigmine treatment (average dose 7.8mg/day) and after the sixth month of treatment. The non-demented PD patients also evaluated in the nature course of the disease by means of the same tests at the start and at the end of the six month.

Results: At the end of six months rivastigmin therapy, PDD patients showed statistically significant improvement in neuropsychological tests related memory and shortening of P300 latency. However we didn't found any statistically significant changes in the measurements of MRCP and RT tests after therapy. But, although PDD patients showed shortened RT after therapy, RT was prolonged in non-demented PD patients after the six months. In conclusion, our study have suggested that while rivastigmine therapy improve cognitive functions in PDD, it doesn't cause any side effects on motor function of patients.

P15.18

RECOGNISE: Rasagiline effects on cognition in Parkinson's patients with mild cognitive impairment

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Objective: Double blinded placebo controlled trial evaluating effects of Rasagiline 1mg on cognition and motor function in patients with Idiopathic Parkinson's Disease [IIT-TN-067]

Background: Numerous patients with Idiopathic Parkinson's Disease (PD) are treated with Rasagiline to help improve their motor function. However, this medication may also help with improving cognitive function as assessed by the Montreal Cognitive Assessment (MoCA), Frontal Assessment Battery test (FAB), and Scales for Outcomes in Parkinson's Disease-Cognition-test (SCOPA-COG).

Methods: Patients meeting the inclusion and exclusion criteria undergo motor and cognitive testing at baseline. They are then randomly assigned a treatment drug which is either placebo or Rasagiline. A phone visit is performed at 6 weeks regarding any problems with drug or any perceived improvements in motor

function or cognition. A final visit is performed at 14 weeks and patients again undergo motor and cognitive testing. Secondary endpoints include assessment of changes in UPDRS, depression, and balance.

Results: The interim analysis includes 16 of 40 anticipated subjects (64.7% male, mean age 69.5 years, diagnosed with PD mean 5.9 years, and mean years of education 16.5). Analysis of baseline data revealed mean MoCA score of 26.4/30, mean FAB score of 10.9/12, and mean SCOPA-COG score of 29.5/43. Additionally, mean baseline Berg Balance Scale score was 50.5/56 and mean UPDRS part III was 21.1.

Conclusion: This ongoing study will provide valuable information for Parkinson's disease patients with cognitive decline. Thus far, no standard-of-care medications for PD have been shown to significantly enhance cognition, so the addition of Rasagiline to a patient's medication regimen could potentially be of great value in addressing this issue along with addressing motor function.

P15.19

Vitamin D in Parkinson's disease

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Objective: To review our research on vitamin D in persons with Parkinson's disease (PD).

Methods: Specifically we have looked at cross-sectional data of vitamin D and measures of cognitive function, mood, and balance performance. These data have come from three different studies.

Results: In regard to cognitive function, baseline data from a study following neuropsychiatric function in persons with PD showed significant correlations between vitamin D concentrations and semantic verbal fluency (vegetables, p=0.01), categorical verbal fluency (animals, p=0.05; vegetables, p<0.01), and memory (Hopkins Verbal Learning Test, immediate recall, p=0.02; delayed recall, p=0.04) in the non-demented subset of the cohort. In regard to mood, data from the above study also showed a correlation between Geriatric Depression Scale (GDS) and vitamin D levels. Baseline data from a vitamin D intervention study showed significant negative correlations between vitamin D concentrations and total PD Quality of Life (PDQ-39 score: -0.46, p=0.02), the depression/dejection subscale of the Profile of Mood States (POMS: -0.43, p=0.03), and the confusion/bewilderment subscale of the POMS: -0.41 (p=0.04). In regard to balance measures, data from a pilot study of the relationship between vitamin D and balance in PD showed correlations between vitamin D concentration and postural response strength asymmetry and stance weight asymmetry. Correcting for the Unified Parkinson's Disease Rating Scale (UPDRS), the correlation coefficients for vitamin D and strength symmetry were 0.41 (p=0.01), 0.34 (p=0.03), and 0.32 (p=0.05) for small, medium, and large perturbation respectively. The correlation coefficients for vitamin D and weight symmetry were similar at 0.32 (p=0.05), 0.42 (p=0.01), 0.30 (p=0.07). It appears that vitamin D might have effects on a number of aspects of PD. These data are all cross-sectional, limiting the ability to infer causation. Intervention studies following multiple measures are needed to determine the full extent of the role vitamin D plays in PD.

P15.20

Response inhibition and emotional facial expression recognition in Parkinson's disease

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Objective: Attention and emotional recognition have often been found altered in Parkinson's disease (PD) individuals. Moreover, some studies have suggested that divided attention problems of patients determine emotional recognition through facial expression. Another attentional process that may influence emotional facial expression recognition in PD patients is the ability to inhibit irrelevant information. The objective of the present study is to assess the influence of this process on facial expression recognition abilities in PD.

Methods: We observe 51 PD patients and 51 healthy controls in two inhibition tasks based on the Stroop paradigm. We design an "emotional Stroop" task in which stimuli consisted of showing an emotion facial expression together with a different emotional category label superimposed on it. So, we compare the performance of both groups in the "emotional Stroop" and in the original color-name Stroop test.

Results: Both groups showed a higher performance in the color-name Stroop task than in the "emotional Stroop" task. However, PD group performed worse than healthy controls in the "emotional Stroop" task but not in the color-name Stroop task. This set of results points to that facial expression recognition problem may not be attributable to a widespread impairment in inhibition ability. Thus, emotional recognition and attention difficulties, when they are found in PD individuals, may be due to different processes and brain mechanisms. This knowledge may contribute to the design of specific intervention programs aimed to improve social communicative abilities in PD.

P15.21

Impact of Cognitive Dysfunction in Patients with Parkinson's disease during the Execution of Gait

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Objective: The aim of this study was to compare the results obtained with the evaluation of gait in single task conditions and multiple tasks in patients with Parkinson's disease (PD) with and without cognitive impairment. **METHODS:** 20 patients with idiopathic Parkinson's disease without cognitive impairment (PDI), mean age 65.5 years (St.Dev. = 7.8) and 20 patients with idiopathic PD and cognitive impairment (CPS), with mean age of 64.5 years (St. Dev = 6.44) in stage 1, 2 and 3 of the disease according to Hoehn and Yahr classification. Patient evaluation consisted of walking for a distance of 12 meters where participants are instructed only to walk as fast as possible to a table placed at the end of 12 meters called the single-task condition (ST). And the condition of multiple-task (MT), the participants performed the same route, with other associated tasks as Task 1, walking holding a glass of water. Task 2, floor and exchanging a coin from one pocket to another. Task 3, walking and holding a tray and Task 4, floor and asked how many times particular bell was played. Participants underwent cognitive evaluation by the Mini-Mental State Examination (MMSE), Montreal Cognitive Assessment (MoCA) and Clock Test and equilibrium by BERG Balance Scale.

Results: The results showed a significant interaction between task

condition (ST and MT) and groups (DPI and DPC), which showed that, under conditions of ST, DPC has impaired performance compared to IPR, and in conditions of MT, patients with CPS are even more disadvantaged than the group of DPI.

P15.22

Age of acquisition effects during verbal fluency task performance in Parkinson's disease

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Parkinson's disease (PD) is characterized by a deficiency in dopamine, a neurotransmitter that has been shown to play a neuromodulatory role in executive function and cognitive control processes. Verbal associative fluency is a task that requires working memory and flexible access to the lexical-semantic knowledge system under time constraints, and hence may be sensitive to dopamine level. Specifically, reduction in dopamine may be associated with a more limited search of long-term knowledge.

Objective: The aim of this study was to investigate the frequency and age of acquisition (AOA) of exemplars produced during verbal fluency tasks in PD patients and matched controls. AOA has been shown to potentially confound frequency effects and may better represent the organization of this system.

Methods: We compared the frequency and AOA of exemplars produced during verbal fluency tasks by two groups of individuals with PD differing in side of motor symptom onset (PD-Right and PD-Left) to a control group matched on age, education, handedness, and Mini Mental Status Exam scores. PD individuals were tested in an off medication state.

Results: A nonsignificant trend was observed for the PD-Right motor onset group to produce a range of exemplars with greater frequency during a semantic fluency trial ($p = .105$). Both PD-Right and PD-Left groups produced a range of exemplars with significantly earlier AOA in comparison to controls ($p = .016$). Hence, PD individuals with dopamine loss may have reduced access to the lexical-semantic knowledge system and limited to earlier acquired words. Further studies are underway to determine if this alteration applies to other domains of knowledge and can be modified by dopamine dose.

CLINICAL SCIENCES: SLEEP DISORDERS/ FATIGUE

P16.01

The use of actigraphy in clinical practice for the assessment of sleep disorders in Parkinson's Disease Dementia

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Objective: Dementia in Parkinson's disease (PDD) and Lewy Body Dementia (LBD) are commonly associated with sleep disturbances, including REM sleep behaviour disorder, which have a significant negative impact on quality of life. Sleep monitoring using polysomnography is poorly tolerated in patients with dementia. An alternative is the use of actigraphy. Sleep wake patterns are

estimated from periods of activity and inactivity and provides statistics of sleep quality. Actigraphy has previously been used in Parkinson's disease to quantify bradykinesia and assess sleep disorders but not specifically in those with dementia.

Methods: 5 patients attending a Consultant Psychiatry Outpatient Clinic in Berkshire, England with PDD OR LBD experiencing sleep difficulties were actigraphed. The patients were monitored with the Respirationics Actiwatch 2 device for 7 days. Sleepiness and quality of life scales and sleep diaries were recorded.

Results: The data analysis highlighted the sleep problems experienced by the patients.

Pt No	Total time in bed	Sleep duration	Number of psychotropic medications	Sleep efficiency (%)	Differential diagnosis
1	11:06:20	6:38:30	4+3	60.40	Free running sleep pattern (non – 24 hr sleep-wake)
2	11:33:23	7:27:58	2+1	63.02	Lewy Body Dementia + REM behaviour disorder
3	14:19:35	12:30:25	3+0	87.27	Lewy Body Dementia + Hypersomnia/ somnolence
4	14:23:37	12:37:08	2+3	88.60	Parkinson Disease dementia + Hypersomnia
5	8:33:11	7:48:58	2+1	91.43	Parkinsons Disease dementia + normal sleep pattern

Behavioural and medical management was offered to patients after analysis to improve their sleep patterns and quality of life. In patient 1, sleep efficiency improved by almost 10% on follow up.

Actigraphy appears to be a well-tolerated, low cost, non-invasive tool for assessing and monitoring of sleep in patients with dementia. Further research to assess its utility and predictive value is needed to elucidate whether this technique can be used in everyday clinical practice.

P16.02

REM sleep behavior disorder in Parkinson Disease: Association with abnormal ocular motor findings

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Objective: REM sleep behavior disorder (RBD) is related with brainstem pathology. We examined whether patients with RBD have abnormal ocular movements suggesting brainstem or cerebellar dysfunction in Parkinson's disease (PD).

Methods: Total 202 patients were included in this study. Ocular movements were examined by video-oculography (VOG).

Results: 116 (57.4%) of the 202 patients have clinically probable RBD, and 32 (27.6%) of the 116 with clinically probable RBD patients had abnormal VOG findings suggesting brainstem or cerebellar dysfunction; whereas 86 of the 202 patients did not have clinically probable RBD, and only 8 (9.3%) of 86 patients had abnormal VOG findings suggesting brainstem or cerebellar dysfunction. ($P = .001$). This study suggests that the presences of RBD are associated with more severe brainstem pathology in PD.

P16.03

High intensity exercise improves skeletal muscle mitochondrial function corresponding with reduced fatigability in Parkinson's disease

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Objective: Parkinson's disease (PD) is a debilitating, neurodegenerative disease that manifests as disrupted motor behavior (bradykinesia, tremor, postural instability, rigidity) which ultimately reduces physical activity and weight-bearing ambulation. Deconditioning as a result of PD often leads to weakness, low muscle power, and fatigability. We hypothesized that a high-intensity exercise training prescription which simultaneously challenges strength, power, balance, and endurance would improve muscle function and fatigability in PD patients.

Methods: Participants ($n=12$, 65 ± 6 y, Hoehn & Yahr 2-3) exercised 3 d/wk x 16 wk. Fatigue was assessed in three domains (patient perception, cardiorespiratory fatigue, and neuromuscular fatigue) and skeletal muscle biopsies were analyzed for changes in muscle fiber size, type distribution (I, IIa, IIx), and mitochondrial function.

Results: Improvements were noted in the Fatigue Severity Scale, UPDRS motor score, voluntary strength (57%), and power (49%) ($p < 0.05$). Muscle fiber size (type I: 14%; type II: 36%) and mitochondrial complex I activity (48%) increased ($p < 0.05$), and fiber type distribution shifted toward the more oxidative, fatigue-resistant type IIa phenotype (IIa from 39% to 55%; IIx from 12% to 2% of total myofibers). In conclusion, PD patients are capable of, and responsive to, high-intensity exercise training with improvements in skeletal muscle phenotype, functionality, and fatigability.

P16.04

Treatment of obstructive sleep apnea with continuous positive airway pressure improves non-motor symptoms in Parkinson's disease patients

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Rationale: We have previously shown that Parkinson's disease (PD) patients with obstructive sleep apnea (OSA) have more non-motor symptoms (NMS) than those without OSA. We hypothesize that OSA treatment with continuous positive airway pressure (CPAP) can improve NMS in PD.

Methods: PD patients without known OSA underwent overnight diagnostic polysomnography. OSA was defined as an apnea-hypopnea index (AHI) ≥ 15 /h. PD was assessed using the Movement Disorder Society Unified Parkinson's Disease Rating Scale (MDS-UPDRS). NMS were assessed using: Montreal Cognitive Assessment (MoCA); Epworth Sleepiness Scale (ESS); Fatigue Severity Scale (FSS); Apathy Scale; Beck Depression Inventory (BDI); and Parkinson's Disease Sleep Scale (PDSS). Patients with OSA were offered CPAP. All patients were reassessed at six months. Linear regression was used to assess change in NMS, comparing the three groups, non-OSA; CPAP-treated OSA (OSA-Tx) and untreated OSA, adjusting for any change in levodopa equivalent dose (LED).

Results: We studied 28 PD patients (60.7% male), mean age 63.0, SD 11.3 years, and motor MDS-UPDRS 21.5, SD 12.3. Sixteen (57.1%) patients had OSA (AHI 21.4/h, SD 18.5/h). Ten accepted CPAP; they had a similar mean AHI to those declining CPAP.

At 6 months, adjusting for change in LED, the following variables improved in the OSA-Tx group, significantly more than in the non-OSA group: Total UPDRS ($p=0.008$); Part 1 (NMS)UPDRS ($p=0.004$); Apathy Scale ($p=0.009$); MoCA ($p=0.048$); ESS ($p=0.02$) and PDSS ($p=0.01$). Motor UPDRS, FSS and BDI did not show significant change. The change in MoCA remained significant after adjusting for ESS ($p=0.01$).

For OSA-Tx patients, the MoCA at 6 months, improved by a mean of 1.6, SD 1.9 versus baseline ($p=0.043$, adjusted for change in LED).

Conclusions: Our preliminary results suggest that, in PD patients, OSA treatment by CPAP can result in improved NMS including cognitive dysfunction.

P16.05

Focus group and quantitative assessment of sleep and fatigue in Patients with Parkinson's disease

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Objective: Focus group and survey data were collected from PD patients to assess sleep problems, beliefs about sleep, strategies used to help initiate and maintain sleep, as well as common sleep disruptions. The purpose of these focus groups was to inform a Cognitive Behavior Therapy for Insomnia (CBT-I) intervention that will be modified for use in a PD-population.

Methods: Participants ($N=25$) completed the Parkinson's Disease Sleep Scale (PDSS), SCOPA-Sleep (SCOPA), Dysfunctional Beliefs and Attitudes About Sleep Scale (DBAS-16), and researcher generated instrument that assessed current sleep habits. In the focus groups, participants discussed strategies used to initiate sleep and maintain energy during the day, problems that disrupt sleep, and general interest in participating in a CBT-I intervention.

Results: Participants endorsed sleep apnea (16%), restless leg syndrome (16%), REM sleep behavior disorder (12%) and insomnia (4%). More than one third reported clinically impaired scores on the PDSS (40%), SCOPA-NS, (44%), and SCOPA-DS (40%). Over half (56%) reported that these problems interfered with their daily functioning, and the majority (84%) reported worry/distress about their current sleep problems. Participants reported a high degree of

dysfunctional beliefs about sleep, with 76% endorsing sleep cognitions that may perpetuate insomnia. Frequently endorsed strategies for initiating sleep included consistent sleep schedule (91%), physical exercise (73.9%), sleep medications (69.9%) and napping (69.6%). Sleep disruptions were attributed to needing to use the restroom (80%) and worry (60%). Physical exercise, activity pacing and naps were frequent strategies for maintaining energy during the day. Over half of the participants indicated moderate to high levels of interest in participating in a CBT-I intervention. Findings are consistent with sleep problems reported in the PD literature and suggest that a CBT-I focused intervention may target dysfunctional cognitions and improve sleep habits among PD patients.

P16.06

What influence most on the quality of sleep in Parkinson's disease patients?

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Introduction: Sleep disturbances are one of the most common nonmotor symptoms of Parkinson Disease (PD) and its prevalence vary from 60-98%.

Objective: To investigate incidence of sleep disturbances in patients with idiopathic PD and to evaluate what kind of sleep disturbance influence most on the quality of the sleep.

Patients and methods: We analysed 104 PD patients treated on the University Hospital Centre Osijek and General Hospital Nasice. All patients were asked if have sleep disturbance or not. To evaluate sleep disturbances we used Parkinson Disease Sleep Scale (PDSS).

Results: sleep disturbance reported 58.7% patients, while 41.3% had not sleep disturbance. In group of patients reported not to have sleep disturbance total PDSS score was 104.4, while in group that have disturbance score was 87.7. We found statistically significant difference between two groups of patients on this items: nocturnal awakening ($t= -2,869$; $p<0,005$), restlessness ($t= 1,941$; $p<0,01$), distressing dreams ($t= -2,947$; $p<0,005$), distressing hallucinations ($t= -1,956$; $p<0,05$), tremor on waking ($t= -2,135$; $p<0,05$) and morning tiredness ($t= -2,494$; $p<0,01$).

Conclusion: Among sleep disturbances nocturnal awakening, restlessness, distressing dreams, distressing hallucinations, tremor on waking and morning tiredness influence most on the quality of sleep in patients with Parkinson Disease.

P16.07

¹H magnetic resonance spectroscopy study of auditory cortex metabolism in obstructive sleep apnea syndrome combined nerve deafness

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Objective: Obstructive sleep apnea hypopnea syndrome (OSAHS) is a sleep breathing disorders in patients with idiopathic Parkinson's disease and it correlates well with the severity of the disease. The patients with OSAHS have a higher incidence rate of nerve deafness, but the underlying mechanism remains to be elucidated.

Recently, studies showed abnormal cerebral metabolism in patients with OSAHS. Therefore we have investigated the characteristic changes of metabolic products in the auditory cortex (transverse temporal gyrus) of OSAHS patients with nerve deafness using ^1H magnetic resonance spectroscopy (^1H -MRS) to discover the prognostic indicator of nerve deafness in OSAHS.

Methods: The electric response audiometry was performed in 47 patients with OSAHS, 21 patients with nerve deafness and 15 healthy control subjects, the patients were classified into three groups: OSAHS with no deafness, OSAHS with deafness, and the control group. Cerebral metabolism was studied by assessing the relative contents of Nitro-acetyl aspartate (NAA) and choline (Cho) and ratio of NAA to Cho in the auditory cortex separately in these groups. We also analyzed the changes between the abnormal and contralateral normal auditory cortex in the group with unilateral nerve deafness.

Results: Significantly lower values of NAA/Cho ratio were found in the auditory cortex of OSAHS patients with deafness compared with 15 age-matched control subjects ($P < 0.05$) and OSAHS without deafness ($P < 0.05$). Auditory cortical NAA and NAA/Cho ratio in OSAHS with unilateral nerve deafness were significantly lower compared with normal control ($P < 0.05$ and $P < 0.01$, respectively), but there is no significant difference between the abnormal and contralateral normal auditory cortex. Based on these data, NAA/Cho and NAA may be the early warning marker of nerve deafness in OSAHS.

CLINICAL SCIENCES: DIAGNOSIS (DIFFERENTIAL, ACCURACY)

P17.01

Clinical correlates of vascular parkinsonism

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Objective: To identify the demographic and clinical correlates of VP in comparison with PD.

Background: Vascular parkinsonism (VP) is the second most common form of non degenerative parkinsonism. In VP, signs and symptoms include disabling features such as early axial signs and minimally responsive to dopaminergic therapy. Also, the diagnosis is not straightforward, frequently misinterpreted for other forms, such as rigid akinetic PD and PSP.

Methods: Diagnosis was based on the presence of lower body predominant parkinsonism, pyramidal tract signs, imaging evidence of multiple vascular lesions, and at least two vascular risk factors. PD was diagnosed using the Queen Square Brain Bank criteria. The scores utilized were UPDRS, to define motor severity; Hoehn & Yahr; DSM-IVR to access dementia. Psychosis was clinically diagnosed. REM sleep behavior disorder was defined by the occurrence of behavioral symptoms during sleep.

Results: A total of 60 patients with VP and 1142 with PD were included. Although males were more prevalent among those with VP, differences were not significant ($p: 0.27$). On the other hand, VP patients were significantly older, had shorter disease duration, had more symmetric signs, worse H&Y scores, were more likely to present with PIGD and only rarely presented with tremor (all variables with $p < 0.0001$). Psychosis was equally common in both groups. Dementia was significantly more common in the VP group and RBD was more common among PD patients.

Conclusions: VP patients present a clinical picture that is significantly distinct from PD. The presence of risk factors, a consistent motor profile, lower prevalence of RBD, and higher frequency of dementia despite shorter disease duration, may help distinguishing both disorders.

P17.02

An investigation of the relationship between clinically-assessed and self-reported measures of side affected in patients with Parkinson's disease

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Objective: Both clinically-assessed and self-reported measures have been used to determine the side that is most affected by PD. However, it is unclear if clinicians' assessment of side affected is representative of the patients' own perceptions. Therefore, the objective was to investigate the relationship between self-reported and clinically-assessed measures of side affected. We also sought to uncover the strongest clinical predictor of self-reported side affected.

Methods: Participants consisted of 254 (66% male) patients with PD from the Sun Life Financial Movement Disorders Research & Rehabilitation Centre (MDRC). Data was collected during participants' initial assessments. Participants completed a self-report questionnaire assessing demographics and side affected (right vs. left). Part III of the Unified Parkinson's Disease Rating Scale (UPDRS) was employed as the clinically-assessed measure of PD. Scores were calculated for total right and left: upper limb severity, lower limb severity, upper limb tremor, lower limb tremor, upper limb voluntary movement, and lower limb voluntary movement.

Results: A Pearson chi-square between self-reported and clinically-assessed side affected was significant ($\chi^2(1) = 71.39, p < .001$), indicating an agreement between patient and clinician. A multiple logistic regression was also performed, with self-reported side affected as the dependent variable, and total limb severity, tremor score, and voluntary movement score entered as covariates. The results indicated that only total right upper limb severity predicted self-reported side affected ($\beta = -.675, p = .05$). Therefore, participants with higher right upper limb severity were more likely to self-report as right side affected.

Conclusion: Taken together, these results suggest that clinicians' ratings of side affected are consistent with patients' own perceptions of side affected; however, when individual predictors were examined, the UPDRS could not significantly predict patients' self-reported side affected and thus may not be fully reflective of patients' own experiences with PD.

P17.03

Neuropsychological testing for the detection of mild cognitive impairment in Parkinson's disease

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Objective: Prevalence of mild cognitive impairment (MCI) in Parkinson's disease (PD) is variable (range 20-58%) likely due to methodological differences in classification criteria and lack of consensus about neuropsychological tests used for cognitive profiling. Our previous work identified most suitable tests for

diagnosis of MCI in PD and defined appropriate cut-off scores. In this study we expanded previous results using a wider neuropsychological battery in a new larger PD cohort to verify statistical validity of those tests and their cut-off scores.

Methods: One-hundred-five PD patients and 20 healthy subjects (HC) performed an extensive neuropsychological evaluation. PD patients were categorized as PD-CNT (PD without cognitive impairment, 35%), PD-MCI (47%) and PDD (PD with dementia, 17%) based on established criteria. Univariate ANOVA and Receiver Operating Characteristic (ROC) curves were adopted.

Results: We found that MoCA, Trail Making test, Digit Ordering test, similarities, semantic fluency task, prose memory test immediate and delayed recall, free clock drawing test, Boston naming test and incomplete letters test reached significant screening and diagnostic validity in predicting PD-MCI (AUC 0.721-0.825) with cut-off scores calculated by ROC analyses lying within normal range for normative data.

Conclusion: These data corroborate and expand our previous results, confirming that a wide spectrum of cognitive tests can detect cognitive abnormalities in PD without frank dementia (verbal memory, attention/executive, visual-perceptive and language impairments). The use of valid cut-off score can ameliorate the accuracy of MCI diagnosis in PD.

P17.04

Development and implementation of a next generation sequencing platform for hereditary Parkinson disease

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Objective: The purpose of this effort was to develop a comprehensive and flexible next generation sequencing platform to diagnose Mendelian forms of Parkinson disease and identify hereditary risk factors for Parkinson disease in a clinical setting.

Methods: After a thorough literature review, an Agilent SureSelect sequence capture was designed to enrich for genes associated with Mendelian forms of Parkinson disease (e.g. *SNCA* and *PARK2*), autosomal dominant risk factors for Parkinson disease (e.g. *GBA* and *LRKK2*), and Mendelian forms of atypical Parkinsonism (e.g. *MAPT* and *GRN*). The efficacy of the sequence capture was evaluated in a small technical validation experiment. Baits were subsequently redesigned to supplement coverage in low coverage regions and Sanger sequencing primers were designed to analyze exons that did not achieve desired coverage levels. A larger clinical validation involving 20 samples was carried out to evaluate the ability of this assay to identify a variety of mutations. Five patients with early onset and/or familial Parkinsonism were analyzed using these methods.

Results: A total of 19 candidate genes, comprised of 321 distinct exons, were identified in the literature review. Greater than 20x coverage was achieved at every base for 316/321 (98.5%) of exons. Sanger sequencing primers were designed for the remaining 5 exons. In the initial 5 patients analyzed, an average of 60 variants per sample were identified. The majority of these variants were interpreted as benign based upon minor allele frequency and/or published data. In addition to one pathogenic *SNCA* mutation, novel variants of uncertain clinical significance were identified, highlighting the need for family studies for accurate interpretation. Targeted next generation sequencing is an effective strategy for comprehensive analysis of known PD genes in patients with suspected hereditary Parkinsonism.

P17.05

Kinematic and kinetic continuous measurement of hand tremor to discriminate Parkinson's disease: a pilot single-case study

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Objective: Tremor is one of the cardinal motor symptoms of Parkinson's disease (PD). Although the quantification of tremors is the object of study for several researchers, a standard method does not exist yet. In this pilot study, we aimed to assess if continuous measurement of kinematic and kinetic characteristics of the tremorous hand could have discriminative value for PD.

Methods: The kinematic (movement analysis) and kinetic (force analysis) characteristics of tremor was measured in the dominant (DH) and non-dominant (nDH) hand of one PD patient and also a healthy individual who was blind to tremor characteristics of PD and was asked to simulate tremor (SH). In kinematic assessment, postural tremor of the index finger was measured by sensor displacement and using four cameras. Data were recorded for two continuous minutes and values were traced in each second (overall 120 seconds for each hand) through projection in three dimensions, X-, Y- and Z-axis. Finally, these continuous measurements were analyzed using orthogonal partial least square (OPLS) method and principle component analysis (PCA).

Results: Kinematic measurements of X-axis (velocity and acceleration) was shown to be the most fitted variables in the PCA model to discriminate DH from the SH ($R^2 > 90\%$ and $Q^2 > 70\%$). Based on the OPLS data, muscle force (Mean=0.42, SE=0.028) and velocity in the Y-axis (Mean=0.37, SE=0.029) were the most strong variables for discriminating DH from the nDH.

Conclusions: These preliminary findings showed that kinematic and kinetic analysis of hand tremor could help not only to distinguish PD patient from control subject, but also the dominant hand from the non-dominant one. It seems that continuous measurement data such as self-quantified symptoms assessment by smart-phone applications could provide worthy information. This pilot case-study should be followed by larger studies to introduce some newer aspects of personalized healthcare approaches in PD.

P17.06

DaTscan™ for prediction of clinical diagnosis of early Parkinsonian syndromes: Sensitivity, specificity, positive and negative predictive values, and diagnostic accuracy in clinically uncertain cases

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Objective: To assess the diagnostic efficacy data from clinical trial Kupsch et al, 2012 (data not previously published) conducted using DaTscan™ ([¹²³I]loflupane Injection).

Methods: Study imaging group (n=92) was used to assess the diagnostic accuracy of DaTscan™ in subjects with early, clinically uncertain Parkinsonian syndromes (PS) after 1 year follow-up. The reference standard was final clinical diagnosis 1 year after imaging, and it was compared to baseline clinical diagnosis and to baseline imaging diagnosis. Visual assessment of DaTscan™ images was performed by local nuclear medicine physicians. Acquisition of SPECT data with DaTscan™ and their reconstruction were performed using a standardized imaging protocol.

Results: The sensitivity of clinical diagnoses at baseline was 92% when compared to final clinical diagnosis at 1 year, but the specificity was only 52.4%. For the comparison of baseline DaTscan™ images to the clinical diagnosis at 1 year, the sensitivity was 93.9%; specificity was 95.4% (p=0.0005 as compared to baseline clinical diagnosis). The PPV, NPV and diagnostic accuracy for baseline clinical diagnosis or baseline imaging diagnosis vs. final clinical diagnosis at 1 year were respectively: 69.7% vs. 95.8% (p<0.0001), 84.6% vs. 93.2%, and 73.9% vs. 94.6%. Performance of DaTscan™ compares favorably in this study to the performance of clinical diagnosis relative to final clinical diagnosis. Study Supported by GE Healthcare.

P17.07

Posturography in differential diagnosis of patients with vascular Parkinsonism

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Objective: Postural dysfunction is one of the major features of vascular Parkinsonism. This study aimed to quantitatively evaluate balance disturbances by means of computerized dynamic posturography(CDP) in patients with vascular Parkinsonism in comparison with Parkinson's disease patients and healthy people

Methods: Thirty-four patients (18 M, 16 F) with a mean age of 73(range 51-79) with vascular parkinsonism were included. Eleven of them were qualified as patients with leukoaraiosis and 23 others were identified as basal ganglia microangiopathy. Patients with vascular parkinsonism (VP) and Parkinson's disease patients with nigral hypotrophy were tested regarding motor function, balance and cognition. CDP, EquiTest (NeuroCom International, Clackamas, OR), was performed both groups of patients and age-matched healthy individuals (HI).

Results: The 35 patients had poorer balance measured with the Sensory Organizing Test (SOT) score in every condition (p=0.01 in SOT 1 and p<0.001 in SOT 2-6) compared to the HI. The greatest difference was in test conditions measuring mainly vestibular function, where loss of balance (LOB) was frequent. There was an increase in the weighted composite SOT score (p<0.05) but no significant change in any of the SOT conditions after Madopar treatment. The sway range was significantly greater in VP in comparison to the control group. CDP showed that the VP patients had a poorer balance than the HI and Parkinson's disease patients. The greatest difference was in SOT 5-6, indicating that the postural disturbance is of primarily central vestibular origin. There was a slight improvement of balance after Madopar therapy.

P17.08

Targeted next-generation sequencing for Parkinson's disease

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Objective: Clinical diagnosis of familial and sporadic parkinsonism can be challenging, with several forms being ascribed to a monogenic etiology. We have developed a cost-effective, targeted assay to simultaneously sequence 172 genes genetically linked/associated with parkinsonism.

Methods: Patients included familial and sporadic parkinsonism, mean age-of-onset 61.8±11.5SD years (range=20-83) of European descent (n=200)². Additional features consisted of dementia (n=6), dysautonomia (n=30), dystonia (n=5) and gaze palsy (n=36); autopsy confirmation (n=76) included alpha-synucleinopathy, tauopathy and nigral neuronal loss. Genes implicated in Parkinson's disease and related neurodegenerative conditions (n=172) were selected from prior linkage and association studies. Target-DNA-capture and next-generation sequencing was executed for 96 barcoded-samples in parallel, on a SOLiD 5500xl™ sequencer. Read alignment to the hg19 human reference sequence and annotation was performed using LifeScope v2.5.1™. Frequency estimates were made using proprietary and public genome databases (NHLBI's Exome Sequencing Project, 1000 Genomes Project). Functional predictions were retrieved with ANNOVAR. Data were filtered into rare known/novel mutations (<1% population frequency), intermediate variants (1-5%) and frequent polymorphisms (>5%). Mutations were confirmed by Sanger sequencing. Disease association analyses were implemented using PLINK and R™.

Results: Re-sequencing was successful for >94% of target exons (average 118 read-depth/exon). Known mutations observed included LRRK2 p.G2019S, DNAJC13 p.N855S, SOD1 p.D90A, and PARK2 p.R275W. Of 293 mutations identified, 38 were novel. The distribution of mutations clustered within specific loci, and differed between patients and control subjects. Targeted next-generation sequencing accelerates discovery of known and novel variants, and may highlight specific molecular pathways in disease pathogenesis. The significance of findings is being assessed in consecutive replication series. For research participants, the approach provides a fast and affordable option for diagnostic screening, without incidental findings unrelated to neurodegeneration. Specific results can inform neurologists and may facilitate a differential diagnosis for their patients.

³see abstract by Silva *et al.*

P17.09

Oro-digital synkinesia in corticobasal degeneration

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Objective: Dyskinesias are common in Parkinson's disease (PD) and atypical Parkinson disorders. Facial-limb synkinesias are rare. We report two patients with atypical Parkinson disorder in whom movements of fingers and hands activated distinct oral movements.

Methods: Patient 1 - An 80 year -old male developed "stiffness" of the left upper and lower limbs over the past 4 years . Examination

demonstrated normal mentation, cranial nerve and cerebellar assessments. There was marked increased tone in the left upper and lower limbs with dystonic left clinched fist, left upper limb apraxia, alien hand and stimulus sensitive myoclonus. Opening and closing of the left hand each time corresponded with mouth opening and closure (Videotape1). This oral digital synkinesia did not habituate and continued over three years of follow up.

Patient 2- A 55 year old male complained from slowing of movements, "stiffness" of the limbs and right hand tremor for the 12 months. Examination showed moderate rigidity and hypokinesia bilaterally; more on the right side and a resting tremor on the right. The right upper limb was apraxic with intermittent action myoclonus. Opening and closing of hands opened the mouth simultaneously.

Results: Magnetic resonance imaging showed diffuse cortical atrophy in both patients and additional mild diffuse microangiopathy in the second patient. Both patients failed levodopa treatment with doses up to 25/100 five times daily.

1- Two patients met the clinical criteria for diagnosis probable corticobasal degeneration presented who demonstrated prominent oral-digital synkinesia in examination.

2- Oral -digital synkinesia did not habituate and once occurred persisted over time.

3- Oral -facial synkinesia in CBD may be caused by activation of supplementary motor cortex as reported for ipsilateral hand-digital synkinesia in PD (Salardini et al *Neurosci Lett* 2012, 523:135).

4- An fMRI study is scheduled for the second patient.

P17.10

Auto-segmentation and evaluation of daily mobility tasks: whole-body kinematic assessment in Parkinson patients and elderly adults

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Introduction: Aging and Parkinson disease (PD) are major causes of restriction in daily mobility. Unconstrained ambulation and its change with age, disease, or medical intervention are difficult to assess. Natural mobility is complex and understanding it requires segmentation into simpler and consistent sub-movements. Sub-movements such as sit, stand, walk, turn can occur as primary movements or have added secondary components such as carrying an object and passing obstacles. In this study, using a full-body network of inertial motion units (IMUs) and multiple variants of a Timed Up and Go (TUG) task a robust segmentation algorithm for segmentation into primary and secondary movements has been developed.

Methods: 11 PD (65±9 years) and 19 healthy (70±9 years) participants performed 5m TUG test at their normal speed along with variants of TUG: 10m normal and fast speeds, with obstacles, L-path, carrying a physical load, and with cognitive loads. TUG-5m trials were used to adjust the parameters for segmentation in both groups. Auto- and visual segmentation performance is compared. Key parameters in performance of each mobility task, such as stability in transitional task, symmetry in straight walking (including in arm swing), and degradation indices with performance of the secondary tasks will be presented.

Results: Optimal parameters for detecting some transitions were different between PD and healthy. Performance of previously proposed algorithms with minimal sensors was improved with multiple IMUs. Auto-segmentation algorithm was able to correctly detect 88-100% of sitting, 89-97% of sit-to-stand, 94-100% of turns,

68-96% of turn-to-sit, 68-94% of stand-to-sit, and 77-97% of straight walking tasks.

Conclusion: This study showed that using a full-body network of IMUs, mobility detection algorithms optimized for a combination of simple tasks could reasonably detect variation of those tasks. This study could eventually help identify the best location of sensors for optimal detection of changes in movement performance.

P17.11

Late-onset hepatolenticular degeneration presenting as Parkinson's disease

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Introduction: Wilson disease (WD) is an autosomal recessive disorder of copper biliary excretion caused by an impaired function of a metal-transporting P-type ATPase (ATP7B) encoded by WD gene. WD is one of the very few chronic neurological diseases for which specific and effective treatment is available. The clinical symptoms and age at onset of WD are highly variable but it usually develop between 3 and 40 years of age and include signs of liver and/or neurological (movement disorders) disease. Unfortunately, a misdiagnosis appears early in the course of the disease and late-onset WD is a frequently overlooked condition.

Objective: To report late-onset WD in 63 year-old man with symptoms of Parkinson's disease (PD).

Patient and Methods: At the age of 60 male patient develop resting tremor of both hands with postural instability. He had slightly abnormal liver function. Levodopa treatment was introduced with mild transient improvement. After 3 years he was referred to Movement disorders centre as idiopathic PD for therapy titration. In addition to tremor, rigidity, bradykinesia and postural instability dysarthria was observed. On examination Kayser-Fleischer ring was demonstrated as well as low ceruloplasmin concentration and serum copper level. Hepatic copper content in liver biopsy tissue was increased (350 microg/g dry weight). Magnetic resonance imaging was unspecific (cortical atrophy). D-penicillamine therapy was introduced (total 600 mg daily).

Results and Discussion: D-penicillamine therapy caused transient exacerbation of tremor. But after 3 months significant clinical improvement was observed and levodopa dose could be reduced. WD presents with a variety of neurological signs and late-onset WD is a frequently overlooked condition. Since early treatment may reverse even long-lasting symptom, WD should be considered also in older patients with symptoms of PD.

P17.12

MIBG scintigraphy and a predictive role in clinically uncertain Parkinsonism

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Objective: Visualisation of the heart using MIBG scintigraphy is an useful method to ascertain Parkinsonism from idiopathic Parkinson's disease (IPD) and is an approved technology in some countries such as Japan but not in the UK. In this single centre study, we describe an UK based experience in order to analyse the predictive

significance of MIBG scintigraphy for the diagnosis of IPD versus Parkinsonism in cases with clinically uncertain Parkinsonism (CUP).

Methods: Using a retrospective single centre analysis/audit we studied the clinical diagnoses of 41 patients (mean age 72±11.28 years) and the related static MIBG images which were classified to 3 types (1= no visualisation of the heart, 2= borderline, 3= clear visualisation of the heart). We then sought of correlation between these types and the clinical diagnoses at a variable clinically determined follow up (FU) period.

Results: Data are shown in Table 1. 60% of CUP cases with type 1 MIBG scans had confirmed diagnosis of IPD at FU while type 3 MIBG scans correlated with a 45.8% cases proving to have Parkinsonism (MSA) and another 41.7% continuing a diagnosis of CUP but not IPD. Majority of the type 2 MIBG scans also had a final diagnosis of atypical Parkinsonian syndrome. 29 of the patients underwent a DAT scan which confirmed striatal dopamine derivation in 75.9% of all patients. Except 1 all patients underwent MIBI scans.

Table 1 Prevalences of type1-3 MIBG scans and clinical diagnosis in our cohort

Type	0 (non-visualisation of the heart)	1 (borderline)	2 (clear visualisation of the heart)
Idiopathic Parkinson syndrome	6 (60%)	2 (28.57%)	3 (12.5%)
Atypical Parkinson syndrome	3 (30%)	3 (42.86%)	11 (45.83%)
Unknown	1 (10%)	2 (28.57%)	10 (41.67%)

In conclusion to our knowledge this is the first study in the UK analysing the effect of MIBG in the differential diagnosis of IPD and CUP. MIBG cardiac scans may play an useful although surrogate role in the final diagnosis of CUP cases.

Acknowledgement: National Institute for Health Research (NIHR) Mental Health Biomedical Research Centre and Dementia Unit at South London and Maudsley NHS Foundation Trust and [Institute of Psychiatry] King's College London

CLINICAL SCIENCES: CO-MORBIDITIES

P18.01

Post-stroke Parkinsonism

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Objective: Parkinsonism is one of the movement disorders that may appear after stroke and complicate the course of the disease.

Aim: To analyse the incidence, anatomical correlation, temporal relationship and associated risk factors of Parkinsonism after stroke. **Material and methods:** We made a prospective analysis of 86 patients with stroke during a period of 1 year. We analysed the CT findings, neurological status and risk factors.

Results: Three patients (3.4%) developed Parkinsonism after median time of 125 days after stroke. All were male, median age 75 years. Two had ischaemic stroke, one was with haemorrhagic stroke. These strokes were in the right hemisphere (2 in the basal ganglia, 1 in the thalamus). Neurological status revealed motor dysfunction and sensory loss, respectively. No statistical difference

was found in the associated risk factors among the groups with and without Parkinsonism ($p>0.05$), with hypertension being the commonest risk factor.

P18.02

Managing Parkinson's disease related co-morbidities at a community hospital outpatient geriatrics clinic for Parkinson's

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Introduction: Ninety percent of patients with Parkinson's disease (PD) are over 60 years of age. In addition to mobility symptoms, patients experience PD related co-morbidities which are often undiagnosed and therefore untreated. A Geriatrics Clinic for Parkinson's with a geriatrics PD specialist - pharmacist team was established under a community hospital's ambulatory service. It provides comprehensive geriatrics assessment and management to elderly patients with PD referred by family physicians, neurologists or discharged from hospital.

Objectives: This study aimed to determine (1) whether comprehensive geriatrics assessment could identify previously unrecognized PD related co-morbidities (2) types and prevalence of co-morbidities in a community-based population of elderly patients with PD.

Method: A prospective observational study was conducted from January 2008 to December 2009. All new patients seen at the clinic during this period were included. Each patient was assessed through a comprehensive geriatrics assessment, including a review of motor, neuropsychiatric and autonomic symptoms. Standardized non-motor symptoms questionnaire and standard validated assessment scales were used.

Results: One hundred and forty patients with the average age of 76 were seen in the clinic during study period. Comprehensive assessment in the clinic identified 379 cases of previously unrecognized co-morbid conditions. These include 80 cases of dementia, 74 of anxiety/depression, 64 of constipation, 54 of osteoporosis, 45 of orthostatic hypotension, 39 of pain and 23 of acid reflux.

Conclusion: Comprehensive geriatrics assessment in this specialized clinic has successfully identified many cases of PD related co-morbidities in a community-dwelling elderly population with PD.

P18.03

Comorbidity in idiopathic Parkinson's disease

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Aim: Comorbidity is common in the elderly and contributes to the complexity of this population subgroup. Our goal is to evaluate the prevalence and contribution of comorbidities on functional decline, disability and cognitive performance in a population of Parkinson's disease (PD) patients.

Patients and Methods: Data on 107 patients with PD (48 men/59 women) followed-up in a neurologic consultation in Salamanca, Spain, were obtained. The mean age of PD patients was 77.2 ± 8.3 years (mean duration of PD 10.7 ± 4.8 years) and Hoehn & Yahr Staging median: 3[1-5]. Comorbidity data included six common conditions (heart/circulation problems, diabetes, arthritis, cancer, respiratory diseases and other neurologic diseases). Also we performed comorbidity (Charlson Index), motor (UPDRS part III),

functional (Hoehn and Yahr), activities of daily living (Schwab and England) and cognition (Mini-Mental State Examination (MMSE)) assessments.

Results: The two most reported comorbidities were heart/circulation problems (50.5%) and arthritis (37.1%), with other neurologic diseases affecting 20.6% of the sample (7.5% stroke, 5.6% essential tremor, 5.6% head injury). Diabetes was diagnosed in 18.4%, cancer in 16.3% and respiratory diseases in 15.3%. Arthritis was more prevalent in women and respiratory conditions in men. The Charlson Index of comorbidity median was 2[0-12]. A higher score in the Charlson Index was associated with an older age and akinesia-rigidity subtype as initial predominant motor sign in PD. Specific comorbidities, particularly heart/circulatory and diabetes, independently contributed to worse cognitive performance ($p=0.04$). However, comorbidity didn't affect functional decline or disability.

Conclusion: Comorbidities are very common in PD, especially heart/circulation problems and arthritis. In some PD patients, essential tremor may precede the onset of PD by several years or decades. Nevertheless, this study only provides evidence for a small detrimental influence of comorbidities on measures of cognition.

P18.04

Pulmonary dysfunction in Parkinson's disease patients attending the Lagos University Teaching Hospital, Nigeria

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Objective : To determine the prevalence and pattern of pulmonary dysfunction experienced by PD patients attending the Movement Disorders (MD) Clinic of the Lagos University Teaching Hospital (LUTH)

Methods: 43 PD attending the Movement Disorders clinic, LUTH were consecutively recruited between March 2011 and September 2012. 81 apparently healthy non-smoking age and sex-matched controls were also studied. The study population did not have any current or past history of respiratory or cardiovascular symptoms/disease capable of compromising lung function. Pulmonary function was assessed by spirometry and the following parameters obtained – forced expiratory volume in one second (FEV1), forced vital capacity (FVC), FEV1/FVC ratio and peak expiratory flow rate (PEFR). Obstructive pulmonary dysfunction was defined as FEV₁/FVC ratio less than 70% while restrictive pulmonary dysfunction was defined as FEV₁/FVC ratio equal to or greater than 70% with FVC percentage predicted below 80%.

Results: There was no significant difference regarding age and gender within the study population. Mean FEV1 was significantly lower for PD ($1.54 \pm 0.70L$) compared to controls ($1.96 \pm 0.66L$); $p = 0.001$. Mean FVC was also significantly lower for PD ($1.81 \pm 0.96L$) compared to controls ($2.22 \pm 0.85L$); $p = 0.02$. PEFR was significantly lower for PD ($4.2 \pm 2.2L/min$) than controls ($5.5 \pm 2.0L/min$); $p = 0.001$. There was no significant difference between the FEV1/FVC ratio of PD and controls ($p > 0.05$). Respiratory dysfunction was present in 37 of 43 PD (86%) and 51 of 81 controls (62.9%); $\chi^2 = 51.4$, $p = 0.00$. The pattern of respiratory dysfunction was restrictive in 89.2% (33 of the 37) PD and obstructive in 10.8% (4 of 37 PD). None of the controls had an obstructive pattern of respiratory dysfunction.

P18.05

The impact of comorbidities and concomitant medications on falling in Parkinson disease

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Objective: To assess the relationship between comorbidities and concomitant medications which are known risk factors of falling in the elderly and falling in Parkinson disease (PD). A number of systemic and neurological disorders and drug categories have been identified as risk factors for falling in an American Academy of Neurology Practice Parameter. We sought to explore the strength of these risk factors in predicting falls in PD patients.

Methods: Detailed medication regimens and 4-week diaries recording falls and near falls were collected in 335 PD subjects. Two sets of partial correlations were obtained with presence of falls as the main outcome measure: in the first set, the presence of neurological, osteoarthritis, and spinal co-morbidities were used as possible predictors, while accounting for presence of any drug risk factors, age, and disease duration; in the second set, concomitant treatment with benzodiazepines, other sedatives, tricyclics, antihistamines, and opioids were used as possible predictors, while accounting for presence of any comorbidity risk factors, age, and disease duration. Chi-square was used to test associations. Statistic significance was set at $p < .05$.

Results: 53% of subjects experienced at least one fall, 35% were on concomitant medications known to increase falls risk and 66% had comorbidities known to increase falls risk. None of the comorbidity categories showed any significant association to the main outcome. Among drug categories known to increase falls risk, only tricyclics were associated with the main outcome ($p=0.009$). Comorbidities and concomitant medications commonly associated with increased falls risk in the general population do not seem to predict falling in PD, with the only exception of tricyclic antidepressants.

CLINICAL SCIENCES: BIOMARKERS AND NEUROIMAGING

P19.01

Usefulness of (123 I)-FP-CIT SPECT (DaT Scan) in diagnosing drug-induced Parkinsonism (DIP): a retrospective study

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Objective: Objective of our study is to differentiate DIP from Neurodegenerative Parkinsonism (NDP) with the help of a DaT Scan. Differentiating DIP from NDP may be a challenge to clinicians. Patients who develop DIP may unnecessarily receive dopaminergic medication due to difficulties in making correct diagnosis. One of the factors distinguishing DIP from NDP involves discontinuation of the suspected medication in DIP should relieve the symptoms of Parkinsonism. However in clinical practice the timeframe between the drug withdrawal and resolution of the symptoms of Parkinsonism could be longer which leads to delay in the diagnosis and treatment of patient with IPD.

Method: We designed a retrospective study of 10 patients including 4 men and 6 women presented to our clinic with suspected

symptoms of DIP. All patients had a history of exposure to the drugs known to cause extrapyramidal side effects (EPS). All patients underwent detailed neurological examination and loflupane (123 I)-FP-CIT SPECT (DaT Scan).

Results: Among nine out of ten patients with suspected DIP the DaT Scan showed the pattern of tracer uptake suggesting normal dopaminergic neuronal terminal density in the striatum. However in one patient there was grade 2 loss of dopaminergic terminal density in the striatum suggestive of NDP. A negative DaT scan in nine out of ten cases correctly predicted a diagnosis of DIP and seems to exclude NDP reliably. One patient with positive DaT Scan had an underlying NDP unmasked by dopaminergic blocking drugs may be suggestive of presynaptic dopaminergic loss. These results also suggest postsynaptic dopamine blocking effect is linked to DIP. In conclusion DIP can be differentiated from NDP with the use DaT Scan and unnecessary use of dopaminergic drugs can be avoided.

DIP: Drug induced Parkinsonism

NDP: Neurodegenerative Parkinsonism

P19.02

Effect of dopamine receptor binding agents on Dopamine Transporter (DaT) scan result

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Background: DaT scans aid physicians in differentiating neurodegenerative vs non-neurodegenerative parkinsonism. Drugs that may interfere with dopamine receptor binding have been labeled as "contraindicated" with a recommendation to stop prior to scan, as they might decrease radioligand uptake and result in a false positive (abnormal) scan. However, many patients taking these contraindicated medications have psychiatric co-morbidities that make it difficult to discontinue medications without the risk of exacerbating psychiatric symptoms.

Objective: To assess the effect of contraindicated agents on DaT scans.

Method: All patients who obtained DaT scan that were ordered by movement disorders specialists at Cleveland Clinic from June 1, 2011 to October 31, 2012 were analyzed, including demographic data, medications prior to scan and the scan results. We excluded scans that were obtained for research purposes and repeat scans on the same patient.

Result: Forty one scans were excluded based on our exclusion criteria, and 175 scans were included in our analysis. 45 out of 175 patients (26%) were on "contraindicated" medications prior to the scan. Only one patient was documented to discontinue the drug prior to the scan. Dopamine receptor binding drugs that patients were taking included Citalopram, Bupropion, Buspirone, Selegiline, Rasagiline, Methylphenidate, Amphetamine, Paroxetine, Sertraline. 25 patients (53%) who were exposed to these medications had negative DaT scans and 20 patients (43%) who were on these contraindicated drugs had positive DaT scans.

Conclusion: Our data suggests that patients who were on drugs that may interfere with dopamine receptor binding can still have a negative (normal) scans. Therefore, at least in this subset of patients, the presence of contraindicated medications did not seem to interfere with the scans. More studies are needed in understanding the effect of dopamine receptors binding agents on DaT scans.

P19.03

A large Turkish Parkinson pedigree with alpha-synuclein duplication: blood expression biomarkers elucidate predictive diagnostics and pathway

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Objectives: To establish a predictive blood test for synucleinopathy.

Methods: Whole blood in PAXgene tubes from twelve presymptomatic and 2 symptomatic carriers of a SNCA duplication in a large Turkish PD family underwent expression profiling.

Results: Eight biomarkers from the vesicle fusion pathway (SNARE machinery) showed the best correlation with genotype.

Conclusions: Excess physiological function of alpha-synuclein leads to detectable significant downstream effects in blood, which may be useful in predictive diagnostics and complement existing methods to diagnose prodromal PD. Furthermore, they help to elucidate a common pathway of PD pathogenesis.

P19.04

A novel blood-brain barrier permeable PET Ligand for Parkinson's disease

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Objective: Development of blood-brain barrier (BBB) permeable biologics that specifically target alpha-synuclein (α -syn) has great clinical potential for early diagnosis, monitoring of disease progression and therapeutic efficacy of drugs in patients at risk or afflicted with Parkinson's disease (PD). We have developed a breakthrough technology, referred to as Picotechnology that unequivocally delivers diagnostic and therapeutic antibody mimics (AbMs) across the BBB to specific targets within the central nervous system (CNS). AbMs display excellent BBB penetration and pharmacokinetics, characteristics that are highly desirable for the use of antibodies as *in vivo* imaging biomarkers. Using this innovative approach, alpha-synuclein-AbM (α -syn-AbM) was generated to detect and visualize toxic α -syn aggregates either as inclusions, pre-Lewy bodies (LBs) or LBs. Our long-term objective is to develop a diagnostic imaging biomarker by utilizing α -syn-AbM as positron emission tomography (PET) ligand. In this study, the specificity and BBB permeability of α -syn-AbM was evaluated in α -syn transgenic (tg) mice.

Methods: To assess tissue specificity of α -syn-AbM *ex vivo*, brain tissue sections from α -syn tg mice and patients with PD were immunolabeled with α -syn-AbM. To determine the BBB permeability of α -syn-AbM *in vivo*, α -syn transgenic and non-transgenic mice were injected intravenously (i.v.) with a single low dosage of α -syn-AbM (1.5 mg/Kg) or a conventional monoclonal antibody against α -syn. Mouse brains were harvested 24 hours post injection and tissue sections were analyzed for the presence of antibodies in the brain by immunostaining.

Results: *Ex vivo* tissue stainings of human PD and α -syn tg mice demonstrated that α -syn-AbM binds and labels LBs and LB-like structures, respectively. The BBB permeability of α -syn-AbM was substantiated in α -syn transgenic mice that received a single low dose injection of α -syn-AbM but not the conventional mouse antibody. α -syn-AbM was shown to cross the BBB and specifically label diffuse aggregated (oligomeric) forms of α -syn and LB-like structures.

P19.05**Longitudinal striatal atrophy during Parkinson's progression**

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Background: Parkinson's disease (PD) is marked pathologically by progressive nigrostriatal dopaminergic cell degeneration. Striatal atrophy has been suggested by postmortem pathological data and cross-sectional imaging studies.

Objective: To test the hypothesis that PD causes accelerated striatal atrophy using a state-of-the-art probabilistic atlas-based segmentation approach.

Methods: High resolution (3-T) T1- and T2-weighted MRI images were obtained from 80 PD patients and 55 healthy controls at baseline and 18 month follow-up. Striatal structures [putamen (PUT), caudate (CN), and global pallidus (GP)] were segmented individually based on both T1 and T2 images using a fully automatic probabilistic atlas-based pipeline implemented in AutoSeg 2.9 (<http://www.med.unc.edu/psych/research/niral/>). For PD patients, clinical measures including the United Parkinson's Disease Rating Scale, disease duration, and levodopa equivalent daily dose also were recorded. The dynamic volume changes between PD and controls were assessed using mixed effects models controlling for age and gender. Associations between striatal volume change and clinical measures were assessed using partial Pearson correlation coefficients.

Results: The dropout rates at 18 months were 20% for PD patients and 15% for controls, respectively. Cross-sectional comparisons between PD and controls indicated that PD patients displayed significant volume loss of PUT at follow-up [p=0.0065], but not at baseline [p=0.090]. Longitudinal analyses demonstrated that PD subjects had significantly faster volume loss in all three striatal structures [p=0.036 for PUT, p=0.005 for GP, and p=0.049 for CN] compared to controls. Volumes of all three striatal structures were correlated with all clinical measures at baseline, but volume change was correlated with clinical measures only in CN.

Interpretation: There is accelerated striatal atrophy in PD, and dynamic volume changes in striatum might be a useful marker for Parkinson's progression.

P19.06**A promising preclinical biomarker for Parkinson's disease based on ocular tremor: support from quantitative DaTscan analysis**

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Objective: Parkinson's disease is known to have a lengthy prodromal period preceding the onset of clinical motor symptoms. Studies suggest that more than half of subjects with REM sleep behavior disorder (RBD) will develop PD and that, on average, RBD predates the onset of PD motor symptoms by over a decade. Our previous study showed that ocular tremor was a universal feature of PD, including in those with de novo, untreated disease. The present study aims to determine the utility of ocular tremor as a preclinical biomarker for PD.

Methods: To date, 17 subjects with polysomnography confirmed RBD were assessed using an EyeLink II binocular eye tracker while following random step displaced stimuli. None of the subjects had symptoms or clinical features of PD or other neurological conditions.

Results: Nine of 17 subjects (53%) had ocular tremor consistent with that seen in PD, while the other 8 subjects exhibited normal eye movements. UPDRS Part III Examination scores did not differ between groups with and without ocular tremor. Three subjects with ocular tremor consented to DaTscan imaging. Quantitative analysis showed unilateral reduction of uptake in the putamen in two subjects and bilateral reduction in the putamen in the third subject.

Conclusions: These compelling findings in a group at risk for PD suggest that ocular tremor could serve as a highly accurate biomarker for the detection of preclinical PD.

P19.07**Metabolomic changes associated L-DOPA induced dyskinesia in a MPTP primate model of Parkinson's disease and the effect of DHA or plasmalogen precursor administration**

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Objective: Development of dyskinesias with long-term treatment of dopamine precursor L-DOPA in Parkinson's disease (PD) remains a serious obstacle in the treatment of PD. We have therefore investigated the metabolomics effects of L-DOPA in MPTP monkeys before and after inhibition of dyskinesias by either docosahexaenoic acid (DHA) or the plasmalogen precursor PPI-1011 using non-targeted Fourier transform ion cyclotron mass spectrometry (FTICR-MS).

Methods: 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP) was administered to monkeys (n=5) to deplete dopaminergic neurons and to make monkeys parkinsonian. The monkeys were then given L-DOPA to induce dyskinesias. Then either DHA (100 mg/kg) or plasmalogen precursor PPI-1011 (50 mg/kg) was administered in a cross-over design with a washout period in-between the treatments. Serum was subjected to aqueous and organic extractions followed by analysis by FTICR-MS. Behavioral studies were done to evaluate parkinsonian symptoms and dyskinesias. Dyskinetic scores and treatment phases were statistically correlated to changes in the intensity of accurate masses in serum to evaluate the metabolic changes associated with dyskinesias.

Results: There was a significant reduction in dyskinesias in monkeys at differing time points with PPI-1011 and DHA treatments. 176 masses were commonly associated with the reduction of dyskinesias in monkeys with either PPI-1011 or DHA (p<0.01). Out of these 176 masses, the restoration of 10 masses were identified as being primarily responsible for reducing dyskinesias. L-DOPA induced dyskinesias create a specific metabolic profile that responds to therapy with either DHA or PPI-1011.

P19.08**Safety of DaTscan™ (Ioflupane I 123 Injection), a radiopharmaceutical indicated for visualization of the striatal dopamine transporter in the brain using SPECT imaging**

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Objective: To assess DaTscan™ ([¹²³I]Ioflupane Injection) is safety data from clinical trials in GE Healthcare's clinical development and post-marketing experience.

Methods: In GE Healthcare's clinical trials, DaTscan™ was administered intravenously to 1236 subjects (1171 patients and 65 healthy volunteers). Clinical trials collected information on adverse events (AEs), and collected data on laboratory parameters, vital signs and ECG. Administered activity of [¹²³I]Ioflupane ranged from 3 to 5 mCi (111 to 185 MBq). The calculated whole body effective dose was 4 to 6 mSv, comparable to 1 year of natural background radiation in the USA (3 to 4 mSv).

Results: There were mild and infrequently reported AEs and no SAEs or deaths that were considered related to DaTscan™ administration. The most common AE ascribed to DaTscan™ by the investigator was headache (1%), followed by nausea, and vertigo, dry mouth, hunger, dizziness, and formication (<1 % each). Most of these AEs were mild. The safety profile established in clinical trials is supported by limited AE reports (including hypersensitivity reported as rash and pruritis shortly after dosing) from post-marketing exposure in over 300,000 patients who have been imaged with DaTscan™. Comprehensive review of the safety data shows that DaTscan™ is a safe product to use. Study Supported by GE Healthcare.

P19.09**MR Volumetry and T2 relaxometry of the Basal ganglia in Sydenham's chorea: A study in the Indian population**

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Objective: The purpose of our study was to evaluate abnormalities of the basal ganglia (BG) in patients with Sydenham chorea (SC) using MR volumetry (MRV) and T2 relaxometry (T2R) on 3 Tesla MRI. Although SC is relatively rare in developed countries, it is often encountered in Indian population due to the higher incidence of rheumatic fever. The disease has recently been implicated in the etiology of Obsessive Compulsive Disorder (OCD).

Methods: Eight patients with SC and sixteen age matched controls were recruited for the study. In addition to the conventional T1W, T2W and FLAIR sequences, a high resolution 3D inversion recovery (IR) sequence was performed for calculating the basal ganglia volumes using the manual region of interest (ROI) method. The subjects then underwent T2 mapping using a multiecho FRFSE sequence on a 3T MR scanner. T2 values were calculated from the caudate nuclei and putamina. Statistical analysis of the data was performed.

Results: Our results indicate that compared with healthy controls, patients with SC have a significant decrease (p value<0.01) in T2R values of the caudate nuclei suggesting increased iron deposition in these structures. The basal ganglia –frontal lobe tracts play an

important role in performing goal-directed movements and hence have been implicated in movement disorders. Increased BG iron deposition has been reported in SC and other such neuropsychiatric movement disorders resulting in shortening of the BG T2 relaxation times on T2R while BG volumes are preserved on conventional MRI sequences. Hence, we conclude that T2R at 3T MRI is a sensitive tool for assessing BG iron content and can serve as a quantitative imaging biomarker in movement disorders like SC.

P19.10**Cortical and subcortical brain volumes and clinical correlates in preclinical and clinical Parkinsonism**

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Objective: To correlate regional volume differences with olfactory function, cognitive measures, and clinical severity in preclinical and clinical Parkinsonism. Individuals with idiopathic REM sleep behavior disorder (iRBD), considered a subclinical synucleinopathy, are at a high risk for the development of Multisystem Atrophy (MSA), Lewy-Body Dementia, or Parkinson's disease (PD).

Methods: 23 confirmed PD, 10 confirmed MSA and 13 confirmed iRBD patients participated. Volumetric measurements were derived from high resolution T1-weighted 3T MR images; volumetric reconstruction and segmentation performed with Freesurfer. Clinical measures included Hoehn & Yahr staging for severity, University of Pennsylvania Smell Identification Test (UPSIT) - 40 odor olfaction, Montreal Cognitive Assessment (MoCA). Pearson correlations of normalized brain volumes and clinical measures were performed using SPSS 21.0.

Results: Significant negative correlations between UPSIT scores and bilateral caudate volumes were found in the iRBD group, demonstrating deficits in olfactory performance were associated with larger caudate volumes and more representative of preclinical PD pathology. Significant correlations were found between MoCA scores and volumes bilaterally in the caudal middle frontal gyrus, but unilaterally in the caudal anterior cingulate, posterior cingulate, precentral gyrus, and precuneus, indicating cortical degeneration is related to decline in cognitive functioning in iRBD patients and less representative of PD pathology. In the MSA group we found significant correlations between UPSIT scores and the volume of left amygdala and frontal pole, right cuneus, pericalcarine, rostral middle frontal gyrus and insula. These results suggest brain volumetric measurements in conjunction with clinical measures may be used as biomarkers, specific for clinical and subclinical Parkinsonism and disease progression.

P19.11**The national institute of neurological disorders and stroke Parkinson's disease biomarkers program consortium**

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Objective: The National Institute of Neurological Disorders and Stroke (NINDS), is establishing a Parkinson's Disease Biomarkers

Program (PDBP) (see <http://pdbp.ninds.nih.gov/>). The overall purpose of the NINDS PDBP is to rapidly identify and develop potential biomarkers to improve the efficiency of Phase II clinical trials and advance therapy for PD.

Methods: The NINDS PDBP coordinates efforts in the identification and development of diagnostic, progression or prognostic PD biomarkers and related assays by: 1) standardizing data and biospecimen collection across new PD cohort studies; 2) enhancing efforts of current PD biomarker studies through ancillary projects that support additional well characterized biospecimen collection; 3) accelerating the discovery of new biomarkers; and 4) fostering and expanding collaborative opportunities. Currently the NINDS PDBP includes four components: 1) Biomarker hypothesis testing and collection of clinical data and biospecimens 2) Technology-based studies 3) Biospecimen banking and distribution through the NINDS Repository and 4) Data management and standardization through a Data Management Resource (DMR).

Results: To date, nine projects have been awarded under this program, with a tenth and eleventh existing project incorporated most recently. Three of the 11 projects are technology development, and the remainder are clinical collections combined with the development of clinical or laboratory methods and tools. In collaboration with the PD research community, NINDS will integrate all of its current and future PD biomarker projects within this program. Broad sharing of data and biological specimens with academic, industry and government researchers is a critical feature of the PDBP. Annual milestones provide clear indicators of a project's continued success.

P19.12

Multi-modal imaging study of the posterior cingulate in Parkinson's disease

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Objective: Our goal was to test the hypothesis that cognitive deficits in Parkinson's disease (PD) are associated with structural and functional changes in the posterior cingulate. To test this hypothesis, we used multi-modal magnetic resonance imaging (MRI) methods including high resolution structural MRI, diffusion tensor imaging (DTI), continuous arterial spin labeling (CASL) perfusion weighted MRI, MRI spectroscopy (MRS), in combination with [18F]-fluorodeoxyglucose positron emission computed tomography (FDG-PET) to assess brain glucose metabolism.

Methods: Twenty-nine PD patients (H&Y: 1-3.5) and 23 controls matched for age, gender, and educational level underwent MRI examination, which included structural MRI, DTI, CASL, and MRS. Thirty-four PD (H&Y: 1-3.5) and 20 control subjects underwent FDG-PET. Antiparkinsonian medications were withheld for 12 hours prior to imaging. Pre- and post-processing imaging were analyzed using statistical parametric mapping (SPM).

Results: Compared with controls, PD subjects had significantly increased mean diffusivity (MD), reduced *N*-Acetylaspartate (NAA)/H₂O levels, and borderline atrophy in the posterior cingulate. PD patients also had decreased fractional anisotropy (FA) in the white matter below the posterior cingulate and motor cortex, consistent with disrupted microstructure and neuronal loss in PD. Significant metabolic increases on FDG-PET were found in the bilateral posterior cingulate extending to the white matter in PD subjects versus controls. This might potentially represent a compensatory mechanism for structural damage in the adjacent region in PD. The DTI MD, DTI FA, NAA/H₂O and glucose metabolism values were all associated with memory decline in PD, as assessed by the California verbal learning test (CVLT). There were no significant cerebral blood flow changes in PD subjects as compared with controls, as assessed by CASL. Together, these findings show evidence for structural damage and functional alterations in the posterior cingulate in PD that might potentially play a role in the pathophysiology of PD-related cognitive impairment.

P19.13

Abnormal functional brain networks in Parkinson's disease: A graph theory analysis of resting-state fMRI data

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Objective: The degeneration of dopaminergic neurons in Parkinson's disease (PD) is accompanied by impairment of not only motor, but also cognitive and emotional functions. The aim of our study was to characterize the whole brain functional connectivity in PD patients compared to healthy age-matched controls (HC) using graph theory analysis of resting-state (RS) fMRI data. **Methods:** RS-fMRI was acquired in twenty subjects, 10 patients with PD (6M/4F, 62.4±7.77 yrs, UPDRS score 16.9±6.8, H&Y staging 1.8±0.4) and 10 healthy controls (6M/4F, 63.5±8.84 yrs) using a 3 T scanner. The whole brain was parcellated in 206 bilateral cortical, subcortical and cerebellum regions based on cytoarchitectonic maximum probability map and macrolabels. Both global [clustering coefficient (γ), path length (λ), global efficiency (E-glob)] and local [nodal betweenness centrality (BC), degree (D), local efficiency (E-loc)] network metrics were computed using Brain Connectivity Toolbox. To ensure an equal number of edges, we thresholded all correlation matrices over a wide range of sparsity (10% ≤ S ≤ 65% with 5% interval).

Results: Both controls and patients with PD showed small-world network properties with normalized clustering ($\gamma=1.2$ HC and 1.3 PD) and path length ($\lambda=1.39$ HC and 1.13 PD). However, clustering coefficient was significantly lower (PD=0.34, HC=0.41; $p=0.001$) in patients compared to controls. In addition, we found statistically significant decreased E-loc in right supramarginal and middle occipital gyri and in left thalamus in PD as compared to HC ($p \leq 0.004$). The number of hubs was lower in PD (12) than in HC (33) based on degree. In comparison to HC, PD patients showed statistically higher BC in right amygdala and superior temporal gyrus, in left thalamus and bilateral insula ($p \leq 0.004$). In summary, our results show that network topological properties are altered in PD not only in motor areas but also in areas involved with cognitive and emotional functions.

P19.14

Breath gas analysis for a potential diagnostic method of Parkinson's disease

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Objective: Exhaled breath analysis is a fast-developing topic to improve the diagnosis and monitoring of the respiratory and systemic diseases, including lung cancer. Not only as a lung biomarker, but also many of exhaled breath components characterize the functioning of the organism as a systemic biomarker. Therefore, we studied the feasibility of a novel method that is based on breath gas analysis to identify neurodegenerative conditions, especially for Alzheimer's disease and Parkinson's disease.

Methods: Exhaled breath was collected in an inert bag from 22 patients with Parkinson's disease and 8 healthy controls. And we also collected breath gas from 28 patients with Alzheimer's disease for another controls. Samples were analyzed using gas chromatography mass spectrometry (GC-MS). All patients and healthy volunteers conducted the neuropsychologic tests such as MMSE (Mini-Mental Status Examination), NPI (Neuro-Psychiatric Inventory) and UPDRS (Unified Parkinson's Disease Rating Scale) motor scales.

Results: Among several compounds that showed statistical difference, phenol was detected on the exhaled breath of most participants (19 out of 28 Alzheimer's disease patients, 13 out of 22 Parkinson's disease patients and 6 out of 8 healthy volunteers) and it showed higher concentrations in Parkinson's disease patients compared to healthy volunteers with statistical significance ($p < 0.01$ for Phenol; GC-MS measurements). Furthermore it also showed a positive correlation with the UPDRS motor scale. Analysis of exhaled breath is a non-invasive and totally painless test, so it could be an ideal method for the diagnosis. In this study we showed the feasibility of a novel method to diagnose Parkinson's disease. However, phenol is usually detected in the environmental sources and it is not well known for human metabolites. Therefore further studies should be conducted to demonstrate more distinctive evidences that could explain the correlation between pathology and clinical diagnosis of Parkinson's disease.

Acknowledgement: This research was supported by the Converging Research Center Program through the National Research Foundation of Korea (NRF) funded by the Ministry of Education, Science and Technology (2012K001351 and 2012K001352).

P19.15

High field diffusion tensor imaging of the Corpus Callosum in Parkinsonism dementia complex

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Objective: The purpose of this study was (a) to examine the regional nature of white matter (WM) abnormalities in Parkinson's disease (PD) using diffusion tensor imaging (DTI) parameters and (b) to determine whether regional changes correlated with cognitive impairment in Parkinsonism dementia complex (PDC). Patients with

Parkinson's disease (PD) often present with cognitive deficits. The corpus callosum (CC) plays an important role in transmitting sensory, motor and cognitive information between cortical regions and both hemispheres. DTI is a recently developed MR imaging technique which enables the noninvasive assessment of white matter microstructural integrity.

Methods: We studied five patients each with PD, PDC and twenty healthy controls using an echoplanar DTI sequence on a 3 Tesla MRI scanner. We measured DTI parameters of the anterior and posterior corpus callosum, including Fractional Anisotropy (FA) and Mean Diffusivity (MD). Statistical analysis across groups was performed using the t tests. The results were correlated with the Mini Mental Status Examination (MMSE) scores.

Results: We found no significant differences in the FA values of CC between PD subjects and controls. PDC subjects had a significantly reduced FA value in the anterior corpus callosum compared with controls and nondemented PD patients.

P19.16

Essential tremor has alterations in regional glucose metabolism and GABAergic system

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Objectives: We investigated whether GABAergic transmission is altered in ET using [¹⁸F] flumazenil (FMZ) PET which has a specific binding affinity to GABA_A receptor. Alteration of regional glucose metabolism was also investigated using [¹⁸F] FDG PET.

Background: Essential tremor (ET) is the most common movement disorder. However, the underlying etiology is not clear. Recently, altered GABAergic neurotransmission has emerged as a key feature of pathophysiology in ET.

Methods: Twelve patients (M:F=4:8, age=55.8±12.1) fulfilling the criteria for definite ET according to the proposal of the Tremor Research and Investigation Group were enrolled. All subjects performed FDG PET and FMZ PET. Regional glucose metabolism and GABA_A receptor availability were compared with those of age-matched 18 healthy controls (M:F=5:13, age =56.2±6.1).

Results: In the patient group, significant glucose hypometabolism was identified in bilateral primary motor cortex and left posterior parietal lobe ($p < 0.005$, uncorrected; extended threshold, $k=100$). GABA_A receptor availability revealed no significant difference between patient and control groups in voxel-based analysis. However, ROI analysis showed a trend of slightly higher cerebral and cerebellar cortical GABA_A receptor availability in ET patients.

Conclusions: FMZ PET revealed mild difference in the GABA_A system between patient and control groups. FDG PET showed that ET patients have glucose hypometabolism in bilateral primary motor cortex and left posterior parietal lobe. Further studies are needed to elucidate the role of alterations in the regional glucose metabolism and GABAergic system in ET.

P19.17

Influence of Dopamine Transporter (DaT) scan on medical management in movement disorders specialists: Cleveland Clinic experience

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Objective: To describe influence of DaT scan on movement disorders specialist decisions on medical management of patient presenting with parkinsonism.

Method: We conducted a retrospective review of all patients, seen by a Movement Disorders neurologist, who received a DaT scan at the Cleveland Clinic. Demographic data including pre scan diagnosis and anti-PD medication use after the scan were collected. We excluded all DaT scans ordered by other clinicians, scans obtained for research and repeat scans in same patient.

Results: Total of 216 DaT scans were performed from June 1, 2011 to October 31, 2012. Forty-one scans were excluded based on our criteria. 175 scans were used for analysis. 45% had positive DaT scans, 54% were negative and 1% was indeterminate. For patients with an abnormal DaT scan, 96% were placed on anti-PD medications. Of those not placed on anti-PD medications, two were due to the minimal degree of symptoms, and one was due to a concern for a false positive scan due to drug interaction. On the other hand, 25% of patients with negative scan remained on anti-PD medications. Reasons for these were: clinician's belief that the scan was false negative (N=6), mixed ET/PD diagnosis (N=2); other diagnosis responsive to anti-PD medications, such as NPH (N=3), drug-induced parkinsonism (N=5), gait disorder of unclear etiology (N=2), psychogenic parkinsonism (N=2), idiopathic camptocormia (N=1), other form of dystonia (N=1), parkinsonism related to liver disease (N=1).

Conclusion: DaT Scan has strong influence on physician decision on initiating or continuing on antiparkinsonian medications especially if the scan was positive. For negative scans, the reasons why clinicians continue anti-PD medications are varied.

P19.18

Differences in striatal dopamine transporter levels regarding predominant motor symptom in Parkinson's disease

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Objective: Loss of striatal dopamine nerve terminal function, a hallmark of neurodegenerative Parkinsonism, is strongly related to decreases of dopamine transporter (DAT) density, which can be measured by single photon emission computed tomography (SPECT) with ¹²³I-FP-CIT. The aim of this study was to quantify the loss of DAT, by means of ¹²³I-FP-CIT SPECT, in patients with Parkinson's disease (PD) regarding predominant motor symptom at the onset of disease.

Methods: ¹²³I-FP-CIT SPECT studies were performed on 36 consecutive patients with clinical diagnoses of PD. 22 males; mean age: 70.67 years (46 to 88 years); Hoehn and Yahr stage: I-II and two cases in III. These patients were classified in two groups regarding predominant motor symptom at the onset of disease: Group 1 consisted of 19 patients with tremor-dominant and Group 2 made up of 17 patients with non-tremor dominant. Specific to nondisplaceable binding ratios (SBRs) were calculated using version 2 of the BasGan software (BasGan V2), that allows automatic quantification of striatal ¹²³I-FP-CIT uptake. SBRs in right and left caudate nucleus and putamen were the dependent variables in a repeated measures general linear model analysis and predominant motor symptom was the independent variable.

Results: The visual analyses of ¹²³I-FP-CIT SPECT studies were pathologic in all patients. The mean values of SBRs in left and right caudate (2.59 and 2.60) and putamen (1.55 and 1.55) of patients of

Group 1 were significantly higher than in Group 2 (1.72, 1.7, 0.85 and 0.82, respectively) ($p < 0.002$), which means higher density of DAT in Group 1. This study confirms that those patients with PD with tremor-dominant at the onset of disease presented lower loss of DAT with regard to non-tremor dominant phenotype, which might explain why the former is being considered a more benign subtype of PD.

P19.19

Discrimination between patients with neurodegenerative syndromes with brain perfusion SPECT

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Objective: To evaluate changes in brain perfusion and the expression of Parkinson Disease Related Metabolic Covariance Pattern (PDRP) in patients with Parkinson's Disease Dementia (PDD), Alzheimer's Disease (AD) and Dementia with Lewy Bodies (DLB).

Methods: 99mTc-ECD/SPECT brain perfusion images were acquired in 14 PDD (age 72 ± 4 yrs, MMSE 24 ± 2), 11 DLB (age 73 ± 4 yrs, MMSE 23 ± 2), 11 AD patients (age 71 ± 8 yrs, MMSE 22 ± 4), and 7 healthy controls HC (age 62 ± 3 yrs). Statistical parametric mapping (SPM8; two group t-test, uncorrected $p < 0.01$, extent threshold > 100 voxel) was used to identify brain perfusion changes in each patient group relative to HC and between patients' groups.

Additionally, the expressions of metabolic brain marker of Parkinson's disease - PDRP was calculated for each individual subject. Topographic Profile Rating technique was applied to brain perfusion images. Expression scores for each subject were calculated and compared among patients' groups and HC; discrimination between groups was found significant if $p < 0.001$.

Results: In PDD comparing to HC hyperperfusion was found in basal ganglia, thalamus, cerebellum, primary motor and frontal cortex. Hypoperfusion was present in parieto-occipital cortex.

In DLB comparing to HC changes in perfusion were similar to PDD but with lower perfusion in frontal cortex.

In AD comparing to HC hyperperfusion was found in primary motor and prefrontal cortex and in cerebellum. Hypoperfusion was present in posterior cingulate and precuneus, medial and anterior temporal lobes.

PDRP expression scores were significantly elevated in PDD and LBD patients but not in AD patients, all relative to HC.

Conclusion: Changes in brain perfusion can help us differentiate among parkinsonism and dementia syndromes. PDRP analysis can be applied to perfusion SPECT images to differentiate between neurodegenerative disorders, although it was first identified from FDG/PET images. PDRP expression is significantly more pronounced in parkinsonian syndromes compared to AD and HC.

P19.20

Clinical study for the identification of autoantibodies in Parkinson's disease by protein arrays

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Objective: Parkinson's disease or idiopathic parkinsonism is the second most common neurodegenerative disorder in the elderly. Because no biomarker is available, the diagnosis and also the monitoring of disease progression are still based on clinical criteria. Especially in early stages, several conditions can mimic PD, which leads to false diagnosis. The trigger for the neurodegeneration is still unknown; neuroinflammatory processes seem to play a crucial role. Besides general mechanisms activating and amplifying neuroinflammation, such as generation of proinflammatory cytokines by local glial cells, a neuronal labeling in the substantia nigra pars compacta with PD IgG was described. Therefore antibodies may play a critical role in the pathological process. Assuming immunological mechanisms involved in PD and the requirements to an optimal biomarker, antibodies are good biomarkers candidates for an early diagnosis, with a high sensitivity and specificity and perhaps the ability to monitor disease progression.

Methods: We performed a case-control study using human protein microarrays to identify human autoantibodies in sera samples for discriminating Parkinson's disease patients from two other reference groups (neurodegenerative/autoimmune diseases vers. non-diseased controls). For the discovery of a new protein microarray platform was used, which allows the simultaneously analysis of around 9.500 human proteins as possible autoantigens.

Results: Finally analysis was conducted with a subset of 72 triplets matched 1:1:1 by gender and age fulfilling all inclusion and exclusion criteria. We identified an autoantibody panel that classify patients from healthy and diseased controls. An average classification accuracy of 73.5% has been achieved. The identified autoantibodies are partially directed against proteins, which are already described in literature in the context with the disease pathology. These findings suggest that a panel of autoantibodies may function as a specific biomarker for Parkinson's disease.

CLINICAL SCIENCES: PHARMALOGICAL THERAPY

P20.01

Changes in troublesome dyskinesia and its relationship with dose in advanced Parkinson's disease patients treated with levodopa-carbidopa intestinal gel infusion

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Objective: To assess the effect of levodopa-carbidopa intestinal gel (LCIG) treatment on troublesome dyskinesia (TSD), as well as examine the relationship between the change in ON-time with TSD and change in dose, in advanced Parkinson's disease (PD) patients with TSD.

Methods: In a double-blind, double-dummy study, patients received LCIG infusion + placebo capsules, or encapsulated LC-Oral tablets + placebo gel infusion for 12 weeks. In a 54-week, open-label study, patients all received LCIG infusion. Change in ON-time with TSD and ON-time without TSD were analyzed in the subgroup with baseline ON-time with TSD ≥ 1 hour/day based on diary

assessment. The correlation between change in total daily dose of levodopa and change in ON-time with TSD was analyzed.

Results: LCIG patients in the TSD subgroup of the double-blind study cohort (N=10) reported a significant decrement (mean [SD]) in ON-time with TSD from baseline (3.13 [1.65]) to final, change= -1.76 [1.83], $P=0.014$. This was accompanied by an increase in ON-time without TSD from baseline (7.35[2.15]) to final, change= 4.43[3.64], $P= 0.004$. In the open-label study (N=139), LCIG treatment resulted in a significant reduction from baseline to final in ON-time with TSD (baseline= 3.37[1.81], change= -1.83[2.92], $P<0.001$) and extension of ON-time without TSD (baseline= 6.84[2.44], change= 5.31[3.88], $P<0.001$). An increase in LCIG dose was not significantly correlated with an increase in ON-time with TSD in either study (double-blind: $R= -0.073$, $P= 0.842$; open-label: $R= -0.001$, $P= 0.992$). Overall, adverse events were common, mild to moderate, and generally related to GI procedure. In patients with TSD, LCIG produced clinically significant improvements by reducing ON-time with TSD and increasing ON-time without TSD. While most patients increased LCIG dose during the study, there was no correlation with increased ON-time with TSD. These results support the effectiveness of LCIG in reducing TSD in advanced PD.

Financial Disclosure: Support: AbbVie

P20.02

Mucuna Pruriens: a possible strategy for Parkinson's disease patients in developing countries

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Objective: Mucuna Pruriens is a tropical legume found in Asia, South America and Africa. It is used for many medicinal purposes and ayurvedic Indian medicine claims that it possesses anti-parkinsonian properties. The seeds of Mucuna Pruriens contain high levels of levodopa (about 5.9 and 6.7%, respectively, for white and black seeds). Our objective was to measure the levodopa content of various legumes and to assess whether they could be used as a therapeutic option for Parkinson's disease patients in developing countries. We have opened clinics for Parkinson's disease patients in Ghana and Zambia, which are already attended by more than 100 patients. Pharmacological treatment is a problem as most patients cannot afford it: levodopa costs on average 1.5\$ daily.

Methods: We have collected 30 different kinds of legume seeds, all sold at low prices in markets in Africa. All the seeds have been sent to a botanist for classification. After dry heating or boiling (soaked in water for 15 h and then boiled in the same water for 1,5 h) they were sent to a laboratory where their levodopa content was measured.

Results: In the group of 30 different legumes, we found Mucuna Pruriens in Togo-Ghana, both in white and black seeds. The levodopa content was: in dry heated seeds 3,99% and 4,93%, respectively; in boiled seeds 2,28% and 2,8%, respectively. In the others 28 legume seeds levodopa was not found. We plan to learn how to use Mucuna Pruriens seeds to offer safe and effective treatment to our patients in developing countries. We are considering the option of genetic engineering to develop a legume containing levodopa and carbidopa in the right concentrations and the right proportions.

P20.03

Taq1A polymorphism improves dopamine agonist therapeutic response in Parkinson's disease

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Objective: Frontal-striatal dysfunction caused by Parkinson's disease (PD) can impair certain aspects of action control. The preferential D2 and D3 Receptor Agonists can differentially impact impulsive action tendencies; some patients improve on therapy, whereas others worsen. This study sought to determine if functional dopamine polymorphisms in the DRD 2 and DRD 3 genes influence the response to Dopamine Agonist (DAA) therapy for PD with respect to inhibitory action control.

Methods: The Simon Manual Conflict task was completed by 28 PD patients On and Off DAA therapy in a counterbalanced manner. For the Off state, participants withheld from DAA for 24 hours. Patients were genotyped for known functional polymorphisms in DRD2 (rs6277 and rs1800497) and DRD3 (rs6280) receptors. Proficiency of inhibitory action control, as measured by the ability to inhibit a prepotent action impulse induced by task irrelevant stimulus information, was defined as the measure of change in the Simon effect at the slow end of reaction time distributions (delta plots). We calculated within-subject effects of DAA therapy on inhibitory control, and grouped genotype results based on known functional polymorphism effects on DRD receptor affinity and availability.

Results: The Taq1A polymorphism in the DRD2 gene (rs1800497) appears to augment DAA therapeutic response. Patients with the A1 polymorphism (A1/A1 or A1/A2: 12 subjects) improved the proficiency to suppress impulsive actions when On DAA. Conversely, patients with the A2/A2 allele (16 patients) became less proficient at suppressing the incorrect response information on DAA therapy (*Medication x Genotype*, $F(1, 26) = 5.22$, $p < 0.05$). Polymorphisms in rs6277 and rs6280 were not associated with a differential medication response. These findings suggest that certain DRD polymorphisms may influence medication response in PD patients. We speculate that DAA therapy may improve the ability to suppress impulsive action tendencies in patients due to alterations in D2 receptor expression.

P20.04

Parkinson's disease tremor profiles across a range of loads with serial neurotoxin injections

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Introduction: While PD tremor is thought to be predominantly at rest (no load = only involuntary muscle activation), rather than during action (with load = range of voluntary and involuntary muscle activation to maximum), tremor can still be present across the whole range of load conditions. Botulinum toxin type A (BoNT-A) is a possible treatment for upper limb tremor in PD. However, the effect of BoNT-A on PD tremor over a range of loads and weakness as a side effect has not been studied.

Objectives: To evaluate in a series of sequential neurotoxin injections the pattern of change in:

- rest versus action tremor across a wide range of loads in PD and BoNT-A effect at each load condition.
- weakness profile in individual fingers along with grip strength.

Methods: 12 PD patients (67.5±6.3) in whom tremor was not adequately controlled were enrolled in the study. Kinematic assessment tools were used at baseline and 4 follow up visits (at 6, 16, 22, and 32 weeks; injections every other visit). Data were analyzed to evaluate tremor amplitudes at all joints and loads, as well as average of finger strength.

Results: 6 weeks after the first injection, wrist tremor at low-load and medium-load reduced by 40% and 12%, respectively. PD patients also benefitted from significant tremor reduction of maximal load in 3 fingers: second (30%), third (24%), and fourth (31%) digits. However, PD patients experienced weakness in 4 fingers: index (28%), second (41%), third (46%), and fourth (37%) digits.

Conclusions: The profiles of the changes over serial injections reveal that PD patients benefitted from the injections over a wide range of load conditions. Kinematic measures allow clinicians to assess both benefits and side effects of injection. So, the effects of selecting appropriate muscles for injection and patients' functional improvement can be monitored.

P20.05

A review of nicotine agonist treatment for cognitive impairment in Parkinson's disease

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Objective: Several population-based studies have reported a dose-dependent diminution of Parkinson's disease (PD) risk associated with cigarette smoking. Nicotine may be one of the components of cigarette smoke that could exert local neuroprotective/anti-inflammatory effects on dopaminergic (DA) neurons. Nicotine may indeed contribute to a DA increase by stimulating cholinergic nicotinic receptors in the nigrostriatal system. Nigrostriatal and other DA alterations in early PD may impact on cognition, as cognitive impairment in PD is reported to affect 19%-36% of *de novo* patients. Therefore, it is possible that nicotine agonists could improve cognitive disorders in PD. This critical review aims at investigating the potential benefit of nicotine administration on cognition in PD patients.

Methods: A search was conducted in Pubmed and ClinicalTrials.gov databases using the keywords «parkinson» AND «cognition» OR «mental status» AND «nicotine» OR «smoking». Inclusion criteria were: 1) articles published in 1993-2013 and reporting cognitive results following nicotine agonists administration in PD patients; 2) use of at least one validated cognitive test; 3) case reports were also included.

Results: Only 6 studies (3 R-DB-PC, 2 open label, 1 case report) met the inclusion criteria. Four studies reported some improvement in measures of attention and global cognition and on a semantic priming/processing task in patients with early PD (H&Y 1-3). However, 1/4 also reported deterioration on digit span and visual tracking tasks. Two studies reported numerous side effects (e.g. headache, dizziness, light-headedness, nausea, intestinal cramps) that led to attrition in 59%-75% of cases. At this point, there is no clear data regarding the therapeutic dosage of nicotine agonists. Moreover, small sample sizes (n=2-22), lack of randomized controlled trials and lack of exhaustive cognitive assessments made it difficult to assess the effects of nicotine in PD-cognition. Nonetheless, ongoing clinical trials (e.g. NCT00873392, NCT01216904) may soon provide additional data.

P20.06**Pill dispensers and medication management strategies: helping patients take medications at the right time, on time, every time**

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Background: Parkinson's disease patients and carepartners report difficulty managing complex pill schedules. Getting the right medication at the right time is a critical part of the management of PD symptoms.

Objectives: 1) To share creative strategies developed by patients and caregivers to manage medication schedules. 2) To demonstrate a variety of pill-taking storage and dispensing systems that can help health professionals and patients be sure that medications are taken at the right time, on time, every time.

Methods: Patients and carepartners at Struthers Parkinson's Center meet with nurse clinicians prior to the clinic visit with their neurologist. While updating the medication list, the nurse asks the family to describe the pill management system they are using, who sets up the medications, and whether their system is working. Patients are counseled about the importance of taking medications on time, every time. The occupational therapist also addresses issues around medication management during Activities of Daily Living evaluations.

We have reviewed the commercially available pill dispenser and timer options, and have catalogued and photographed some systems that patients and families have devised.

Results: Over 100 dispenser options are available, with designs ranging from simple one day or week systems to multiple dosing automatic dispensers. Cost ranges from \$1.27 to \$500.00. We will show some commercially available options, as well as ideas and dispensing systems that patients have come up with independently.

Conclusions: Many of the commercially-available pill dispensers have proven impractical for patients with limited computer skills, decreased dexterity, poor eyesight, cognitive impairment, or financial restrictions. "Homegrown" dispenser systems, using basic household items, are preferred by many people. There is an opportunity for nurses and others who care for people with PD to learn of these simplified systems and share with other patients as appropriate.

P20.07**Effects of levodopa on gait variability of backward walking in Parkinson's disease**

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Objective: Levodopa treatment has been shown to improve gait performances in patients with PD. We found previously that levodopa decreased gait variability of forward walking in individuals with PD (Bryant MS et al. 2011). The effects of the levodopa on gait variability of backward walking in individuals with PD, however, have not been reported. This study is to investigate the influence of levodopa treatment on gait variability of backward walking in patients with Parkinson's disease (PD).

Methods: Forty-one subjects with idiopathic PD were recruited. The mean age was 68.44 ± 7.56 yr. The average time since diagnosis was 9.34 ± 5.67 yr. Patients were "off" levodopa for 12 hours before the first gait test. The gait test was performed again during "on" state when the optimal motor response was achieved after administration of levodopa. The tests were to measure the gait variability during states of "off" and "on" medications when the subjects walked backward at their usual speed.

Results: Variability of step time, stride length and stride velocity decreased by 2.8% (p < 0.0005), 1.66% (p = 0.036), and 1.63% (p = 0.014), respectively, from "off" to "on" levodopa state. Variability of double support time also decreased by 1.27% but the difference was not statistically significant (p = 0.137). The gait speed during "on" time increased by 15.51 cm/s (p < 0.0005). In conclusion, Levodopa reduced certain measurements of backward gait variability. This indicates that dopaminergic medications may have positive effects on gait stability of backward walking in individuals with PD. More samples will be needed to further prove this hypothesis.

P20.08**IPX066 dose conversion in patients with advanced Parkinson's disease**

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Objective: To evaluate IPX066 dosing regimens used in three trials.

Background: IPX066 is an oral investigational extended-release formulation of carbidopa-levodopa (CD-LD; 1:4 ratio) designed to provide rapid increase in LD plasma concentrations followed by sustained concentrations allowing a dosing interval of ~6h. IPX066 was studied in 2 active-controlled double-blind studies with immediate-release CD-LD (IR) and CD-LD+entacapone (CLE) as active controls, respectively, and in 1 open-label study in patients previously treated with controlled-release CD-LD (CR) alone or with IR.

Methods: All studies enrolled advanced Parkinson Disease (PD) patients with ≥2.5h "Off" time. All dose conversion to IPX066 was not blinded. The recommended initial IPX066 LD conversion dose was ~30% higher for CLE than for IR regimens with or without CR. All patients were started with IPX066 approximately every 6 hours. IPX066 dosing >5X/day was not permitted. IPX066 regimen was individually adjusted for 6 weeks. IR rescue was not allowed.

Results: The final IPX066 LD daily dose averaged ~2X IR LD dose when converting from IR alone, and ~2.7X when converting from CLE. The ~35% higher conversion ratio with CLE regimen is consistent with higher LD exposure (35-40%) when IR is dosed with entacapone. The conversion ratios were ~1.8X when converting from IR+CR, and ~1.5X from CR alone; these lower conversion ratios are generally consistent with reduced bioavailability of CR relative to IR in PD patients. The dosing frequency of IPX066 (median 3X/day) was similar regardless of patients' previous LD regimens. The higher dose of IPX066 represents an ~30% higher LD exposures than the controls after adjusting for lower bioavailability of IPX066.

Conclusions: Conversion ratios from various LD regimens to IPX066 are generally consistent with the pharmacokinetic profiles of IPX066 and LD regimens presented above. IPX066 dosing

frequency is similar (median:3X/day) regardless of previous LD regimen.

P20.09

Developing Usp14 inhibitors as disease-modifying therapeutics for neurological proteinopathies

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Objective: Neurological proteinopathies such as Parkinson's (PD) disease are associated with the accumulation of misfolded proteins in the brain. Such protein aggregates can be cleared by a number of mechanisms including protein ubiquitination followed by proteasome-mediated degradation. The catalytic activity of proteasome-associated deubiquitinating enzymes, such as Usp14, limits the proteasomal turnover by trimming the associated ubiquitin chains prior to substrate degradation. We have developed a drug discovery platform to evaluate whether selective inhibition of Usp14 by small molecules can decrease the accumulation of neuropathogenic misfolded proteins, such as α -synuclein in PD, tau in AD, or TDP-43 for ALS, by enhancing their proteasomal degradation.

Methods: We have used HTS and medicinal chemistry optimization to identify and develop Usp14 inhibitors that enhance the clearance of disease-relevant proteins prone to aggregation. Protein levels are determined in various cellular and neuronal models after genetic knockdown of Usp14 or following treatment with small-molecule Usp14 inhibitors.

Results: We are progressing two chemical series with different mechanisms of action that exhibit drug-like properties including *in vitro* potencies (IC₅₀) below 150 nM for Usp14 inhibition. Some of these compounds show lowering of α -synuclein in various cellular models including human iPS neurons and lowering of tau in primary neurons. Compounds in the lead series are well tolerated *in vivo*, displaying high free brain exposures in rodents with no overt toxicity. The *in vivo* pharmacokinetic and pharmacodynamic relationships of Usp14 inhibitors are being investigated. Consistent with our pharmacological findings, genetic knockdown of Usp14 also results in the lowering of soluble and aggregated α -synuclein and tau. Our results support the development of Usp14 inhibitors as a disease-modifying strategy for the treatment of neurological proteinopathies, which by selectively modulating proteasomal activity, enhance the degradation of disease-relevant, aggregation-prone proteins.

P20.10

Caffeine, has antiparkinsonian and hipouricemiant effects, what else?

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Objective: Aim of this study, was to determinate caffeine potential as antiparkinsonian drug in an animal PD model (apomorphine induced circling behavior) and to know its impact on uric acid serum levels.

Methods: Animal PD models and circling behavior. In Wistar rats, intracerebral unilateral 6-OHDA injections (n=6) were performed, a month after it all animals did receive intra peritoneal caffeine injection (7.5mg/Kg), plus Apomorphine (APO) to induce circling. Uric acid serum levels. Wistar rats, CAFFEINE group (n=6) receive caffeine intraperitoneal injections (7.5mg/kg) and CONTROL group (n=6) only vehicle, and were immediately placed in metabolic cages, to recollect and quantify urinary production by 12 hours. After it, both groups according bioethics guidelines were anesthetized and intra cardiac blood sample was obtained and uric acid in serum was determinate.

Results: Circling behavior. Intraperitoneal caffeine did increase contralateral circling behavior and it indicates a clear antiparkinsonian effect at used dosage. Uric acid serum levels. At same used dosage than in Circling behavior, CAFFEINE group did have a significant decrease in uric acid serum levels, respect to CONTROL group, and also a significant decrease in urinary concentration without significant differences on urinary volume, between two groups. Our results suggest that Caffeine is a promissory molecule in PD management, with another favorable effects to patients such decreasing uric acid serum levels. What else? Give us a few time, we are working to know it.

P20.11

The effects of age on adverse event reporting in Parkinson's disease patients treated with IPX066 extended-release carbidopa-levodopa capsules

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Objective: To evaluate the effects of age on adverse event (AE) reporting in a population of Parkinson's disease (PD) patients treated with IPX066.

Background: IPX066 is an investigational extended release capsule oral formulation of carbidopa-levodopa (CD-LD 1:4 ratio), designed to provide a rapid increase in plasma concentrations of levodopa followed by sustained stable concentrations allowing a dosing interval of ~6h. IPX066 was studied in three Phase 3 controlled trials, one in early PD vs. placebo and two in advanced PD, one vs. CD-LD immediate release (IR) and one vs. CD-LD IR + entacapone (CLE).

Methods: For each study, AEs were collected at each visit and were summarized using preferred terms from MedDRA 12.1. Comparative summaries were examined in patients categorized by age groups of <65, 65-74 and ≥75 years old.

Results: Of the 849 patients treated with IPX066 in controlled trials, 431 (50.1%) were of age <65, 186 (38.0%) were 65-74 and 108 (12.7%) were ≥75 years old.

The table below displays the AEs that occurred in at least 5% in any age group.

	Treated with IPX066			
	Age (years)	< 65	65-74	≥ 75
	N	431	310	108
Number of patients reporting at least one AE		233 (54%)	186 (60%)	70 (65%)
Nausea		42 (9.7%)	34 (11%)	12

			(11.1%)
Headache	34 (7.9%)	22 (7.1%)	4 (3.7%)
Dizziness	26 (6.0%)	29 (9.4%)	9 (8.3%)
Dyskinesia	25 (5.8%)	15 (4.8%)	6 (5.6%)
Insomnia	23 (5.3%)	11 (3.5%)	4 (3.7%)

Conclusions: In this population of PD patients treated with IPX066 in the Phase 3 clinical studies, the number of patients reporting at least one AE increased with increasing age. Of the most common AEs, headache decreased with increasing age but no clear pattern of AE frequency emerged for nausea, dizziness, dys kinesia or insomnia.

P20.12

Safety analyses from open-label clinical trials of levodopa-carbidopa intestinal gel in patients with advanced Parkinson's disease: Events not related to device or procedure

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Objective: To evaluate non-procedural or -device adverse events (AEs) during treatment with levodopa-carbidopa intestinal gel (LCIG) in patients with advanced Parkinson's disease (PD).

Methods: LCIG provides continuous drug infusion via an intrajejunal percutaneous gastrostomy tube. Data from 3 open-label studies of LCIG were pooled. 412 patients were analyzed, with mean (SD) exposure of 512 (320) days and total exposure of 577.8 patient treatment years.

Results: AEs occurred in 379 (92.0%) patients and lead to discontinuation of treatment in 45 (10.9%). The most common AEs were procedure- or device-related (e.g. abdominal pain). 367 (89.1%) subjects experienced an AE not associated with the procedure or device (Table 1), which lead to discontinuation in 35 (8.5%). 64.8% of subjects experienced a non-procedure or -device AE onset during titration (Days 1-28), 84.1% during maintenance (\geq Day 29, up to Day 1284), and 40.0% experienced an onset during titration that lasted into maintenance with duration \geq 7 days. AEs of interest include compulsive behavior (10.2%, by MIDI assessment), polyneuropathy (7.3%), sleep attacks (4.1%, by Sleep Attack Questionnaire), and melanoma (0). In conclusion, the profile of AEs in this long-term data set is similar to that in a 12-week, active-controlled trial (Olanow et al, Movement Disorders Society Meeting, 2012) and comparable to AEs observed with oral levodopa-carbidopa.

Table 1. AEs reported in \geq 5% of patients, excluding procedure- and device-associated AEs

Preferred Term	N (%) of patients	Preferred Term	N (%) of patients
Insomnia	80 (19.4)	Orthostatic hypotension	37 (9.0)
Nausea	77 (18.7)	Vitamin B ₆ decreased	37 (9.0)
Fall	74 (18.0)	Diarrhoea	36 (8.7)
Constipation	69 (16.7)	Sleep attacks	34 (8.3)
Urinary tract infection	55 (13.3)	Blood homocysteine increased	33 (8.0)
Anxiety	49 (11.9)	Dyspepsia	29 (7.0)
Parkinson's disease	47 (11.4)	Oropharyngeal pain	26 (6.3)

Weight decreased	47 (11.4)	Hallucination	25 (6.1)
Depression	44 (10.7)	Arthralgia	24 (5.8)
Dyskinesia	42 (10.2)	Pain in extremity	24 (5.8)
Vomiting	38 (9.2)	Decreased appetite	23 (5.6)
Back pain	38 (9.2)	Musculoskeletal pain	22 (5.3)
Headache	38 (9.2)	Dizziness	21 (5.1)

P20.13

Effective treatment of Parkinson tremor using kinematics to optimize Botulinum neurotoxin type A injection

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Introduction: Clinically assessing the complexity of multi-joint tremor in Parkinson Disease (PD) patients is difficult through traditional visual observations. Results from past studies showed injection of Botulinum neurotoxin type A (BoNT-A) to have the potential to alleviate tremor symptoms, however efficacy was often poor with severe hand weakness. Our study deconstructs the tremor on the arm using kinematic sensors, thereby providing a detailed and comprehensive assessment of PD tremor which can improve the efficacy of BoNT-A.

Methods: Kinematic recordings were done while patients were in rest, posture, and kinesis states in 24 PD patients. The 8 month assessment utilized 3D accelerometers, electrogoniometers and torsionmeters to measure tremor at the wrist, elbow, and shoulder, along with clinical tremor rating scales at each visit. Flexion-extension, pronation-supination, radial-ulnar movements were determined at the wrist, as well as flexion-extension at the elbow and flexion-extension with abduction and adduction at the shoulder. The information was then used by the clinician to determine injection sites and dosage needed.

Results: 6 weeks after the first injection the total tremor amplitude for shoulder, elbow and wrist was reduced in PD patients by 80% overall. PD patients had only 20-30% reduction in grip strength 6 weeks after each injection. The rest tremor UPDRS score (item 20) had decreased over 16 weeks from 2.75 to 1.81. Likewise for action tremor (item 21) there was a decrease from 1.67 to 0.77. The Fahn-Tolosa-Marin tremor rating scale over 8 months showed significant improvement while quality of life assessment in PD patients had no change.

Conclusions: PD patients showed significant reduction in their tremor and improvement in clinical scores. Using kinematics to determine injection parameters of BoNT-A is an effective tool to improve the standard of care to patients, not previously possible with visual assessment alone.

P20.14

4-aminopyridine improves gait in a patient with Parkinson's disease.

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Objective: Walking impairment represents a significant therapeutic challenge in patients with Parkinson's disease (PD). 4-aminopyridine (4-AP) is a potassium channel blocker that has favorable effects on several neurological diseases associated with gait dysfunction including multiple sclerosis and episodic cerebellar

ataxia. We aimed to evaluate the effects of a 4-aminopyridine in a patient with PD and freezing of gait resistant to dopamine therapy.

Methods: One patient with Parkinson's disease has been evaluated in ON state before and after administration of 5 mg of 4-AP three times daily. Clinical evaluation of gait has been performed using Timed Up and Go Test, Timed 25 Foot Walk, Freezing of Gait Questionnaire, MDS-UPDRS. Objective measures of gait have been collected using wireless sensors attached to ankles (APDM Inc, Portland).

Results: While the velocity of gait and stride length remained overall unchanged, improvements in TUG, freezing of gait and axial UPDRS were significant after 48 hours. The FOG score improved 50 % (from 16 points before 4-AP to 8 points after), axial UPDRS from 10 points to 3, and TUG improved from 16.7 +/-1 to 14.0 +/-0.5. The effects on freezing of gait and axial UPDRS have maintained 4 weeks after initiation of treatment. 4-AP was well tolerated at 5 mg tid with no side effects. Interestingly, besides freezing of gait, festination has improved and this correlated with reduction in the coefficient of variation of stride time, a marker of gait rhythmicity (11.6% +/- 4.6 before treatment, 6.3% +/-0.5 at 48 hours). Given the recent studies that showed the 4-AP improves gait variability in patients with various type of cerebellar disorder we posit that 4-AP can act as a regulator of arrhythmic neuronal networks in PD. Controlled clinical trials are necessary to evaluate the 4-AP effects on gait in patients with PD.

P20.15

Function and expression differences between ergot and non-ergot dopamine D2 agonists on heart valve interstitial cells

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Objective: The symptoms of Parkinson's disease are alleviated by dopamine D2 agonists, which are classified as ergot dopamine D2 agonists and non-ergot dopamine D2 agonists. Among the former, pergolide has been associated with valvular heart disease, since it has serotonin 5-HT2B agonistic properties. We aimed to analyze the function and expression differences between pergolide, an ergot dopamine D2 agonist, and pramipexole, a non-ergot D2 agonist, on heart valve interstitial cells (VICs).

Methods: We procured porcine VICs and analyzed the [³H]thymidine incorporation on them treated with pergolide or pramipexole by using of [³H]thymidine incorporation assay. Moreover, we performed Microarray global analysis on them and validated the varied genes between pergolide and pramipexole by using of Real-time PCR.

Results: We demonstrated that the 5-HT2B receptor was abundantly expressed in porcine VICs. The 5-HT2B receptor agonist pergolide induced an increase in [³H]thymidine incorporation accompanied by a decrease in 5-HT2B receptor mRNA expression. [³H]thymidine incorporation was blocked by lisuride, a 5-HT2B receptor antagonist, and by LY-294002, a specific inhibitor of PI3K and Akt. Moreover, we showed that type 2 iodothionine deiodinase (Dio2) expression in porcine VICs treated with pergolide was markedly increased by global analysis of mRNA compared with that induced by pramipexole. Such changes in VICs may be correlated to the mechanism of heart valve disease pathogenesis.

P20.16

Levodopa bioavailability and variability in plasma concentrations: levodopa-carbidopa intestinal gel infusion versus oral tablets

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Background: Maintaining constant levodopa concentrations is critical for reducing motor complications in Parkinson's disease (PD). Levodopa-Carbidopa Intestinal Gel (LCIG) provides continuous levodopa-carbidopa delivery by infusion through an intrajejunal percutaneous gastrostomy tube.

Objective: Using a population modeling approach, compare levodopa bioavailability and intra-subject variability in plasma concentrations following 16-hour jejunal infusion of LCIG or frequent oral administration of immediate release levodopa-carbidopa tablets (LC-oral) in subjects with advanced PD.

Methods: A nonlinear mixed-effects model of levodopa pharmacokinetics (PK) was developed using serial data from an LCIG Phase 1 PK Study and a Phase 3 12-week double-blind, double-dummy study of the efficacy and safety of LCIG in comparison to LC-oral in advanced PD patients (N=68 included in model development; 45 on LCIG and 23 on LC-oral). The final model was evaluated using stochastic simulations against observed data from the above studies and sparse PK data from 311 subjects with advanced PD evaluated in a 12 month long term safety study of LCIG.

Results: The final levodopa population PK model was a two-compartment model with a transit compartment for absorption, first order elimination, bioavailability for LCIG relative to LC-oral, different first-order transit absorption rate constants (LCIG = 9.2 hr⁻¹ vs LC-oral = 2.4 hr⁻¹) and residual (intra-subject) variability for LCIG versus LC-oral. Levodopa bioavailability was 97% (95% bootstrap confidence interval = 95% to 98%) for LCIG relative to LC-oral. The proportional residual error was 15% for LCIG versus 29% for LC-oral. Standard deviation of the additive residual error in levodopa concentrations was 0.3 µg/mL for LCIG versus 0.59 µg/mL for LC-oral.

Conclusions: Levodopa bioavailability is comparable for LCIG and LC-oral administration. LCIG administration results in approximately half the intra-subject variability in levodopa concentrations observed with LC-oral administration. LCIG is absorbed faster than LC-oral, consistent with direct delivery of LCIG to the jejunum.

P20.17

Lack of association between the intensity of dopaminergic treatment and falls in Parkinson disease

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Objective: To assess the relationship between the potency of dopaminergic treatment and falling in Parkinson disease (PD). Falling is considered a symptom of PD that is not responsive to changes in dopaminergic medications.

Methods: Detailed medication regimens and 4-week diaries recording falls and near falls were collected in 324 PD subjects. Simple and partial correlations were obtained for the following outcomes: Presence or absence of falls; number of falls; number of near-falls; and, number of all events (falls and near-falls). Total daily levodopa equivalent dose (LED), Age, and Disease Duration, were considered as possible predictors. The same analysis was then restricted within the subgroup of PD subjects who experienced falls. Chi-square was used to test relationships. Statistical significance was set at p < .05.

Results: 54% of subjects experienced at least one fall. LED was significantly associated with presence ($p=0.014$) and number of falls ($p=0.032$), and total events ($p=0.033$); Age was associated with number of near falls ($p=0.028$); Disease Duration was associated with presence ($p=0.001$) and number of falls ($p<0.001$), and total number of events ($p=0.018$). When accounting for Disease Duration, LED was no longer a significant predictor for any of the outcomes. When the same analysis was performed in the subgroup of PD subjects with falls, LED was not a significant predictor for any of the outcomes. The intensity of dopaminergic treatment is not associated with the occurrence or frequency of falling in PD.

P20.18

Lack of association between central anticholinesterase treatment and falls in Parkinson disease

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Objective: Cognitive dysfunction is associated with falling in PD. A recent clinical trial indicated that a centrally acting anticholinesterase medication may reduce falling in PD.

Methods: Detailed medication regimens and 4-week diaries recording falls and near falls were collected in 322 PD subjects. Simple and partial correlations were obtained for the following outcomes using chi square statistics: Presence or absence of falls; number of falls; number of near-falls; and, number of all events (falls and near-falls). Use of a centrally acting anticholinesterase agent (donepezil, galantamine, or rivastigmine), Age, Disease Duration, MMSE score, and cognitive dysfunction defined as MMSE<26 were considered as possible predictors. The same analysis was then restricted within the subgroup of PD subjects who experienced falls.

Results: 53.7% of subjects experienced at least one fall, 14.6% were on an anticholinesterase and 21.1% had MMSE scores less than 26. Anticholinesterase treatment, MMSE, and cognitive dysfunction were not significantly associated with presence or number of falls and total events; Age was associated with number of near falls ($p=0.027$); Disease Duration was associated with presence ($P=0.001$) and number of falls ($p<0.001$), and total number of events ($p=0.020$). The lack of association between anticholinesterase treatment and falling persisted after accounting for disease duration and severity of cognitive dysfunction. Concomitant treatment with centrally acting anticholinesterases is not associated with the occurrence or frequency of falling in PD.

P20.19

Antidepressants and falling in Parkinson disease

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Objective: To assess the relationship between the use of antidepressant medications and falling in Parkinson disease (PD). Antidepressant use is associated with falling in the general population and in patients with PD.

Methods: Detailed medication regimens and 4-week diaries recording falls and near falls were collected in 322 PD subjects. Simple and partial correlations were obtained for the following outcomes using chi square statistics: Presence or absence of falls; number of falls; number of near-falls; and, number of all events (falls and near-falls). Use of any antidepressant medication, number of antidepressant medications prescribed, antidepressant category (SSRI or tricyclic), Age, Disease Duration, and cognitive dysfunction defined as MMSE<26 were considered as possible predictors. The same analysis was then restricted within the subgroup of PD subjects who experienced falls.

Results: 53.7% of subjects experienced at least one fall, 40.4% were on an antidepressant, 29.8% on an SSRI, and 3.1% on a tricyclic; 21.1% had MMSE scores less than 26. Antidepressant treatment was not significantly associated with presence or number of falls and total events, with the only exception of tricyclics, which was significantly associated with the presence of falls ($p=0.003$); Age was associated with number of near falls ($p=0.027$); These findings persisted when accounting for disease duration and age, and when the analysis was restricted only to subjects experiencing falls. Among commonly used antidepressants, treatment with tricyclics is associated with the occurrence or frequency of falling in PD.

P20.20

Potential of novel mTOR modulator to treat dyskinesia in a 6-OHDA rat model of Parkinson's disease (PD)

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People with PD who are treated with L-DOPA long-term often develop involuntary movements, i.e. L-DOPA induced dyskinesia (LID). A suggested underpinning of LID is overstimulation of mTOR (mammalian target of rapamycin), a nutrient-regulated serine/threonine kinase. Rapamycin treatment, which results in mTOR inhibition, reduces LID in rodents. Unfortunately, rapamycin has unacceptable side effects rendering it suboptimal for LID treatment. A novel insulin sensitizer (MSDC-0160, approved for clinical testing in diabetes and Alzheimer's disease patients) modifies a mitochondrial complex mTOT (mitochondrial target of thiazolidinedione insulin sensitizers), improving mitochondrial oxidative metabolism and leading to reduced mTOR activation. We hypothesize that MSDC-0160 can reduce mTOR activity in the striatum in a rat model of LID, thereby reducing LID in the absence of side effects. We generated unilateral 6-hydroxydopamine (6-OHDA) lesions in Sprague-Dawley rats by stereotactic injection into the right medial forebrain bundle. Lesioned rats are given L-DOPA daily for 4 weeks to induce L-DOPA-induced abnormal involuntary movements (AIMs) Two groups receive either control chow or chow containing MSDC-0160 (30 mg/kg/day) to assess if MSDC-0160 can mitigate AIMs that have already developed following L-DOPA priming. We are also pre-treating with MSDC-0160 to determine if the initial development of AIMs, can be prevented. At molecular level we determine S6 phosphorylation (to assess activation of mTOR), P-ERK and c-fos, and quantify tyrosine hydroxylase to determine lesion changes. In brief, there is evidence that mTOR over-activation participates in the molecular-cascade that causes LID; thus MSDC-0160 has potential to reduce AIMs. Due to its safe profile in humans, MSDC-0160 could be used to prevent LIDs in PD patients.

P20.21

Non-interventional study of caregivers' and physicians' attitudes to drug administration via a transdermal patch in patients with Parkinson's disease who require caregiver support

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Objective: To provide real-world data on caregiver and physician assessments of advantages/disadvantages of rotigotine transdermal patch versus oral PD medication.

Methods: Cross-sectional, non-interventional study in routine clinical practice in Germany (NCT01330290). Patients had PD with documented need for care, and had received rotigotine as add-on to oral PD treatment for ≥ 1 month (following physician's independent decision to prescribe). Caregivers and physicians assessed rotigotine transdermal patch versus oral PD medications for each patient at a single timepoint using questionnaires comprising questions on: swallowing dysfunction, nausea/vomiting, monitoring therapy, once-daily application, application independently from meals, application to sleeping patients, caregiving efforts (caregivers only) and clinical aspects (physicians only). Each question was assessed on a 5-point scale ranging from -2 (major disadvantage) to 2 (major advantage compared with oral treatment). Multiple patient assessments by one caregiver/physician were averaged to obtain a single response. Primary outcomes were mean total scores of all questions for caregivers and physicians who provided responses for ≥ 4 questions.

Results: Questionnaire responses from 128 caregivers and 41 physicians were documented for 147 of 148 patients. 100 (68%) patients had a caregiving family member (spouse in 72 cases); 36 (24%) were cared for by a nurse in a nursing home. Mean PD duration was 8.2 ± 6.3 years; 136 (93%) patients were additionally taking levodopa. Mean total score of caregivers' questionnaires was 1.32 ± 0.67 and of physicians' questionnaires was 1.46 ± 0.32 . Mean scores for individual questions were in the range 1.03-1.54 for caregivers and 1.15-1.87 for physicians. When given a choice about their rationale to prescribe for each patient, physicians cited the pharmaceutical form (patch) in 139 (95%) cases and the active agent (rotigotine) in 89 (61%) cases.

Conclusions: In the opinions of caregivers and physicians, rotigotine transdermal patch had some major advantages over oral PD medication in everyday life for patients in need of care.

P20.22

Botulinum Toxin treatment for primary and secondary blepharospasm

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Objective: Blepharospasm (BS) is a focal dystonia characterized by involuntary eyelid closure due to spasmodic contractions of ocular muscles. BS can be idiopathic (primary) or secondary to other disorders such as Parkinson's disease (PD). Botulinum toxin type A (BTX-A) is considered the treatment of choice. The objective of this study is to compare the efficacy of BTX-A treatment for patients with primary versus secondary BS associated with PD (with or without DBS).

Methods: 27 consecutive patients [15 males, age: 65.11 ± 13.66 years, disease duration 7.7 ± 8.2], newly or routinely treated by BTX-A were recruited including patients with primary BS (N=10), secondary BS associated with PD (N=6), PD+DBS (N=5), and other various types of BS (N=6). Patients were evaluated before and 4 weeks following BTX-A injections, using the Blepharospasm Disability Scale (BDS), the Blepharospasm Disability Index (BDI), the Jankovic Rating Scale (JRS), the Blepharospasm Movement Scale (BMS), and the Clinical Global Impression of Improvement (CGI-I). Additionally all were recorded on a 5-minute videotape and scored by a blinded rater.

Results: Following the BTX-A injections, our sample as a whole showed a statistically significant improvement in Severity of Illness (1.74 ± 1.27 vs. 2.34 ± 1.05 , $p=0.013$), JRS severity scale Illness (1.37 ± 1.04 vs. 1.96 ± 1.22 , $p=0.0018$), BMS severity scale (4.01 ± 1.27 vs. 5.04 ± 1.79 , $p=0.039$), and the severity rating scale (1.19 ± 0.84 vs. 1.61 ± 0.80 $p=0.013$), with the other outcome measures showing the same improvement trend. 21 patients reported improvement on CGI-I. When these effects were compared by diagnosis group, the best beneficial effect was evident in patients with BS secondary to PD and was maximal for the group of PD patients without DBS demonstrating a significant improvement in Severity of Illness compared to the other two groups. The study conclusion is that BTX-A was an effective treatment for BS. Patients with PD associated BS showed a better response than those with primary BS.

P20.23

Pharmaceutical quality of seven generic Levodopa/Benserazide products compared with original Madopar® / Prolopa®

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Objective: To compare the pharmaceutical quality of seven generic levodopa/benserazide combination products marketed in Germany with the original product (Madopar® / Prolopa® 125, Roche, Switzerland).

Introduction: Madopar® / Prolopa® is a combination of levodopa (L-Dopa) and benserazide. Generics assume the same pharmaceutical characteristics as the reference product.

Materials: Madopar® / Prolopa® 125 tablets and capsules were used as reference materials. The generic products tested (all 100mg/25mg formulations) included four tablet formulations (Betapharm, CT, MYLAN and ratiopharm) and three capsulated formulations (HEXAL, STADapharm and TEVA).

Methods: Shape, colour, appearance and hardness (tablets) or surface, colour, imprint and content (capsules); mass (tablets) or fill-mass (capsules); content, degradation products, disintegration and dissolution were tested.

Results: For all seven generic products at least one of the tested parameters fell outside specifications. Content requirements were unmet by two tablet formulations for L-Dopa (specs: 100mg $\pm 5\%$; test results: -5.6% and -7.6%) and for benserazide (specs: 28.5mg $\pm 5\%$; -6.6% and +8.4%). Average mass (specs: 275mg $\pm 3\%$) was not reached for two tablet formulations (+3.3%), and average fill mass (specs: 150mg $\pm 5\%$) was not reached for three capsule formulations (+48.2%, +99.1%, +99.3%).

Conclusions: All seven analysed generic L-Dopa/benserazide products exhibited at least one deviation. Deviations for the active ingredients ranged from +8.4% (benserazide) to -7.6% (L-Dopa) in two tablet products, with potential clinical consequences. Furthermore, two of the degradation products were 26.5% above standard. These results should lead to caution when prescribing a generic of Madopar® / Prolopa®, and also invite further investigations, both pharmaceutical and clinical.

P20.24

Non-interventional study of the switch from oral treatment to rotigotine transdermal patch in patients with Parkinson's disease and gastrointestinal symptomsDirk Woitalla¹, Jan KassubeK², Lars Timmermann³, Thomas Lauterbach⁴, Reinhard Berkels⁴, Frank Grieger⁴, Thomas Müller⁵¹St Josef-Hospital Universitätsklinik, Bochum, Germany²Universität Ulm, Ulm, Germany³Universität zu Köln, Cologne, Germany⁴UCB Pharma, Monheim am Rhein, Germany⁵St Joseph-Krankenhaus Berlin-Weißensee, Berlin, Germany

Background: Gastrointestinal (GI) symptoms are common among patients with Parkinson's disease (PD), significantly affecting quality of life. Transdermal systems of drug administration bypass the GI tract and may result in fewer GI problems.

Objective: We investigated the effect of switching from oral PD medications to transdermal dopaminergic therapy in patients with PD and GI symptoms in daily practice.

Methods: This observational study was conducted in a routine clinical practice setting in Germany (ClinicalTrials.gov: NCT01159691). Patients presenting with GI symptoms (heartburn, bloating, nausea, vomiting, abdominal pain, diarrhoea) and receiving oral PD drug treatment were switched to rotigotine transdermal patch based on the independent decision of their physician. Effectiveness was assessed using a visual analogue scale that measured intensity of GI symptoms from 0 (no disorder) to 100 mm (extremely severe disorder) and questions on the frequency and intensity of individual GI complaints, as well as patient satisfaction regarding GI symptoms over approximately 6 weeks after switching.

Results: Of 65 patients with baseline and follow-up data, 58 had follow-up data available for final analysis. Intensity of GI complaints improved on the visual analogue scale from an average of 47.5 mm at baseline to 19.7 mm after ~6 weeks. At baseline, heartburn was reported by 39 of 65 patients, bloating by 37/65, nausea by 38/65, vomiting by 8/65, abdominal pain by 31/65, and diarrhoea by 10/65. Fewer patients reported individual GI symptoms after ~6 weeks: heartburn 12/58, bloating 12/58, nausea 10/58, vomiting 1/58, abdominal pain 9/58, and diarrhoea 2/58. Fifty of 58 patients who completed the "assessment of satisfaction referring to GI complaints" after ~6 weeks were "Satisfied" or "Very satisfied".

Conclusion: This study suggests that a switch from oral PD medication to rotigotine transdermal patch may improve existing GI symptoms among patients with PD. Additional studies are needed to confirm this finding.

CLINICAL SCIENCES: SURGICAL THERPAY, INCLUDING CELL AND GENE THERAPY

P21.01

Chromospheres: a new source for cell replacement therapy in Parkinson's diseaseAlejandra Boronjat-García¹, Paulina Montoya-Guerrero¹, Arturo Hernández-Cruz¹, Magdalena Guerra-Crespo¹, Diana Millán-Aldaco¹, Marcela Palomero-Rivero¹, Monika Enhart-Bornstein², René Drucker-Colin¹¹Universidad Nacional Autónoma de México, Instituto de Fisiología Celular, Mexico City, Mexico²Technische Universität Dresden, University Hospital Carl Gustav Carus, Dresden, Germany

Objective: Mammalian chromaffin cells located in the adrenal medulla synthesize and release dopamine (DA) as well as other neurotransmitters. Due to their neuronal properties, chromaffin cells have been used as a source for cell replacement therapy in Parkinson's disease (PD). However, despite more than 20 years of extensive effort, such cells have not yielded the expected results, mostly because differentiated chromaffin cells have been unable to reach the long-term survival required to treat this neurodegenerative disorder. Recently, Enhart-Bornstein and coworkers (2009) isolated chromaffin progenitor cells (CPC) from bovine and human adult adrenal medulla. These progenitor cells share significant properties with neural stem cells as its self-renewal capacity and the ability to form clonal secondary spheres, named chromospheres. *In vitro*, 21% of CPC are able to differentiate into dopaminergic (DA) neurons. This percentage increases to 46% in the presence of retinoic and ascorbic acids. In our laboratory, we have been studying the potential of these cells to differentiate *in vivo* as well as their functional integration capacity in a rat model of PD.

Methods: In order to form chromospheres, CPC were isolated from adult bovine adrenal medulla and cultured in low-attachment conditions in presence of fibroblast growth factor-2. Chromospheres were transplanted into the striatum of 6-hydroxydopamine-lesioned rats.

Results: We found by immunofluorescence assays that these grafted precursors cells were capable to survive and differentiate into DA neurons. Moreover, we observed a gradual and sustained behavioral improvement of dopamine-mediated motor asymmetry (induced by apomorphine and amphetamine) and motor coordination, as evaluated with the beam test. Together, our results suggest that chromospheres obtained from adult tissue can be a potential source for autologous cell replacement therapy in PD.

P21.02

Case report: transplantation of fetal porcine ventral mesencephalic cells (FPVMC) for Parkinson's disease (PD): long term results and pathologySamuel Elias¹, Jeffrey H. Kordover²¹Boston University Medical Center, Boston, MA, USA²Rush University Medical Center, Chicago, IL, USA

Objective: To study the long-term efficacy and pathology of unilateral transplantation of FPVMC in PD.

Background: An open-label 1 year study of unilateral FPVMC in PD reported 3 of 12 patients with excellent response. Six patients received chronic cyclosporine (CyA), 6 received FPVMC pretreated with an F(ab')₂ antibody fragment directed against MHC class I. No patients developed off-medicine dyskinesia. (Neurology 2000;54:1042-1050). Subsequently, a double-blind placebo-controlled trial with bilateral transplantation of FPVMC using only CyA did not show clinical efficacy. In both studies ¹⁸F-fluoro-L-DOPA PET was unchanged and no porcine endogenous retrovirus was detected. Here, results of an F(ab')₂ patient are presented with 15 year follow up.

Methods: UPDRS and timed motor tests were performed according to a CAPIT protocol with videotaping. Testing for Parkin and PINK1 was conducted. Immunohistological investigation was done at autopsy.

Results: Pre-surgery, gait freezing and dyskinesia were troublesome and patient could not walk during off-periods. Surgery was performed at age 47 (PD duration-18 years, Off UPDRS/H&Y-90/4.0). By 3-6 months post-surgery there was no gait freezing or wearing-off. Levodopa was reduced from 700 to 500mg/d. Twelve hours off-medicine scores improved for bilateral arm movements and stand-walk-sit test. UPDRS/UPDRS III at (presurgery, 3 mo, 3 yr, 7.5 yr, 9 yr.) were respectively (90/26, 51/31, 54/27, 54/29, 61/36). On-medicine UPDRS/UPDRS III scores were: (35/17, 22/16,

17/4, 28/13, 31/13). At 9-15 years Ldopa dyskinesia gradually increased, and balance and gait stability decreased. Tests for Parkin/PINK1 were negative. Pathology was consistent with PD. No viable cells were observed with TH or a porcine specific marker. Hence, a patient with pathology proven PD given unilateral transplantation of FPVM cells with an F(ab')₂ antibody fragment had long term efficacy without side effects. [Some clinical results were presented previously at the 2006 International Congress of Movement Disorders, Kyoto, Japan]

P21.03

Effects of bilateral STN-DBS on non-motor and axial symptoms in patients with Parkinson's disease

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Introduction: Studies have shown that bilateral deep brain stimulation of the subthalamic nucleus (STN-DBS) is associated with improvements of Parkinson's disease (PD) motor disability and levodopa-related complications. Controversy remains however with regard to the effects of bilateral STN-DBS on non-motor and axial symptoms associated with PD.

Methods: Ten patients with PD were evaluated in the ON-medication state both pre- and post-surgically using tests and scales measuring axial (gait, balance and speech) and non-motor features (mental status, word fluency, sleep-related problems, mood, fatigue and quality of life). Measures of caregiver/family burden and patients' subjective experience of change were also documented. Patient demographics and motor characteristics are summarized in Table 1. The Wilcoxon signed-rank test was performed to compare pre-surgical to post-surgical within group differences. P values are 2-sided and were calculated at the 0.05 significance level.

Results: With a mean post-surgical follow-up period of 48.9 weeks, we analysed data for 10 patients with PD treated with bilateral STN-DBS. Results for axial tests are shown in Table 2 and Table 3 summarizes scores for non-motor symptoms.

Discussion: Our initial findings reveal a mild but significant decrease in balance while an amelioration of depressive symptoms was observed following bilateral STN-DBS. Results on all other axial and non-motor features measured in this study as well as results for caregiver burden did not reveal significant changes following surgery. Approximately one year after surgery, the average subjective patient response concerning changes following surgery was "Better, and a definite improvement that has made a real and worthwhile difference."

P21.04

Long-term safety considerations of deep brain stimulation in treatment of Parkinson's disease

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Introduction: In the last two decades, DBS became a standard intervention for treatment of advanced Parkinson's disease.

Moreover, indications for DBS in PD continue to extend, since DBS showed benefits compared to medical treatment for patients with early motor complications. Although, DBS is usually considered a pretty safe procedure, it could be related to different complications that worsen the general effect of therapy.

Objective: To evaluate the safety of DBS therapy in PD patients in a single functional neurosurgery centre.

Methods: 129 PD patients underwent surgery for continuous high-frequency DBS between 2002 and 2013: 99 received DBS of subthalamic nucleus, 15 had DBS of globus pallidus internus, and 15 had DBS of ventrointermediate nucleus of thalamus. Mean age at surgery was 54.6±0.8 years (range 25–72). Follow-up duration ranged from 6 months to 10 years. We performed the detailed assessment of complications encountered.

Results: In all patients, 300 electrodes were implanted: 222 targeted in STN, 35 in GPi, and 43 in Vim. Among hardware-related complications, electrode or connector fractures (4 cases) and migration of pulse generator (4) were observed. There was an evidence of unexpected IPG end-of-service (1). Surgery-related infections occurred in 5 patients. Two cases of symptomatic cerebral hemorrhage (0.7%) were registered. In 2 patients, intraoperative seizures occurred. To optimize the clinical effect, correction of electrode position was required in 25 cases. The prevailing adverse effect of DBS was dysarthria (15 patients, 8.5%). In 2 cases, DBS-components were permanently explanted due to different reasons. Four patients died from the unrelated causes in prolonged follow-up. 37 patients underwent pulse generator replacement (totally, 53 IPG).

Conclusion: DBS therapy seems to be rather safe for treatment of PD patients. The overall rate of persisted surgery-related disability is definitely low. At the same time, unpredictable technical and stimulation-related complications might be a challenge.

P21.05

Intraoperative subthalamic microelectrode recording for deep brain stimulation in Parkinson's disease

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Introduction: For successful DBS in Parkinson's disease, accurate placement of electrodes into sensorimotor part of subthalamic nucleus is essential. Microelectrode recording (MER) of specific neuronal firing became a widespread technique for precise targeting the basal nuclei during stereotactic surgery for movement disorders, particularly PD. However, MER is associated with the higher operative risks and costs.

Objective: To assess the role of MER for STN-DBS in PD patients.

Methods: In the last 5 years, 75 PD patients were operated for continuous high-frequency STN-DBS in Burdenko NSI: 47 without intraoperative MER (98 electrodes implanted) and 28 using MER (56 electrodes). Disease duration was 12.3±3.9 years, PD severity, 3–4, according to Hoehn&Yahr, age at surgery – 54.0±8.8 years, without significant difference between two groups. Analysis of intraoperative strategy and related complications was performed.

Results: In patients without MER, central MRI-calculated trajectory was used for the final electrode placement in 96%. Implantation depth adjustments were made for 9% of electrodes. Stereotactic correction of electrode position in early or long-term follow-up was needed in 6 patients. Stimulation-induced dysarthria occurred in 8 patients (10.7%). In patients with intraoperative MER, 1 to 5 microelectrodes were used per one side, mean 2.3(±0.9). Image-based tracks corresponded the best neurophysiologically defined

trajectory only in 68%. For implantation of 21% of electrodes, medial track was chosen and in 7%, lateral one. Additional correction in placement by depth was necessary in 77% of implantations (range - 3.0–1.5mm). No electrode replacement was required postoperatively and only 1 case (3.6%) of stimulation-related dysarthria was noticed. In one case, symptomatic intracranial hemorrhage from meningeal vessels occurred.

Conclusion: MER serves to improve the accuracy, optimize the placement of electrodes, and reduce side effects in STN-DBS. Nevertheless, direct impact of MER on clinical outcome is unclear and needs to be verified in long-term follow-up studies in larger population.

P21.06

Weight modifying effect of deep brain stimulation: results of a case-control study

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Objective: Deep brain stimulation (DBS) is a well-recognized treatment for Parkinson's disease (PD). Weight gain has been consistently reported following DBS of a variety of subcortical nuclei in PD.

Methods: A case-control study of PD patients undergoing DBS of the subthalamic nucleus (STN) and a control group of age, gender, and diagnosis-matched controls who did not undergo DBS was performed. Demographic data, baseline and follow up weights, and body mass index were collected. Pre- and post-operative Unified Parkinson's Disease Rating Scale (UPDRS) scores and levodopa equivalent dose (LED) were collected at baseline and 6 months postoperatively. Descriptive statistics were calculated for the population. For binary variables, chi square and Fisher's exact test were used, and for continuous variables, t-tests were used to determine significance of weight change at follow up and over time.

Results: Thirty-five cases were identified and matched to 34 controls. Cases had a significantly longer duration of diagnosis than controls (10.3 vs 5.76, respectively, $p=0.0015$). Cases and controls had similar baseline weights (80.4 vs 80.4 kg, respectively, $p=0.99$). Cases gained an average of 2.9 kg while controls lost an average of 1.8 kg ($p=0.02$) over a mean follow up of 634 vs 645 days ($p=0.85$). At baseline, 63% of cases and 77% of controls were overweight (BMI>25) while at follow up 69% and 56% were overweight, respectively. Confirming surgical efficacy, UPDRS scores improved by an average of 21 points and LED by 157 points. While not statistically significant, patients who underwent bilateral lead implantation gained 3.4 kg compared to only 1.7 kg with unilateral implantation ($p=0.62$).

Conclusion: DBS has a weight modifying effect on PD patients undergoing STN stimulation compared to age, gender, and diagnosis-matched controls. Whether this owes to increased food intake, lowered metabolic demands, improved motor complications, or other etiology is unclear.

P21.07

Stereotactic neurosurgery for Parkinson's disease in a world perspective: results from the WSSFN-supported survey

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Objective: Most studies in the field of neurosurgical treatment of movement disorders have been published by a small number of leading centers in developed countries. This study aimed to investigate the clinical practice of stereotactic neurosurgery for PD worldwide.

Methods: Neurosurgeons were contacted via email to participate in a worldwide survey. The results obtained are presented in order of the countries' economical development according to the World Bank, as well as by the source of financial support.

Results: A total of 353 neurosurgeons from 51 countries who operated on 13,200 patients in 2009 were surveyed. Surgical procedures performed in high-income countries were more commonly financed by a public health-care system. In contrast, patients frequently financed surgeries themselves in lower-middle and upper-middle income countries and lesions were most commonly performed. Unexpectedly, ablative surgery is still used by about 70% of neurosurgeons, regardless of their country's economic status. This study provides a previously unavailable picture of the surgical aspects of PD across the globe in relation to health economics and socio-demographic factors. Global educational and training programs are warranted to raise awareness of economically viable surgical options for PD that could be adopted by public health-care systems in lower income countries.

P21.08

Modulation of glutamate receptors in dyskinetic MPTP monkeys receiving a unilateral subthalamicotomy

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Objective: Subthalamicotomy is a surgical option to alleviate disabling L-DOPA-induced dyskinesias (LID) in parkinsonian patients. Despite the fact that this surgery is known to reduce LID, the mechanisms remain largely unknown. The subthalamic nucleus is the sole glutamatergic nucleus within the basal ganglia and its lesion may exert changes in the expression of glutamate receptors.

Methods: AMPA, NMDA (containing NR1/NR2B), mGlu2/3 and mGlu5 receptors were investigated using receptor binding autoradiography in four MPTP monkeys displaying LID that underwent unilateral subthalamicotomy and were compared to four controls and four L-DOPA-naïve MPTP monkeys.

Results: Behaviorally, subthalamicotomy allowed a 40% reduction of the L-DOPA dose for a similar antiparkinsonian response as before the lesion, but was associated with higher LID. Increases induced by MPTP in AMPA receptors in the dorsal putamen and ventrolateral caudate nucleus returned to normal values with L-DOPA and subthalamicotomy. AMPA receptors were reduced by subthalamicotomy in the ventral putamen compared to controls. Striatal and pallidal NMDA receptors remained unchanged, except for the ventrolateral putamen which decreased after MPTP, L-DOPA and subthalamicotomy. Striatal and pallidal mGlu2/3 receptors were found to be highly decreased in the L-DOPA-treated MPTP-monkeys that underwent subthalamicotomy compared to controls and L-DOPA-naïve MPTP-monkeys, whereas mGlu5 receptor displayed

an opposite pattern and increased in the same brain regions. In the caudate nucleus of MPTP monkeys receiving L-DOPA and a subthalamotomy, increases in NMDA and mGlu5 receptors correlated with higher dyskinesia and putaminal increases in NMDA receptors correlated with a better motor response to L-DOPA. Pallidal decreases in mGlu2/3 receptors correlated with a better improvement in motor response and lower dyskinesia. Decreases in mGlu2/3 receptors and increases in mGlu5 receptors observed in the basal ganglia may be the result of the subthalamic lesion and L-DOPA. These changes could participate in the alleviation of parkinsonian symptoms and LID after subthalamotomy.

P21.09

Usefulness of the personality assessment inventory in the patient evaluation process for deep brain stimulation surgery in Parkinson's disease

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Objective: Selection of patients appropriate for deep brain stimulation (DBS) for Parkinson's disease (PD) is focused on the likelihood of improvement of motor symptoms, yet concern remains about the possibility of emerging behavioral symptoms following DBS surgery. There is general consensus that thorough pre-operative assessment of non-motor symptoms is needed but little agreement on which methods are most practical and informative. A few studies have used validated scales of non-motor symptoms; none has focused on the use of scales of personality and psychopathology. This study will evaluate the use of the Personality Assessment Inventory (PAI), a self administered and validated scale of personality and psychopathology, in patients with PD undergoing DBS evaluation. The PAI is a questionnaire with 22 separate, non-overlapping scales including clinical, treatment, interpersonal and validity scales. The purpose of this pilot study is to evaluate the usefulness of the PAI in the DBS evaluation process, quantify personality and psychopathology in this population, and evaluate possible effects of DBS on personality as measured by this tool.

Methods: The PAI was administered to PD patients undergoing DBS evaluation and 6 months post surgery. Results were compared to PDQ39, QUIP-RS and UPDRS I-IV scores. PAI results were discussed in interdisciplinary DBS team conference and compared to clinical assessment by the health care providers on the team.

Results: PAI scores were completed for 7 patients undergoing DBS evaluation. The most notable results are elevated scores for somatization (mean: 65.6 range: 48-79) and depression (mean: 62 range: 42-98). The mean scores for all other subscales, including positive and negative impression management, fell in the normal range. There were abnormal values in individual patients, and in one patient high scores on the depression subscale led to further psychiatric and social work evaluation before surgery was performed.

P21.10

Effects of low-frequency deep brain stimulation of the subthalamic nucleus or globus pallidus internus on gait in Parkinson's disease

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Objective: Gait difficulties in Parkinson's disease (PD), especially freezing of gait (FoG) in later stages of the disease does not

respond well to pharmacological treatment and high-frequency (HF) deep brain stimulation (DBS) of subthalamic nucleus (STN) or globus pallidus internus (GPI). Recent studies indicate that low-frequency (LF) stimulation of these structures may improve gait and FoG. We are quantitatively examining the effects of changing frequency of stimulation of these structures on gait in PD.

Methods: In this ongoing study, four PD patients (two with STN-DBS and two with GPI-DBS) have been recruited and examined so far. On the day of evaluation, the subjects were first tested in their usual high frequency DBS setting (HF) and Med-off condition (12-hours or more after the last dose of PD medications). They were reevaluated twice at Med-off, DBS-80 Hz (Intermediate frequency (IF)) and Med-off, DBS-30 Hz (low frequency (LF)) after random selection of the sequence of these conditions, with a minimum of 30 minute wait after changing stimulation frequency. Several quantitative gait indices and motor part of the Unified Parkinson's Disease Rating Scale (MDS-UPDRS) were obtained in each condition.

Results: Two of the four subjects (one with STN-DBS and one with GPI-DBS) showed improvements in gait in the IF condition when compared to HF condition. The gait velocity, double support duration, and stride-time variability improved in these two subjects at IF condition compared to LF and HF conditions. The subject with GPI-DBS who exhibited above mentioned improvements also showed increased cadence and swing time duration. Generally, gait worsened at LF condition when compared to IF and HF conditions. These preliminary results indicate that IF stimulation of STN or GPI can improve gait in PD and will be confirmed by including more subjects.

P21.11

Review of published outcomes of subthalamic nucleus deep brain stimulation (DBS) in Parkinson disease supports hypothesis of disease-modifying effect of DBS

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Objective: To conduct a systematic review of literature regarding outcomes of Subthalamic Nucleus (STN) Deep Brain Stimulation (DBS) in Parkinson disease (PD) in order to: 1) examine the long-term effects of STN DBS on the progression of motor disability, measured by Unified Parkinson Disease Rating Scale motor subscore (UPDRS-III) off treatment (Off medication, Off stimulation); and 2) compare the rate of progression with estimated expected natural progression.

Methods: An extensive PubMed search of literature published between 1998 and 2012 was conducted using the key terms: DBS, STN, neurostimulation, and PD. Included in the analysis were the publications reporting bilateral STN DBS outcomes, UPDRS-III off treatment before and after DBS implantation, and a minimum one year follow-up. The rate of natural decline of motor symptoms was defined, based on previously reported placebo controlled clinical trials, as an annual increase in the UPDRS-III of 5 points.

Results: 38 articles matched the search criteria and were included in the analysis. The number of subjects per study varied from 5 to 103, the total number was 1,341. The maximum follow up time was 11.7 years. The majority of studies demonstrated unchanged UPDRS-III scores, some demonstrated improvement. In studies that reported worsening, the annualized change was lower than expected from natural progression. On average, no significant change in UPDRS-III was observed in DBS treated patients. This finding is remarkable for an otherwise progressive

neurodegenerative disorder and supports the notion that chronic STN DBS results in persistent electrophysiological, neurochemical, and synaptic changes in the brain, known as neuromodulation.

P21.12

A Gene Therapy for Parkinson's disease – modifying ProSavin® to increase specific activity

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Objective: Oral dopaminergic treatments have remained the primary standard of care for Parkinson's disease (PD) for the last 40 years. Although these are highly efficacious in the early stages of disease, over time they lead to debilitating long term side effects that seriously impact on the quality of life and restrict the longevity of such treatment. The severity of PD, the lack of a cure and the limited long term effectiveness of current therapies strengthen the need of novel therapeutic approaches.

Methods: We have developed a lentiviral vector (ProSavin®) derived from the equine infectious anaemia virus (EIAV) expressing the three key dopamine biosynthetic enzymes (tyrosine hydroxylase, aromatic L-amino acid decarboxylase and GTP cyclohydrolase-1). Clinical evaluation of the safety and efficacy of ProSavin® in mid to late stage PD patients is currently ongoing in fifteen patients in three dose cohorts. There have been no serious adverse events related to ProSavin® or the administration procedure and no severe immunological responses. In terms of efficacy, an improvement in the primary endpoint, UPDRS Part III, has been observed.

Results: In order to support further dose optimisation we sought to increase the specific activity of the vector in order to increase the production of dopamine. By refining the gene expression cassette for the three genes we were able to increase dopamine production significantly. This construct is being evaluated in vitro in primary neuronal cells and in the MPTP NHP animal model of PD and results will be presented.

P21.13

Lower urinary tract Interventions in Parkinson's disease: The Indian experience at KDAH

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Objective: Recognition of bothersome and progressive urinary complaints by patients in Parkinson's disease (PD) helps a clinician to make changes in his fast deteriorating urinary health. It affects the quality of life with bothersome obstructive and irritative voiding symptoms in such physically challenged individuals. Stabilisation of lower tract symptoms in the long run is a management challenge in view of ever changing presentation with age and state of disease.

Methods: The Neuro-urology team recognized patients with secure neurological diagnosis of PD referred with persistent and disabling urinary symptoms and evaluated the same with symptom score, Uroflowmetry and Urodynamics, then categorized and managed as A. Watchful waiting with combination pharmacological therapy B. Active intervention. 62 patients

Interventions undertaken were cystoscopy- urethral dilatation, Cystoscopy- Botulinum toxin intravesical injection, Transurethral resection of prostate (TURP) and Botulinum toxin intrasphincteric injection as indicated

Results: 38 patients ranging in age from 51 to 77 years underwent TURP, 10 patients (males- 9, females- 5) with refractory detrusor hyperreflexia underwent Intravesical botulinum toxin injection, 12 underwent Intrasphincteric botulinum toxin therapy. 2 female patients underwent urethral dilatation along with anticholinergics. Repeat injections were considered in all except when they reverted to catheter in view of the progressive disease and refractory bladder state.

Conclusions: All patients tolerated TURP well; Four patients were placed on catheter after surgery in view of gross urgency and urge incontinence and treated with prolonged anticholinergics with minimal benefit. No patients developed urinary incontinence after transurethral resection of prostate. Thirty one patients post-TURP status showed satisfactory flow and continence at median follow up of 6 months. Patients on medical management were followed closely with stable results. Three patients with progressive PD had recurrence necessitating finally requiring suprapubic cystostomy. Thus, carefully planned interventions in Parkinson's disease go a long way in maintaining urinary health.

P21.14

Botulinum Toxin is the Final answer in refractory Neurogenic Overactive bladder and Sphincter dyssnergia in Parkinsonism: Kokilaben hospital Experience

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Objective: Gross neurogenic overactive bladder symptoms associated with Parkinson's disease and progressive obstructive voiding resulting directly from detrusor external sphincter dyssnergia are two most debilitating and refractory urinary symptoms that have no satisfactory medical management till date. Use of Botulinum toxin in carefully chosen and diagnosed cases go a long way in relieving symptoms and treating these difficult situations.

Methods: All 22 patients with above debilitating symptoms underwent urodynamics studies. Group 1 (10pts)-Neurogenic overactive bladder group were treated with Intravesical botulinum toxin 200IU injected in the bladder wall spread across the bladder dome, lateral and posterior walls by cystoscopy route. Group 2 (12pts)- Detrusor external sphincter dyssnergia group with obstructive voiding under Intrasphincteric Botulinum toxin injection 150 IU under cystoscopic guidance. All patients were observed with overnight admissions as institute protocol. They were prepared with pre and post intervention urine cultures towards beneficial effects thus decreasing morbidity from any urinary infections. All patients were chosen for a second session of therapy after 6-9 months or on return of symptoms which ever was earlier.

Results: All patients reported vastly improved quality of life after Botulinum toxin therapy in both subgroups. The neurogenic overactive bladder group showed significant improvement in all domains of frequency, urgency and urge incontinence without any change in nocturia. The dyssnergia group had improved obstructive voiding commencing third week that was sustained between 4-6 months as proven by repeat urodynamics studies. The two groups being completely refractory to any oral medications were vastly benefited with the above intervention and improved quality of life in face of progressive Parkinson's disease.

P21.15

Social support and motor outcomes after deep brain stimulation in patients with Parkinson disease

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Objective: Levodopa response is the only known predictor of motor outcome after deep brain stimulation (DBS) surgery in Parkinson disease (PD). We have anecdotally observed that PD patients with better social support seem to have more favorable motor outcomes after DBS. The Social Provisions Scale (SPS) examines the amount of social support that a patient perceives. We examined whether baseline SPS scores were associated with motor outcomes after DBS in PD.

Methods: We performed a retrospective data analysis of 15 PD patients (10M/5F) undergoing bilateral subthalamic nucleus DBS who had completed the SPS prior to surgery (baseline) and approximately six months following initial programming and compared them to their MDS-UPDRS motor scores.

Results: There was no change in total SPS score at 6 months, but the SPS reliability alliance subscale (which measures the reliability of someone's social support network) worsened after surgery (15.4 ± 1.2 at baseline vs. 14.5 ± 1.8 at 6 months, $p=0.05$). The MDS-UPDRS motor score improved by 38% with stimulation (43.3 ± 10.8 at baseline vs. 26.9 ± 9.3 at six months, $p=0.001$), but there was no correlation between baseline SPS scores and change in MDS-UPDRS motor score. Overall, baseline social support does not correlate with DBS motor outcomes; however, one measure of social support worsened after DBS. There are often numerous visits after DBS surgery for stimulation adjustments, which may stress a patient's support network. Though we hypothesized that social support would affect DBS outcomes, it seems that DBS may instead affect social support.

demographics and clinical data, we assessed patients with the Unified Parkinson's Disease Rating Scale (activities of daily living and motor sections), Freezing of Gait Questionnaire (FOG-Q) and Activities-Specific Balance Confidence Scale (ABC). Subjects were classified as freezers if they scored one or more on the FOG-Q, item three. Mann-Whitney and Pearson Chi-Square tests were performed. Results are shown as median (Q1; Q3).

Results: The sample had a median age of 70 years and 60 subjects (58.3%) were male. Forty-one (39.8%) subjects were classified as freezers. Freezers had longer disease duration, and increased disease severity and functional limitations ($p \leq 0.001$). Median score on the ABC for freezers was 60 (31.87; 82.19); for non-freezers median score was 75.94 (49.22; 93.12) ($p=0.017$). Median scores were significantly lower for freezers on items: walking around the house, reaching on tiptoes, standing on chair to reach, sweeping the floor, walking across a parking lot/in the mall/being bumped/on a slippery surface ($p \leq 0.037$). We found borderline p value for the following tasks: walking outside ($p=0.071$), walking down/up a ramp ($p=0.086$) and riding an escalator without holding the rail ($p=0.062$).

Conclusions: Our data suggest that freezers have lower self-perceived balance confidence on tasks that are more challenging to their postural control and that have been described as likely to elicit FOG. These results suggest that people with PD who freeze know when they are at risk of falling, and support the validity of the self-report ABC scale for measuring fear of falling in this group.

P22.02

Associations of freezing of gait with fear of falling and falls in people with Parkinson's disease

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Objective: To examine associations of freezing of gait (FOG) and clinical characteristics, fear of falling and falls in people with Parkinson's disease (PD); and to identify the correlation between FOG and fear of falling.

Methods: Eighty-four patients with PD and independent walking ability were evaluated during the "on" phase of the medication cycle. Exclusion criteria were cognitive impairment (assessed by the Mini-Mental Status Examination), presence of neurological conditions other than PD, and visual disturbance. Demographics and clinical data were gathered and individuals were assessed with the modified Hoehn and Yahr scale, Freezing of Gait Questionnaire (FOG-Q) and Falls Efficacy Scale-International (FES-I). The FES-I is useful to assess concern about falling while performing certain activities of daily living, with possible scores ranging from 16 to 64 points, and higher scores reflecting more fear of falling. Subjects were classified as freezers if they scored one or more on the FOG-Q, item three. The Mann-Whitney and the Pearson Chi-Square tests were used to identify associations and the Spearman correlation was performed.

Results: The overall sample had a median age of 70 years. Thirty-two patients (38.1%) were classified as freezers. Freezers had longer disease duration, increased disease severity and higher levodopa equivalent dose ($p \leq 0.018$). Motor fluctuations were also associated with FOG ($p=0.004$). The median FES-I score was 39 points for freezers versus 27 points for non-freezers ($p < 0.001$). Among freezers, 13 (40.6%) had a history of two or more falls in the preceding 12 months, while among non-freezers six (11.5%) reported recurrent falls in the last year ($p=0.002$). A moderate correlation was found between the FOG-Q and FES-I ($r=0.58$; $p < 0.001$).

CLINICAL SCIENCES: REHABILITATION SCIENCES (PT, OT, SLP)

P22.01

Impact of freezing of gait on self-perceived balance confidence for functional activities in people with Parkinson's disease

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Objective: To identify associations of freezing of gait (FOG) and fear of falling in people with Parkinson's disease (PD); and to compare self-perceived balance confidence between patients with and without FOG.

Methods: One hundred and three subjects in two countries with a diagnosis of PD were included in this study. In addition to collecting

Conclusions: Our data suggest that freezers have more advanced disease and degree of fear of falling. These clinical aspects have been found to be important risk factors for falls in people with PD.

P22.03

Comparison of the effects of exercise programs conducted at home or hospital Parkinson's disease patients

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Purpose: This study compares the effects of home exercises and those of exercises performed with a physiotherapist on the functionality, balance, walking and severity of the disease in Parkinson's patients.

Methods: This study included 21 patients followed in the Movement Disorders Clinic of Neurology Department of Dokuz Eylul University Hospital. The patients were divided into two groups: those attending a 3-day exercise program in the hospital (n=10) and those who regularly exercised at home (n: 11). The exercise program took 45-60 minutes, 3 days a week for a period of 10 weeks. The stages of the disease were evaluated with the Modified Hoehn-Yahr Scale and the severity of the disease with the Unified Parkinson's disease Rating Scale (UPDRS). The static and dynamic balance was evaluated with Berg Balance Scale (BBS) and Functional Reach Test (FRT), functionality with (Time up-go test (TUG), turning in bed, from lying to sitting position, from sitting to standing position, 5-repetition sit-to-stand) and walking with the dynamic walking index.

Results: The pre-exercise scores for UPDRS part I, II (activities of daily living) and III (motor examination), all functionality tests (except for TUG), walking, and balance significantly improved after the hospital exercise program (p<0.05). In the home-exercise group, after the exercise program, part II scores of UPDRS, some functionality and balance tests (from sitting to standing position, FRT) improved (p<0.05). The comparison of the two groups revealed that scores for walking, some functionality tests and BBS were better in the hospital group.

Conclusion: Balance, walking and some functionality scores in the hospital group were better than those in the home group were. However, the patients' balance, functionality and UPDRS scores improved with exercise in both groups. Therefore, we think that medical treatments should be accompanied with exercise programs when Parkinson's patients are treated.

Key Words: Parkinson's disease, Exercise, Functionality, Balance

P22.04

Can singing be a treatment option for speech and language therapists?

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Objective: Previous research data inspired Parkinson's UK Derby branch and a specialist Speech and Language Therapist (SLT) to set up a singing group for local people. The scope of this group was to be therapeutic and prove that singing can benefit people with Parkinson's disease, evaluate how it benefits and view the impact it has on people at different stages of Parkinson's Disease.

Method: A working party established an initial 10-week trial (April-June 2012) followed by weekly singing sessions from September 2012 to the present day. The style and approach of the musical director was evaluated, as was the seating arrangements and the music choice. The group participants were between 60-70 years of age, with British origin. All 12 individuals who completed a pre and post evaluation form were under the care of the specialist SLT. 50% of the evaluated group could be considered to be in the 'maintenance' phase of Parkinson's disease and the other 50% in the 'complex' phase.

Results: The data collected provides strong support for the socio-emotional benefits of singing as a form of therapy. The difficulty lies in generalising the vocal gains from this therapy into everyday talking situations. This would be the primary aim for an NHS Speech and Language Therapist. Unfortunately, the information obtained so far has shown that intelligibility in conversation is not affected by attending a singing group. Clinically, singing should facilitate improvements in breath support and aspects of voice (including pitch range and voice quality). The scope of future work will look at the same data subjects with a view to measuring improvements in vocal performance. This will allow us to fully evaluate the benefits of offering singing as a treatment option in the NHS.

P22.05

Functional improvements associated with upper extremity motor neurorehabilitation in individuals with Parkinson's disease

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Objective: Non-traditional exercise neurotherapy is proving beneficial in symptom management for people living with Parkinson's disease (PD). Whilst traditional therapies promote motor function, the benefits may be limited by compounding physical, cognitive, and attentional barriers. Preliminary research from our laboratory has shown that some people living with PD preserve the capacity to safely and effectively ice skate despite displaying marked deficits in a range of functional movements. Furthermore, a brief period of ice skating has been shown to positively influence balance and coordination. We hypothesised that adding an upper body motor coordination task (stickhandling) to ice skating may provide upper extremity neuromotor benefit. Accordingly, the purpose of this study was to explore the effects of a stickhandling exercise session on motor performance amongst people with moderate PD.

Methods: Nine people with moderate PD and seven control subjects (CTRL) completed three trials of a reaching-to-eat (fine motor) task and a button push (gross motor) task with their dominant arm PRE-and POST-intervention. The intervention involved completing two dynamic stickhandling tasks (ice hockey stick and puck) either on- or off-ice depending on the physical abilities of the subject. Reaching-to-eat trials were captured in sagittal plane video and manually scored for movement quality. Button push trial data were collected automatically. Reaching-to-eat and button push scores were compared between groups (PD, CTRL) and time periods (PRE, POST).

Results: All subjects performed the stickhandling tasks safely and effectively. The PD group demonstrated deficits in both tasks when compared to CTRL. Both groups demonstrated an improvement in reaching-to-eat (Figure 1A) and button push (Figure 1B) scores immediately following the intervention. The observed improvements in upper extremity motor performance amongst the people living with PD following a period of exercise imply that sport-derived

exercise programs may provide neurotherapeutic benefit to PD patients in sustaining upper extremity functional mobility.

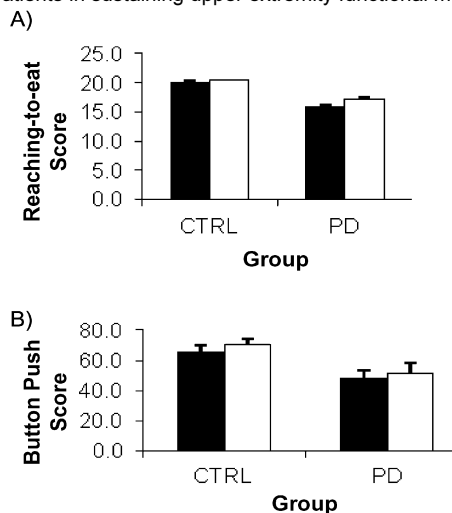


Figure 1. Mean score for A) reaching-to-eat task and B) button push task. Dark bars represent pre-intervention data; light bars represent post-intervention data.

P22.06

Non-gait related benefits of auditory cueing in Parkinson's disease

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Objective: Parkinson's disease (PD) is a neurodegenerative disorder that targets mainly dopaminergic neurons of the basal ganglia. PD is characterized by motor symptoms typically leading to dysfunctional gait. External auditory cues have shown beneficial effects on gait kinematics in PD patients. However, little is known about potential benefits of auditory cueing on non-motor functions. In the current study we investigate whether auditory cueing has a positive effect on perceptual timing.

Methods: Fifteen PD patients were submitted to a standard auditory cueing program (3 times a week for 30 min, for one month). Gait performance was evaluated using motion capture. In addition, motor (via tapping tasks) and perceptual timing abilities were assessed using a new Battery for the Assessment of Auditory Sensorimotor and Timing Abilities (BAASTA). The patients' sensitivity to temporal regularity, a crucial element in rhythmic auditory stimulation, was also monitored using a perceptual oddball paradigm task using electroencephalography event-related potentials (ERP; Schwartz et al. 2011). Participants were asked to count deviant tones presented in a sequence of either regular or random stimuli. The patients were evaluated before the program, immediately after, and one month after the therapy. Their performance was compared to a

baseline which was established by data collected from healthy age-matched controls.

Results: Improved gait kinematics (i.e., greater walking speed and step length) were observed as a result of the therapy and persisted one month later. Interestingly, these benefits extended to perceptual timing. Improved duration discrimination, detection of a deviant beat in a musical stimulus and enhanced detection of misaligned sounds to the beat of music were observed. These effects are complemented with a reduced response to temporal regularity visible at the level of the P300 late ERP component linked to deviance detection.

References: Schwartz M, Rothermich K, Schmidt-Kassow M, Kotz SA., Temporal regularity effects on pre-attentive and attentive processing of deviance, *Biol Psychol.* 2011 Apr;87(1):146-51.

P22.07

Effects of Parkinson's medication on the performance of different exercises before and after dosing

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Objective: As a researcher with Parkinson's, I executed a series of controlled experiments on myself to see the relationship between exercises, before and after dosing with Parkinson's medication. Four physical activities were done typically 5 to 7 days per week for up to 12 weeks. Activities were done in triplicate immediately before and one hour after taking medications. Three activities were based on Wii Fit games, two of which were balance activities and one aerobic. The fourth task involved small motor skills of sorting shapes.

Methods: All activities showed improvements following medication dosing. The least responsive activity was small motor skills sorting. Medication increased the performance of balance activities to a typical ratio of 60% of scores before/after. Balance exercises requiring quick, random actions trended downward with time compared to exercises with predictable, repetitive patterns, which improved due to learning. Variances for all tasks were lower before medications, suggesting the body's superior ability to regulate internal dopamine levels versus externally administered. Small motor shape sorting activity showed performance changes smaller and more variable than larger motor skills.

Results: Exercise studies should account for timing and dosing of medication to get understandable trends. Large motor skills respond more to medication than small motor. Exercises requiring random, rapid responses behave differently than repetitive, predictable activities. Performance variability increases with medication dosing.

P22.08

Influence of music therapy to improve quality of gait and balance in PD patients – a pilot study

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Objective: The aim of this research was the evaluation of influence of music therapy to improve gait, balance and associated motoric functions in a group of patients with Parkinson's Disease. Research approach assumed the use of functional therapy combined with music therapy techniques taken from Neurologic Music Therapy Concept (NMT). The main hypothesis was that NMT sensorimotor techniques can improve the kinematics gait parameters and balance reaction in group of patients with PD.

Methods: To evaluate therapeutical activities objective

measurement of gait by optoelectronic complex biomechanical analysis BTS Smart was used. Static balance and dynamic balance reactions were assessed by stabilographic platform CQ STAB. Patients were also assessed according to author's "Therapeutic approach schema during session". Measurements were done before and after one month research cycle. Therapeutic program was conducted in The Neurology and Neurosurgery Clinic in Krakow. 10 patients selected to the pilot group for 4 weeks, 4 times a week, attended 45 minutes individual, therapeutic sessions of functional therapy based on neurologic music therapy techniques. During therapeutic session metronomes, simple percussion instruments and rhythmical music from MP3 was used. It was all combined with functional movement focusing on improvement of balance reactions, gait components, muscles strengthening and movement smoothness.

Results: The pilot study shows that neurological music therapy can help patients with PD improve gait and balance. Still, to confirm the results this research should be continued on a bigger group of patients. Expected results in a wider group of patients can contribute to better recognition and understanding of mechanisms of therapeutic influence on the symptoms which significantly impair in the course of Parkinson's Disease. Also it can help develop therapeutic strategy based on music and rhythm to improve and maintain good functional state and help this group of patients come back to social activity.

P22.09

Dancing and drumming with individuals with Parkinson's disease: a community based program

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Objective: Current research supports the use of dancing, specifically the partnered tango, to improve functional deficits related to Parkinson's disease (PD). Recent literature has indicated that music can positively influence quality of gait in people with PD. While the type of dancing reported to be most beneficial is the Argentine tango, there have not been any studies that focus on the use of modern/ interpretive dancing (MID) and drumming. Similar to tango, MID is a flexible, improvisational form of dancing that can incorporate multi-directional movements and rhythmic variations.

This pilot study aim to evaluate the benefits of a 12-week community based dancing and drumming program in individuals with idiopathic Parkinson's disease with Hoehn and Yahr stages I-II.

Methods: A cross-over study design will be used to divide ten individuals who have been discharged from physical therapy service. The individuals and their care-partners will be divided into a control and an experimental group to participate in weekly dancing and drumming sessions. These sessions will be lead by licensed physical therapists. The participant will also perform a progressive home exercise program. Data collection will be conducted by the same blind evaluator at pre assessment, 12 week, and 24 week post assessment periods. Various tools will be use to collect data on functional outcome, quality of life, and individual's satisfaction with socialization and engagement in physical activity.

Results: This ongoing pilot study will be complete in July 2013. Result will be use to further develop a long term community based dancing and drumming program for individuals with PD at varies disease stages.

P22.10

A novel approach to testing freezing of gait in patients with Parkinson's disease: the clover test

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Objective: (1) To assess the effectiveness of a newly designed freezing of gait (FOG) functional assessment tool. (2) To determine if the FOG questionnaire (FOG-Q) total scores correlated with FOG episodes captured in the clover test.

Methods: A convenience sample of 31 subjects (mean age 69.58) with idiopathic Parkinson's disease (PD) who experienced FOG, and 22 controls without PD were recruited from the PD and Movement Disorders Center in Philadelphia, Pennsylvania. Subjects completed the FOG-Q and then performed the clover test. This test had four numbered chairs placed in an "X" pattern. Chairs 1, 2, and 3 faced in and chair 4 faced out. Chairs were spaced at 18 inches and subjects began ambulating at five feet away from chair 1. Subjects walked to chair 1, sat in the chair, stood, and continued on to perform the same at chairs 2, 3, and 4. The test ended when subjects sat in chair 4. The entire test was timed and episodes of FOG were noted.

Results: The mean time to complete the clover test was 21.8 seconds for controls, and 38.55 seconds for subjects. It captured FOG episodes (ranging from 0-15), with the top three causes being: turns, initiation of gait, and reaching for the chair before turning to sit. Total scores on the FOG-Q ranged from 7-23 (mean = 12.45). The total scores on the FOG-Q did not correlate with the clover test times, showing that the subjects' perception of their FOG generally did not match their actual ability.

P22.11

Using timed tasks to determine change after LSVT® BIG treatment in three patients with young onset Parkinson's disease

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Objective: To present a case study showing how timed tasks can show improvement in the function of individuals with young onset Parkinson's disease (YOPD) using LSVT® BIG treatment. Many current functional assessment tools do not adequately capture the deficits of bradykinesia and hypokinesia that those with YOPD suffer.

Methods: A random sample of 3 patient charts detailing LSVT® BIG treatment received at the Dan Aaron Parkinson's Rehabilitation Center in Philadelphia, Pennsylvania were chosen. Each patient reported functional limitations. An initial assessment was performed on each patient, followed by LSVT® BIG treatment 4x/week for 4 weeks, in hourly sessions. Prior to discharge, each patient was reassessed, in part using timed tasks.

Results: The time to perform tasks such as typing, shoe-tying, transfers, single leg stance, and retrieving items from the floor all decreased, indicating improved functional ability and decreased bradykinesia. All patients improved their step size which decreased their likelihood of LOB, and indicated less hypokinesia. Each patient also self-reported that they felt "much better" on their global rate of change scale. Timing functional tasks can capture improvements in mobility gained through LSVT® BIG treatment.

P22.12

Novel GaitReminder™ technology for use in treadmill rehabilitation using cadence matched musicAlexandra Cihal[†], Kailie Luan[†], Nicole Meyer[†], Bin Hu[†][†] Equal Contribution¹Department of Clinical Neurosciences, University of Calgary, Calgary, AB, Canada

Objective: Treadmill training (TT) and rhythmic auditory stimulation (RAS) are recommended gait rehabilitation methods in Parkinson's disease (PD). The aim of the present study was to develop a paradigm of RAS that can be used safely for treadmill walking under harsh weather conditions.

Methods: We first obtained step length and cadence data from 6 healthy subjects walking under 9 different treadmill settings of varying speeds and inclines. Data was continuously acquired using GaitReminder™ (GR), an Apple iPod touch-based application. Average cadences of each treadmill setting were used to determine the songs with matching beats per minute (bpm). The final songs were compiled into a playlist with auditory instructions directing users to change treadmill settings prior to each matched song. Questionnaires regarding aspects of music most enjoyed were administered.

Results: 24 different, healthy subjects listened to the playlists during the same 9 treadmill conditions, while wearing the GR. BPM accuracy was tested by comparing actual walking cadences to the BPM of the song chosen for that treadmill condition. We found a mean difference of $1.7 \pm 0.97\%$ and $3.7 \pm 0.80\%$, for the tall and short subject groups respectively. 81% of participants indicated on the questionnaire that the beats and tempo were the aspect of the music most enjoyed. Music triggers physiological arousal, whereas rhythm provides an external time keeper, influencing step timing and fluidity, and increasing the pleasure associated with exercise. Combining musical RAS with TT may create an enjoyable rehabilitation and gait training method for people living with PD. Such a program may be also applicable to other disorders affecting gait, such as stroke, spinal cord, or head injuries.

P22.13

Enhanced walking function with boxing training for persons with Parkinson diseaseStephanie A. Combs¹, M. Dyer Diehl¹, Michelle Bentz¹, Katelund Hojnacki¹, Lindsay Sewell¹, Stephanie Steider¹¹Krannert School of Physical Therapy, University of Indianapolis, Indianapolis, IN, USA

Objective: The purpose of this preliminary study was to compare walking function outcomes over time between people with PD who participate in boxing training and those who do not.

Methods: Eighty-eight participants with PD were enrolled in a 2-year longitudinal cohort study. Participants who completed all testing at baseline, 6, and 12 months were included in the current analysis [n=65; mean age 67.1(8.7) years; male 71%; mean months post diagnosis 71.8(55.4), mean Hoehn and Yahr 1.75]. Participants were categorized as "boxer" if at each testing session they reported participating in boxing training (n=39) or as "non-boxer" if at each testing session they reported participating in other exercise activities (n=26). Demographics and PD characteristics were collected at baseline. Exercise behaviors and walking function were collected at each testing session. Walking variables included the comfortable and fast 10-meter walk tests and the 6-minute walk test. Data were analyzed with a 2x3 mixed-model ANOVA ($p < 0.05$).

Results: Groups did not significantly differ in age, gender, month since diagnosis, Hoehn & Yahr levels, or self-reported readiness to

exercise ($p > .05$). Boxers demonstrated significantly greater comfortable 10-meter walking speed compared to non-boxers [mean speed, boxers 1.29(0.23)m/s vs. non-boxers 1.18(0.24)m/s; $p = .048$] and increased gait endurance on the 6-minute walk test [mean distance, boxers 503.5(120.3)meters vs. non-boxers 433.5(108.0)meters; $p = .012$]. Significant differences in fast walking speed were not found between groups. Neither group demonstrated significant changes in walking function over the 12-month period. Boxers reported significantly more minutes of exercise per week ($p = .007$) and a higher rate of perceived exertion during exercise ($p = .002$) than non-boxers.

Conclusion: Those who participated in boxing training maintained better walking function over the course of one year than those who did not box. Future study of persons with PD is warranted to determine the effectiveness of boxing on both overall fitness and PD symptoms.

P22.14

Do clinical tests of balance performance correlate with physical activity level in Parkinson's disease?David Conradsson^{1,2}, Håkan Nero¹, Niklas Löfgren¹, Maria Hagströmer^{1,2}, Caroline Paquette³, Erika Franzén^{1,2}¹Karolinska Institutet, Department of Neurobiology, Care Sciences and Society, Division of Physiotherapy²Karolinska University Hospital Department of Physical Therapy Stockholm, Sweden and ³Department of Kinesiology and Physical Education, McGill University and Centre for Interdisciplinary Research in Rehabilitation, Montreal, QC, Canada

Objective: Tests of balance performance are commonly used in clinics to assess whether individuals with Parkinson's disease (PD) are safe to ambulate independently, however it is uncertain if these clinical assessments relate to physical activity (PA) in real life. Hence, the aim of this study was to examine the association between clinical test of balance performance and objectively assessed PA in elderly with PD.

Methods: Sixty-five participants (29 female), mean age 73 years (range 61 - 86) with mild to moderate idiopathic PD (Hoehn & Yahr 2-3) were included in this cross-sectional study. Balance performance was tested for mini-BESTest (total score), modified figure of eight test, timed up and go, one leg stance and pull test (normal/abnormal response). As a measure of total PA, average steps per day was assessed using accelerometers (Actigraph GT3X+, 30Hz) worn around the waist during daytime for 3 to 7 consecutive days. Based on PA data, the participants were categorized into an active (>5000 average steps/day, n= 26) and an inactive group (<5000 average steps/day, n= 39). Non-parametric statistics ($P < 0.05$) were used to compare clinical balance performance between the two groups and test associations between clinical tests and level of PA. P-values and correlation coefficients (r_s) are presented here.

Results: Significant differences between the active and inactive group and correlations to PA level were found for mini-BESTest ($P = 0.004$, $r_s = 0.51$) and modified figure of eight test ($P = 0.034$, $r_s = -0.35$). No group differences were found for the other tests, however a significant correlation was found between timed-up and go and PA level ($r_s = -0.40$). This study implies that clinical tests that target multidimensional and dynamic abilities of balance control, such as mini-BESTest and modified figure of eight, reflect more PA levels than single item or more static balance tests.

P22.15**Impact of exercise on the motor and non-motor symptoms of Parkinson disease**

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Objective: To determine and compare the effects of the two different exercise programs on the motor and non-motor symptoms of Parkinson disease (PD).

Design/Methods: Nine patients with early-middle stage PD went through a prospective, double-blind, randomized clinical trial to compare the effect of the training BIG vs. one-to-one exercise program. Baseline evaluations of Unified Parkinson's Disease Rating Scale (UPDRS), Beck Depression Inventory (BDI), Beck Anxiety Inventory (BAI) and Iowa Fatigue Scale (IFS) were taken before exercise intervention. Both groups received 16 one-hour supervised exercise sessions; five patients underwent one-to-one exercise while four underwent BIG therapy. Three follow-up evaluations were performed at 1-3 month intervals. Wilcoxon rank-sum testing was used to assess outcomes based on changes in UPDRS, BDI, BAI, and IFS as compared to baseline.

Results: The combined cohort demonstrated an average decrease from baseline across all scales at all follow-ups, with statistical significance for UPDRS and BDI ($p < .05$). No significant differences between the groups were detected, except for IFS, for which exercise group showed a significant decrease from baseline at the final evaluation ($p = .02$) while the group with BIG therapy had returned to baseline after an initial, insignificant decrease.

Conclusions: This pilot study showed the positive effect of exercise or BIG physical therapy on motor and non-motor symptoms of patients with PD. Our study suggested that one-to-one exercise could be as effective as BIG physical therapy on symptoms of PD.

P22.16**Digital inclusion for telerehabilitation speech therapy in Parkinson's disease**

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Objective: The purpose of this study is to identify, among the general population of PD patients, those who could be best candidates for enrolling in a program of speech therapy telerehabilitation.

Methods: Fifty patients with diagnosis of PD participated in the study. Forty-eight percent ($n=24$) were male, ages ranged from 45 to 87 years old and all were in stages II to IV (Hoehn & Yahr). All patients were treated with the Lee Silverman voice therapy and submitted to voice intensity evaluation with VoxMetria 4.7 during the on phase both before and after therapy. Patients were then asked to fill a questionnaire aimed to evaluate technological competence regarding basic computer operations and internet. Also, patients were asked to inform their impression about conventional therapy and about the possibility of receiving similar treatment at home using a computer connected to the internet.

Results: After speech therapy, an increase of 18 dB SPL in mean voice intensity was observed (pre and post treatment mean intensity were 45 dB and 63 dB, respectively). All patients reported a positive impression regarding the effectiveness of the speech therapy. Most patients (76%, $n=38$) informed they would seriously consider receiving speech telerehabilitation but only 10 out of these

38 patients reported basic knowledge of computer and internet. From the other 12 patients who were not willing to receive treatment at distance only two were familiar with computers. There were no correlations between considering or not telerehabilitation and sex, age or stage of the disease.

P22.17**Treatment effects of Attention Process Training for an individual with Parkinson disease: A single-subject study**

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Aim: Evidence finds ~70% of individuals with PD demonstrate cognitive deficits (Cooper et al., 1991), possibly due to dopamine depletion in the frontal-striatal circuitry (Owen 2004). However, no one has proposed clinical treatment. We investigated whether *Attention Process Training* (APT; Sohlberg et al, 2001) could improve attention in a person with PD, as it has in TBI survivors with frontal lobe dysfunction (Sohlberg & Mateer 1987).

Methods: This Phase I, multiple-baseline A₁-B-A₂-A₃, single-subject study measured change in percent accuracy and timed performance. The university's Institutional Review Board approved the study. The participant, an independent, college-educated, 79-year old female, with self-reported attention problems, 7 years post-PD diagnosis, Hoehn & Yahr stage 2.5, no apathy, depression or dementia, disabling hearing or vision loss, received informed consent prior to the study's start. Baseline, post-treatment and treatment withdrawal phases included 3 probes of attention components, attention and working memory testing. She received APT (B phase) 120-minutes, once a week for 6 weeks (12 hours total). Treatment was administered by second-year Master's student (KF) APT trained by ND.

Results: We found large change in sustained attention for both % accuracy (A₁ to A₂ $d=5.196$; A₁ to A₃ $d = 13.279$; A₂ to A₃ $d=1.443$) and timed performance (A₁ to A₂ $d=2.951$; A₁ to A₃ $d = 3.153$; A₂ to A₃ $d=0.287$), based on single-subject effect size calculations (Busk & Serlin, 1992; Olive, 2005) and Cohen's (1988) effect size interpretation. Selective and Divided attention also improved, but not as much or as consistently although they were untrained. Alternating attention did not improve.

Conclusion: APT led to large effects when delivered at high intensity (120 minutes per session) for six weeks. The treatment effect carried over to 2 of 3 untrained attention components. We cannot generalize these findings, but have preliminary evidence to continue this line of study.

P22.18**Introducing the Communicative Effectiveness Survey: an objective measure of communicative participation for people with Parkinson's disease and dysarthria**

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Objective: Up to 80% of people with Parkinson's disease (PD) eventually experience communication disorders. People with communication deficits do not receive the same quality healthcare as those without (Hoffman et al., 2005). Reduced healthcare utilization may lead to isolation, depression, reduced independence and quality of life, and increased caregiver and societal burden (Hoffman, et al., 2005; Parkinson's Disease Society, 2012). Patient Reported Outcome (PRO) measurement is becoming widely accepted in healthcare (Fries, Bruce, & Cella, 2005). PRO developers use Item Response Theory and Computer Adaptive Testing to develop precise and efficient measures that reduce

burden for testers and respondents leading to increased cost effectiveness. This study aims to investigate the content and construct validity of the 24-item *Communicative Effectiveness Survey* (CES) for people with PD using an IRT methodology–Rasch analysis.

Methods: Prospective, validation study, between-group, approved by the university's Institutional Review Board, informed consent obtained. 123 participants 65 to 89 years old (63 NO PD, 60 PD) participated based on the inclusion criteria: no active or prior neurological disorders; hearing and vision within functional limits; passed cognitive, apathy, and depression screenings; PD group only: stable on medications, Hoehn & Yahr ratings and Dysarthria Severity Ratings 1-4.

Results: The CES represented a unidimensional construct and adequate item local independence to perform a partial credit model Rasch analysis. Item-level psychometric properties were strong: participants used all four units of the rating scale reliably; item difficulty matched person ability well; a strong, significant relationship existed between an *a priori* item difficulty and the actual item hierarchy ($r_s = .96$, $df = 25$, $p < .01$). Three misfitting items were eliminated; no floor or ceiling effect. PD group mean ($M=71.93$, $SEM=13.65$) was significantly lower than the NOPD group mean ($M=85.794$, $SEM=11.12$) [$t(121) = -6.187$, $p < .001$]. Clinical and research implications will be discussed.

P22.19

A study of the effect of a one year community-based group exercise program for people with Parkinson's disease in Mumbai, India: A quasi-experimental design.

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Objective: The Parkinson's Disease and Movement Disorder Society conducts group therapy sessions where patients at different stages of the disease (Hoehn and Yahr stages 1 to 4) exercise together at a community centre under the supervision of a physiotherapist. This study aimed to investigate the effects of participation in such an exercise program in people with Parkinson's disease (PD) after a duration of 1 year.

Methods: Unified Parkinson's Disease Rating Scale (UPDRS) was administered to 50 people with PD at baseline. Group therapy sessions were conducted once weekly for PD patients who voluntarily participated in the program which consisted of exercises aimed at improving posture, range of motion, strength, balance and gait. Those participants who attended at least 45 of the 48 sessions were allocated to Group A (cases) and those who didn't attend more than 2 of the 48 sessions were allocated to Group B (controls). UPDRS was administered at the end of 1 year to all patients in Group A and B.

Results: At baseline, there was no statistically significant difference between the mean scores of Group A and Group B ($U=163.5$, $N_A=20$, $N_B=19$, $P=0.456$) however at the end of 1 year the mean score of Group B was significantly higher than Group A indicating greater progression of the disease in patients in Group B ($U=79.0$, $N_A=20$, $N_B=19$, $P<0.05$). There was a statistically significant difference between the pre and post UPDRS scores for Group B ($N_B=19$, $Z = -3.724$, $P<0.001$) while there was no statistically significant difference between the scores for Group A ($N_A=20$, $Z = -1.169$, $P=0.243$) indicating the effectiveness of the exercise program in retarding the progression of the disease.

P22.20

Balance differences between people with and without freezing of gait in Parkinson disease

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Objective: To determine whether balance impairments differ between groups of people with PD who either have or do not have a history of freezing of gait (FOG), taking into account differences in disease severity, disease duration and age. Balance was assessed using the Balance Evaluation Systems Test (BESTest) total and section scores, Mini-BESTest total score, and Berg Balance Scale (BBS) total score.

Methods: Balance of 78 participants (58% male; mean age \pm SD = 68.1 ± 9.3 years; H&Y frequency (stage(n)): I(5), II(30), II.5(28), III(8), IV(7)) with PD was assessed using the BESTest, Mini-BESTest, and the BBS. Participants completed the FOG Questionnaire; those reporting a score greater than one on item three were classified as freezers. The Movement Disorder Society- Unified Parkinson Disease Rating Scale subsection III (MDS-UPDRS III) was administered to measure motor symptom severity. Analyses of covariance were used to determine differences between freezers and non-freezers in BESTest total and section scores, Mini-BESTest total score, and BBS total score, using a PD severity composite score (MDS-UPDRS III score, years since diagnosis, and age) as a covariate ($\alpha=0.05$).

Results: Thirty-two (41.0%) participants were classified as freezers. After accounting for disease severity and duration as well as age, freezers had significantly lower BESTest ($F(1,76)=7.33$; $p=0.008$) and Mini-BESTest ($F(1,76)=12.26$; $p=0.001$) total scores compared to non-freezers. There were no differences in BBS scores for freezers compared to non-freezers ($p=0.27$). With respect to the individual BESTest sections, freezers had significantly lower scores on sections IV (postural responses) ($F(1,76)=14.39$; $p<0.001$) and VI (stability in gait) ($F(1,76)=9.16$; $p=0.003$) than non-freezers. In conclusion, regardless of motor symptom severity, years since diagnosis, and age, freezers had more severe balance impairment than non-freezers as measured by the BESTest and Mini-BESTest. Physical therapists should consider addressing postural response and stability in gait problems in PD patients with FOG.

P22.21

Benefits of task-specific learning-principled practice to improve freezing of gait for individuals with Parkinson disease in a small group community setting: a case series study

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Objective: Freezing of gait (FOG) is one of the most disabling symptoms of advanced stage PD and is associated with frequent falls and reduced quality of life (QoL). Researchers and clinicians define FOG as: An episodic inability to generate effective stepping...most commonly experienced during turning and step initiation, but also when faced with spatial and time constraints, stress, and distraction. Despite the multifactorial nature of FOG, task-specific training has not yet been applied to counteract the

multiple motor/cognitive/emotional triggers that lower threshold for the occurrence of FOG and that may interact and deteriorate synergistically. In addition, learning principles of practice have not been applied to task specific “antifreeze” exercises. Instead, more general gait and balance training with attentional strategies and external cues are typically used to circumvent freezing episodes.

Methods: In this case series study, we investigated the effects of a task-specific learning principled approach that targeted each person’s unique “triggers” directly. In addition to specificity of training, other learning principles were integrated into the program including: feedback, intensity through high effort and dosage (5 days; 3 hours/day), and progressive difficulty by manipulating environment, balance requirements, distractors, and variability of practice. Attentional strategies and external cues were integrated to enhance learning by allowing for greater success during the practice of complex multitasking conditions. The study was held in a community setting with a small group “boot camp” approach to take advantage of social/emotional interactions shown to impact learning and quality of life.

Results: 5/6 S’s showed improvement in the FOG questionnaire and objective measures including dual tasking conditions. These improvements were related to QoL for 4/5 S’s. One subject with mild FOG did not show improvement on any FOG outcomes. We will report on the trends across 6 individuals and discuss the implication to future studies and real world implementation.

P22.22

Mobility training with popular music in persons with Parkinson disease

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Objective: To study the effects of walking with music on the walking parameters of people with Parkinson disease (PD).

Methods: 35 persons with PD were recruited to participate in this study. Participants were stratified according to walking speed (< 0.8 m/s; 0.8 – 1.1 m/s; > 1.1 m/s) and randomized to one of three training groups. Group 1 walked at a comfortable pace without music. Group 2 trained with popular music that matched their comfortable walking cadence, measured at baseline. Group 3 trained with popular music that was progressively increased. Training progression in Group 3 was determined by regularly (3 times/session) assessing the changes in walking speed, stride length, and cadence in response to increasing the training rate. Training consisted of walking for 30 min/session, 3 sessions/week for 6 weeks.

Results: According to preliminary data, subjects from group 1 ($n = 5$) had a mean decrease in cadence of 0.99steps/min (SD=7.82), group 2 ($n = 6$) had a mean decrease of 3.52steps/min (SD=4.7), and group 3 ($n = 5$) had a mean increase of 2.47 steps/min (SD = 7.33). Average stride length for group 1 decreased by 0.01m (SD= 0.06), group 2 increased by 0.05m (SD=0.12), and group 3 increased by 0.05m (SD=0.08). Mean speed gains were 10.02m/min (SD=0.11) for group 1, 0.01m/min (SD=0.14) for group 2, and for group 3 it was 0.08m/min (SD=0.12). The between-group and within-group differences were not found to be significant for walking parameters due to the small sample size. Baseline PDQ-39 scores for group 2 is significantly different from group 3 (difference = 22.69, $p=0.0236$) and resulted in a significant decrease by -5.58 points (95% CI -10.94, -0.23).

P22.23

Fusion training: the effects of combined strength and aerobic training on persons with Parkinson disease

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Objective: The objective of this study was to examine the effects of an exercise program on strength, aerobic capacity, and fatigue in persons with idiopathic Parkinson disease (PD).

Methods: 12 persons PD (Hoehn and Yahr II – III; mean = 2.4) to date have participated in a 16 week exercise program at the UAB Center for Exercise Medicine. Participants were screened by a movement disorder specialist in order to confirm a diagnosis of PD. One rep max was used to assess strength, Peak VO₂ for aerobic capacity, and Fatigue Severity Scale (FSS) for fatigue. Participants trained 3x/wk (M,W,F) with a personal trainer. Fusion training (FuT) consisted of a combination of exercises that challenges strength, power, balance, and endurance. Exercise sessions consisted of: (i) five movements to improve strength and muscle mass (leg press, knee extension, chest press, overhead press, pull down), each performed for 3 sets of 8-12 repetitions (~30 total repetitions); (ii) trunk exercises to improve postural stability (trunk extension and flexion); and (iii) 3-4 bodyweight exercises (selected from a menu) to improve power and balance (e.g., step up, squat, jump squat, lunge, side lunge, push-up, assisted pull-up, assisted dip). Heart rate (HR) was monitored during training with participants maintaining a minimum of 50% heart rate reserve (HRR). Wilcoxon Signed Ranks Test were used to assess the differences in strength, aerobic capacity, and fatigue before and after training.

Results: Analyses revealed statistically significant improvements in bench press, leg press, shoulder press, and leg extension strength after 16 weeks of training, however there were not improvements in aerobic capacity. Participants did perceive that their fatigue was less (FSS; $p < .02$) after 16 weeks of training.

P22.24

Intensive rehabilitation treatment improves sleep quality in Parkinson’s disease

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Objectives: Sleep disturbances are among the most common non-motor symptoms of Parkinson’s disease (PD). Pharmacological treatments have not been satisfactory because of side effects and interactions with antiPD drugs. While studies in normally aging subjects with sleep complaints have shown that regular exercise improves sleep quality, there is no such evidence in patients with PD. Here we explore whether an intense physical exercise program improves sleep quality in a large group of patients with PD and sleep complaints.

Methods: PD Sleep Scale (PDSS, a 15-question visual analogue scale evaluating sleep quality, nocturnal psychosis, nocturia, nocturnal sensory-motor symptoms, daytime somnolence) was administered twice, 28 days apart, to two groups of patients with PD (Hoehn and Yahr stage 3) of comparable age, gender, disease duration and pharmacological treatment. UPDRS III scores were measured at the same times. The control group (50 patients) did not receive rehabilitation treatment. The treated group (100 patients) underwent a 28-day intensive rehabilitation program (three one-hour daily sessions comprising cardiovascular warm-up, relaxation, muscle-stretching, balance and gait training with stabilometric platform and treadmill, occupational therapy to improve daily living activities).

Results: At enrolment, control and treated groups had similar UPDRS III scores, PDSS scores and profiles. At re-test, 28 days later, UPDRS scores significantly improved in the treated ($p < 0.0001$), but not in the control group ($p = 0.23$). Similarly, the total PDSS scores improved in the treated group ($p = 0.0001$), but not in the control group ($p = 0.32$). In particular, the treated group showed significant improvement in the PDSS scores for sleep quality, motor symptoms and day-time somnolence, but not for psychosis and nocturia. The control group did not show improvement in any of the items. These results suggest that intensive rehabilitation treatment may have a positive effect on sleep quality, nocturnal motor symptoms and day-time somnolence in patients with PD.

P22.25

An acoustic and perceptual investigation of speech and voice in Parkinson's and in depression

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Objective: Most people with Parkinson's experience changes in their speech and voice. The purpose of this study was to establish why people with Parkinson's sound depressed when they are not.

Methods: Participants were 30 people with Parkinson's and no depression, 30 with Parkinson's and depression; 18 with depression without Parkinson's, 30 without Parkinson's or depression. Speech and voice samples were acquired employing standard clinical tasks: reading a passage, monologue, sustained vowel, diadochokinetic repetitions (DDK). Based on these acoustic and auditory perceptual measures were derived: speech and articulation rate, pause number and duration, mean fundamental frequency (F0) and variability, mean intensity and variability, duration of sustained vowel, and DDK rate; loudness/pitch level and consistency, rate of speech and voice quality. Sixty-six listeners transcribed low-predictability sentences to gain a measure of intelligibility.

Results: Three blind speech-language pathologists judged the groups with Parkinson's as significantly more 'depressed' than the groups without Parkinson's, with the group with Parkinson's and depression perceived as significantly more 'depressed' than the others. Based on acoustic analyses, pause duration in reading was significantly longer in both groups with Parkinson's compared to those without. For the perceptual analyses, significant reduced loudness level and loudness/pitch consistency during reading and monologue tasks was reported for both groups with Parkinson's compared to the groups without Parkinson's. Regarding intelligibility people with Parkinson's produced significantly more impaired speech than those without, with those with Parkinson's and depression being most impaired. No differences were found for both groups with Parkinson's according to Hoehn and Yahr stage and disease duration. These findings suggest that people with Parkinson's sound depressed because their speech features do not differ significantly from people with depression, whereas on these key elements they do differ from people without Parkinson's or

depression. Some features of speech and voice are uniquely linked to depression.

P22.26

The efficacy of a group exercise program using large amplitude movements and functional activity training on improving mobility and quality of life in older adults with Parkinson's disease

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Objective: The effect of an exercise program using large amplitude movement and functional mobility training in those with Parkinson's disease (PD) has not been evaluated when delivered in a group delivery format or in an older adult population (i.e. average age 80 years). The purpose of this study was, therefore, to determine if an eight week biweekly group exercise program using large amplitude movement and functional mobility training was effective at improving mobility and quality of life in old, older adults with PD. To determine the long term training effects of the program, a follow up assessment was conducted at four months post intervention.

Methods: 20 participants with PD were recruited through a hospital-based Seniors Outpatient Clinic. Participants were assessed before starting (PRE) and upon completion (POST) of the intervention. To decrease the likelihood that the results would be affected by day-to-day fluctuations in mobility, 3 measures were gathered at both PRE and POST. A single follow-up assessment was conducted four months after completion. Outcome measures included: MDS-Unified Parkinson's Disease Rating Scale-Part III, Timed Up and Go, Berg Balance Scale, Chair Stand Test, Gait characteristics (GaitRite system), Parkinson's Disease Questionnaire – 39 and Goal Attainment Scale. Data was analyzed using repeated measures ANOVA and paired dependent t-tests.

Results: Results indicate significant improvements ($p < 0.05$) in all measures of physical function (effect sizes (ES) ranging from 0.33-0.88), QOL (mobility dimension, ES=0.35) and personal goal achievement (ES=3.0). Results of four month follow up assessments are pending.

Conclusion: This group exercise program model was very effective in improving mobility and QOL for an older adult population with PD, while being cost effective to deliver. Further the program frequency and duration made it manageable for our population to attend as well provide adequate duration to achieve desired training effects.

P22.27

Correlations between performance-based balance measurement, self-report balance confidence and freezing of gait in people with Parkinson's disease

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Objective: To analyze patients with Parkinson's disease (PD) scores on a performance-based balance measure and on a measure of self-perceived balance confidence; and to identify their correlation with freezing of gait.

Methods: One hundred and three subjects in two countries were included in this study. Besides demographics and clinical data,

patients were assessed with the Freezing of Gait Questionnaire (FOG-Q), Berg Balance Scale (BBS) and Activities-Specific Balance Confidence Scale (ABC). Subjects were classified as freezers if they scored one or more on the FOG-Q, item three.

Results: The sample had a median age of 70 years. Forty-one (39.8%) subjects were classified as freezers. Median score on BBS for freezers was 51 (46;54); for nonfreezers was 53 (51;56) ($p=0.014$). Median score on ABC for freezers was 60 (31.87;82.19); for nonfreezers was 75.94 (49.22;93.12) ($p=0.017$). BBS and ABC total scores showed moderate correlation with FOG-Q ($r=-0.44$; $r=-0.45$; respectively) ($p<0.001$). All BBS tasks, except sitting unsupported, standing with eyes closed/feet together, were significantly correlated with FOG-Q (range from $r=-0.22$ to -0.42 ; $p\leq 0.025$). All ABC tasks were significantly correlated with FOG-Q (range from $r=-0.23$ to -0.5 ; $p\leq 0.019$). For individual items on the two scales, 7/14 on the BBS and 13/16 on the ABC were moderately correlated with FOG-Q ($r\geq 0.3$).

Conclusions: Although both the BBS and ABC scores correlated with FOG-Q, critical analysis reveals important differences between these scales. Total BBS scores were high even for freezers, and fewer individual items correlated moderately with FOG-Q scores. Total ABC scores were lower among freezers, and a majority of individual items correlated moderately with FOG-Q. This suggests that the ABC may be a more valid and informative measure in freezers and nonfreezers. This is likely related to the different constructs measured in the two scales (balance and fear of falling) and the measurement method (performance and self-report).

P22.28

Influence of multimodal therapies on life quality and motor performance in Parkinson's disease

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Objective: Evaluation of a 3 to 4 week hospital multimodal complex treatment in Parkinson's disease (PD). Outcome parameters: Motor performance and life quality.

Methods: 35 patients with PD were treated during 3 weeks by daily visits of a neurologist, by physiotherapy, ergotherapy, speech therapy and physical therapy. UPDRS, CGI and PDQ 39 were assessed before and after 3 weeks. Outcome was expressed in terms of mean value, standard deviation and percent change. We divided in 2 groups: Group A with L-dopa equivalent (LED) change lower 50 mg and group B more than 50 mg LED. Age, PD duration and severity were similar in both groups.

Results: UPDRS III was reduced from $36,2 \pm 11,3$ to $29,1 \pm 10,3$ pts according 7,1 pts in all patients. In group A the reduction was 7,1 pts, in group B 6,9 pts. CGI was estimated as $2,4 \pm 0,6$ in all. PDQ 39 was improved from $41,7 \pm 16,3$ to $32 \pm 15,9$ by 9,3 PDQ according 21,3% in all. Group A: From $42,9 \pm 13,4$ to $31,9 \pm 15,9$ according 11 PDQ or 25,6%. Group B: From $41,8 \pm 18,6$ to $33,1 \pm 15,4$ according 9,7 PDQ or 20,1%. We observed amelioration higher than 20% within the subscores mobility, emotional wellbeing, stigma and bodily discomfort. No significant differences were found in the above mentioned groups with different amount of LED. Our results demonstrate a clear clinical benefit according the minimal clinical important changes (MCIC) in motor outcome and life quality for PD treated by a multimodal hospital therapy over 3 weeks. Interestingly we could not observe significant differences concerning UPDRS and PDQ 39 with different LED in our 2 groups.

P22.29

The impact of high intensity exercise on outcome in people with Parkinson's disease: A systematic review

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Objective: The objective of this systematic review with meta-analysis is to examine the effectiveness of high intensity exercise therapy when compared to conventional therapy on functional outcome in people with PD.

Methods: A systematic literature search was performed to identify all studies that met the inclusion criteria: (a) study design; randomised controlled trials (RCTs), (b) population; individuals with PD, (c) intervention; high intensity exercises (as defined by the individual study), (d) comparison; conventional exercises or sham/no intervention, (e) outcome; measures of impairment, activity or participation. Two reviewers independently assessed the risk of bias of each study against Cochrane criteria. Cochrane Review Manager Software was used to conduct statistical analyses to determine the treatment effect.

Results: A total of 3,155 records were identified and 9 RCTs were included, ranging in size from ten to 44 participants. The RCTs delivered the intervention using a variety of modalities including resistance, eccentric, treadmill and cycling training. Duration of interventions ranged from 8 weeks to 4 months. The frequency and duration of sessions also varied. Overall, the methodological quality of the studies was unclear. Preliminary results from the meta-analysis indicate that high intensity exercises have a significant favourable impact on gait speed [SMD -0.66, 95% CI -1.07- -0.26, $I^2=0\%$] and no significant difference on motor impairment [Unified Parkinson's disease rating scale (UPDRS) – motor subsection; -7.75, 95% CI -18.21- 2.71, $I^2=84\%$] when compared to conventional therapy.

Conclusion: This systematic review shows high intensity exercise significantly improves levels of activity limitation in people with PD when compared to conventional therapy. However, there is no significant change in motor impairment despite promising results in some studies. More research is needed to clarify the frequency, intensity and timing of high intensity exercise, in order to optimise the chance of motor impairment improvements using standard outcome measures.

P22.30

Patients with Parkinson's disease: their working capacity and employment in Sweden

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Objective: The aim of the present study is to investigate the working capacity and employment of patients with Parkinson's disease in southwest Sweden in order to obtain knowledge and to set up relevant management of multidisciplinary rehabilitation in the future.

Methods: The data were obtained with a postal survey questionnaire answered by 264 patients, aged from 42 to 67 years old. The patients were identified and confirmed to have a diagnosis of idiopathic Parkinson's disease. A comparison of years lost in working time was performed between patients with Parkinson's disease and a population without diseases. Ethical approval was obtained from the local ethical committee. All patients received information leaflets.

Results: 53% of the patients have reduced working time the same year when they received the diagnosis, some of the patients had already a part time work before they get their diagnosis. A further 19% of the patients reduced their working time one year after the diagnosis. Only a few patients had only temporarily decreased working time after the diagnosis. These patients were satisfied with their medication. The most disabled symptoms were hyperkinesia, tremor and stress sensitivity. About 40% patients have psychological symptoms (depression, anxiety and sleep disturbance). The high sickness absence causes a significant socioeconomic burden. This study shows that most of the patients reduced their working time immediately or one year after the diagnosis, which could be correlated with that only a few of the patients had received help from a professional rehabilitation team.

P22.31

AmbuloSono: A sensorimotor contingent musical walking program for Parkinson's disease rehabilitation

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Objective: Postural instability and gait disorder are important hallmarks of PD progression. They are often associated with non-motor symptoms, such as fear of falling, anxiety, depression and excessive avoidance of physical and social activities. Our aim is to develop a reward and behavioural reinforcement-based music walking program that can help patients in gaining automatic gait control while transforming naturalistic walking into a pleasurable habit of daily activity and exercise.

Methods: Ambulosono program utilizes GaitRminder iPod application to create a contingency between walking step size and musical cues enriched with rhythm, vocal singing and uplifting emotional salience. We recruited 46 patients, including those living in rural areas with no rehabilitation services. After giving formal written consent and a baseline screening test, patients were instructed to utilize the walk kit at home for regular exercise. The weekly target of walking time was set from 60 to 350 minutes. Their walking data was automatically sent to a central server for daily analysis and monitoring.

Results: Participants of Ambulosono can undertake large step walking over long distance with the walking time and speed regularly approached or surpassed the NIH guidelines. Significant improvements were also reported in terms of gait awareness and the amplitude of arm swings during walking. More importantly, a sub-group of subjects reported a marked reduction in fear of falling and increase in confidence. Our pilot study suggests that Ambulosono is an effective behavioural training paradigm that can improve multiple domains of motor and non-motor function for patients living with Parkinson's disease.

Acknowledgments: CIHR, Parkinson Alberta Society, the Movement Disorders Clinic-Alberta Health Services, Markin Undergraduate Student Research Program, and Branch Out Neurological Foundation.

P22.32

Using the SpeechVive to treat speech impairments in Parkinson's disease

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Objective: The purpose of this study was to examine the effectiveness of the SpeechVive device for improving speech production in individuals with Parkinson's disease.

Method: Forty-five patients with Parkinson's disease were enrolled in the study. Thirty-nine completed the study. Patients were, on average, 67 years old and had been diagnosed for 8.7 years. Speech and motor impairments ranged from mild to severe but were most often rated as moderate. Patients were assessed before and after an 8-week treatment period during which they wore the SpeechVive device for 2-8 hours per day. The SpeechVive device was developed at Purdue University and plays multi-talker babble noise in one of the patient's ears while they are talking. The noise induces the Lombard effect, a reflex to talk louder and clearer in the presence of noise. Patients were also assessed 4 weeks after treatment had ended to assess detraining. Half of the patients were assessed for an 8-week no-treatment period prior to treatment.

Results: There were no significant changes in sound pressure level (measure of vocal intensity/loudness), length of utterance, or speech rate during the no-treatment period. Ten of the patients demonstrated a decrease in sound pressure level after treatment, potentially due to disease-related changes. These subjects were not included in the statistical analysis, leaving a sample size of twenty-nine. Sound pressure level was significantly higher after treatment and remained significantly higher after the detraining period. Ratings of communicative effectiveness by patients and their caregivers were significantly higher after treatment. Speech rate declined across the treatment period and was significantly lower by the end of the detraining period, as compared to pre-treatment.

Conclusions: The SpeechVive was demonstrated to significantly improve vocal intensity and communicative effectiveness in a group of patients with Parkinson's disease.

Note: A portion of this data (subset of the subjects and measures) was presented at the Speech Motor Control Conference in 2012.

P22.33

Rehabilitation using blowgun in patients with Parkinson's disease

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Objective: To evaluate the effects of rehabilitation using the blowgun in patients with Parkinson's disease (PD). Pneumonia is the important complication in the patients with advanced PD. Maintenance of lung volume and breath holding might make effective coughs and prevent patients with PD from pneumonia.

Methods: We conducted rehabilitation using blowgun according to the Japan Sports Fukiya Association once a week. Patients with PD were evaluated about the Unified PD rating scale (UPDRS), pulmonary function test, Geriatric Depression Scale (GDS) and EuroQoL (EQ-5D) before and 3, 6 and 9 months after the intervention. We applied the formula of Japanese lung age using height and forced expiratory volume 1.0 (FEV_{1.0}), and evaluated

peak expiratory flow (PEF). Statistical analyses were performed by Wilcoxon signed-rank test.

Results: Fourteen patients (male 9) were included. The mean age and disease duration were 74.3 years and 7.3 years. Before the intervention, the mean modified Hoehn and Yahr was 2.6 on time / 3.2 off time and 8 patients had wearing off. The mean total UPDRS score was 33.9 on time (male 43.3, female 23.0). The lung age was older than real age + 5.93 years (male +15.87, female -5.17) and the mean PEF was 4.50 L/sec (male 4.65, female 4.29). The mean GDS and EQ-5D were 12.7 and 3.8. The male lung age became younger 3 months after the intervention than before (from +15.87 to 10.75; $p=0.027$). PEF in total and male increased at 6 and 9 months significantly from 4.50 to 5.35 ($p=0.008$), 5.23 ($p=0.041$); from 4.65 to 4.84 ($p=0.036$), 4.35 ($p=0.036$). The total UPDRS on time, GDS and EQ-5D did not change. However speech and posture (sub-scores of UPDRS) improved at 6 and 9 months significantly. The rehabilitation using blowgun is effective to improve PEF, speech and posture in patients with PD.

P22.34

European physiotherapy guidelines for people with Parkinson's disease

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Objective: We aimed to develop the 1st European physiotherapy guideline for Parkinson's disease, which can be used in any country but also be tailored to country specific possibilities and constraints (e.g. concerning healthcare organisation). The 2004 Parkinson's guideline of the Royal Dutch society for Physical Therapy¹ (KNGF) is unique in its field, but needed an update. Members of the Association of Physiotherapists in Parkinson's disease Europe (APPDE) had expressed their preferences to update and adapt the KNGF guideline into a collaborative European guideline.

Methods: Initiated by the KNGF and ParkinsonNet², 19 member organisations of the European Region of the World Confederation for Physical Therapy (ER-WCPT) collaborated to develop the guideline according to international standards (e.g. AGREE and GRADE). First, barriers in delivering optimal care were identified, e.g. though a survey in which over 3,000 physiotherapists throughout Europe participated. These were transformed into key questions for which conclusions were drafted based on systematic literature search. Other considerations to the conclusions (e.g. on availability) were collected, to finally create the recommendations. A panel of the European Section of the MDS was involved to develop MDS-supported referral criteria. Patients (e.g. through the European Parkinson's Disease Association, EPDA) were involved at all stages of the development process.

Results: Through a unique collaboration of 19 national professional physiotherapy organisations, we have developed the 1st European physiotherapy guideline for Parkinson's disease. It is available for free in English and Dutch (more languages to follow) at www.ParkinsonNet.nl/guidelines. The guideline provides decision support towards evidence-based, patient-centred care. Currently, several countries have started its implementation. At the MDS Congress 2012, the main recommendations of the guideline will be presented.

References: ¹Keus SH et al. *Mov Disord* 2007;22(4):451-460; ²Munneke M et al, *Lancet Neurol*, 2010;1:46-54

P22.35

A comprehensive dance-based movement program improves mobility in Parkinson's disease

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Objective: Mobility in Parkinson's disease (PD) is restricted due to impairments in gait, balance, and rigidity. Generally in PD, balance and gait difficulties do not respond to pharmacological and surgical treatments resulting in decreased independence and increased risk of falls. Recently, application of dance training and practice of large and faster movements has been shown to be beneficial in PD. This research study examined the effects of a new comprehensive dance-based Movement and Motion (M&M) training program created by one of the authors (CM), on mobility in people with PD.

Methods: Nineteen subjects (11 females and 8 males; mean age: 66.7 ± 7.2 years; range 55 – 80 years) with mild to moderate PD were recruited to participate in the 10-week M&M training (two 1-hour sessions per week) of which 15 subjects completed the study successfully. Several quantitative gait, balance control, and range of motion indices and clinical scores were obtained pre- and post-training to investigate the effects of M&M training. Gait indices were obtained during overground walking, balance control parameters were calculated from dynamic weight shifts tasks, and range of motion were obtained from different joints. Non-parametric Wilcoxon signed rank test was used to compare the changes in the above mentioned indices due to the training and changes were considered significant at $p \leq 0.05$.

Results: Gait velocity, stride length, double support and stance duration, degree of arm swing, and turning parameters improved after training. Regarding posture measures, the time taken to initiate movement shifts and to reach targets decreased significantly due to training. Also, range of motion at many joints increased significantly. These results suggest that the comprehensive M&M training can be utilized to improve mobility by improving gait, balance control, and range of motion which can subsequently lead to improved quality of life in people with PD.

P22.36

Effects of polestriding training on gait in Parkinson's disease

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Objective: Gait impairment is one of the most disabling of the symptoms of Parkinson's disease (PD) and often it does not respond well to pharmacological or surgical treatment. It has been shown that regular practice of polestriding (walking with poles) can improve quality of living, exercise capacity, and some gait measures in people with PD. This research study has quantitatively investigated if regular 12-week polestriding exercise training could improve gait in individuals with PD by obtaining spectrum of gait indices.

Methods: Sixteen subjects (8 males, 8 females; mean age: 63.9 ± 5.0 years; range 53-73 years) with mild to moderate PD (Hoehn-Yahr score: 2.5 – 3) were selected to participate in a 12-week (three 45-minute sessions per week) polestriding exercise program. Gait patterns were quantitatively measured during overground walking in medication-off condition (at least 12 hours after the last usual dosage of anti-parkinsonian medication) at four time points, each separated by 12 weeks: baseline, pre-training, post-training, and follow-up.

Results: Comparison of pre-training and post-training gait assessments indicated significant increases in step length, speed, and swing power as well as significant decreases (indicating improved gait) in step-time variability, Hoehn-Yahr score, and the gait and balance related items of the Unified Parkinson's Disease Rating Scale ($p < 0.02$ after Bonferroni correction of multiple comparisons). Since step-time variability and step length are associated with an increased risk of falls in PD, these results suggest that regular practice of polestriding may reduce the risk of falls. The observed improvements in gait due to polestriding may improve mobility for people with PD.

P22.37

Physical activity levels and disease severity in individuals with Parkinson's disease

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Objectives: To evaluate the association between physical activity level and disease severity in individuals with Parkinson's disease (PD); to investigate the physical activity level in individuals on different disease severity stages and in different PD subtypes.

Methods: Participants were evaluated with the UPDRS and the Human Activity Profile (HAP). They were also classified through the Hoehn & Yahr Scale (HY). Using UPDRS items, each patient received a final ratio score and based on its distribution, patients were assigned to one of three clinical subtypes: tremor-dominant (T), akinetic-rigid (AR), and mixed (MX). Correlation coefficients were used to investigate the association between physical activity level and disease severity (motor UPDRS and HY). An independent samples t-test was used to analyze the difference in HAP scores between two groups of disease severity (mild group HY= 1 to 2,5; moderate/severe group HY= 3 to 4). One-way anova was used to investigate the difference in the HAP between PD subtypes.

Results: 45 PD patients (65,3±10,9 years; 30 men, 15 women) participated in the study. Their UPDRS motor score was 12,9±7,4 and it was 65,3±20,7 in HAP. 24 individuals were classified as AR, 12 as T and 9 as MX. There were inverse, significant ($p<0,01$) correlations between the HAP and the motor UPDRS ($r= -0,64$) and the HY ($s= -0,54$). We found a significant difference in the HAP score between mild (72,13±16,24) and moderate/severe (48,47±23,22) PD groups ($p<0,05$). Individuals with mild disease presented a higher score in the HAP, showing a higher physical activity level. We did not find any difference in physical activity levels between the subtypes of the disease. Although the level of physical activity was not different between subtypes of PD, it was reduced with disease progression. The improvement in the level of physical activity should be prioritized in rehabilitation programs.

P22.38

Analysis of the psychometric properties of the Human Activity Profile in individuals with Parkinson's disease: Rasch Model

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Objective: The aim of this study was to evaluate the reliability and construct validity of the Human Activity Profile (HAP) in individuals with Parkinson's disease (PD).

Methods: PD patients classified in stages 1 to 4 in Hoehn & Yahr scale were evaluated with the HAP. The reliability and construct validity of the instrument was evaluated by the Rasch Model. This model determines if the level of difficulty of the items is appropriate for the skill level of individuals. It also reports the reliability of measurements and the calibration of items, which provide a degree of consistency or stability, ranging from zero to one. The coefficients higher than 0.80 are considered good and higher than 0.90 are excellent.

Results: 44 individuals with PD (65,3±10,9 years; 29 men, 15 women; disease duration of 11,36±7,3 years). The reliability coefficient of calibration of the items ranged from 0.90 to 0.92 indicating stability of measurements, and it ranged from 0.94 to 0.95 for subjects indicating that the measures can be reproduced in subsequent applications. Participant's ability showed a good distribution, as well as item's difficulty. The easiest item was "walk 1 minute" and the most difficult item was "run 3,2 km". Only three items of the HAP did not fit to model expectations. These items are related to reading and writing skills. The set of items that constitute the test seems to be divided in more than one dimension, suggesting that the HAP is a multidimensional test for individuals with PD. Since the multidimensionality does not preclude the use of an instrument as a clinically valid tool, the HAP seems to be a reliable and valid tool for assessing physical activity level in subjects with PD.

P22.39

Muscular power training improves gait and balance in individuals with Parkinson's disease: A Proof-of-Concept Study

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Objective: To determine whether muscular power training is tolerated and to gather preliminary data regarding the potential benefit in people with Parkinson's disease (PD).

Methods: This study was a within-participant, repeated-measures design. Patients participated in two baseline assessments and at the end of the intervention. Subjects with PD received training three times a week for ten weeks. The lower limb muscle groups trained were: hip flexors, extensors, adductors, abductors; knee flexors and extensors; ankle dorsiflexors; and plantar flexors. The Borg Scale of Perceived Exertion was used in order to investigate the subject's tolerance to the exercise. Work and muscular power were measured by isokinetic dynamometer. A lower limb bradykinesia subscore was derived by summing the Unified Parkinson's Disease Rate Scale motor exam items 26, 27, 29 and 31. Walking velocity, stride length and cadence were measured by GAITRite system, and balance was assessed by the Berg Balance Scale (BBS). Descriptive statistics and repeated-measures ANOVAs were employed for analysis.

Results: 13 subjects with PD (eight men; five women), with a mean age of 63.8±12.3 years (50-87), participated in the training program. Participants reported average perceived exertion by 12.8±1.1 (11-14), which corresponds to 'somewhat hard' on the Borg Scale. Participants increased their work ($p = 0.001$) and muscle power ($p = 0.0001$) compared with baseline. There was a significant improvement of bradykinesia (95% CI -1 to -3) and the BBS score increased 5 points (95% CI 2 to 7) with training. Walking speed increased significantly after the intervention (0.22 m/s, 95% CI 0.14 to 0.30), there was significant gain of stride length (0.09m, 95% CI 0.04 to 0.13) but this did not occur with the cadence (6 steps/min 95% CI 0 to 11). Preliminary data suggest that this intervention is tolerable and may be beneficial for balance and gait disorders in PD.

P22.40

LSVT Big Physical Therapy: Does it improve quality of life?

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Objective: Parkinson's disease is a neurodegenerative disease that causes a decline in motor function. Overtime, a person's disability increases leading to a decline in their overall quality of life. Physical therapy is used to improve functional mobility. Big and Loud therapy was developed specifically for patients with Parkinson's disease. Our goal is to show that patients who participate in Big physical therapy experience an improvement in their quality of life. This will be assessed using the PDQ-39.

Method: Patients who were to begin Big physical therapy completed the PDQ-39 on day 1 prior to beginning therapy. They were then asked to fill out the PDQ-39 after completing their 16th and final therapy session. Only patients who completed Big therapy within five weeks were included in the study. The mean difference in each of the eight subcategories of the PDQ-39 was calculated as well as the standard deviation.

Results: The average age was 68.6 years old. Improvement in PDQ-39 scores following Big therapy was noted in mobility (6.79 points), ADL's (6 points), emotional (1.39 points), cognitive (1.78 points) and bodily discomforts (6.75 points). No change was noted in stigma and social support. Worsening was noted in communication (1.19 points).

Conclusion: Our study did show that quality of life was improved in five subcategories of the PDQ-39 which were related to mobility. One category had some worsening, and the remaining two subcategories had no change. Due to the small sample size, this study did not achieve statistical significance, but the results deserve closer examination. A study with a larger sample size and one comparing traditional physical therapy to Big physical therapy should be done to further evaluate the benefit of Big therapy on the quality of life in our Parkinson's patients.

P22.41

Characterization of motor performance front of the functionality of elderly with Parkinson's disease

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Objective: Know the level of functional performance in elderly patients with Parkinson's Disease (PD) and correlate it to the scale of Hoehn Yahr staging (HY) and time to clinical progression

Methods: Field study, exploratory cross-sectional descriptive correlational approach were evaluated in 145 elderly patients with PD were divided into three groups according to age groups: G1 (60-69), G2 (70-79) and G3 (80-89) outpatients at the Division of Movement Disorders Department of Neurology, Hospital das Clínicas, Federal University of Parana - UFPR, Curitiba - Brazil. To collect data, we used two instruments: the Sociodemographic and Functional Independence Measure (FIM). We performed statistical analysis of comparison (Kruskal-Wallis), Pearson correlation and descriptive analysis of data.

Results: The sociodemographic characteristics revealed a higher frequency of women aged 80 to 89 years with a low education level (38.89%), mostly coming from remote areas of the city (90.48%). High scores were observed in MIF indicating functional independence. The comparison between the scores of FIM and FIM HY and mean time to clinical progression through the G1, G2 and G3 indicate the time of onset of disease and staging of HY did not affect the performance of these functional groups and the relationship between the three groups also showed no statistical difference between them.

P22.42

The question of long-term compliance to the recommendations made by a specialized interdisciplinary team

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Background: The Renata Hornstein Center, part of the Movement Disorders Unit at CHUM, offers an interdisciplinary approach for patients with advanced Parkinson's disease and loss of autonomy. At the end of the assessment, a treatment plan is proposed to the patient and his family and a team member follows-up with the patient 3 months later.

Objective: To evaluate if patients keep going with team recommendations after one year following their evaluation.

Methods: Quantitative and qualitative data on the adherence or not to the team recommendations were collected through phone contact with 25 patients and/or their caregivers.

Results: Of the 25 patients (17 male, 8 female), 65% had Idiopathic Parkinson's disease, others had Parkinsonian syndrome; the mean age was 72.3 years. The majority (80%) had difficulty with their balance and 72% cognitive deficits. Recommended interventions that were followed or maintained included changes made to medication, advice on management for dysphagia and installation of safety equipment to assist with mobility. Recommendations that met with resistance included changes in behaviour, suggested modifications to the home and the use of tools to assist with ADLs. Exercise programs and voice training exercises were abandoned after a few months.

Conclusion: For this clientele, the success of the treatment plan is largely left up to the caregiver who is already overwhelmed by the activities of daily life. Motivation to implement changes in behaviour

or to keep on with exercises is hard to maintain. Issues to reflect upon: ensure long-term follow-up particularly with physiotherapy; encourage attendance in exercise classes, ensure a link with community resources and offer respite care for the caregiver.

P22.43

Walking difficulties is the strongest contributing factor to fear of falling among people with mild Parkinson's disease

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Objective: Fear of falling is common among people with Parkinson's disease (PD) and may cause activity limitations and restrictions in participation. The aim of this study was to investigate contributing factors to fall-related self-efficacy in a clinical sample of people with PD.

Methods: The study included 104 people with PD that visited a neurological clinic during 2006-2011. Those >80 years of age, requiring support in standing or that did not understand the instructions were excluded. Mean (SD) age and PD-duration were 68 (9.4) and 5 (4.2) years, respectively; the mean (SD) "on" phase UPDRS III score was 14.5 (8.1). Fall-related self-efficacy (the dependent variable) was investigated with the Swedish version of the Falls Efficacy Scale, i.e. FES(S). Multiple linear regression analysis included independent variables targeting walking difficulties in daily life, freezing of gait, dyskinesia, fatigue, need of help in daily activities, age, PD-duration, history of falls/near falls, and pain.

Results: The median FES(S) score was 117 (q1-q3, 70-129; min-max, 11-130). Three significant independent variables were identified explaining 66% of the variance in FES(S) scores. The strongest contributing factor to fall-related self-efficacy was walking difficulties (explaining 60%), followed by fatigue and need for help in daily activities. These observations suggest that walking difficulties in daily life is the strongest contributing factor to fall-related self-efficacy in a mildly affected PD-sample. Targeting walking difficulties may help reduce fear of falling among people with PD.

P22.44

Test-retest and inter-rater reliability of the mini-BESTest in mild to moderate Parkinson's disease – a clinical approach

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Objectives: The inter-rater reliability of the mini-BESTest, previously found to be a reliable tool for balance assessment in individuals with Parkinson's disease (PD), have generally been studied using one test leader with different observers scoring the test. However, in daily clinical practice the same person instructs and scores the test, and the instructor may change between test sessions, warranting for reliable tests under similar conditions. Hence, the aims were to, in a clinical context, investigate the test-retest and inter-rater reliability of the mini-BESTest in elderly with mild-to-moderate PD.

Methods: Twelve individuals, diagnosed with idiopathic PD (66 – 79 years, mean age: 73; Hoehn & Yahr: 2-3; 1-13 years since diagnosis) were included. To achieve a clinically relevant assessment of the inter-rater reliability, two test leaders with

different experience of the test instructed and scored the test separately in similar facilities at a hospital. To limit the possible effects of bias, the subjects were randomized regarding which test leader to begin with. For the test-retest assessment, all participants returned 7 days after the first test session to perform the mini-BESTest under similar conditions (regarding time of day, time since medication etc.). Intraclass correlation coefficients (ICC), standard error of measurement (SEM) and smallest real difference (SRD) was used.

Results: Mini-BESTest had good to very good agreement (inter-rater: ICC= 0.775 and test-retest: ICC=0.895). On group level, the measurement error (SEM) was 1 point for test-retest and 2 points for inter-rater reliability, whereas on individual level, the error (SRD) was 3 and 5 points, respectively. This indicates that the mini-BESTest is a reliable tool for assessing balance of elderly with mild-to-moderate PD. However, on an individual level the results emphasize the importance of each patient being assessed by the same clinician. Future studies, including greater number of participants, needs to investigate this further.

P22.45

Development and feasibility of a novel conceptual framework for balance training in Parkinson's disease

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Objective: Balance training needs to be designed to challenge specific impairments of the targeted group. Moreover, to optimize a training regime, the theoretical approach needs to be tested in practice to enable modifications for further improvement. In addition, it is essential that the outcome measures used are appropriate, regarding the studied population and their specific impairments. Our aims were therefore to 1) to develop a highly challenging, progressive and varying group balance training regime specific to Parkinson's disease (PD) symptoms and 2) to investigate the feasibility of a this intervention as well as the outcome measures in elderly with mild to moderate PD.

Methods: The intervention (12 weeks, 3 x 45 minutes/week) was developed through discussions and workshops by a group of researchers and physiotherapists. Subsequently the feasibility of this intervention was evaluated in five subjects with idiopathic PD, mean age 72 years (range 69 - 80) and Hoehn & Yahr score 2 to 3. Indicators of feasibility included adherence, safety, progression, perception and adequacy of the outcome measures.

Results: Adherence was high (78%) and adverse events, fatigue and pain were scarce. The majority of the participants and trainers, respectively, considered the training as adequately progressive. All participants also considered the training regime as motivating, stating that they would recommend it to others. However, some perceived that the training period was too long. The outcome measurements were adequate as the participants were able to complete all assessment tools. On the other hand, a critical examination of the measurements revealed that sensory integration and physical activity were not adequately covered by the outcome measures. These findings support the overall feasibility of this new highly challenging group balance training program in elderly with mild to moderate PD. However, a RCT is required to evaluate the efficacy of the program.

P22.46

An acute Parkinson's Therapy Pathway; bridging the gap between hospital and homeChristopher Lovegrove¹, Helen Guppy¹¹Royal Devon & Exeter NHS Foundation Trust, Exeter, Devon, UK

Objective: People with Parkinson's can often experience long hospital admissions, and are frequently not discharged to their own homes to continue their rehabilitation. Reports from people living with Parkinson's show that the hospital environment does not replicate their own home set-up, and home-based rehabilitation programmes have been shown to be effective (Ashburn et al 2007, Antonini et al 2008). Furthermore, home based therapy has been shown to have positive advantages over day hospital based rehabilitation (Parker et al 2009). The authors aim to develop a Parkinson's Therapy Pathway for the acute hospital setting, integrating early home-based assessment and therapy sessions, with seamless transition to community services.

Methods: The early home assessment aims to focus and specify further rehabilitation in the hospital environment, using photographs of key home areas to allow the full MDT to enable the patient in hospital. Home based therapy sessions and a staggered discharge aim to reduce readmission rate and ease transfer to the community services. We have found that an exercise program that works in hospital has not always been successful at home and may need adjusting. The staggered discharge allows the patient and MDT to troubleshoot any problems at home, which can subsequently be solved in the hospital environment. We aim to create a template therapy discharge summary which is e-mailed to the community services and PD nurse on discharge, to give a comprehensive therapeutic account of admission and expedite therapy at home.

Results: The measured outcomes will be patient satisfaction, length of stay and readmission rates, alongside Lindop and UPDRS scores.

P22.47

Changes in vowel (co)articulation following intensive voice treatment (LSVT) in Parkinson's diseaseVincent Martel Sauvageau^{1,2}, Johanna-Pascale Roy^{1,3}, Mélanie Langlois⁴, Joël Maccoir^{1,2}¹Centre de recherche de l'Institut Universitaire en Santé Mentale de Québec, Canada²Université Laval, Faculté de médecine, Québec, Canada³Université Laval, Département de langues, linguistique et traduction, Québec, Canada⁴Centre hospitalier universitaire de Québec (HEJ), Québec, Canada

Objective: LSVT (Lee-Silverman Voice Treatment) is an intensive speech therapy program designed to reduce the symptoms of hypokinetic dysarthria, a speech disorder frequently associated with Parkinson's Disease (PD). Even though the effects of this treatment on voice intensity and intelligibility have been well documented in past studies, changes it might generate on vowel articulation and consonant-vowel sequences (C-V) coarticulation has been overlooked. These acoustic variables are of particular interest because they are known to contribute directly to speech intelligibility and they have not been studied in a systematic way.

Methods: The present study was designed to investigate the impact of LSVT on vowel articulation and coarticulation in C-V sequences. We report the acoustic data of 10 PD subjects with moderate hypokinetic dysarthria, before, immediately after, then one and two months after receiving the LSVT program. F1 and F2 formant values of the vowels /i/ /u/ and /a/ were measured at the initial and stable portion of the vowel in different consonant contexts: voiced and

voiceless occlusive (/b/ /d/ /g/ /p/ /t/ /k/) and voiceless fricatives /f/ /s/ "ch").

Results: Preliminary results show a small increase of F1/F2 vocalic space in the post-treatment conditions as well as reduced vowel dispersion, which are the acoustic correlates of better vowel articulation and increased stability. Other measures such as "Locus of Equation" and "Contrasts between consonant contexts" suggest an increase in C-V coarticulation, post-treatment. This ongoing study will help clarify the impact of LSVT on vowel articulation and coarticulation in PD. The project will also investigate the relationships between these measures and other acoustic variables such as speech rate and intensity.

P22.48

The type of secondary task matters in dual task walking during the Timed Up and GoTara L. McIsaac¹, Franchino Porciuncula¹¹Teachers College, Columbia University, NY, USA

Objective: Walking while simultaneously performing a cognitive or manual task typically alters gait, particularly in people with Parkinson's disease (PD). Difficulties in turning are also associated with the disease and can be related to falls. However, the relationship of the attention requirements of different types of secondary tasks and walking with turns is unclear. Therefore, we examined the effects of the type of secondary task on performance costs to dual-task walking and turning.

Methods: Twelve participants with PD and six healthy controls were assessed using wearable inertial sensors during the instrumented Timed Up and Go (TUG) under six conditions; single-task and in five dual task conditions: 1) carrying water, 2) serial-3 subtractions, 3) combined water and subtraction tasks, 4) dialing a cell phone, and 5) buttoning a coat. The cost to performance from dual tasking was compared across conditions and groups for the sit-to-stand, 7-meter walk, turn, walk back, and turn-to-sit components of the TUG, using mixed design ANOVAs on each component (total duration, stride length, sit-to-stand peak velocity, turn duration, and turn-to-sit peak velocity).

Results: All participants sustained performance costs in all gait measures to different degrees according to the type of secondary task ($p < 0.005$), with the greatest costs during walking while carrying water and subtracting, and the least cost in the serial-3 subtraction condition. Compared to controls, participants with PD sustained greater costs to stride length in all dual task conditions ($p < 0.05$), and greater costs in time spent turning when also carrying the water or buttoning the coat ($p < 0.05$). We conclude that the type of secondary task performed exacts different costs on walking and turning components of the TUG. For individuals with PD, everyday activities such as buttoning a coat or carrying a cup while walking may pose particular risks to balance, especially when turning.

P22.49

Pre-stepping postural preparation in patients with Parkinson's disease with and without freezing of gaitSusanna Mezzarobba¹, Alice Pellizzaro², Sgubin Giulia¹, Marcovich Roberto¹, Valentini Roberto²¹Physiotherapy Degree, University of Trieste, Italy²Orthopaedics and Traumatology Clinic, Cattinara Hospital, University of Trieste, Italy

Objective: investigate variability in postural adjustments prior to first step of Gait Initiation (GI) in Parkinson's Disease (PD) patients with freezing of gait (FOG) compared to patients without FOG (NO-FOG) and their healthy elderly peers. People with Parkinson's disease

frequently have difficulties with generating anticipatory postural adjustments (APAs) for forward propulsion and lateral weight transfer when initiating gait, and frequently occurring FOG episodes in GI. Detect differences between subjects NO-FOG and FOG in GI, outside actual FOG episodes, can support the hypothesis of FOG as a specific disorders of load regulation.

Methods 18 patients were enrolled and divided into 3 different groups: subjects with PD NO-FOG (7), subjects with PD-FOG (6), healthy subjects (5). All PD subjects (ON-phase) underwent clinical (H&Y, UPDRS III, FOG-Q, BBS), and kinematic-kinetic evaluation by means of motion analysis laboratory. COP displacement, COM-COP distance (stability limit), stepping features including length, width of the first step of GI were compared between groups during simple and dual task.

Results: No differences were found in clinical data between both PD patients group. In PD FOG group COP displacement results greater than PD NO FOG, but similar to healthy group. In APA-phase they showed increased posterior ($p=0,008$) and lateral toward stepping limb COP displacement ($p=0,014$). PD FOG patients also showed reduced forward propulsion ($p=0,07$) in taking the first step. In PD FOG subjects distance COP-COM increased backwards and lateral toward stance limb compared to PD NOFOG subjects ($p=0,008$). Posterior COP displacement is also increased in dual-task ($p=0,03$). Only patients PD FOG initiated gait with a significantly shorter step as compared to healthy ($p=0,03$) and with a significantly reduced speed ($p=0,04$). In PD patients the ability to generate a consistent stepping pattern during GI may be altered but PD FOG patients show a higher instability (not clinically manifested) and reduced forward propulsion.

P22.50

Neurocognitive rehabilitation with motor imagery vs treadmill training for freezing of gait in Parkinson's disease: A randomized controlled study

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Objective: compare the efficacy of a neurocognitive rehabilitation based on explicit motor learning using Motor Imagery (MI) versus a more implicit motor learning treatment with treadmill, to improve Freezing of gait (FOG) in Parkinson's Disease (PD) subjects.

Methods: 21 PD patients with FOG (median age $75\pm 4,9$, disease duration years $9\pm 3,6$, H&Y 1,8 range 1-3), no evidence of dementia (MMSE >24) or depression (BDI <16), were enrolled and randomly assigned to different treatment groups. Selected patients performed 20 sessions of a rehabilitation program based on MI for Group 1, while Group 2 underwent treadmill training. Disease stage (H&Y and UPDRS III), FoG (FOGQ), quality of life (PDQ-39), locomotion (Timed up and go-TUG, six minute walk test-6MWT), balance (Berg balance test-BBT) and disability (Modified Parkinson's Activity scale-MPAS) were assessed at baseline, after treatment, at follow up of 4 and 12 weeks in stable pharmacological therapy; furthermore patients underwent a brief neuropsychological test to assess frontal and executive functions to define motor learning ability. A neurocognitive rehabilitation treatment program, aiming to modify wrong strategies in motor planning and improve movement control, was administered to 11 patients, while other 10 patients underwent treadmill training.

Results: At baseline both groups did not differ for clinical variables, neuropsychological scores or rehabilitation scales. After treatment in Group 1 a significant reduction in FOGQ ($p=0,01$) and an

improvement in some rehabilitation scales (MPAS=0,01 BBT $p=0,02$) were detected and retained at the second follow up 12 weeks after (FoGQ $p=0,02$ MPAS=0,002 BBT $p=0,09$). While no significant changes were shown in Group 2. This improvement maintained at the second follow-up suggests that learning effects were retained in daily life. The rehabilitation program with MI could represent an interesting rehabilitation strategy to treat FOG in PD patients.

P22.51

Assessment of gait therapy effectiveness in the patients with Parkinson's disease on the basis of three-dimensional movement analysis

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Objective: The purpose of this study was to assess: gait pattern disorders based on three-dimensional gait analysis and effect of physical therapy in a group of people with Parkinson's Disease (PD).

Methods: 32 subjects with PD (14 women and 18 men; age range: 50-75) were qualified for research which run for 3 weeks and included 18 PNF therapeutic sessions. 35 control subjects were included in research (13 women and 19 men; age range: 52-77). Gait analysis using the Vicon 3D system took place in the Biokinetics Laboratory in the University School of Physical Education in Krakow. Research group were conducted before and after treatment, control group were tested once.

Results: Comparing the average peak angle changes and average standard time results (%gait cycle) corresponding with angles of movement in cervical spine, elbow and shoulder joint statistically significant changes were observed. The study indicates the differences in both groups in spatio-temporal parameters and angular changes of gait.

P22.52

Dancing to enhance mobility in people with Parkinson's disease

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Objective: Although therapeutic dance is increasing in popularity, the feasibility of Irish dancing for older adults with idiopathic Parkinson's disease (PD) remains open to question. The aim of this study was to test the feasibility and safety of Irish set dancing compared to standard physiotherapy for the management of movement disorders in PD.

Methods: We tested 24 individuals with idiopathic PD from Venice, Italy. Each was randomly assigned to either Irish set dancing classes or traditional physiotherapy classes for a period of 6 months, coupled with a home program. The main outcome measure was mobility measured on the Unified Parkinson's Disease Rating Scale. We also measured gait freezing and balance.

Results: In older adults with PD, both the Irish set dancing and the physiotherapy exercise program were shown to be feasible and safe. Adverse events such as falls, serious injuries, death or rates of admission to hospital were similar in the two groups. Improvements were made in both groups although the dance group showed great gains in motor disability. Dancing classes are safe and feasible in

people with mild to moderate levels of disability associated with Parkinson's disease.

P22.53

An Australian model of inter-professional rehabilitation for Parkinson's disease

Meg E Morris

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Objective: Parkinson's disease is a chronic and progressive condition that can affect movement, balance, mobility, the ability to perform daily activities, autonomic function, cognition, and psychosocial function. It affects individuals as well as families and caregivers. Each person living with Parkinson's disease is unique and services need to be comprehensive and tailored to individual needs.

Methods: In Melbourne Australia we have led comprehensive inter-professional rehabilitation services to assist people with Parkinson's disease and the significant others in their lives to live well with this condition. Rehabilitation interventions are research led and based on current scientific findings on responses to movement rehabilitation strategies, strength training, cognitive training, and physical activities such as walking, dancing and hydrotherapy. Services are provided in home, community and hospital settings. As well as adopting science informed clinical guidelines, emphasis is placed on teaching health professional how to work effectively and efficiently within a team and how to ensure client centred and family focussed outcomes.

Results: In both young adults and older people with PD, a comprehensive inter-professional team based model of rehabilitation has been found to be effective, feasible and safe. As well as optimising mobility, functional task performance and physical activity, it is argued to reduce care-giver burden by empowering people to be more independent. The aim is to optimise quality and life and well-being through targeted and effective services provided at the right time by the right person in the right environment.

P22.54

Home-based gait improvement in Parkinson's disease: using video to support self-cueing

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Objective: Individuals with Parkinson's disease (PD) who experience gait impairment may benefit from external cueing, such as statements like "take big steps". This external cueing approach is often successful in establishing short-term gait improvement; however, long-term improvements are more difficult to achieve. This study tested the effects of a novel home-based video intervention designed to facilitate longer-term gait improvement in individuals with mild to moderate PD.

Methods: Five participants (mean age = 71.4) with PD related gait impairment completed a two-week home-based gait improvement intervention, designed to help participants learn to cue themselves. Video of each participant walking with and without verbal cueing (e.g. take big steps) was captured in a laboratory setting, edited, and delivered to participants for home-based viewing every-other-day for two weeks. The video-intervention consisted of alternating periods of active viewing of oneself walking (3x1 minute), timed walking practice (3x3 minutes), and embedded audio coaching. Participants step length, gait speed, and functional mobility were

assessed before and after the two-week intervention, and after a two-month period of unprescribed practice.

Results: Immediately after the two-week intervention, all five participants showed improved step length, four of the five participants showed improved gait speed, and four of the five participants showed improved functional mobility. Four participants returned for testing after two-months of unprescribed practice. At this time, compared to pre-intervention measurement, all four participants showed improved step length, three of the four showed improved gait speed, and all four showed improved functional mobility. Feedback from participants and researchers established feasibility for larger-scale intervention testing and implementation.

P22.55

The impact of physical environmental barriers on accessibility problems- very old people with self-reported Parkinson's disease versus controls

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Objective: To investigate which physical environmental barriers that contribute the most to accessibility problems among very old people with self-reported Parkinson's disease (PD) versus matched controls.

Methods: Data collected for the cross-national ENABLE-AGE Survey Study were used to identify people with self-reported PD (n=20), and to select three matched controls per individual (n=60). The matching criteria were age (mean=82 years), sex, country, and type of housing. By means of the Housing Enabler instrument, data on individual profiles of functional limitations and 188 physical environmental barriers (EB) in the housing environment were collected. In addition, accessibility problem scores were generated that represent a function of the individual profiles of functional limitations and the presence of physical environmental barriers.

Results: The number of EB did not differ (p=0.727) between the two samples. The PD-sample had however significantly (p<0.001) more accessibility problems than controls: median (q1-q3) was 192 (112-232) versus 63 (14-128). The top three physical EB that induced the most accessibility problems were similar for the two samples: Wall-mounted cupboards and shelves placed extremely high; No/too few seating places (exterior surrounding); No grab bars at shower/bath and/or toilet. In all instances, these barriers induced significantly (p≤0.016) more accessibility problems among very old people with self-reported PD than among controls. This was due to that the PD-sample had more (p=0.004) functional limitations. Importantly, the 20 environmental barriers that generated the most accessibility problems differed between the two samples. That is, six of the EB in the top 20 list for the PD-sample did not appear in the list for the controls: e.g. three concerned exterior surroundings and two concerned indoor design features requiring hand use.

Conclusions: Our findings suggest that accessibility problems and physical environmental barriers need specific attention among very old people with self-reported PD.

P22.56

The changes of gait pattern after arm load in Parkinson's disease

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Objective: Gait disturbances characterized by slow velocity, short-step, decreased arm-swing and festinating gait are common features in Parkinson's disease. Due to unsatisfactory response to dopaminergic medication, much research has focused in physical therapy for treatment. It is known that gait pattern is influenced by amplitude of arm-swing. The purpose of this study is to evaluate the effect of weight load to arms on gait pattern in Parkinson's disease.

Methods: Thirty patients with Parkinson's disease were enrolled in our study. We estimated gait parameters using three-dimensional motion analysis system. We checked spatiotemporal parameters such as walking speed, stride length, stride width and cadence. Kinematic parameters including arm-swing amplitude, trunk and pelvic rotation are also obtained. The patients walked for 6 meters with and without 0.45kg bag of sand tied in each forearm. We compared gait parameters between two conditions.

Results: Gait disturbance was generally improved after weight load in both arms. Arm swing amplitude is more increased in walking with arm load. Spatiotemporal parameters such as walking speed, stride length and cadence significantly improved after arm load. Amplitude of arm-swing is highly correlated with walking speed and stride length. Our result support that increased arm-swing magnitude enhanced locomotion in Parkinson's disease. The effect of weight load on arm-swing is obvious, and might result in substantial changes in gait pattern. These findings might be useful information for gait training in Parkinson's disease.

P22.57

A pilot study based on a proactive exercise program (PEP) for mild to moderate stage Parkinson's disease

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Objectives: Exercises are essential in the none-pharmacological treatment of Parkinson's Disease (PD) however guidelines for their application (type, frequency, intensity, and duration) remain unclear. Based on new approaches (Training Big, Tai Chi, Task oriented, Multi tasks...) a new proactive exercises program (PEP) was developed, however its feasibility was still unproven.

The objective of the pilot study was to evaluate the feasibility and to determine which incapacities resulting from Parkinson's disease could be improved using the PEP program in this population.

Methods: 11 subjects with idiopathic PD (Hoehn & Yahr stage 1-3) participated in PEP program twice a week for 6 weeks. The feasibility criteria, amongst others, were the subjects' ability to perform the exercises and the occurrence of adverse events. Axial articular mobility, balance, motor performance and quality of life were measured to evaluate the effectiveness of the program.

Results: The majority of subjects were able to perform the PEP exercise program with no occurrence of serious adverse events. Significant improvements ($p < 0.05$) were observed with the sit to stand test (STS), in bed mobility with and without blanket and the time up and go (TUG) test. However the results show a reduction in the extension range of cervical motion.

Conclusion: The feasibility of the PEP program was shown within the PD population that was targeted. In fact, there was significant improvement with certain variable measures which suggests the PEP exercise program could improve the subjects' ability to perform activities. However further studies would be necessary to confirm this.

P22.58

Bradykinesia and timed up and go are improved after dynamic cycling in Parkinson's disease

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Objective: Parkinson's disease is a neurodegenerative disorder and is estimated to affect 7-10 million individuals worldwide. Bradykinesia or slowness of movement, a primary symptom, can cause significant disability. Previous studies have shown that active-assisted cycling improves bradykinesia. However, it is important to correlate changes in clinical measures of bradykinesia with performance during functional mobility tasks. The aim of this study is to document changes in bradykinesia after bouts of dynamic cycling and to establish a relationship between the UPDRS clinical scores and the Timed Up and Go (TUG) test.

Methods: Individuals with mild to moderate PD were randomly assigned into either a static or dynamic cycling group. Each subject was first evaluated using the UPDRS Motor III scale, a quantitative measure of bradykinesia (Kinesia 3.0), and the TUG and then completed three days of cycling with one day of rest between. A post-exercise evaluation was completed one day after the last cycling session.

Results: Analysis of combined Kinesia 3.0 bradykinesia measures shows an improvement in amplitude for both the static and dynamic groups of 40.0% and 50.6% respectively. Frequency of movement scores indicate a similar trend with the static group improving by 17.9% while the dynamic group improved by 42.6%. The overall UPDRS scores show a 1.1% and 9.8% improvement in UPDRS, for the static and dynamic groups respectively, and TUG self-selected speed worsened by 16.1% in the static group but improved by 17.3% in the dynamic group. TUG scores show improvements in functional movement alluding to improved motor planning and improved speed of movement. These findings are consistent with the findings of the UPDRS motor scale as well as findings from the Kinesia 3.0.

P22.59

Efficacy of mental practice mnemonic coupled with physical practice in improving gait of patients with Parkinson's disease

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Objective: Strategies to minimize the gait disruption typical of PD patients have posed a great challenge for Physical Therapy Science. Mental practice associated with physical practice can be an important approach to improve the efficiency of attention control on the gait. Thus, the aim of this study was to verify the efficiency of mental and physical training in improving gait performance of patients with Parkinson's disease (PD patients).

Methods: A total of 24 PD patients participated in the present study, comprising 14 men and 10 women, having a mean age of 68.3 (SD = 10.86), 8 in stage 2; 10 in stage 2.5 and 8 in stage 3 of evolution of disease, according to the Hoehn and Yahr Classification. Patients were randomly divided into two groups: Mental Practice group (MP), which carried out 8 sessions (twice a week) of physical training coupled with mental practice; and a Physical Practice group (PP), which performed only physical training. Patients were tested whilst on levodopa medication, which remained unchanged throughout the study. All participants signed the free informed term of consent, previously approved by the local Ethics Committee.

Results: There was a significant improvement of performance in gait with regard to speed, exclusively in the MP, and independent of stage of evolution of disease (p-value < 0.001). In contrast to results at study baseline, there was a significant difference in the gait speed between the groups after training (p-value < 0.01).

Conclusions: Physical training coupled with mental practice leads to significant improvements in gait performance compared with the same training without mental practice. Thus, mental practice can be useful in the motor rehabilitation of such patients, constituting a straightforward, inexpensive and swift form of training for non-demented patients.

P22.60

A vision of improved postural stability in Parkinson's disease: enhancing balance through visual training under dual-task conditions

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Objective: It is well documented People with Parkinson's disease (PWP) experience mobility impairments and an increased risk of falls secondary to deficits in balance, posture, and vision.^{1,2} These deficits can cause enhanced difficulty for PWP when performing under dual-task conditions. Research reveals PWP utilize visual feedback to maintain upright posture and control balance as a compensatory strategy for inaccurate processing of proprioception and sensory feedback.³⁻⁷ Vision as a secondary task under dual-task conditions has yet to be explored. The purpose of this poster is to discuss the relevant literature and describe dual task treatment concepts to enhance balance and visual abilities in PWP.

Methods: Recent literature suggests visual deficits and difficulty performing under dual-task conditions in PWP add to the challenges of maintaining effective balance. Pertinent visual deficits include: decreased visual attention, saccades, smooth pursuits, peripheral vision, depth perception, and vertical eye movements.⁸⁻¹⁰ Studies indicate an increase in postural sway secondary to saccadic suppression, difficulty initiating saccadic movement, a hypometric saccadic gaze response, and decreased peripheral vision contribute to PWP difficulty in detecting and reacting to visual stimuli.^{5,8,9}

PWP are known to experience increased fall risk when completing simultaneous tasks.¹ The 'dual-task paradigm' suggests the performance in a primary task deteriorates while a secondary task is simultaneously being performed.¹¹ However, studies have also shown improved performance in a primary task as well as two concurrent tasks under dual-task conditions.^{1,12,13} This infers with appropriate challenges, PWP have the potential to improve under dual-task conditions.

Results: The authors will introduce, describe, and outline the need for dual-task training that includes visual strategies for saccadic movement, visual attention and processing speed, pursuits, and head turning which assist PWP in stabilizing postural control for improved balance performance. These treatment ideas will incorporate effective dual-task visual methods for use in the rehabilitation and home setting.

P22.61

A unique community group rehabilitative exercise and therapy (GREAT) program for people with Parkinson's disease

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Lack of activity is a major risk factor for morbidity and mortality in the aging population. There is growing evidence that therapeutic exercise is an effective method to significantly increase activity, function and quality of life for people with Parkinson's disease (PD). However, availability of appropriate community programs is rare. The Group Rehabilitative Exercise and Therapy (GREAT) program fills a gap that exists in the rehabilitation spectrum between traditional therapy and community gyms in an effort to improve function and activity levels.

Objective: Our aim was to test the feasibility and impact of a unique tri-therapeutic program that merges physical, occupational, with speech language therapy techniques.

Method: This study utilized a single group repeated measures design. Testing was completed at baseline, 3, and 6 months post start of group exercise. Fifteen volunteers with PD were enrolled into a one hour (2x per week) group session run by physical or occupational therapy assistants under the supervision of licensed therapists. This 12 week program incorporated vocalizations, breathing exercises, memory and recognition, fine and gross motor mobility exercises for extremities and trunk, balance activities and progressive distance walking techniques.

Analysis: Repeated measures ANOVA was used to analyze significant differences in physical performance, function and quality of life measures.

Results: Significant improvements were seen in walking speed (6 meter walk test), voice loudness, quality of life (PDQ-39, communication), cognition (MOCA), and disability (UPDRS, total). Additionally, subjects reported improved clarity of voice. Post intervention interview indicated that socialization was exceedingly important to the groups' adherence.

Conclusions: People with PD benefit from this tri-therapeutic program. The PT, OT and speech components were easy to integrate during all exercise classes and demonstrated significant clinical benefits.

P22.62

Evaluation of the upper limb in people with Parkinson's disease: a systematic review

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Objective: Treatments for people with Parkinson's disease (PD) include interventions to address upper limb movement disorders. To measure the efficacy of these interventions, measurement tools which are reliable, valid and responsive in this population are needed. A two part systematic review was designed to examine these measurement properties in upper limb measurement tools used in PD. The aim of part one was to identify evaluative measurement tools described in the literature.

Methods: A systematic search was conducted in July 2012. Studies were included if they evaluated the effects of a treatment intervention or disease progression on upper limb impairments, activity limitations or participation restrictions in people with PD. Studies which utilised laboratory based equipment or measurement techniques which could not be replicated using the information provided in the study were excluded. The study was limited to articles published in English.

Results: Following screening, a total of 17 measurement tools were identified. The effects of medical, surgical and other interventions such as exercise, or changes occurring with disease progression were evaluated, and impairments, activity limitations and participation restrictions were quantified. The identified measures were largely generic upper limb measures, tools developed for conditions other than PD, and single or grouped upper limb items taken from global PD-specific scales such as the UPDRS. One PD-

specific upper limb measurement tool, the Modified Bradykinesia Rating Scale,[1] was identified. There remains the need to understand the measurement properties of each of these tools, and to examine their clinimetric properties and clinical utility for the evaluation of people with PD.

P22.63

Parkinson's disease and forced exercise: A preliminary study

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Objective: The concept of forced exercise has drawn attention for the treatment of Parkinson's disease with anecdotal reports of success. To ascertain any significant effect of forced exercise on Parkinson's disease symptoms.

Method: We examined 23 patients (13 experimental and 10 controls) in a blinded, randomized, controlled study on a number of standard Parkinson's measures after participation in eight weeks of twice weekly forced exercise using a motorized stationary bicycle. Dependent measures were UPDRS-III, Berg Balance Scale, Fingertapping, and the PDQ-39. Scores were obtained immediately after the eight week period of exercise and then after a three month period had elapsed.

Results: Results did not demonstrate any differences between the exercise and control groups on any measure at any point in time. A within subjects effect was demonstrated for forced exercise on overall UPDRS-III scores, but no other within group effects were noted. Results suggest that early enthusiasm for forced exercise may need tempering. Limitations of the study are discussed as well as numerous logistical challenges to this type of study.

P22.64

Randomized Clinical Trial (RCT) of Voice treatment for Parkinson disease

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Objective: This RCT was designed to evaluate the short and long-term impact of voice treatment in PD. 89% of individuals with PD have a speech and voice disorder that negatively impacts quality of life. Our research team has developed and advanced an intensive, exercise-based voice treatment for PD, known as the Lee Silverman Voice Treatment (LSVT). Published data document improvements in variables critical to functional speech production: vocal loudness (sound pressure level (SPL)) and pitch variability (fundamental frequency variability) during reading and monologue that are maintained 24 months post-treatment. The current study was designed within the RCT structure to advance the quality of research on voice treatment for PD.

Method: Eighty four subjects (64 with PD, 20 without) ranging in age from 45-85 years old were enrolled. Subjects with PD were assigned at random to one of three groups: intensive voice

treatment (LSVT), intensive articulation treatment (ARTIC), or no treatment (NOTX). Both treatments were administered by expert clinicians, four 1-hour sessions per week for 4 weeks. The primary outcome variable was: SPL across a range of speech tasks. Acoustic data were collected on two separate days during the week immediately before (PRE) and after (POST) treatment, and again six months later (6MO).

Results: Following treatment, the LSVT group increased SPL significantly on all tasks ($p < 0.0001$) and the ARTIC group increased SPL significantly on all but one task ($p < 0.05$). The increase in SPL for the LSVT group was significantly larger than those of any other group ($p < 0.05$). Only the LSVT group maintained significant increases in SPL ($p < 0.001$) from PRE to 6MO. Subjects who received LSVT had the greatest magnitude and duration of treatment effects. The implications of these outcome data will be discussed in the context of treating disordered speech and voice in Parkinson disease. (NIH-NIDCD R01-DC01150)

P22.65

Development of an intelligent bicycle for rehabilitation in Parkinson's disease

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Objective: The benefits of exercise for people with Parkinson's disease (PD) have been documented but it is unclear what constitutes an optimal exercise intervention. Every individual with PD is unique and it is likely that exercise responses are not "one size fits all". The aim of this study is to construct a novel, automatically controlled cycling test-bed to investigate the factors and features that are responsible for significant improvements in motor skills from accelerated cycling.

Methods: Individuals with mild to moderate PD were randomly assigned into either a static or dynamic cycling group. Each subject was first evaluated using the UPDRS Motor III scale and then completed three days of cycling with one day of rest between. A post-exercise evaluation was completed one day after the last cycling session.

Results: Following three days of cycling, improvements in the UPDRS motor scores were observed in both the static (1.1%) and dynamic (9.8%) groups to lesser degrees. Improvement in the upper extremity (UE) subscale (8.1% and 12.4%) and changes in the lower extremity (LE) subscale (4.3% worsening and 15.6% improvement) were also observed for each group. Differences were also observed between groups for posture (improvements of 1.2% and 9.5%), tremor (9.8% improvement and 1.4% worsening), bradykinesia (6.0% improvement and 0.4% worsening) and gait (improvement of 5.1% and 5.3% worsening score). UPDRS scores for UE and LE scores suggests a systemic effect, driving UE improvements with LE cycling. In three days of dynamic cycling, participants improved their Parkinson's symptoms. This automated cycle provides rigorous test-bed for correlating cycle operation with the rider's physical state and resulting improvement in motor skills. Future studies will use programmable aspects of the system enable customized cycling regimens for individuals with widely varying capabilities to be easily implemented.

P22.66

Gait velocity and step length predict aerobic capacity in patients with Parkinson's disease

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Objective: To investigate if specific gait parameters can predict aerobic capacity in patients with Parkinson's disease (PD).

Methods: PD patients (n=95) were evaluated on the Unified Parkinson's Disease Rating Scale motor section (UPDRS III), maximum oxygen consumption (VO₂ max), and a GAITRite® electronic walkway to measure motor symptom severity, aerobic capacity and spatiotemporal aspects of gait respectively. Significantly correlated variables were entered into a linear regression model to determine what gait parameters predict aerobic capacity in patients with PD.

Results: After accounting for age and gender, gait velocity was a significant predictor of VO₂ max (R²=0.473; p<0.001). However due to the colinearity among gait measures, step-length was also a predictor of VO₂ max (R²=0.461; p<0.001), accounting for the same variability as velocity. The results suggest slower gait speed/shorter step length are predictive of lower aerobic capacity.

Conclusion: We suggest gait velocity and step length should be measured when performing aerobic capacity tests in patients with PD. It is important to account for the severity of gait impairments as they influence aerobic capacity. Furthermore, rehabilitation strategies focused on improving aerobic capacity in patients with PD may also want to consider limitations of gait velocity and step length.

P22.67

Parkinson's disease: The addition of a concurrent task changes postural reactions

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Objective: This study aimed to determine the effects of a concurrent task on postural stability in subjects with Parkinson's disease (PD).

Background: Postural instability is one of the most disabling features of PD. Studies have shown that the individuals with PD have difficulty performing dual-tasks. However, few studies have investigated the postural reactions during the performance of a concurrent task and its relationship with executive function.

Method: Twenty subjects with Hoehn and Yahr 2-3 were tested under two conditions: standing quietly and standing while enumerating animals. The following descriptive measures of the centre of pressure (CoP) displacement were collected by posturography: the total CoP trajectory over the support surface, the circular area covered by the CoP, and the velocity of the CoP sway. Participants also performed the Trail Making Test (TMT).

Results: T-tests showed that the three posturographic measures differed significantly when single- and dual-task conditions were compared (p<0,001; p=0,033; p=0,040, respectively). The CoP

trajectory and velocity correlated to the delta of TMT on dual-task condition (r=-0,567, p=0,034; r=-0,567, p=0,034), but not on single-task condition (r=-0,176, p=0,545; r=-0,177, p=0,545).

Conclusion: The addition of a concurrent test changed postural reactions and postural reactions correlated to an executive function measure, suggesting the relation between balance strategies and executive function in individuals with PD.

P22.68

The effectiveness of occupational therapy in Parkinson's disease

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Objective: Evidence for the added value of occupational therapy (OT) in the care for patients with Parkinson's disease (PD) is inconclusive due to a lack of rigorous studies. The aim of this trial is to evaluate the (cost) effectiveness of OT in improving daily functioning of patients with PD.

Methods: A multicentre, assessor blinded, two armed randomized controlled clinical trial, with evaluation at three and six months. Home dwelling patients with PD and with an OT indication are assigned to the experimental group or the control group (2:1). Patients and their caregivers in the experimental group received 10 weeks of home based OT according to recent Dutch guidelines. The intervention is delivered by occupational therapists who have been specifically trained to treat patients according to these guidelines. Participants in the control group do not receive OT during the study period. The primary outcome for the patient is self-perceived daily functioning at three months, assessed with the Canadian Occupational Performance Measure. Secondary patient related outcomes include: objective performance of daily activities, self-perceived satisfaction with performance in daily activities, participation, impact of fatigue, proactive coping skills, health related quality of life, overall quality of life, health related costs, and effectiveness at six months. All outcomes at the caregiver level are secondary and include self-perceived burden of care, objective burden of care, proactive coping skills, overall quality of life, and care-related costs. Effectiveness is evaluated using a covariance analysis of the difference in outcome at three months. An economic evaluation from a societal perspective is conducted, as well as a process evaluation.

Results: Hundred and ninety one patients were included in the trial. Seven patients have dropped out. The final follow up assessments take place in April 2013. The outcomes will be presented at the congress.

P22.69

Perceptions of participation among people with Parkinson's disease

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Objective: To describe and deepen the knowledge of perceptions of participation in everyday life among people with Parkinson's disease (PD).

Methods: The qualitative method of conducting focus groups was used, and each group was interviewed once. The participants were recruited at the Department of Neurology, Skåne University Hospital in Lund, Sweden, and they should have had their PD diagnose for > one year. Strategic sampling was used to ascertain that the participants represented men and women, different ages and a variety regarding living arrangements, work and family situations. Recruitment continued until saturation was reached, and the final sample consisted of 29 participants. Their mean (SD) age was 68 years (6.2) and the mean (SD) PD-duration was 11.1 (7.9) years. Homogeneity within each focus group was based on self-rated disease severity (mild, moderate or severe). In total, nine focus groups were conducted (three groups per severity grade): mild (n=11, min-max: 3-5), moderate (n=10, min-max: 3-4), and severe (n=8, min-max: 2-3). The focus groups were led by an experienced researcher and a PhD student.

Results: The preliminary analyses indicate that unchanged participation is important for people in the early stages of the disease, even if it is under new circumstances. The participants with moderate or severe symptoms express that they are more dependent on surrounding people's attitudes and awareness of the disease in order to be able to participate in desired activities. Situations considered by all focus groups as important to participate in, involved being with other people and/or performing activities in order to maintain a meaningful everyday life. This study provides valuable knowledge about perceptions of participation at different stages of PD. These findings are of importance for health care professionals in order to support people with PD towards maintained participation in everyday life.

P22.70

Feasibility, safety and efficacy of dance for people with Parkinson's disease: A systematic review

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Objective: To conduct a systematic review of the feasibility, safety and efficacy of dance interventions for adults with Parkinson's disease.

Methods: Relevant studies were identified by electronic searches of databases including CINAHL, MEDLINE, Scopus, PEDro and PsycINFO. Studies were included if: (1) the primary focus was to examine the feasibility or effect of dance intervention in people with PD; (2) and the study was a primary publication in English with an available full text. The quality of the studies was assessed by two independent authors using the PEDro scale and a customized quality appraisal tool. Reports of feasibility and safety were explored and an overview of the content and conduct of the dance interventions was provided. Data were synthesized to assess the effectiveness of dance interventions on balance and mobility.

Results: Ten trials (12 articles) with a total of 332 participants were identified. Study designs included five RCT's and five case series studies, with reported sample sizes ranging from 11-75. The dance styles reviewed included both partnered and nonpartnered tango, waltz and a variety of modern dance styles. In general, studies varied from low to moderate in quality, with considerable variation in the level of detail provided regarding feasibility and safety. Although well reported, attrition rates varied widely from 0% to 50%. Limited information was available regarding adherence, monitoring or the occurrence of adverse events, and in-class supervision. The data synthesis revealed that there was a positive trend toward improvements in balance and functional mobility when compared to a control group. Dance has the potential to improve physical function and quality of life in people with PD. More detailed reporting

of feasibility and safety are encouraged to enhance the application of research into clinical practice.

P22.71

Identifying when changes to Parkinsonian gait occur within a vibratory intervention study

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Objective: The aim of this study is to identify if a statistically significant change in unilateral step duration, stance duration, and swing duration occurs during Parkinsonian gait when exposed to step-synchronized vibratory feedback.

Methods: Five subjects with Parkinson's disease were recruited. While wearing the PDShoe volunteers walked 10 meter laps for a total of 22 minutes, twice a day for 4 days as part of a vibration intervention gait study. Each subject performed the following walking protocol: two-minutes without vibration (pre-therapy), three bouts of six-minutes each step-synchronized vibration (therapy), and two-minutes again without vibration (post-therapy). Two minute rest breaks occurred between each walking bout.

Analysis: Gait data was collected using the instrumented shoe. Only the first session of the study was considered; five twenty-two minute sessions were considered in all. Data was sampled at greater than 10 Hz. Turns were removed from the data stream so that all analysis was performed on straight path walking. Each step of the left foot was analyzed for step, stance, and swing duration. We merged consecutive bouts from each walking session (pre-therapy, therapy, and post-therapy), with rest periods removed. Change point analysis was performed on each session with 1000 bootstrap resamplings. The largest change point for step, stance, and swing duration was identified and tested for significance using a confidence level of >90%.

Results: Change point analysis illustrated significant changes in all three measures for each subject. These change points were only present in the therapy bouts, indicating an effect of therapy on Parkinsonian gait. Change to step duration was not exclusively reflective of a change to either stance or swing duration since both of those also changed. Continued analysis will include cluster analysis to identify common change points across additional study sessions.

CLINICAL SCIENCES: COMPLICATIONS OF THERAPIES

P23.01

Medication administration errors and In-Hospital Complications for Patients with Parkinson's disease: A Retrospective Review

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Objective: To determine the occurrence of errors in medication administration or administration of medications contraindicated for

Parkinson's disease in the inpatient setting over 1 year. The secondary endpoints of this study are to determine reason for errors in medication administration, reason for usage of medications contraindicated in Parkinsonism, difference in medication administration schedule in the hospital compared to in-clinic, reasons for admission, reason for in-hospital complication, length of stay as function of medication errors or contraindicated medications recorded.

Methods: Our hospital electronic health record will be used to retrospectively identify patients who were diagnosed with Parkinson's disease or any form of parkinsonism and admitted to the hospital over a year. Demographics; type of Parkinsonism; co-existing diagnoses; daily levodopa equivalent dose; anti-parkinson medication dose and frequency as outpatient prior to admit; anti-parkinson medication dose and frequency from EHR MAR during admission; actual medication administration dose and frequency from EHR MAR; reason for admission; new diagnoses at time of discharge; deterioration during admission; reason for deterioration; duration of hospitalization.

Results: We anticipate examining approximately 1200 PD medication administrations for the time period in question (100 patients x 3 days in hospital x 4 PD medication administrations per day). Descriptive statistics such as means, proportions and prevalence, along with their respective 95% confidence intervals will be calculated. Comparisons between groups with high versus low rates of medication error will utilize either chi-squared and Wilcoxon rank sum tests for non-parametric/non-normal data or Student's t-test for normally distributed data. Logistic regression may be utilized to model patient outcomes.

P23.02

Nicotine and nicotinic receptor drugs reduce L-dopa-induced dyskinesias in a nonhuman primate model of Parkinson's disease

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Objective: Although L-dopa is one of the primary therapies for Parkinson's disease, it can lead to disabling dyskinesias for which there is little treatment. Nicotine has recently been shown to decrease L-dopa-induced dyskinesias (LIDs) in several parkinsonian animal models. The goal of the current study was to identify the optimal nicotine treatment regimen for reducing LIDs in nonhuman primates and to test if nicotine improved LIDs in both L-dopa-primed and L-dopa naïve monkey. In addition, we investigated the effectiveness of the nicotinic receptor drugs varenicline and ABT-089, which acts selectively in the brain thus minimizing side effects.

Methods: Monkeys were given MPTP until parkinsonian. Nicotine or nicotinic receptor drugs were then given to L-dopa-naïve or L-dopa primed monkeys, with L-dopa (10 mg/kg) gavaged twice daily. Dyskinesias were scored every 30 min. Parkinsonism was also measured.

Results: Nicotine was given to nonhuman primates in the drinking water before L-dopa treatment was started and also to animals with pre-existing dyskinesias. Nicotine decreased LIDs by 60-70% after several weeks of treatment in both the L-dopa-naïve and L-dopa primed animals. The beneficial effect of nicotine was consistently observed for the entire course of the study, which lasted up to 23 weeks. Nicotine did not worsen parkinsonism. We also tested the effect of the nicotinic receptor drugs varenicline, which has been approved for use in humans as a smoking cessation aid, and ABT-089, which has been evaluated in phase 2 clinical trials for other

indications. Both ABT-089 and varenicline reduced dyskinesias by about 50%. The effect of these drugs persisted for the entire length of the study (several months). These combined data suggest that treatment with nicotine and nicotinic receptor drugs has potential as a successful antidyskinetic therapy for L-dopa-treated Parkinson's disease patients. These studies were supported by NIH grant NS59910

P23.03

Task-coupled dyskinesias in patients with Parkinson disease

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²Great Lakes Neurotechnologies

Objective: To characterize interactions between voluntary and involuntary movements in individuals with Parkinson disease (PD) and levodopa-induced dyskinesias (LID).

Background: Levodopa-induced dyskinesias are a common complication of chronic levodopa therapy in patients with PD. The phenomenology includes both choreiform and dystonic movements, and is thought to involve abnormal signaling in basal ganglia circuits that regulate the activity of motor pattern generators. We hypothesized that execution of voluntary movements would modulate the severity of dyskinetic movements in body segments engaged in the task, whereas dyskinetic movements in remote body segments would be unaffected by the task.

Methods: We enrolled 15 subjects with idiopathic PD and predictable motor fluctuations with Off period akinesia and peak dose dyskinesias. A network of 10 triaxial inertial sensors (Kinetisense, Great Lakes NeuroTechnologies) was used to monitor head, trunk, and extremity movements during a set of standardized tasks, with simultaneous video recording for blinded clinical ratings of dyskinesia severity (modified Abnormal Involuntary Movement scale). Tasks were performed prior to, and repeated after a usual dose of medication. For this report, we focused on the subset of tasks that engaged only one hand for voluntary movement: drinking from a cup and combing hair.

Results: During video review, we noted that in individual patients, specific voluntary movements were temporally coupled to a dyskinetic movement in a body segment not engaged in the task. For example, stereotyped head movements were also seen during tasks that engaged the upper extremity. Angular velocity plots from the inertial sensors confirmed coupling between voluntary movements and involuntary movement of a body segment that was not engaged in the task.

Conclusions: The observation of task-coupled dyskinesias suggests that dyskinesias are not random but rather, may be triggered by motor pattern generators that are somatotopically remote from body segments involved in carrying out the specific task.

CLINICAL SCIENCES: CLINICAL TRIALS: DESIGN, OUTCOMES, RECRUITING, ETC.

P24.01

Improving health workers' effectiveness in Sub-Saharan Africa Skyler Jayden Demebe¹, Ryan Evans Ntambi¹, Derrick Kawuma², Mary Nambi²

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²Makerere, University, Kampala, Uganda

Objective: The aim of the study to investigate effectiveness of human resource management initiatives in Sub-Saharan Africa (SSA).

Methods: Effectiveness not only explores whether an intervention has shown to be effective, but also through which strategies an intervention produces outcomes and which contextual factors appear to be of critical influence. Forty-eight published studies were reviewed.

Results: The results indicated that human resource management initiatives can improve health workers' effectiveness, but that different contexts produce different outcomes. Critical implementation aspects were involvement of local authorities, communities and management; adaptation to the local situation; and active involvement of local staff to identify and implement solutions to problems. Strategies that triggered change were increased knowledge and skills, feeling obliged to change and health workers' motivation. Strategies to contribute to motivation were health workers' awareness of local problems and staff empowerment, gaining acceptance of new information and creating a sense of belonging and respect. In addition, staff was motivated by visible improvements in quality of care and salary supplements. Only a limited variety of human resource management initiatives have been evaluated in the health sector in SSA. Assumptions underlying human resource management initiatives are usually not made explicit, hampering our understanding of how human resource management initiatives work.

Conclusion: Application of a realist perspective allows identifying which human resource management initiatives might improve effectiveness, under which circumstances, and for which groups of health workers. To be better able to contribute to an understanding of how human resource management initiatives could improve health workers' effectiveness, a combination of qualitative and quantitative research methods would be needed and the use of common indicators for evaluation and a common reporting format would be required.

P24.02

Which treatments are in the pipeline for the management of falls in Parkinson disease?

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Background: Tremendous efforts are being made to develop effective treatments for preventing falls in Parkinson disease (PD). To determine which therapeutic interventions are being developed in this area, we conducted a review of clinical trials listed in the open access registries for ongoing trials.

Methods: We searched the World Health Organization International Clinical Trials Registry Platform, Clinical Trials gov and the European Clinical Trials Database for ongoing controlled trials that proposed to evaluate therapeutic interventions for the management of falls in PD. Data was extracted on characteristics of trial design, participants, interventions and outcomes.

Results: Thirty trials met the inclusion criteria for this review with a total of 5669 participants planned to be recruited. There were 23 trials evaluating a non-pharmacological intervention and 7 trials for pharmacological interventions. There were 18 randomized trials with a parallel group design and 3 with a cross-over design. Physiotherapy treatments were a main component of non-pharmacological interventions and included: treadmill training with virtual reality, balance programs, home-based programs, multifactorial fall prevention program, and exercise programs.

Pharmacological treatments were in smaller number and included studies testing the efficacy of vitamin D, Donepezil, Rivastigmine, Methylphenidate, Droxidopa and Rasagiline. Outcomes related to falls included: rates of falling, falls frequency, fear of falling, frequency of near falls, number of fallers, and number of injurious falls. This was measured by using falls diaries, calendars, postcards, and telephone reminders or interviews. The majority of the studies included patients in Hoehn & Yahr stage II-III.

Discussion: There are clinical trials evaluating pharmacological and non-pharmacological interventions for falls in individuals with PD on-going. The non-pharmacological trials include several different interventions which reflects the heterogeneity of physiotherapy therapeutic interventions. The heterogeneity of the study designs and outcomes reflects the absence of accepted recommendations for the design of trials in this increasingly relevant field.

P24.03

Barriers to traditional research design: a study of exercise and disease progression in persons with Parkinson's disease (PD)

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Objective: The objective of this project was to assess the effects of participant attrition on longitudinal study of physical activity and exercise characteristics in persons with PD.

Methods: 263 persons PD (Hoehn and Yahr II – III; mean = 2.4) participated in a two-year longitudinal study at four different sites (Boston University; University of Alabama at Birmingham; University of Utah; Washington University in St. Louis). Participants were assessed at baseline and every six months after baseline assessment for two years. Investigators collected data on patients' health, PD symptoms, falls, physical activity/exercise habits, quality of life (QOL), walking and balance. Over the course of the study participants withdrew for various reasons, the most common being worsening disease and problems with transportation. For this analysis we categorized those participants who did not attend their 24-month post-baseline assessment as dropped from the study. T-tests were used to compare baseline and follow-up (12-month) characteristics between participants who did and did not drop out of the study. Paired t-tests were used to compare baseline to 12-month characteristics within each group. Finally, t-tests were used to compare the change in characteristics from baseline to follow-up by dropout status.

Results: 172 remained, while 94 dropped from the study. Participants that remained in the study were significantly different than those that dropped out when comparing baseline characteristics (Table 1). Furthermore, when comparing the changes over 12 months, these groups (remaining vs. drops) showed significant differences in # of comorbidities, # of falls, 6 minute walk distance, quality of life (PDQ-39), and physical activity (PASE).

Table 1. Baseline characteristics of participants by dropout status

	Dropouts (n=94) Mean (SD)	Remained in study (n=172) Mean (SD)	p-value ¹
# of co-morbidities	3.4 (1.9)	2.8 (1.6)	0.0091
# of falls	1.0 (1.0)	0.7 (0.9)	0.0020
UPDRS Total	75.6 (29.3)	55.8 (22.3)	<0.0001
10 MWT (self-	65.2 (16.5)	72.3 (15.4)	0.0010

selected speed) ³			
10 MWT (maximum speed) ³	87.6 (23.4)	100.2 (24.6)	<0.0001
6 MWT ²	369.0 (124.3)	499.9 (122.0)	<0.0001
FGA (balance) ⁴	18.1 (7.0)	21.8 (5.6)	<0.0001
BERG (balance) ²	47.3 (8.2)	51.8 (5.4)	<0.0001
PDQ-39 ⁵	27.7 (15.7)	17.6 (11.4)	<0.0001
PASE (physical activity)	111.9 (79.2)	146.2 (82.3)	0.0014

¹t-test

²n=1 missing data

³n=2 missing data

⁴n=3 missing data

⁵n=4 missing data

Note: Last observation carried forward used.

Table 2. Change in characteristics from baseline to 12-month follow-up (12-month minus baseline) by dropout status

	Dropouts		p-value ¹
	Mean (SD)	Remained in study Mean (SD)	
# of co-morbidities	-1.2 (1.8)	-1.8 (1.9)	0.015
# of falls	0.1 (0.7)	-0.1 (0.7)	0.0027
UPDRS	1.6 (11.6)	-0.3 (15.0)	0.26
Total			
10 MWT (self-selected speed)	-3.6 (10.3)	-2.2 (10.4)	0.29
10 MWT (maximum speed)	-3.9 (11.3)	-1.8 (11.5)	0.17
6 MWT	-4.2 (60.8)	11.7 (65.1)	0.052
FGA (balance)	-0.9 (3.9)	-1.2 (3.7)	0.55
BERG (balance)	-1.3 (4.7)	-0.2 (3.6)	0.058
PDQ-39	1.0 (7.3)	-1.0 (6.5)	0.023
PASE (physical activity)	-61.1 (82.1)	-8.6 (73.3)	<0.0001

¹t-test

P24.04

Initial choice of dopaminergic therapy in the NINDS Exploratory Trials in Parkinson Disease (NET-PD) Longitudinal Study-1 (LS-1)

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Objective: Selecting the initial dopaminergic therapy in early Parkinson disease (PD) is a major clinical decision, yet associated factors for that decision have not been extensively studied. The NINDS Exploratory Trials in PD (NET-PD) Longitudinal Study-1 (LS-1) is a randomized, multicenter, placebo-controlled trial designed to determine the disease modifying efficacy of creatine in early/mild PD. Participants were enrolled in the LS-1 study after they were on stable doses of dopaminergic therapy for at least 3 months, but not longer than 24 months. Importantly, the selection of dopaminergic

therapy was made by providers in the community and occurred prior to entry into clinical trial, which increases the likelihood that the results will be relevant to treatment decisions for the general PD population. Given the large sample size (N=1741) and relatively broad inclusion criteria, the baseline data from the LS-1 study provides a unique opportunity to investigate factors that may be associated with the choice on initial dopaminergic therapy to treat early, mild PD. The hypothesis that younger age, availability of health insurance, and lower medical comorbidities is associated with the initial choice of dopamine agonist therapy was tested in LS-1 study participants.

Methods: Multivariable analysis was used to identify factors associated with the initial selection of dopaminergic therapy (levodopa, dopamine agonist, or the combination of levodopa+dopamine agonist) in the NET-PD LS-1 study. Health insurance availability, education, family history of PD, time since diagnosis, use of non-dopaminergic adjunctive medications, medical comorbidities and socio-demographic factors were evaluated at baseline among 1616 participants with early, mild PD selected from the overall LS-1 study.

Results: Younger age, higher education level, greater years since PD diagnosis and use of an adjunctive, non-dopaminergic medication were associated with more frequent use of dopamine agonist compared to levodopa or combination therapy.

P24.05

Home-based motion sensor monitoring for Parkinson's disease clinical trials

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Objective: The objective was to determine the sensitivity and reliability of a home-based motion sensor system compared to traditional measures for gauging Parkinson's disease (PD) motor symptoms. Clinical trials typically rely on subjective rating scales, which can suffer from bias, placebo effects, limited resolution, and poor intra- and inter-rater reliability. Additionally, symptoms that tend to fluctuate throughout the day cannot be monitored in a single visit. To compensate for this lack of temporal resolution, subjects in clinical trials are often asked to complete daily diaries; however, these diaries yield suboptimal data due to poor compliance, recall bias, and inaccurate self-assessment.

Methods: Eighteen PD patients treated with subthalamic deep brain stimulation (STN DBS) performed tasks evaluating tremor and bradykinesia while wearing a wireless motion sensor unit on the index finger. The sequence of three tasks was performed three separate times with DBS turned off and on at 10 separate stimulation amplitudes, as DBS provides a unique opportunity slowly modulate symptom severity. This study paradigm provided a wide range of symptom severities with relatively few subjects. It also simulated subtle motor symptom progressions in individual subjects in a manner that otherwise might take years to observe. Each task was digitally videoed for subsequent clinical rating.

Results: The reliability and sensitivity of the motion sensor system was comparable to the clinician ratings for rest and postural tremor, but significantly better for finger tapping speed, amplitude, and rhythm. This suggests that, when applied in the home environment, motion sensors can provide significantly increased resolution in both amplitude and time compared to traditional measures, which in turn could decrease the number of subjects, costs, and time to detect significant motor changes in clinical trials.

P24.06**Apokyn for morning akinesia trial (AM IMPAKT)**Stuart H. Isaacson¹, Jean Hubble², Kristen Gullo²¹Parkinson's Disease and Movement Disorders Center of Boca Raton, Boca Raton, FL, USA²US WorldMeds, LLC, Louisville, KY, USA

Objective: The primary objective of this study is to assess the effect of APOKYN (apomorphine HCl subcutaneous injection) in Parkinson's disease (PD) patients with morning akinesia resulting from delayed or unreliable onset of effect of first morning dose of L-dopa. A secondary objective is to assess APOKYN's effect on gastric motility in a subset of study patients with symptoms of gastroparesis. The primary study outcome is a comparison of patient self-reported, diary-recorded Time to On (TTO) following first morning dosing of L-dopa at baseline for one week compared to TTO when using APOKYN each morning for one week. The study will additionally provide data on the effects of APOKYN, a potent dopamine agonist that bypasses the GI tract, on gastroparesis, a common, yet often undertreated, non-motor symptom of PD that may exacerbate L-dopa motor fluctuations.

Methods: This Phase IV, multi-center, open-label study is enrolling eligible PD patients at 12 US study sites with a target enrollment of 100 subjects. Subjects complete a Baseline Period recording daily TTO following their regularly scheduled L-Dopa morning dose for 7 days. At the end of the Baseline Period, subjects start trimethoprimamide antiemetic therapy and begin APOKYN titration. Once the investigator identifies an optimal dose, subjects self-inject APOKYN at their regularly scheduled L-Dopa morning dose time (L-Dopa first morning dose is delayed by 40 minutes) during a 7-day APOKYN Treatment Period and record TTO following the APOKYN injection. In the gastric motility sub-study, subjects participate in a gastric emptying imaging study following a standardized meal during the Baseline Period (taking their usual L-Dopa dosing) and during the APOKYN Treatment Period (following morning APOKYN injection).

Results: An interim analysis of the primary TTO change from baseline endpoint, key secondary endpoints and gastric emptying time results from the sub-study participants will be available for presentation in October.

P24.07**The group exercise program for improving self-body image and posture for Parkinson disease**Nami Kawano¹, Kayo Nakamoto², Yutaka Uchida³, Takeshi Miyazaki⁴, Ken Koguchi², Kazuo Abe^{3,4,5}¹Osaka Electro-Communication University, Shijonawate, Osaka, Japan²Shirahama Hamayu Hospital, Nshimuro, Wakayama, Japan³Konan Hospital, Kobe, Hyogo, Japan⁴Garacia Hospital, Mino, Osaka, Japan⁵Osaka Health Science University, Osaka, Osaka, Japan

Objective: We attempted to develop a novel innovative group exercise program that improving self-body recognition and postural impairment. We studied effectiveness of this exercise program for Parkinson's disease (PD) patients in several hospitals.

Methods: We recruited 33 PD patients who gave informed consent for the purpose, method of the research and voluntarily participated in the program; mean age was 72.1 years (range, 48 to 90 years), and the severity of disease corresponded to stages 1 (n = 2), 2 (n = 4), 3 (n = 22) and 4 (n=5) evaluated by the Hoehn and Yahr stage. The exercise program developed for improving self-body recognition and posture. During exercise, patients leaned and push a ball on the

back of the seat by the level of the lower thoracic. Patients were told to keep moving with paces of themselves and move without a command or music. Patients conducted 30-minutes exercise supervised by physical and occupational therapists every week for 2 months. The unified Parkinson's disease rating scale (UPDRS) score, posture, and grip strength were assessed at the first session and after 2 months. Results were analyzed by paired t-test and nonparametric Wilcoxon test using statistical software (PASW Statistics 18).

Results: Twenty-two patients with camptocormia and scoliosis were improved. Three patients with aids to keep standing position improved to keep standing position without aids. Sixteen patients improved UPDRS scores. Seventeen patients increased grip strength. On the basis of our results, our exercise program may be useful for improving disease severity, postural impairment in PD patients.

P24.08**Measuring clinically important changes in disability ratings using IV levodopa for phase IIa trials of new-anti-dyskinetic drugs in Parkinson's disease**Tiago A. Mestre¹, Nicolas Phiellip¹, Camila Henriques de Aquino¹, Jane Lui², Yu Yan Poon¹, Julie So¹, Susan H. Fox¹¹ Morton & Gloria Shulman Movement Disorders Centre, Toronto Western Hospital, University of Toronto, Toronto, Canada² Investigational Pharmacy Services, University Health Network, Toronto Western Hospital, Toronto, Canada

Objective: 1. To test the feasibility of using patient-reported outcomes in the IV levodopa model as methods of evaluating change. 2. To determine clinically important changes in dyskinesia or parkinsonism as per patient report.

Methods: We included patients with advanced PD (UK PD Society Brain Bank criteria), age 30-80 years, stable bothersome dyskinesia (LFADLDS \geq 1; peak-dose dyskinesia for >25% of the daytime) and stable anti-parkinsonian medications (>1 month). A randomized, double blind, placebo-controlled crossover design was adopted, with an initial run-in phase. A video protocol was used for assessment of patient-reported clinically important events as determined by a 5-point Likert scale. The following clinically important events were considered: onset of dyskinesia, maximum intensity of dyskinesia, remission of dyskinesia and onset of improvement in parkinsonism, best ON and onset of wearing-OFF. Two blinded raters individually rated dyskinesia and/or parkinsonism by video assessment of the clinically important events, using the UDysRS-III and MDS-UPDRS-III, respectively and the scores averaged. Non-parametric paired testing (Wilcoxon signed-rank paired test) was used to compare median scores at baseline and at each clinically important event. A P value of 0.05 was significant.

Results: We recruited 6 individuals. One of those was excluded due to issues with venous access. All patients were able to report all parkinsonism-related clinically important events, but were less often able to identify onset of dyskinesia (n=4) and maximum intensity (n=2) or remission of dyskinesia (n=2). The minimal clinically important change as reported by the patient was, for dyskinesia, 11.8 points (IQR =12) in the UDysRS-III and, for the antiparkinsonian effect, 7.3 points (IQR =18.3) in the MDS-UPDRS-III. There were no reportable side effects.

P24.09**Clinical research participation among people with Parkinson's: examining the importance of travel assistance when deciding to join a study**

Karlin Schroeder, David Blomquist, Veronica Todaro, Robin Elliott
Parkinson's Disease Foundation, New York, NY, United States

Objective: To determine the importance of travel assistance to people with Parkinson's who participate in clinical studies.

Methods: An online survey was administered in April 2013 to people with Parkinson's who have participated in a clinical study. The survey data will be analyzed to determine how travel assistance ranks in comparison to other factors when considering whether or not to participate in a clinical study. Data will also be analyzed to determine if study participants are provided with travel assistance and if so, what type of assistance is offered (reimbursement for travel, provision of a voucher for a hotel stay, etc.).

Results: Data will be analyzed via descriptive and correlational analysis. Patient demographic data and study enrollment history will also be included in the analysis.

P24.10**Pair up for Parkinson's research: the impact of local clinical research education forums on study inquiry and enrollment**

Karlin Schroeder, David Blomquist, Veronica Todaro, Robin Elliott
Parkinson's Disease Foundation, New York, NY, USA

Objective: To determine the impact of Parkinson's Disease Foundation Pair Up for Parkinson's Research Educational Forums on increasing study inquiry and participation among people with Parkinson's disease and care partners.

Methods: An on-site survey was administered to people with Parkinson's and care partners who attended one of two (Arizona and Colorado) PAIR Up for Parkinson Research educational forums in April 2013 to determine if knowledge about clinical research increased and the likelihood of participating in clinical research increased among attendees. A survey will be administered in June to people with Parkinson's and care partners who completed the on-site survey to determine if individuals contacted a study site and if so, whether they were eligible to participate in the study, and if they enrolled. This survey will be administered online, with follow-up phone calls utilized to maximize the response rate of survey recipients.

Results: Survey data will be collected, tabulated, analyzed and reported. A comparison will be made between individuals who have previously participated in a clinical study and those who did not make an inquiry or participate in a clinical study prior to attending the educational forum.

P24.11**A cohort study of Parkinson's disease in British Columbia**

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Objective: Approximately 100,000 Canadians have Parkinson's disease (PD)¹ yet our understanding of disease etiology,

pathogenesis, and response to treatment remains inadequately defined. We have initiated a study to assess the role of genetic susceptibility variants/pathogenic mutations in PD. Herein we describe: 1) our clinic-based cohort, recruitment efforts and impediments to subject participation; 2) preliminary data on the frequency of pathogenic mutations. We hypothesize genetic analysis, made possible through province-wide participation, may improve the diagnosis/prognosis of patients and may ultimately yield disease-modifying therapies.

Methods: In BC, subjects have been primarily recruited through the UBC Movement Disorder Clinic, a community neurologist clinic, support groups and various lay publications. Participants provide detailed information on ancestry and family history of neurologic disease. For most patients, standardized clinical questionnaires including motor and cognitive assessments are administered and neurologic exams performed. Blood samples are collected. Extracted DNA is screened for: i) Pathogenic mutations in genes known to cause PD (LRRK2, DNAJC13, SNCA, VPS35, EIF4G1, PINK1, and PARK2) and; ii) genes implicated in neurodegenerative disease². Clinical, genealogic and genetic data are organized in a database designed to ensure participant confidentiality.

Results: Patients (n=713), affected/unaffected family members (n=159) and control participants (n=120) provided informed consent to participate. The mean age for patients was 64±13SD years (range=21-91) with early-onset PD (≤45 years) totalling 17% of the cohort. A total of 232 patients had sporadic PD whereas 321 reported a family history. For PD patients, where data were provided on initial symptoms (n=154), 71% had resting tremor, 14% bradykinesia, 8% rigidity and 7% postural instability. Mutations were found in 1.5% (11/713) of patients. In conclusion, although we have established a substantial cohort, increased effort is needed to expand recruitment across BC. As analysis continues, a more standardized method of collecting clinical assessments is essential to effectively correlate clinical with genetic data.

¹Parkinson Society Canada

²see abstract by Lin, Evans *et al.*,

P24.12**Efficacy, safety and tolerability of rasagiline as add-on to suboptimal dopamine agonist monotherapy in Parkinson's disease (PD): The ANDANTE study**

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Background and Objective: Dopamine agonists (DAs) are often used as initial PD monotherapy. However with disease progression DA monotherapy alone becomes sub-optimal and patients often require additional dopaminergic therapy to maintain symptomatic efficacy. Traditional options at this stage include levodopa (associated with risk of dyskinesia) or increasing DA dose (associated with higher risks for ICDs and other side-effects). Rasagiline is a selective, irreversible MAO-B inhibitor, and this distinct mode of action provides a rationale as add-on therapy to DAs for additional symptomatic benefit. The objective of this study was to determine the efficacy, tolerability and safety of add-on rasagiline therapy for early-PD patients sub-optimally controlled by DA monotherapy.

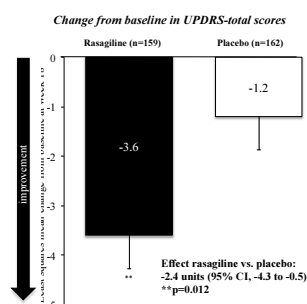
Methods: ANDANTE was an 18-weeks, placebo-controlled (randomized 1:1) study of PD patients (Hoehn&Yahr 1-3) aged ≥30 years taking stable DA dosages with suboptimal control. The primary outcome was change from baseline in total-UPDRS score.

Secondary outcomes were changes from baseline in UPDRS motor and ADL scores, and CGI. Exploratory outcomes were changes from baseline in Scales for Outcomes in Parkinson's Disease (SCOPA)–Sleep, SCOPA–Cognition, Brief Smell Identification Test, and Parkinson's Disease Questionnaire. Safety was assessed by AE frequency/severity. Out of 328 patients randomized, 321 (mean age 62.6; duration PD 2.13 years) were included in the efficacy analysis.

Results: Treatment with add-on rasagiline significantly improved total-UPDRS scores versus placebo (Figure). Significant improvements in UPDRS-motor scores were also observed ($p=0.007$). There were no significant differences between groups for ADL, CGI or any exploratory measures. Rasagiline was well-tolerated, with no significant difference in percentage of patients with AEs (64.2% vs. 61.0%) or serious AEs (4.9% vs. 3.0%) versus placebo. Only 11 patients required rescue levodopa during the study.

Conclusions: Addition of rasagiline significantly improved motor symptoms in patients sub-optimally controlled with DA monotherapy, and was well-tolerated.

Figure: Change from baseline in total-UPDRS scores



P24.13

Expectations of Parkinson's patients from the next decade of research

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Introduction: Patient expectations of future treatment prospects are influenced by the views of their treating physician, literature from patient organisations and information gleaned from Internet sources. Although these sources can differ substantially in credibility and optimism, the extent to which patients views mirror these external influences is unknown. The present study, conducted by Parkinson's Movement (PM) examines Parkinson's (PD) patient perceptions of future treatments and research.

Methods: A series of 4 brief (single question, multiple choice answer) Internet polls were posted on the PM community website (www.parkinsonsmovement.healthunlocked.com). The questions asked (Q1) the perceived timeframe of a cure for PD, (Q2) patient expectations over the next decade, (Q3) top three areas where PD-related funding should best be targeted, and (Q4) the most promising areas of research toward a cure. Between 107 and 187 responded to each poll.

Results: The PM cohort was mainly young (76% aged 50-69), highly educated (68% with at least 1 degree), with mild Parkinson's (Hoehn & Yahr stage 1/2: 66%) for 4-6 years. Results were as

follows: Q1: 41% felt that a cure for PD was attainable within 10 years, 16% within five. Only 6% felt that a cure was unattainable in any timeframe. Q2: a cure for PD (20%), treatments with fewer long-term side-effects (21%), more effective drugs (25%) and more available treatments (20%) were the most likely expectations of patients for the next decade. Q3: 81% felt that funds were best directed to finding a cure. 50% wanted new symptomatic treatments for PD. 32% prioritised long-term social support. Q4: 58% felt that stem cells were the most promising route to a cure while 22% supported gene therapy. 6% felt that the cure lay in surgery.

Conclusion: PM patient views generally reflect optimistic realism and sophisticated understanding of future treatment prospects.

P24.14

Effects of a community-based balance program on enhancing the balance performance in people with Parkinson's disease

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Objective: To examine whether an 8-week blended indoor-outdoor program is effective to enhance balance performance after treatment completion and at 2-month follow-up in people with Parkinson's disease (PD).

Background: Previous studies demonstrated that multi-modal balance training program was effective in improving balance performance in people with PD. However they did not include all the balance domains and outdoor fall-prone activities have been overlooked. We designed an exercise program based on the framework of the Balance Evaluation Systems Test (BESTest) to target six balance domains including biomechanical constraints, stability limits and verticality, anticipatory postural adjustments, reactive postural responses, sensori-motor integration and dynamic gait control.

Methods: It is a randomized controlled trial with 39 subjects completed the 8-week program, pre-training, post-training and 2-month follow-up assessments. Subjects were randomly assigned to an experimental group (EXP) receiving 4-week indoor and 4-week outdoor balance exercises, or a control group (CON) receiving 8-week upper limb exercises. Outcome measures included BESTest total score (%), MDS-UPDRS III and postural-instability-gait-difficulty (PIGD) scores. Two-way repeated measures ANOVA was used to analyze within-group and between-group differences.

Results: Immediately after training, only the EXP group significantly increased BESTest score (by 14%, $p<0.001$) and decreased PIGD score (by 34%, $p<0.001$). Both groups significantly reduced MDS-UPDRS III scores (by 22-27%, $p<0.001$). At 2-month follow-up, only the EXP group significantly increased BESTest score (by 14%, $p<0.001$) and decreased PIGD score (by 31%, $p<0.001$). Both groups significantly maintained the reduced MDS-UPDRS III scores (by 21-31%, $p<0.001$). Between-group comparisons indicated that the changes of BESTest and PIGD scores were significantly larger in EXP than CON group at both post-training and 2-month follow-up ($p<0.001$ and $p<0.01$).

Conclusions: Our blended indoor-outdoor balance program, which based on the BESTest framework, enhanced balance performance in people with PD at post-training and 2-month follow-up.

P24.15

Xiaoyao Pill for the treatment of depressive symptoms in patients with Parkinson's disease: a randomized, double-blind, placebo-controlled trial

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Objective: Depression is common in Parkinson's disease (PD). There are seldom studies concerning alternative therapies. The objective of this trial was to investigate the effects of herb extracts of Xiaoyao Pill, an antidepressant medicine approved by the People's Republic of China Pharmacopoeia, on clinically relevant depressive symptoms in PD.

Methods: A total of 58 patients with PD and reaching DSM-IV Criteria were enrolled to this 12-week, double-blind, placebo-control, randomized trial. The primary efficacy endpoint was the mean change baseline and 12 weeks in total score on the Hamilton Depression Scale (HAMD 17), the percentage of recovered, and the responder rate. The secondary outcome included the 30-items-Geriatric Depression Scale (GDS-30), the Parkinson's Disease Questionnaire (PDQ-39), and the Pittsburgh Sleep Quality Index (PSQI).

Results: There was a trend favoring Xiaoyao Pill group, but no significant differences were found between groups. The mean change of HAMD 17 score is highest in the Xiaoyao Pill group (-7.69 vs -4.57 and -4.20, $p=0.001$). The percentage of recovery is 46.2% for Xiaoyao Pill, 14.3% for Bupleurum+Ginkgo, and 20% for placebo. Response rate: Xiaoyao Pill 46.2%, Bupleurum+Ginkgo 7.1%, and placebo 30%. There was a significant decrease in GDS score (from baseline to the endpoint: 20.62 ± 3.80 to 16.38 ± 5.88 , $P=0.007$), while no significant decrease in GDS overtime in group 2 and placebo group. The same is the dimension 3, emotion well being, of PDQ-39 ($P=0.015$). Though the sample size is limited, this is the third largest placebo-controlled trial done to date in PD patients with depression. Our study shows that Xiaoyao Pill has better efficacy and is tolerated.

CLINICAL SCIENCES: RATING SCALES

P25.01

3D sensors, the new paradigm for assessing Parkinson's Disease

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Objective: Create objective, automatic and relatively inexpensive tools for the evaluation of Parkinson's disease using the new 3D sensors like the Microsoft Kinect.

Methods: We selected 10 healthy subjects and 10 patients with Parkinson's disease. Each participant performed a set of manoeuvres designed to assess their capabilities and functions while recorded by one of these 3D movement sensors (in our specific case, we used the Microsoft Kinect). 20 corporal reference points were recorded for each instant of time, with an average frequency sampling of 30 fps. For each of them, the time course of the measurement was assumed as a time series. A set of descriptive parameters was extracted for each independent manoeuvre, which were then analysed and compared for individual and group comparisons.

Results: The Kinect system is useful for the evaluation of motor control and movement disorders. Distinguishes normal pattern of gait and posture and provides quantitative measurements of gait, posture, hypokinesia and dyskinesia.

This research demonstrates the utility of the Kinect sensor to record and evaluate the postures and movement sequences and opens new possibilities for assessment, diagnostic and treatment of movement disorders.

P25.02

Discriminant capacity of four Fear of Falling rating scales in people with Parkinson's disease

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Objective: To evaluate the discriminant capacity of four Fear of Falling (FOF) rating scales in people with Parkinson's disease (PD).

Methods: The FOF rating scales were: the Falls Efficacy Scale-International (FES-I; possible scoring range 16-64, higher=worse), the Swedish version of the Falls Efficacy Scale (FES(S); 0-130, higher=better), the Activities-specific Balance Confidence scale (ABC; 0-100, higher=better) and the modified Survey of Activities and Fear of Falling in the Elderly (mSAFFE; 17-51, higher=worse). A postal survey was mailed to 96 non-demented people with PD. The survey contained the four FOF rating scales and dichotomous questions on FOF, activity avoidance due to the risk of falling and falls and near falls during the past six months. PD-severity was self-rated as mild, moderate or severe (in the analysis dichotomized as mild or moderate/severe). Non-parametric group comparisons (Mann-Whitney U-test) were used to investigate if the FOF scales were able to separate people with and without FOF, activity avoidance, previous falls, near falls and people with different disease severity.

Results: Fifty-six persons (52% men) responded within three weeks and were included in the preliminary analyses. Mean (SD) age and PD-duration were 73 (7.8) and 7 (5.3) years, respectively. Thirty-two participants (57%) stated that they had FOF according to the dichotomous question. Median (q1-q3) scores for the four FOF rating scales were: FES-I; 25 (19-36), FES(S); 109 (67-128), ABC; 72 (39-90) and mSAFFE; 24 (19-32). All four scales detected significant ($p\leq 0.003$) differences in relation to the dichotomous questions that targeted PD-severity, FOF, activity avoidance and falls, as well as significant ($p\leq 0.029$) differences in relation to near falls.

Conclusion: Preliminary analyses indicate that when using dichotomous questions, all four scales discriminate between PD-severity, FOF, activity avoidance, falls and near falls.

P25.03

The Exo-Imaging test: using a markerless motion tracking system to detect and monitor motor symptoms in patients with Parkinson's disease

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Background: Assessment of motor symptoms in Parkinson's disease (PD) is currently done using clinical scales. However, these evaluations must coincide with rare visits to the treating physician; hence they are not done often enough to appreciate sudden changes in health status of patients.

Objective: Accordingly, we intend to develop an automated tool to assess motor symptoms of patients with PD; the Exo-Imaging test.

Similar to other types of imaging, this system could be installed anywhere. The test could also be repeated multiple times so as to provide a better clinical picture of the evolution of symptoms.

Methods: A markerless system (Biostage, Organic Motion) is used to record movement of patients while they will perform tasks, such as standing, walking, drinking and performing rapid alternating movements. The level of involuntary movement is also assessed during quiet standing. To be detected by the system, the patient only has to go into the recording zone and take a "T" pose for 2 seconds, without wearing any marker. The Biostage system integrates videos from 14 cameras to provide position of 16 different body segments. Using this information, we are able to compute biomechanical parameters in order to assess motor performances. Finally, motor performances is associated with severity of PD symptoms using statistical methods, such as neural networks.

Results: Our preliminary results show that the Biostage is able to detect dyskinesia and tremor, as well as to capture key differences during gait between healthy participants and patients with PD. Ultimately, we hope to develop a fully-automated test for the detection and follow-up of motor symptomatology in PD that will provide the same information available through currently-used clinical scales.

P25.04

Can single-leg stance time be used to assess bilateral progression of Parkinson's disease?

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Objective: Reduced body balance time based on single-leg stance test (SLST) is associated with increased postural instability and risk of fall in Parkinson's disease (PD). This study sought to determine whether the wide range of SLST data obtained from both lower limbs clinically actually consists of discernible statistical pattern, corresponding to bilateral disease progression.

Methods: Demographic and disease history information were collected from 38 people with PD. The mean age of our study participants was 66.3 years (SD 10.7) and the mean disease duration was 7.6 years (SD 5.7). Each participant performed the SLST and was timed with a stopwatch by an independent observer.

Results: SLST scores obtained among individuals were quite variable, ranging from 1-60 seconds. Using 10 seconds, a previously recommended cut-off level for potential fallers, as a classifier, we classified our data into two sub-groups: those who were able to balance for at least 10 seconds on both legs (N=22) and those who could not (N=16). When looking at the participants who had at least one leg scored below 10 seconds, two additional sub-groups of participants emerged: 62.5% had *both* legs scoring below the 10 second cut-off ($p < 0.05$ for both legs; Wilcoxon signed-rank test) while 37.5% had only *one* leg score below the 10 second cut-off ($p < 0.05$ for only one leg; Wilcoxon signed-rank test). We postulate that the *inter-leg* difference SLST, combined with 10s cut-off, has the statistical power and sensitivity to identify three patient groups: 1) those with both leg above 10s and relatively good balance; 2) those with only one leg below the cut-off whose postural instability could remain unilateral, and 3) those with both legs below the 10s cut-off, in which postural stability appeared to have progressed bilaterally. Our results indicate that SLST may be a useful indicator for assessing bilateral disease progression.

Acknowledgments: CIHR, Parkinson Alberta Society, and the Movement Disorders Clinic-Alberta Health Services, and MITACS.

P25.05

Postural balance evaluation in a outpatient population with Parkinson disease

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Objective: Evaluate the dynamic postural balance of patients with Parkinson Disease (PD) in order to know the potential risk of falls

Methods: Field study, exploratory cross-sectional descriptive correlational approach were evaluated in 145 elderly patients with PD were divided into three groups according to age groups: G1 (60-69), G2 (70-79) and G3 (80-89) outpatients at the Division of Movement Disorders Department of Neurology, Hospital das Clínicas, Federal University of Parana - UFPR, Curitiba - Brazil. To collect data, we used two instruments: the Sociodemographic and Functional Independence Measure (FIM). We performed statistical analysis of comparison (Kruskal-Wallis), Pearson correlation and descriptive analysis of data.

Results: The sociodemographic characteristics revealed a higher frequency of women aged 80 to 89 years with a low education level (38.89%), mostly coming from remote areas of the city (90.48%). High scores were observed in MIF indicating functional independence. The comparison between the scores of FIM and FIM HY and mean time to clinical progression through the G1, G2 and G3 indicate the time of onset of disease and staging of HY did not affect the performance of these functional groups and the relationship between the three groups also showed no statistical difference between them.

P25.06

Dual-task performance assessment (DTPA): a novel test for assessing motor and cognitive performance during dual-task

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Objective: The aim of this study was to analyze results following the application of a novel protocol devised to assess motor and cognitive performance on dual-tasks, comparing performance of healthy elderly and Parkinson's disease (PD) patients.

Methods: Thirty healthy elderly, mean age 67.5 years (S.D. = 7.8), 45 patients with idiopathic PD, mean age 66.5 years (S.D.=6.44) at stages 1,2 and 3 of disease evolution according to the Hoehn and Yahr Classification, took part in the study. The DTPA was split into four tasks: (1) GAIT, assessing distance traveled and number of paces taken in 1 minute; (2) BALANCE, assessing ability to balance in unipodal support for 1 minute; (3) POSTURE, quantifying the number of times the participant is able to stand up and sit down within 1 minute; and (4) HAND SKILL, assessing the number of cards turned over on a table top within 1 minute. The four tasks were assessed: (i) independently i.e. under single-task (ST) conditions; (ii) simultaneously with a cognitive test; and (iii) simultaneously with a motor task. The impact of DT between healthy elderly group and PD patient group was compared using ANOVA.

Results: The results revealed significant difference in impact of DT on the groups (ANOVA, $p < 0.001$), confirmed by Tukey's test which showed greater impairment between PD patients than healthy elderly across all four DTPA sections. **CONCLUSION:** The DTPA was shown to be effective for measuring differences in impact of DT between healthy elderly and PD patients and also proved sensitive to disease progression in patients with PD. The DTPA was shown to be a straight-forward and rapid tool, representing the first

standardized protocol for assessing the impact of dual-tasks not only on gait but also balance, posture and manual skill.

P25.07

Quality of life assessments using the MDS-UPDRS

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Objective: Depressive symptomatology and motor impairments have been frequently associated with quality of life in Parkinson disease (PD). This pilot study sought to determine what factors measured by the Movement Disorder Society revised Unified Parkinson's Disease Rating scale (MDS-UPDRS) correlate with quality of life in PD patients.

Methods: We recruited PD patients from the Johns Hopkins Morris K. Udall Center and movement disorder clinic. Participants were administered the MDS-UPDRS. Part I and II of the MDS-UPDRS evaluated non-motor and motor experiences of daily living, respectively, and Part III measured motor function. Part IV examined complications from therapy. Quality of life was assessed with the Parkinson's Disease Questionnaire 39 (PDQ39).

Results: Thirteen PD patients are currently enrolled with an average age of 66.74 years (SD=2.69). Participants were primarily early in the disease (Hoehn and Yahr II: 9 participants; Hoehn and Yahr III: 2 participants; Hoehn and Yahr IV: 2 participants). Higher Hoehn and Yahr stages corresponded with increasing age ($p=0.02$) and higher MDS-UPDRS scores ($p=0.02$). Total mean MDS-UPDRS score was 63.86 (SD=20.00) and the average PDQ39 score was 29.25 (SD=16.70). As the total MDS-UPDRS score increased, patients reported a poorer quality of life ($r=0.70$). Motor experiences of daily living (part II) and motor complications subscales (part IV) were also associated with poorer quality of life ($r_{\text{MDS-UPDRS II}}=0.60$; $r_{\text{MDS-UPDRS IV}}=0.62$). However, motor function (part III) and non-motor experiences of daily living (Part II) had less impact on quality of life ($r_{\text{MDS-UPDRS III}}=0.50$; $r_{\text{MDS-UPDRS I}}=0.39$).

Conclusion: Total MDS-UPDRS scores had the strongest correlation with quality of life, followed by motor experiences of daily living and therapeutic complications. Non-motor experiences of daily living and motor examination had the least impact on quality of life. Larger investigations are needed to confirm these findings and determine the ability of the MDS-UPDRS to assess quality of life.

P25.08

Measures of quality care reveal large variation across NPF Centers of Excellence

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Objective: Meaningful improvements in health outcomes have been achieved through quality improvement. For the first time, the National Parkinson Foundation Quality Improvement Initiative (NPF-QII) has measured the quality of care across a sample of NPF Centers of Excellence.

Methods: NPF-QII is an observational clinical study with comprehensive data on patients with Parkinson's from 19 NPF Centers of Excellence. It includes both patient-reported and clinically-measured outcomes, together with broad measures of

demographics and treatments. The data was adjusted for age, disease duration, and sex. Quality of care was measured by examining the means and standard deviations (SD) for the two year change in patient outcomes (data is collected annually), examining the PDQ-39 summary index (PDQ-39), the time to complete the timed up-and-go test (TUG), and a cognitive measure that combined verbal fluency (animals) and delayed recall and was scaled to parallel the MoCA cognitive exam.

Results: Six of nineteen centers had two year follow-up data on over 80 subjects (n=921 subjects). At baseline, the average PDQ-39, TUG, and cognition scores were 23%, 12.9 seconds, and 24.3. The results achieved at each center showed little variability in the two-year change in PDQ-39 (average change for all subjects: 1.3%; center averages: 0.7%-1.4%) but more significant two-year change in both the TUG (average, all subjects: 0.85 second increase; center averages: 0.12-2.0 seconds) and cognitive score (positive values show improvement; average, all subjects: 0.03; center averages: -0.25 to 0.26). Further, the SD also showed wide variation for the PDQ-39 ranging from 3.5% to 5.6% and the TUG from 1.79 to 3.59 seconds, but for the cognitive measure the SD varied less: 1.23 to 1.53. Lower SD indicates more predictable outcomes and clinics with higher SD require higher recruitment to measure an impact of care change. Future studies will evaluate the factors contributing to this observed variability.

CLINICAL SCIENCES: E-HEALTH AND TECHNOLOGY

P26.01

PDaily: mobile application to monitor patients with Parkinson Disease

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Objective: To design, develop and validate a mobile system that would support the evaluation and monitoring of people diagnosed with Parkinson's disease in a specialized medical institution in Cali, Colombia.

Methods: In an interdisciplinary work we developed a mobile application designed to be used by the patient or caregiver, and thought with a medical approach. To develop the software was used an agile methodology with iterative and incremental cycles based on Prototyping. We defined four cycles of development, each one with differential internal cycles according to the progress of the project.

Results: The obtained mobile system, PDaily, has 5 software components: (1) to keep registration of the person, condition and treatment, (2) to identify medicines through augmented reality, (3) to notify the next dose of the drug, (4) to analyze motor fluctuations and dyskinesias through objective measurement using accelerometers, a brief questionnaire about dyskinesias and impact on daily activities using Unified Parkinson's Disease Rate Scale (UPDRS: section 2.10), and (5) to contact a family member, doctor or emergency call system of the city for help in an emergency. These components are supported by a core component enabling interoperation between them and facilitate the extensibility of the system with additional modules. The collected information is stored locally on the Smartphone, then the patient, shares it with the specialist through a web main system. PDaily provides a summarized report about detailed records on the onset and ending of symptoms and their temporal relation to treatment. Accurate information will allow adjust the treatment plan, monitor the adherence and to detect complications early.

P26.02

Multisensor system as a clinical aid in evaluation differentiation of tremor disorders

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Objective: Develop a multisensor system for the measurement of tremor, providing the visualization and analysis of signals to help differentiating tremor disorders.

Background: The differentiation of the etiology of tremor disorders is a challenging task for most specialists. In the case of Essential (ET) and Parkinsonian tremor (PT), this is specially difficult. From a physiological standpoint, these tremors have their own characteristics, however the measurement of these parameters are not part of routine clinical practice.

Methods: The system sensors (accelerometers) were placed in eight body parts of interest in lower and upper limbs, positioning the measuring axes perpendicular to the longitudinal axis of the limb. Registration assessed the limbs at rest, as well as with postural and kinetic tests. Analyses were focused in function of the specific features of each disease and also the signals for their RMS amplitude and frequency.

Results: seventeen patients with ET (6 men, mean age 62 years) and 62 with PT (30 men, mean age 65.3 years) were analyzed. Cases of PT presented with a mean frequency of 5.3Hz at rest, 5.8Hz with posture and 6.5Hz kinetic (average for the 3 tests 5.8Hz). Cases of ET have an average tremor frequency of 6Hz at rest, 6.2Hz with posture and 6.5Hz kinetic (average for the tests 6.2Hz).

Conclusions: Our system was able to differentiate ET and PT in regards to frequency. In addition, the system allowed us to analyze amplitude parameters, identifying cases in which there was a significant overlap between both forms of tremor.

P26.03

Performance evaluation of an optical analysis technique based on passive markers in the characterization of voluntary and involuntary muscle movements in patients with Parkinson's disease

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Objective: This study aims to evaluate a system using video motion analysis (Parksys®) correlated with different items of the rating scale for Parkinson's disease.

Methods: 28 patients (14 men and 14 women) with PD with an average age of 63.7 ± 9.5 years who fulfilled the diagnostic criteria of the Brain Bank of London and 15 healthy subjects (8 men and 7 women) with an average age of 59.8 ± 9.3 years. EP duration was 11.6 ± 6.2 years. All cases were on treatment with levodopa. Subjects were evaluated using an optical motion analysis. Each of the individuals performed the tests 20 and 23 of the motor section of the UPDRS in both sides of the body. It was considered the amplitude and frequency of each of the movements. In the statistical analysis were used descriptive measures of correlation between variables, principal component analysis (PCA), analysis of variance and the nonparametric alternative when the data were not normally distributed.

Results: In the analysis using PCA it was determined that there are significant differences between the control group and the case group, with a P value of 0.013, for the right hand UPDRS23. In this analysis the amplitude in the axis X, Y and Z gathered 89% of variability. There are also differences between the control group and the group of cases in the UPDRS20 in the left hand, with a p-value of 0.008. The results indicate there are differences in the UPDRS test 20 for left hand and UPDRS test 23 for right hand between the groups. The used technique allow to measure and characterize quickly and accurately the muscular movements in subjects with PD.



P26.04

Application of iPod Touch motion sensing technology for Gait measurements

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Objective: Brisk walking is a commonly recommended form of exercise for patients living with Parkinson's disease (PD). In this study we developed and validated an Application (GaitReminder™; GR) using 4th generation iPod Touch technology that can monitor and record stepping data during treadmill and level ground walking.

Methods: 18 control subjects and 15 PD patients walked on a treadmill and on level ground while wearing the GR. We compared gait parameters (step size, walking speed, and distance) obtained through GR to known benchmarks as indicated by treadmill speeds, or pre-measured distance markers on the ground. Within this data, we looked for relationships between cadences and changing inclines and speeds during treadmill walking, and at GR sensitivity to differences between the PD and control group.

Results: We found the mean percent errors of GR-recorded walking speed and distance on a treadmill was 2.94% and -0.36% respectively, and that GR-derived step length has a mean error of -5.15% when compared to the line distance. GR measurements are also sensitive to walking instructions such as walking with larger vs. smaller steps. When the subjects were instructed to maintain their amplitude of walking steps, GR accurately recorded a linear increase in cadence with increased treadmill speeds, but not the increase in incline. PD patients performing the ground line-walking test showed a significantly higher mean error rate due to their shorter step length than controls. Our data indicates that iPod Touch can be utilized as a versatile device for tracking gait parameters with acceptable accuracy and reliability in both healthy subjects and PD patients.

Acknowledgments: CIHR, Parkinson Alberta Society, the Movement Disorders Clinic-Alberta Health Services, Markin Undergraduate Student Research Program, and Branch Out Neurological Foundation.

P26.05**Parkinson's disease patients' opinions on use of technology for communication and education**

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Objective: Parkinson's disease (PD) is the most common neurodegenerative movement disorder in the U.S. Patients' opinions of technology-based tools for education and communication as related to PD are unclear, with little documented research addressing the issue. The goal of this research was to investigate patient opinions about technology-based tools. Education and communication using technology may affect satisfaction and adherence to treatment regimens. Prior to developing technology tools for clinical use, establishing the relevance from the patients' perspective, specifically accounting for the needs of geriatric patients, is crucial.

Methods: A quality assessment survey was administered to PD patients at the Parkinson's Disease Treatment Center at the New York Institute of Technology. The survey assessed patient opinions on willingness to use electronic methods including electronic forms, video education, emailed home-care instructions and the ability to email with healthcare providers. Additionally, patients were asked whether they felt that using technology (online tools, etc.) to communicate with the healthcare provider would result in a better understanding of their care or the healthcare-provider better understanding their needs. Associations between patient opinions of technology, having unmet needs related to PD, and being age 65 or older were assessed.

Results: 109 PD patients completed the survey. 27.2% (n=28) of the subjects reported having unmet needs related to PD. The majority of the patients were age 65 and older (78.0% (n=85)). Those who were age 65 and above were less likely to believe that using technology would result in a better self-understanding of patient care (OR=0.30, 95% CI:0.12, 0.79, p=0.01) and less likely to want an email summary of care/home instructions (OR=0.39, 95% CI:0.15, 0.98, p=0.05) than those under age 65. The results of our study indicate that PD patients over age 65 appear to have a less favorable view regarding the role of technology in communicating with healthcare providers and self-understanding of their care.

P26.06**A smartphone-based Interactive Rhythmic Auditory Cueing Evaluation (iRACE) for gait impairments**

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Objective: Rhythmic auditory cueing (RAC) continues to receive attention as a promising therapy for gait impairments in Parkinson's disease. By synchronizing their movements to an external cue, patients can reduce their motor timing variability (MTV);

MTV has been retrospectively and prospectively linked with fall likelihood. Currently, however, there exist no easy-to-use diagnostic tools to evaluate whether a given patient might benefit from a longer-term therapy program with RAC, or to optimize RAC parameters.

Methods: iRACE has been developed for Apple (iOS-based) iPhone/iTouch. The touchscreen of the device is used to quantify upper-motor timing during bimanual alternate index finger tapping, and the device's built-in tri-axial accelerometer to quantify lower-motor timing while walking. Both self-paced and externally-cued

conditions may be evaluated. Based on each participant's self-paced cadence, a "yoked" playlist is created to determine the precise tempo at which MTV is minimized. Accuracy of the accelerometer-derived step time series was validated using a Biometrics wireless tri-axial accelerometer system (www.biometricsltd.com/datalog.htm). Time-domain estimates of MTV were quantified using a widely-used method (percent coefficient of variation) for both finger tapping (i.e., inter-tap intervals) and walking (i.e., inter-step intervals, with steps identified using peaks in anterior-posterior acceleration). Walking and tapping statistics are presented directly to the user (i.e., therapist/neurologist) on the device's screen, and automatically uploaded to a central server for data management.

Results: The flexibility, portability, and validity of iRACE offers both prognostic and analytic applications, including (1) evaluating whether a given patient may benefit from the longer-term therapeutic application of rhythmic auditory cueing; and (2) tracking the improvement of motor timing performance after behavioral, pharmacological, or neurostimulatory interventions. Further work from our group will provide a large library (~3 million items) of music that has been carefully analyzed for tempo, enabling further customization.

P26.07**SENSE-PARK: measuring Parkinson's disease in the home environment in an objective, continuous and minimally obtrusive fashion**

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Objective: The future treatment of Parkinson's relies on the accurate assessment of how it affects people with Parkinson's (PwP's) as individuals. SENSE-PARK is a pioneering project which combines expertise from technology with the experiences of those who live with Parkinson's and the scientific know-how of those who treat it. The objective of SENSE-PARK (EU funded, INFISO-ICT-2011-288557) is to develop a patient-centered, minimally obtrusive and empowering information system for use in the home environment, which provides PwP's with practical and motivating tools to monitor their condition in a continuous and objective way. In more detail, the SENSE-PARK system will inform the users about motor and non-motor functioning in daily life activities ('being', data collection via a wrist-worn data logger), leisure activities ('belonging', data collection via gaming console and adapted interface) and scientific environment ('becoming', validation purposes).

Methods: (i) Participatory approach; (ii) needs and requirements analysis; (iii) adapt and develop a PwP's-friendly interface; (iv) define relevant parameters to monitor disease progression; (v) sensor system development and data interpretation; (vi) hardware and software integration, IT infrastructure and telemedicine; (vii) iterative testing; (viii) scenario-based multicentre study.

Results: Through conducting a needs and requirements analysis that was facilitated by Cure Parkinson's Trust, project partners were able to define usability criteria and to prioritize symptomatic domains and parameters for measurement of Parkinson's. The symptomatic

domains of the SENSE-PARK system are: Gait, Sleep, Bradykinesia, Cognitive function, Tremor and Sway. Pilot systems for the measurement of these domains including hardware, software and interface are being developed, used and systematically tested by PwP's whose feedback will direct modifications and improvements. Validation and relevance of the SENSE-PARK system with respect to the selected domains and parameters have been identified as the key issues for the use by PwP's as well as for eventual application in PD trials.

P26.08

Automatic assessment of touch-pad tapping performance in Parkinson's disease

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Objective: To develop and evaluate a computerized method for automatic scoring of finger tapping performance in Parkinson's disease (PD), using a touch-pad device.

Methods: Sixty-five patients diagnosed with advanced PD have utilized a test battery in a telemedicine setting over the course of a 3 year clinical study. On each test occasion, they were asked to perform fine motor tests including alternate tapping of two buttons on a touch-pad screen as fast and accurate as possible, for 20 seconds in duration. The tapping performance was visualized by displaying graphs in a web interface. Information presented included distribution of taps over the two buttons, horizontal tap distance vs. time, vertical tap distance vs. time, and tapping reaction time (Figure 1a). A neurologist (DN) used a scale between 0 (normal) and 4 (severe) to rate firstly four tapping properties: Speed, Accuracy, Fatigue, Arrhythmia, and secondly a Global Tapping Severity (GTS). Different quantitative measures (Table 1) were calculated for representing symptom severities of the said dimensions. An ordinal logistic regression model, using stratified 10-fold cross-validation, was used to map these measures to the corresponding GTS, and to calculate and evaluate an automated GTS score.

Results: The Spearman's rank correlations between first principal components of the quantitative measures and their corresponding ratings of dimensions were as follows: Speed (-0.91), Accuracy (0.69), Fatigue (0.46) and Arrhythmia (0.77). The agreement between computer ratings and neurologist ratings was very good with a weighted Kappa coefficient of 0.89 ($p < 0.001$, Figure 1b). In conclusion, the computer method could automatically assess tapping performance of PD patients similarly to the visual assessments of the neurologist.

Figure 1. a) An illustrative example of visualization of tapping performance to the neurologist, with Speed rated as 0 (normal), Accuracy as 1 (mild inaccuracy), Fatigue as 0 (normal), Arrhythmia as 1 (mild) and GTS as 0 (normal). b) Ratings of tapping tests by the neurologist and computer method.

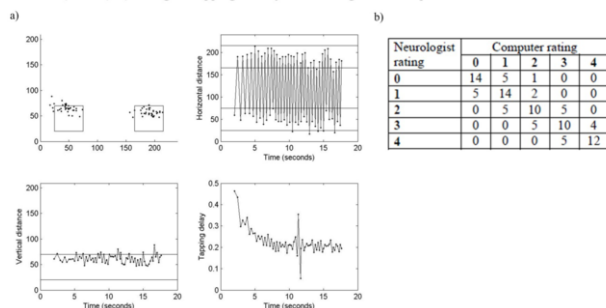


Table 1. Description of quantitative measures

#	Measure	Description	Tapping dimension
1	No_taps	Total number of taps	Speed
2	Avg_vel	Average tapping velocity	Speed
3	Avg_vel_L_R	Average tapping velocity of moving from left to right button	Speed
4	Std_vel_L_R	Standard deviation of tapping velocity of moving from left to right button	Speed
5	Avg_vel_R_L	Average tapping velocity of moving from right to left button	Speed
6	Std_vel_R_L	Standard deviation of tapping velocity of moving from right to left button	Speed
7	Ent_vel	Entropy of velocity	Speed
8	Avg_dfb	Average deviation from button centers	Accuracy
9	Cv_dfb	Coefficient of variation of deviation from button centers	Accuracy
10	Ts_rb	Spread of taps in the right button	Accuracy
11	Ts_lb	Spread of taps in the left button	Accuracy
12	Avg_s	Average spread of taps in two buttons	Accuracy
13	Avg_vpc	Average velocity per tapping cycle	Fatigue
14	Diff_T_1_2	Mean difference of number of taps between the first part (2-10 seconds) and second part (10-18) of the test	Fatigue
15	Diff_dt_1_2	Mean difference of tapping reaction time between the first and second part of the test	Fatigue
16	Avg_rho	Average correlations of jackknife samples between test time and tapping reaction time	Fatigue
17	Ae_vel	Approximate entropy of tapping velocity	Arrhythmia
18	Ae_x	Approximate entropy of horizontal tap distance	Arrhythmia
19	Ae_y	Approximate entropy of vertical tap distance	Arrhythmia
20	Std_jitter	Standard deviation of the horizontal distance variation	Arrhythmia
21	Std_shimmer	Standard deviation of the vertical distance variation	Arrhythmia
22	Avg_rhythm	Average of joint horizontal-vertical distance variation	Arrhythmia
23	Std_rhythm	Standard deviation of joint horizontal-vertical distance variation	Arrhythmia
24	Corr_r	Cross-correlation coefficient of distance-time slopes	Arrhythmia
25	Xapentr_R	Cross approximate entropy of distance-time slope	Arrhythmia

P26.09

Quantitative motor assessment of gait and lower extremity bradykinesia following the discontinuation of deep brain stimulation

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Objective: One of the challenges of outpatient programming of deep brain stimulation (DBS) parameters in Parkinson's disease (PD) is the delayed effect on gait. Therefore, the objective was to quantify the change in gait function and lower extremity bradykinesia in PD patients treated with DBS after stimulation is turned off using body-worn motion sensors.

Methods: Forty sub-thalamic DBS-treated PD patients with residual gait impairment were recruited. Evaluation took place in the "practically defined OFF state", the morning after overnight withdrawal of anti-parkinsonian medications. Compact and wireless motion sensors were positioned on the feet, wrists, and torso. Subjects were then guided through a subset of the Unified Parkinson's Disease Rating Scale (UPDRS) motor section: toe taps and leg lifts while seated and walking in a straight line at a normal pace, turning in place, and returning to the starting position. Motion sensor data were wirelessly transmitted to a computer for storage and analysis while subjects were also videotaped for later clinical scoring. The battery of tasks was performed first with stimulation turned on and then repeated with stimulation turned off at approximately 15 and 30 minutes and 1, 2, and 3 hours later. Subjects were set to their previously optimized stimulation parameters at the conclusion of the study. Multiple linear regression scoring models were developed based on the kinematic features extracted from motion sensor data and clinician UPDRS scores.

Results: On average, model scores and kinematic features extracted from motion sensor data were highly correlated to clinician scores ($p > 0.80$). When plotted over time, kinematic features and

model scores demonstrated a gradual worsening that continued more than an hour after stimulation was turned off. These scoring models and study results could be used to more efficiently manage DBS programming by accounting for the delayed response of gait to changes in stimulation.

P26.10

Metronome-paced square step test (MPSST) in Parkinson's disease

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Objective: Midline or axial symptoms in PD are frequently associated with poor balance and gait, reduced physical activity and cognitive decline. Here we developed a metronome-paced square-step task (MPSST) that requires auditory timed, bilateral midline, and diagonal stepping. We examined the relationship among MPSST, level of physical activity, and cognitive function.

Methods: 11 age-matched controls and 21 PD participants were recruited. As part of *Ambuloso*, a home-based music walking therapy program, PD patients were further classified as frequent vs. infrequent walkers. We developed a global performance score for MPSST using visually rated errors and step time consistency. Specific MPSST parameters were obtained using GaitReminer™ and the Montreal Cognitive Assessment (MOCA) examined cognitive functioning.

Results: The global performance score showed the control group performed the MPSST significantly better than the PD group as a whole ($p < 0.01$). The coefficients of step-length variances acquired during MPSST were significantly smaller in controls than that of infrequent, but not frequent, PD walkers ($p < 0.05$). Correlation analysis between MPSST and MOCA scores from individual patients showed those patients who scored lower on the MOCA also tended to score lower on the MPSST (Spearman $r = 0.57$; $p < 0.01$), despite mean MOCA scores being comparable between groups ($p > 0.05$). Logistic regression further revealed that MPSST was a significant predictor of MOCA score outcome, able to identify patients as being above or below the published optimal screening cut-off of 26/27 with an overall correct percentage of 81% ($p < 0.05$). Hence, the MPSST is a useful tool for evaluating motor and non-motor impairments in PD patients.

Acknowledgments: CIHR, Parkinson Alberta Society, and the Movement Disorders Clinic-Alberta Health Services.

P26.11

E-Motion capture system for movement disorders

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Objective: To develop a system based on human-computer interface (HCI) motion capture, to quantify motor (stride length, width and length step) and spatiotemporal (velocity and acceleration) variables, to support the clinical evaluation of patients with Parkinson's disease.

Methods: To develop the software was used an agile methodology with iterative and incremental cycles that used Agile methodology base on Prototyping. We defined four cycles of development, each one with differential internal iterative cycles according to the

progress of the project. The project required an interdisciplinary work, where was selected a team of neuroscientists who worked with the main team at regular meetings, they provided and validated the software requirements.

Results: The obtained motion capture system, E-Motion, is prototype software able to calculate motor (stride length, width and length step) and spatiotemporal (velocity and acceleration) variables. Kinect sensor was selected as the main capture device because compared to conventional gait laboratories, has advantages such as low cost, portability and the lack of markers for capture. The Kinect provides the location in space (3D) joint required to calculate the motor and spatial-temporal variables. The E-Motion capture system would fit to the conditions to the neurology clinics in low and middle income countries.

P26.12

Objectively measuring characteristics of gait in Parkinson's disease

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Parkinson's disease (PD) has a profound effect on the ability to walk. Unique features of PD gait include shuffling and freezing of gait (FOG). Research supports walking can be improved with medical and non-medical interventions such as exercise and vibration therapy. However, these studies largely rely on self-report or direct observation of gait to assess their effectiveness. Currently, no identified "gold standard" assessment provides a direct measure of gait and mobility in a real-life setting. Therefore, it is difficult to assess the real impact of treatment. This study takes a look at a unique method of objectively assessing PD gait patterns.

Objectives: The aim of this study is to test the ability of a novel insole (SEnsole) that can be worn in a person's shoe to reliably and accurately assess the quality and characteristics of PD gait.

Methods: Volunteers with and without PD were recruited. Participants were asked to walk back and forth a 10 meter path wearing the SEnsole device; sessions were video recorded.

Analysis: SEnsole data was sampled at greater than 20Hz for several bouts of walking. Steps during turns were removed so that analysis was based on straight path walking only. A representative healthy step cycle was formed from a composite of 40 non-PD subjects averaged step data. The average shuffle step was similarly processed, but on a single subject experiencing shuffling gait. Spectral analysis was used to characterize FOG data as stride analysis is not possible during FOG episodes.

Results: Clear differences in gait characteristics between PD and non PD subjects were identified. The SEnsole and analysis program accurately detected normal gait from shuffled gait, and FOG. In addition to the observed sensitivity, the simplicity of the SEnsole supports its usefulness in the assessment of gait and the testing of interventions.

P26.13

Retraining function with exercise based computer games for people with Parkinson's disease: PD-Kinecton

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Objective: Develop and pilot test an exercise based computer game to rehabilitate dynamic postural control in people with Parkinson's disease (PD) using the Xbox Kinect; and assess accuracy of the Kinect to monitor clinically relevant movement in people with PD.

Methods: An exercise based computer game aimed at training dynamic postural control was developed in collaboration with people with PD and their carers. The game consisted of multi-directional reaching and stepping, with increasing complexity across 12 levels of difficulty. Nine people with PD pilot tested the game. Participant feedback to identify issues relating to acceptability, feasibility and safety of the game was collected in a semi-structured interview. Concurrent validity to measure functional movements (such as sit-to-stand, multi-directional stepping and reaching, foot tapping, hand clapping and walking on the spot) was established by comparing movement in nine PD participants and 10 controls concurrently measured with a 3D motion analysis system (VICON) and the Kinect.

Results: Participants generally enjoyed the gameplay and all felt safe whilst playing the game. Participants performed a high volume of reaching and stepping, reaching on average 328 times (range 167-628) and stepping 167 times (74-276) during the ~30min session. However, some participants found interacting with game objects appearing to move towards them difficult and some had difficulty combining the stepping and reaching tasks. The Kinect accurately measured the timing of movements (Intra-class correlations (ICCs) >.9) and the range of motion for gross movements (ICCs >.9) but did not monitor smaller movements such as hand clapping as accurately (ICCs <.3).

P26.14

The Edmond J Safra visiting nurse faculty program: innovations in the nursing care of people living with Parkinson's disease

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³Edmond J Safra Visiting Nurse Faculty Program

Objective: The Edmond J Safra Visiting Nurse Faculty Program was launched in 2009 to address the paucity of content on Parkinson's disease (PD) in undergraduate schools of nursing. Through engaging nurse faculty in intensive didactic, clinical, and PD support group experiences in collaboration with leading interdisciplinary movement disorder teams in the US, the program has exceeded expectations. Since its inception, scholars attending the program have incorporated scientific care guidelines in PD for over 5,800 nursing students. In addition, faculty scholars have developed numerous creative projects to enhance nursing education and patient care, thereby, greatly influencing the care of people living with Parkinson's. This poster will highlight several unique projects undertaken by Edmond J Safra Nurse Faculty Scholars.

Methods: Nursing faculty have achieved excellence in teaching content on PD and concurrently have developed a scholarly interest in the field. This poster highlights faculty projects focused on unique contributions in the areas of: nursing models of care, curricula design, nursing outreach, patient care, and nursing research.

Results: To date, 78 nursing faculty have completed the Edmond J Safra Visiting Nurse Faculty Program, representing over 35 schools of nursing in the United States and Canada. While enhancing nursing students' understanding of PD care remains the key objective of the program, nursing faculty attending this 37 CEU accredited course are independently pursuing scholarly work through unique projects presented in this poster.

CARE DELIVERY & QUALITY OF LIFE: CAREGIVING, RELATIONSHIPS, RESPITE CARE, FAMILIES

P27.01

The relationship between patient symptoms and caregiver burden in advanced stage Parkinson's disease

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Objective: This study aimed to describe the characteristics of the caregivers for patients with advanced stages of Parkinson's disease (PD) and to analyze the association between PD symptoms and caregiver burden.

Methods: Thirty caregivers for advance PD patients were recruited. Caregivers completed self-reported questionnaires on the clinical aspects of partner's PD, Hospital Anxiety and Depression Scale (HADS), and Zarit Caregiver Burden Inventory (ZCBI). Within the questionnaire, caregivers ranked patients' symptoms by the impact on the caregiver's life from 8 clusters: motor, balance, medication related, cognitive, speech, neuropsychiatric, autonomic, and sensory deficits.

Results: PD patients (76.6 % male) had a mean age of 72.8 years (± 10.9) with median disease duration 10 years. Caregivers (16.6 % male) had a mean age of 67.2 years (± 8.9), and 86.6 % were patients' spouses. All but 1 patient were at home. Average hours per week caregiving were 31.7 (range 4 – 168). Nine caregivers had outside help and an additional 4 had home health services. On the basis of HADS scores, 46.6% of patients and caregivers experienced anxiety equally, and 50 % of patients and 60 % of caregivers experienced depression. Only 20% of caregivers were on medications for mood. On ZCBI, 14 (46.6%) experienced mild-to-moderate, and 7 (23.3 %) reported moderate-to-severe burden. There was a positive correlation between ZCBI and caregiver HADS depression scores ($r = 0.60$, $p < 0.05$). By impact on their life, caregivers subjectively ranked balance deficit as #1, followed by cognitive, motor and speech deficits. Multiple linear regression analysis showed balance ($R^2 = 0.53$, $p < 0.001$) and cognitive ($R^2 = 0.6$, $p < 0.001$) changes having the biggest impact on ZCBI. In-home support with balance and cognitive therapy for advance PD patients, psychological support, and treatment of affect for caregivers could positively impact advance PD care.

P27.02

The relationship between caregiver burden and negative social exchanges in Parkinson's disease

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Objective: Caregiver burden has a negative impact on both people with Parkinson's disease (PWP) and their family members. Given the heightened rate of caregiver stress associated with the non-

motor complications of Parkinson's disease (PD), depressed PWP and their social supports are particularly vulnerable to its detrimental effects. The purpose of this study is twofold: 1) to identify predictors of emotional burden in a high-risk sample of PD caregivers, and 2) to describe the relationship between emotional burden and the caregivers' provision of negative social feedback (i.e., criticism, rejection, reinforcement of negative thoughts) to depressed PWP.

Methods: Baseline data from 80 PWP and their caregivers enrolled in a National Institutes of Health-sponsored treatment trial of cognitive-behavioral therapy (CBT) for depression in PD (dPD) were examined. Caregiver and patient variables that predicted caregiver provision of negative feedback to PWP (as reported by both PWP and caregivers) were explored.

Results: The caregivers' past receipt of psychotherapy and the depressed PWPs' quality of life and coping style were significant predictors of caregiver emotional burden. Caregiver emotional burden was significantly related to the caregivers' provision of negative feedback (i.e., "Your future is hopeless") to depressed PWP on two separate measures (caregiver measure: $r = .349$, $P = .002$ & PWP measure: $r = .337$, $P = .002$). Emotional burden and history of psychotherapy (caregiver variables), as well as working memory, impairment in activities of daily living, coping style, motor disability, anxiety, and negative thoughts (patient variables) were all significant predictors of the caregivers' provision of negative social feedback to PWP (as assessed by both PWP and caregivers). In conclusion, caregiver burden significantly increases the risk that caregivers will offer negative social feedback to depressed PWP, which may make dPD more difficult to treat. Thus, caregiver burden remains a critical target for intervention in dPD treatment protocols.

P27.03

Carer benefit from a domiciliary multidisciplinary specialist rehabilitation service for people with Parkinson's and their carers: the SPIRITT project

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Objective: To evaluate carer benefit from a domiciliary multidisciplinary specialist (MDT) rehabilitation service for people with Parkinson's and carers compared to usual care.

Background: Although co-resident carers provide most care for people with Parkinson's, thereby reducing the need for more costly arrangements, the burden can result in strain and adverse health effects. An MDT approach to rehabilitation is recommended to provide coordinated care and support to patients and carers, but has not been widely researched.

Methods: Pragmatic three parallel group randomised controlled trial – the Specialist Parkinson's Integrated Rehabilitation Team Trial (SPIRITT), Surrey, England involving people with Parkinson's (all stages), and live-in carers. Groups A and B received domiciliary MDT rehabilitation for six weeks, Group B received ongoing support for a further four months from a trained Parkinson's care assistant (PCA), control group (C) received usual care. A per protocol analysis was undertaken; effects of the MDT intervention were calculated within and between groups using change scores at 6, 24

and 36 weeks. Primary outcome: Modified Caregiver Strain Index; secondary outcomes: generic health-related quality of life (General Health Questionnaire, EQ-5D, SF-36), psychological wellbeing (Hospital Anxiety and Depression Scale (HADS)).

Results: 155 carers (A - 52, B - 50, and C - 53) were analysed. At baseline, carer strain, SF-36 Mental component and HADS Depression were positively associated with hours spent caring. The MDT intervention (Groups A and B) had a beneficial effect on psychological wellbeing of carers. In Group B, caregiver strain improved marginally over weeks 6-24, and psychological wellbeing improved slightly over 36 weeks. Carers in Groups A and C reported increased strain and decreased psychological wellbeing over the study period.

Conclusion: A domiciliary specialist multidisciplinary rehabilitation service delivered short-term benefits to co-resident carers, which continued when additional PCA support was provided.

ISRCTN: 44577970

Financial Disclosure: This project was funded by the National Institute for Health Research Health Services and Delivery Research (NIHR HS&DR) programme (project number 08/1909/251). Visit the HS&DR website for more information.

The views and opinions expressed therein are those of the authors and do not necessarily reflect those of the NIHR HSDR programme or the Department of Health.

P27.04

Determinants of psychosocial impact of being a carer of people living with Parkinson's disease: a systematic review

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Objective: There is evidence to suggest that the support provided by carers leads to improved health outcomes and quality of life (QoL) and prevention of early nursing home placement for people with Parkinson's disease (PwP). Being a carer, however, can have a variety of physical, psychological, social and financial consequences that may challenge their ability to continue caring for a PwP. This systematic review aimed to identify the factors which influence psychosocial outcomes of caring for a PwP.

Methods: A search of the MEDLINE, PsychINFO, EMBASE, AMED, BNI and CINAHL databases (between 1996-January 2012) and hand searches of key journals and reference lists yielded 48 relevant articles. The psychosocial outcomes studied were varied, including carer burden, psychological well-being, QoL and social functioning.

Results: This review found that PwP disease factors, carer involvement (e.g. amount and duration of care-giving), social support and other related psychosocial factors were consistently associated with psychosocial outcomes. PwP and carer demographics were less consistent factors. PwP QoL and carer physical health, coping styles and personality showed consistent associations, however, further research in these areas is needed to draw confident conclusions. This review builds on previous PwP carer theory and highlights the need for more theoretically-grounded and longitudinal research to guide the development of psychosocial interventions for PwP carers.

P27.05

Hanging by a shoestring: respecting spouses' desire to remain at home in advanced Parkinson's disease

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Objective: The majority of care for people with Parkinson's disease (PD) is provided at home by family members. PD is characterized by a slow progressive decline with care needs often exceeding a decade. The experience of having advanced PD and what the family preferences are at the advanced stages has not been studied.

Methods: Data were collected on two occasions over a one month period utilizing semi-structured interviews, with both individual and couple interviews. The sample was 14 couples with a mean age of 73.3 years for the person with PD and 72.1 years for the spouse. The person with PD had been diagnosed on average for 12 years and the couples had been married for 49 years on average. All persons with PD were dependent on assistive devices. Data was coded by three members of the research team.

Results: All participants discussed the strong desire to remain in their homes for as long as possible. Some participants had made housing modifications in order to support this goal. For the persons with PD, placement was not an option to be considered. However for spouses, acknowledgement there may come a time when they could no longer continue to provide care was discussed. During the study three persons were placed in a nursing home and in each case this was unplanned. Wanting to care for a spouse in the home is common but the care needs may be overwhelming. Interventions to support the couple in their planning and decision making are needed.

P27.06

Reduction of care partner burden through care partner training

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Objective: Patients living with Parkinson's have a higher risk for isolation and require coordinated care services. As PD progress, patients rely on care partners for assistance with daily living and socialization for quality of life. Many care partners are not prepared and struggle resulting in burnout. Our goal is to cycle through six sites in 19 counties, a 50 mile radius, over 2 years, reaching 10% of the "at risk" patients and care partners. Twenty patients and care partner pairs per site will be given disease-specific education. We expect to see higher quality of life scores in care partners who participate in the training program.

Methods: Members of a multi-specialty health team, specially trained in Parkinson's care have designed "stations" for small groups. In these stations, specific tasks are presented. Stations cover safe mobility, adaptive equipment, falls, medication compliance, monitoring declines, assessing medication response, weight loss, lightheadedness, bowel and bladder issues, handling hospitalizations, and maximization of resources. Care partners rotate through stations over two hours. Training is offered one day a month rotating through the 19 counties. Reinforcement is available on DVD or on line.

Results: Care partners completing training are compared to those receiving routine education and support through a Parkinson's clinic. Both groups are surveyed at three weeks, three months, and six months, looking at retained knowledge, activities implemented and SF – 36 scores. Our primary outcome measure will be care partner burden in our intervention group by use of SF – 36 scores. We expect higher quality of life scores in care partners who participated in the program.

P27.07

"Do I look like I care?" Parkinson's disease and its potential effects upon relationships

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Objectives: To gather information from people living with Parkinson's disease about communication-related symptoms—e.g., facial masking, flat affect, lower speech volume and altered body language—and whether any personal relationships have been affected by those specific symptoms. To educate family, friends, health professionals, staff who interact on a regular basis with people living with Parkinson's disease, and the general public about masking, speech effects and altered body language symptoms in order to foster greater tolerance, respect and understanding of the disease and those affected by it.

Methods: Two voluntary self-selecting surveys were created. They were not built with statistical analysis in mind. Rather, they were intended to provide "snapshots" and anecdotes from the lives of those who completed them. In addition to demographic information, questions regarding the specific symptoms listed above, relationship changes attributed to those symptoms, and anecdotes were collected in the surveys (available upon request). Data were collected by the two surveys posted on Survey Monkey, each for three months. Availability of surveys publicized was through email and social media. Data and anecdotes from two surveys were compiled and prepared for future publication.

Results: Data from surveys showed that certain symptoms of Parkinson's disease have deleterious effects on interpersonal communication. These effects were found to impact relationships of all kinds—those with life partners, potential life partners, family, friends, healthcare providers, even complete strangers. Better education about Parkinson's disease and increased awareness that one cannot rely on typical body language or means of expression to interpret mood or intent are needed in order to maintain (or create) important life relationships and to reduce the isolation so common in people living with Parkinson's disease.

P27.08

Different impact of Parkinson's disease symptoms on patients and caregivers

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Objective: Symptoms of Parkinson's disease (PD) influence QOL of patients and their caregivers. We examined the difference of distress of each PD symptom for patients and their caregivers.

Methods: Pairs of PD patients and ones caregivers who were able to answer the question were enrolled to the study. We asked each pair to pick up presenting PD symptoms of patients, and then asked if the symptoms disturbed their daily life or not.

Results: 184 patient-caregiver pairs were assessed in the present study. Among motor symptoms, freezing gait (28.3%), postural instability (27.4%), bradykinesia (21.6%), frequent falls (21.4%), and tremor (19.7%) were the main symptoms for PD patients to feel distress. Among non-motor symptoms, constipation (25.1%), low back pain (17.7%) and frequent nocturnal micturition (16.9%) were

complained frequently to feel distress by patients. The distressing symptoms for caregivers were frequent falls (27.3%), postural instability (25.1%), bradykinesia (22.3%), and freezing (21.3%) as motor symptoms, and cognitive impairment (20.5%) and apathy (18.1%) as non-motor symptoms. The 3 most distressing symptoms for patients were gait freezing, constipation and postural instability, and they were frequent falls, postural instability and cognitive impairment for caregivers. The symptoms of which patients felt distress more prominently than their care givers were gait freezing, constipation, pain (low back pain, head ache, and the other pain), frequent nocturnal micturition, insomnia, drooling, orthostatic hypotension, and taste impairment. Whereas, the ones of which caregivers felt distress more than patients were frequent falls, cognitive impairment, apathy, psychosis, aggression, irritability, vocalization during sleep, and sweating. Symptoms including nocturnal vocalization, irritability, aggression, impotence, and sweating were the symptoms of which PD patients do not care as well as caregivers.

P27.10

Parkinson's Spousal Caregivers and Health Care/Work Issues

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Objective: Determine what health care and work related issues cause problems for spousal caregivers, and to bring awareness within the Parkinson's community of non-medical effects of the disease on the family.

Methods: The link to the online survey was posted to several PD and Caregiver-related Facebook pages, and emailed to a variety of support group participants. It was also posted on the NPF Caregiver and the Well Spouse Association Online Forums.

Results: These results are preliminary, based on the first 92 respondents. Caregivers as well as their partners are approximately 3 times more likely to be no longer working now than at the time of diagnosis. Both groups appear to have health insurance or Medicare coverage, with the exception of a few caregivers. Two-thirds of caregivers have experienced anxiety since their partner's diagnosis, and just over half indicated that depression has also been experienced. A significant number report pain in the back, neck, knee, leg, arms, hands and/or shoulders. About half have received mental health counseling in the past, and about 30% currently receive counseling. Caregivers report that the PWP is least likely to be able to independently work outside the home, handle yard work, and/or do household chores/repairs. Activities that caregivers have typically taken over include making important decisions, driving, paying the bills, doing household chores/repairs, and helping the PWP with entertainment. Respondents were split evenly in terms of their financial situation relative to time of diagnosis, however one in five each rated their level of concern regarding future financial obligations as quite or extremely concerned. One third of the caregivers say they are getting by, but barely, right now, and 5% are having to use savings or borrow to stay afloat.

P27.11

Providing instruction of Reiki first degree as a complementary therapy to help improve the lives of Parkinson's disease (PD) carepartners/caregivers

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Objective: To instruct and educate the Parkinson's disease community about how the teaching of Reiki (RAY-KEY) first degree as a complementary therapy to Parkinson's disease carepartners/caregivers can be beneficial to their self-care. To give carepartners/caregivers another tool to reduce stress, increase relaxation, and provide mental & physical calmness. Reiki is a non-invasive therapy that uses light touch to increase and enhance one's personal energy. Reiki first degree instruction focuses on self-care, a self-treatment protocol, and seated chair protocol to give Reiki to another person.

Methods: The workshop is a twelve hour workshop in Reiki first degree. The current workshop held in six two-hour sessions, allowing the carepartner to absorb the material. The workshop includes instruction in Mindfulness Meditation, Energy anatomy, Qigong, and Reiki self treatment & seated chair protocols. The workshop highlights the importance of the caregiver/carepartner to take care of themselves on a daily basis. Examples of how Reiki can be incorporated into daily life are presented.

Results: Carepartners/Caregivers will be able to treat themselves with Reiki and have a general understanding of Reiki which can be used to enhance and complement their current self-care strategies. Workshop participants will be able to use Reiki to increase one's relaxation, reduce stress, and enhance the body's own healing properties. Carepartners/Caregivers will also be able to provide Reiki to help their love one who is living with Parkinson's disease.

P27.12

Quality of life and caregiver burden among Hispanic subjects with Parkinson's disease living in the US and Mexico

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Objective: Ethnic and sociocultural factors may play a role in quality of life (QoL) and caregiver burden perception. The objective is to compare the QoL and caregiver burden between Latin-American subjects with Parkinson's disease living in the United States (US) and Mexico.

Methods: Immigrants or first-degree relatives of Latin-American immigrants to the US participating in the Muhammad Ali Parkinson Center's Promotores Program and diagnosed by a Movement Disorder Neurologist in Phoenix or Mexicans at the National Institute of Neurology and Neurosurgery in Mexico City and who fulfilled UKPDBB criteria for Parkinson's disease were included. QoL was assessed using the PDQ-39 while caregiver burden was evaluated with the Zarit Caregiver Burden Interview (ZCBI).

Results: A total of 27 subjects from Phoenix (63% Mexican) and 30 subjects from Mexico City were included. No differences were found in regards to gender ($p=0.58$), years of schooling ($p=0.59$), age ($p=0.86$) and disease duration ($p=0.98$). PDQ-39 total score was slightly higher (worse QoL) in subjects living in the United States but without statistical significance (38.6 ± 20.7 vs 31.6 ± 19.3 , $p=0.20$). From the eight dominions of the PDQ-39, the only difference found was on social support where US subjects reported higher scores (41.3 ± 31.7 vs 15 ± 25.5 , $p=0.001$). Caregivers from both groups did not differ in the number of days per week spent with the subject nor in the total years of caregiving. Little or no caregiver burden was reported by 93% of caregivers in the US in comparison to the 80% from Mexico (chi square $p=0.17$). Our data shows a statistically significant difference in the social support dominion, being worse in subjects from the US. Caregivers in the US reported less burden than their counterparts in Mexico. Whether these findings are due to sociocultural factors merits further study in a larger sample.

P27.13

Documenting the lived experience of unconditional love in Parkinson care givingRamon Ruiz Sampaio¹ and Sheree L. Loftus²¹Ramon Ruiz Sampaio, Mexico City²Beth Israel Medical Center, NY, NY, USA

Modern technology fosters longevity. Degenerative diseases are more common with age. There are 65 million family caregivers in the United States. At some point it is likely we will provide family care or receive it. Most of us are untrained and unprepared to assume this responsibility. Awareness of this vital issue is crucial to support and integrate family caregivers in the health care system. Parkinson disease is an increasingly common degenerative condition. This disorder of the central nervous system presents with movement - related symptoms of shaking, rigidity, slowness, and difficulty with walking and speech. As the disease progresses, difficulty with sleep, cognitive, emotional, and behavioral problems may arise. Parkinson disease has a relentless progression. The care needs of the person diagnosed becomes increasingly demanding over a lifetime. The role of the caregiver is essential. This photo documentation focuses on family managing to overcome the challenges in the care giving journey of Parkinson disease. The psychological, physical, and everyday aspects of care giving are starkly depicted. The long - lived experience of Parkinson disease - related progressive symptoms takes a toll. The once free human being is now immobilized by the disease, with soft speech rigid limbs, unable to turn the body axis freely, swallowing difficulty, and inability to initiate the simplest gait. The Parkinson mind well - aware of the altered body, but unable to translate this awareness into action. The family caregiver is ever present with encouragement, kindness, a helping hand, concise direction and unconditional love. Every day is important, and living in the present moment arrives with clarity as movements of freedom are limited by Parkinson disease. Symptoms progress and family life is undermined by increasing limited movement. The family caregiver struggles with multiple roles, yet is a cherished resource and at once creative, resilient, flexible and frustrated.

P27.14

What measures of disability predict caregiver burden in Parkinson's diseaseM. Kwasny¹, O. Oguh², D. Klein¹, T. Simuni¹, on behalf of the NPF QII Investigators¹Northwestern University, Chicago, IL, USA²University of Florida Jacksonville, Jacksonville, FL, USA

Background: Caregiver burden is significant and increases with progression of disability in Parkinson's disease (PD).

Objective: To determine what measures of PD disability and patient quality of life are associated with caregiver strain among carers of patients with PD.

Methods: Data was collected from PD patients and their caregivers enrolled in the NPF-QII registry. 1470 patients who indicated non-professional caregivers, with complete Multidimensional caregiver strain inventory (MCSI), and at least two clinic visits were included in the analysis. Multivariate logistic and linear regression models were fit to examine the relationship between caregiver burden (MCSI \geq 30) and PD quality of life (PDQ-39), as well as several aspects of PD disability including stage of disease, disease duration, concomitant medication use, cognition, utilization of mental health care and social services at baseline, and predicting change in MCSI at a subsequent visit.

Results: Similar to a larger analysis of cross sectional data from the NPF-QII registry, PDQ-39 was the strongest predictor of caregiver

burden at baseline ($c=0.80$, $p<0.001$). After adjusting for PDQ-39 (OR=1.07, $p<0.001$), decreased verbal fluency (OR=0.93, $p=0.003$), history of mental health referrals (OR=1.99, $p=0.006$), were also predictive of caregiver burden. At the next clinic visit, there was a small, but statistically significant increase in MCSI (mean 1.31, SD 11.2, $p<0.001$). The change in caregiver burden was most related to changes in PDQ-39 ($p<0.001$), and to decreases in verbal fluency ($p=0.028$) after adjusting for baseline age ($p=0.005$), Hoehn and Yahr stage >3 ($p=0.015$), and disease duration ($p=0.398$).

Conclusions: These results demonstrate the caregivers are afflicted with strain and burden in many psychosocial and somatic domains of PD care. PDQ-39 total score is the strongest predictor of caregiver burden.

P27.15

Turning Strain into Strength: Investigating caregiver growth in the loved ones of persons with Parkinson's disease (PD)Deborah Worboys¹, Associate Professor Anne Tolan¹, Dr Andrea Langmont-Mills²¹Australian Catholic University, Brisbane, Queensland, Australia²University of Southern Queensland, Toowoomba, Queensland, Australia

Objective: There is a plethora of research into Caregiver burden. However, Caregiver growth is an important, yet less-explored phenomenon. It is important to focus on the positive side of PD caregiving and its benefits; not only because experiencing growth is valuable in its own right, but also because personal growth (such as deriving pleasure and gratification, developing skills, and finding meaning) may buffer against the common detrimental consequences of caregiving (such as depression, burden, and health problems). This PhD project adopted a strength-based perspective. This project aimed firstly to investigate whether caregiver growth is experienced, secondly to examine psychological aspects associated with caring for a loved one with PD, and thirdly to make recommendations for possible psychological interventions aimed at assisting in empowering loved ones to positively adjust and grow throughout their caregiving journey.

Methods: A Qualitative research project, consisting of two studies. Study 1 involves in-depth interviews (N=30) and Study 2 involves a group discussion (N=3) with the loved ones of people with PD, about their overall caregiving experience.

Results: Interpretative Phenomenological Analysis of data has shown emerging themes and patterns associated with personal growth in a PD caregiving sample. Overall findings show that the majority of loved ones report some positive transformation and growth as a result of their caregiving experience. Many loved ones reported becoming more patient, independent, assertive, compassionate, and empathetic, with a greater sense of life purpose and meaning as a result of caring for their loved one with PD. These findings support Dementia caregiving research findings.

P27.16

Quantitative assessment of home and community mobility of persons with Parkinson disease and their spousal caregiversLynn Zhu^{1,9}, Catherine Lavigne-Pelletier^{2,3,9}, Margaux Blamoutier^{2,3,9}, Simon Brière^{4,9}, Matt Dibsedale⁵, Patrick Boissy^{4,6,9}, Mandar Jog^{7,8,9}, Christian Duval^{2,3,9}, Mark Speechley^{1,9}¹Department of Epidemiology and Biostatistics, Western University, London, ON, Canada²Kinanthropology Department, L'Université du Québec à Montréal, Montréal, QC, Canada³Centre de recherche de l'institut universitaire de gériatrie de Montréal, Montréal, QC, Canada

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⁸Clinical Neurological Sciences, Western University, London, ON

⁹Ecological Mobility in Aging and Parkinson's (EMAP) Research Team, Canada

Objective: Spousal caregivers of people with Parkinson disease (PwP) can experience increased level of caregiver stress. However, whether Parkinson disease affects the day-to-day activities and mobility of each partner in the spousal dyad has not been evaluated. This study compares the daily physical activity (PA) duration and community mobility of PwPs and their spousal caregivers.

Methods: Thirteen pairs of community dwelling PwPs (nine males, four females; Hoehn and Yahr stages I and II; 67.6 ± 7.9 years) and their spousal caregivers (four males, nine females; 65.3 ± 7.7 years) participated in this study for 14 days. Analysis of covariance (ANCOVA) was conducted to compare between spousal dyads and across the spousal caregiver and PwP groups for: 1. same-day average daily PA duration, measured using energy expenditure armbands (PA: > three METs for > two minutes) and 2. same-day average daily area of travel outside the home (km²), measured by a wireless inertial measurement unit with GPS. Age and self-perceived social support received by the PwP were added as covariates.

Results: A statistically significant difference ($p = 0.04$) was observed between the PA duration of PwPs (mean = 1 hour and 6 minutes) and spouses (mean = 2 hours). Average daily area travelled by spousal caregivers spanned 906.9 ± 1558.2 km² versus 821.6 ± 1386.1 km² travelled by PwPs; this difference was not statistically different, after adjusting for age and social support ($p = 0.43$).

Conclusion: Results suggested spousal caregivers maintained an active lifestyle during early PD, and spouses and PwPs may be travelling together outside the home. It is unclear whether the difference in PA durations is due to PD related caregiving duties, spousal pairs maintaining pre-PD PA routines, or both. The interpretation of results is complicated by the high variability in distance travelled; hence it is important to consider each spousal partner individually.

CARE DELIVERY & QUALITY OF LIFE: FITNESS, WELLNESS, NUTRITION

P28.01

How does a self directed exercise class increase quality of life for people with Parkinson's disease from a local community perspective?

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Objective: The objective is to provide the opportunity for PWP to exercise together three times a week at local community recreation centres which are accessible to PWP. There are many barriers to exercising, including; accessing trained exercise therapists, cost, motivational issues, isolation and transportation. PWP are capable of teaching each other exercises and providing feedback and support as long as they have been educated themselves on the

benefits of specific fitness- focused exercises for PWP and the latest research to back it up.

Methods: The local recreation centre is approached and educated about Parkinson's disease and the importance of exercising in a self- directed group. This limits costs for facility fees. Each PWP is initially assessed by a trained PWR!Moves physical therapist to obtain information about underlying pathology preventing participation, baseline function and to identify individual exercise needs to increase present function. Small groups are taught their deficits to target. There must be set times for PWP to go to the community recreation centre so it becomes routine. All group members are responsible for helping each other with the exercises and encouraging each other to push and achieve higher function. As PWP are all different each are working independently but using similar equipment. Reassessment by a trained therapist is advised every three months. The trained therapist support is available as needed but need not attend all sessions.

Results: PWP can get better and feel better by attending an exercise group with their peers. The above barriers are broken down. The group feels comfortable exercising with other PWP and helping each other. New friendships are made; information is shared resulting in better quality of life and EMPOWERMENT!

P28.02

Postural sway among elderly women with and without Parkinson disease: a cross-sectional study

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Objective: To compare the postural sway in a static position with and without the aid of the visual system among Parkinson's disease (PD) physical exercise practitioners and healthy elderly women classified as physical exercise non-practitioners (HE).

Methods: A total of 26 elderly women paired by age and body mass index (BMI) were divided into two groups, PD (n=13) 69,31±5,45 years with a BMI:27,28±5,24kg/m² and HE (n=13) 69,15±5,50 years with a BMI:27,15±4,99kg/m². The Hoehn & Yahr scale was used to classify the disease level (1-4). The center of pressure sway was measured using a force platform of two balance tasks with eyes open (EO) and closed (EC). The subjects were instructed to stand as still as possible with their feet 2 cm apart and arms at their sides. Data was collected with a sampling frequency of 100 Hz and filtered with a cut-off frequency of 10 Hz. Each test was performed twice for 30 s and the average was calculated. Descriptive (median, average and standard deviation) and inferential statistics (Mann-Whitney U test) were used with a significance level of 5%.

Results: There was a difference between groups in EC protocol for the Sway Range AP variable ($p = 0,001$) with HE showing lower anteroposterior displacement range than the PD. However, for the other variables in the two protocols no differences were found ($p>0,05$) (Table 1). The results suggest that elderly PD physical exercise practitioners present values of postural sway comparable to similar subjects older in terms of age and body mass but non-practitioners.

Table1. Main descriptive postural sway variables (Median) characterizing postural control in PD and health elderly women.

	Closed Base	Group		p-level
		PD	HE	
Sway Range AP (cm)	EO	2,42	1,96	0,204
	EC	3,01	1,19	0,001
Sway Range ML (cm)	EO	2,84	2,20	0,335
	EC	3,03	2,58	0,091
Area 95 (cm ²)	EO	4,76	3,28	0,139
	EC	6,50	3,92	0,153
Path Length (cm)	EO	40,25	41,69	0,801

	EC	55,12	54,65	0,807
Average velocity (cm/s)	EO	1,34	1,39	0,801
	EC	1,91	1,82	0,570

EO: Eyes open; EC: Eyes closed; Area 95: Area 95% of ellipse; AP: Anteroposterior; ML: Mediolateral

P28.03

Pilates for Parkinson's disease: an interdisciplinary perspective

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Pilates is an exercise-based approach to strengthening and flexibility based upon the work of Joseph Pilates. The emphasis on core strengthening, axial rotation and breath work makes this approach well-suited to the treatment of Parkinson's disease. In addition, there is an inherent awareness of movement and an emphasis on controlling and maximizing function of each component of the body during performance of exercises. By incorporating resistive breath training and voice exercise into the activities, it is possible to unlock the interdisciplinary potential for these activities in rehab and exercise settings. Pilates exercises improve symptoms of postural dysfunction by reducing kyphosis associated with Parkinson's disease in addition to enhancing core stability and axial range of motion, resulting in numerous benefits from an interdisciplinary perspective. Enhancing upright posture and rotational flexibility can result in improved balance and walking abilities. It can also also facilitate enhanced breath support which can result in louder phonation ability. Speech production will be more properly directed upwards towards communication partners and non-conversational pragmatics such as eye contact may also be enhanced. Upright positioning can improve transit of food materials from the stomach to the mouth. Enhanced breath support also facilitates stronger cough reflex (improving airway protection). If drooling is present, enhancing upright posture can mitigate this dysfunction. There is only a minute amount of published material discussing improving symptoms of Parkinson's disease with a Pilates approach and no publications in peer-reviewed journals. There have been a handful of peer-reviewed articles regarding the benefits of Pilates interventions on gait and balance in the general population. Further study into the efficacy of this treatment approach for Parkinson's-related deficits in all rehab disciplines is merited.

P28.04

In the Clinic, in education and in the Community: A capacity building strategy for comprehensive supportive services and wellness programs through community partnership

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Background: In 2007, the NYU Langone Medical Center's Parkinson and Movement Disorders Center (NYULMC-PMDC) embarked upon an experimental pilot program with the Jewish Community Center in Manhattan (JCC) to develop Parkinson's-specific wellness programs for those impacted by Parkinson's. Six years later, this pilot program has evolved into the award-winning Edmond J. Safra Parkinson's Wellness Program (EJSPWP) and become a national model for innovative community-based Parkinson's care.

Aims: The EJSPWP is a welcoming hub for the regional Parkinson's community and remains in high demand. With a focus on dignity, hope, respect and possibility, the program offers fitness classes, support groups and educational and socialization events for patients, caregivers and loved ones. A range of PD-specific fitness classes with varying curriculum impacts include: Alexander Technique; Chair Exercise; Rhythm and Functional Movement; Water Exercise; Tai Chi/Qi Gong; Nia: Movement and Music; Chair Exercise; PD Bootcamp; and Yoga. Psycho-educational Support Groups for Patients and for Caregivers are facilitated by licensed social workers and monthly education, socialization and creative expression events are provided.

Methods: The EJSPWP has become the dynamic cornerstone of the NYULMC-PMDC's unique and innovative Supportive Services Program (SSP). The SSP has further developed to build much needed capacity through partnership in education, in the clinic and in the community to meet the needs of patients, caregivers and families. The SSP's mission is this: 1) To keep our patients, caregivers and families active, educated, empowered and connected in an effort to achieve the highest possible quality of life throughout the disease spectrum and continuum of care; 2) To build a replicable model of supportive and wellness care and; 3) To provide support for our medical, scientific, and healthcare professionals team. Integrated, on-site clinical social work services, including psychotherapy, supportive counseling, education, resource referral and limited case management for advanced patients are provided to families within the clinic. Support Group and professional education delivery is provided in collaborative partnership with the Hebrew Home at Riverdale's Geriatric Care Management Program to build the network of PD trained supportive service providers. And the SSP has developed a nationally unique Social Work Educational Initiative to train the next generation of PD supportive care leaders in collaborative partnership with the NYU Silver School of Social Work.

Results: The SSP is popular with patients and with providers, as it provides a range of proactive and empowering supportive care options that complement medical care. The supportive and wellness program partnership model has expanded our capacity to provide services, increased access to care and extended the boundaries of clinical dialogue into the community. The trust relationships that are built with patients, families and providers in the community and in the clinic are allowing us greater ability to communicate and coordinate effectively as we partner in transitions related to disease progression and medical to community transfer.

Discussion: This poster will demonstrate in graphics and narrative the growth, development and vision of this innovative, replicable and popular supportive services and wellness program model.

P28.05

Aerobic exercise training improves health and the acquisition of new motor skills in early Parkinson's disease.

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Objective: Aerobic exercise training (AET) has been shown to have many health benefits in individuals with Parkinson's disease (PD), including improvement in previously automatized motor skills (i.e., locomotion). Yet, it is unknown whether AET can also facilitate the acquisition of *new* motor skills in PD. To this end, we assessed the

effects of 3-month AET on learning of a *new* motor sequence, as well as on different health-related indicators (i.e., functional capacity, cognitive functioning, cardiorespiratory fitness, and quality of life).

Methods: Twenty-five individuals (14 healthy, 11 early PD) participated in a supervised stationary recumbent bike training program (3 times/week; 12 weeks). Exercise prescription started at 20 minutes high intensity training based on participant's maximal volume of oxygen uptake (VO_2 peak or estimate). This duration was increased by 5 minutes every week until it reached a total of 40 minutes. Participants' ability to learn a new motor sequence was assessed using a bimanual version of a sequence learning task before and after AET. Functional capacity, cognitive functioning and cardiorespiratory fitness were also assessed in both groups, while severity of PD symptoms and quality of life were evaluated in the PD group only.

Results: Cardiorespiratory fitness improved significantly in all participants indicating that the AET program was effective. Moreover, the ability to learn a new motor sequence increased significantly in both groups as a result of training. Cognitive functioning improved in elderly individuals, but only marginal gains were observed in their PD counterparts. UPDRS scores were reduced in 6 out of 11 individuals with PD, whereas a significant reduction of social stigma (quality of life indicator) was recorded after training in PD patients. Our results suggest that AET can be a valuable non-pharmacological intervention to promote fitness and wellness in early PD, and that it helps them to acquire new motor skilled behaviours.

P28.06

Community Wellness for people with Parkinson's

Annette Edwards

Banner Neuro Wellness, Gilbert, AZ, USA

Background: Studies continue to show evidence that specialized exercise and stimulating activity in conjunction with medical treatment slows the disease progression and increases quality of life. Up until now, individuals with Parkinson's disease have few if any resources to receive specialized disease specific support.

Banner Neuro Wellness was developed to bridge the gap between gains made during formal medical treatment and therapies into sustainable results that enhance wellness through activities and socialization in a supportive community setting. This approach promotes quality of life and maintains function.

Aim/Objective: The objective of Banner Neuro Wellness is to provide an environment that empowers people with Parkinson's to stay engaged and active members of society. The Parkinson's specific exercise programs and activities aim to promote quality of life and maintain function. Through this highly specialized program, individuals have a place to meet their physical, social, and emotional needs. Banner Neuro Wellness helps individuals to stay active members of the community.

Method: Banner Neuro Wellness provides PWR! exercise, fitness training, yoga, Tai Chi, speaking groups, art, support groups and special interest classes to its members weekly. Members are encouraged to attend 2 to 3 PWR! exercise classes per week and at least one special interest class. The community based center allows the individual with Parkinson's an avenue to engage in multiple exercise and wellness activities weekly.

Results: Banner Neuro Wellness meets the need of the Parkinson's community by facilitating physical activity and stimulating activities in a positive wellness environment. Membership has grown to over 100 members in a year and offers over 30 classes per week. Members report their ability to maintain function with fewer falls and a higher quality of life.

P28.07

Nutritional status correlates with non-motor and motor symptoms of Parkinson's disease: A cross-sectional analysis in 143 patients

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Objective: Nutritional status has attracted less research attention than it should be in Parkinson's disease (PD). Numerous features of PD including motor and non-motor (NMS) symptoms could make the patients susceptible to malnutrition, and nutritional impairment may itself exert a significant influence on PD complications to make a vicious cycle. The aim of this study was to evaluate the relationship between nutritional status and severity of the NMSs and motor symptoms in PD patients.

Methods: This cross-sectional study was performed in a referral movement disorder clinic in Tehran, Iran during 2011-2012. A total number of 143 PD (96 males and 47 females) patients with the mean age of 61.4 (SD=10.5) yr were recruited in this study. Mini-Nutritional Assessment (MNA), Hospital Anxiety & Depression Scale (HADS), Fatigue Severity Scale (FSS), PDQ-39 and Hoehn & Yahr and Schwab & England score of disability were filled up in PD patients.

Results: Univariate Pearson correlation showed that depression score was the strongest symptom to associate with MNA score ($r=-.596$, $P<.001$). More severe anxiety ($P=.023$), depression ($P<.001$) and fatigue ($P=.006$) were observed in cases at risk of malnutrition. Multiple regression showed that communication ($Beta=-.271$, $P=.001$) and bodily discomfort ($Beta=-.208$, $P=.003$) domains of PDQ-39, depression ($Beta=-.251$, $P=.003$) and Schwab & England score ($Beta=.233$, $P=.001$) were independently associated with MNA score.

Conclusions: Negative association was found between NMS's especially depression suggesting that nutritional status needs to be more highlighted in PD care. Even more interestingly, NMS's were more correlated with nutrition than motor symptoms, which must be taken into account in further causality evaluations.

P28.08

Tai Chi, Zumba, drumming and golf: An integrative approach to promote PD wellness

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Objective: There are increasing reports in both the professional and lay press supporting the role of exercise on the health and wellbeing of patients with Parkinson's disease. Many patients actively seek treatments "beyond the pill box", searching for therapeutic activities focused on positive health initiatives. Over the past 3 years, at our National Parkinson's Foundation Center of Excellence, we have fully integrated 4 different exercise programs into a Wellness Program. We describe these specialized programs: Tai Chi, Zumba, Drumming and Golf. Videos support the rationale for the Tai Chi and Zumba programs and capture the enthusiasm of the participants. Program challenges and future directions are presented.

Methods: Introduce and integrate 4 wellness programs into a hospital-based clinical program for PD patients. Posters and flyers to market the programs emphasize the health and social benefits of participation in these programs. Classes are carefully designed for patients with relatively recent diagnoses who have mild symptoms. Yearly patient surveys guide the programs which we offer. Members of our interdisciplinary team routinely generate patient referrals to our programs. Education and training concerning Parkinson's disease is provided to instructors so they can modify classes to meet the needs of participants. Ongoing feedback from participants is elicited from the instructors so that classes can be "tweaked" as needed. Partners of patients are invited to participate to enhance social aspects of the program.

Results: To date, over 200 participants have enrolled in exercise classes. Our success depends on the training and skills of our instructors, the appropriate selection of participants and the full support from the team. Patients uniformly report improved wellbeing while participating in these programs. We are currently planning formal research projects to quantify the benefits to our patients.

P28.09

A continuous care model: education to rehabilitation to wellness.

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¹Southeast Alabama Medical Center, Dothan, AL, USA

²The University of Alabama at Birmingham, Birmingham, AL, USA

Objectives: The goals of the Southeast Alabama Medical Center health and wellness program include: 1) to provide a comprehensive education, rehabilitation and wellness for people with Parkinson's through experienced staff, 2) to provide the framework for a replicable program that ensures known outcomes and 3) to provide a sense of community and services previously unavailable for PWP and their families.

Methods: SAMC provides access to high quality educational, rehabilitation and wellness opportunities in one facility in a rural community. All program staff were identified to have an interest in treating PWP and have participated in additional professional training to more effectively work with PWP. The program began in January 2013. A program participant initiates the program with a 2 hour initial evaluation comprised of education and needs assessment. The participant transitions to any combination of physical, occupational and speech therapy. Once rehabilitation is completed, the participant has the opportunity to join a structured wellness program. Systematic data is collected at the initial 2 hour visit, completion of rehabilitation and every 6 months in the wellness program. The program creates a sense of community by providing regular digital newsletters, assists the local Parkinson's support group and organizes social events. SAMC receives guidance and assistance from SAMC Foundation, University of Alabama at Birmingham – Department of Neurology, APDA – Birmingham, Parkinson's Association of Alabama and Lakeshore Foundation.

Results: To date 33 people with Parkinson's have entered the program. 19 PWP have completed rehabilitation demonstrating improvements in functional mobility, ADLs, balance, physical activity levels and quality of life measures. 14 PWP have initiated the post-rehab wellness program and participate in aquatic, walking, balance and cardio/strengthening classes. All wellness classes are instructed and supervised by an exercise specialist(s) with specialized training to work with PWP.

P28.10

Evaluation of a rhythmic exercise program for patients with Parkinson's disease

Audun Myskja

Objective: To evaluate a structured training program using a series of rhythmic exercises for a group of patients with Parkinson's disease (PD).

Background: There is increasing interest in the potential benefit of systematic exercise in the management of PD. However, there is still insufficient knowledge about what type of exercise may be most beneficial, for which symptoms, and how exercise programs may be best applied to aid PD patients.

Methods: PD patients (n=20) were recruited in a Norwegian region, with patients on waiting list as controls. The group followed a structured program with rhythmic exercises once a week, led by physiotherapist. The mean age was 62.4 (SD 7.3) years and the mean disease duration was 8 (SD 5.2) years. Participants were evaluated by UPDRS, Hoehn & Yahr, Senior Fitness, Up and go before project start, at 6, 12 and 18 months. Quality of life issues were evaluated by interactive qualitative interviews, Montgomery-Aasberg depression rating scale and Herth Hope Index before project start, at 6, 12 and 18 months.

Results: Functional tests showed stability in the exercise group compared to control group (findings will be discussed in the presentation). Quality of life measures showed low values for depression compared to control group and emphasized the value of group training and the importance of collaboration with participants responses. Interview data suggest a higher rate of follow-up on home training would further improve results.

Conclusions: Our data suggest benefit of a rhythmic exercise program developed in collaboration with participants, effects becoming more marked over time. Further research to specify benefits of structured exercise is recommended.

P28.11

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Conclusions: Our data suggest benefit of a rhythmic exercise program developed in collaboration with participants, effects becoming more marked over time. Further research to specify benefits of structured exercise is recommended.

P28.12

Improving nutritional status in Parkinson's disease and the effects on Parkinson's disease symptoms

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Objective: People with Parkinson's disease (PD) are at an increased risk of protein-energy malnutrition (PEM). Increasing energy and protein intake is a useful strategy in PEM. However, protein intake in PD may interfere with dopaminergic medication absorption and increase "off" times. The aim was to assess the effect of a high protein-high energy (HEHP) nutrition intervention for PEM on nutritional status and Parkinson's disease symptoms.

Methods: Nineteen people with Parkinson's disease at risk of malnutrition or malnourished participated in a randomised controlled nutrition intervention. The participants were treated as one group for data analysis. Participants recorded dietary intake using photographic 3-day food diaries at 3 time points. Nutrient analysis was completed using Foodworks (2009, v6). PD symptoms, freezing of gait and "off" times were assessed using the UPDRS assessment, Freezing of Gait Questionnaire (FOG-Q) and a 3-day on/off diary, respectively. Objective movement assessments included the Timed Up and Go (TUG) and finger tap count in 30 seconds. The Beck Depression Inventory (BDI) recorded depressive symptoms.

Results: Energy intake ranged from 54.9-237.4kJ/kg and protein intake from 0.4-2.9g/kg at baseline and increased by up to 83.1kJ/kg and 2.9g/kg, respectively. Median weight gain was 2.2% of starting body weight. Increased protein intake was associated with decreased freezing of gait ($r_s = -.325$, $p = .014$) and fewer depressive symptoms ($r_s = -.304$, $p = .022$). Linear mixed models analysis resulted in no effects of protein on UPDRS score or "off" times. TUG times and finger taps did not significantly change. The use of a HEHP nutrition intervention resulted in improved intake and nutritional status in this group of malnourished/at-risk people with Parkinson's disease. There was no reported effect on Parkinson's disease movement symptoms, and there may potentially be a beneficial effect on gait and depression.

P28.13

Exercise has sustained benefit for Quality of Life in Parkinson's disease

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¹Northwestern University, Chicago, IL, USA

²University of Florida Jacksonville, Jacksonville, FL, USA

Objective: To explore the effects of physical activity on disease related quality of life (QoL) in Parkinson's disease (PD).

Background: There is emerging but still limited data on the impact of exercise on PD progression.

Methods: Data was obtained from the National Parkinson Foundation (NPF) Quality Improvement Initiative database. Dataset includes demographics, disease severity, exercise program, health care utilization, and PD quality of life (PDQ-39).

Results: 2605 PD participants who had data on exercise use and at least two annual visits were included in the analysis. The median exercise at the first visit was 2 hours per week [0, 40], (0, 4) [min, max] (25th, 75th). Subjects were divided into three groups: no exercise (NE) (n=881, 34%), casual exercise (CE) (0.2-2hours/week, n=528, 20%), and regular exercise (RE) (≥ 2.5 hours/week, n=1196, 46%). Factors associated with regular exercise included better total PDQ-39 (OR per 5 unit increase 0.93, $p < 0.001$), lower BMI (OR=0.95, $p = 0.002$), less comorbid disorders (OR=1.69, $p = 0.033$). At the subsequent visit, 639 (25%) of patients increased activity levels, (214 NE became CE; 218 NE became RE; and 207 CE became RE), whereas 479 (18%) decreased exercise levels (129 CE became NE; 216 RE became CE; 134 RE became NE), (p for symmetry < 0.001) After adjusting for age, sex, duration, Hoehn & Yahr > 3 , and baseline PDQ-39 total, regular exercise at both visits correlated with the lower PDQ-39 (mean difference from non-exercisers -3.4, $p = 0.03$) at follow-up.

Conclusion: Regular but not casual exercise is associated with improved and sustained PD QOL. This data provides a strong rationale to encourage regular physical activity and explore factors that enforce sustained exercise in PD patients.

P28.14

Benefits of a community based whole body voice strengthening program for persons with Parkinson's

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²Parkinson Place, Sarasota, FL, USA

Objective: To evaluate benefit from a weekly class which couples vocal function exercises with movement. A mixed design study was developed to determine which components of the intervention were perceived to yield benefit (i.e. socialization and weekly contact with the instructor and class members or specific content of the program or both). Improvement in voice use and overall communication, and independent home practice were outcome measures. Qualitative and quantitative data were collected.

Methods: Voice Aerobics™, a whole body voice strengthening program, led by a speech-language pathologist was offered weekly at a community based Parkinson center. Participants included persons without prior speech/voice therapy, and those who had completed speech therapy, with LSVT® most commonly reported. A recorded version of the class was also available for independent home use. Pre and post class surveys were administered, and included a voice self-rating scale.

Results: Final results will be reported at the WPC, as surveys are still being completed. Surveys reviewed thus far indicate: age range between 65-86 years, average time since diagnosis of Parkinson's is 5 years, and an equal number of women and men responding to the survey. 60 % reported no prior speech therapy, and 40% reported speech therapy within the last 1-2 years, most often reported was LSVT®. Most participants, including those who had speech therapy, self-rated speech clarity pre-class participation 1 (poor) - 2. Those with the lowest pre-class scores continued to self-rate low on post class surveys, but with an improvement shift of at least 1 point. Approximately 25% of class participants report using a recorded version of the class independently at home for guided practice.

P28.15**Multi-year observational study of community-based exercise for individuals with Parkinson disease**¹Rebecca States, ¹Anayo Ikeme, ²Yasser Salem, ¹David Spierer¹Long Island University Brooklyn, Brooklyn, NY, USA²University of North Texas Health Science Center, Fort Worth, TX, USA

Objective: Community-based group physical activity has immediate functional benefits for people with Parkinson's disease (PD). Evidence on long-term effectiveness is limited however, especially for programs that allow participants to attend selectively and don't individually track and progress exercise protocols. The purpose of this study was to document changes in physical function for people with PD who participated in such a community-based group exercise program over several years.

Methods: Thirty-one people with mild to moderate PD (Hoehn and Yahr stages I to III) participated for up to 4 years. Participants attended an ongoing series of 1-hour exercise classes (2 times/week x 10 weeks/session x 3 sessions/year) which included resistance training for 12 muscle groups, floor exercises for aerobics, core strengthening, stretching, and balance. Physical function via gait speed, Six Minute Walk (6MW), Timed Up and Go (TUG), Berg Balance Scale (BBS), grip strength, chair stand, and Single Leg Balance (SLBal) was evaluated before and after the initial 10-week series and annually.

Results: High rates of participation were seen throughout, ranging from 90% at year 1 to 62% at year 4. Significant improvements were seen for 6MW and chair stand ($p < .05$) after the initial 10-week session, and for BBS and grip strength after one year. The only significant declines throughout the four years were for SLBal after year 2. All change scores remained within the minimum detectable change threshold.

Conclusion: Results suggest that long-term participation in community-based exercise is feasible, can keep the interest of individuals with PD over long periods, and assists in maintaining initial levels for most aspects of physical function. These findings suggest that a community-based group exercise program can be beneficial for people with PD, and may provide a valuable adjunct to traditional rehabilitation programs at relatively low cost.

P28.16**Effects of resistance training on bradykinesia, functional performance and disease severity in individuals with Parkinson's disease**Ariel Vieira¹, Samuel Vidal¹, Grassyara Tolentino¹, Lorena Resende¹, Ricardo Jacó de Oliveira¹¹University of Brasília, Brasília, Brazil

Objective: Explore changes in the bradykinesia, disease severity and functional performance following the completion of a 9-week program of resistance training in individuals with mild-moderate level of involvement of Parkinson disease (PD).

Methods: Were evaluated 27 individuals with PD (Hoehn e Yahr scale between 1-3) before and after 9 weeks: 3 weeks of familiarization with light loads exercises and 6 weeks of training with progression of loads. The intervention consisted on 5 exercises for upper and lower limbs with 2 sets of 10 to 12 repetitions. To explore the objectives were evaluated clinical assessment of bradykinesia by gait speed, using the Ten Meters Walk Test (TMW) and by dynamic balance, using the Timed Up and Go Test (TUG). Section III of the UPDRS was applied covering bradykinesia and disease severity. The functional performance was assessed by TMW, TUG and functional strength tests – 30 seconds Chair-Stand Test (T30). To compare the pre and post intervention was performed Paired-

Samples T-Test for variables pread TUG, TWM and UPDRS III; for the T30 used the Wilcoxon Test. The level of significance was $p \leq 0.05$.

Results: The results indicate a decrease in TUG scores ($p = 0.001$) and TMW ($p = 0.001$). The same behavior was observed in the results of the motor examination - UPDRS III ($p = 0.019$). The T30 obtained an increase of score ($p = 0.001$). These results suggest that resistance training show be considered positive in clinical bradykinesia, verified into increased functionality and reduced disease severity scores.

P28.17**Development of a community-based Nordic walking program for persons with Parkinson's disease**Maria Walde-Douglas¹¹Struthers Parkinson's Center, Minneapolis, MN, USA

Objective: To outline a framework of a community-based Nordic Walking program for persons with Parkinson's disease (PD). Research has shown the benefits of Nordic walking in individuals with PD. Organized Nordic walking groups with trained leaders are an effective way to implement community programs to improve mobility, gait and conditioning in the Parkinson's population.

Methods: An individual with PD sought out a Nordic walking instructor to lead community walks for persons with PD. This led to collaboration with a physical therapist specializing in PD to develop a program to train others to lead community Nordic walking groups for people with PD. A comprehensive 4 hour training curriculum was developed with the following components: basic Nordic walking technique and use of poles, group safety and education on the effect of PD on balance and gait. Practice sessions were carried out with instructor feedback.

Results: Eleven persons completed the training curriculum. Following completion of the training, PD Nordic walking groups were formed at area parks and indoors at a shopping mall during the winter months. Average attendance was 10-12 people stages I-III PD. Participants reported enjoyment of the activity, reduced fear of falling, improved posture and ability to walk with less pain and fatigue using the poles. Four individuals involved in the original group leader training went on to complete an official Nordic Walking instructor training. A community-based PD Nordic walking program offers a practical approach to an evidence-based form of exercise. Education on Nordic walking and PD offer a "train the trainer" approach to the development of qualified individuals to lead community groups. This offers the opportunity to expand programming to other communities and locations resulting in improved physical abilities and quality of life for persons in the PD

CARE DELIVERY & QUALITY OF LIFE: ALTERNATIVE & COMPLEMENTARY THERAPIES/ CREATIVITY

P29.01**Generating Rhythm: Music Therapy in Parkinson's Care**Amy Clements-Cortes¹¹ Wilfrid Laurier University, University of Windsor, Baycrest, Canada

Objective: To provide participants with an overview of music therapy treatment in the care of Parkinson's disease.

Method: This presentation will describe music therapy interventions and techniques in the care and treatment of Parkinson's disease,

highlighting Neurologic Music Therapy, songwriting and improvisation. Case studies of music therapy clinical work will illuminate the efficacy of music therapy in holistic, alternative and complimentary therapy interventions. Strategies for Parkinson's patients using music at home will also be presented.

Results: The use of music therapy as an alternative therapy is proven in several areas of need and concern in the care of Parkinson's including: rhythm and gait, rhythm and speech, entrainment, and rhythm and dyskinesia. Specific aspects of neurological music therapy will show the results of music therapy in the areas of sensorimotor, speech and language and cognitive training. Music therapy has also been established to assist with additional symptoms related to Parkinson's such as anxiety, depression, isolation, self-esteem and sleep assistance.

P29.02

Long-term effectiveness of Alexander Technique (AT) in managing motor symptoms of Young Onset Parkinson's disease (PD)

Candace Cox¹

¹Big Sky Alexander Technique Studio, Castleton, ON, Canada

Objective: To look at the long-term effectiveness of regular AT lessons in combination with medication therapy.

Methods: The patient in this case study was diagnosed with PD in 2003, at which point she already suffered from chronic stooped & painful posture; knee pain presented in 2005. Standard rehabilitation therapies yielded no improvement. Cumulative damage in the left knee due to severe tremor prompted knee replacement surgery in November 2008. Alexander Technique is an educational, empirical treatment developed to change functional patterns. Our focus was restoring normalcy to external functions. Lessons involved discussion and hands-on guidance to facilitate a mental and physical ability to access stability, and to improve static and dynamic balance. From May 2009 through June 2011, the student received weekly or twice-weekly 45-minute AT lessons. From July, 2011 through March, 2013 she received intensive groupings of 4 – 6 lessons every 8 – 12 weeks.

Results: A greater range and control of motion resulted, which facilitated a re-learning of daily activities. The orthopaedic surgeon who performed the knee-replacement surgery observed that the subject was his only patient (including non-PD patients) to recover full movement without a limp within a year. 7.5 years after diagnosis and 2 years after knee surgery, the subject was rated 56/56 on the Berg Balance Scale. Since AT treatment, TUG (Timed-up-and-go) score and UPDRS Subscale III (Motor Examination) rating continue to decrease. Only 2 minor adjustments in medication were made since 2007. Subject reports: improved posture far beyond pre-PD state; immediate recovery from semi-freeze; ability to walk normally even in the midst of severe tremor; improved singing voice; ongoing ability to travel and live with reasonable normalcy; hope.

P29.03

Yoga for Parkinson's disease: a competency-based course for yoga teachers

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²LIM Yoga for Parkinson's and other Movement Disorders,

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⁴Department of Neurology, Boston University Medical Campus, Boston, MA, USA

⁵TriYoga of Boston, Waltham, MA, USA

Objective: To describe a competency-based yoga training course where a collaborative model is used. Healthcare professionals with

expertise in PD and yoga teacher trainers provide educational training to yoga teachers about the symptoms and needs of people with PD, as well as specific yoga postures and practices that best address the symptoms of PD. The 5-day program provides attendees the opportunity to gain proficiency in the practices and gain the confidence and expertise needed to start providing yoga classes to meet the needs of students with PD.

Methods: This 5 day course evolved from one and two day workshops that were previously piloted. The shorter courses lacked the depth of information for this curriculum and did not include assessment of the participants or certification. In this course, Clinical Nurse Specialists practicing in neurology and psychiatry presented an overview of the unique motor and non-motor features of PD and the role of yoga in depression and anxiety. A physical therapist presented an overview of how these features relate to gait and balance limitations in people with PD and safety concerns related to mobility and fall risk. In addition, target areas for stretching and strengthening exercises unique to this population were highlighted. Yoga faculty presented research and practices on yoga techniques including breathing, meditation, chanting, and mantra. Participants had the opportunity to present different types of classes with input and feedback from course instructors and were assessed at the conclusion of the course. Post program evaluations were completed by participants.

Results: Seventeen participants demonstrated proficiency and received certification in this competency-based course. Additional yoga teachers have been trained in three one-day workshops, and one two-day workshop. A total of sixty yoga teachers from the USA have been trained to lead yoga classes for students with PD.

P29.04

Comparative biomechanics from ice skating and regular terrain locomotion amongst people living with Parkinson disease

Jon Doan¹, Natalie de Bruin², Patrick Bartoszyk¹, Mike Amatto¹, Kevin McLarty¹, Lesley Brown²

¹Engineering and Human Performance Lab, University of Lethbridge, Lethbridge, AB Canada

²Balance Research Lab, University of Lethbridge, Lethbridge, AB Canada

Objective: Recent research suggests that non-traditional exercises may be highly effective in the management of Parkinson disease (PD) symptoms, encouraging PD patients with stimulating activities at greater rates and regularity. The purpose of this project was to compare kinematics and muscle activities in ice skating and standard gait amongst people living with PD, with the long-term goal of developing the paradoxically persistent skill of ice skating into an exercise neurotherapy for PD.

Methods: Seven mild to moderate PD patients and seven matched control subjects completed fourteen trials of walking and ten trials of ice skating, each 12 m in length at self-selected rate. Trials were captured in sagittal plane video, and muscle activation in lower extremity agonists and antagonists was collected through electromyography. The central 4 m of walking and skating trials were hand-digitized, providing Cartesian coordinate data for critical anatomical landmarks in each video frame. Three kinematic parameters were compared between groups (PD, CTRL) and conditions (PRE-WALK, SKATE, POST-WALK): a) arm swing – maximum resultant distance between hip and hand; b) step length – maximum resultant distance between left and right heels; and c) trunk inclination – average angle between trunk and vertical. Mean muscle activation ratios (SKATE:POST-WALK) from the tibialis anterior, gastrocnemius, vastus lateralis, and biceps femoris muscles of the right leg were also compared between groups.

Results: For the 5 PD participants with full EMG data, SKATE:WALK activation ratios exceeded 1.5 for all muscles, and

those ratios were significantly increased compared to CTRL subjects for TA and VL. PD had increased arm swing, greater step length, and smaller trunk inclination during skating trials compared to pre-walking trials. Post-walking was also improved compared to pre-walking, suggesting short-term benefit from skating exercise. Control participants also changed performance in the skating trials. No PD patients fell in the course of the skating trials.

P29.05

Developing a collaboration in music therapy and physiotherapy for older adults with Parkinson's disease: A pilot project

Hélène Gaudreau¹, Annie Bélanger¹

¹Grace Dart Extended Care Centre, Montreal, QC, Canada

Objective: This research pilot project presents a collaborative approach between music therapy and physiotherapy with a group of older adults with Parkinson's disease and (or) dementia. The main goal of this project was to examine the benefits of such collaboration for the residents in order to prepare for an intervention research. Studies have shown the positive effects of physiotherapy on patients with Parkinson's disease (Keus, 2007; Morris, 2000). Music therapy also has been proven an effective approach to help people with this diagnosis (Tomaino, 2002, 2011). No extensive research on a collaborative approach of these two fields has been found.

Methods: This collaborative inquiry was initiated by the physiotherapy program. The music therapist was invited to join in an already existing exercise group conducted by the physical rehabilitation therapist at Grace Dart Extended Care Centre in Montreal. This group consists of sixteen (male and female) subjects, all residents of the centre. Sessions are being held once a week. The pilot project was conducted during 20 sessions and allowed the music therapist and physiotherapist to gather observations on patients' improvements. These will be measured in phase 2: the intervention research.

Results: The initial phase, the pilot project, showed several positive effects on the participants. Observations were made in three important areas: participation, communication and motor abilities. Residents started to arrive earlier at their session, passive participants started to be more engaged and various expressions of happiness and pride were demonstrated on many occasions. Furthermore, manipulation of small instruments and singing seemed to diminish tremor. According to these observations and the literature, the anticipated results of an intervention research program would benefit the residents of this group in the areas of motor abilities (control, coordination) and communication abilities (breathing, pronunciation). Therefore, the next phase will be to continue developing the program through the creation of evaluation tools and the development of a therapeutic intervention plan. The data collected during the pilot project and the evaluation tools will be presented.

P29.06

Neurologic music therapy interventions: a whole picture approach for people with Parkinson's disease

Sandra Holten¹

¹Struthers Parkinson's Center, Golden Valley, MN, USA

Objective: A songwriting process with 8 members of a therapeutic adult day program diagnosed with Parkinson's disease and related movement disorders is chronicled.

Background: Neurologic Music Therapy (NMT) is the therapeutic application of music to cognitive, sensory and motor dysfunction due

to neurologic disease. NMT treatment techniques are research-based and directed towards functional therapeutic goals. Standardized Therapeutic Music Interventions are adaptable to the patient's needs. NMT techniques for sensorimotor dysfunction have been well researched and provide the underpinnings of the application of NMT techniques to Parkinson's disease.

Methods: This poster focuses on the use of NMT techniques beyond the sensorimotor domain with which they are more commonly associated. At Struthers Parkinson's Center, music therapy is an integral part of the therapeutic adult day program, Club CREATE. Over the course of 7 weeks, a group of 8 clients in Club CREATE participated in Neurologic Music Therapy Interventions that included music improvisation, vocal intonation therapy, rhythmic speech cuing, musical attention control training and songwriting. Although the song, "Our Fight" was a final product from the process, the process itself addressed numerous domains of functioning and provided a creative outlet for self expression and improved connection with each other. Clients described ways this had an impact on their coming to terms with Parkinson's.

Results: Although the song, "Our Fight" was a final product from the process, the process itself addressed numerous domains of functioning and provided a creative outlet for self expression and improved connection with each other. They described ways that this had an impact on coming to terms with Parkinson's. Staff and carepartners noted these outcomes as well. These results will be depicted in narrative description of series process, pictures and comment samples from clients.

P29.07

An arts & movement program designed to link exercise, creativity and social interaction

Renee Le Verrier¹, Jane Arsham², Michael S. Kleinman³, Cathi A. Thomas³, Marie Saint-Hilaire³

¹LIM Yoga, Newburyport, MA, USA

²Moving Easy Tai Chi, Arlington, MA, USA

³Boston University Medical Campus, Boston, MA, USA

Objective: Exercise reduces severity of symptoms and increases a sense of wellbeing in people with PD. In addition individuals with PD can experience an increase in creativity, most likely related to the use of dopaminergic medications. Research shows that loneliness in the general population of older patients hastens a decline in motor function. Patients with PD often identify a reduction in socializing. Evidence demonstrates that increased social interaction has a high impact on a person's quality of life. People living with Parkinson's disease should be provided opportunities to experience creative and exercise-based therapies in a socially supportive environment.

Methods: The Art's and Movement Program is a two night retreat with two full days of workshops. An alternative one day program can also be implemented. Facilitators with expertise in a number of specialties lead interactive workshops that encourage and focus on ability. The rotating schedule ensures that participants experience each subject area in a small-group setting. Workshop topics include activities that have been shown to be beneficial for persons with PD including: creative writing, music, storytelling, visual arts, dance, tai chi, and yoga.

Results: 110 participants have attended one of three Arts and Movement Programs. Participants expressed overwhelming satisfaction in a post program survey. An outline of the details of the Arts & Movement Program has been developed to allow other communities to set up similar interventions that tailor sessions specifically designed for people living with PD.

P29.08

Providing instruction of Reiki first degree as a complementary therapy to help improve the lives of those living with Parkinson's diseaseKarl Robb¹ Angela Robb²¹Person with Parkinson's disease & Reiki Master, GiveReiki.com, US²PD Carepartner & Reiki Master, GiveReiki.com, USA

Objective: To instruct and educate the Parkinson's disease community about how the teaching of Reiki (RAY-KEY) first degree as a complementary therapy to people with Parkinson's disease can be beneficial to their self-care. To give those living with PD another tool to reduce stress, increase relaxation, and provide mental & physical calmness. Reiki is a non-invasive therapy that uses light touch to increase and enhance one's personal energy. Reiki first degree instruction focuses on self-care, a self-treatment protocol, and seated chair protocol to give Reiki to another person.

Methods: The workshop is a twelve hour workshop in Reiki first degree. The current workshop held in six two-hour sessions, allowing the person with Parkinson's time to absorb the material. The workshop includes instruction in Mindfulness Meditation, Energy anatomy, Qigong, and Reiki self treatment & seated chair protocols. The workshop highlights the importance of the person with PD to take care of themselves on a daily basis. Examples of how Reiki can be incorporated into daily life are presented.

Results: People with PD will be able to treat themselves with Reiki and have a general understanding of Reiki which can be used to enhance and complement their current self-care strategies. Workshop participants will be able to use Reiki to increase one's relaxation, reduce stress, and enhance the body's own healing properties. Previous students who attended the workshop reported: "I always feel relaxed and hopeful after attending the class" and "I felt like I was walking away with a treasure, suited to my particular needs".

P29.09

Incorporating community based artists into an established Parkinson's disease care program at a National Parkinson Foundation Center of ExcellenceRose Wichmann¹, Sandra Holten¹¹Struthers Parkinson's Center, Golden Valley, MN

Objective: To maximize quality of life for people with Parkinson's through creative arts programs in collaboration with community artists. Research has shown that creative activities such as music, dance, painting, and theater can improve feelings of well being for young and old alike. People with Parkinson's (PD) have compromised physical/cognitive skills, interfering with participation in creative arts programs. Since 1995, Struthers Parkinson's Center (SPC) CREATE program has collaborated with community artists to design programs for people living with PD.

Methods: Weekly programs include nature based therapies (with University of MN Landscape Arboretum), music (utilizing a neurologic music therapy fellow), dance programs (with nationally recognized Kairos Dance Theatre), visual arts (with Artsy Smartsy, offering programs to seniors/people with disabilities), dramatics (with CLIMB Theatre), and SPC "Arts Café" (featuring interaction with community artists on a monthly basis.) Funding has been obtained through the Metropolitan Regional Arts Council, MN State Arts Board, and Park Nicollet Foundation.

Results: Weekly arts programs at SPC average 15 participants in each group. The average monthly Arts Café attendance has grown from 9 to 25. Participants report benefits including increased energy, feelings of joy, opportunities for self exploration, improved creativity,

and pride in accomplishments, deeper social connections, physical exercise, relaxation, and reduced stress. Community artists report greater awareness of PD, heightened sensitivity to the needs of those with physical/cognitive challenges, and improved comfort levels in communicating /interacting with PD clients. Involvement in creative arts provides opportunities for improving mobility, mood, and communication for individuals with PD. Engaging community artists in collaborative relationships with PD programs offers unique opportunities to access artists' talents and abilities, encourages those with physical and cognitive deficits to explore new avenues of self expression, and contributes to quality of life.

P29.10

Combination treatment of Osteopath and Chinese deep tissue massage improve Parkinson disease

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Objective: Improve parkinson disease patient's bodily functions.

Methods: Record the symptoms of each control PD patient's major claims of abnormal bodily functions by words and video. Design some behaviors to present the abnormal bodily functions of each patient for each major claim. Observe and analysis control PD patient's skeleton structure problem, give relative deep tissue massage and osteopath treatment to the control patient. Compare the skeleton structure before and after the treatment; Compare the designed behaviors the control patient can finish by video and words before and after each treatment.

Results: Combination treatment of Osteopath and Chinese deep tissue massage can comprehensively improve Parkinson disease. Some control patients can obtain a great progress.

P29.11

School "Health" in the lives of patients with Parkinson's diseaseIrina Zhukova¹, Maria Nikitina¹, Olga Izhboldina¹, Natalya Zhukova¹, Valentina Alifirova¹, Anna Agasheva², Alexey Povalyaev³, Marina Titova¹¹Department of neurology and neurosurgery, Siberian State Medical University, Tomsk, Russia²Hospital N° 2, Tomsk, Russia³State Medical and Social Examination Service, Tomsk, Russia

Objective: Show the importance of continuing medical rehabilitation in outpatients with Parkinson's disease (PD) from the perspective of impact on life quality and severity of affective disorders.

Methods and materials: 68 patients with PD (28 males, 40 females) were included. The average age was 64.3±8.2. The average stage for the Hoehn & Yahr scale was 2.6±0.8. All patients were divided into two groups (homogeneous by sex, age, stage of PD): I- 33, engaged in the school of rehabilitation "Health" regularly, II- 34, who didn't. The patients' life quality was estimated with the help of "The Short Form (36) Health Survey" (The SF-36). Affective disorders were estimated by: Hospital Anxiety and Depression Scale, Apathy Scale. Examination conducted twice: at the first visit and after 6 months.

Results: Analysis of life quality, affective disorder (anxiety, depression, apathy) hasn't shown significant difference between groups at the first visit (p>0.05). At the second visit the SF-36 showed that 1st group's life quality was higher by item: General Health, Vitality, Social Functioning, Role Emotional, Mental Health (p<0.05). In group I proportion of subjects without depression increased by 18.1%, with subclinical- by 24.2%; in group II- did not change (p<0.05). According to the Apathy Scale on the second visit

the proportion of people without disturbance increased by 15.1% in group I, in the II— clinically significant apathy appeared in 8.8%. The estimation of anxiety hasn't shown significant difference between visits in both groups.

Conclusion: The medical rehabilitation PD patients could reduce the severity of apathy and depression and improves quality of life.

CARE DELIVERY & QUALITY OF LIFE: LAY & PROFESSIONAL HEALTH LITERACY

P30.01

Improving support for those affected by Progressive Supranuclear Palsy: Phase 2

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Background: Although PSP is the most common type of atypical parkinsonism, there is almost no data available from the perspectives of people with PSP or their caregivers. In Phase 1, focus groups and surveys were used to assess the needs of people with PSP, as well as their families and professional caregivers. Four categories of challenges were identified: symptoms, services, lack of research, and lack of knowledge. Dissemination of information about PSP diagnosis, symptoms, and care was identified as the priority need. This information needed to reach physicians, community workers, long-term care staff, patients, and families

Objective: To improve support for patients with PSP and their families by addressing their expressed need for knowledge dissemination.

Method: Three activities were completed: (a) development of a brochure summarizing possible symptoms and care options and testing of the brochure with patients, families, General Practitioners (GPs) and geriatric Nurse Practitioners (NPs); (b) revision of the CurePSP 'Physician Packet' and testing of the packet with GPs and geriatric NPs; and (c) testing of a revised PSP care presentation through a webinar offered to staff in long term care and community settings.

Results: The feedback on each of these new resources was positive. Meaningful feedback for improvement was also received from the respondents. Where possible and appropriate, their suggestions were incorporated and are reflected in the final versions of the brochure, primary care practitioner packet, and webinar. These three new resources are being disseminated through clinic visits, mail, internet, publications, and this presentation. It is expected that improved knowledge will translate into more skillful, timely, and supportive care for individuals affected by PSP.

P30.02

Awareness of Parkinson's disease Questionnaire (APDQ) in an Urban Asian setting

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Objective: Public awareness of Parkinson's disease (PD) is important for early symptom recognition. However, the literature on this is very limited. We aimed to address this in our study.

Methods: An Awareness of Parkinson's Disease Questionnaire (APDQ) was designed by neurologists with expertise in PD, and vetted by experts in PD epidemiology and questionnaire design, and by patients, caregivers and lay members of the public. Respondents are instructed to tick a box for "problems experienced by people with PD" (14 symptoms that occur commonly in PD are presented); and to provide a True or False answer for ten statements regarding PD. English, Chinese and Malay language versions of the APDQ were administered on 1,261 members of the Malaysian public attending a health fair in Kuala Lumpur. Demographic data of the respondents were collected.

Results: 74.5% of respondents were tertiary-educated. 19.0% knew someone with PD. Tremor was the most widely recognized symptom (78.9%); however, 83.6% of respondents believed that *all* patients with PD will have tremor. Memory problem was the most widely recognized non-motor symptom (51.8%); however, 30.2% considered PD and Alzheimer's disease to be the same disorder. Motor symptoms such as slowness of movement (73.0%), imbalance (52.6%) and rigidity (47.1%) were better recognized than non-motor symptoms such as depression (33.9%), weight loss (24.3%), urinary urgency (21.0%), insomnia (19.3%), pain (18.0%), excessive daytime sleepiness (15.5%), visual hallucinations (15.1%), reduced sense of smell (11.6%), and constipation (9.2%). Common misconceptions were that there is a cure for PD (50.2%) and that PD is usually familial (41.6%). 78.4% felt that patients with PD often feel socially isolated.

Conclusion: There are significant gaps in public knowledge about PD. This could present a barrier to early diagnosis and timely treatment of symptoms. This highlights the need for further education and research in this area.

P30.03

Knowledge among senior medical students on diagnosis and management of Parkinson's disease: views from Kenya and Uganda

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Objective: To assess the knowledge among senior medical students on diagnosis and management of Parkinson's disease.

Methods: This was a cross-sectional study where 350 senior medical students were sampled from two medical schools each in Kenya and Uganda and recruited. Data on their demographic characteristics and knowledge on recognizing the clinical features, diagnosis, and treatment of Parkinson's disease were captured using researcher-administered questionnaires. Data entry and analysis were performed using Epi-data 7 and SPSS 20.

Results: 85% of the students were able to state the clinical features of Parkinson's disease. 5% of the students reported using neuroimaging as part of the diagnostic criteria in ruling out parkinsonian-like disorders. 3% of the students noted the importance of neuropathology during autopsy as a diagnostic marker, and 70% of the students were aware of levodopa being used in the management of Parkinson's disease.

Conclusion: Despite significant knowledge on recognizing Parkinson's disease, there are still gaps as far as diagnosis and management is concerned and more attention should be paid in general to the teaching of movement disorders in medical school.

CARE DELIVERY & QUALITY OF LIFE: DIABILITY AND QUALITY OF LIFE OUTCOME MEASURES

P31.01

The impact of clinical symptoms on quality of life in patients with advanced stage Parkinson's disease

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Objective: Clinical status and health-related quality of life (HQOL) of advanced stage Parkinson's disease (PD) patients have not been well documented. This study aimed to identify the most bothersome clinical symptoms of advanced stage PD and their impact on HQOL.

Methods: Advanced stage PD was defined as Hoehn & Yahr stages 4 and 5, loss of independence in 2 or more activities of daily living, and cognitive impairment. Thirty PD patients were recruited from the UNC Movement Disorders Clinic. Questionnaires on clinical aspects of PD, PDQ39, and Hospital Anxiety and Depression Scale (HADS) were administered. Within the questionnaire, patients indicated whether they had experienced each of 46 symptoms, from 8 clusters: motor, balance, medication related, cognitive, speech, neuropsychiatric, autonomic, and sensory deficits, and they were asked to rank them by the most impact on their QoL.

Results: PD patients (76.6 % male) had a mean age of 72.8 years (± 10.9) with median disease duration 10 years. Twelve patients (40 %) were post deep brain stimulation surgery. All except 1 patient were living at home with a family member as a regular caregiver (96.6%), and 7 patients used home health services (23.3%). By impact on HQoL, patients ranked balance/falls/freezing of gait #1, followed by motor, speech, cognitive, and lastly autonomic deficits domains. Multiple linear stepwise regression analysis, with PDQ39 as the dependent variable and 8 symptom clusters of the PD symptoms checklist as the independent variables, showed balance ($R^2 = 0.67$, $p < 0.001$) and cognitive ($R^2 = 0.45$, $p < 0.0005$) changes have the biggest impact on HQOL. Our findings highlight the impact of balance and cognitive problems on overall QoL in advanced PD. Thus, policies to improve in-home support with balance and cognitive therapy will be crucial in maintaining patients at home with substantial improvement of the QoL.

P31.02

Quantifying the effect of deep brain electrical stimulation on postural behavior of patients with Parkinson's disease, in the initial weeks post-surgery

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Objective: Quantify the effect of deep brain electrical stimulation (DBS) on postural behavior in Parkinson's disease patient, in the initial weeks post-surgery.

Methods: Women with PD (stage 2, H&Y) with DBS surgery, performed posturographic tests with the aim of quantitatively evaluate the postural motor changes up to 9 weeks post-surgery. The posturography evaluation was carried out in a pre-surgery phase (one month before surgery) and 3 times after surgery (1st, 3rd and 9th weeks). This study analyzed the results of four posturographic tests: mCTSIB-modified Clinical Test of Sensory Interaction on Balance; LOS-Limits of Stability; WA- Walk Across and TW-Tandem Walk.

Results: When comparing the values obtained in pre-surgical with the values obtained in successive post-surgical evaluations, we verified that in LOS test the reaction time remained similar, the velocity of center of gravity increased, and the maximum distance did not change. In mCTSIB test, the sway velocity increased when the patient stood with eyes open on firm surface and decreased with closed eyes. Same results were obtained on unstable surface. In WA test, the step width decreased and the step length and stride velocity increased. In TW test, the step width and the end sway velocity decreased but the displacement velocity increased. Some parameters related to postural behavior did not change after surgery until 9 weeks, but gait parameters tended to return to normal control values in a post-surgical early phase.

P31.03

Motor dysfunction, quality of life, physical activity and life-space in advanced Parkinson's disease: what is the impact of STN DBS

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Background: Understanding how Parkinson's disease (PD) motor dysfunctions affect mobility, physical activity and quality of life (QoL) is essential. Furthermore, identifying the impact of interventions such as STN DBS on these issues will help better adapt our treatments.

Objectives: 1. Identify differences in life-space, physical activity and QoL between advanced PD patients and healthy controls. 2. Assess the impact of STN DBS on these variables.

Methods: Thirty patients with idiopathic PD and 30 age- and gender-matched healthy controls filled out questionnaires on mobility (Life-Space Assessment), physical activity (Phone-FITT), and QoL (SF-36). Results were compared to establish normative values in advanced PD. Then, 20 of the PD patients underwent surgery for STN DBS and filled-out the same questionnaires 6 months after surgery. Pre-operative and post-operative results were compared with results from the same age- and gender-matched healthy controls to assess the effect of treatment.

Results: A statistically significant reduction in life-space, physical activity and QoL was observed between healthy controls and advanced PD patients. While STN DBS significantly improves motor dysfunction, not all aspects of mobility, physical activity and QoL are equally improved.

Conclusion: As mobility and physical activity are inter-related and both are related to QoL, interventions should be aimed at improving these factors so as to lessen the burden of disease on patients and the health-care system. Furthermore, while STN DBS drastically improves motor symptoms in PD, there is not a systematic normalization in mobility, physical activity or QoL. As such, interventions should be developed to address these issues.

P31.04

The ParkinsonAtlas: transparency in medical practice variations in PD care in the Netherlands

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Objective: ParkinsonNet, a national multidisciplinary network of specialized health professionals, aims to improve the quality of care for patients with Parkinson's disease (PD). The concept has nationwide coverage in The Netherlands with 66 regional allied health networks in the catchment areas of Dutch hospitals. Within each network a selected number of expert therapists are trained according to evidence-based guidelines. To date, 2500 neurologists, PD nurse specialists, physical-, occupational therapists, speech-language pathologists and dieticians are involved. Recently, we introduced the ParkinsonAtlas, an online tool which provides insight in the quality of care within all ParkinsonNet regions [1].

Methods: The following outcome-, process- and structure indicators are visualized in the ParkinsonAtlas to assess the quality of PD care in each region: *Outcome indicators:* patients' quality of life (PDQ-39), patient-experiences (PCQ-PD), (hip-) fractures, costs per patient, hospitalization rate, home care and admission to rehabilitation- or nursing homes. *Process indicators:* utilization of allied healthcare, anti-Parkinson medication, professionals' adherence to medical guidelines and healthcare team-effectiveness. *Structure indicators:* the estimated number of PD patients, density of specialized health professionals and healthcare services. The data is collected from health insurance companies, patient- and professional surveys and the ParkinsonNet membership database. All indicators are calculated on a national- and regional level. Each indicator is separately visualized in online maps.

Results: Large medical practice variations were found for all three types of indicators. For instance, the utilization of physical therapy per region ranged from 45% to 75%. Additionally, the percentage of PD patients consulting a ParkinsonNet physiotherapist could be improved in several regions. The ParkinsonAtlas is now used to provide feedback to health professionals to enhance internal quality improvement, by insurance companies to contract high-quality PD care, and by patients to choose excellent health professionals specialized in PD.

P31.05

Comparison of the psychological symptoms and disease-specific quality of life (QoL) between early- versus late-onset Parkinson's disease patients

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Objective: The impact of Parkinson's disease (PD) on psychological status and quality of life (QoL) may vary depending on age of disease onset. The aim of this study was to compare the psychological symptoms and disease-specific QoL between early- versus late-onset Parkinson's disease (PD) patients.

Methods: This cross-sectional study was performed in a referral movement disorder clinic in Tehran, Iran during 2011-2012. A total number of 140 PD (95 males and 45 females) patients with the mean current age of 61.3 (SD=10.4) yr were recruited in this study. Conventionally, PD patients with the onset age of ≤ 50 yr are defined as "early-onset" (EO) group (n=45); while, the ones with > 50 yr at the time of diagnosis are categorized as the "late-onset" (LO) PD patients (n=95). Different questionnaires and scales were used for between-group comparisons including PDQ39 (PD-specific QoL), HADS (hospital anxiety & depression scale), FSS (fatigue severity scale), MNA (mini-nutritional assessment), Schwab & England (activity of daily living) and Hoehn & Yahr scales (progression and level of disability).

Results: Univariate comparisons showed that depression score was significantly higher in EO group (6.3 \pm 4.5 vs. 4.5 \pm 4.2, $P=0.023$). Among different domains of QoL, emotion score was also significantly higher in EO group (57.1 \pm 21.2 vs. 48.9 \pm 21.2, $P=0.033$). Results of multivariate linear regression model showed that anxiety ($P=0.0002$), depression ($P<0.0001$), fatigue ($P=0.033$) and level of morbidity (Schwab scale) ($P=0.048$) are the independent factors significantly related to PD patients' quality of life.

Conclusions: Our findings showed more severe depression and more impaired emotional domain of QoL in early-onset PD patients. Moreover, decreased QoL in PD was related to depression, anxiety, fatigue and lower level of activity in daily living. It is important to consider these psychological disturbances for improvement of QoL in PD especially among the early-onset patients.

P31.06

The effect of disease severity on postural control behavior in Parkinson disease

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Objective: Most of the research concerning postural behavior in Parkinson Disease (PD) integrates patients from different stages in the same sample. This methodology of analysis gives us limited

information about the progression of the disease. The present research aims to characterize the variations associated to different PD patient's postural sway. This allows us to identify important indexes of balance impairment regarding each particular level of the disease progression. In this study, we have analyzed quantitative data of the time series parameters of the center of gravity (CoG), during different posturographic tests.

Methods: The sample was composed of 103 patients (45 female and 58 male, 70.5 ± 8.4 years) diagnosed with PD stages 1 to 4 according to Hoehn and Yahr rating scale (H&Y) (Stage 1 – 15; Stage 2 - 33; Stage 3 - 47; Stage 4 - 8). Clinical information concerned patient's diagnosis, stage of the disease and UPDRS-II scale. The posturographic tests included the *modified Clinical Test of Sensory Interaction on Balance (mCTSIB)* and the *Limits of Stability test (LOS)*. Statistical analyses integrated different tests (One-way MANOVA, one-way ANOVA and Factor Analysis) in order to compare the postural behavior presented by patients with PD in the different stages.

Results: In mCTSIB test, the alignment of the center of gravity (CoG), was significantly altered by disease progression ($p = 0.037$). A forward projection of the CoG within each stage was also observed, related to the stimulus manipulation. In LOS test, a small decrease with disease progression was suggested for the distance of the CoG sway in the forward direction ($p = 0.057$). Balance changes during PD progression are possible to be better identified. The future development of physiotherapy programs to reduce postural instability and prevent future falls should consider these changes.

P31.07

Neuropsychiatric symptoms impact quality of life and caregiver burden in Mexican population with Parkinson's disease

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Objective: The aim of this study is to determine impact of neuropsychiatric symptoms in PD patients' quality of life and caregiver burden.

Methods: We applied the Scale for Evaluation of Neuropsychiatric Disorders in PD (SEND-PD) and PD Quality of Life, eight-item scale (PDQ-8) to PD patients and the Zarit Caregiver Burden Interview (ZCBI) to their caregivers. Disease stage was classified according to Hoehn and Yahr scale. SEND-PD was considered abnormal with a score greater than or equal to 1.

Results: A total of 174 PD patients and their main caregiver were included. Of PD patients, 55% were male. Mean age was 62.23 more or less 13.06 years. Mean school years were 8.26 more or less 5 years. Association between PDQ-8, ZCBI and abnormal SEND-PD scores are shown in Table 1 and Table 2. After performing a linear regression model, disease severity ($p = 0.002$, $B = 2.37$), educational level ($p = 0.035$, $B = -0.96$) and SEND-PD total score ($p < 0.001$, $B = 7.33$) were predictive factors for PDQ-8 score. Multinomial regression showed that mild disease ($p = 0.006$, $B = 1.73$) and SEND-PD total score ($p = 0.001$, $B = 2.48$) were significant factors for caregiver burden. Caregiver burden seems to be influenced by an increase in PD motor and neuropsychiatric symptoms such as depression, hallucinations or confusion and decreased quality of life in PD patients (1, 2). It has not been established whether non-motor or motor symptoms have a greater

impact on caregiver burden. We report an association between SEND-PD and PDQ-8 scores, with a greater impact in mild (HY lesser than or equal to 2) and moderate (HY = 3) disease stages. Educational level and disease severity are independent factors influencing PDQ-8. In our study motor and neuropsychiatric symptoms have an equal impact on caregiver burden.

P31.08

Factors, disabling patients on the early stages of Parkinson's disease

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Parkinson's disease (PD) is one of the most frequent neurodegenerative diseases. Social adaptation of PD patients is significantly reduced, work capacity is limited, quality of life and daily activities of patients are impaired even on the early stages of the disease.

Objectives: to determine the range of factors, disabling patients on the early stages of PD.

Material and methods: 80 patients with PD on the early stages were included (male: female = 30: 50). 20% of our patients had 1-1,5 stage of modified H&Y scale, 35% - 2nd and 45% - 2,5. The mean age was $58 \pm 8,0$ years; the mean duration of the disease - $3,0 \pm 2,5$. The mean age of the onset was $54,5 \pm 8,5$ years. The mixed form of PD predominated over others (75%). Disabled were 42,5% of patients with early stages PD. Dates of treatment: 47,5% early, 10% - late, 42,5% - delayed treatment onset. We used Hoehn and Yahr scale modified by Lindvall to assess PD severity (Hoehn M., Yahr M., 1967, O. Lindvall, 1989); to assess the severity of the main symptoms of Parkinson's disease - UPDRS scale (II and III) (Fahn S., Elton R.L., 1987); assess affective disorders - Hamilton Rating Scale - (M. Hamilton, 1959, 1999); cognitive disorders - Montreal cognitive assessment scale (MOCA, Nasreddine M.D., 2004); non-motor symptoms - scale of non-motor symptoms PD NMS (Chaudhuri K. R. et al., 2004); to assess the quality of life - a questionnaire Boer (Boer A.G. et al., 1996) and the PDQ-39 (Peto V. et al., 1995), scale EuroQoL (Rabin R. et al., 2001).

Results: Quality of life (PDQ-39) were $40,5 \pm 26,5$; on (Boer) - $141,5 \pm 31,95$. Non-motor disturbances were observed in 87,5%. Cognitive impairment in 37,5% cases had cortical-subcortical type. Affective disorders were diagnosed in 57,5% cases. There was a positive correlation between disabilities and start of treatment ($p = 0,000001$). Positive correlation ($p < 0,05$) of disability with the gender, stage, form, duration of disease and type of progression. Conclusions: Cognitive, affective disorders and other non-motor symptoms significantly deteriorate social adaptation of patients with PD even on the early stages of the PD, leading to disability.

P31.09

Quality of life in Parkinson's disease patients with motor fluctuations and dyskinesias in five European countries

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Background: Parkinson's disease (PD) patients treated with levodopa frequently develop long-term motor complications. However, little is known about the relationship between specific subtypes of motor complications and quality of life (QoL). In addition, potential differences in the QoL of PD patients from different countries have not yet been investigated.

Objective: To assess QoL and its association with on-off fluctuations, peak-dose dyskinesias, biphasic dyskinesias, and dystonias in patients with PD in five European countries.

Methods: Data from 817 PD patients and their physicians from the Adelphi Parkinson's Disease Specific Programme were collected cross-sectionally. Generic and disease-specific QoL was measured with the EuroQoL 5-Dimension (EQ-5D) and the Parkinson's Disease Questionnaire-39 (PDQ-39). Multivariable analyses were performed to test the adjusted association of motor complications and country with QoL.

Results: Approximately 30% of the patients suffered from any type or combination of motor complications. On-off fluctuations significantly worsened generic QoL ($p < 0.001$) and PD-specific QoL ($p = 0.01$). Dyskinesia subtypes did not affect generic QoL but had detrimental effects on the PD-specific QoL dimensions activities of daily living, cognitions, stigma, and bodily discomfort. Significant differences in QoL were found between the countries with patients from Spain, Italy, and France having poorer QoL scores than patients from Germany and the UK.

Conclusion: Motor complications, primarily on-off fluctuations, may adversely affect QoL in patients with PD. This substantiates the importance of targeting their prevention and delay in the treatment of PD. Country differences in QoL of PD patients should be further explored.

P31.10

Club CREATE- A program to improve quality of life for late-stage Parkinson's disease

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Purpose: For many diagnosed with Parkinson's disease (PD), late stages of the disease lead to a poor quality of life with declining movement, interests, connections and isolation. Club CREATE is a therapeutic day program to address these concerns. Club CREATE's goal is to improve quality of life for people with PD by providing programs, support, and assistance in adapting to the challenges of PD. The program focuses on six areas: move your body, train your brain, build a community of support, make yourself heard, express yourself creatively, and expand your horizons.

Methods: The program draws upon an interdisciplinary team consisting of nursing, music therapy, occupational therapy, social work, chaplaincy, community artists, horticultural therapy and support staff. The team provides intervention and care at various times, matched to the client's current needs and abilities. Both structured groups of 8-12 members and larger group activities are offered to carry out goals. To better understand the impact of the program on members' quality of life, members were surveyed using

the PDQ-8 to assess their overall health status. Questions were asked from a staff person and data was collected at intervals over three years.

Results: Members have been in the program an average of two years, ranging from two months to seven years. The overall scores of the members whose PDQ-8 scores were measured consistently over the three year period either improved or maintained. The greatest increase in scores came in the social support category, increasing on average 1 point per member.

Conclusions: As the numbers of those living longer with PD increases, it is important to develop and expand programs that can improve quality of life, especially for those in the late stages of the disease.

P31.11

Quality of life in patients with newly diagnosed untreated Parkinson's disease

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Objective: In order to plan an optimal treatment in patients with newly diagnosed Parkinson's disease (PD), it is important to gain knowledge about the patient's disability and quality of life (QoL) in relation to the clinical factors, such as the motor and non-motor symptoms.

Methods: Fifty patients with newly diagnosed PD were included. The QoL was measured by the Parkinson's disease quality of life questionnaire (PDQL). The clinical aspects of the disease were assessed using the UPDRS II, III, UPDRS sub-scores (tremor, bradykinesia, rigidity, PIGD, ADL-axial), MMSE, Beck Depression Inventory (BDI), Pittsburgh Sleep Quality Index (PSQI), Epworth Sleepiness Scale (ESS), the nonmotor symptoms questionnaire (NMSQ).

Results: The mean age of onset of parkinsonian symptom was 58.9 (SD=12.2) years and the average duration of disease was 14.2 (SD=16.0) months. The PDQL total scores correlated most strongly with UPDRS III (-0.749), NMSQ total score (-0.676), BDI score (-0.663), and UPDRS II (-0.598, all $p < 0.0001$). Among UPDRS sub-score, PIGD (-0.638) and ADL axial (0.736, both $p < 0.0001$) scores were the most significant predictors of poor QoL. In multivariable regression models, UPDRS and BDI (model 1) or UPDRS and NMSQ (model 2) were almost equivalent predictors.

Conclusions: This study demonstrates that patients who were depressed, had more nonmotor symptoms, axial motor impairment, and had high levels of disability are most likely to experience poor QoL. The improvement of both motor and nonmotor symptoms should therefore become an important target in the management of newly diagnosed PD.

P31.12

Does home-visiting improve quality of life of those living with Parkinson's disease living in rural areas? – a program evaluation

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A unique home-visiting program was established in partnership with Medicine Hat College Nursing Program and the Parkinson's Alberta Society Medicine Hat office in 2010. Third year nursing students were matched with person's living with Parkinson's disease and

caregivers (if applicable) to provide home visits over an 8-week duration to learn what it is like to live with a chronic illness such as Parkinson's disease in the community, to assess their needs, strengths, and to provide community-based nursing interventions that provide positive health outcomes. Anecdotal evidence from participants suggested the program was successful and improved participants quality of life; a formal evaluation of the program was desired.

Objectives: One objective was to explore if quality of life improved for the person living with Parkinson's disease and their caregiver. Second to see if over-all-health improved for the person living with Parkinson's disease and the caregiver. Finally, ideas on how to maintain and improve the program were desired.

Methods: Thematic analysis was used to evaluate 11 audio-taped interviews (transcribed) of past home-visit participants. Informed consent was provided. Data was coded for demographic data, and five themes emerged. Information was validated with the participants.

Results: Results showed that quality of life and over-all-health for both the caregiver and the person living with Parkinson's disease improved by participating in the program.

Participants were happier, loneliness diminished; participants had increased socialization, self-confidence, self-esteem, coping skills, patience, and overall enjoyment; participants felt safe in expressing their feelings and felt listened to; communication improved between couples; and, participants were empowered by educating students nursing and by 'giving back' to the community. Results indicated that student-led home-visits were an effective way to increase understanding of what it is like to live with Parkinson's disease in the community for future nurses and quality of life was improved for participants.

P31.13

Quality of life and the relative importance of motor and non-motor symptoms in Parkinson's: the patient perspective

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Introduction: Most investigations of quality of life (QoL) in Parkinson's (PD) have focussed on the comparison or validation of measurement scales. Others have assessed the contribution of general affect (depression and anxiety) to QoL. Few have addressed the contribution of motor and non-motor symptoms (NMS). Fewer still have taken a patient-centred stance, answering questions posed by fellow patients. The present study, conducted by Parkinson's Movement (PM) looks at personal QoL in PD.

Methods: A series of 5 polls (single question, multiple choice answer) were posted on the PM community website (www.parkinsonsmovement.healthunlocked.com). The questions asked (Q1 & Q2) the first motor and non-motor symptoms experienced, (Q3) current motor symptom burden, (Q4) motor influence on QoL and (Q5) relative role of motor and non-motor symptoms on personal QoL in patients. Between 165 and 286 responded to each poll.

Results: The PM cohort was mainly young (76% aged 50-69), highly educated (68% with at least 1 degree), with mild Parkinson's (current Hoehn & Yahr stage 1/2: 66%) for 4-6 years. Results were as follows: Q1: Tremor was usually the first symptom motor experienced (57%), with rigidity in 21%. Q2: Anosmia (25%), sleep problems (24%) and changes in affect (19%) were the first NMS experienced. Q3: Most common motor symptoms currently experienced were micrographia (77%) balance problems (76%) and tremor (73%). Q4: 28% felt that their QoL was directly related to their motor symptoms while 30% and 33% felt their QoL was better

or worse than predicted by motor symptoms. Q5: Key movement problems (bradykinesia, rigidity, tremor) were the most common predictor of QoL in 71%. Other factors noted were sleep disruption (49%), balance (43%), cognition (36%) and pain (35%).

Conclusions: Motor problems, although pivotal to diagnosis, are only one factor in a complex raft of symptoms affecting individual patient QoL.

P31.14

Patient-centered care for PD patients in the Parkinson centers of excellence: a multicenter study

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Objective: Patient experience questionnaires are increasingly recognized as an essential part of quality of care assessment. We developed and validated the Dutch Patient-Centeredness Questionnaire for PD (PCQ-PD). Here we describe the validation of the English PCQ-PD and its initial application to a representative patient sample from American and Canadian Parkinson centers of excellence.

Methods: First, the PCQ-PD was translated from Dutch into English, based on a forward-backward translation process. Second, the applicability was evaluated by an expert consultation round with 17 center directors. Third, the questionnaire was pre-tested within cognitive interviews with professionals (n=7), patients (n=6) and caregivers (n=6). Fourth, psychometric validation was performed in a multicenter study within 20 centers. Data-analysis focused on psychometric properties of the questionnaire and the level of patient-centeredness by calculating scores for overall patient-centeredness [0-3], subscale experiences [0-3] and quality improvement scores [0-9].

Results: 972 PD patients completed the questionnaire (mean 49 per center, range 37-58). After the validation procedure, the PCQ-PD addressed 44 items in six subscales of patient-centeredness. The internal consistency, expressed in Cronbach's α per subscale, ranged from 0.677 to 0.889. The mean overall patient-centeredness score was 2.09 (SD 0.44). The 'providing information' subscale received the lowest experiences ratings (Δ 1.62, SD 0.62). 'Were you informed about what your health professionals discussed with each other regarding your treatment?' obtained the highest quality improvement score (4.61). Centers differed significantly on the overall patient-centeredness score and information-, collaboration-, accessibility-, and patient-involvement subscales ($p < .001$). Centers had comparable scores on the empathy- and emotional support subscales. The PCQ-PD is a valid instrument to measure patient-centeredness in PD care in America and Canada. Psychometric properties of the instrument were good. Application of the PCQ-PD revealed the level of patient-centeredness in the centers of excellence. The main outcome was a compelling call for the provision of information.

P31.15

Quality of life and neuropsychology assessment in Nigerians with Parkinson's disease

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Introduction: Parkinson's disease (PD) is a chronic neurodegenerative disease characterised by motor features. However growing evidence suggests that this is usually preceded by non-motor features. PD is associated with negative quality of life and mood impairment.

Objective: To assess the self-determined quality of life measures and mood disorder among patients living with PD.

Method: Twenty-one consecutive consenting patients were assessed using the Parkinson's Disease Quality of Life Questionnaire (PDQ-39), Schwab and England Activity of daily living scale, Modified Hoehn and Yahr Staging (MHYS), and the Hospital Anxiety and Depression scale (HADS).

Result: Twenty-one PD patients made up of 7 females (33.3%) and 14 males (66.3%) with mean age of 60 years and mean age of onset at 56.6 years were screened. 66.6% of the patients were of MHYS stage 2 or below, while the rest were of stages 3-4. On the Schwab and England Activity of daily living scale 66.1% of the patient performed at levels between 70-100%, while only 4.8% of the patient performed at $\leq 40\%$. The average PDQ-39 score was 31.5%. Score of 30-50% were recorded mobility, activities of daily living, stigma and bodily discomfort. The proportion of patients that were depressed and anxious was 9.5% and 14.3% respectively.

Conclusion: There is a significant impairment in mood and quality of life measures among Nigerians living with PD.

CARE DELIVERY & QUALITY OF LIFE: SHARED DECISION-MAKING: PWP- CAREGIVER- DOCTOR

P32.01

Effects of group-delivered improvisational dance on balance in adults with middle stage Parkinson's disease: a two-phase pilot with fMRI case study

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Objective: The purpose of this two-phase pilot was: (1) To examine the effects of group-delivered dance improvisation on balance and mobility and, (2) for one participant, to examine changes on Functional Magnetic Resonance Imaging (fMRI) in a subsequent neuroplasticity study.

Methods: Seven community-dwelling adults (mean age 69), with middle stage Parkinson disease, completed a 7-week (21-hour) class in improvisational dance. The protocol emphasized individual and group movement creation without teacher mimicking or music

entrainment. At termination, one participant with significant functional gains consented to fMRI in a neuroplastic protocol conducted two months later. After two weeks of being sedentary, the participant underwent a brain imaging protocol: resting and reaction (button-pressing) task. The parent group gathered again for one week of improvisational dance (five consecutive days, same protocol). Post-fMRI scans followed immediately.

Results: Posttest balance outcomes for the group-delivered dance protocol were significant for the Fullerton Advanced Balance Scale $p=.017$), with an average improvement of 5 points. TUG scores were not significant, though group performance variability decreased with a trend toward decreased timing. For phase 2, fMRI recordings showed increased connectivity in long-range anterior-posterior neural network communities after the intensive trial. Previously isolated neural networks in the basal ganglia showed significant connections with the premotor cortex.

For this sample group, dance improvisation resulted in significant functional gains. For one participant, functional improvements appeared to correlate with positive neuroplastic changes in brain connectivity both in global efficiency and strength of network connectivity between the basal ganglia and cortical motor centers. Larger studies are warranted to substantiate correlations between functional gains and neural efficiency through improvisational dance in adults with middle stage Parkinson disease.

P32.02

Shared decision making in current treatment choice in advanced Parkinson's disease

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Introduction: In advanced Parkinson's disease (PD), three therapies are available: deep brain stimulation, duodenal levodopa infusion, and subcutaneous apomorphine infusion. These therapies differ in procedures, daily care and outcomes. Evidence for first choice of treatment is lacking as no trial has compared these therapies directly. Therefore, therapy-selection should be personalized and shared decision making (SDM) could stimulate active patient involvement. In this study we evaluated the current decision making process in advanced PD and the role of SDM.

Methods: Questionnaires on current decision making and SDM in advanced PD were developed based on qualitative data and literature research. Questionnaires were sent to all eligible registered Dutch neurologists ($n=869$) and PD nurse specialists ($n=86$) in the Netherlands. A convenience sample of patients who had undergone one of the treatments in the past three years ($n=179$) were recruited through online requests and via neurologists.

Results: Neurologists (42% response rate): 88% considered SDM useful and 54% said they regularly/ always applied SDM for this decision. An important barrier to SDM was a lack of knowledge about all treatments. 66% expressed a need for a decision aid.

PD nurse specialists (73% response rate): 29% were actively involved in decision-making and 36% gave information only.

Patients (68% response rate): 40% were informed about all three options. The majority of patients (63%) would have preferred SDM for this treatment choice; 41% had actually experienced SDM and a small proportion was referred (11%). An important facilitator for

SDM was trust between the professional and patient.

Discussion: Most professionals and patients have a positive attitude towards SDM, however in practice it is not used optimally. It is important to provide equivalent information on all options to facilitate professionals and to increase patients' involvement. A decision aid can be such a facilitator for SDM in advanced PD.

P32.03

Equal options; shared decision? Development of a decision aid for treatment choice in advanced Parkinson's disease

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Introduction: The three available therapies in advanced Parkinson's disease (PD), deep brain stimulation, duodenal levodopa infusion, and subcutaneous apomorphine infusion, differ in procedures, daily care and outcomes. Evidence for first choice of treatment is lacking as no trial has compared these therapies directly. Therefore, therapy-selection should be personalized through shared decision making (SDM). In a previous study most professionals were positive about shared decision making (SDM) in therapy selection. However, professionals expressed a need for a decision aid (DA) to support this process. A decision aid helps people to make deliberative choices and facilitates the cognitive processes, thereby stimulating patient involvement in the decision making process. Here we describe the development of our DA.

Methods: The process map of Elwyn et al¹ was used to develop the DA. Qualitative and quantitative data from professionals and patients provided information about the format, content and constraints. SDM models plus general and PD specific cognitive decision processes gave input for the theoretical basis of the DA. These together with the evidence synthesis of the treatments and brainstorm sessions with stakeholders resulted in a first prototype. The prototype was tested in several rounds by treated patients, treatment naïve patients, caregivers, neurologists, PD specialists with expertise on these treatments, PD nurse specialists, and a patient communication expert.

Results: Both patients and professionals expressed a need for equivalent treatment information. PD specific cognitive processes taken into account were impulsivity, reduced cognitive flexibility and limited capacity to organise new information. Our qualitative data showed patients often focused on one treatment, not searching for equivalent information on alternatives. Using the theoretical framework, strategies were build into the DA to reduce these possible biases in decision making and to stimulate SDM.

References: Elwyn et al. How to develop web-based decision aids for patients: a process map. PEC. 2011

P32.04

Providing information equals Shared Decision Making: the professionals' view on treatment choice in Early Parkinson's disease

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Objective: The Dutch guideline on Parkinson's disease (PD) regards levodopa and dopamine agonists as equipotent pharmaceutical therapies in early PD. It recommends that the choice for treatment is based on the individual patients' characteristics, preferences, and the neurologists' experience. Patients increasingly express a desire for unbiased, comparative information regarding treatment options, and active involvement in decision making. Considering the preference-sensitivity of the choice, this decision is well equipped for shared decision making (SDM). The aim of this research is to clarify if and how professionals apply SDM for this particular decision in current practice.

Methods: Semi-structured interviews were conducted with 15 neurologists and 7 PD nurse specialists. Saturation was pursued in both groups. Transcripts of the interviews were independently coded by two researchers following the rules of grounded theory.

Results: Neurologists regarded the moment to start with pharmaceutical treatment more suitable for SDM than the choice of treatment. They often offered their patients the freedom to wait with treatment until they considered the disease to interfere with their daily activities. Nonetheless, the neurologists considered not all patients suitable for a postponed patient-directed decision, due to disease severity and the fact that levodopa response can be used to support the diagnosis. With regard to treatment choice, the majority strongly favoured levodopa, and did not regard dopamine agonist as equipotent. Although all neurologists emphasized that they informed their patients about both treatment options, they admitted that this information is likely to be biased according to their preferences. Nurse specialists seldom discussed the possibility of choice with patients, but offered complement information. For true SDM, substantial efforts will be needed to overcome the perception that sharing (biased) information equals SDM.

CARE DELIVERY & QUALITY OF LIFE: PALLIATIVE CARE/ END OF LIFE CARE/ LONG-TERM CARE

P33.01

Improving end of life care in Parkinson's disease

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Objectives: Management of end of life care in patients with Parkinson's disease (PD) is complex. Medications commonly used for symptom relief at the end of life (metoclopramide and haloperidol) often worsen Parkinsonian symptoms. Furthermore, patients with PD may be inappropriately deprived of anti-Parkinsonian drugs at the end of life. We aimed to identify current end of life prescribing practices in PD patients admitted to a District General Hospital in England.

Methodology: All patients with PD who died at the Royal Berkshire NHS Foundation Trust, Reading, England between 1st January 2010 and 31st December 2012 were identified using the Hospital death Registry. Three physicians analysed medical notes and drug charts for end of life care and involvement of specialist PD and palliative care services. Clinical data was recorded in a proforma.

Results: 98 patients were identified from the Hospital death Registry. 2 patients did not have PD and notes were unavailable for 8 further patients. Clinical notes from 88 patients were reviewed. Drug charts were available for 80 patients. 55 male and 33 female patients were identified. Haloperidol was prescribed in 24% (19/80) whilst metoclopramide was given in 9% (7/80) of patients. 35 patients (44%) were started on a formal end of life care pathway (Liverpool Care Pathway). Of those 60% (21/35) patients had their Parkinson's medications discontinued. Our results demonstrate that patients with PD frequently receive inadequate end of life care. We have designed a clear end of life pathway for use in patients with PD. We emphasise the importance of continuing some of the PD medications, considering alternative routes of administration, avoiding antidopaminergics, and seeking specialist PD and palliative care advice. Education of medical and nursing staff regarding appropriate medication has since been undertaken.

P33.02

End of life experience in Parkinson's disease and related movement disorders from the caregiver perspective

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Objectives: To better understand the experience of patients / families at end-of-life with parkinsonism.

Background: Although there is recognition that needs of patients with parkinsonism and their families are complex, actual end-of-life experiences are poorly documented.

Methods: Primary caregivers (CG) of Struthers Parkinson's Center patients who had died within the last 24 months were contacted for this study. The first contact was one-page survey; those who were willing participated in a semi-structured phone or in-person interview. Data were stored MS Excel and MS Access.

Results: Sixty-nine CGs were identified. Forty-eight (70%) responded to survey, and 42 were interviewed. Thirty-eight (79%) were spouses, 81% female, average number of years caregiving was 7.3 (range 0-24). Thirty (63%) utilized hospice average of three months, (range 3 hours – 11 months). Interview findings included: profound and complex neurological handicap of those dying in hospice, pneumonia as terminal event was relatively uncommon (12%) and "slow shutting down" due to disease itself rather common (56%). Changes in care setting and medical care teams in the months before death were common. While 23% of the 42 patients died at home, 41% of non-hospice users died in hospital. Caregivers reported that their lives had been consumed by the caregiver role, that they continue to experience deep grief months after patient's death, and identified nurses, aides, social workers as most significant to care and support during terminal stage.

Conclusions: Strategies to prepare patients and caregivers for, assist with, and coordinate transitions in care team, medical goals, and care setting could impact the care process and reduce the burden to caregivers in final stages and during the dying process.

P33.03

Struthers Parkinson's Care Network

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Objective: Build sustainable partnerships with community-based residential & home care agencies dedicated to delivery of high quality care for persons with PD and related movement disorders.

Methods: Agencies applied for one year pilot program designed to build capacity to provide high quality PD care and agreed to: designate two "site champions" as key leaders and provide training

for at least 80% of all staff in core module TULIPS PD education program and 60% of direct care providers in two additional modules; support continuing education days at SPC for 4 nurses, 1 social worker & 2 rehabilitation professionals; demonstrate evidence of facility initiative to insure "pills on time" and track / minimize falls; sponsor and facilitate a support group; collect data and distribute satisfaction surveys for PD families. Struthers Parkinson's Center (SPC) provides education for site champions and professionals; facilitates ongoing communication; conducts site visits; collects and reports outcomes.

Results: Six programs were selected. Two "site champions" from each facility attended two day orientation and conducted TULIPS training in their facility. A total of 1,200 staff completed TULIPS core and 774 direct care staff have completed additional modules. Site champions attend quarterly network calls and submit bi-monthly reports. All sites report policy of "pills on time" and tracking / minimization of falls. All exceed required numbers for professional education. Each agency hosts a support group. Seventy-five client satisfaction surveys have been received to date at SPC.

Conclusion: "Buy-in" from administration and lead staff is essential. As the process unfolds and staff becomes knowledgeable, leaders describe increasing staff enthusiasm and comfort in providing PD care. All agencies express interest in continuing and SPC will expand the program to additional sites.

CARE DELIVERY & QUALITY OF LIFE: HEALTH ACCESSIBILITY/ UNDERSERVED POPULATIONS

P34.01

An outreach model to educate Hispanics living with PD in Phoenix, Arizona

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Objective: To develop a culturally appropriate model to educate Hispanics with PD and their caregivers who don't attend community programs due to barriers including transportation, mobility, cultural beliefs, and economic constraints.

Methods: A group of 7 volunteers were trained in partnership with a community college, Community Health Worker networking organization and the Muhammad Ali Parkinson Center. All volunteers had a close family member with PD or had worked as caregivers of a client with PD. All of them attended many of the Hispanic Outreach community programs offered by the MAPC, including support groups and recreational classes. Volunteers had bi-monthly meetings with the MAPC Hispanic outreach coordinator and completed a total of 30 hours of practice required by the college class.

The volunteers identified 12 topics they considered important for Hispanic families to better understand the disease. A flipchart was designed that tells the story of a Hispanic family dealing with PD. Each page explains one of the 12 topics. The language used is easy to understand and includes every day expressions to keep it conversational. The flipchart was used to educate Hispanics with PD in their homes. The volunteers conducted once weekly home visits for twenty-nine families for a total of 12 visits per family.

Results: Paired samples t-tests were used to compare PDQ-39 subscale and summary scores before and after program involvement. Social Support and Communication are statistically significant.

PDQ -39 n=21	T=1 mean	T=12 weeks mean	Change	P value
Mobility	54	53	-1	.78
ADL	46	42	-4	.46
Emotional	42	43	+1	.98
Stigma	34	38	+4	.67
Social Support	48	21	-27	.00
Cognition	32	36	+4	.43
Communication	31	9	-22	.00
Discomfort	43	44	+1	.86
Summary Score	38	35	-3	.50

P34.02

Increasing return on investment and access in the health sector in developing countries

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Objective: This paper focuses on the different mechanisms of how to maximize return on investment and access to health care services developing countries. One of the most inhibiting factors to health care service access and utilization is cost sharing and/ or health insurance.

Methods: A random sampling technique was employed to 300 households and individual interviews conducted.

Results: Health insurance mechanisms render access to health services affordable for low income groups. Conditional cash payments showed promise for improving uptake of initiatives, but could also create a perverse incentive.

Conclusion: There is a need for improved quality of research in the area of conditional cash transfers for health services. An evaluation of health financing initiatives is required to ensure an evidence base that correlates to conditional cash transfers.

P34.03

Developing a network of interdisciplinary Parkinson's rehabilitation teams in nontraditional settings: providing high-quality treatment to populations in underserved settings

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Objective: Interdisciplinary approaches to treating Parkinson's disease can be extremely effective to treating the wide range of deficits associated with this disorder. Many of the top programs are associated with large movement disorders clinics. However, access to this level of expertise can be difficult for individuals in underserved regions due to barriers such as distance as well as a lack of qualified professionals with sufficient training and experience in treating this disorder.

Methods: By developing a network of Parkinson's rehab teams based in subacute rehabilitation facilities with skilled nursing, we are attempting to improve access to the local community as well as for inpatient and long-term care populations that are demographically likely to be represented in higher numbers due to their age.

Members of an interdisciplinary Parkinson's team typically include physical, occupational and speech therapy as well as dietitian, social worker, neuropsychologist in addition to the movement disorders specialist (a neurologist with specialized training in the treatment of Parkinson's disease). In contrast, the core of our

program relies on rehab disciplines (physical, occupational and speech therapy) with specialized training in the treatment of Parkinson's disease based on the Allied Team Training Program (ATTP) through the National Parkinson Foundation. We refer our clients to Parkinson's specialists in other disciplines as needed. In 2012, our program concept was integrated into 12 other Life Care facilities throughout Colorado and Wyoming, modeled after the ParkNet program in the Netherlands.

Results: Pending a successful trial of this concept in this region, we hope to develop an easily replicable program for providing access to high-quality treatment to underserved regions around the United States.

P34.04

Relationship between patient age and resource utilization among newly diagnosed Parkinson's disease patients

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Objective: Examine differences in resource utilization in newly diagnosed with Parkinson's disease (PD) patients.

Methods: Study utilized Truven Health MarketScan® Commercial Claims and Encounters and Medicare Databases, from 1/1/2006 through 12/31/2011. Patients received at least 2 diagnoses of PD, with first date identified as index date. Patients were required to have continuous insurance coverage 1 year prior through 3 years post index date and be at least age 35. Unadjusted comparisons of characteristics and resource utilization based upon patient age (<65 v ≥65) were conducted using chi-square statistics for categorical variables and t-tests for continuous variables.

Results: 16,022 individuals met inclusion criteria: 4,739 < 65 and 11,283 ≥65. Older patients were more likely to be female (63.20% v 56.80%; P<0.0001), less likely to reside in the South (27.86% v 35.01%; P<0.0001) and less likely to be diagnosed by a neurologist (51.83% v 67.35%; P<0.0001). Older patients were more likely to reside in Northeast (19.49% v 13.42%; P<0.0001) and be diagnosed by a general or family practitioner (39.16% v 24.37%). In one year prior to initial diagnosis, older patients were significantly more likely to have an office visit (77.34% v 69.11%; P<0.0001), an emergency room (ER) visit (30.97% v 12.83%; P<0.0001), a neurologist visit (19.70% v 18.17%; P=0.0246) or a hospitalization (22.31% v 7.22%; P<0.0001). After PD diagnosis older individuals were significantly less likely to have an office visit (96.26% v 99.43%; P<0.0001) or a neurologist visit (72.22% v 83.60%; P<0.0001). Older age is generally associated with poorer health and increased healthcare resource utilization, the lower utilization of office and neurologist visits suggests potential gaps in treatment for these individuals.

P34.05

Our experience developing a service for in-patients with Parkinson's

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Objective: In our region there are 10,500 people living with Parkinson's disease (PD). 1 in 3 patients with PD are admitted annually. 75% of admissions are emergency admissions.

There are on average 10 PD in-patients at the RD&E per day. The average length of stay is 24 days (1.94 days higher than expected). In-patient care is often sub-optimal and only 40% of PD patients

receive an accurate medication regime within 24 hours of admission.

Methods: In January 2013 we opened a PD ward focusing on multidisciplinary, patient-centred care. We have also designed a PD care pathway. It identifies patients at the earliest stage of their admission ensuring they receive specialist care whether on the PD ward, or elsewhere in the hospital. These arrangements will improve care for PD patients, in particular medication management.

A PD Nurse Specialist will see emergency PD admissions on arrival. These patients can then be diverted to the appropriate setting. This will make the patient journey less fragmented and will improve their in-patient experience. This may also prevent unnecessary admissions, ward transfers and ensure patients 'get to the right ward at the right time.'

Outcomes: Our aims from developing this service:

- Reduced length of stay – target 20%
- % accurate PD medication prescribed and taken within 24 hours from 40 to 80%
- Reduction in prescribing errors from 27% to <5%
- Reduction in unplanned readmissions
- Patient satisfaction measured by a patient questionnaire
- % of patients self-medicating increase from 30 to 70%

P34.06

Developing an innovative model of care for a Nurse Managed Health Center - Parkinson's disease telemedicine clinic

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There is ample evidence that medical, surgical and exercise interventions have potential to significantly improve the symptoms and quality of life of people living with Parkinson's disease (PD). It has been demonstrated that regular visits to a neurologist was associated with better control of symptoms, lower risk of injury and long term facility placement, and greater survival. However, in many areas of the USA access to PD focused care is lacking. On the Delmarva peninsula PD patients can travel up to 10 hours for treatment by a movement disorder specialist in one of the surrounding states. We will use a telemedicine approach to import the expertise of a movement disorder specialist to care for the medical needs of our PD patients.

Purpose: Describe the development of a unique PD Telemedicine Clinic designed to specifically meet the complex needs of PD patients.

Methods: Stakeholders included people living with PD, caregivers, a movement disorder specialist with expertise in telemedicine, the state Division of Services for Aging and Adults with Physical Disabilities, BCBS, local neurologists, and Advanced Practice Nurses with PD expertise. Each was included in discussions regarding the development, composition, and evaluation of the clinic. Evaluation will occur at the end of three months of operation for feasibility, cost, impact and satisfaction by users.

Results: Educational needs were identified for patients, caregivers and staff of the Nurse Managed Health Center. Access to PD knowledgeable providers such as movement disorder specialists, advanced practice nurses, psychologists, speech, physical and occupational therapists was requested. Access to relevant exercise programs, and clinical trials were also requested. State and private insurance stakeholders requested evaluation of impact on quality of care and cost-effectiveness of this new model of care.

Conclusion: This information will inform the structure and function of our new PD telemedicine clinic.

P34.07

Does a specialist unit improve outcomes for hospitalised patients with Parkinson's disease? A prospective study

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Objective: Suboptimal management of Parkinson's Disease (PD) medication in hospital may lead to avoidable complications and increased length of stay. We introduced an in-patient PD unit for those admitted urgently with general medical problems. We explored the effect of the unit on medication management, length of stay and patient experience.

Methods: We conducted a single-center prospective feasibility study. The unit's core features were defined following consultation with patients and professionals: specially trained staff, ready availability of PD drugs, guidelines, and care led by a geriatrician with specialty PD training. We compared patient outcomes before and after introduction of the unit. Mandatory staff training comprised four one-hour sessions: PD symptoms; medications; therapy; communication and swallowing. Most medication was prescribed using an electronic Prescribing and Administration system (iSOFT). A patient experience survey was administered.

Results:

	General Ward Care	PD Unit care	p-value
Baseline characteristics			
Number	20	24	
Age – median (Interquartile range)	81 (75-84)	81 (73-84)	0.611
Gender: male – no. (%)	16 (80%)	16 (67%)	0.498
Stage (% Hoehn-Yahr 4 and 5)	6 (30%)	14 (58%)	0.160
Outcomes			
PD medication doses given (% of all prescribed doses)	1,827 (82%)	1,307 (86%)	0.022
PD medication given on time [within 30 minutes of scheduled time] (%)	949 (44%)	904 (60%)	<0.001
Patients with any PD medication prescription error(s) (%)	12 (67%)	11 (46%)	0.221
Length of stay – days: median (IQR)	13 (9 - 27)	9 (5-16)	0.043
Patient experience – overall experience of care (higher scores better): median (IQR) (n=31)	3 (2-3)	3 (3-4)	0.016

Discussion: If replicated and generalisable to other hospitals, reductions in length of stay would lead to significant cost savings. The apparent improved outcomes with Parkinson's unit care merit further investigation. We hope to test the hypothesis that specialized units are cost-effective and improve patient care using a cluster-randomized controlled trial design.

CARE DELIVERY & QUALITY OF LIFE: DAILY LIFE ACTIVITIES INCLUDING WORKING & DRIVING

P35.01

Freezing of gait symptoms in Parkinson's impairs vision for perception but not action: evidence from gait with obstacles

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Objective: The aim of current study was to evaluate whether the foot elevation (to step over an obstacle) in PD patients with FOG symptoms would be influenced during height judgements of an obstacle's height during static condition.

Methods: Fourteen PD patients with FOG (PD-FOG), thirteen PD patients without FOG (PD-nonFOG) and thirteen healthy control participants (HC) judged the height of an obstacle using a measuring tape, from the starting position (perceptual estimate) prior to walking toward, and stepping over the obstacle. Participants had to inform the experimenter to stop opening the tape when they perceived that the length of the tape matched the obstacle height. Active iRED markers were placed on the 5th metatarsal of each foot to measure the max toe elevation of each foot when stepping over the obstacle.

Results: A group effect ($F_{(2, 38)}=5.8047$; $p=.006$) showed that PD-FOG had significant greater variable error and lower accuracy (typically underestimating the obstacle height) ($p=0.047$) when estimating the obstacle height compared to HC participants. There were no differences between groups for foot elevation performance when actual walking trials were completed. Pearson's correlations revealed that only HC had a significant positive correlation between perceptual estimate of the obstacle height with: i) foot elevation ($r=0.554$; $p=0.03$) and, ii) actual obstacle height ($r=0.674$; $p=0.008$).

Conclusion: In sum, our results demonstrated that FOG symptoms in PD affect the perceptual judgement of the obstacle height; however it does not affect the control involved in physically stepping over an obstacle. A selective perceptual impairment is suggested by these results, and needs to be carefully considered for its influence on tripping and falling in this specific population.

P35.02

The experience of motor and non-motor symptoms during daily life with Parkinson's disease

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Objective: People with Parkinson's disease (PD) have a variety of symptoms, yet there is very little research on how they spontaneously describe motor and non-motor symptoms in their daily life. The purpose of this study was to examine how people with PD experience their symptoms relative to their participation in daily life activities.

Methods: Open-ended interviews of 38 participants with PD (Hoehn & Yahr Stages I–III) discussing their daily life experiences in the past few weeks were transcribed verbatim and content analyzed. A coding system was developed to detect participants' spontaneous talk about symptoms and daily life activities. Motor symptoms were coded as a general movement problem, hypokinesia, hyperkinesia,

or an axial or functional motor control impairment. Non-motor symptoms were coded as a general non-motor problem, a problem in cognition, affect, sensory experience, fatigue, sleep, or autonomic function. Nonspecific symptoms were coded when participants referred to the disease affecting their activity without providing distinctions between motor and non-motor symptoms. Activities were coded as rest or sleep, basic activity of daily living, instrumental, low-demand leisure, high-demand leisure, social or other. The coding system demonstrated adequate inter-rater reliability.

Results: Participants described 145 daily life activities, 68 (47%) of which were experienced with PD symptoms (average = 1.7 activity-related symptoms per participant). Motor symptoms were mentioned more frequently (31 times, 46%) than non-motor (22 times, 32%) and nonspecific (15 times, 22%) symptoms. Motor symptoms, especially axial or functional motor control impairments, were mentioned most frequently during basic activities of daily living, high-demand leisure, and social activities. Non-motor symptoms, especially sleep problems, were mentioned most frequently during instrumental, low-demand leisure and social activities. Nonspecific symptoms were spread in roughly equivalent rates across activity categories. People with PD spontaneously mention motor and non-motor symptoms as linked to specific types of daily life activities.

P35.03

Working with Parkinson's disease: extent and nature of problems and adaptations

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Objective: Inability to maintain employment has considerable consequences for the person with Parkinson's disease, employers and society. The aim of the study was to investigate in which way and to what extent Parkinson's disease impacts on work and what kind of support and adaptations patients receive.

Methods: A descriptive quantitative research was conducted (2011/2012). Data were received from the National Social Security Institute of Employee Insurances and a one-time survey was executed. For the survey, persons who have (had) experienced being employed while having the diagnosis Parkinson's disease were invited to participate via various media. The questionnaire was developed on the basis of the literature, expert opinions and patient perspectives and with use of the International Classification of Functioning, Disability and Health.

Results: In 2011, 1467 Parkinson's disease patients in the Netherlands received disability benefits due to (partial) incapacity to work, of whom 88% was considered completely unable to work. The questionnaire was completed by 293 patients; 63% were still employed. Fatigue was the most reported complaint impacting on work (61%); diminished fine hand use (58%) and undertaking multiple tasks (51%) were most reported activity limitations. Adaptations to work were realized in 66% of the respondents. Accommodation of task content and working hours were most frequent adaptations. Only 38% received information, advice or support about working with Parkinson's disease. One year after diagnosis 9.4% stopped paid employment; this increased to 50% after 8 years (Kaplan Meier survival analysis). Factors significantly associated with giving up work were age of diagnosis (hazard ratio 1.16; 95% CI: 1.096-1.219; $p=0.000$) and moment of first adaptations at work (hazard ratio 0.76 (95% CI: 0.680-0.839; $p=0.000$) (Cox proportional hazard analysis). So, the older the age

at diagnosis and the earlier adaptations at work are necessary, the sooner a Parkinson's disease patient gave up work.

P35.04

Utilization of occupational therapy in management of impairments in Parkinson's disease

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Objective: 1) Describe current occupational therapy interventions to assist individuals in minimizing disability using exercise, compensatory strategies, and adaptive equipment. 2) List examples of strategies, exercises, and adaptive equipment frequently found to be effective in PD.

Methods: In sample of 207 patients, referred for outpatient occupational therapy treatment, the reported problems resulting in OT referral were difficulties with performance of functional ADL's (89.9%), bed mobility (68.1%), and instruction in PD-specific exercises to promote functional ability (76.8%), medication management (22.7%), cognition (7.7%), driving (6.8%), falls prevention (5.3%), and writing (3.9%). Patients were trained in home exercises to promote trunk rotation, shoulder flexion, fine motor coordination with emphasis on stretching and large amplitude motions. These movements were incorporated with instruction in alternate methods of performing tasks to compensate for decreased motor control, bradykinesia, rigidity, perceptual deficits, balance impairment, tremor, and decreased coordination. Instructions were determined by the patient's specific strengths and difficulties. When appropriate, adaptive equipment was recommended.

Results: Patients reported feeling benefits of upper body exercises relative to performing functional tasks more easily. They reported less difficulty and demonstrated increased independence in performance of common ADL tasks, by effectively using alternate methods and adaptive equipment appropriate to their needs.

Conclusions: Individuals with PD report and demonstrate benefit from instruction that addresses their specific priorities and difficulties to increase and preserve their ability to function in daily life. This involves the current understanding of exercise and instruction in methods immediately addressing the functional difficulties the person experiences.

CARE DELIVERY & QUALITY OF LIFE: SELF-MANAGEMENT, EMPOWERMENT, COPING STRATEGIES

P36.01

Reclaiming positive perspective: secrets to success living life to the fullest with Parkinson's disease (PD)

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Objective: The objective of this presentation is to enlighten Parkinson's patients about the substantial control they have over the quality of their own life.

Methods: By being forewarned about the less desirable common emotional stages of PD, patients have the opportunity to move through the difficult stages more quickly. Some form of shock is experienced when diagnosed, followed by disbelief. Denial occurs because PD is frequently misdiagnosed, and no definitive

confirmatory test exists. We have a right to be angry and depressed. Having PD is not our fault. PD will likely eventually affect our ability to talk, walk, think, swallow, have sex, drive, and even go to the bathroom. These emotional stages should be communicated to all, especially newly diagnosed patients.

Results: By explaining the emotional stages involved with PD, patients can accept, and even embrace, PD sooner. When I was diagnosed, shock, disbelief and denial paralyzed me and anger and depression were poison to my soul. My new "job" became to sustain the highest quality of life for the remainder of my life. My Plan was to envision myself with the highest quality of life; to remember to live in the moment; to create a "bucket list" and experience each item; to keep a positive attitude; to have faith in myself; to eat healthy, organic food; to exercise daily, gradually getting out of my comfort zone; to perform activities that keep me mentally sharp; to discover my life's purpose as an inspirational speaker and author; to be more loving, kind and compassionate; and to accept, and even embrace, PD by finding meaning (silver linings) in the disease. The ultimate result of enacting this plan is that I am healthier now, over ten years into my PD, than I ever was before I started exhibiting symptoms of PD.

P36.02

Learning experience from a family intervention research project: benefits for couples living with Parkinson's disease

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Background: Around the world, Parkinson disease (PD) affects millions of people and their families. The majority live at home and are cared for by an elderly spouse. The complex changes and trajectory of the illness often leave these couples ill prepared to face the challenges ahead. Many clinicians and researchers emphasize the need for studies that examine specific family interventions oriented towards this clientele.

Objective: Describe a family intervention and the approach underpinning its development and evaluation.

Frameworks: Transition Theory (Meleis et al., 2000), the Calgary Family Assessment and Intervention Models (Wright & Leahey, 2009) and the Intervention Mapping Scheme (Bartholomew et al., 2006) were selected as frameworks for this study.

Methods: A qualitative design and a participative process were utilized. Ten elderly couples, four health care professionals and two consultants collaborated in the intervention development. Three new couples took part and evaluated the intervention (contents, structure, process, usefulness). Couples were recruited from a Movement Disorders Clinic (Montréal, Canada). Data from semi-structured interviews with these couples was subjected to constant comparative analysis.

Results: The intervention consisted of seven bi-monthly sessions of ninety minutes. The themes of the sessions were based on the couples' needs and preferences. The intervention was oriented towards the couples' concerns and specific objectives; health promotion, problem solving, access to resources, communication and role adjustment. The study results showed the feasibility, the acceptability and the utility of the intervention. The main benefits observed by the couples were; the ability to find solutions adaptable to various situations which are favorable to both partners, the skills to get help and services, an increased feeling of mastery, mutual support, pleasure and hope.

Conclusion: Our study provides a guide for the development and the evaluation of family interventions tailored to the context and the needs of elderly couples living with PD.

P36.03

The Advantages of Parkinson's and other (un)likely stories

Paul MacDonald, Philip Beckett

Background: Two individuals who each had that unusual combination of characteristics: Parkinson's; a penchant for sharing ideas; a skill in communicating and a wry sense of humour, met and fed from each other's ideas. A cartoonist who uses his skill to illustrate many aspects of life and a poet who can only occasionally suppress his instinct for a humorous punch line came together and produced a series of words and pictures that look at Parkinson's in a light hearted way, focusing on things we all might recognise, but often we need to have it pointed out to make us smile – and we all need to smile!

Aims/objectives:

- primarily to bring a smile to the faces of people by making them realise that Parkinson's can be laughed at
- to produce material for an exhibition and a book, including work from artist and poet together, inspired by each other, as well as work from each that stands alone.
- to keep Parkinson's in perspective by commenting through their various mediums on life in general
- to attract attention, increase awareness and to have fun doing it.

Method : We each had a stock of work already completed and the idea of combining those in a book and an exhibition was suggested. But linking the two, poetry and cartoons, sparked inspiration. Not only could the artist illustrate the poetry, but the artwork could inspire the poet – this was a rich source of raw material for both men. The focus on searching out and depicting advantages that Parkinson's might give an individual generated many ideas, from ridiculously funny to sublime. At the congress, we propose handing out postcards containing Parkinson-related cartoons and a short poem, limerick or similar and ask individuals to write on the card a comment about the thoughts, emotions or feelings the images or words induced in them. To collect, analyse and report upon the responses. Also at the congress, we will write topical poems and draw relevant cartoons as the event progresses, picking up aspects of the congress from people's experiences and reporting these as a live blog, maintaining a positive and "good fun" stance.

Outcomes: The poster will present information on progress towards our aims, information about the book and exhibitions and any proceeds to be donated to Parkinson's charities, but our wish is to spark positive attitudes through laughter and looking at life from new perspectives, thus to broaden people's awareness. Measuring this will be possible if sufficient numbers of postcards are returned.

P36.04

Developing Northumbria Parkinson's information service: exploring health professionals' perceptions of information provision

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Objective: Improving information provision is fundamental to supporting people with Parkinson's disease (PD) to manage their condition. It has been a primary driver in recent UK government policies. Few research studies have focused on information provision in PD. Participatory research was used to improve information provision for people with PD and their carers. Specifically, this phase aimed to: (1) Explore how information is provided within Northumbria Parkinson's Service; (2) Explore health professionals' perceptions of the facilitators and barriers to information provision; (3) Develop recommendations for practice.

Methods: Fourteen semi-structured interviews were carried out on a purposive sample of health professionals, including four PD nurse specialists, three doctors, six allied health professionals and one community specialist nurse. Interviews were analysed using thematic analysis (Braun & Clarke, 2006).

Results: Four main themes emerged: (1) 'information provision systems' described the systems that were needed to provide information to people living with PD, including participants' perceptions of what and how information should be delivered and how information provision should be recorded; (2) 'providing the right information at the right time by the right person', included participants' perceptions of how to avoid information overload, how to assess people's individual information needs and who should provide information; (3) 'perceived barriers to information provision'; and (4) 'impact of information provision', including participants' perceptions of whether information provision always has its intended impact. These findings were corroborated with findings from patients and carers consultations to make service-level and organisational recommendations on improving information provision. An action plan was created for Northumbria Parkinson's Service including the development of health professional-led and patient-led information provision models; information events for newly diagnosed patients and their carers; new information resources; and personal health records.

P36.05

An introduction to the Voices of Hope Choir for people with Parkinson's disease

Jennifer Grundulis, Christine O'Mahony

Move4Parkinson's, Dublin, Ireland

Objective: To provide information on the current Move4Parkinson's Voices of Hope choir (VoH), created specifically for PwP, their family and friends.

Methods: The VoH was created in September 2012 after SLP Jennifer Grundulis gave a talk on choral singing for PwP at the Move4Parkinson's Empowerment Day in Dublin, in June 2012.

No formal evaluation of the choir has been undergone at present, though choir members do submit an anonymous 'check-in' form which they fill out upon beginning and then ending of rehearsal, which asks members to identify how they are feeling at those moments. Personal statements and surveys have been collected from members.

Results: Anecdotal evidence from choir members has been overwhelmingly positive. Weekly check-in forms have demonstrated an immediate positive impact on choir members:

Pre-Rehearsal Statement

Jittery and nervous

Self-conscious/ under-confident

Nervous with the shakes- but looking forward to the practice

Post-Rehearsal Statement

Much happier and at ease

Heart feels wide open! Amazing

So enjoyed the evening. I feel uplifted

Member statements collected in December 2012 indicate a positive impact. One wrote, "(The Voices of) Hope choir has shown me that there are no limits. Thursday is my oasis. Move4Parkinson's has got me living again and provided lots of practical support with love and kindness... This is world changing for all of us and more."

Survey of choir members in April 2012 indicated 100% of participants felt their voice had improved since joining choir. Of those with PD, 85% noted an improvement in how good they feel, 71% an improvement in how loud they sing, and 57% an improvement in how loud they talk, how deep a breath they can take and how well they can follow a rhythm.

P36.06**Evaluation of a maintenance exercise program for people with Parkinson's disease over a three year period**Christine Huston¹, Juliette Looker¹¹Nottingham University Hospital NHS Trust, Nottingham, UK

Objective: To evaluate the uptake and effect of a weekly physiotherapy led exercise class for people with Parkinson's disease in maintaining physical function.

Methods: Weekly exercise groups consisting of stretching, core stability training, strength and balance exercise was set up in a local church hall with places for forty individuals at any one time. Participants self referred and were permitted to attend as frequently or infrequently as they chose. On first attendance Berg Balance Scores, Timed Up and Go test, Lindop Scores, Parkinson's disease questionnaire 39 and PD Non motor symptom questionnaires were completed. These tests were repeated at 4 monthly intervals and a record of attendance kept. Test scores were collated for individual participants over the period of time they attended the group and results shared with the individual. Individual data sets were then collated and analysis of data undertaken in 4 months blocks (e.g. cohorts of individuals attending for 4 months, 8 months 12 months etc)

Results: Preliminary results Total number of participants over three years 89. 16 individuals attended over three year period. During the first 4 months of attending there was a 3.18% ($p > 0.05$) improvement in Berg Balance score, trend towards improvement was noted in TUG. This improvement was maintained in 81% who continued to attend 75% of the classes over a period of 28 months. Beyond this individuals required targeted physiotherapy to restore TUG, and Berg Balance score to normal ranges. (Analysis of additional scoring and correlations not yet completed)

P36.07**An evaluation of an occupational therapy memory group for those with mild cognitive impairment in Parkinson's**

Clare Johnson

Derby Hospitals NHS Foundation Trust

Objective: This is an evaluation of the content and outcomes of a group ran by Occupational Therapists for people with mild cognitive impairment in Parkinson's. The group aims to educate patients and carers about memory impairment and to teach strategies to use daily to maintain independence and confidence. With a score between 21/30 and 27/30 on a Montreal Cognitive Assessment (MOCA) patients were invited to attend.

Methods: The group is 90 minutes per week for seven weeks, consisting of six patients. The weekly format included an education topic, practical exercise and learning strategies. Topics for education included; what is memory, how it relates to Parkinson's, external factors and other cognitive difficulty in Parkinson's (dysexecutive function). Focus was made on attention and concentration impairment. Written information was given to take to read and share with carers. Strategies provided varied from white boards / diaries to prompt, to association. At the beginning and the end a memory questionnaire was completed. An evaluation of content and format was completed at the end. A MOCA was completed following.

Results: The memory questionnaire rated how often they have difficulties with everyday activities. There was a reduction overall in frequency of memory problems. In the evaluation questionnaire, education was the most useful part of the group, the exercises were difficult to manage within the group setting. An evaluation of the number of strategies used found there was an increase used by all patients following the course. It was evident though that the most

beneficial part of this group was that they felt they were not alone and were able to share memory difficulties with others without shame.

P36.08**Application of the Integrated Chronic Care Management model using LSVT BIG and LSVT LOUD protocol framework for care of people with PD in the home**Bernadette Kosir¹, Kerry Wilson¹¹Residential Home Health, Madison Heights, MI, USA

Objective: Health coaching models have become prevalent and successful in facilitating effective patient care transitions across care settings and in reducing rehospitalization of high risk patients with chronic or progressive conditions, including people with Parkinson's disease. The implementation of such models with PD using LSVT BIG and LSVT LOUD treatment protocols will be presented.

Methods: Successful coaching models, such as the Integrated Chronic Care Management (ICCM) model, train and equip health coaches with a knowledge base of best practices for self-management support which ultimately focus on a patient's unique goals. Residential Home Health clinicians certified in LSVT BIG and LSVT LOUD are trained in parallel self-management support techniques that engage and empower patients for improved quality of life using evidence-based protocol techniques. These sensory calibration techniques have been applied by physical, occupational, and speech therapists at all stages of Parkinson's disease with over 500 patients, with improvement noted in OASIS comprehensive data set scores of critical functional skills required to maintain safety in the home and engagement in the community.

Results: Our experience with implementation of ICCM techniques and tools including Motivational Interviewing, team conferencing, assessment of Confidence to Change, and assessment of Importance of Behavior Change, to home-bound patients using LSVT BIG and LOUD treatment framework will be discussed. Data related to improved OASIS functional data set scores as well as a significant reduction in rehospitalization rates for this at-risk population will be presented through case study examples.

P36.09**Twenty-five years of discovery: A longitudinal study of Parkinson support groups**Sheree L. Loftus, PhD^{1,2}¹Beth Israel Medical Center, NY, NY, USA,²Hunter-Bellevue School of Nursing, NY, USA

Objective: Alzheimer's and Parkinson's have emerged as increasingly common neurodegenerative diseases associated with the aging population. Support groups are a missing link in the continuum of care for those with chronic illness and their caregivers. Documentation and presentation of twenty-five years of discovery of the cumulative lived experience of Manhattan Parkinson Groups, with focused attention to the content and purpose of groups.

Methods: Support groups play an integral role in the chronic care community. Data on the activities, concerns, and experiences of support group members during meetings were recorded through transcribed meeting minutes and longitudinal documentation. Manhattan Parkinson Group ideas and themes were identified through the data written as text. The three Manhattan Parkinson Groups where data was recorded were at Columbia University Medical Center from 1985-1988, New York University Medical Center from 1990-1994 and Beth Israel Medical Center 1994-2013. Complete anonymity was maintained as names of participants were

never recorded for this study. Consent for transcription of meeting minutes was given by all.

Results: Group themes include maintaining dignity, independence, social and family roles, and being informed. Groups provide a confidential oasis in the drought of chronic illness care in the United States. They provide an opportunity for patients to share issues with others living with and experiencing the same disease. Non-motor symptoms of Parkinson disease such as hypotension, insomnia, incontinence, depression, constipation, skin care, difficulty with sex, exercise, speech, swallowing, mobility, balance, falls and pain, were consistently identified as Nursing care concerns needing attention. Family caregivers and those with long term Parkinson disease identified the medical community "forgot" them once medical or surgical treatment options were expended. Support groups are for patients and families alike to discuss concerns about care, health, life, relationships and subjects too time-consuming or controversial to discuss with their primary health care provider.

P36.10

The effect of a music cue on gait and impact on quality of life in Parkinson's: two case studies

Fiona Lindop

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Objective: To investigate the effect of music on gait and impact on Quality of life (QoL)

Methods: Patient A, diagnosed with Parkinson's in 2001, now experiences marked freezing of gait (FOG), no longer responding to cognitive, visual, verbal or metronome cueing. Patient B, diagnosed 2009, experienced FOG, axial rigidity on turning (especially when dual tasking), reduced stride length and ground clearance. Reduced confidence in going out was a direct result of FOG and anxiety a prominent non-motor symptom. For both patients, gait was measured using three tasks on the Lindop Parkinson's Assessment Scale: timed up and go (TUG) and 180° turn to right and left. These were immediately repeated while listening to music through headphones.

Results: Improvements in TUG and turn scores when using the music can be seen in Tables 1 and 2. Patient A found "easy listening" music most helpful while Patient B experimented with different genres, finding marching music most beneficial. Using the MP3 player she demonstrated the ability to walk backwards safely and dance a "jig", neither of which were possible without the music. She reported that "playing the right music is like turning on a power switch, and when the music stops it's like turning off the power again". Using a music cue has positively impacted both patients' mobility, reducing FOG and improving QoL, particularly for Patient B, with improvement in all questions on the PDQ-39 stigma domain and some areas of mobility. She reports decreased anxiety and feels she can "walk more naturally and feel less awkward". A larger study is planned to compare the effectiveness of a metronome with listening to music.

Table 1: Patient A

	Timed Up and Go (with 3-wheeled frame)	180° turn to Right	180° turn to Left
No Music Cue	1 minute 33seconds	34 steps	36 steps
With Music Cue	34.8 seconds	14 steps	22 steps

Table 2: Patient B

	Timed Up and Go (no walking aid)	180° turn to Right	180° turn to Left
No Music Cue	14.7 seconds	5 steps	5 steps
With Music Cue	9.2 seconds	3 steps	3steps

P36.11

The effectiveness of self-management support strategies used by health care professionals

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Objective: Parkinson's care constitutes an ongoing process of team treatment and support provided by clinicians and lay personnel based on the changing condition. In addition to providing optimal medical care, health care professionals (HCP) recognize that outcomes are largely mediated through patients' own behaviour and lifestyle which occurs after they leave the clinical setting. The goal of self-management support (SMS) is to empower and prepare patients to make decisions and to engage in healthy behaviors and acknowledges the patients' central role in their care.

Methods: To address client behaviour, clinicians are becoming skilled to incorporate SMS strategies including behavioural counselling interventions into routine practice. Two methods were employed to investigate the relative effectiveness of various SMS strategies: a) the development of "evidence-based" best practice guidelines on SMS by the Registered Nurses Association of Ontario; and b) an investigative report examining SMS in primary health care by the Health Council of Canada.

Results: Varying levels of evidence ranging from "Expert Opinion" to "Systematic Reviews of Randomized controlled trials" have been allocated to 10 strategies that can be utilized by HCP's in clinical practice.

P36.12

Home-based training with Nintendo Wii Fit and balance board in Parkinson's disease: Is it a tool for self-management motor activities in long term care?

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Objective: evaluate the efficacy on postural control of a home based training using Wii Fit with Balance Board in subjects with Parkinson's disease (PD), comparing the effects with a control PD group performing the same exercises without Wii Fit. Furthermore we checked patient compliance to motor activity to ensure regular self-management for implementing long term benefit of rehabilitation program.

Methods We enrolled 20 subjects with PD, recruited on a voluntary basis throughout PD meeting group. Patients performed a daily home based training program in "on" condition for 3 months. They independently managed after a proper supervision and guidance of

the first training session plus four scheduled physiotherapist's supervision meetings. Two groups were determined. Group 1 based on exercises with Wii Fit and Group 2 with the same exercise protocol without Wii Fit. Disease stage (H&Y and UPDRS III), quality of life (PDQ-39), balance (Berg balance scale-BBS and force platform analysis) and disability (Schwab and England) were assessed at baseline and after 3 months treatment. Patients underwent a brief neuropsychological test to assess frontal and executive functions and compliance to treatment. Caregiver burden was also assessed.

Results At baseline both groups did not differ in clinical variables. Group 1 significantly improved ($p < 0.05$) in UPDRS, PDQ39, BBS and in force platform data after treatment, compared with Group 2, with a mean of 70^h of self-managed motor activities in Group 1 and 45^h in Group 2. Furthermore neuropsychological data highlight a positive effect on depressive state (BDI) and coping strategies. Home based balance training using Wii Fit could improve postural control in people with Parkinson's disease with a better compliance for independent motor activities. In our hypothesis visual feedback and motivating environment, continuous reinforcement and results obtained in games are pleasant components of training that can maximize compliance with motor activity.

P36.13

Applying the self-determination theory to gait retraining in people living with Parkinson's disease: potential directions for intervention

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The Self-Determination Theory provides a framework that might be useful in understanding and shaping rehabilitation interventions. The Self-Determination Theory describes different types of motivation, as well as ways that self-determined forms of motivation can be developed or enhanced. According to this framework, the satisfaction of three basic psychological needs of autonomy, competence, and relatedness facilitates the development of self-determined motivation. These types of motivation are particularly relevant in the context of rehabilitation, because they can be related to the initiation and maintenance of behaviour (Deci & Ryan, 1985, 2002), such as rehabilitation activities. According to Sirur, Richardson, Wishart, and Hanna (2009), rehabilitation interventions should be theoretically informed such that the intervention supports practice adherence. Incorporating the Self-Determination Theory into intervention design can enhance the possibility of achieving adherence and, as a result, meaningful participant outcomes. Recently a home-based gait-retraining intervention for individuals with Parkinson's disease was piloted in London, Ontario, which resulted in 100% home-practice adherence. Although not initially developed as a motivational intervention, it appears that the three basic psychological needs were implicitly supported due to the intervention design. This pilot intervention will be discussed in relation to the Self-Determination Theory, highlighting the potential use of this framework in rehabilitation programs for people living with Parkinson's disease.

P36.14

Health information seeking in young-onset Parkinson's disease: sources and foci

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Health information seeking refers to the purposeful behavior of trying to acquire information on a particular health-related topic. For those with young-onset Parkinson's disease (YOPD), the diagnosis often leads to a number of difficult questions that require engagement in health information seeking.

Objective: Subjects living with YOPD, for periods ranging from one to 15 years, were asked to report on their health information seeking behavior.

Methods: Using grounded theory methodology, individuals with YOPD participated in at least one of three means of data collection: multiple interviews, focus groups and/or an online discussion board. Part of the discussion within each of these methods focused specifically on the sources of information used to acquire health information, the value of the information sought, difficulties encountered, and how they perceive that their information seeking has changed over time.

Results: Based on initial data from 24 individuals with YOPD (14 male / 10 female), a number of important categories have emerged. In terms of the types of sources used to acquire information, participants drew distinctions between personal sources of knowledge (physicians, other individuals with PD, discussion boards, etc.), extant sources of knowledge (books, articles on the Internet, etc.) and knowledge gained from one's own experience living with YOPD. The value placed on each of these sources varied greatly and was influenced by a multitude of factors, such as one's relationship with their physician, the age of a person with PD, and one's expectations for finding answers to health questions. It also appears that over time information seeking shifts from 'general' information about YOPD being sought immediately after diagnosis, towards more 'specific' information being sought later in the disease; depending on the unique issues confronting an individual. Understanding health information seeking will help to optimize health education for persons with YOPD.

P36.15

Self-monitoring in Parkinson's disease – exploring traveling over multiple time-zones

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Introduction: Function and wellbeing of people with Parkinson's are highly dependent on dosage and consistent timings of medication. Travelling across multiple timezones poses particular challenges for people with Parkinson's with respect to medication timings.

Objective: Exploring the effects of a changed medication schedule and of jetlag induced by traveling over multiple timezones on the physical functions of the author.

Methods: Data were collected during the first 48 hours of a 10 day trip Stockholm – Chicago, departing Stockholm at 10.15 am 27/10/2012 and arriving Chicago 12.20 pm the same day (local times). Normally the time difference is 7 hours but during the night of 27/28 Oct, the US shifted to daylight savings time, resulting in a time difference of 6 hours for the remainder of the trip. The author took her medications less often during the day of travelling to be able to start the next day synchronised with local time.

Times for medication intakes and other relevant observations were noted. For evaluating physical function, a 30 second smart phone finger tapping test was used (iOS app Fast Fingers). Tapping tests are used in clinical evaluation of medication efficiency in Parkinson's (Westin, 2010). In all 29 measurements were recorded with tapping at maximum speed with right and left hand respectively.

Results and conclusion: Scores spanned from 69 (right hand)/53 (left hand) to 135 (right)/119 (left) taps per 30 seconds. The 5 highest values for both hands were recorded during the first 24 hours and the 5 lowest during the second 24 hours.

Data indicate that self-monitoring can be helpful when deciding the best method for changing medication timings when travelling across multiple time-zones. More data will be collected when the author travels to WPC in Montreal.

References: Westin, J. (2010). Decision Support for Treatment of Patients with Advanced Parkinson's Disease. Uppsala University

P36.16

Expressive writing improves psychosocial functioning of patients with Parkinson's disease and their caregivers

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Objective: Expressive writing is a novel psychosocial intervention that may effectively target both non-motor symptoms (NMS) and caregiver stress in order to enhance quality of life (QOL) for patients and caregivers coping with Parkinson's disease (PD).

Methods: A randomized, controlled trial was conducted at an interdisciplinary movement disorders specialty clinic to determine the psychological, cognitive, and QOL effects of journaling for twenty minutes on three occasions about an emotionally stressful topic (expressive writing) ($N=17$) compared to a neutral topic (control writing) ($N=12$) among patients with a confirmed PD diagnosis ($N=19$) and their caregivers ($N=10$).

Results: Initial results were analyzed using multivariate analyses of variance to determine the effects of the different writing exercises on patient NMS and health-related QOL and caregiver burden from baseline to immediate post-intervention, 4 month follow up, and 10 month follow up. Trends in the results indicated that patient NMS and QOL remained relatively stable over time in the overall sample; however, patients in the expressive writing condition showed reductions in NMS and improvements in QOL, while patients in the control group showed the opposite pattern. Caregiver burden was generally alleviated over time, but larger improvements were observed for caregivers in the expressive writing condition than for caregivers in the control group. Expressive writing appears to improve non-motor functioning, QOL, and caregiver stress over time, but neutral writing does not. Use of expressive writing and other psychosocial interventions may attenuate the typical symptom progression and increasing caregiver burden of PD and other movement disorders.

CARE DELIVERY & QUALITY OF LIFE: PHARMACIST, SOCIAL WORKER & NONPROFIT TEAM MEMBERS

P37.01

Multidisciplinary care in professional networks for Parkinson's disease

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Objective: The ParkinsonNet concept, a national multidisciplinary network of specialized health professionals, aims to improve the quality of healthcare for patients with Parkinson's disease (PD) in the Netherlands. A major challenge is to optimize multidisciplinary collaboration between health professionals. This study examined whether the introduction of ParkinsonNet enhances multidisciplinary collaboration between professionals involved in PD management.

Methods: A regional ParkinsonNet network involving 101 health professionals from 10 different disciplines was newly established. Using a parallel, mixed-methods design, participants received two surveys (one aimed at documenting network connections; and the other aimed at evaluating team-effectiveness); these were delivered at baseline (T0) and after one year (T1). Additionally, thirteen health professionals were interviewed at T0 and T1. Data analysis focused on collaboration within sub-networks around three community hospitals.

Results: After one year, the number of professionals that knew each other and worked together increased significantly compared to baseline ($p < 0.001$). However, large differences between sub-networks were found, positive changes being associated with a prominent role of a neurologist and PD nurse specialist committed to allied health interventions. Team-effectiveness showed a small but non-significant improvement. Interviewees reported improved communication lines between health professionals one year after the establishment of the network. However, participants acknowledged that interdisciplinary communication and information exchange could be further improved. For example, professionals were not aware of the other providers engaged in the healthcare team of individual patients. The introduction of a regional professional network of professionals specialized in PD made a connection between healthcare professionals, without having a major impact on multidisciplinary collaboration. One year after the introduction of the network, communication and information exchange across traditional echelons and institutions could still be improved. Neurologists and PD nurse specialists committed to allied health interventions play a vital role in the delivery of optimal multidisciplinary care.

LIVING WITH PARKINSON'S: PUBLIC EDUCATION OR AWARENESS PROGRAMS

P38.01

The chain that bonds not binds – a project in awareness

Phillip Beckett

Background: The Parkinson chain is a project intended to visually represent the links between people around the world whose lives are affected by Parkinson's. Every link in the chain – similar to a paper chain – is signed by an individual. The symbolism of the chain linking people from around the globe is powerful and its visual

impact is an important factor in generating interest from picture editors and the media as well as individuals.

Aims/ objectives:

- To attract attention and provide opportunities for discussion and increased awareness about Parkinson's.
- To illustrate the significant number of people affected and the geographical spread of the condition
- To collect inspirational, amusing or heartfelt comments of those adding a link.

Method: a chain made from robust material was constructed. Each link was written on by an individual affected by Parkinson's, showing name, home location and comments. As the chain grows in length it attracts more attention. At events, attendees are encouraged to add to the chain. The multi-coloured chain contains some 530 links at present and is 66 metres (215 feet) long and growing! It represents people from 23 different countries. A document is maintained recording the details of each link in the chain.

The chain is used to attract attention and to afford the opportunity to gain publicity, so that awareness about Parkinson's is enhanced.

A website has been developed and social media use is planned to broaden the appeal and accessibility of information about the chain, publish pictures and statistics and provide links to reliable websites where individuals or media can obtain information, support and contacts. There is a proposal to provide a blank link to each individual at the Montreal WPC in their joining packs and an encouragement to add to the chain. The longer it gets the more impact it will have!

Outcomes: The chain has been used at events in several countries, including England, USA, Portugal, Belgium, Scotland and Sweden. People from many other nations have attended those events and contributed to the chain. It has attracted attention and appeared on TV and in newspapers and has helped, in a visual way to increase awareness about Parkinson's. It will continue to do so.

P38.02

Implementing get it on time: a Canadian perspective

Jon Collins¹

¹Parkinson Society Canada Central & Northern Ontario, Toronto, ON, Canada

Objective: The recently published Canadian Guidelines on Parkinson's disease acknowledges the primacy of medication timing as a priority for Canadian's living with Parkinson's. (per guideline C27[1]) Implementing the Get it on Time program meets the established best practice standard to ensure improved care for people living with Parkinson's.

Method: Based on design and text created by Parkinson's UK, Parkinson Society Canada launched the Get it on time campaign in English and French to educate staff and improve the quality of life of people with Parkinson's. The Central & Northern Ontario Region is engaged in a large scale dissemination of this international, collaborative message through a variety of channels, which we will share in our poster presentation.

Results: Our program has received overwhelming positive reviews from staff including an average 4.65/5 rating from over 2000 respondents who indicated that the program materials and presentation conveyed the importance of medication timing and would help them ensure better care of people living with Parkinson's. The same evaluations indicated that 96.55% of respondents indicating that they had made changes in their management as a result of the program and 100% acknowledging that this led to a higher quality of life for people living with Parkinson's. In addition to educational materials and in-services, we have developed tools to empower people living with Parkinson's in their transition from home to the long term care and/or hospital

environment. Resources include an 'official' letter written from the perspective of someone who has Parkinson's and a hospital preparation kit; both designed to ensure more positive interactions with health care professionals by creating prepared, personal advocates out of people living with Parkinson's and their loved ones. These materials have been found to be successful by all who have used them.

P38.03

Making the most of expert practice: The association of physiotherapists in Parkinson's disease Europe case study project

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⁴Independent Physiotherapy Consultant, Sheffield, UK

Introduction: Physiotherapists specializing in exercise and health promotion for people with neurological conditions are ideally placed to enhance quality of life in individuals with Parkinson's; Association of Physiotherapists in Parkinson's Disease Europe (APPDE) is a network of such physiotherapists. APPDE supports educational initiatives amongst its members – clinicians, researchers, people with Parkinson's and carers - and recently developed a restricted area on its website (www.appde.eu) for members to share case examples based on clinical evidence (<http://www.appde.eu/members/logon.asp>).

Objectives: 1. To build a communication platform for therapists with specific Parkinson's knowledge.

2. To develop clinical reporting skills transferrable to the workplace.

3. To accumulate evidence of similarities and differences in practice for a future APPDE case series peer-reviewed publication.

Methods: An educational tool - a template, based on the European Physiotherapy Parkinson Disease Guideline - was created to guide the writing of case studies by members. Topics such as maintenance, prevention and treatment of motor problems across the lifespan of the condition were included to enable (differences in) practice to be discussed amongst APPDE members. Cases will be peer reviewed by the Case study review group (poster authors); one case will be presented quarterly.

Expected Results: APPDE anticipates two key outcomes of the project for organization and members:

1. Improvement in patient care by:
 - Providing guidance on recording and reporting evidenced-based clinical reasoning for individual cases in practice; and
 - Sharing evidence-based physiotherapy treatment options for Parkinson's.
2. Improvement of scientific and educational activities through:
 - Stimulating debate about potential future clinical studies; and
 - Generating evidence-based material for clinical education.

Discussion: This project will assist the APPDE in advocating for the application of research to clinical practice in each clinical encounter and in the full range of settings and contexts in which physiotherapy is delivered across Europe.

P38.04**Project – What if you had it all in one setting? An Innovative Parkinson Intensive Multi-Program Rehabilitation Approach (PIMPRA)**

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Background: Parkinson's disease (PD) still presents many challenges in its management for both patients and health care professionals. In this changing era, programs for the treatment of specific disease, such as Parkinson disease, must be adapted for three reasons: the global burden of these neurologic diseases is increasing, non pharmacological intervention programs have a supporting role in developing health systems, and the health benefits of these programs may go beyond the prevention of complications. Recent research suggests that intensive rehabilitation programs can provide both short and long-term benefits to individuals with PD and their carers. Given the variety of rehabilitation programs that exist, the true use, safety and combination of these programs is still unknown in the scientific and clinical community. Which treatment programs better optimizes motor function? Should we focus on one program or the combination of such programs when they have complementary objectives?

Objectives: To expand and enhance care of patients and families through combining and articulating non-pharmacological treatment options in PD.

Methods: (1) Application and combination of current disease-specific programs, such as Parkinson Wellness Recovery Programs®, LSVT LOUD™ and LSVT BIG™ therapy programs, Ronnie Garden Method®, Dance for PD® and Lisbon Intensive Fall Treatment (LIFT) program, applied according to patient functional impairments, preference, capacities, disease stage and context.

(2) Developing a multi-strategy research-based intervention model capable to produce efficiently and safely results with best possible long term benefits.

Discussion: This innovated multi-strategy model of rehabilitation care for patients with PD may prove to be a valuable addition to standard rehabilitation programs. We believe our model will be unique in its integrated approach to PD care. To our knowledge, there is still no care offered in such a manner or that has shown the ability to join several existing rehabilitation programs in one setting.

P38.05**Parkinson's disease sensitivity training for first responders; the 411 for the 911**

Gretchen Garie-Church, Michael J. Church
Movers & Shakers Inc. USA, Naples, FL, USA

Background: People with Parkinson's face a wide variety of health & life issues that will at some point require the assistance of a first responder; i.e. Paramedics, firefighters, police, ER staff. This project evolved from speaking with many people with Parkinson's who had disastrous results with first responders.

Aim/Objective: To educate all "first responders" about the special care people with Parkinson's require. This special care includes such topics as:

- Timing of medications
- Contra-indicated medications
- Dementia
- Psychological issues
- Speech issues

Methods: This program has been presented several times to a variety of professionals including:

- Nursing Students
- County Emergency Responders
- Leaders within the Parkinson's Community

Presentation involves:

- Comprehensive PowerPoint presentation
- Discussion involving people with Parkinson's
- DBS demonstration and DBS discussion that helped those in attendance understand the complexities of issues
- Video of a person with PD in a very OFF state
- Several real life scenarios were included to help them understand who they may assist

Results:**Attendees:**

- Gained greater understanding of Parkinson's
 - Understood effective and ineffective treatments
 - How DBS affects EKG readings
 - How DBS surgery complicates some medical treatments
- A random survey was sent to participants, the results indicated:
- A comprehensive understanding of PD and issues faced by PWP
 - The county is currently working on a medication change on ambulances that will alleviate a contra-indication for widely used nausea medications
 - Interaction with people with PD very helpful
 - Greater sensitivity
 - A desire for more information

Discussion/Conclusions: This is shown to be a powerful tool to further awareness and education of Parkinson's disease. We believe that by working with advocates from around the world, the presentation could be changed to fit the needs of people with Parkinson's in other countries.

P38.06**Through Our Eyes Speakers Panel: Health Care Professional and Educator/Advocates with Parkinson's are indispensable to, and uniquely equipped to complement training of health-care professional and educate fellow PWP's about Parkinson's disease**

Leonore Gordon¹, David Spierer²

¹New York University; New York, USA

²Long Island University, Brooklyn, NY, USA

Objective: People with Parkinson's disease (PWPs) have unique motor and non-motor symptoms. Specifically, they face lesser-known cognitive challenges having to do with diminished executive functions. By educating PWPs, their friends, and families about specifics of our diminishing "executive functions," we plan to correct misconceptions and teach compensatory strategies.

Methods:

- 1) Educational Handouts of "Lesser-Known Symptoms" for graduate student "helpers" in Long Island University Exercise Class.
- 2) PWP Speakers Panel serve as guest speakers in graduate programs

- Long Island University: PT and Exercise Physiology
- NYU/ Langone Medical Center: PhD Research

3) PWP's participate in Q&A's hosted by Mark Morris's "Dance for PD" 3-day trainings for new PD dance teachers. Training packets include articles written by PWP dance students

4) Presentations of "Empowerment Strategies To Deal with Our Diminishing Executive Function's", offered to PD Folks & Caregiver Support Groups in following venues:

- JCC/NYU Langone Sunday Education Series
- Beth Israel Medical Center for Dr. Sheree Loftus' PD Support Group)

Results:

- Grad students and their professors rate Speakers Bureau guests as "favorite class."
- PhD research students report a new passion to find a cure for PD.
- Many LIU Grad student "EXERCISE CLASS helpers" have gone on to specialize in PD.
- At "Empowerment Strategies to Deal with Our Diminishing Executive Function," presentations, both PWPs and family members have responded with relief, and expressed new compassion for symptoms previously seen as stubbornness, laziness, or perplexing incompetence in multi-tasking exhibited by a once highly-functioning spouse.

P38.07**Pass the baton for Parkinson's awareness and fundraising program**

Shelby Hayter

Parkinson's Research Consortium, Ottawa, ON, Canada

Objective: In 2005, I was diagnosed with Young Onset Parkinson's Disease. Using my strengths of being an educator, marathon runner and public speaker, I created a program for the school system which has been successfully presented to various schools in the Ottawa Carleton Public School Board over the past 8 years. The name of the program is; "Pass the Baton for Parkinson's." This program accomplishes two goals; awareness for Parkinson's Disease and fundraising for continued research at the University of Ottawa's Parkinson Research Consortium.

Methods: The awareness is attained through a presentation at an elementary school in which a "TEAM" of speakers (a person with Parkinson's, a medical professional and a researcher) explain how they work together towards a common goal of finding a cure for Parkinson's disease. The presentation is upbeat and interactive and each speaker describes their role on the "TEAM" towards finding a cure before passing a relay-runners baton to the next team member. The fundraising component is introduced the following day to the same student audience, who is invited to join the "TEAM". Donations are collected as every class in the school is led by a facilitator through a series of exercises; specifically chosen to reinforce the mobilities affected by Parkinson's disease; strength, flexibility, speed and balance. The awareness assembly concepts are reinforced while the students run and exercise and have fun!

Results: The attractiveness of this program to the School Board is that students learn about a debilitating disease, take ownership of sharing what they have learned with family members, and contribute to Parkinson's research through donations. They are now a part of the "TEAM". To date, the program has touched approximately 30,000 students and raised over \$75,000.

P38.08**Training police about Parkinson's**Judy Hazlett¹, Roger Buxton¹¹Unionville, Ontario, Canada

Objective: Increase the awareness and knowledge about Parkinson's in police services to lessen the likelihood that uniformed officers and civilian employees will mistake the symptoms of someone with Parkinson's for anti-social behaviour, some other medical condition, or even criminal activity. Expose police personnel to the types of predicaments that people with Parkinson's can

experience, especially when out in public. Provide the police with advice on how to respond and assist if needed.

Methods: Created a presentation entitled STOP AND ASSIST supported by graphics, video clips, and live demonstrations illustrating pertinent examples of Parkinson's symptoms and circumstances. Broadened the scope to include other types of disabilities. This was followed by advice on how to assist a person in public, a discussion of legal and human rights issues, and sources of further information. Beginning in 2000, this presentation has been given frequently ever since by a person with Parkinson's and a companion to classes of officers and civilians in several police services in Ontario, and most often in Toronto. Also created a short video of the highlights and printed materials which were distributed for reference and use by others who were unable to attend the classes.

Results: Educated thousands of police personnel over the past twelve years. Feedback reveals that the presentation was well received and was considered appropriate and valuable. People with Parkinson's have also reported that they are pleased with the project because they feel more secure in their communities knowing that the police are familiar with their situation.

P38.09**Drive Right**Judy Hazlett¹, Roger Buxton¹¹Unionville, ON, Canada

Objective: Educate people with Parkinson's about the consequences of their condition on their ability to drive from first onset to cessation of driving. The goal is to ensure the safety of all those on the roads while allowing people with Parkinson's to continue to drive for as long as they can do so safely. Furthermore, when the time comes, they can cease driving with dignity, having alternative methods of transportation available to retain their independence.

Method: Created a presentation entitled Drive Right supported by graphics and video clips containing descriptions and demonstrations of: the physical and mental requirements of driving; the effects of Parkinson's and of medications and their side effects on these requirements; the similarity of Parkinson's symptoms to an impaired driver's condition and how to avoid being incorrectly charged with a criminal offence; methods of evaluating one's driving skills; understanding the costs of driving and of accidents; and choosing alternative methods of transportation. The presentation has been given by a person with Parkinson's, usually in conjunction with a police officer, at conferences for people with Parkinson's and to support groups in Ontario. In a modified form, the presentation has also been given to Drug Recognition Expert police officers to educate them on the distinction between Parkinson's and the effects of prohibited drugs.

Results: Exposed hundreds of people with Parkinson's and police officers to this strategy of balancing transportation needs with highway safety. Originally undertaken in 2000, the lecture has been revised in recent years to account for changes in understanding, laws, and technologies.

P38.10**My Parkinson's Story: Parkinson's disease research, Education and Clinical Center's online educational videos**Susan Heath¹, Jeff Kraakevik,²¹San Francisco VA Medical Center, San Francisco, CA, USA²Portland VA Medical Center, Portland, Oregon, USA

Objectives: To share online videos filmed with Parkinson's disease experts who discuss clinical insight(s) and management strategies about commonly encountered problems for persons with limited access to specialty care services. To increase awareness within the Parkinson's disease community and non-Movement Disorders specialists about 16 common Parkinson's disease clinical issues.

Methods: We filmed 16 persons with Parkinson's Disease seen in the Veterans Affairs (VA) Medical Centers with their local Movement Disorders Specialists and team members (nurse, allied health or rehab team member) discussing how to best manage their clinical issues. Tips for the management of these issues were highlighted using short eight-ten minute vignettes. Topics were chosen from a recent unpublished Parkinson's disease Research Education and Clinical Center (PADRECC) needs assessment survey of VA primary care providers. Grant funding was obtained for the series through VA Employee Educational System. Videos were shot on location at PADRECC sites using PADRECC staff. Videos are posted online on the VA PADRECC website and on YouTube.

Results: The following video titles were posted on February 2013 (# of YouTube views as of 4/15/2013): Early Parkinson's disease (1,132 views); Depression (589); Impact of Falls (617); Memory and Thinking Problems (720); Sleep Problems (808); Deep Brain Stimulation (715). DVD only subject titles include: Genetics and Environmental Exposures. Eight additional videos are soon to be published: Medications, Impulse Control Disorders, Hospitalization Issues, Caregiving, Exercise, Advanced Parkinson's Disease, Speech/Swallowing and Driving in Parkinson's disease. These videos are an effective and novel way of delivering information in an online setting.

P38.11

Community rehabilitation for people with Parkinson's - a social worker's perspective

Deborah Herbert¹

¹ Parkinson's Disease and Movement Disorder Society, Mumbai, India

Background: In a country as socio-culturally varied as India, the Parkinson's Disease and Movement Disorder Society (PDMDS) had to draw on the very factors which seemed like obstacles to reach out to people with Parkinson's. The low levels of education, cultural and religious practices, joint family considerations, lack of quality medical care made available to the masses and a skewed ratio of neurologists available for the existing population – 80 neurologists for the 18 million people living in Mumbai, forced the PDMDS to find a solution within the very problem.

Objective: The objective of the project was to involve all the stakeholders in the treatment and community rehabilitation for people with Parkinson's in the city of Mumbai.

Methods: The process began by getting together a team of medical and allied health workers to pool in their resources; the result being awareness material about Parkinson's Disease was translated into local languages, so that people of different linguistic and cultural backgrounds could be educated. By networking with non-governmental organisations working with the different communities, we were able to understand the social and economic difficulties of the people (isolation of the person within the family or ostracising of the family within the community, financial burden on the family if the male member has Parkinson's) and be the link for them to access government services. Therefore, the PDMDS decided to make its services more accessible to people with Parkinson's by initiating support centres within the community. From conducting its first support group in a community hall in 2005 the Society now reaches out to over 800 patients across 10 centres.

Results: The PDMDS created a network of support centres by providing free treatment and rehabilitation to people with Parkinson's in their local community.

P38.12

Tango everyone? A perpetual community program providing tango lessons to individuals with Parkinson's disease: A mentorship program

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¹Department of Physical Therapy, Northern Arizona University

Objective: Participation in ongoing community programs is critical for the functional success of persons with Parkinson's disease (PWP). Engaging in regular tango dance classes has been shown to improve symptoms specific to PD 1,2,3. However, such programs, such as tango, are difficult to maintain due to the transient nature of teaching commitments, volunteer availability, and space requirements. The physical therapy (PT) students at Northern Arizona University (NAU) have solved this dilemma.

Methods: For the past three years, NAU PT students have been teaching weekly tango lessons to PWP. The novelty of this program is its legacy, passed down from year to year. Not many PT students have prior tango or dance teaching experience. To accommodate for this, our tango program incorporates a lengthy mentoring protocol to assure that all involved have mastered the skills required to teach. The fall term begins with 2nd year PT students at the reins. Assistant volunteers are recruited from the 1st year class. This opportunity gives them exposure to the program at an introductory, no commitment-required level. As the spring term begins, 1st year volunteers are again recruited. Those students ready to commit to learning the dance and teaching the following year are folded into the weekly schedule. Now the assistants are encouraged to take a more participatory role, creating warm-up exercises or providing feedback to the dance participants. At mid-term, the roles reverse. The 2nd year PT students step back and assume the role of assistants and the 1st year students assume leadership, under the guidance and insight from the more senior class.

Results: Tango for Parkinson's attracts approximately 5-6 regular participants with new dancers joining every semester. The continued success of this program relies on the strength of its instruction, its creative outlet, enthusiastic volunteerism and the sense of community it builds.

P38.13

Parkinson education program for community caregivers: maximizing outreach to health Care Professionals

Tracey Jones

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Objective: The Parkinson Education Program (PEP) for Community Caregivers was developed by Parkinson Society Southwestern Ontario as a profound need for information and support was identified by both health care professionals and families caring for people with advanced Parkinson's. Launched in 2007, PEP for Community Caregivers has been sustainable through the engagement of volunteer health care professionals in a train the trainer model. Community caregivers have embraced this unique form of education and training. The tremendous success of this educational program has directly impacted other areas of our mission including increases in our support services. PEP for Community Caregivers supports:

- helping people with advanced Parkinson's to remain in their homes longer;
- reducing the number and duration of hospital stays;
- people with advanced Parkinson's to enjoy increased dignity and a better quality of life whether at home, in the hospital or in long-term care; and
- Community Caregivers to feel better equipped with knowledge that will help ease the burden of both the person with advanced Parkinson's and themselves.

Methods: The unique train the trainer aspect of *PEP for Community Caregivers* maximizes the number of local Parkinson's experts through recruitment of qualified health care professional volunteers to increase our outreach and ensure that the best possible information about Parkinson's is provided. The program consists of two parts: a resource manual for Community Caregivers and ten interactive In-service training presentations. An online discussion forum for health care professionals has additionally been created to compliment this program.

Results: The poster presentation will provide statistics on the number of health care professional volunteer trainers engaged for this program as well as the number of community caregivers trained across the region. Additional qualitative measurements including changes in best practices, and testimonials that show clear improvements in quality of care will be shared as well.

P38.14

Speaking with a unified voice: National Parkinson Foundation Minnesota's Medical Team Advisory Board

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Objective: In 2012, National Parkinson Foundation Minnesota created a Medical Team Advisory Board, with the goals of 1) bringing together physicians with Parkinson's expertise from multiple neurology practice groups around Minnesota, 2) bringing together allied health professionals (nurses, social workers, rehab therapists) who are part of the Parkinson's teams in those practice groups, in order to 3) address issues of common interest.

Methods: The team meets quarterly, with telephone/internet conferencing available for those who are unable to attend in person, with communication by email between meetings.

The group has identified several issues of common interest and concern: 1) the lack of levodopa products on the first tier of a major insurer's formulary; 2) hospitalization in PD patients; 3) the diagnosis and management of very early PD; and 4) the possibility of creating templates for annual PD visits that meet American Academy of Neurology guidelines. A number of other areas have also been discussed.

Results: An action plan for the first two issues was created and is underway. 1. All members of the group jointly signed a letter to health plan leaders regarding the formulary issue. Further work has identified other health plans that lack a levodopa product on the first tier. 2. Members of the group were familiarized with the National Parkinson Foundation's Aware in Care kits about hospitalization in PD, and agreed to give presentations in their local hospitals or clinics on this topic. This novel approach to identifying and addressing issues common to PD subspecialty practices within a region has the potential to improve care throughout the region, as well as strengthening interactions among programs at both the physician and the allied health levels.

P38.15

The European Parkinson's disease standards of care consensus statement

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¹European Parkinson's Disease Association (EPDA), London, UK

Objective: To provide guidelines for policy makers on how people with Parkinson's (PwPs) should be managed to ensure their effective participation within society and areas that need to be focussed on to realise this.

Methods: The European Parkinson's Disease Standards of Care Consensus Statement combines evidence of the European emotional and economic cost (€13.9 billion annually) of 1.2 million European PwPs, reinforcing that prevalence is forecast to double by 2030. It was developed, reviewed and endorsed by a number of European key Parkinson's opinion leaders as well as representatives of the multidisciplinary team, PwPs, carers and 45 patient organisations. All worked with the EPDA over a period of twelve months to try to define and standardise the care, treatment and management of the disease that will improve the quality of life of PwPs. This consultation resulted in an 8-point plan that European policymakers need to do: 1. Support initiatives that ensure equal access to good quality, specialised Parkinson's care across Europe; 2. Reduce inequalities in the treatment and management of Parkinson's; 3. Improve funding for Parkinson's research and define research priorities; 4. Invest in optimum treatment and maintenance strategies; 5. Increase public and professional awareness of Parkinson's; 6. Minimise stigma and discrimination; 7. Strengthen the level of neurological care within European healthcare systems; 8. Provide adequate funding that supports the continued work of national Parkinson's organisations.

Results: It is the first document of its kind to support and encourage the drive for equality and optimisation of Parkinson's management at both a European and national level. Following its launch (November 2011) in the European Parliament, Brussels it has been translated into a number of European languages; has been read, supported and endorsed by a number of European policymakers, with over 50 Member of European Parliament (MEPs) joining the EPDA's MEP Parkinson's support group.

P38.16

Move for change part I – A pan-European survey evaluating impact of EPDA charter for PwP on disease management and QoL

Knut-Johan Onarheim¹, Susanna Lindvall¹, Lizzie Graham¹

¹European Parkinson's Disease Association (EPDA), London, UK

Objective: To evaluate what difference the Charter for people with Parkinson's (launched in 1997) has made to present-day healthcare services throughout Europe.

Methods: the EPDA is conducting the Move for Change campaign which is a three-year, three part pan-European on-line survey (translated in 24 European languages, across 36 countries) that asks people with Parkinson's (PwPs) whether their lives have improved since the launch of the 1997 EPDA Charter for PwPs that outlines their rights in terms of standards of care. It states that all people with Parkinson's have the right to: be referred to a doctor with a special interest in Parkinson's; receive an accurate diagnosis; have access to support services; receive continuous care; and take part in managing their illness. The first survey (23 questions) focused on the Charter's two initial points (see above) and of the 2149 forms completed, 2068 (96.2%) were analyzed.

Results: The majority of PwP who completed the survey were diagnosed within 2 years from the onset of their first symptoms (82.7%; range 1 year to >5 years). 45.3% stated that the diagnosis delivery was 'poor' or 'very poor' with 43.8% reporting that during the 2 years following diagnosis they had never seen a Parkinson's disease specialist with their treatment being overseen by generically active neurologists (92.5%) or family doctors (81.0%), with considerable overlap between the two. The findings highlight the challenges that PwP continue to face during the diagnosis period, despite the introduction of the Charter and provides the evidence that can help healthcare professionals and policy makers to improve PwPs management and their families across Europe.

P38.17

Move for change part II – A pan-European survey evaluating impact of EPDA charter for PwP on disease management and QoL

Knut-Johan Onarheim¹, Susanna Lindvall¹, Lizzie Graham¹

¹European Parkinson's Disease Association (EPDA), London, UK

Objective: To evaluate what difference the Charter for people with Parkinson's (launched in 1997) has made to present-day healthcare services throughout Europe.

Methods: The EPDA is conducting the Move for Change campaign which is a three-year, three part pan-European on-line survey (translated in 24 European languages, across 36 countries) that asks people with Parkinson's (PwPs) whether their lives have improved since the launch of the 1997 EPDA Charter for PwPs that outlines their rights in terms of standards of care. It states that all people with Parkinson's have the right to: be referred to a doctor with a special interest in Parkinson's; receive an accurate diagnosis; have access to support services; receive continuous care; and take part in managing their illness. The second survey (9 questions) focused on the third right of the Charter (all PwPs have the right to have access to support services'). The definition for accessibility of support services was services /medication/multidisciplinary health care professions etc., being available and on hand to manage PwP when required.

Results: Neurologists and General Practitioners (GPs) received highest accessibility results (90.0 and 87.0% respectively) with moderate results for physiotherapists (68.0%) and patient organisations (72.0%), Parkinson's disease nurse specialists (26.0%), occupational therapists (23.0%) and counsellors (27.0%). The support provided by neurologists (59.0%) and Parkinson's disease Specialists (55.7%) was considered to be 'very helpful' whilst (31.8%) of GPs were considered the same. Across Europe, the funding of services was variable. This data demonstrates the challenges faced by PwPs in accessing the adequate management and support they require throughout the course of their Parkinson's journey and provides the evidence that can help healthcare professionals and policy makers to improve PwPs and their families level of access to support across Europe.

P38.18

Two centers are better than one: joining forces to build capacity and provide robust services for the Parkinson's community

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Background: In 2001, the Department of Veterans Affairs allocated funding to establish six centers of excellence for American military Veterans affected by Parkinson's Disease (PD). McGuire Veteran's Affairs Medical Center (VAMC) in Richmond, Virginia was designated as a Parkinson's Disease Research, Education, and Clinical Center (PADRECC). From 2002 through 2009, PADRECC was the only comprehensive PD center in Richmond, with services limited to Veterans. In 2005, members of the Richmond community launched a fundraising and advocacy campaign to establish a comprehensive center for non-veterans. In 2010, the Virginia Commonwealth University (VCU) Parkinson's and Movement Disorder Center was established to combine research, clinical care, and education in a coordinated approach to combat PD.

Objective: To demonstrate how the two centers partner to plan programs, and leverage resources to expand community outreach, enriching the quality and number of education and awareness events in Richmond and across Virginia.

Methods: Tracking data was collated and analyzed for lay community and professional education events produced by the centers from inception through 2013.

Results: Services for those impacted by PD in Virginia have increased exponentially with the creation of the PADRECC in 2001, and nearly doubled with the formation of the VCU center in 2010. Partnering allowed the centers to produce an additional 26 programs for the community, reaching over 2,800 attendees. Through collaboration, the centers are able to capitalize on shared resources, additional subject matter experts, collective creativity, and identify gaps in services to best address the needs of the community.

P38.19

The social movement: building the More Than Motion™ Facebook community for people living with Parkinson's disease

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Objective: The non-motor symptoms (NMS) of Parkinson's disease (PD) can be challenging for healthcare providers, people living with PD (PLWP), and caregivers to recognize¹. Our aim was to: provide an educational social media community built around the concept that PD is more than a movement disorder; allow PLWP and caregivers to connect with each other and receive helpful information; inspire the community to share their own stories, learn from others, and get involved in PD advocacy.

Methods: We developed a program, called Parkinson's More than Motion™, to educate PLWP and caregivers about the broad impact of Parkinson's disease. Parkinson's More than Motion™ is a multi-media resource designed to inform this audience via: Facebook, a reality video series, a Parkinson's Well-being Map™, a magazine, and advocacy events. We launched the program for U.S. PLWP in April 2012.

Results: After one year in the public domain (April 2012-April 2013), Parkinson's More than Motion™ has reached a significant number of U.S. PLWP:

- 42,937 "likes" on Facebook (as of April 5, 2013)
- 1,000+ people "talking about" our content by commenting on it, liking it, or sharing it
- 7,000+ Facebook users reached per week
- 1,000+ magazine subscriptions
- Exhibited at neurology and PD events
- Shared information from PD advocacy groups

Conclusion: Increased awareness of NMS is needed among healthcare providers, PLWP, and their caregivers. PLWP and caregivers are impacted by NMS and respond well to multi-dimensional education programs. The increasing popularity of social media among older adults makes sites like Facebook an ideal setting for creating an educational support community.

P38.20

Parkinson's Movement: Operationalisation and evaluation of the web-based presence (2011-2013)

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Introduction: Parkinson's Movement (PM), outlined in principle at the 2010 WPC in Glasgow [1], was predicated on the view that, of all involved with Parkinson's, the insights of people with Parkinson's were particularly pertinent. The intention was to create a hub combining "the best aspects of the fora, integrated into a vehicle for information gathering, dissemination and lobbying". Here we review progress with the web presence of PM since WPC 2010.

Methods: The web presence of PM comprises the central website (parkinsonsmovement.com: PMC), a forum/polling website (parkinsonsmovement.healthunlocked.com: PMHU) and associated social media. Google analytics data harvested on 7 April 2013 were supplemented where necessary by internal data from PM, Survey Monkey and social media.

Results: Since 8 August 2011, PM has conducted 72 polls, interviewed 14 neurologists on film, broadcast 5 webinars, appointed 24 ambassadors, attended 6 scientific conferences, submitted 10 abstracts on polls to meetings, and conducted 2 pilot research studies. In 20 months, PMC has had 21,491 unique visitors and 79,983 page views from 4389 towns/cities in 141 countries. Peak daily visits (424) occurred on 14 April 2012. data extend from 30 November 2011 with data loss (24-29 May 2012) for site maintenance. During the logged period, PMHU had 86,049 visitors and 734,182 page views from 7585 towns in 168 countries. Peak daily visits (644) occurred on 13 January 2013. PM's Youtube channel had 8593 views, 2638 from the US since inception (17 November 2011). PM has 684 Facebook 'likes'.

Conclusion: following an initial surge, PM statistics suggest consolidation of interest in the organisation. PM has exceeded all anticipated metrics and, following ambassador consultation, anticipates greater focus on key patient driven deliverables in 2013 and 2014.

P38.21

www.discoverMI.org – Helping patients with Parkinson's disease get a clear view of modern molecular imaging technology

Frederick Woodlief

Member, SNMMI's Patient Advocacy Advisory Board, USA

Background: The Society of Nuclear Medicine and Molecular Imaging (SNMMI), with

over 50 years history and representing 19,000 professionals worldwide, supports a mission

"to improve human health by advancing molecular imaging and therapy". SNMMI created a Patient Advocacy Advisory Board (PAAB) whose members "help insure patients' concerns, ideas, experiences and recommendations are reflected in the Society's endeavors". With PAAB input, SNMMI developed the discoverMI.org website as a public resource for patients seeking information on diseases using molecular imaging. Parkinson's Disease is a progressive, neurodegenerative disease involving movement disorders as well as extensive life style issues. It affects approximately 1 million people in the United States and an estimated 5 million worldwide. With advances in technology in the past several decades and the development of radiotracers to assist in brain imaging, more physicians and researchers are referring their People with Parkinson's (PWP) for advanced molecular imaging. CT and MRI imaging allows a view of the structure of the brain. Newer PET and SPECT scans allow for the visualization of brain function and a measure of its chemical processes, which can lead to detecting the early onset of neurological disorders. Neuroimaging also provides for the study of brain circuitry or neurotransmission.

Objective: "Healing begins with seeing precisely" The objective is to provide a comprehensive and user-friendly website where the public can interact to get reliable information about molecular imaging and therapy in the areas of brain disorders, heart disease, cancer, and radiation safety. This can be especially helpful to the Parkinson's patient.

Discussion: This award winning website was launched in 2011 with its 2nd edition to be released in June, 2013.

LIVING WITH PARKINSON'S: GOVERNMENT ADVOCACY/ CAMPAIGNS/ PUBLIC POLICY

P39.01

Experiencing Parkinson's Disease and dealing with the health system in Colombia: the point of view of an informed patient

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Objectives: To describe a personal experience as an informed patient dealing with the Colombia Health Care System.

Methods: It is a case report from an informed patient living with PD. Using literature review and my own experience. To analyze clinical registry, I selected two categories: administrative processes to get health care (i.e. medications, surgery, and therapies) and relationship with my colleagues (i.e. neurologists, neurosurgeons, and general practitioners)

Results: I have identified barriers and facilitators related to context, processes and actors to get health care services. In Colombia both medications and the bilateral subthalamic nucleus stimulation are not part of the obligatory plan of health services, so patients must face an exhausting legal (i.e. tutela) and different administrative process (i.e. surgical boards) in order to get them. My experience show that: a. Even though I wanted discuss with doctors about causation, all of them showed any interest in causation inquiry in PD; b. Doctors just know about their specialty and in the Colombian Health System there are not teams to treat patients integrally which is essential among people with PD; c. Doctors focus on treatments of motor symptoms which is a consequence of available treatments

and medical training in Colombia; and d. I was able to deal with surgical boards (ex. using technical jargon) and legal processes because I know very well my health condition, the latest scientific evidence related to PD, and the Colombian Health System. Doctors have limited options to attend PD, for example levodopa remains as the gold standard treatment, access to neurostimulation is difficult, and treatments focus on motor symptoms. Moreover, strategies to cost containment, using legal and administrative mechanisms, do not allow offering integrated services to PD patients. Finally, medical training is still fragmentary which is reproduced within health care process, affecting the quality of life of Parkinsonian patients.

P39.02

The effect of Medicare Part D on Parkinson's disease patients: a four year retrospective study

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Objective: Compare behavior of Parkinson's Disease (PD) Medicare patients reaching coverage gap (CG) and out of pocket (OOP) expenditures over 4 years, from 2008 through 2011. Assess changes in medication usage and spending patterns during and after implementation of Affordable Care Act which provided a 50% reduction in patient burden for Medicare Part D CG beginning in 2011.

Methods: 4 year retrospective study using the IMS Longitudinal prescription database, LRx and Plantrak managed care data. Patients were evaluated on medication usage and spending patterns before, during and after the CG by payer type.

Results: Percentage of patients reaching coverage gap diminished from 51% in 2008 to 39% in 2011. Proportion of CG patients who reached catastrophic coverage (CC) slightly increased from 26% to 29%. The percentage of patients who remained in the gap was relatively stable (74% in 2008 and 71% in 2011). The average time spent in the gap remained at 4.8 months. The percentage of patients who stayed on therapy remained high and increased from 77% in 2008 to 81% in 2011. Out-of-pocket (OOP) cost of drugs was reduced by half in 2011, we only observed an increase of 1% in the proportion of patients who remained on therapy. The percentage of patient who reduced therapy went from 2% to 1% over the same period. The proportion of patients who stopped therapy declined from 12% in 2008 to 10% in 2011. Whereas the percentage of PD Medicare Part D patients reaching the CG diminished between 2008 and 2011, mean OOP costs for PD medications declined but compliance to PD medication remained unchanged.

P39.03

The growth, accomplishments and challenges of the international Parkinson advocacy movement: social history, literature review and call to action

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Objective: to demonstrate the positive effect Parkinson advocacy has had in the global PD community and to illustrate some of the projects including those using internet tools for self-care, participating in research and encouraging reforms in areas of concern to those with PD.

Methods: survey Parkinson disease history; identify significant issues; record actions of people with Parkinson disease (PwP) and include historical materials such as interviews and literature

reviews. At key turning points in the history of Parkinson advocacy, we will show what was involved and how people participated on many levels. Examples will illustrate issues such as: using new technology, educating the whole PD community and encouraging new thinking to cure PD. From the collected, factual material plus contemporaneous and later commentary, we will summarize PD advocacy and develop a timeline of significant events.

Results: This work will educate and increase public awareness of many significant issues and accomplishments in PD advocacy. It will encourage individuals to become active participatory patients and join others working to improve PD care and contribute to finding a cure for PD.

P39.04

Policy Advocacy on Parkinson's Diseases in Nepal

Shrestha, Hom L.

Non-Smokers' Rights Association of Nepal

Objective: To create environment and system for policy, legal and media advocacy on Parkinson's Diseases (PD) in Nepal; and to design conceptual framework, national policy and legal framework for the diagnosis, treatment and rehabilitation for the PD patients through policy reform, formation of Parkinson's Diseases Society of Nepal, tripartite partnership and collaboration among government, NGOs and donors or international charitable institutions, etc.

Methods: A few available patient data from neurology departments of some hospitals and National Neurology Hospital; scientific articles published in the *Lancet*, *Neurology*, *Journal of the Royal Society of Medicine*, *Neuroepidemiology*, *Indian J. Psychiatry*, etc., national health policy and second long term health plan and stories of young lady PD patient and 88 years old women patient, have rigorously been reviewed.

Results: The concept and idea of PD is new in Nepal. There is no such practice to neither question about symptoms of Parkinson's diseases among neurology patients nor diagnose even doing MRI test. MRI test is so expensive to look for signs of a stroke and brain tumor in Nepal but not examine PD due to lack of guidelines, protocol and training for the diagnosis of PD by neurology professionals. Also, there is no such policy and facilities even for geriatric health care in hospitals of Nepal, the health care policy should be reformed to address geriatric health care including dementia, Alzheimer's and Parkinson's disease treatment and rehabilitation facilities in particular. The PD lady patient 20 years and 88-years old women both are survived by regular physical exercise without physiotherapy to maintain and improve mobility, flexibility, strengthen and gait speed and quality of life from support of family. The further policy-relevant research and advocacy should be undertaken to create public and media education and awareness among health care professionals, media and family as global health issue.

LIVING WITH PARKINSON'S: LIVING WELL WITH PD

P40.01

A smart phone-based application for medication compliance and user motivation in Parkinson's disease

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Introduction: There is much current interest in patient empowerment and personal engagement.

Methods: A 6 week, randomised, double blind trial compared two versions of an app - a minimal version (MIN), with the uMotif 10-petal tracker and a FULL version including medicine reminders and cognitive games. Pre and post trial surveys included two widely used Parkinson's questionnaires (PDQ-39 & Non Motor Symptoms survey), the Oxford Happiness Inventory, the Quality of Life Scale a medicines management questionnaire and several freeform responses about the app and the trial.

Results: 26 patients joined the trial. Participants provided very positive feedback on the ease of use of the software and value of symptom tracking. Unfortunately, the small numbers of users that completed the study (10 MIN, 6 FULL) obviated statistically significant differences but FULL users saw Parkinson's symptoms slightly *improve* and happiness *increase*. If anything the opposite was true for MIN. Trial participants used the app for 55 days (mean), and entered data on at least 70% of days. Comparing the first and last 5 days, there were statistically significant increases in ratings of *Energy, Water & Exercise* (all $P < 0.05$) and marginal improvement in the *Meds* rating (0.15). There were no significant changes in any of the Parkinson symptoms (*Bradykinesia, Suppleness, Dyskinesia & Tremor*). There was marginal improvement in *Sleep* rating ($p < 0.07$) which was strongest in the FULL condition. Similarly, *Mood* improved for users in the FULL but not for MIN condition ($P < 0.08$).

Conclusion: The tracker was used regularly by participants and gave some significant positive results that were not picked up by more traditional questionnaires, demonstrating the value of the uMotif tracker for research and as a monitoring tool. The positive feedback from the participants and the overall positive trends from this limited sample suggest that a follow up study is warranted.

P40.02

Managing Parkinson's disease symptoms while hospitalized for non-PD related conditions.

John Ball¹

¹Team Parkinson, Whittier, CA, USA

Objective: Management of Parkinson's symptoms to minimize impact of treatment of unrelated conditions on PD, to shorten hospital stays, and to improve treatment outcomes.

Methods: The treatment—as well as the stress—of many conditions that require hospitalization, such as infectious disease, respiratory ailments, or trauma, can interfere with the efficacy of treatments for PD and cause a temporary worsening of PD symptoms. Self-identified Parkinson's patients who require admission to the infectious disease or respiratory ward, or the trauma center of a hospital will typically have a neurologist assigned to their care, and will not be under the care of their usual Movement Disorders Specialist. Thus it is essential for patients and care-partners to advocate for self-management of their PD symptoms since it is unlikely that hospital staff assigned will have the level of PD management expertise required to manage individual patient needs. A pre-hospitalization admission agreement to allow PD patients and care-partners to manage PD medications, both dosage and timing, is a dramatic step towards gaining positive control. I will present tools to prepare a PD patient for a hospital stay from both patient and physician (neurologist/MDS) points of view.

Results: With the proper education, preparation and tools, the PD patient and care-partner can negotiate for self-management of both timing and dosage of PD medications prior to entry into the hospital, thus reducing the potential for misunderstanding, mistreatment and medication conflicts. This will additionally minimize stress and enhance the quality of life during the recovery process while enduring hospitalization.

P40.03

Effect of organized physical activity on the quality of life of people living with Parkinsons

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Objective: This is a patient driven study. The objective of this project is to demonstrate whether or not participation in organized physical activity improves the quality of life of People with Parkinsons.

Methods: At least 25 Participants in organized physical activities such as Group Exercise Classes at the YMCA, Chair Yoga at the YMCA and Dance for PD by the NC Dance Theater will be asked to complete one of the quality of life measurement tools such as PDQL, PDQ-39 and PDQUALIF. The results will be compared to the application of the same measurement tools as reported in existing published research over age of onset, years since diagnosis and the age and sex of participants. The results will be tabulated analyzed and reported.

Results: Results will be reported.

Discussion: Anecdotal evidence obtained through informal discussions with participants, caregivers and leaders of physical activities of all types support the conclusion that engaging in group activities improves quality of life for people with Parkinsons.

Topic: Living well with Parkinsons

P40.04

Shou ... shou ... bang: moving more quickly through the stages of the emotional rollercoaster in order to embrace your Parkinson's disease on solid ground

John Baumann¹

¹Faculty, University of Louisville, KY, USA

Objective: To enlighten and empower Parkinson's patients as to the significant influence that each of us has over the quality of our own life.

Methods: I identified the emotional issues or phases that typically result from a Parkinson's diagnosis (shock, disbelief, denial, anger, difficulty disclosing to others, social awkwardness, isolation and depression) and determined what can be done to eliminate, or, at least move through, these difficult and undesirable emotional phases more quickly. I identified what could be done to accept and embrace life with Parkinson's, including what I could do to reverse, if not, slow the progression.

Results: I concluded that there are action steps that can be followed to be more successful. I then applied these steps to my life with Parkinson's. I conducted an assessment of what I could still do. I envisioned myself with the highest quality of life possible doing what I was still able to do. On a daily basis, I reminded myself to live in the moment; to continually update my "bucket list" and experience each item; to keep a positive attitude; to have faith in myself; to eat healthy, organic food; to exercise daily, gradually moving every day further out of my comfort zone; to perform activities that keep me mentally sharp; to discover and rediscover my life's purpose (currently as an inspirational speaker and author: *Decide Success – You Ain't Dead Yet*); to be more loving, kind and compassionate; and to accept, and even embrace, Parkinson's by finding meaning (silver linings) in the disease. The ultimate result of enacting this plan is that I am healthier now, over ten years into my Parkinson's, than I ever was before I started exhibiting symptoms of Parkinson's. My conclusion is that anyone with Parkinson's can take steps to improve the quality of their life.

P40.05**Parkinson's disease + music therapy = higher quality of life***Concepcion Bentz¹*¹Asociacion Catalana para el Parkinson, Barcelona, Spain

Objective: To show the importance and effectiveness of music therapy in the treatment of Parkinson's disease.

Methods: Music therapy is very effective in the treatment of a wide variety of disorders. By itself, music triggers a stimulating process which benefits various areas of the brain. The author's own musical oeuvre (intended especially for Parkinson's disease patients) on which her specific treatment is based, was composed in such a way that its rhythmic and melodic patterns facilitate and promote the motion and mobility of these patients.

In patients treated with the RAS and PSE methods, 50% of those in stages 1 and 2 have experienced a great improvement in their unilateral and bilateral symptoms.

Regarding speech loss, hypophonesis and slow speech disorders, the best results have been obtained by means of MIT, VIT and RSC therapies. Three of the author's musical compositions have been very effective when applying CPMT and ISO principle techniques, obtaining an improvement in 100% of patients. With the RAS technique and two of the author's compositions, very positive results have been obtained when treating walking disorders. By means of the TIMP technique, tremor at rest can be eliminated and movement and coordination can be controlled. With two of the author's compositions, along with the use of the musical travel technique, micrographia improves substantially.

In order to treat facies amimica, the face and body movement therapy has been used, with the aid of one the author's compositions.

Results: From the author's practical experience and observations, the above conclusions can be drawn regarding the motor, psychological and cognitive benefits of this music therapy treatment, as well as regarding the patients' evolution, progress and improvement in their quality of life.

P40.06**Accessibility to Parkinson's specific exercise***Madonna Brady*

Background: Research shows the right kind of exercise can slow the progression of symptoms of Parkinson's disease. There is a lack of accessible exercise based initiatives for people with Young Onset Parkinson's Disease in Brisbane. The level of awareness of Young Onset Parkinson's disease (YOPD) in general medical practitioners is delaying prompt diagnosis and early intervention possibilities.

Aims and objectives: Become an advocate for people with YOPD, lobbying the Government, health professionals and fitness centres to facilitate affordable accessible Parkinson specific weekly exercise classes. Free gym use to maintain fitness and agility, thus promoting social interaction and boosting quality of life for all people with Parkinson's (PwP) is the ultimate goal.

Methods: Early commencement of Parkinson's specific exercise enables PwP to take charge on a personal practical level.

- Lobbying Government and organisations for funding enabling PwP to free use of gym facilities.
- Working with Parkinson's Queensland Inc. to recognise the needs of people with YOPD.
- Encouraging mandatory referrals to allied health professionals on diagnosis of Parkinson's for assessment, leading to individual exercise programs. At this stage, exercise can be managed independently; meeting for weekly classes would be beneficial and encourage social interaction.

- Embracing PwP and their families with a combination of informative, social and recreational initiatives.
- Review progress with Physiotherapist regularly to assess and adjust.

Results and benefits:

- Improved balance, agility and capability, thus preventing falls.
- Increased fitness levels and confidence.
- Maintain PwP's working potential, increased social interaction helps preserve self-esteem.

The poster will cover the following:

- Author's personal experience of benefits.
- Author's photos at the beginning of regular Parkinson's specific exercise and after.
- A description of exercises.

Anecdotal evidence from people with Parkinson's

P40.07**My Blessing - Living With Parkinson's***Mark F. Burek*

Objective: To instill hope in the lives of people with Parkinson's through personal experience.

Methods: I have lived with Parkinson's for over six years and I am an active advocate in the fight against Parkinson's. I refuse to live my life for however long God sees fit without being a part of the effort in finding a cure. Like many, when I was first diagnosed I felt as though I was diagnosed with a disease which in fact is true. However, what was once initially thought of as a disease has turned into a blessing. The reason I use the word blessing is because through my diagnosis I found my purpose in life. To be part of a group of people called advocates. In short extraordinary people doing extraordinary things in their search for a cure. So many people go through life wondering what if or what could have been. Never experiencing the awakening of the inner self, Pondering days gone by, never to be retrieved. Doors remain closed and behind those doors are opportunities unchallenged. When we accept life's challenge no matter how difficult they may appear, we choose to travel a road seldom traveled but filled with blessings. Blessings full of friends we would have never found on any other road. The choice is up to us. Travel the road or remain at life's intersection.

P40.08**Don't run and hide from stage 4 and 5! Optimizing function and quality of life for persons with late stage Parkinson's disease***Valerie Carter¹ Karen Mueller¹*

Northern Arizona University Flagstaff, USA

Objective: Persons with Parkinson (PWP) disease who are in the later stages are often treated as if they are not capable of making improvements. For example, when PWP who are in later stages of the disease stop walking due to illness or injury, it is common for them to not be referred to rehabilitation allowing the negative sequel of immobility ensue. PWP who are in the later stages are capable of improved mobility even after months and years of postural instability and immobility. This retrospective case study series will introduce the possibility of functional gains such as improvements in gait and postural instability in persons with late stage Parkinson disease.

Methods: This case study series will discuss the emerging literature that will indicate that PWP who are in the later stages can make cognitive and mobility gains as well as describe valid and

reliable outcome measures for PWP who are in the later stages. Discussion will also contain treatment concepts that are designed around the patient's cognitive and mobility deficits and lasting outcomes to interventions for PWP who would not have normally been referred to rehabilitation.

Results: The data of 4 PWP who were in late stages of PD will be shared. Three of these PWP had gains in their functional mobility post intervention and one which had an appropriate referral to hospice and continued physical therapy interventions to improve function and maximize comfort in the terminal phases of PD. All 4 of these case studies demonstrated benefits such as improved mobility and enhanced QOL from physical therapy interventions

P40.09

Persistence: Reform to rehabilitation in people with Parkinson's Condition

Sergio Contreras Varas, Parkinson's Community of La Serena

This paper is written from the perspective of a user with Parkinson Condition and shows the results from a joint work venture of users, their careers and family, which eventually founded a Parkinson's Community of La Serena, Chile.

The main purpose of this research is to try answer the following question: What else can we do to improve our quality of life beyond the normal treatment? What we are looking to date, with interesting results, has been walking our lives, watched Parkinson User binding.

Methodology: what we have done is to define what we call a Route Parkinson, from the point of view of the physical rehabilitation, divided in three phases:

1. Pre / Post Diagnosis
2. Reinvention process towards Persistence (Reform)
3. Reformed Rehabilitation

For phase 1, Our main effort is to try to collect information / cases on similar experiences in childhood time, environmental characteristics, personal traumas, in other words, a history that would indicate some overlap between users, and try to create a correlation between this issue in order to explain previous life, development of the disease. It can be an important antecedent empirical complement to contribute to early diagnosis.

Phase 2, Which we have called Reformation which from our point of view contains innovative element which objective is to facilitate user behaviors with the creation of systematic methods to the user and also the caregiver (s), to educate through an appropriate teaching methodology to achieve high levels of persistence, which favors the User be in continuous therapy, both physical exercise as primarily oriented toward serving others (be server rather than being served). All this is explained as part of a process of reinvention person, reconstructive action that leads to users, to recognize, accept (RAA in Spanish) our condition. For Phase 3, we have special contributions beyond what is required for good link this reform phase.

P40.10

Persistence: A New Approach for Patients with Parkinson's disease

Sergio Contreras Varas¹

¹Amigos del Parkinson, La Serena, Chile

Objective: This paper tries to demonstrate a new approach for Parkinson condition which links traditional pharmaceuticals treatment along with social support from people exposed to this disease, where the main focus is what factor(s) really improve(s) their quality of life.

Methods: We tried this new approach in a Parkinson's disease group in La Serena, Chile. In order to determine their goals we conducted a focus group with patients, doctors, family and people involved in this condition. In addition, we conducted a reach to find similar patterns in other groups in Chile. Also we tried to find links between treatment and religion focused on Jesuit's catholic spirituality and the impact on rehabilitation.

Results: The research showed us that the Parkinson disease treatment can be approached from we called Parkinson rehabilitation Plan. We defined three stages:

1. Pre / Post Diagnosis: collect information on similar experiences in childhood time, environmental characteristics, personal traumas, in other words, a history that would indicate some overlap between one user and another, and so they attempt a correlation between , somehow permitting explain previous life, development of the disease. It can be an important antecedent empirical complement to contribute to early diagnosis

2. Reinvention process towards Persistence (Reform): which contains innovative elements what we have called it Reformation, in order to facilitate user behaviors with routinize methods and also the caregiver (s). All this strategy is explained as part of a process of reinvention person, reconstructive action that leads to users, to recognize, accept (RAA) our condition.

3. Reformed Rehabilitation: This stage shows the results of this combined strategy toward Parkinson's treatment.

We have not clinically tested due that is not our intention but gives a new hope of relief to the parkinsons patients.

P40.11

Six month interim report on the effectiveness of a self-efficacy learning program for newly diagnosed Parkinson's disease (PD) patients and their care partners

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²University of Denver, Denver, CO, USA

Background: Study is based on the positive results of two existing education-focused support groups for newly diagnosed Parkinson's (PD) patients. This program adds an additional component focused on increasing self-efficacy skills.

Objective: Purpose of the overall study is to evaluate whether this 12-month program results in specific physical, psychological and Quality of Life (QOL) improvements for the person with Parkinson's (PWP) and less perceived burden for the care partner, as measured against standard care PWP and care partners. The purpose of this interim 6 month assessment was program evaluation of the self-efficacy component.

Methods: Led by two trained lay facilitators with PD, 14 participants and their care partners attend monthly 2-hour meetings designed specifically to inculcate self-efficacy behaviors. Patients with PD, care partners and wait-list controls are evaluated at baseline and 12 months using the MDS-UPDRS Parts I, II and III, and self-report psychosocial measures.

Results: Participants with PD reported a high level of self-efficacy (mean = 40.83 [\pm 5.69] of 48 possible points) on the 8 item self-efficacy scale (alpha = .93) developed for this study. A high degree of certainty regarding making positive lifestyle changes was indicated by scores on 3 individual items (all 5.42 [\pm .67] on a 6-point scale). The 12 item care partner questionnaire developed for this study (alpha = .83) showed the program is meeting their needs (44.14 [\pm 4.98] of 48 total points) and is helping them understand what their partner is experiencing (3.86 [\pm .38] on a 4-point scale).

Conclusion: Findings of this assessment suggest that introducing the self-efficacy concept, and modeling and supporting self-efficacy enhancing skills is helping Parkinson's patients and care partners.

The final assessment is expected to verify that these skills play an important role in improving disease management and QOL.

P40.12

Assessment of individuals with Parkinson's disease participating in Rock Steady Boxing

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¹Rock Steady Boxing, Inc., Indianapolis, IN, USA

²Indiana University Medical Center, Indianapolis, IN, USA

Objective: Rock Steady Boxing, located in Indianapolis, Indiana, is the first non-contact boxing program dedicated to people with Parkinson's disease. Founded in 2006, the organization is steadily growing and currently offers 16 classes/week to over 125 participants. Over time the need to define classes appropriate for individuals in different stages of PD was recognized. Assessment with standardized methods was initiated early in 2011 and used as part of the evaluation by the trainer and for placement of new individuals in classes. The class levels are roughly based upon the Hoehn & Yahr stages. Reassessments are performed at approximately 6, 12, 18 and 24 months and the reassessment information is shared with the boxers, their caregivers and the trainers who use the information to enhance the class plans.

Methods: Physical assessments are completed in the following order: Fullerton Balance Assessment (FAB, 10 test measures), Timed Up and Go (TUG, 1 measurement), Sit & Reach (1 measurement), Davies Test (performed in push-up position), Jump Rope Test (number jumps/minute) and Purdue Pegboard Test (average of 3 tests on each hand).

Results: Assessments for class placement and reassessments after approximately 6, 12 and 18 months are continually in process. Some individuals go through the Rock Steady assessment process, but never join a class. Between early 2011 and early 2013, initial assessments were performed on 116 individuals, 30 reassessments after 6 months, 9 at 12 months and 1 at 18 months; assessments of newcomers and reassessments of boxers are ongoing. Preliminary results indicate that the majority (>75 %) of boxers demonstrate improvement in one or more functions including balance, coordination and strength after 6 months of class participation. Other non-quantifiable improvements are noted by Rock Steady Boxing trainers and PD caregivers; many boxers are more positive, outgoing and enjoy socializing with fellow boxers.

P40.13

Combining Hatha yoga approaches with Bones for Life® processes for teaching people with mild to moderate Parkinson's disease

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¹Inward Focused Movement, LLC, Indianapolis, IN, USA

²Rock Steady Boxing, Inc., Indianapolis, IN, USA

Objective: Many individuals, diagnosed and undiagnosed with Parkinson's disease, participate in senior exercise classes. We developed a class structure suitable for people living with PD; their caregivers are invited and welcome to participate in these classes. Symptoms and effects of PD can be managed and progression of the disease delayed through regular practice of focused movements based upon Hatha yoga combined with Bones for Life processes, breath awareness, relaxation, mental and vocal stimulation.

Methods: Providing a calming, balanced 75 – 90 minute session which exercises all major functions (physical, mental and emotional). Classes are designed to insure that some form of success is experienced by each and every participant. Processes

used during each class are adapted to the functional level of the class participants.

Process Sequence	Focus on benefits	Minutes
Centering/breath awareness – Ujjayi breath	Emotional calming, centering	10
Torso movement – spine movement in 3 planes with Ujjayi	Flexibility, coordination	15
Sitting or lying – hand, arm, leg, foot and knee exercises	Control, coordination, flexibility	15
Moving to standing – standing, supported exercises	Control, coordination, balance	15
Walking using combination of BFL processes, vocalizing (music used to stimulate movement, vocalize, fun)	Balance, coordination, mental stimulation, voice projection	20 - 30
Standing to sitting or lying; meditation with visualization	Emotional calming, self healing	10 - 15

Results: Combining Hatha yoga approaches with Bones for Life processes provide well-rounded classes for individuals living with PD and their caregivers. These classes are complimentary to other more active PD classes, offered at Rock Steady Boxing, since emotional calmness, flexibility, coordination, balance, movement control, mental and vocal stimulation are encouraged without the challenges of more intense and vigorous exercise. This class design is suitable for active boxers and other people living with PD who prefer to "leave off the gloves" and participate in a gentler class.

P40.14

The Parkinson's Well-Being Map™ – a visual tool to support patient communication with their care team

Lizzie Graham¹, Maria Gálvez², Helen Matthews³, Elisabeth Dohin⁴, Ursula Davis⁴

¹European Parkinson's Disease Association

²Federación Española de Párkinson

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Objective: Motor symptoms have so far been the predominant focus of treatment for people with Parkinson's (PwP). However, it is now increasingly recognized that non-motor symptoms (NMS), which can present at any stage of the disease, may be as disabling as motor symptoms. Common NMS include sleep disturbances, mood disorders, gastrointestinal problems and pain. NMS can significantly reduce the quality of life of PwP and importantly, PwP do not frequently report these to healthcare professionals (HCPs). To encourage PwP to discuss their condition, the Parkinson's Well-Being Map™ (WBM) was developed as a visual tool allowing them to monitor their symptoms over time and to facilitate communication about these with HCPs.

Methods: The WBM was developed in consultation with PwP and their caregivers and in collaboration with the European Parkinson's Disease Association, The Cure Parkinson's Trust (UK) and the Federación Española de Párkinson. It consists of a radar chart with eight radial axes, each representing a functional domain: sleep disturbances, attention/memory, digestion and the gut, movement, bladder and sexual function, pain, mood and other NMS. PwP rate

how frequently they experience symptoms on a scale of 0–4 (Never, Occasionally, Sometimes, Often, Always) across the axes.

Results: The WBM was refined and developed in both print and online formats following user feedback. Since launch, it has been translated into 10 languages and downloaded over 7000 times. The WBM provides an 'at a glance' visual representation of disease status encompassing a variety of symptoms. Indeed, physicians who have used the WBM cite the visual nature of the map as a unique feature aiding the identification of problematic symptoms. Ultimately, the WBM could facilitate communication between PwP and physicians, resulting in focused, in-depth assessment and effective management of symptoms over time.

P40.15

Cultivating community care

Sue Jackel

South Sunshine Coast Parkinson's Support Group, Sechelt, BC, Canada

Introduction: In small communities, a diagnosis of Parkinson's reveals the strengths and limits of local healthcare supports and skills available to residents, especially aging ones. What can Parkinson's-affected individuals and families do to build needed medical expertise so that longtime residents can feel confident about continuing to live amid familiar surroundings?

Background: One answer, emerging from published scholarship¹, is to recruit or train nurse specialists in the management of Parkinson's. PD Nurse Specialists have won recognition for their multifaceted role as translator, medication teacher, self-care coach and research manager. Their training and practice have taught them to be respectful, resourceful and well grounded in people's everyday circumstances. They can contribute immensely to better quality of life, and better care, for Parkinson's-affected families, especially those with limited access to neurologists and other medical specialists.

Method: This abstract proposes a real-life project in community care resource development, on the Sunshine Coast of British Columbia (pop. 30,000). Drawing on the experience and networking of affected residents, the project will seek strategic partnerships with healthcare providers, community organizations, regional health authority managers and Parkinson Society British Columbia. The goal is to have one or more PD Nurse Specialists join our community's established chronic disease care team within three years.

Outcomes: The project will be a form of action research, minuted and summarized for the benefit of other small communities facing similar constraints and challenges. Thus it will be a combination of public education and awareness raising, and a demonstration of the feasibility of community capacity building in the face of provincial healthcare funding restraint.

P40.16

Parkinson's disease: It's just all in your head

Andrew Johnson

www.youngandshaky.com, Auckland, New Zealand

Objective: A diagnosis of Parkinson's Disease can be devastating, especially for those people diagnosed well before the average age. Managing the condition and its effects on someone's day to day life is challenging for patients, their families and the medical professionals entrusted with their care. This poster discusses the hypothesis that quality of life in People with Parkinson's can be

improved by increasing self awareness of their condition and its effects and by subsequent actions based on that awareness.

Methods: Diagnosed four ½ years ago at age 35, the author has subsequently undergone successful

Deep Brain Stimulation surgery, and the paper explores this argument as he attempts to navigate towards better outcomes during the course of his disease. Living with the uncertainty that comes with a progressively degenerating neurological disorder can be almost as difficult as the insidious changes to your mind and body caused by Parkinson's. It is argued here that developing an awareness and understanding of the unique characteristics of your condition can help you, your doctors and loved ones understand and track the progression of your illness and the difficulties you face. Furthermore, this knowledge can assist in maintaining a sense of control over the illness. It is then how you use this state of mind that can help you maintain your functionality as long as possible.

Results: There is no doubt that Parkinson's is a game changer. But that is no reason to let your disease dictate the rules of the game. How a patient perceives their illness can be a strong indicator of their quality of life. Simply put, if you consider that Parkinson's is literally and figuratively just all in your head, a patient may in fact be able to enhance and preserve a good quality of life over an extended period of time.

P40.17

The perception of people with Parkinson's by others

Ann Keilthy

Parkinson's Association of Ireland, Dublin, Ireland

Abstract: The objective was to gauge the ability of those who might not be familiar with the signs and symptoms of Parkinson's disease to understand what it is they are seeing, and therefrom to assess people's preconceptions about others [in this situation the people are pwps at the wide arena is the assessment of presumptions made and whether educating on one prejudice will cause the subjects to assess their presumptions in the future. and their resulting behavior. A small sample of health professional students at universities in Ireland received a questionnaire to fill out, after hearing a talk given by the lead author, on their perceptions of people with Parkinson's, and what they thought was going on in terms of understanding the symptoms and side effects. Were they drunk? Would they be safe to approach? A majority said they would have no problem, would recognize Parkinson's and would be willing to assist. A second group, the same age and also at university in a health related area, saw the speaker arriving while in a Parkinsonian state, and in this situation a significant percentage of people said that they would not know what to do and some would retreat from the situation.

P40.18

Tai Chi: Eight steps to keep you stepping

Bonnie Lyons-Cohen

Toronto, ON, Canada

Objective: This poster will inform and educate viewers that Tai Chi is of great benefit to People with Parkinson's. The gentle, repetitive movements benefit the body physically and the mind emotionally. Tai Chi increases muscle mass and strength, improves balance, improves flexibility and ease of movement and prevents worse injuries from falling. Individuals as well as groups can practice Tai Chi, indoors or outdoors, making it an excellent social experience. This information will be presented in a graphically pleasing way to inform and persuade people to take up this form of exercise.

Method: Creation of a poster showing the 8 basic steps (plus the

start and end positions) of the Tai Chi form, with each form drawn as a silhouette and the name of that position and the benefits to the body for each one. This will be original artwork, as photos of my Shifu and classmates practicing the form will be used to create the art. Studies will be cited that comment on the effects of Tai Chi on Parkinson's symptoms as well as interviews/comments/quotes from people with Parkinson's who have incorporated Tai Chi into their exercise routines and from those who teach this art.

Results: The poster will educate people about both the medical advantages and the better quality of life that Tai Chi provides. If a picture is worth a thousand words, then this poster will be worth ten thousand words. It will inform and convince more People with Parkinson's, their caregivers and others in their lives to take up Tai Chi and more doctors and health workers to recommend it to their patients.

P40.19

The Parkinson's Tracker - A database management tool for People with Parkinson's

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Objective: Parkinson's is such a unique and complex disease that, often people living with it (PWP) experience very different responses to medications, diets, or even the environment. Thus the goal of this project is to develop a user-friendly tool designed for PWPs to a) help them better understand and document their bodies' shift from "On" to "Off" and vice versa, and b) serve as a communication tool amongst PWPs and their care partners; so that the overall disease management process can be streamlined and quality of life may be enhanced.

Methods: The Parkinson's Tracker is a personal electronic diary designed for PWPs and their care partners to document their Parkinson's journey. This health data management software offers an unbiased and consistent approach in documenting a user's disease progression and well-being by utilizing a database runtime engine to compile and analyze data collected through a 60-item questionnaire organized into 6 correlated categories.

Comprehensive graphical reports are then obtainable in soft or hard copy, detailing the user's current well-being scores and probable disease progression trend line. Additional features of the program include an e-journal for comments or observations and a medications e-organizer. Users are encouraged and reminded to share these reports with their healthcare providers.

Results: With a minimal use of medical terminology and a straightforward interface, this peer-developed application is suitable for PWPs in documenting and trending their PD progression at their own convenience. During a focus group session held in fall 2012, the software was well received by its participants, confirming the need/desire of such tool. Currently the software is available in disk format but a downloadable free app version will be available shortly.

P40.20

Off-Park: impact of wearing-off symptoms on quality of life; matched survey of both people with Parkinson's (PwP) and their care partners

Helen Matthews¹, Jon Stamford² on behalf of the Off-Park survey steering group

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²Parkinson's Movement (PM), UK

Background: The symptoms of wearing-off in Parkinson's affect PwP in different ways with varying impacts on quality of life (QoL). Preliminary evidence suggests Partners/Carers/Family Members ('care partner, CP') notice symptoms of wearing-off before PwP. This is the first survey believed to capture data from both PwP and matched pairs of PwP and their CPs.

Aim(s) / Objectives: To identify the impact of wearing-off symptoms (motor and non-motor) on PwP and their CPs and identify patient defined 'QoL' language which could support more effective QoL discussions between PwP, their CPs and their healthcare professionals (HCP) to improve PD management and daily life for PwP.

Method: This is an ongoing anonymous survey comprising open-ended and multiple-choice questions, available online or via soft/hardcopy. Respondents are recruited through CPT and PM contact databases. Respondents comprise individual PwP and matched pairs PwP and their CPs. PwP respondents have a specialist confirmed diagnosis of idiopathic PD with a disease duration of >2 years. The goal is to gather 200 completed surveys. Survey domains include daily QoL situations and impact of wearing-off symptoms (motor and non-motor).

Discussion: The results will provide insights into the PwP definition of wearing off, its recognition by CPs and PWPs and its impact on QoL issues. This may produce fresh opportunities to improve PD management and daily life for PwP.

Conclusion: The survey may raise awareness of QoL issues and the impact of wearing-off motor and non-motor symptoms for PwP and, for the first time, their CPs.

P40.21

Effects of Dance for PD® on activities of daily living among persons with Parkinson's disease

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Introduction: Dance for PD® (DFPD) was developed by the Brooklyn Parkinson Group (BPG) and Mark Morris Dance Group (MMDG) in 2001. Previous research has indicated that individuals have benefitted in a variety of ways, including significant improvement in the UPDRS assessment of gait, from a brief intervention of DFPD classes. The present study assessed the effects of DFPD on activities of daily living (ADL) among individuals who had attended classes for an extended period of time.

Methods: Participants in three well-established DFPD classes were invited to complete a survey related to effects of the program. Usable responses were received from 53 individuals. The majority of participants were female (76%). Average age was 67 (SD = 12.8). Average length of attendance at DFPD classes was 12 months and more than half the participants (53%) reported attending classes an average of once a week. In addition to items related to effects of DFPD, measures of ADLs, self-efficacy, and QoL were included. Descriptive analyses and correlations were calculated.

Results: Results indicated that 67% of participants rated QoL as "Excellent" or "Very Good," 58% reported they were able to perform several ADLs with more ease because of the class, and 66% indicated they had more confidence in performing daily activities. More than 88% reported that class helped improve mood and sense of well-being and more than 82% reported improved motor functioning and less isolation. Strong correlations (ranging from .58 to .77) were found between effects of DFPD, self-efficacy, and ADLs.

Conclusions: Participants in the DFPD program reported improvements in ability to perform ADLs and in physical, social, emotional functioning as a result of the class. It appears that participants benefited from DFPD and gained a sense of competence in activities outside the studio resulting from increased confidence and activities in the class.

P40.22

"My Life" and the positive power of singing with the Tremble Clefs

Patti Meese

Tremble Clefs, Scottsdale, Arizona, USA

Objective: The healing power of music through the Tremble Clefs choral group provides positive therapy for people with Parkinson's and their Caregivers. After Parkinson's diagnosis in May 2008, Patti Meese realized she was losing her singing voice; couldn't project or hold a note the way she had in past performances and became embarrassed when others couldn't hear or understand her. She would often stay at home and not socialize.

Methods: Meese attended a conference in which the keynote speaker, Sun Joo Lee, Director of the Scottsdale Arizona Tremble Clefs, discussed the importance of singing and the clinical benefits the program provides. She explained that a common symptom is decreased vocal volume with a monotone quality. Lee, who acquired a Master's degree in Music Therapy and Voice Performance from Arizona State University in Tempe, Arizona went on to explain that participation in the choir strengthens a patient's voice, increases the volume and quality of their voices while engaging in a safe, fun environment.

Results: Patti Meese joined the Tremble Clefs and with continued vocal and movement exercises has now regained her singing voice. Her confidence has returned, she has more energy and now describes Music therapy and singing as her 'natural' drug in hopes that everyone will take their 'daily dose' of Music. Many PD patients enjoy the powerful results the same way that Meese has done and are generally healthier and happier. Meese has enjoyed the positive benefits of musical therapy with her Tremble Clef friends so much so that she recently competed in the Ms Senior Arizona Pageant where she won a 1st Place Trophy for Talent by singing an uplifting rendition of 'Get On Your Feet' made famous by Gloria Estefan. Patti Meese often enjoys telling audiences that she now has her life and JOY back because of the Tremble Clefs program under the excellent direction of Sun Joo Lee. Other positive comments by Tremble Clef members: "Since being diagnosed with Parkinson's some 12 years ago, I have learned how difficult this journey is. Now that I'm singing with the Tremble Clefs, my spirits have lifted." "My wife has speech problems. She looks forward to Tremble Clefs every week and being with everybody. We also enjoy the special performances we give." "I enjoy having my voice again and am thrilled to watch the faces of audiences as we perform for them." "Rehearsal days are the BEST of the week because we look forward to singing with the Tremble Clefs. We love it! It's great to have music in our lives again." "We have Tremble Clef withdrawals if we miss a rehearsal!"

P40.23

CHEER>UP: drama therapy support groups for Parkinson's

Anissa Mitchell¹, Anne Curtis¹

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Objective: To address mental, emotional, social and physical issues arising from Parkinson's disease through the use of drama

therapy and humor. To empower Parkinson's patients and caregivers by demonstrating ways to improve wellness, re-frame thought patterns, build resilience skills and live mindfully in the present.

Methods: Cheer>Up (Creativity, Humor, Education, Encouragement, Resilience, (>) Greater Understanding of Parkinson's) is an emerging drama therapy intervention to improve quality of life for Parkinson's patients and caregivers. Using an innovative therapeutic model, "trauma drama", that harnesses metaphor, drama and humor to address Parkinson's issues related to mind, body and spirit. Drama techniques may enhance verbal and non-verbal expression, movement, social skills, socialization, mood, motivation, resilience and cognitive function.

cheer>up sessions target specific "living well with Parkinson's" objectives using drama therapy activities including breathing exercises, vocal practice, movement, pantomime, art, dance, singing and improvisational comedy. Metaphor links elements of each session together and offers participants a novel approach to expressing difficult emotions. The pilot program meets monthly for six months and includes surveys regarding life satisfaction or caregiver strain.

Results: Evaluation of the pilot program will emerge through surveys. The authors hypothesize that participation in cheer>up will cause a positive shift mentally, physically and emotionally for Parkinson's patients and caregivers.

P40.24

The five elements: the implementation of a self-management tool for people with Parkinson's ('PWP's')

Margaret Mullarney¹

¹Move4Parkinson's, Ireland

Objective: Provide a framework for PWP's to better understanding of the management of the complexity of Parkinson's disease in order to achieve an improved quality of life. Based on our founder's personal experience of living with Parkinson's we have developed the Five Elements framework ('The Framework').

Method: The Framework was developed and an educational leaflet produced. A self-management workshop based on the Framework is in development phase.

The Five Elements:

1. **Medication Awareness & Medical Support**
This is the key to the self-management process.
Important questions to ask yourself are 'Do I know what I'm taking? How to take it? When to take it? What it is supposed to do?'
Be aware of potential side effects of any medication.
2. **Nutrition**
What you eat and when you eat may affect the impact of your medication.
Stay hydrated.
3. **Exercise**
Studies have shown that while exercising may not increase the levels of dopamine, it can make your brain use the dopamine you have more efficiently.
4. **Emotional Well-Being**
Be aware of changes in mood/behaviour.
Mindfulness therapies can be an effective tool.
5. **Optional Treatments**
Any interventions that can support your well-being in addition to taking your medication.

Results: 18 recipients of the brochure were surveyed. 100% confirmed the framework was clear & easily understood. 100% reported content provided information that would support PWP's to better manage their condition. 94% would have benefited from this

information at diagnosis. 80% confirmed they will make changes to their lifestyle based on the framework. Comments included 'The whole message is Positive, Punchy and Proactive' 'I wish I'd had something of this quality. The fact that the information has been provided by PWP for PWP is even better'.

P40.25

Why Dance?

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Objective: To explain why dance has been found to be an especially useful form of therapy for PD.

Method: See chart below. It shows how dance embodies many elements that help manage PD symptoms.

PD PROBLEM	DANCE AID
Initiation, continuation and coordination of movement	Dance uses aural (music) and visual (copying someone else) cuing as substitutes for normal automatic movement. Music provides rhythmic, even structure to equalize movement on both sides of the body.
Contraction of muscles, overall stiffness	Dance uses touch to relax contraction and to guide movement; dance involves stretching to improve flexibility.
Poor posture and balance	Intrinsic to dance is the study and practice of alignment, posture and balance.
Poor self-image; self consciousness	Dance teachers demonstrate how to present one's self graciously.
Poor physical memory	Learning new movement and repeating it until it is familiar is an essential part of the dance form. Repetition of movement helps it become habitual.
Isolation	Dance is social
Loss of different qualities of movement	Dancers, stretch, float, jiggle, punch, etc.
Your body won't respond to your direction	Dancers continually direct themselves physically; they move consciously all the time.
Depression	Dance is uplifting and spiritual without being dogmatic.
Difficulty in accessing movement quality	Dance uses imagery to communicate how to move; images provide students with references they can use at other times.

There isn't one exercise form that covers all needs for everyone. But dance is particularly suited to address initiation of movement, rhythmic coordination, social contact and joy in living. Can you name another physical activity that is responsive to so many aspects of PD?

P40.26

Grounding advice: words of wisdom for physicians and those newly diagnosed with young-onset Parkinson's disease

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Individuals newly diagnosed with young onset Parkinson's disease (YOPD) and their treating physicians struggle with many unknowns and unanswered questions. Those who have been living with YOPD for some time have important insights that can be shared, based on their personal experiences managing with the disease.

Objective: Subjects with YOPD were asked to share some of these insights; specific to information and resources they perceived to be invaluable after their diagnoses and the care provided by their physicians.

Methods: Using grounded theory methodology, individuals with YOPD participated in at least one of three means of data collection: multiple interviews, focus groups and/or an online discussion board. Part of the discussion within each of these methods focused specifically on soliciting from participants the advice they would give to someone newly diagnosed with YOPD, as well as the advice they would give to a physician responsible for caring for someone with YOPD.

Results: Based on initial data from 24 individuals with YOPD (14 male / 10 female), a number of important categories have emerged. In terms of the advice given to newly diagnosed individuals with YOPD, there was a focus on the need for information that enables one to be proactive in various facets of life that directly impact health (e.g., exercise and employment), as well as the importance of taking time to manage the emotional side of receiving the diagnosis. Advice directed towards physicians from participants addressed the distinction between information that participants thought should and should not be shared with patients at the time of diagnosis. Other advice related to the importance of following-up with patients after delivering the diagnosis, and elements of the patient-physician relationship. It is anticipated that the knowledge generated will inform the development of future education materials for physicians and those newly diagnosed with YOPD.

P40.27

Living, learning and laughing with Parkinson's disease

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¹ParkinsonsHumor.com, Yuma, AZ, USA

Objective: Teach people about Parkinson's disease; how it affects people's lives and how to use laughter as medicine for all of us, by Blogging and using Social Media.

Methods: In July of 2011, I started writing my funny stories about my life as a Parkinson's patient in blog form and later on, in book form. The title of my blog and book are Parkinson's Humor.

Results: My results were amazing. Within a month, I had 1000 visitors from six continents reading my Parkinson's Humor stories. Now, a year and a half later, my blog counter is at 80,000 and I have had readers from 132 different countries. I write about everything and anything Parkinson's, and always seem to make it funny. I even detailed my recent DBS surgery (with pictures taken in the operating room). I have a knack of turning confusing medical jargon into user friendly stories. My stories have been shared by various Parkinson's groups around the globe and on the Michael J Fox website. I am donating all the profits from the sale of my book to various Parkinson's Foundations.

P40.29**Argentine Tango as a rehabilitation therapy for Parkinson's disease patients**

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Objective: Activities such as exercise programs could be helpful in the management of gait and balance disorders in Parkinson's disease patients (PDp). Argentine Tango could be a good choice of motor rehabilitation of gait in PDp: 1) Specific movement strategies, 2) External cues for initiation and continuation of movement, and 3) Control of dynamic balance. The objective of this study is to evaluate changes in motor and emotional aspects in (PDp) that participated in the Dance Therapy Program using Argentine Tango (DTPAT).

Methods: We recruited 20 PDp, 2 p dropped out. All were evaluated by a Movement Disorder (MD) specialist at baseline and at the end with the following scales: UPDRS; MOCA test; Gait and balance Scale (GABS); Six-Minute-Walk Test (6MWT) and PDQ-39. All p had an interview with a clinical psychologist. Over 16 weeks, p attended 120 minutes (min) tango sessions per week: 20 min: breathing, proprioception, and postural correction; 30 min: basic step of tango; 10 min: break; 30 min: new steps, and 30 min: Tango dance.

Results: Mean age: 65 years; male:11; years with PD: 5 [3-7]; H&Y II:13p and III:5p; MOCA: ≥ 26 : 14p. UPDRS: using Wilcoxon test matched samples we found statistical difference between baseline and final visit in: part II ($p=0.02$), part III ($p=0.01$), and total score ($p=0.0005$). Other evaluations did not show statistical difference. In psychological interview p extremely enjoyed the program with high compliance (assistance >90%). They reported benefits dancing tango and discovered that their bodies are able to do it beyond the restrictions that PD may present.

Conclusion: DTPAT showed to be useful improving PD symptoms. Patients felt tango as a valid form of exercise, making this modality a suitable and interesting rehabilitation tool.

Acknowledgments: We thank the collaboration of Boehringer Ingelheim-Argentina with an unrestricted grant.

P40.30**Rhythm of Life Cranial Sacral Therapy Explained**

Rosemary Craig and Linda Rose

Our Objective is to contribute to the developing dialogue between the international, medical and alternative health communities as well as people living with Parkinson's on the effectiveness of alternative therapies for Parkinson's Disease.* A review of the available literature** suggests the current consensus is in the need for more research about the effectiveness of such healing modalities. We describe the experience of a Craniosacral Practitioner and a Patient with a 15 year history of Parkinson's *** from a serendipitous meeting at a farmers market to significant improvement in the Parkinson's Patient's Quality of Life. By offering experiential evidence of the potential benefits of this therapy, we hope to capture people's imagination and to inspire them to reach for the potential relief in other healing modalities.

Cranial sacral therapy is a method of alternative healing used across the globe. Working with light pressure and deep patience, the Practitioner guides the Patient into deep relaxation and awareness of their body. The Therapy sessions were given at 6-8 week intervals over a three year period, following the methods of Hugh Milne. **** The Craniosacral Therapy approach has brought consistent results, for this patient. After each session the Patient's posture was straighter, the arm swing more noticeable, the stride length more even, walking more fluid and movement easier. These improvements in functional performance ***** have allowed an increase in complex techniques in the Patient's hobby of woodcarving. This enhanced function has also led to a General feeling of well being and the sense of knowing her place in the world.

P40.31**Parkinson en mouvement: evolution and current focus**

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Intention: This poster presents the evolution of *Parkinson en mouvement* Montreal, Quebec, Canada. The aim of the initial dance classes for people with Parkinson's (2007) was to provide an environment of creativity, joy, and movement through access to professionally taught dance classes designed to meet needs of those living with Parkinson's. Classes of 5 grew to 10 and more classes were added each year. The classes are documented in film, television programs and news articles; there have been several public performances. A complementary singing group emerged in 2010. Parkinson en mouvement is now incorporated as a not for profit organization with a team of teachers with training and experience in dance therapy, physiotherapy, and medicine. The initial framework transitioned into a team model of one dancer/dance therapist with a physiotherapist with dance training; in 2010 the physiotherapist of the team completed training and certification in LSVT/BIG (an intensive whole body amplitude-based training protocol for people with P. D.). This added a tool to the teaching approach; with class warm-ups and choreographies designed around principals of LSVT BIG. Evidenced based LSVT/BIG was presented to class members via verbal explanation, example, articles and demonstration; most importantly it was experienced.

Method: There are numerous published observations of how dance, movement and exercise classes affect people with Parkinson's; few are based on the experience people living (and dancing) with Parkinson's. Our research integrates the written and stated perspective of the dance class members who experience Parkinson's.

Results: This process led to the development of a teaching template with the goal of training more professionals to lead similar classes supporting the development of classes throughout the Montreal region and to contribute to work across Canada. Training templates are being formalized and internship opportunities developed. Please see Parkinsonenmouvement.com

This poster session will be discussed in English, French, Czech, Ukrainian and Russian by the current teaching team: Joanabbey Sack (dance therapist), Maura Fisher (physiotherapist), Zuzana Sevcikova (dance therapist/physiotherapist) and Tetiana Lazuk (MD/psychotherapist).

P40.32

Parkinson's Buddy Program: piloting a new support model for people living with Parkinson'sLouise Leblanc¹, Marjie Zacks², Barbara Snelgrove³¹Parkinson Society Canada, Central & Northern Region, Toronto, ON, Canada²Chair, World Parkinson Congress 2013, Communications Committee³Parkinson Society Canada, Toronto, ON, Canada

Objective: To pilot the buddies concept as a model support program for people living with Parkinson's. Parkinson's is a complex condition that impacts people on an individual basis. Often they feel isolated and search for a way to connect with others who understand their experience. Support Groups are one option, but often people are not comfortable discussing problems in a large group because they are either shy or may be very private people. There may not be a local support group nearby and transportation may present challenges. A one-on-one buddy program may address many of the issues that prevent people attending a Support Group and may lead to ongoing, individual support.

Methods: World Parkinson Congress 2013 launched a new Buddies Program matching registrants from around the world with a Canadian buddy to share experiences about living with Parkinson's. Based on the tremendous response to the Buddies Program, we recognized its potential for ongoing support beyond the WPC experience. One of the Parkinson Society Canada WPC Buddies Co-ordinators is interested in piloting the program so there will be consistency in delivery based on WPC experience.

Results: We will gather feedback from WPC Buddies on the benefits of the program. As part of the WPC poster presentation, we will seek ideas and suggestions on how this model might best work as a support program. Building on the success of the WPC Buddies Program, we will develop an application similar to the WPC application. We will create promotional material for over 50 support groups in our region, using our newsletter and web site. We will offer appropriate training for the buddies and ongoing educational support. We plan on piloting this project after WPC and will share our success with other global partners with the hope that they would implement the buddies program in their country.

P40.33

Living Well with PD: Vocal Strengthening and Singing GroupMerrill Tanner¹, Lili Liu²¹Glenrose Rehabilitation Hospital, Edmonton, AB, Canada²University of Alberta, Edmonton, AB, Canada

Background: The weekly "Vocal Strengthening and Singing Group for People with Parkinson's Disease" provided in Edmonton, Alberta by Speech Language Pathologist and singer Merrill Tanner evolved from a research study on the use of singing to improve the vocal skills and quality of life of people with PD. The treatment portion of the study was completed in 2010 as a part of a PhD program at the University of Alberta. The results of the study (presented at the CAG and the GSA in 2012) showed that physical vocal parameters (loudness range and average pitch during a reading task) and 'Quality of Life' as it relates to voice and communication (Speech Intelligibility Inventory: Self Assessment Form) both improved as a result of the six-week intervention. The study participants initiated a weekly group at the beginning of 2011 led by Merrill Tanner.

Treatment: During the first 45 minutes of each session participants perform vocal exercises taken from speech and voice therapy and choral and vocal pedagogy that condition the vocal and breathing mechanisms and release tension that interferes with optimal voice use. A break of 15 minutes encourages socialization with an

energized voice. The second hour involves choral and unison singing focused on maximal vocal effort, emotional expression, body movements to enhance breath support and having fun! Professional piano accompaniment and improvisation is provided throughout the session.

Benefits: This ongoing group is much more than an ordinary sing-along and should be offered in every town! It is an enjoyable, therapeutic, community-based activity that does not feel like therapy. It strengthens the support network around those with PD, as relatives, caregivers, etc. may be present. Participants choose whether or not to attend, thus contributing to self-empowerment and self-management. No prior musical knowledge or experience is necessary and all skill levels are easily accommodated.

P40.34

Creativity and personal story as a healing modalityGary Turchin¹¹PD Active, Berkeley, CA, USA

Background: Gary Turchin is an award-winning poet, performance and visual artist with 40 years of experience riding his creative edges (see www.garyturchin.net). Diagnosed with Parkinson's in 2004, he has published three books in the last three years, and wrote and performed a one-man show, "The Healthiest Man On Earth; A Poet's Journey With Parkinson's," which is also the title of a documentary film about him (see: <http://youtu.be/craVH8mzpuQ>). He says that as long as he remains creative, then he feels like "the healthiest man on Earth."

Objectives: The aim of this session is to inspire a creative practice in PwPs and their caregivers, in response to their physical and emotional challenges. A creative practice grounds one in a milieu of hope and excitement. It is the best anti-depressant on the market. Turn your symptoms into symbols, your Parkinson's to poetry.

Methods: Remember being diagnosed? How did it happen? What did you feel? Everyone's story is different. How can you tell yours? Record it? Write it? Sing it? Paint it? Cook it? Through fun exercises, sharing, and Gary's keen artistic sensibility and inspired enthusiasm, we'll explore our creative edges, and begin to see the arc of story, which is the connective tissue to the human experience. Let's give you something to think about, other than your symptoms, or caring for someone with symptoms.

Results: Participants will leave this session with a new curiosity about their creativity and personal story, and some tools for incorporating that into their lives. They may very well leave with a seed of what they want to do with their story. They will definitely leave with a kick in the pants to come home to their creativity, and with a network of like-minded PwPs to stay connected to.

P40.35

Hamilton City Ballet's Dance for Parkinson's: bringing hope through dance

Jody White, Melania Pawliw

Hamilton City Ballet, Dundas, ON, Canada

Objective: To provide a safe and inspiring ballet class for people with Parkinson's and their families, with opportunities for nurturing friendships after class with indulgent cupcakes. Hamilton City Ballet (HCB) is a classical ballet school, located in Hamilton, Ontario, Canada, founded by Artistic Directors Max Ratevosian and Melania Pawliw. Jody White, Program Manager has combined her love of ballet with her career in health sciences to this program.

Methods: HCB offers *Dance for Parkinson's* classes to families living with Parkinson's. Classes are based on classical ballet techniques and storylines, with the added enjoyment and benefits of

live classical musical accompaniment. We were inspired by both the English National Ballet's *Dance for Parkinson's* and the pioneering, *Dance for PD* which is reflected in the choreography and delivery of our classes. HCB spring 2013 session consists of 3 monthly two hour classes which follow the storyline of *Coppelia*. The first hour is the ballet class, followed by Cupcakes & Friendship in the second hour. Sponsorship was secured from *Tiny Cakes* who provide cupcakes. The teachers trained with David Leventhal, of *Dance for PD*, whose model and theory provides the framework for the class.

Results: Hope and joy are the foundation for HCB's *Dance for Parkinson's*. Through the course of the first hour of class, students appeared to acquire a sense of belonging and were mindful of their dance movements, instead of the limitations of having Parkinson's. These results are achieved through dancing to live classical music in an environment that is challenging while at the same time, respectful of limitations. According to Pam, a *Dance for Parkinson's* student, "Sometimes when I can't walk, I can still dance". The inaugural class was a success as evidenced by student's feedback and registration for further classes. Monthly classes continue through June and weekly classes begin in September.

P40.36

Dancing for exercise, well-being and making friends

Richard Windle¹, Janet Roberts¹, David Stanfield¹

¹Volunteer, Parkinson's UK, West Hertfordshire

Objective: To set up a dance class for people with Parkinson's. To produce a 'best practice' guide that might help other Parkinson's UK branches to do the same. To examine how participants benefitted from this activity.

Methods: The first steps were to find a teacher, someone who could provide live music and a suitable venue. We worked with the London-based charity Musical Moving who helped us to find a teacher and provided invaluable advice. A timetable was agreed and an enrolment form devised. The classes were well publicised and took place weekly.

Each session began with warm-up exercises followed by movement, initially sitting, then standing and finally moving around the room, accompanied by live music. It was noticeable that some participants seemed to take on a new lease of life and were able to move much more freely.

We were aiming for up to twenty participants each week. A few carers took part, others helped out. Two sessions of six weeks were planned with a gap between them (around Christmas 2012). This was to enable changes to the programme to be made at the half-way stage.

Results: The project was evaluated in two ways; by monitoring the numbers attending and by means of a structured questionnaire that was given to all those who took part. On average there were sixteen participants each week. Almost all thoroughly enjoyed the experience and said that they had benefitted from it. It was apparent from the questionnaire responses that there are three themes running through these comments that contributed to their enjoyment:

- The dance movements as a form of exercise
- The 'inner peace' that the activity brought
- That participants generally got on well and bonded as a group

A practical guide for setting up dance classes is being written based on everything we learned.

LIVING WITH PARKINSON'S: ADVANCING RESEARCH: FUNDRAISING, TRIALS, CAMPAIGNS

P41.01

The answer is in all of us: how fox trial finder empowers patients and powers research

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Background: PD patients report wanting to participate in research, but fewer than 10% ever do. Meanwhile, 30% of authorized clinical trials never happen because they fail to recruit enough participants. Research progress depends on more patients taking part.

Objectives: The Michael J. Fox Foundation for Parkinson's Research (MJFF), wanted to make participation in clinical trials as easy as possible for patients, and to help clinical trial coordinators find qualified participants. Another goal was raising awareness and providing education about the importance of clinical trials.

Methods: Using input from patients, researchers, and industry, MJFF developed Fox Trial Finder (FTF), an online tool designed to match patients and controls with clinical trials. FTF lists all ethically approved PD clinical trials, regardless of funding source. It provides information about trials in general, informed consent, and patient rights and responsibilities. Registrants search for trials without commitment, and communicate securely, directly and anonymously with trial coordinators at the university or institution conducting the research; they can be notified when a new trial is posted that matches their profile. FTF also allows registered trial team members to search the anonymous profiles of PD and control registrants, and communicate with those who may be a fit for their research. While created by MJFF, FTF is an independent database; registrants will never be contacted by MJFF unless they opt-in.

Results: Since its launch in April, 2011, 15, 600+ people have registered (75% PD, 25% control), and 200+ PD trials have been posted. More than 300 researchers are using FTF to find trial participants. FTF is now live in the USA, Canada, the UK, Ireland and Australia. In fall 2013, FTF will be available in 4 additional languages and will list trials in France, Germany, Spain, Italy and Austria. FTF raises awareness and provides education through its Ambassadors and Clinical Trial Recruitment Community Partners programs. FTF Ambassadors receive toolkits for grassroots outreach; they also use quarterly calls to share ideas. The Community Partners program facilitates connection among key stakeholders.

Conclusions: Fox Trial Finder empowers patients to become directly involved in research, and powers research with the trial participants needed for success. A cure and better treatment for PD will not be found without patient participation – the answer is in all of us.

P41.02

Information and support groups in growth strategy the Run for Parkinson's Brazil

Janette de Melo Franco

Run For Parkinson's Brasil, Belo Horizonte- Minas Gerais – Brasil

Summary: The Run for Parkinson's Brasil brought up Parkinson's disease and the subjects about it, in an event that mobilized thousands of people and touched various sections of the society. Although, to make sure this event wouldn't happen only on April and its effects would be limited, the benefits out of social network would

be necessary, like the creation support groups in the countryside, not necessarily linked to any specific Association.

Methods: The information and support group was a path to make sure the information would get through ailing people and their relatives. The group brings high quality information at low cost, emotional support with the similar, exchange of experiences, supported by professional volunteers. If we can reach the patients and their relatives or helpers in the group, at the event "Run for Parkinson's" we will reach more people and various sections of society besides Parkinson's people. The search for sponsors for the achievement of the RUN, always try the locals first with priority of social service institutions, like nonprofit companies. The goal isn't to get money, but benefits for raise awareness and the maintenance of the groups.

Results: In a year, after the event, four support groups had been formed, besides the group which already worked in Belo Horizonte. Our Parkinson support group served five or six people, and nowadays we serve close to fifty and these numbers keep raising. In 2012, only Belo Horizonte city had the RUN, by the time, counting with four hundred people, and, in 2013, this number had doubled in participants and a new sportive competition had been added. Before, there was only one city participating, now, there are seven.

P41.03

Parkinson's UK Research Support Network – working together to find a cure

Emily Hughes¹, Ken Bowler¹, Geoff Butcher¹, Michael Cranfield¹, Richard Hill¹, Harry Pearman¹, Janice Russell-Taylor¹, Richard Windle¹.

¹Parkinson's UK, UK

Objective: Our Research Support Network was set up to provide opportunities for anyone with an interest in Parkinson's research to get involved in the search for a cure and better treatments. We believe that involvement by volunteers will lead to more and better research. This will be achieved: through awareness-raising, fundraising, increased participation in trials, and input by people with Parkinson's and carers into project selection and design.

Methods: The Research Support Network is managed by one full-time manager, one administrator, and a Development team of 9 volunteers. The network has over 700 members, many of whom have proactive roles. We support researchers to encourage them to involve people with Parkinson's in their work as well as promoting participation opportunities in their studies. Volunteers review every application to the Charity for research funding, as one step in our selection process. We encourage initiatives developed by volunteers across the UK to support research. These include raising awareness through events; newsletters and helping other supporters to find out about research; as well as donations by local volunteer groups to specific research projects.

Results: Through the Research Support Network, volunteers and supporters from across the UK are involved in research. 100 specific opportunities were promoted to the network in 2012, encouraging supporters to participate in studies, share their experiences to help researchers develop projects and information, and raise awareness of Parkinson's research. Through the Research Funding Programme, fundraisers from 88 local groups transferred a total of £431,619 to support Parkinson's UK-funded projects. Lay grant reviewers submitted 403 reviews of applications for funding from researchers.

P41.04

A ten-year follow-up analysis of investments made in Parkinson's disease research

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Objective: To analyze investments made in Parkinson's disease research over the past ten years by a non-profit organization.

Background: The Parkinson's Disease Foundation (PDF) is a non-profit organization located in the United States whose mission is to improve the lives of people affected by Parkinson's disease. PDF works to achieve this goal through three distinct yet complementary mechanisms: supporting Parkinson's disease research, providing educational resources, and advocating on behalf of those with Parkinson's. In supporting research, the Foundation seeks out the most promising ideas to understand and potentially solve Parkinson's disease by challenging the scientific community to brainstorm and develop novel scientific hypotheses for testing. In addition, reflecting PDF's long-term commitment to battling Parkinson's disease, PDF supports the development of young scientists and clinicians on their path to becoming new leaders in Parkinson's disease research. We now seek to ascertain the impact of the research PDF has funded over the past ten years.

Methods: From 2000 to the present, the Parkinson's Disease Foundation has provided over \$69 million for Parkinson's research to more than 400 individual scientists as part of a comprehensive and multifaceted approach to support both research and training.

Results: We will provide an analysis of the impact PDF support has had in the realm of Parkinson's disease research. Outcomes of specific projects will be highlighted and how these results may have altered the research landscape will be subsequently examined. We will also analyze the success PDF has had in providing "seed" support to enable grant recipients to compete for larger grants from other sources. PDF will also show how funding young scientists in their formative years has influenced their ability to stay within the field of Parkinson's disease, supporting PDF's efforts to ensure a steady pool of talented scientists dedicated to curing this disease. By utilizing these metrics, it is PDF's goal to identify potential areas in need of support and improve upon the Foundation's existing research programs.

LIVING WITH PARKINSON'S: OTHER

P42.01

Experiencing Parkinson's disease and the Reward System: the point of view of an informed patient

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Objectives: To explore how the reward system works in an informed patient and to implement induced behavior strategies to increase reward sensations.

Methods: It is a case report from an informed patient living with PD. Using literature review and my own experience, I was able to identify and implement strategies to increase reward sensations.

Results: I describe my particular experience as physician living with PD. Because the human biology is designed for pleasure and both pleasure and displeasure are susceptible of reframing, I started a

process of reframing my personal experiences, moving other neurotransmitters, in order to influence my lack of dopamine and to review my reward system. Last year, I started to write reports of my daily experiences and I developed an exhaustive literature review about the relationship between anhedonia and PD. I found that there is a research gap between pathophysiology and quality of life among Parkinsonian patients. Based on both my own experience and literature review, I identified a set of strategies to compensation related to: physical activity routine; food and diet characteristics (taste, nutritive, simple); increasing opportunities to laugh (seeking for funny experiences); modifying my affective relationships (pets and reencounter with significant others); redefining my sexual life; and changing my leisure time activities. Overall, my objective was to revalue my quotidian activities filling them with hedonic value in order to change my distorted reward system. This case report suggests that it is necessary to evaluate the reward system through hedonic enjoy of life and to identify practical and individualized strategies to balance wellbeing among PD patients. Moreover, informed Parkinsonian patients can do an important contribution to increase the understanding of mental health complexities on PD, taking into account that non-motor symptoms are important factors affecting patient's quality of life, particularly, in early onset and rapid progression subtypes of PD.

P42.02

Wilson's disease in southern Brazil: genotype-phenotype correlations and description of two novel mutations in ATP7B gene

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Objective: Clarify the regional distribution of ATP7B mutations in Wilson's disease (WD), genetically analyzing a WD population of southern Brazil.

Methods: 36 WD subjects were studied and classified according to their clinical and epidemiological data. In 23 subjects the ATP7B gene was analyzed.

Results: Mean age at the initial symptom was 23.2±9.3(10–41) years. Mean time since the first symptom and the diagnosis was 27.5±41.9(1–194) months. This population presented a high predominance of an exclusively European origin (74.2%). Nine patients (25%) showed predominantly neuropsychiatric symptoms, 14 (38.9%) predominantly hepatic symptoms, 11 (30.6%) mixed presentation and 2 (5.5%) were asymptomatic. Fourteen distinct mutations were detected in at least one of the alleles. The c.3207C>A substitution at exon 14 was the most common mutation (allelic frequency=37.1%) followed by the c.3402delC at exon 15 (allelic frequency=11.4%). The mutations c.2018-2030del13 at exon 7 and c.4093InsT at exon 20 are being reported for the first time. Subjects homozygous for the most common mutation (n=5) had a mean age of disease onset of 33.4±4.82 years, compared to 15.7±3.21 years for heterozygotes (n=3) and 19.5±8.55 years for the remaining individuals (n=15).

Conclusions: Almost half of the mutations of the ATP7B gene were located at exons 14 and 15. Identification of these most prevalent mutations provide basis to design appropriate regional screening strategies for genetic diagnosis of WD in southern Brazil.

P42.03

Not Only An Old Person's Disease

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Objective: The objective of this research was to assess the gaps in knowledge about 'younger onset' Parkinson's Disease (PD) in order to identify needs for improved support services and information. 'Stage-of-life' factors make the challenges faced by 'younger onset' group (under 65) people particularly significant and worthy of separate consideration.

Method: An online survey of 38 questions plus focus groups were used. The project was promoted via a media campaign. The survey collected a range of demographic, experiential and attitudinal data from respondents. It also assessed HRQoL using the Assessment of Quality of Life (AQoL) instrument.

Results: Of the 297 respondents 56% were men diagnosed between 46 and 65 years. Nearly a quarter had children under 18 living at home. The following themes emerged from the focus groups : young onset people face additional challenges relating to the impact of PD on: a) their ability to continue work or build careers; b) to maintain active social lives; c) maintain their parenting responsibilities and d) plan for a secure financial future. The AQoL results showed the QoL of younger onset PD patients is severely impaired. The QoL scores of H&Y 4-5 scale people reflects the worst possible health state being in the bottom 2% of the Australian population.

Conclusion:

- This research supports the need for improved health and support services including: addressing stage-of-life issues (including counselling related to employment, retirement, financial and future planning and supporting parents of young children)
- PD community nurses
- Better access to neurologists
- Better support for those newly diagnosed

P42.04

How the nonprofit sector can help people living with Parkinson's receive quality voice treatment: two successful models

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Objective: To educate the rehabilitation community on two new service delivery models that enable people with Parkinson's to receive quality voice treatment.

Methods: In 2008, Parkinson Voice Project, a nonprofit organization dedicated to preserving the voices of those with Parkinson's, developed a new service delivery model to ensure that people with Parkinson's would receive the treatment they needed to regain and maintain their speaking skills: Pay It Forward. The challenge with voice treatment for Parkinson's is that patients require intensive individual therapy followed by ongoing maintenance groups; however, Medicare/insurance limits the number of treatments a patient receives and does not reimburse "maintenance therapy." With Pay It Forward, patients receive intensive voice therapy (SPEAK OUT!®) followed by ongoing group therapy (The LOUD Crowd®) at no cost. Each patient is given an opportunity to "Pay It Forward"-- make a donation to help the next patient receive treatment. Through Pay It Forward, no patient has ever been denied

treatment. This unique service delivery model could be implemented in University Speech Clinics or Nonprofit Organizations. Since hospitals bill insurance, Parkinson Voice Project facilitated a second type of service delivery model whereby hospitals partner with a nonprofit organization to provide quality speech services. Hospitals provide the services that are covered by insurance, while the nonprofit organization provides the services and therapy materials not covered.

Results: Pay It Forward covers 22-25% of the Dallas clinic's expenses, while fundraising events cover the remaining budget. Since implementing the Pay It Forward model, Parkinson Voice Project has treated over 650 patients. The "hospital/nonprofit partnership" model has been successfully implemented in Oklahoma. In 2012, over 70 patients received SPEAK OUT! and The LOUD Crowd in Oklahoma. By having the nonprofit sector supplement services provided through hospitals, patients receive the quality voice treatment they need.

P42.05

Going for the Goal!

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Objective: A Parkinson's diagnosis issues the challenge: you can try to take flight or enter the fight!

Methods: Our non-profit foundation is excited to introduce our self-motivated, goal-oriented PDFit program, which intentionally creates a variety of customized nine-minute targeted exercise routines, as well as specialized yoga classes and choreographed PD dance instruction. Designed by ability levels, individualized sets of balance, stability and strength-training exercises help participants concentrate on "competing" against their Parkinson's symptoms-similar to an athlete in training. They challenge themselves and fellow members to consistently increase their endurance and mobility goals through the aid of boxing, step hurdles, weight, agility ladders, pitch back devices, etc.

Results: Following an initial Parkinson's diagnosis, everyone eventually asks: "So, what do I/we do now?" Concerned about future physical and emotional challenges, many people will diligently seek out physicians who will listen and guide, join clinical trials, research the Internet and read the newest written articles, consider whether or not to join a support group, and participate in Parkinson's assessment programs, where they learn the importance of regular exercise to increase endurance, improve balance and mobility, and help injury. Our vision for presenting the multi-faceted PDFit program in communities in our area is to educate otherwise healthy individuals and families affected by Parkinson's in learning that proactive, resilient living equates to having confidence in one's physicians; using medications correctly and participating in a professional mobility assessment' establishing empowering physical goals through consistent, focused exercise; and finding a welcoming, non-intimidating location for sharing interactive resourcing and social interaction with others who understand the questions, fears, frustrations, limitations and triumphs associated with Parkinson's.

P42.06

Parkinson disease in history

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Objective: It is well known that Parkinson disease is a very old disease, which was historically mentioned and discussed by some

old civilizations, about 7000 years ago. The aim of this paper is to provide the historical different stages in which Parkinson disease developed.

Methods: This paper accomplished by going back to some historical texts of an old medical books such as Al-Qanunn book of Avicenna. Some other books related to history of medicine were reviewed as well to trace this disease.

Results: Symptoms and possible treatments for Parkinson's disease are discussed in Ayurveda, an ancient Indian medical practice that has been around since as early as 5000 BC. It is claimed that there are references to the symptoms of Parkinson's Disease in both the old and new testaments of the Bible. In the Iliad, which, along with the Odyssey are claimed to have been written by Homer in the eighth century B.C., the septuagenarian King Nestor describes symptoms that appear to be those of Parkinson's Disease. Avicenn (c980-1037), discussed the various forms of motor unrest in his chapter on nervous disorders in the "Qanunn of Medicine". There is a reference to shaking palsy in the second part of Henry VI, during an exchange between Dick and Say. Parkinson's disease was first formally described in modern times in "An Essay on the Shaking Palsy" published in 1817 by James Parkinson (1755-1824). James Parkinson systematically described the medical history of six individuals who had symptoms of the disease that eventually bore his name. It was not until 1861 and 1862 that Jean-Martin Charcot (1825-1893) with Alfred Vulpian (1826-1887) added more symptoms to James Parkinson's clinical description. The underlying biochemical changes in the brain were identified in the 1950s, due largely to the work of Swedish scientist Arvid Carlsson (born 1923). Lastly, Sinemet was developed by DuPont during the 1970's for the treatment of Parkinson's disease.

P42.07

The central and essential role of the nurse clinician at a movement disorder clinic

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Context: The Andre Barbeau Movement Disorder Unit of the University of Montreal Hospital Center is comprised of an interdisciplinary team that includes a nurse clinician.

Objective: To describe the characteristic role played by the nurse clinician serving a clientele suffering from Parkinsonism.

Method: Over a period of 3 consecutive months (4 days/week), all interventions performed by the nurse clinician were listed and documented in detail. Clinical, administrative and telephone interventions were included.

Results: Based on 534 actions related to 272 patients and performed by the nurse clinician, the majority (41,2%) were related to the evaluation of the needs of the patient, changes in disease progression and overall disease management. Coordinating with other members of the interdisciplinary team and establishing links with community resources came in second place with 20,2%. The third role function involved medication review (19,9%). Lastly, teaching and transmitting information to patients constituted an important aspect of the role of the nurse clinician (18,7%).

Conclusion: The role of nurse clinician specialized in Parkinson's disease is varied and essential. Clinician to the patient, she is also a pivotal member with neurologists, health care professionals and community resources. The nurse clinician plays an essential supportive role to the Parkinson patient and a central role in the interdisciplinary team.

P42.08

Clinical Profile of Parkinson's disease Patients with Pneumonia
 Manor Y¹, Shpant - Llivshiz D¹, Rosenberg A², Ezra A¹ Judith Knaani¹, Giladi N^{1,2}, M. Guttman³, Gurevich T^{1,2} on behalf of the NPF QII Investigators

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Objective: Swallowing disorders (SD) are a common symptom in Parkinson's disease (PD) and may cause pneumonia. A clinical profile of PD patients who experienced pneumonia should be investigated.

Methods: Data was obtained from the National Parkinson's Foundation (NPF) Quality Improvement Initiative (QII) database an observational, prospective longitudinal study, conducted at 18 NPF sites. All PD patients are eligible for enrolment into NPF-QII registry. Dataset filled in retrospectively for the last year includes demographics, causes of hospital admission including pneumonia, PDQ-39 (quality of life questionnaire), cognitive status, treatments and medications.

Results: 4907 patients were included in the study. Mean age 67.20±9.91, age of PD onset 58.40±11.04, body mass index (BMI) 26.73 ± 4.61, H&Y 2.41± 0.82. Thirty two (0.7%) patients self-reported hospital admission due to pneumonia (PWP), 4875 - had no pneumonia (PNP). The PWP's H&Y was significantly higher than PNP's (2.88±0.93, 2.41±0.81, p=0.003). PWP had lower scores on verbal fluency test (14.56±7, 17.78±6.36, p=0.004), PDQ emotional, (7.81±4.94, 6.04±4.85, p=0.039) cognitive (6.34±3.63, 4.29±3.23, p<0.001), and total scores, (35.18±16.95, 25.32±15.94, p<0.001) than PNP. PWP received significantly more antidepressants, antipsychotic medications, cognitive enhancers (51.3%, 30.5%, p=0.006, 21.9%, 8.3%, p=0.002, 18.8%, 5.9%, p=0.006) and more speech and physical therapy (37.5%, 12.9%, p<0.001, 68.8%, 37.3%, p<0.001) than PNP. Logistic regression revealed the strongest association between PDQ cognitive score and pneumonia (O.R=1.14, p = 0.016).

P42.09

The effect of STN-DBS's laterality on voice and perception of speech intelligibility of patients with Parkinson's disease
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Objective: To assess and compare the effect STN-DBS's laterality (bilateral, unilateral-right and left) on voice and perception of speech intelligibility of patients with PD.

Methods: 48 PD patients with STN-DBS (unilateral right 8, unilateral left 13, bilateral 27 patients) were studied. We compared Pre and Post DBS evaluations of objective acoustic analysis and speech perception ratings by the patients, caregivers, and a clinician using the voice handicap index (VHI) and voice visual

analogue scale (VVAS) while patients were On-drug. GRBAS (Grade, Roughness, Breathiness, Asthenia, and Strain) and UPDRS-Speech scores were carried out.

Results: 48 PD patients (19 females, 46 right-handed), age 58±8, PD duration upon surgery 10.5±4.5 years, total UPDRS score (69±22/36±16, Off/On drugs) were evaluated. Pre-DBS voice and speech evaluations did not significantly differ between groups (Bi-STN/Right/Left for VVAS 28/26/28±13, p=0.9, VHI 26/19/15±23, p=0.5 and UPDRS-Speech 1.7/1.2/1.7±1, p=0.5). Post-DBS mean scores tended to worsen (Pre/Post-DBS clinician evaluation 5.2±0.8/4.5±1, p=0.006; GRBAS-total 1.9±1.6/3.4±3, p=0.03; UPDRS-Speech 1.6±1/2.8±1.8, p<0.001). Post-DBS scores significantly differ as a function of laterality: deterioration was significant Post bilateral and left STN-DBS (Bi-STN/Right/Left regarding VVAS 40/20/30±19, p=0.09, VHI 42/15/24±10, p=0.09 and UPDRS-Speech 3.6/1.1/2±1.8, p=0.0004).

P42.10

La Salpêtrière's contribution to the study of Parkinson's disease

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Objective: Jean-Martin Charcot (1825-1893) and his colleagues at la Salpêtrière in Paris contributed significantly to our knowledge of Parkinson's disease (PD). Early in the 1860s, Charcot provided an enlightening clinical description of PD that greatly helped to single out this disease from other tremor-associated neurological disorders, particularly multiple sclerosis.

Methods: Although tremor was a cardinal feature of PD, Charcot insisted that it was not necessarily present in all PD patients. Hence, he argued that the term *paralysis agitans* used by James Parkinson (1818-1892) in his 1817 essay was improper and suggested to change it for Parkinson's disease.

Results: Charcot was the first to describe the masked facies and writing problems associated with PD. In 1867, he introduced treatment with the anti-cholinergic alkaloid drug hyoscine (scopolamine), which was used until the advent of levodopa a century later. However, Charcot erred in classifying PD as a *névrose*, an error was later corrected by some of Charcot's students, principally Georges Marinesco (1863-1938) and Édouard Brissaud (1852-1919). Marinesco's description with Paul Oscar Blocq (1860-1896) of a case of parkinsonian tremor due to tumor in the substantia nigra (SN), in 1893, led Brissaud to propose in 1895 that parkinsonism occurs as a consequence SN damage. However, it was Constantin Tretiakoff (1892-1956) who validated Brissaud's hypothesis in a remarkable thesis defended at la Salpêtrière in 1919 and which reported highly convincing evidence of SN cell losses in cases of PD and lethargic encephalitis. Tretiakoff's findings were definitively confirmed in 1938 by the German neurologist Rolf Hassler (1914-1984), whose doctoral studies in the laboratory of Cécile and Oskar Vogt in Berlin elucidated in unprecedented detail the neuropathology of both PD and post-encephalitic parkinsonism. More recently, various Canadian clinicians and researchers played a crucial role in the elucidation of the pathogenesis of this highly incapacitating illness.

P42.11

ParkNC: a referral network for enhanced Parkinson's disease care throughout North CarolinaLindsay Prizer¹, Jessica Katz², Nina Browner²¹Department of Health Promotion and Behavior, University of Georgia, Athens, GA²National Parkinson Foundation Center of Excellence, University of North Carolina, Chapel Hill, NC

Objective: The complex and chronic nature of Parkinson's disease (PD) demands the support from a variety of specialized healthcare professionals and resources, yet few healthcare settings are able to accommodate such a wide range of services onsite. As a result, physicians often refer their PD patients out for additional care, often to nearby allied health clinicians who may not have the expertise in PD necessary to meet the unique needs of this population. Aware that it has been found that people with PD receive higher quality of care from clinicians who have specialized knowledge in this area, the Movement Disorders Center at UNC Chapel Hill developed a referral network program to expand specialized PD services throughout North Carolina.

Methods: This task was implemented through three primary efforts: 1) creating an on-site, bi-monthly Interdisciplinary PD Clinic, 2) helping to organize a workshop on clinical presentations of PD and PD multidisciplinary care in order to increase the number of PD-trained healthcare professionals in the state, and 3) connecting patients to local expert allied health clinicians through an online referral network, ParkNC.

Results: The Center worked with multiple stakeholders within UNC hospital and across the state to execute these efforts. As of April 2013, the UNC Interdisciplinary PD Clinic has served 37 patients from across NC as well as 4 other states. The ParkNC referral network website currently lists over 70 Parkinson's-trained allied health clinicians, and this list is growing. The process undertaken by the UNC Movement Disorders Center can serve as a model for healthcare organizations in other states to develop similar programs and networks, with the goal of enhancing the quality of care for the more than 1 million individuals living with PD in the United States.

P42.12

The science behind Parkinson's disease: a Wikiversity learning projectJohn Telford¹, Harry Pearman²¹Wikiversity, Leicester, UK²Wikiversity, London, UK

Objective: To enable people affected by Parkinson's (patients, carers, professionals and others)

* who are keen to follow progress in research into Parkinson's, * to share what they have learnt

* by writing about it in accessible language

* and making it available as a constantly updateable on-line resource

Methods: The open, global, non-proprietary medium of Wikiversity has been chosen as the platform for establishing a structured resource which anyone can add to and amend.

The project aims to attract people already attempting to follow the progress of Parkinson's research. This includes many with the ability to explain and write about complex scientific ideas in language understandable by the non-specialist.

The value of this project is to enable such people to share what they discover and make it available in a structured way to the wider Parkinson's community. The wiki format, by which people can build on the work of others and add fresh material, is an ideal vehicle for this. A wiki can allow references to be made to source documents and other background information and thus help to ensure accuracy and scientific integrity.

Results: This Wikiversity learning project has been set up at <http://en.wikiversity.org/wiki/ParkinsonsScience> and already a lot of high quality, interesting and interlinked material has been amassed by a growing number of active volunteers. The main section is for tracking Progress and Prospects in Parkinson's Research and is arranged by topics within fields of research. There is a Magazine subsection for standalone articles and a step-wise Introduction to Parkinson's Science. WPC participants including researchers and health professionals are invited to explore the project and to join the growing band contributing high quality and accurate material to it.

P42.13

What really matters to people with Parkinson's?Richard Windle¹, Janice Russell Taylor, Simon Cran, McGreehin, Emily Hughes, Stacey Shorey, Mary Sinnathanmby¹Volunteer, Parkinson's UK

Objective: The objective is to involve people with Parkinson's, carers and health professionals in a wide-reaching consultation that will identify whether there are any gaps in the coverage of current treatments and research programmes. This information will be useful in discussions with Government on policy issues and to support funding applications, as well as giving people with Parkinson's a voice in the research process.

Methods: The methodology is based on a framework developed by the James Lind Alliance (JLA), a non-profit making body funded by the UK Government. The project will be managed by a steering group where all the stakeholders are represented and will include a consultant from the JLA. Questionnaire-based methods are used. The patient/carer questionnaire seeks to ascertain the symptoms/side-effects that respondents experience and, via open-ended questions, any new developments/improvements in existing treatments they would like to see. The questionnaire for healthcare professionals focuses on their perceptions of what is needed. Some of the unmet needs identified by respondents may already have treatments available and this is determined by cross-checking against the UK's Database of Uncertainties about the Effects of Treatments (DUETS). The final part of the process is a 'priority setting' meeting where the objective is to identify a 'top ten' of unmet treatment/research needs. This is done in a workshop where the merits of different suggestions are debated. Specially adapted techniques based on decision-making theory are used to ensure that all participants have an equal say and the proceedings are not dominated by those with the loudest voices.

Results: By October the consultation will be underway, but it will be too early for results – these should be available in mid-2014 and can be made available to other WPC participants for whom this work is of interest. Examples can be given from priority setting projects carried out in other fields.

Oral Presentations

O144

Overview: Exercise, physical therapy, and benefits to the brain of Parkinson's patients

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Public health recommendations endorse sustained activity throughout life because of its protective effects on health, recommendations that have been extended to chronic health conditions such as Parkinson's. In Parkinson's evidence supports the role of exercise to manage symptoms with improved symptom severity, muscle strength and endurance translating to improvements in function. Exercise targets the effects of deconditioning due to reduced activity and typically includes advice to engage in endurance training such as cycling, treadmill or walking, together with strength, co-ordination and flexibility exercise. Most likely a combination of these types of exercise will provide optimal benefits. Another area of interest is training of functional movements and skills which includes complex task practice with dual and multi-tasking where movements are practiced along with cognitive tasks. Complex exercise in older adults that engage thinking processes and problem solving combined with physical exercise may be beneficial to maintain cognitive function which is also of importance for Parkinson's. Dancing could be considered to engage brain activity involved in cognition and movement. There is also increasing interest in the role of exercise to protect the brain – so called 'neuro-protection'. Studies in animal models suggest that a variety of molecular repair mechanisms restore motor function and tap into the body's own mechanisms of neuro-protection with potential for a neurodegenerative disease such as Parkinson's, although the neuro-protective effects of exercise are yet to be demonstrated in humans. Type and dose of exercise is currently unknown however studies suggest that aerobic forms of exercise at moderate intensity are required although even less intensive activities such as walking can be health-protective in older adults and may be easier to implement. This session will explore the role of different modes of exercise (physical and mental) and discuss optimal ways people with Parkinson's can engage in these types of activities.

Late-Breaking Poster Presentations

BASIC SCIENCE: ETIOLOGY, GENETICS, EPIDEMIOLOGY, AND TOXICANTS

LBP01

Neuropsychological performance in LRRK2 G2019S carriers and non-carriers with Parkinson's disease

Roy N. Alcalay^{1,2}, Helen Mejia-Santana¹, Anat Mirelman^{3,4}, Rachel Saunders-Pullman⁵, Deborah Raymond⁵, Laurie Ozellus⁶, Avi Orr-Urtreger^{7,8}, Lorraine Clark^{9,10}, Nir Giladi^{3,7}, Susan Bressman⁵, Karen Marder^{1,2}¹Department of Neurology, College of Physicians and Surgeons, Columbia University, NY, USA²Taub Institute for Research on Alzheimer's Disease and the Aging Brain³Movement Disorders Unit, Department of Neurology, Tel-Aviv Medical Center, Sackler School of Medicine, Tel-Aviv University, Tel-Aviv, Israel⁴School of Health Related Professions, Ben Gurion University, Beer Sheva, Israel⁵The Alan and Barbara Mirken Department of Neurology, Beth Israel Medical Center, NY, USA⁶Departments of Genetics and Genomic Sciences and Neurology, Mount Sinai School of Medicine⁷Sackler Faculty of Medicine, Tel Aviv University, Tel Aviv, Israel⁸Genetics Institute, Tel Aviv Sourasky Medical Center, Israel⁹Department of Pathology and Cell Biology, College of Physicians and Surgeons, Columbia University, NY, USA¹⁰Center for Human Genetics, College of Physicians and Surgeons, Columbia University, NY, USA

Objective: To compare the cognitive and psychiatric phenotype of Ashkenazi Jews (AJ) with Parkinson's disease (PD) with and without LRRK2 G2019S mutations

Methods: We administered a neuropsychological battery to PD participants in the Michael J Fox AJ consortium. Participants (n=290, including 86 from Beth Israel Medical Center, NY, 80 from Columbia University Medical Center, NY and 124 from Tel Aviv Medical Center) included 146 LRRK2 G2019S carriers and 144 non-carriers. GBA mutation carriers were excluded. Five cognitive domains: psychomotor speed, attention, memory, visuospatial function, and executive function, were created from transformed z-scores of individual neuropsychological tests. Participants in NY were evaluated with the entire battery. Participants from Tel Aviv were evaluated for psychomotor speed, attention, and executive function, but not for memory and visuospatial function. Demographics, clinical characteristics, performance on the Geriatric Depression Scale (GDS) and the neuropsychological domains were compared between carriers and non-carriers. The association between LRRK2 mutation status (predictor) and neuropsychological performance (outcome) was assessed using linear regression models, adjusted for site, gender, age, disease duration, education, UPDRS motor score (UPDRS-III), GDS score and levodopa equivalent daily dose.

Results: Age at onset, gender, UPDRS-III and GDS performance did not differ between mutation carriers and non-carriers. Carriers were older, had a longer disease duration and were taking higher levodopa equivalent daily doses. In adjusted regression models, carriers performed better than non-carriers in executive (p=0.014) and attention (p=0.042) domains. In conclusion: in AJ-PD, LRRK2 G2019S mutation status is associated with better attention and executive function. Given the reduced power to detect differences in memory and visuospatial domain scores, it is possible that LRRK2 carriers perform globally better than non-carriers.

LBP02

Age Specific Penetrance of the LRRK2 G2019S mutation in the Michael J Fox Ashkenazi Jewish (AJ) LRRK2 Consortium; Are there gender differences?

Karen Marder^{1,2}, Ming-Xin Tang¹, Roy N. Alcalay^{1,2}, Lorraine Clark^{9,10}, Helen Mejia-Santana¹, Deborah Raymond⁵, Rachel Saunders-Pullman⁵, Laurie Ozellus⁶, Anat Mirelman^{3,4}, Avi Orr-Urtreger^{7,8}, Nir Giladi^{3,7}, Susan Bressman⁵¹Department of Neurology, College of Physicians and Surgeons, Columbia University, NY, USA²Taub Institute for Research on Alzheimer's Disease and the Aging Brain

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Objective: Estimates of the penetrance of LRRK2 G2019S vary widely (24-100%) and may depend on ascertainment, ethnic group, gender, and other genetic or environmental modifiers. Using the kin-cohort method, we reported a lifetime penetrance of 26.2% to age 80 (95% CI 16.4-43.0) in 983 relatives of 181 Ashkenazi Jewish (AJ) cases, similar to the penetrance of 24% (95%CI 13.5-43.7%) in 2975 relatives of 459 AJ and non-AJ Parkinson's Disease (PD) cases combined (Clark 2006). Here, we estimate the penetrance of the G2019S mutation in the AJ Consortium.

Methods: PD cases completed a validated family history interview (FHI) for PD, age at onset (AAO) of PD, current age, or age at death for each first-degree relative. The kin-cohort method uses the mutation status in PD cases to infer unobserved genotypes in relatives and combines this with PD AAO to estimate penetrance of LRRK2 G2019S in relatives.

Results: 96 G2019S+ probands (39 Beth Israel (BI), 26 Columbia (CU), 31 Tel Aviv (TA)) and 310 G2019S- probands (WT) (95 BI, 106 CU, 118 TA) provided FHI on 383 relatives predicted to be carriers and 1264 predicted to be non-carriers (WT). 74 relatives had PD based on FHI (45 WT and 29 G2019S). Cumulative risk in predicted WT relatives to age 80 was 0.057 (0.035-0.080) and 0.218 (0.128-0.311) in predicted G2019S carriers; RR 3.846 (95%CI 1.990-7.850). Cumulative risk in WT female relatives was 0.027 (95%CI 0.004-0.051) and 0.249 (95%CI 0.071-0.413) in carrier relatives; RR 9.12 (1.98-49.92). In male relatives, WT: 0.091 (95% CI: 0.047-0.139) and carrier relatives (0.180 (95% CI: 0.029-0.377) RR: 1.973 (95%CI: 9.226-6.455).

Conclusions: We confirm that the penetrance of LRRK2 G2019S is low in AJ. The relative differences in penetrance in female and male relatives, may explain the similar frequency of male and female LRRK2 G2019S PD cases.

LBP03

The Autonomic profile of Ashkenazi Jewish Parkinson's disease patients carriers of the G2019S mutation in the LRRK2 gene

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Objective: Autonomic disturbances are common in Parkinson's disease and are often manifested early in the disease. The aim of this study was to characterize the autonomic profile of Ashkenazi Jewish (AJ) patients with PD who carry the G2019S mutation in the LRRK2 gene.

Methods: 285 Parkinson's disease patients participating in the Michael J Fox AJ consortium study (84 from Beth Israel Medical Center, 66 from Columbia University Medical Center, and 135 from Tel Aviv Medical Center) completed an in-depth autonomic evaluation. Assessment included completing the Non Motor Symptoms Questionnaire (NMS), Scale for Outcomes in Parkinson's Disease-Autonomic questionnaire (SCOPA-AUT) and the Rapid Eye Movement (REM) Sleep Behavior Disorder (RBD) questionnaire. Demographics, clinical characteristics, and autonomic data were compared between carriers and non-carriers of the G2019S mutation and were adjusted for differences in disease duration.

Results: 141 patients (mean age 69.6±9.7yrs; 45% females) carried the G2019S mutation. Age, gender, UPDRS-III, and scores on the Montreal Cognitive Assessment and Geriatric Depression Scale did not differ between mutation carriers and non-carriers. Carriers had an earlier age of motor symptoms onset (58.0±10.2yrs vs. 61.8±11.6yrs; p<0.001) and longer disease duration (10.9±6.6yrs vs. 7.1±5.2yrs; p<0.001). On the SCOPA-AUT questionnaire, carriers were less likely to report constipation than non-carriers (34% vs. 43.5%; p=0.038), but reported more urinary incontinence and sweating (0.6±0.9 vs. 0.4±0.7; p=0.01 and 0.6±0.9 vs. 0.3±0.7; p=0.02 respectively). In addition, carriers reported less motor expression of RBD (limb movements: 16.5% vs. 30.3%; p=0.006, shouting 24.5% vs. 40%; p=0.005, hurting of the spouse 7.2% vs. 18.8%; p=0.004). PD carriers of the G2019S mutation may have a distinctive autonomic profile to suggest a unique autonomic degenerative process and less prominent motor manifestations of RBD.

LBP04

Microarray analysis of differentially deregulated striatal gene expression between striatopallidal and striatonigral pathways following Deep Brain stimulation in BacTRAP mice

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Objective: Deep brain stimulation (DBS) is arguably the most effective extant treatment for Parkinson's disease (PD). Although the major pathology of PD is believed to be degeneration of nigrostriatal dopaminergic neurons, the neural mechanisms involved in therapeutic effect of DBS have been explained in pathways sparing the striatum. In order to investigate the role of striatal pathways in the deep brain stimulation we analyzed the changes in the striatal gene expression following DBS in 6-OHDA lesioned mice.

Methods: Two groups of mice, namely BacTRAP D1 and BacTRAP D2 mice were used. The samples thus represent differential expression of genes in striatonigral and striatopallidal medium spiny neurons. Both groups are injected with 6-OHDA to mimic Parkinsonian state. Operations are performed on all mice to place DBS electrodes in the subthalamic nucleus (STN). Half of mice in each group received the actual DBS while the other half kept the electrodes in a sham operation. Samples from each of the four groups (sham D1, sham D2, stimulated D1 and simulated D2) were prepared for gene expression analysis. Samples were tested using microarray technology on an Illumina platform.

Results: Comparison of expression level between the four groups reveals profound genetic changes in the striatum following deep brain stimulation in the STN. Significantly altered genes were grouped into several functional clusters using different bioinformatics tools. Main gene clusters found to go through significant changes include those involved in G-protein coupled receptor signal transduction pathways, chromatin remodeling, inflammatory responses as well as neuropeptide synthesis,

trafficking and release. The results can shed light on exploring novel striatal therapeutic targets for Parkinson's disease.

BASIC SCIENCE: PROTEIN MISFOLDING AND HANDLING

LBP05

Tau oligomers as novel therapeutic target for Parkinson's disease and neurodegenerative synucleinopathies

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Objective: The accumulation of tau protein is an important pathogenic factor in Parkinson's disease (PD) and other neurodegenerative disorders; still it is less well characterized in PD and synucleinopathies. Aggregated α -synuclein can induce tau aggregation *in vitro* and *in vivo*, which indicate that tau aggregation and the formation of neurotoxic tau oligomers mediates α -synuclein toxicity. In this study, we investigated the role of tau oligomers in PD and synucleinopathies and the effects of anti tau oligomer passive immunotherapy in a well established using α -synuclein mouse model of PD.

Methods: We performed systematic biochemical and immunohistochemical analyses of human tissues and brains extracted from different synuclein animal models using a number of novel antibodies. Then we specifically targeted tau oligomer in an α -synuclein mouse model of PD by passive immunotherapeutic approach a novel tau oligomer specific antibody-TOMA- which was administered, intravenously, to aged animals and its effects on the PD-like phenotypes were assessed by multiple approaches. After the final behavioral evaluation, animals were sacrificed and are being systematically analyzed.

Results: We discovered that the synergy between synuclein and tau is dependent on the formation of synuclein oligomers which cause tau aggregation and oligomerization. Moreover, we established that tau oligomer levels in fractions of brain tissues from PD patients are elevated compared to the age-matched controls, and tau oligomers formation coincide with behavioral deficits in the synuclein mouse models. Finally, passive immunotherapy using TOMA reversed the phenotypes in aged synuclein animals. Collectively, these results argue that oligomers represent a potential target for a disease-modifying immunotherapy, either alone or in combination with anti α -synuclein immunotherapeutic approaches.

BASIC SCIENCE: MITOCHONDRIA, OXIDATIVE STRESS, INFLAMMATION, PATHOGENESIS

LBP06

LRRK2 and oxidative stress: can we turn genotypes into phenotypes?

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Objective: As most of the LRRK2-linked animal models of Parkinson's disease (PD) fail to recapitulate the clinically relevant symptoms and pathology, we set out to evaluate whether coupling a genetic susceptibility with an environmental toxin could illicit changes in cell viability. We tested whether an oxidative stress insult could manifest a LRRK2-induced cell survival phenotype *in vitro* and *in vivo*, using various mammalian models of LRRK2.

Methods: Primary, embryonic neuronal cultures harvested from LRRK2 R1441C Knock In (KI) mice, the WT and R1441G-hLRRK2 (WT and RG-hLRRK2) over-expressing animals, and the LRRK2 Knock Out (KO) animals were treated with the active neurotoxic metabolite of MPTP (MPP+) and cell survival was assessed *in vitro*. Simultaneously, we performed *in vivo* MPTP neurotoxin studies on 10-week-old male LRRK2 KI, WT and RG-hLRRK2 expressing mice and their respective wild-type littermate controls. Animals were exposed to sub-chronic and/or acute MPTP treatment paradigms and the brain tissue was collected for sectioning and immunohistochemistry. Dopaminergic cell survival was assessed at the level of the striatum, via optical densitometry of dopamine transporter (DAT) staining, and at the substantia nigra *pars compacta* (SNc) region, using stereological quantification of the surviving tyrosine hydroxylase (TH)-positive neurons.

Results: Our results illustrate that the presence of mutant LRRK2 does not sensitize neurons to death induced by the Parkinsonism-related neurotoxin MPTP. These results suggest that traditional PD-linked oxidative stress insults may not be a major contributing factor in the pathogenesis of LRRK2-linked PD.

LBP07

Deciphering the mechanisms of action of parkin during mitophagy using a structure-based FRET-reporter system

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Objective: To understand the structural basis of parkin's function and to gain insight on its mechanism of activation, Gehring and coworkers have determined the structure of parkin using X-ray crystallography in collaboration with our group. The structure reveals that parkin exists in an auto-inhibited state and its activation must be associated with conformational changes at the C-terminal domain. We investigated the structural changes of parkin during the activation of parkin using fluorescent probes, and set out to characterize the activity of parkin in mitochondrial autophagy (mitophagy) based on insights obtained from the structure of parkin.

Methods: Time-lapse fluorescent microscopy was used to examine the kinetics of wild-type and mutant parkin recruitment to the mitochondria after their depolarization with carbonyl cyanide m-chlorophenyl hydrazone (CCCP). To monitor conformational changes in parkin during the course of mitophagy, we used a Förster Resonance Energy Transfer (FRET) -reporter, consisting of the Cerulean fluorescent protein fused to the N-terminus of parkin, and a tetracycline motif that binds with high affinity to the biarsenical dye FIAsh at the C-terminus.

Results: Wild-type parkin was found to recruit to the mitochondria beginning at 30 mins after CCCP treatment, with half of the cells showing recruitment at 45 mins, whereas no recruitment of the

catalytically inactive mutant was observed during the first hour. In contrast, the W403A mutation that releases the auto-inhibition of parkin predisposes parkin for mitochondrial recruitment, and recruits earlier (10 min) than wild-type. Preliminary experiments with the FRET reporter constructs show that labelling at specific positions does not interfere with parkin's function, and that a FRET signal is detected. Thus, it is possible to use FRET to monitor conformational changes in parkin.

LBP08

Balanced ubiquitination and deubiquitination of MFN regulates mitophagy and affects cell viability

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Parkin, an E3 ubiquitin ligase and a Parkinson's disease related gene, translocates to impaired mitochondria upon mitochondrial intoxication and drives their elimination via autophagy, a process known as mitophagy. Mitochondrial pro-fusion protein Mitofusin (Mfn) was found to be a target for Parkin mediated ubiquitination. In the absence of Parkin, Mfn fails to be ubiquitinated, affecting mitochondrial dynamic. We found that under stressful conditions, the pattern of Mfn ubiquitination changes, leading to the disappearance of the ubiquitinated Mfn isoforms and the concomitant increase in the steady state levels of Mfn. This process is dependent on the activity of deubiquitination enzyme Usp8, which, in our model, is opposing Parkin in the ubiquitination of Mfn, ultimately impinging on mitophagy. We therefore identified a novel pathway where balanced ubiquitination and deubiquitination of Mfn regulates mitophagy and affects cell survival.

BASIC SCIENCE: ANIMAL AND CELLULAR MODELS OF PARKINSONISMS

LBP09

Translational profiling reveals novel gene expression changes in the direct and indirect pathways in a mouse model of L-DOPA-induced dyskinesia.

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Objective: The molecular mechanisms underlying the response of the direct and indirect pathway to chronic L-DOPA that underlie dyskinesia are poorly understood. Here we employ two novel transgenic mouse lines, combining translating ribosomal affinity purification (TRAP) with bacterial artificial chromosome expression (Bac), to selectively isolate RNA from either D1-expressing striatonigral or D2-expressing striatopallidal neurons and study changes in translational gene expression following repeated L-DOPA treatment.

Methods: 6-OHDA lesioned D1 and D2 bacTRAP mice were treated with either saline or L-DOPA/benseraside (6/15mg/kg) bi-daily for 21d over which time they developed abnormal involuntary movements reminiscent of dyskinesia. On day 22 all animals received L-DOPA/benseraside (6/15mg/kg) 1 hour prior to sacrifice.

The striatum of the lesioned hemisphere was dissected and subject to TRAP assay. Purified ribosomal RNA was amplified (Nugen), purified (Quiagen) and gene expression was quantified using microarray (Mouse WG-6 v2.0 BeadChip, Illumina).

Results: 195 significantly varying transcripts were identified among the 4 treatment groups (1-way ANOVA with a Benjamini-Hochberg FDR of $p < 0.05$). Pathway analysis revealed an overrepresentation of calcium signaling (HSA04020; Enrichr p value 0.0012) and long term potentiation (LTP) (HSA04720; Enrichr p value 0.0171) in the direct pathway, with significant involvement of long term depression (LTD) (HSA04730; Enrichr p value 0.04) in the indirect pathway following chronic treatment with L-DOPA. Several MAPK associated genes (Nr4a1, Gadd45g, Stmn1, Fos, Dusp1, and Pak1) were upregulated in the direct pathway after chronic L-DOPA treatment. Strikingly the MAPK pathway activator PAK1 was downregulated in the indirect pathway but upregulated in the direct pathway strongly suggesting a role for PAK1 in regulating the opposing effects of L-DOPA on these two pathways in dyskinesia.

Future studies will assess the potential of targeting these genes and pathways to prevent the development of L-DOPA-induced dyskinesia.

BASIC SCIENCE: BRAIN PHYSIOLOGY AND CIRCUITRY

LBP10

Impairment of cerebral auto-regulation in multiple system atrophy and Parkinson's disease

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Objective: To investigate the characteristics of cerebral auto-regulation in multiple system atrophy (MSA) and Parkinson's disease (PD).

Methods: 23 patients with probable MSA (MSA group) and 15 patients with PD (PD group) were studied. Additionally, 16 patients with orthostatic hypotension (OH) without neurodegenerative diseases (OH group) and 15 normal controls (control group) were recruited for comparison. All subjects underwent tilt test with transcranial Doppler (TCD) monitoring. Blood pressure (BP), heart rate (HR) and blood flow velocity in middle cerebral artery (MCA-FV) were measured at supine position and at an angle of 70° from supine on the tilt table. Pulsatility index (PI) and cerebrovascular resistance (CVR) were also calculated. We used the orthostatic subsection (9 items) of composite autonomic symptom scale (COMPASS) for investigating symptoms of orthostatic hypotension (Suarez GA, et al., 1999).

Results: Of 23 MSA patients, 10 patients (43.5%) are classified as MSA-parkinsonian (MSA-P) subtype. Between MSA-P and PD, there was no significant difference in levodopa equivalent dose and Hoehn-Yahr stage. OH group had DM, HTN, cardiac disease and peripheral neuropathy more frequently than other groups. OH was detected in 15 subjects (65.2%) in MSA group and 7 subjects (46.7%) in PD group by tilt test. In COMPASS orthostatic subsection, there was no significant difference between MSA (16.26 ± 14.52) and PD (11.29 ± 10.52) groups. In tilt test, significant differences were found in supine PI and CVR, post-tilt systolic MCA-FV, PI and CVR between MSA, PD and OH groups. In MSA group, positional change of systolic BP showed a significant positive correlation with the alteration of mean MCA-FV ($r=0.468$, $p=0.024$), and COMPASS score ($r=0.527$, $p=0.010$), while COMPASS score was not correlated with change of mean MCA-FV.

Conclusions: The pattern of cerebral vasomotor control between MSA/PD and OH group was different, resulting from the change of CVR.

BASIC SCIENCE: DOPAMINE, RECEPTORS AND OTHER NEUROTRANSMITTERS

LBP11

Striatal and extrastriatal dopamine correlates with cognition in Lewy body disorders: an ¹¹C altropane PET study

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Objective: The biological basis of cognitive impairment in Parkinson disease is believed to be multifactorial, including dopaminergic loss, degeneration of basal forebrain cholinergic nuclei, cortical Lewy-related pathology, and amyloid deposition. We investigated the contribution of dopamine deficiency to cognition in Lewy body disorders (Parkinson Disease (PD), Parkinson disease with dementia (PDD) and Dementia with Lewy bodies (DLB)) with dopamine transporter (DAT) imaging.

Methods: We performed MRI and PET with ¹¹C altropane in 19 nondemented subjects with PD, 14 with parkinsonism and dementia (PDem, including PDD and DLB) and 17 healthy control subjects (HCS). We analyzed DAT concentration in putamen, caudate, anterior cingulate (AC), orbitofrontal and prefrontal regions, using the Standardized Uptake Volume Ratio with partial volume correction, and we related DAT concentration and global cortical thickness (GCT) to neuropsychological performance.

Results: DAT concentration in putamen and caudate was similar in PD and PDem groups and lower than in HCS. Adjusting for putamen DAT concentration, as a measure of severity of motor disease, caudate DAT concentration was lower in PDem than in PD. Diagnostic group, adjusted for putamen DAT, GCT, and their interactions, related to AC DAT concentration ($p=0.03$), and this association was modified by both putamen DAT and GCT. In PDem but not PD, lower putamen DAT concentration related to higher AC DAT concentration. In PDem, loss of caudate DAT concentration was associated with worse CDR-SB scores and visuospatial function, while higher AC DAT concentration related to greater impairment in semantic memory and language. In conclusion, striatal and extrastriatal dopamine dysfunction both contribute to cognitive impairment in the Lewy body dementias.

CARE DELIVERY & QUALITY OF LIFE: CAREGIVING, RELATIONSHIPS, RESPITE CARE, FAMILIES

LBP12

Experiencing Parkinson's disease: A PhotoVoice Story

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Objective: The intent of this research project is to better understand how Parkinson's disease affects a care partner's everyday life. The PhotoVoice methodology used in the study empowered these care

partners to share, through photographs they take, their perceptions and views of how the disease affects their day-to-day living environment. The broader aim of this research project is to raise awareness of Parkinson's disease with community and health care providers, potentially improving the delivery of care and services to these and other families.

Methods: Twelve adult care partners living with someone diagnosed with Parkinson's disease were invited to participate in the project. Using PhotoVoice methodology, participants were asked to photograph images or situations that illustrate the day-to-day realities and challenges of living with someone with Parkinson's disease.

The PhotoVoice methodology enables individuals to use photography to self-select issues of importance to them. A semi-structured interview is conducted with each participant using their photographs to guide the interview. Content analysis is used to identify themes among the interviews.

Results: The PhotoVoice methodology has three main outcomes: empowerment of the participant, awareness-raising, and the potential to bring about dialogue and change. At the time of this submission, both researchers are conducting post-photography interviews. By August 2013, the research project will be completed. The photos, stories, and themes will be shared with health care providers and the community at public events in August and September 2013. Elements of this PhotoVoice project will be incorporated into nursing curriculum to further educate nurses on evidenced based research for improved care delivery for families living with Parkinson's disease.

CARE DELIVERY & QUALITY OF LIFE: DAILY LIFE ACTIVITIES INCLUDING WORKING & DRIVING

LBP13

Living with Parkinson's: Impact and importance of 'on' and 'off time'

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Objective: This study aimed to develop understanding of the experience of living with Parkinson's, in particular the impact and importance of 'on' and 'off time'.

Methods: This two-stage study was conducted using mixed methods. Semi-structured interviews were conducted with People with Parkinson's (PwP) ($n=20$), informal carers ($n=6$) and physicians ($n=6$) in UK and Spain. Qualitative analysis of interview transcripts informed development of an online stated preference discrete choice experiment (SPDCE) and survey that was completed by PwP experiencing ≥ 2 hours 'off time' daily. Participants were from Spain ($n=100$), UK ($n=98$), France ($n=57$) and Italy ($n=50$). The survey, completed with assistance from informal carers if needed, explored PwP's experience of 'on' and 'off time'; including the impact on health-related quality of life (HRQL, using EQ-5D-5L) and important usual activities (mapped to those covered by UPDRS and PDQ-39). The relative value to PwP of increasing 'on time' and the ability to predict the start of 'off time' was quantified using SPDCE.

Results: PwP reported considerably worse HRQL during 'off' compared to 'on time'. Activity limitations during 'off time' that were of most concern to PwP were self-care (washing and dressing

themselves), mobility at home and communicating effectively. PwP relied heavily on informal carers for help with 'off time' activity limitations. Treatments offering increased daily duration of 'on time' and ability to predict the start of 'off time' to within 1 hour of symptoms returning were valued most highly by PwP.

Study findings highlight and quantify the relatively greater impact of Parkinson's during 'off time' and the value to PwP of increasing daily 'on time' and the predictability of 'off time'. These findings have relevance for considering PwP's priorities in treatment selection and meaningful measurement of treatment benefit. The study also increases awareness of the broader impact of informal carers supporting PwP.

Financial Disclosure: Funded by GSK (Study HO-11-802). The views expressed are those of the authors and not the funding body.

CLINICAL SCIENCES: SYMPTOMS, SIGNS, FEATURES & NON-MOTOR MANIFESTATIONS

LBP14

The clinical features of asymptomatic, first degree relatives of Ashkenazi Jewish Parkinson patients, carriers of the G2019S mutation in the LRRK2 gene

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Objective: To assess differences between healthy non-manifesting carriers and non-carriers of the G2019S mutation in the LRRK2 gene.

Methods: 264 Ashkenazi asymptomatic first degree relatives of Parkinson's disease (PD) patients, carriers of the G2019S mutation in the LRRK2 gene participated in this double blind observational cross sectional study (58 from Beth Israel, 50 from Columbia University and 156 from Tel Aviv Medical Center). Participants underwent a battery of tests including the Montreal Cognitive Assessment (MoCA), neuropsychological tests, the Unified Parkinson's Disease Rating Scale (UPDRS), the Spielberg State and Trait Inventory, the University of Pittsburgh Smell Identification Test (UPSIT), the Geriatric Depression Scale (GDS) and the non-motor symptoms (NMS) questionnaire. Mixed procedures were used to assess differences between carriers and non-carriers. Differences between carriers and non-carriers were also assessed based on age (older and younger than the median age of the cohort=48yrs). Analyses were adjusted for age, sex, pedigree, years of education and site.

Results: A total of 139 individuals (mean age 51.3±15.2yrs; 54% males) carried the G2019S mutation. Genetic groups were similar in age, gender, UPDRS-III, MoCA, GDS, and UPSIT. Carriers tended to have slightly higher scores on the NMS questionnaire than non-carriers (3.1±3.0 vs. 2.2±2.1; p=0.07). Carriers also tended to perform worse on the Stroop color-word test (49.6±11.5 vs. 52.9±10.8 number of words; p=0.06). 42 carriers and 31 non-carriers were in the "older group". Carriers in the 'older' group showed more interference effect during the Stroop than the 'older' non-carriers (p= 0.04) and presented more trait anxiety than non-carriers (p=0.05). Subtle differences in non-motor symptoms can be detected between non manifesting carriers and non-carriers of the

G2019S mutation in the LRRK2 gene. These subtle differences are more apparent in older age and may perhaps be related to changes in the prodromal phase of the disease.

LBP15

Crucial contribution for asymmetric reduction of arm and leg swing in Parkinson's disease: Rigidity versus Bradykinesia?

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Objective: Asymmetric reduction of arm and leg swing during gait has been investigated in the field of Parkinson's disease (PD). Although it has been shown that rigidity and bradykinesia are related to the reduction of arm and leg swing representing gait hypokinesia, the precise pathogenic mechanism of such abnormality remains to be unknown.

Methods: Through visual analysis of video clips recording normal walking and standing, we compared dominant side of rigidity/bradykinesia with more affected side in arm swing, leg swing, low shoulder, and laterally rotated foot, respectively. Nineteen patients showing discordance between severe rigidity and bradykinesia as well as 21 patients revealing concordance between both were enrolled in the current study.

Results: More rigid limb is significantly and moderately agreed to more reduction in arm swing ($p < 0.001$, $k = 0.592$) as well as in leg swing ($p = 0.011$, $k = 0.432$). However, severe bradykinetic limb is not related with arm swing ($p = 1$, $k = 0.014$) or with leg swing ($p = 1$, $k = 0.036$). Taken together, our results indicate that decreased arm and leg swing is more connected with rigidity than bradykinesia. In addition, both lower shoulder position and external foot rotation were not significantly associated with rigidity or bradykinesia, implying that asymmetric posture might be affected by more complicated factors. We suspect that our findings will contribute to the future research elucidating gait hypokinesia for the pathophysiology of PD.

LBP16

Impaired perception of facial expressions of emotion and its link to facial masking in Parkinson's disease

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Objective: There is evidence that the ability to label facial expressions of emotion is impaired in Parkinson's disease (PD). An embodied simulationist account of perception of emotion would predict a link between the ability to perceive expressions of emotion and facial masking symptoms, the ability to voluntarily contract facial musculature. The experimental objectives were to investigate basic abilities involved in perception of facial expressions of emotion and its relationship to facial masking symptoms.

Methods: Across two experiments (Experiment 1: PD $n = 34$, control $n = 32$; Experiment 2: PD $n = 25$, controls $n = 24$) we took psychophysical measures of (1) the ability to discriminate graded intensities of facial expressions of emotion from neutral expressions and (2) the ability to discriminate emotional expressions of graded intensity for each of the four commonly expressed emotions, anger, disgust, happiness and sadness. We also explored the relationship between measures of discrimination of emotion and measures of facial masking, the ability to extract other information from faces, and overall disease severity.

Results: Those with PD were as a group impaired in discrimination of all facial expressions of emotion. However, some with PD performed as well as some of the best-performing controls. In support of embodied simulation, we found a strong, positive relationship between measures of discrimination of emotional facial expressions and measures of facial masking. We also found strong correlations between discrimination of emotion, the ability to extract other information from faces, and overall disease severity. The results indicate a broader impairment in extracting from faces emotional and non-emotional information where impairment in extracting emotional information is in part contributed by a reduced ability to voluntarily contracting facial musculature.

LBP17

Olfaction in LRRK2 G2019S Mutation Carriers

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Objective: Olfaction is not impaired in all genetic forms of PD, and the relative impairment in PD due to LRRK2 G2019S mutations (manifesting carriers, MC) is disputed. It is also not clear whether there is an olfactory endophenotype in mutation carriers without PD (non-manifesting carriers, NMC).

Methods: 126 PD non-carriers (PD-NC), 132 MC, 131 NMC, 106 relative non-carriers (NC-Family) and 35 controls from the MJFF LRRK2 Ashkenazi Jewish Consortium (Tel Aviv Medical Center, Columbia, Beth Israel) completed University of Pennsylvania Smell Identification Tests (UPSITs). Mixed effects models, including family as the random effect, and adjusting for age, gender, Montreal Cognitive Assessment (MoCA) score, site and ever a regular smoker assessed differences in UPSIT; GEE, accounting for correlated data within clusters of families, and adjusting for the other co-variables were used to assess odds of hyposmia ($\leq 15^{\text{th}}$ percentile). Simple mixture models were used to identify subgroups based on olfaction status.

Results: Lower UPSIT score and hyposmia were associated with male gender, older age, worse MoCA, and testing site (all $p < 0.05$). All PD had impaired olfaction, however LRRK2 carriers had better UPSIT (difference 3.5, $p < 0.001$) and reduced odds of hyposmia (OR 0.44, $p = 0.01$) than PD-NC. NMC did not differ from NC-F or controls. NC-F had worse olfaction than controls (difference -2.30, $p = 0.03$), although the odds of hyposmia were not different. Three latent classes were identified in the MC and three in the NMC. In conclusion, olfactory differences between LRRK2 PD and other PD are confirmed in our sample. The existence of subgroups of MC suggests that there may be pathophysiologic heterogeneity in the LRRK2 PD group. Mixture models might be utilized to facilitate identification of clusters of NMC with olfactory phenotypes. Site differences in UPSIT should be considered in cross-cultural comparisons.

CLINICAL SCIENCES: PROGRESSION & PROGNOSIS

LBP18

Modifiable Cardiovascular Risk Factors and Axial Motor Impairments in Parkinson disease

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Introduction: Cerebral changes attributable to cardiovascular comorbidities may aggravate clinical morbidity in various age-related neurodegenerative disorders, including Parkinson disease (PD). Cardiovascular risk factors may contribute to extranigral pathologies, which are thought to associate with dopamine resistant (DR) features including axial motor impairments in PD.

Methods: In this cross-sectional study, we explored differences in the estimated rate of axial motor feature accrual between PD subjects with and without elevated cardiovascular risk factors as estimated by the Framingham General Cardiovascular Disease risk-scoring algorithm. All subjects underwent motor evaluations with the Movement Disorders Society revised Unified Parkinson's disease Rating Scale (MDS-UPDRS), [¹¹C]dihydrotrabenazine (DTBZ) monoaminergic brain PET imaging, and MRI imaging.

Results: PD subjects with elevated Framingham risk (FR) scores ($n=63$, 74.1%) showed higher unadjusted rates of total MDS-UPDRS ($t=3.60$, $p=0.0006$) and axial motor scores ($t=3.98$, $p=0.0001$) per year of motor symptoms compared to subjects with normal risk scores ($n=22$, 25.9%). After controlling for gender, Montreal Cognitive Assessment score, frontal leukoaraiosis severity, and striatal DTBZ activity, elevated risk factor status associated with the rate of accrual of axial motor impairments ($t = 2.62$, $p = 0.011$) but not with total MDS-UPDRS motor score ($t = 1.51$, $p = 0.135$). Frontal leukoaraiosis associated with the rate of axial and total MDS-UPDRS scores per year of symptoms and also associated with elevated systolic blood pressure ($t=2.54$, $p=0.0132$) in a separate risk-factor model.

CLINICAL SCIENCES: COGNITION/ MOOD/ MEMORY

LBP19

The roles of dorsal and ventral striatum in stimulus-response learning: implications for Parkinson's disease

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Objective: Dorsal striatum (DS) function is impaired whereas ventral striatum (VS) processes are relatively spared in Parkinson's

disease (PD). These brain regions are also differentially affected by dopaminergic medication in PD. Our aim was to increase our understanding of the cognitive functions associated with DS and VS to better anticipate, explain, and treat cognitive symptoms arising in PD.

Method: Young, healthy adults performed a task during which they learned to associate abstract images with one of three button-press responses while in a functional magnetic resonance imaging (fMRI) machine. During Session 1 (i.e., learning phase), feedback was provided after each response, facilitating learning through trial and error. Participants then performed Session 2 where they provided previously learned, button-press responses for abstract images. Feedback was not provided in this session to preclude further learning.

Results: DS activation was seen when participants selected a response (i.e., during decision making) in Sessions 1 and 2 but not when they received feedback (i.e., during learning) in Session 1. DS activation increased across the learning phase, opposite to the learning pattern observed in behavioural data, and correlated with response accuracy, not learning efficiency. In contrast, VS activity occurred during the feedback phase, peaked early and decreased over Session 1, mirroring learning behaviour, and correlated with learning efficiency. These data suggest that DS is implicated in decision-making, whereas VS mediates learning stimulus-response associations. In PD, DS-mediated functions are impaired at baseline and improved with dopaminergic therapy, whereas VS-mediated operations are normal at baseline and worsened by dopamine replacement. We anticipated impaired decision-making but not learning in PD, with improvements in decision-making versus impairment in learning owing to dopaminergic therapy. The implications of this study inform cognitive complaints and medication strategies in PD. Understanding striatum-mediated cognition can guide medication titration in PD, considering individualized motor and cognitive symptoms.

LBP20

Associations of cognitive domain impairments and gait disturbance in Parkinson's disease

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Objective: Cognitive impairments are prevalent among people with Parkinson's disease (PD), but the relationship between gait impairments and specific cognitive deficits is poorly understood. This study examined associations between gait and cognitive function, both global and within specific cognitive domains, in a large, well-characterized sample of persons with PD.

Methods: A standardized neuropsychological battery was administered based on published consensus guidelines. Neuropsychological testing included assessment of global cognition, executive function (including attention and working memory), language, memory, and visuospatial function. Multiple linear regression analysis was used to examine the relationship between cognitive domains and gait disturbance after adjusting for age, sex, education, disease duration, and motor symptom severity (MDS-UPDRS III). Separate models were used to examine associations between cognitive domains and gait outcomes determined from the MDS-UPDRS, Part III: (1) score on the individual gait items; and (2) postural instability gait disturbance (PIGD) sub-score, calculated as

the sum of gait, freezing of gait, and postural stability items. Significance was set at $\alpha = 0.001$ to adjust for multiple comparisons.

Results: The sample included 635 individuals with PD who met the UK Brain Bank criteria for PD. Average age was 68 years, and 69% of the participants were male. In fully adjusted models (for age, gender, education, disease duration, and MDS-UPDRS III), single-item gait scores were associated with global cognitive function and executive function, but not memory or visuospatial function. In fully adjusted models, PIGD scores were associated with global cognitive function and executive function (i.e., Digit Symbol scores). More severe gait and PIGD scores were significantly associated with worse scores on tests of global cognition and tests of executive function, even after adjusting for covariates. An improved understanding of the relationship between gait and cognition can inform the development of more targeted rehabilitation strategies for people with PD.

LBP21

The Montreal Cognitive Assessment across English and Hebrew

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Objective: The Montreal Cognitive Assessment (MoCA) is a cognitive screening instrument recommended by the Movement Disorders Society task force for cognitive screening in Parkinson Disease (PD). The MoCA is validated in 21 languages including Hebrew and English, however, it remains unknown whether scores in different languages are comparable. Here, we compare the Hebrew and English versions of the MoCA.

Methods: The MoCA was administered to 528 Ashkenazi Jewish (AJ) PD patients in three sites, one in Tel-Aviv and two in New York. Participants were further evaluated by the Unified Parkinson's Disease Rating Scale (UPDRS). Each section of the MoCA was compared between the English and Hebrew versions. Linear regression models were used to test the association between MoCA performance (outcome) and language, adjusted for gender, PD duration, UPDRS-III and levodopa equivalent daily dose. We repeated analyses restricted to participants with post-secondary education and those with total scores $\geq 28/30$.

Results: Total MoCA scores were lower in Hebrew than in English (24.09, SD=3.89 versus 25.19, SD=3.49; $p=0.001$), even after adjustment for gender, PD duration, UPDRS-III and levodopa equivalent dose in a linear model ($\beta=1.19$; $p<0.001$). However, when language tests (sentence repetition, two points, and fluency,

one point) were removed from the total scores, scores were similar between the languages (Hebrew 22.46, SD=3.44, English 22.61, SD=3.20, $p=0.598$). When individual questions were compared, percent correct in Hebrew was significantly lower in sentence repetition (40.8% versus 75.8%, $p<0.001$) and verbal fluency (41.4% versus 84.6%, $p<0.001$). Similar differences were noted when analysis included only those with post-high school education and those with scores $\geq 28/30$. We conclude that the language section of the MoCA is more difficult in the Hebrew version than the English version. Attention should be directed to comparability of items across languages.

LBP022

Recasting the role of dorsal striatum in learning and decision-making: A study in Parkinson's disease

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Objective: Changes to cognitive functions are now recognized in Parkinson's disease (PD). Our aim was to investigate learning and decision-making in PD, as well as the effect of dopaminergic medication on these separate cognitive processes.

Methods: In Session 1, 36 PD patients and 36 age-matched, healthy control participants learned to associate abstract images to key-press responses through trial-and-error based on feedback. Half of the PD patients learned these stimulus-response relations ON medication whereas the other half learned associations OFF medication. In Session 2, on a separate day, patients and controls were asked to select key-press responses associated with abstract images learned in Session 1. No feedback was provided, precluding new learning. Half of the PD patients performed response selections ON whereas the other half performed selections OFF medication. For each ON and OFF group in Session 2, an equal number of participants had learned stimulus-response relations ON as OFF medication, to reduce carry-over effects from learning efficiency in Session 1.

Results: PD patients learned stimulus-response associations significantly more poorly ON relative to OFF medication in Session 1. Further, learning was impaired in PD patients ON medication relative to controls, though no differences in learning arose between PD patients OFF medication and controls. In contrast, PD patients ON and OFF medication performed key-press responses based on previous learning equally well in Session 2. ON medication PD patients performed equivalently to controls, however, OFF medication PD patients performed these decisions more poorly than controls. In PD, learning is unimpaired but decision-making seems deficient at baseline. Dopaminergic medication worsens learning stimulus-response associations. At present there is incomplete understanding of cognitive impairments in PD and the effect of dopaminergic medication on cognition. Our results help to anticipate these concerns and guide medication strategies, taking into account motor and cognitive symptoms, and individual patient priorities.

CLINICAL SCIENCES: DIAGNOSIS (DIFFERENTIAL, ACCURACY)

LBP23

Metrics to analyze micrographia using signature samples

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Objective: As a result of the increased aging population, the total prevalence rates for Parkinson's disease (PD) will increase. The debilitating nature of this medical condition involving hand tremors can negatively impact use of upper limbs for tasks such as handwriting, potentially resulting in reduced sense of independence, identity and well-being. More than 75 percent of people with PD have issues with abnormally small, cramped writing that tends to taper to smaller size (micrographia). An objective method is sought after here for analyzing micrographia from individuals' signatures.

Methods: Here, we apply a series of metrics on previously published signature samples of patients for analyzing their micrographia status and the effect on their signature legibility. The series of metrics measure the global features and local features of signature samples to detect micrographia progression in different aspects.

Results: With micrographia progression, either global features or local features have been detected to show similar changing trends. The studied metrics could therefore correlate with the general trends of how micrographia progresses. Further experimental data needs to be collected in order to generalize the approach and its statistical reliability.

Financial Disclosure: The authors gratefully acknowledge funding from US National Science Foundation, CBET1133992.

CLINICAL SCIENCES: REHABILITATION SCIENCES (PT, OT, SLP)

LBP024

The effect of dopaminergic medication on muscle performance in people with Parkinson's disease-related fatigue

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Objective: Excessive fatigue is a major cause of disability and activity limitation in people with Parkinson's disease (PD). Additionally, withdrawal of dopaminergic medication (DMed) has been reported to reduce muscle contractile force in people with PD. The underlying mechanisms of PD fatigue, the response to DMed and the effects of normal aging are poorly understood. The purpose of this study was to assess thigh muscle performance of people with PD-fatigue whilst on and off DMed compared to younger and older control subjects.

Methods: Eight PD-fatigue (6M, 2F; age=63.4±6; UPDRS III=4.0±3.8; Parkinson's Fatigue Scale=10.7±1.6), 10 younger unimpaired (6M, 4F; age=25.1±3) and 4 older (3M, 1F; age=56.0±3) volunteers were assessed. Subjects with PD-fatigue were tested twice (minimum of 4 days apart), on and off DMed. Maximum

voluntary isometric knee extensor and flexor torque was determined while monitoring quadriceps and hamstring surface EMG. Superimposed electrical stimulation was applied to the quadriceps to determine percent voluntary activation via twitch interpolation (%Activation). The primary outcome was peak torque (extension and flexion) normalized to body weight (nPT). Secondary outcome measures included %Activation and EMG co-activation index of the quadriceps and hamstrings.

Results: DMed withdrawal produced a significant decrease in quadriceps knee extension nPT (-14%; $p=0.02$) and a 7% decrease (not statistically significant; $p=0.35$) in knee flexion nPT (Figure 1). Younger controls produced statistically higher nPT for both muscle groups (Younger vs PD-ON $p<0.01$; Younger vs PD-OFF $p<0.01$; Younger vs Older $p<0.01$). The older controls produced nPT comparable with the ON medication state of the PD-fatigue. A significant difference in %Activation of the quadriceps activation was present between younger and older groups ($p=0.03$). There was no difference in %Activation comparing PD-Fatigue On vs OFF (Figure 2). EMG co-activation of knee flexors/extensors was not significantly different between groups although PD-fatigue tended to have higher co-activation.

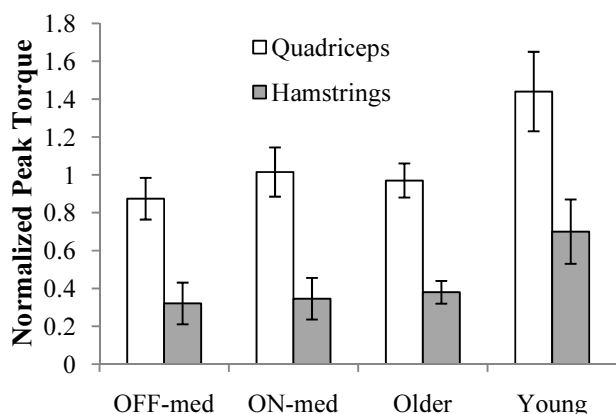


Figure 1.

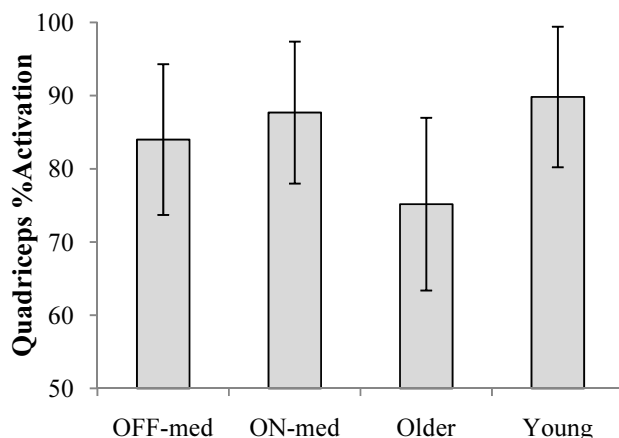


Figure 2.

LBP25

The role of optic flow on locomotion in young adults during overground walking

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Objective: This study serves as the first that investigates the effects of optic flow speed and texture density on gait patterns during overground comfortable speed walking.

Methods: Fourteen healthy young adults were instructed to walk straight forward under two visual conditions: eyes-open, blindfolded. Subsequently, optic flow speed (OS) and dot density (DD) manipulations were implemented. A virtual hallway consisting of two sidewalls with random white dots on a black background was displayed via a head-mounted display. Individual comfortable walking speed (CWS) was estimated while walking through the virtual hallway. OS manipulations included forward flow of equal velocity at the CWS, zero OS and backward flow 1, 2 and 3 times faster than the CWS, with a DD of 50 dots/m². The DD conditions were 10, 30, 50, 70, and 90 dots/m² with backward flow equal to the CWS. All the orders were randomized.

Results: Significant effects of visual conditions were observed for walking speed, stride frequency, stride length, and the phase and frequency relations between arm and leg movements. There was a significant effect of OS on the relative phase between left arm and leg but not on other variables. Walking speed and stride length increased with increasing DD from 10 to 70 dots/m², and slightly decreased from 70 to 90 dots/m². These findings suggest that the richness of texture embedded in the optical array influenced the coordination of overground walking, with participants being more responsive to the changes in DD than OS. These outcomes testified the important role of visual input in modulating gait patterns which could lay the foundation for the prospective development of treatments for movement abnormalities on Parkinson's disease (PD) patients. Currently, we are investigating the effects of visual cues displayed on the walking path on gait regulation in PD patients.

LBP26

Long-term observation of speech and language in patients with Parkinson's disease under continuous Levodopa/Carbidopa intestinal gel therapy

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Objective: The investigators' subjective impression combined with reports from carers suggest that some patients with Parkinson's Disease (PD) benefit from Levodopa/Carbidopa intestinal gel (LCIG) therapy in terms of intelligibility of speech and verbal expression of language. Our objective was to analyze audio-recorded speech samples post-hoc to either refute or confirm this impression.

Methods: 15 patients with LCIG therapy were recorded during a picture description task at 5 different times (before switching from oral to LCIG therapy and 6, 12, 18, 24 months with LCIG therapy). As cognitive decline over time cannot be ruled out, these results are discussed in the light of the Mini Mental State Examination (MMSE), which was conducted at the times of investigation.

The speech samples were analyzed in terms of number of meaningful units per minute (MUM). In addition all samples were judged regarding intelligibility of speech by a student of speech and language therapy using the intelligibility scale of the Lee Silverman Voice Treatment (LSVT). These scores were summed up with the judgments of investigator and carers and the arithmetic average scores were determined.

Results: The following differences in scores before the switch and with LCIG therapy after 24 months were observed: in 5 patients the cognitive function according to MMSE improved, in 3 it remained unchanged over time. The verbal expression in 4 of the 5 patients did not correlate, only one of them improved his rate of MUM, the 3 patients with constant MMSE scores correlated positively in their MUM scores and 3 patients improved their MUM score while decreasing slightly (1-2 points) in their MMSE score. Overall intelligibility of speech improved slightly in 8 patients over two years, 3 remained stable.

LBP27

Central components of quadriceps fatigue are dopamine dependent

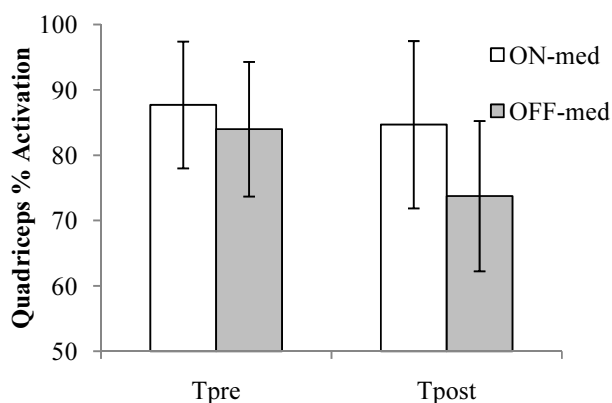
A. Joseph Threlkeld, Sam K. Morton, Dimitrios Katsavelis, Terry L. Grindstaff

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Objective: Excessive fatigue is a major cause of disability and activity limitation in ~58% of people with Parkinson's disease (PD). Additionally, withdrawal of dopaminergic medication (DMed) has been reported to reduce muscle contractile force in people with PD. The purpose of this study was to compare the effects of DMed on the ability of people with PD-fatigue to maximally activate the unfatigued vs fatigued quadriceps muscle.

Methods: Eight volunteers with PD-fatigue were assessed (6M, 2F; age=63.4±6.4; UPDRS III=4.0 ±3.8; Parkinson's Fatigue Scale=10.7±1.6). Two testing sessions were conducted ≥ 4 days apart: one ON prescribed DMed (ON-med) and another session OFF DMed (OFF-med). The order of ON- vs OFF-med testing was alternated between subjects to minimize the effect of testing order. Using superimposed electrical stimulation of the quadriceps and the twitch interpolation technique, percent activation (%Activation) of the quadriceps muscles was measured prior to (Tpre) and immediately after (Tpost) a fatiguing-inducing exercise protocol. The fatiguing exercise consisted of repeated 7-second maximum voluntary knee extension contractions followed by 3 seconds of rest. The 7-3 contract-relax cycle was repeated until reaching ≥35% decrement of each subject's pre-fatigue peak torque.

Results: At Tpre, the %Activation was not different between the ON- vs OFF-med state (ON-med=87.7±9.7; OFF-med=84.0±10.3; p=0.35). At Tpost, %Activation was significantly different between the ON- vs OFF-med (ON-med=84.7±12.8; OFF-med=73.8±11.5; p=0.022). The reduction in %Activation in the OFF-med state following exercise-induced fatigue implies a strong dopamine-dependent central component of exercise-induced fatigue. This finding has implications for disability, activity limitation and community participation related to DMed fluctuations over time. Further studies are underway to discern the interaction of aging and the effects of disease sub-type (people with and without PD-fatigue).



LBP28

To explore the experiences of people with Parkinson's disease of the treatment and care received from a specialist multidisciplinary team at a particular Parkinson's Unit

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Objective: The primary purpose of the study is to understand the experiences of patients with Parkinson's disease of the treatment and care received from a specialist health care team at a particular Parkinson's Unit, rather than from separate places.

The secondary purpose is to inform managers and commissioners of the value of the treatment received from the specialist healthcare team at the particular Parkinson's Unit, rather than from separate places.

Methods: A qualitative study using phenomenological approach and semi-structured interviews was conducted. Purposive sampling by third party was carried out using a cross-sectional design. A digital dictaphone was used for recording the data that was analysed using framework analysis.

Results: Eight people with Parkinson's disease and one carer were interviewed for this study. People recognised that the care received at the large teaching hospitals was impersonal and dealt "purely" with their medical needs. They acknowledged the value of receiving coordinated care at the EPU. Participants appreciated that their progressive needs were being met with continuing support from the integrated multidisciplinary team at the EPU. Participants adopted their own specific strategies for coping with limitations. Thus the findings suggest that the multidisciplinary team at the EPU is meeting the holistic disease-specific needs of people with Parkinson's disease compared to the care received at the large teaching hospitals. The findings also demonstrate that the disease-specific care management by the multidisciplinary team at the EPU may promote self-efficacy for individuals with Parkinson's disease. However, participants highlighted a need for ongoing psychological support onsite as this is currently lacking.

CLINICAL SCIENCES: RATING SCALES

LBP29

Olfactory Capability in Patients with Parkinson's disease

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Objective: Using the „Sniffin' Sticks Screening 12" in assessing patients with Parkinson's disease (PD) during their in-patient neurorehabilitation we investigated:

- olfactory capability (anosmia, hyposmia, normosmia) amongst patients with Idiopathic PD (IPD) and patients with Atypical or Secondary Parkinson Syndromes
- correlation of olfactory capability and disease progression
- self perception of olfactory dysfunction
- changes in olfactory capability over time
- differences in identification between odors.

Methods: Case series comprising 298 patients (60% male, 40% female) who were assessed during routine care in our neurorehabilitation clinic over a period of 30 months with „Sniffin' Sticks Screening 12". Idiopathic PD: 94%, Atypical Parkinson Syndromes: 5%, Secondary Parkinson Syndromes: 1%. Analyses in terms of type of PD, time since diagnosis (1-5 years, 6-10 years, 11 and more years), self perception of olfactory dysfunction, differences between odors and changes in olfactory capability over time.

Results:

- a) IPD (n=280): anosmia: 36%, hyposmia: 55%, normosmia: 9%; Atypical and Secondary Parkinson Syndromes (n=18): anosmia: 27,8%, hyposmia: 27,8%, normosmia: 44,4%.
- b) Date of diagnosis was known for 276 IPS patients: as expected, the proportion of normosmia decreased while hyposmia and anosmia increased steadily over time.
- c) Of 100 IPD anosmics 30% did not judge their olfactory capacity as impaired; of 154 IPD hyposmics 52% did not realize they had impaired olfactory capability. Of 18 patients with Atypical or Secondary PD 10 were anosmic or hyposmic and of these 7 (70%) did not think they had olfactory dysfunction.
- d) 38 patients with IPS were assessed at different times: consistent normosmia: 3; consistent hyposmia: 17; consistent anosmia: 10; normosmia changed to hyposmia: 3; hyposmia changed to anosmia: 3; hyposmia changed to normosmia: 1; anosmia changed to hyposmia: 1.
- e) More than 50% misidentifications: cinnamon (53,9%), lemon (62,5%), licorice (65%), pineapple (60%). Highest correct identification: orange (73,6%).

LIVING WITH PARKINSON'S: PUBLIC EDUCATION OR AWARENESS PROGRAMS

LBP30

The impact of Parkinson's disease on community-dwelling Canadians

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Objective: A national population-based survey was conducted to assess the impact of neurological conditions, including Parkinson's disease (PD), on community-dwelling Canadians.

Methods: The 2011 Survey on Living with Neurological Conditions in Canada was administered to 4,409 respondents age 15+. Targeting 18 neurological conditions, questions covered diagnosis, social support, changes to work/daily living, and general wellbeing. Data specific to people with Parkinson's disease (PwP) were analysed using SAS 9.3; estimates were weighted to represent the Canadian population, and bootstrapping methods were used to estimate variance.

Results: A total of n=356 (unweighted) respondents had PD, representing over 47,000 PwP in Canada. One quarter (27.5%) of responses was by proxy on behalf of PwP. The majority of respondents with PD were men (65.2%) and age 65+ (77.8%). Mean age of symptom onset was 63.8 (range= 12 to 89)(no difference by sex). Mean age of diagnosis was 65 (range = 21 to 89). The majority of PwP experienced limitations in at least one usual activity (79.4%). Only 8.8% were working at the time of survey; 67.1% were not working and a further 23.4% were permanently unable to work. Of PwP who did work, 80.3% reported experiencing changes to their work activities because of their PD. The sense that some people felt uncomfortable around them was the most frequently reported experience of stigma (80.3%). A lower yet considerable proportion of PwP reported feeling embarrassed by their condition (45.4%), perceiving that they were left out of things (34.4%), or perceiving that some people avoided them (24.1%).

Conclusion: The SLNCC is being used to identify the impacts of conditions such as PD on Canadians. This information may support federal and provincial governments, as well as non-government organizations, to better plan policies, health services, and awareness strategies for community-dwelling PwP.

LIVING WITH PARKINSON'S: LIVING WELL WITH PD

LBP31

Young Onset Parkinson's Support Group improves our Quality of Life

Anne Dowling

Objective: To inform others of how connecting with a support group made a difference in coping with the disease.

Method: In January 2005 two people with Parkinson's disease made a commitment to forming a support group for those with young onset Parkinson's. George and Norma found a venue: a small library in White Plains Hospital and advertised through their doctors and on Parkinson's websites. For months they showed up at the designated time and sat alone. Gradually the group expanded to 4, then 6. By 2006 there were 10 members. Now in 2013, we are proud to say that our mailing list contains 40 names! We meet once a month; our current location is Burke Rehabilitation in White Plains New York. We invite guest speakers to inform us and allow time to share and support each other. We also organize social activities such as holiday parties, dining out and attending Parkinson's symposiums and workshops. We participate in the annual Parkinson's Unity walk and this year raised over \$21,000.

Results: We encourage anyone who has recently been diagnosed to connect with a support group. Parkinson's is a lonely disease. People with Parkinson's exert a great deal of energy attempting to minimize the symptoms to appear "normal". No one understands this but someone else with Parkinson's.

LBP32

Achieving the Impossible Together

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¹Center for Music Therapy, Inc., USA

²Team Dopamine, USA

Objective: To change the environment of fitness programs, events and trainings to facilitate Parkinson's patients of all levels to successfully participate.

Methods: The creation of teams which use neurologically based training techniques for Parkinson's patients. Examples of techniques used are music therapy to improve timing and synchronization of movements and treadmills with harness support systems for indoor higher speed cardio training. Personalized tempo music, including tango and other favorites, is very effective with treadmill and body weight support system (if appropriate) for gait training, aerobic exercise, and quality of life enjoyment. Each team member has the goal to participate a minimum of two times yearly in a 10k event with the Team as a relay member. Each team member must agree to focus 60% or more of their thoughts on what they can do.

Results: Team I am / I can was formed in 2005. In October of 2006, five people with moderate to advanced stages of Parkinson's disease successfully participated in their first 5k event. Since this time that Team has successfully competed in 11/10k events. The team size has grown to 40 participants incorporating those who have all stages of Parkinson's disease as well as other neurologic movement disorders. Team Dopamine was formed for early onset Parkinson's disease? Many who were using walkers now use only canes or walking sticks. All have decreased the frequency of their falls. All have slowed the rapid decline of quality of life and decreased the prominence of the symptoms of their disease. The creation of these Teams has energized its team members to regularly exercise at a level that demands higher cardio

performance.

Discussion: Although research supports exercise as beneficial to Parkinson's patients of all stages very little has been done to fund or organize fitness programs for Parkinson's patients. Most programs that do exist are targeted only to early stage patients. Team I am/I can provides a safe model to empower living healthier.

Note: Earl Dumitru was unable to present in Glasgow due to an aortic dissection in August 2010.

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