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Oral Sessions

Oral Presentations A. Epidemiology

A-1
The INTERNATIONAL CLASSIFICATION OF VESTIBULAR DISORDERS OF THE BARANY SOCIETY AND WHO'S INTERNATIONAL CLASSIFICATION OF DISEASES*

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Introduction: The World Health Organisation is in the process of elaborating the eleventh version of its International Classification of Diseases (ICD11), which is projected to be introduced in 2017. ICD is a tool for standardized capture of mortality and morbidity data. It codes health information that is used for statistics and epidemiology, health care management, allocation of resources, monitoring and evaluation, research, primary care, prevention and treatment.
Methods: ICD11 will have new aspects like an up to 100 word definition of each disease or disorder, extensive cross linking between various fields due to multiple parenting, meaning that disorders are not considered to "belong" to a particular field or specialty. The Bárány Society's Committee on Classification is actively involved in the development of ICD11 for vestibular disorders. WHO gathers proposals to update ICD from multiple scientific societies in all fields, for vestibular disorders it is the Bárány Society's mission. Later on all proposals undergo an internal WHO review process.
Results: The present proposal includes the layered approach to decide first if you deal with an acute, episodic or chronic vestibular syndrome before the actual specific disorder. Exactly the same classification for vestibular disorders can be accessed through the parents of ear and nervous system diseases. It gives the opportunity to include newly recognized disorders and provide updated definitions of diseases.
Conclusion: It will be a contribution to ease the coding for vestibular disorders world wide according to modern standards. This should make vestibular disorders more visible to health professionals, politicians and the public.

*This abstract is an invited status report related to the International Classification of Vestibular Disorders and was not reviewed by the scientific committee.

A-2
MANAGEMENT OF PATIENTS WITH VERTIGO IN THE COMMUNITY

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Introduction: Vertigo and dizziness count among the most frequent symptoms in outpatient practices. Although most vestibular disorders are manageable, they are often under- and misdiagnosed in primary care. This may result in prolonged absence from work, increased resource use, and, in case of insufficient therapy, chronification. However, there is so far only limited information on health services utilization of patients with vertigo in the community.
Objectives: To reveal the utilization of diagnostic tests and therepeutic measures in vestibular syndromes in the community.
Methods: Retrospective cohort study on a convenience sample of patients referred to a tertiary care balance clinic. All patients have been seen before by an ENT and/or Neurology service. Patients were included if they had a confirmed diagnosis of benign paroxysmal positional vertigo (BPPV), vestibular migraine (VM), Menière's disease (MD), vestibular paroxysmia (VP), bilateral vestibulopathy (BVP) or psychogenic vertigo/phobic postural dizziness (PSY). Patients were asked to answer questions on previous diagnostic and

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therapeutic measures that they had been assigned to prior to their first visit to the clinic. Log-linear models were used to analyse predictors of utilization.
Results: We included 2374 patients presenting at the clinic between 2010 and 2012 (40.6% PSY, 19.7% BPPV, 14.1% VM, 12.7% MD, 5.8% VP, 7.2% BVP). 61.3% of patients had had more than two prior consultations. Most frequent laboratory examinations were magnetic resonance imaging (76.2%) and electrocardiography (53.5%). For instance, 71% of patients with BPPV had received MRI of brain or cervical spine. Most frequent therapies were medication (61.0%) and physical therapy (41.3%). 37.3% had received homeopathic medication (39% in BPPV), 25.9% were treated with betahistine (20% of those with BPPV). All in all, patients had undergone on average 3.2 (median 3.0, maximum 6) laboratory examinations, had received 1.8 (median 2.0, maximum 8) therapies, and 1.8 (median 1.0, maximum 17) different drugs. Diagnostic subgroups differed significantly regarding number of diagnostic measures, therapies and drugs.
Conclusions: These findings in a large group of patients emphasize the need for establishing systematic training to increase oto-neurological skills in primary care physicians, but also in ENT and Neurology services not specialized on the treatment of dizzy patients.

A-3
EVALUATION OF THE OUTCOME OF THE DIZZINESS HANDICAP INVENTORY (DHI) IN AN OUTPATIENT DATABASE OF 568 VESTIBULAR PATIENTS

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Introduction: The DHI is a well accepted and clinically widely used questionnaire for evaluating the self-perceived handicapping effects of dizziness in patients with vestibular complaints.
Objectives: In this retrospective study, the outcome of the DHI is investigated with respect to symptomatic and diagnostic parameters.
Methods: The DHI contains 25 questions and is comprised out of 3 subscales: emotional, functional and physical. The questionnaire was completed (as part of the standard diagnostic protocol) by 568 vestibular patients (359 women, 209 men; mean age = 54,5 years ($\pm$ 16.3 years); age range from 12.4 years to 90.4 years). Patients were categorized in different diagnosis groups according to the current diagnostic criteria and the self-perceived handicap was evaluated between the different diagnosis groups. Moreover, we investigated the effect of symptom duration (acute versus chronical), symptom frequency ('single episode', 'daily', 'weekly', 'monthly', '2-12 times/year' and 'yearly'), presence or absence of certain symptoms (vertigo, lightheadedness, instability, gait abnormalities, nausea, tinnitus, aural fullness, headaches/migraine and other neurological signs) and caloric (a)symmetry on the DHI score.
Results: There was a significant ($p = 0.002$) gender effect: the total DHI score was significantly higher in female patients (mean = 44.3 ($\pm$ 22.2)) than in male patients (mean = 34.4 ($\pm$ 20.1)). The self-perceived handicap was not significantly different between the different diagnosis groups and there was no correlation between the DHI scores and the level of caloric (a)symmetry. The total ($p = 0.015$) and emotional ($p = 0.001$) DHI-score was significantly higher in patients with chronical complaints (total: mean = 41.4 ($\pm$ 21.0); emotional: mean = 12.2 ($\pm$ 8.1)) in comparison with acute pathologies (total: mean = 35.4 ($\pm$ 22.1); emotional: mean = 9.0 ($\pm$ 8.1)). Patients with daily (mean = 44.1 ($\pm$ 21.3) and weekly (mean = 38.5 ($\pm$ 18.8) complaints had a significantly higher ($p < 0.001$ and $p = 0.011$ respectively) total DHI-score (total: mean = 44.0 ($\pm$ 21.3)) than patients with a single episode of balance complaints (mean = 23.1 ($\pm$ 17.3)). There was a significant effect of symptoms ($p = 0.034$, $r = 0.09$) on the self-perceived handicap (total DHI-score): patients experiencing instability and gait abnormalities had significantly increased DHI-scores ($p < 0/001, r = 0.24$) and patients having no gait abnormalities had significantly lower DHI-scores ($p = 0.021$, $r = 0.16$). No additional effects were found for other symptoms.
Conclusions: The outcome of the DHI-score is neither correlated with the diagnostic group the patients belongs to, nor with the level of (a)symmetry on the caloric test. Experiencing instability and gait abnormality result in a greater self-perceived handicap. Patients with chronical complaints consider their handicap significantly higher than patients with acute complaints.

A-4
THE DIZZINESS/VERTIGO CAREPATH – APPLYING EVIDENCE BASED CLINICAL GUIDELINES TO A LARGE MULTINATIONAL HEALTH CARE SYSTEM. CLEVELAND CLINIC, OHIO
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Introduction: Evidence-based clinical care guidelines for the management of dizziness and vertigo, including benign paroxysmal positional vertigo (BPPV)from the American Academy of Otolaryngology - Head and Neck Surgery and the American Academy of Neurology and acute management of dizziness and vertigo from the American Academy of Emergency Medicine have recently been released, advocating 1) Dix-Hallpike positioning testing to identify BPPV and 2) recommending against head computed tomography (CT scan) except in patients with acute neurological findings in addition to dizziness and vertigo. A project to operationalize these recommendations into a system-wide "CarePath" utilizing electronic medical records within a large multi-national health care system is reported here.
Objectives: Describe the process of identifying and operationalizing multidisciplinary clinical guidelines for Dizziness/Vertigo in an electronic medical records based multi-national health care system.
Methods: Case report.
Results: Over 50 providers from numerous specialties and international locations collaborated to establish an electronic medical records assisted clinical CarePath for Dizziness and Vertigo. Consensus recommendations included 1)Perform Dix-Hallpike positioning to identify BPPV at all entry points into the health care system, across multiple specialties. 2) Head CT scans are recommended only for patients with acute neurological findings in addition to Dizziness/Vertigo. Education materials were developed to support these recommendations, and will be presented.
Conclusion: Establishing clinical guidelines across muliple specialties and international locations within a large health care system necessitates collaborative effort. Electronic medical records support and educational materials are helpful once specific guidelines are identified.

Oral Presentations B. Microgravity Investigations

B-1
VERTICAL AND TORSIONAL OCULAR MISALIGNMENTS ELICITED BY ALTERED GRAVITY-LEVELS PROVIDE EVIDENCE FOR MULTIPLE CENTRAL COMPENSATORY MECHANISMS
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Introduction: Slight asymmetries between the left and right otoliths, resolved on Earth through central compensatory mechanisms, have been linked to motion sickness in altered gravity environments; symptoms persists until compensations are adapted for the new g-level. We examined these innate otolith asymmetries through vertical and torsional ocular positioning misalignments elicited by parabolic flight (0 g and 1.8 g). Ocular misalignments were quantified through Vertical and Torsional Alignment Nulling (VAN and TAN), novel perceptual tests that incorporate a hand-held device developed as part of a larger NASA-directed project. From these results we propose a model that facilitates compensation of saccular-ocular and utricular-ocular reflexes.
Objective: The motivation behind developing such a model was to enhance our understanding of otolith-ocular processes, specifically in regards to binocular positioning driven by static changes in otolith signaling. Examining these eye movements under unusual gravity conditions allowed us to explore their pure, reflexive nature that is typically masked in 1 g by central compensation.
Methods: In VAN and TAN testing, subjects wear red-blue eyeglasses (one lens red, the other blue) and view red and blue lines on a tablet computer. Subjects align the red and blue lines, initially vertically offset from one another in VAN or rotated relative to one another in TAN, until they perceive a single continuous line. Ocular misalignments are inferred from residual offsets in the final line positions. In this experiment, VAN and TAN captured ocular misalignments during parabolic flight in six healthy test subjects. Testing was performed under a shroud to eliminate extraneous visual cues.
Results: All subjects showed significant increases in vertical and torsional misalignments in the altered g-levels, as expected from 1 g-tuned central compensatory mechanisms that are unsuitable for the parabolic

flight environment. However, while the direction of torsional misalignment in 0 g versus 1.8 g reversed, the direction of vertical misalignment did not. These results were repeatable, both early and late inflight. We can show that a central compensation model of the form a+bg å (where a, b, and å are the model parameters and g is the current gravity-level) accounts for both our VAN and TAN results. Small variations in the numerical values of the model parameters for vertical versus torsional oculomotor control facilitate the VAN and TAN results observed inflight. This can be interpreted as distinct central compensatory mechanisms for utricular (the primary driver of torsion) and saccular (the primary driver of vertical eye movements) processes, which is reasonable to expect, given the different functional roles of the utricle and saccule and their corresponding dominant projections to various divisions of the vestibular nuclei and cerebellum.

Conclusion: Our VAN and TAN parabolic flight results characterize the behavior of the otolith-ocular system, but they do not explain how neurophysiological pathways might be organized to produce such results. We present one potential model by which these results may have arisen. Understanding the underlying neural circuitry has important implications for developing various interventions, such as countermeasures for astronauts to expedite adaptation to novel g-levels, or rehabilitation protocols for vestibular patients to promote terrestrial compensation for various pathologies.

B-2
ROBERT BARANY REVISITED 100 YEARS LATER; REVISING THE EXPLANATION FOR CALORIC RESPONSES

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Introduction: One hundred years ago Robert Barany was awarded the Nobel Prize for his explaining why caloric induced nystagmus is generated. Strong support for his theory was his evidence that the nystagmus was generated only "if the canal is not horizontal", and could be reversed by using water warmer or colder than body temperature. Bergstedt in 1961 showed that caloric nystagmus is enhanced under higher G forces, which could not be fully explained by the convection theories, and supposed that the "caloric test may have influence on the otolith organ". Evidence that suggested the "inadequacy of Barany's convection theories" was provided by several groups with NASA experiments showing that caloric responses were similar in 0 G and 1 G conditions. Several groups (e.g. Scherer and Clarke, 1985) hypothesized that modulation of the response intensity by body position change (initially described by Coats and Smith in 1967), initially used to support the convective theory, might be carried out by the otoliths. Suppression of nystagmus during parabolic flight (another finding supportive of Barany's theories) has also been theorized to result from a concomitant reduction of the otolithic signal, although Scherer and Clarke admit that evidence for this is "indirect".

Objectives: We wondered what contributions to caloric response, if any are made by the otoliths, and what influences on caloric response we might see in the patient with otolithic pathology? Preliminary pilot studies carried out in our lab suggest that there is a caloric response with the lateral semicircular canal in the horizontal position. We wondered if this might be an otolith mediated response. Previous studies with caloric testing have been helpful but in these studies there is no detail supplied about calorics being carried out in the meticulous manner that should be used. Caloric testing carried out in the clinical lab can be a robust quantitative measure of labyrinthine response, if carried out in a carefully controlled fashion, with the techniques of Barber and Stockwell being used, and careful analysis of maximal response to water calorics with appropriate alerting. To our knowledge, no accurate studies using carefully administered protocols have been carried out. With the new availability of otolithic testing, we can now delineate patients with otolithic pathology and wondered if caloric testing in different positions might be able to detect otolithic impairment.

Methods: Ten normal subjects underwent eight calorics using the strict protocol laid out by Barber and Stockwell. Four calorics were carried out in the normal fashion and four in the horizontal plane. The ratio of horizontal response/vertical response was calculated. We also looked at five patients with unilateral documented otolithic pathology and five with bilateral otolithic pathology. We calculated the horizontal/vertical response ratio in both groups.

Results: We compared the horizontal response/vertical response ratios in the two groups of patients and compared them to normals. Conclusions: We will discuss our hypothesis that Barany's convection theories are valid but incomplete, and that the otoliths have a definite influence on the caloric response, which results in a certain amount of response in the horizontal (uninfluenced by gravity) position.

B-3
ASSESSMENT OF OPERATOR PROFICIENCY AFTER LONG-DURATION SPACEFLIGHT
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Introduction: The purpose of this NASA funded study is to assess the impact of 6 months microgravity exposure aboard the International Space Station on the ability of astronauts to perform operationally-relevant simulations.
Methods: Testing consisted of two phases; 1) a battery of cognitive and sensorimotor tests (reaction time, match to sample, perspective taking, manual tracking, dual tasking [tracking plus data entry task], manual dexterity [Perdue Pegboard test], and motion perception during random roll and pitch en bloc tilts) and 2) three operationally relevant simulations; landing a T-38 aircraft, driving a car, and operating a Mars rover. These simulations were performed in a custom built 6 degree-of-freedom motion simulator situated at Johnson Space Center in Houston, Texas. Subjects were tested four times prior to flight, and on the day of landing, and 4 and 8 days post-landing.
Results: To date testing has been completed on 3 subjects (out of a planned total of 8). All 3 subjects exhibited significant decrements in driving performance post-flight, particularly in the ability to maintain lane position. Piloting ability was maintained in two out of three subjects. Preliminary results from the test battery showed a small but significant decrease in manual dexterity, significantly larger tracking error during dual tasking, and impaired motion perception during roll tilt below 0.3 Hz.
Conclusions: Although preliminary, the results from the first 3 astronauts suggest significant impairment in operator proficiency post-flight. Decrements in dual tasking performance suggest a lack of cognitive reserve, and low frequency motion perception is compromised. Supported by NASA grant NNX12AM25. I. Tópico 02 Investigations microgravity.

Oral Presentations C. Visual-Vestibular Interaction

C-1
DISTORTED SPATIAL MOTOR TRANSFORMATIONS INDUCED BY VISUO-VESTIBULAR STIMULATION
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Background: Recently it has been demonstrated that modulation of interhemispheric balance via viewing specific visual stimuli (i.e. binocular rivalry; Arshad et al. 2013) or cortical electrical stimulation (Arshad et al. 2014) can result in asymmetric modulation of the vestibular ocular reflex As the vestibular system plays an important role in spatial navigation, we explored whether combining a visual stimulus that is known to activate the right hemisphere with vestibular stimulation would introduce biases in simple external spatial-motor transformations.
Methods: Ten healthy volunteers (mean age: 23.2 $\pm$ 3.9 years) participated in this study. Participants were seated in a chair reclined such that the head was angled at 30o to the horizontal with their eyes closed. The participants were first required to draw a standard clock face with their right hand without resting it on the drawing pad ("Baseline"). Following this, participants received either a cold caloric ("caloric only") or a cold caloric combined with binocular rivalry ("caloric + BR") using differently orientated retinal afterimages for each eye, and subsequently asked to reproduce the clock faces. The clock drawings were analysed by calculating the centre of mass of each drawing, and by creating heat maps for each condition to illustrate the position of any relative representational changes.
Results: In the "caloric only" condition we found no significant effect of irrigation of either the left or right ear on the clock drawings, as indexed by the position of the centre of mass of the each drawing with respect to baseline. In the "caloric + BR", we found that right ear irrigation produced a significant shift in the centre of mass of the clock drawings towards the right side of space, whereas the left caloric was not associated with any significant effects.
Conclusions: These preliminary findings suggest that the combination of a right cold caloric vestibular stimulation and concurrent binocular rivalry viewing can distort external spatial-motor transformations (clock face drawings). The effects are not vestibulo-spinal as

they do not occur during caloric-only conditions. The effects are likely to be mediated by the combination of vestibular and visual stimuli primarily associated with spatial processing in the right cerebral hemisphere.

References: Arshad, Qadeer, Yuliya Nigmatullina, and Adolfo M. Bronstein. 2013. "Handedness-Related Cortical Modulation of the Vestibular-Ocular Reflex." Journal of Neuroscience 33 (7): 3221–27. Arshad, Qadeer, Yuliya Nigmatullina, R. Edward Roberts, Vamsee Bhrugubanda, Paladd Asavarut, and Adolfo M. Bronstein. 2014. "Left Cathodal Trans-Cranial Direct Current Stimulation of the Parietal Cortex Leads to an Asymmetrical Modulation of the Vestibular-Ocular Reflex." Brain Stimulation 7 (1): 85–91.

C-2
THE ROLE OF VESTIBULAR EFFERENTS IN VESTIBULO-OCULAR REFLEX GAIN ADAPTATION: A STUDY IN α9-NACHR DEFICIENT MICE

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Introduction: Precisely what mechanisms underlie vestibular adaptation and compensation in mammals remain to be determined, but a poorly understood candidate that appears to be involved in both forms of plasticity is the predominantly cholinergic Efferent Vestibular System (EVS). Anatomically, the EVS is a well-established and extensive efferent pathway from the brainstem to the inner ear that can modify the output of peripheral vestibular organs. However, little is known about how EVS exerts its influence during the process of adaptation.

Objectives: This study investigates the normal response and adaptive potential of the vestibulo-ocular reflex (VOR) in α9-knockout mice. Nicotinic acetylcholine (nACH) and nACh receptors assembled from α9 subunits form the main signalling pathway of vestibular efferents. Thus, a disruption of the α9 subunit gene in these mice allows study of VOR adaptation with reduced or no input from the EVS.

Methods: We measured the vestibulo-ocular reflex (VOR) gain (eye velocity/head velocity) in 24 α 9-knockout mice and 24 CBA129 controls. Mice were randomly assigned to one of three groups: gain-increase adaptation (x1.5), gain-decrease adaptation (x0.5) or no adaptation (x1). A custom-built servo planetarium projector system, which projected a random pattern of light spots onto a surrounding dome, was used to generate the visual-vestibular mismatch feedback signal that drove VOR gain adaptation. The adaptation stimulus consisted of synchronised sinusoidal rotations (0.5 Hz, peak-velocity 20°/s) of the animal in the horizontal plane (restrained atop a servo controlled platform) and rotation of the visual projection in the opposite direction with a gain of x0.5 or x1.5. Adaptation was kept strictly to 40 minutes. Following adaptation we measured the sinusoidal (0.1–5 Hz, at peak velocities 20, 50 and 100°/s) VOR gain in darkness using a binocular 3D video-oculography system sampling at 220 fps.

Results: Alpha9-knockout mice had significantly lower baseline gains (x1) compared to control mice. The difference in gain was dependent on stimulus frequency, with a decrease of $\sim 25\%$ at frequencies >1 Hz compared to $\sim 5\%$ at lower frequencies. The capacity for vestibular adaptation, measured as the respective difference in VOR gain of gain-increase and gain-decrease adaptation groups, was significantly reduced in α9-knockout mice. VOR gains of controls ranged from ~ 0.41 after gain-decrease adaptation to ~ 0.88 after gain-increase adaptation, a difference of $(0.47) \sim 53\%$. In contrast, VOR gains of α9-knockout mice only ranged from ~ 0.60 to ~ 0.73, a difference of only $(0.13) \sim 17\%$.

Conclusions: Our results show that the EVS moderately affects the VOR, but severely affects VOR adaptation. A preliminary single-unit afferent-recording study in α9-knockout mice showed reduced distribution and sensitivity of irregular (phasic) afferents. If the signals carried by irregular afferents are the ones predominantly used by central vestibular adaptation mechanisms to modify the VOR gain, then one might predict a reduced ability for vestibular adaptation in animals lacking a fully functioning EVS. Our data appear to confirm this line of reasoning.

C-3
ANTICOMPENSATORY QUICK EYE MOVEMENTS AFTER HEAD IMPULSES: A PERIPHERAL VESTIBULAR SIGN IN SPONTANEOUS NYSTAGMUS

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In acute vestibular syndrome assessing gaze-evoked nystagmus, skew deviation, and head impulses quite accurately differentiates strokes from peripheral vestibular disorders. Quantifying the vestibulo-ocular reflex (VOR) gain by the video head impulse test (vHIT), further increases diagnostic accuracy. However, performing vHIT together with oculomotor tests requires expertise not always available. Looking for a simple single sign of peripheral disease in vHIT, we noticed anticompensatory quick eye movements (AQEM; peak velocity above 50°/s) that overshoot the target into the direction of the contralateral head movement in patients with peripheral etiologies of spontaneous nystagmus (SN). To access the diagnostic accuracy of AQEM we tested fourty-eight consecutive patients (12 with central, 36 with peripheral disorders) with acute vestibular syndrome. All peripheral patients had AQEM (latency 231 $\pm$ 53 ms, amplitude 3.4 $\pm$ 1.4°, velocity 166 $\pm$ 55°/s). Central patients did not have AQEM. VOR gain was 0.30 $\pm$ 0.20 for ipsilesional and 0.77 $\pm$ 0.17 for contralesional impulses in peripheral patients, and 0.72 $\pm$ 0.30 for right and 0.74 $\pm$ 0.32 for left head impulses in central patients. We suggest that AQEM are a sign of vestibular imbalance in a peripheral deficit. In addition to VOR gain, which in our study had a diagnostic accuracy of 96%, they should be added to the evaluation of the head impulse test.

C-4
THE EFFECT OF RETINAL IMAGE ERROR UPDATE RATE ON HUMAN VESTIBULO-OCULAR REFLEX GAIN ADAPTATION

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The primary function of the angular vestibulo-ocular reflex (VOR) is to stabilise images on the retina during head movements. The VOR can modify its response for different viewing contexts. For example, during near viewing the VOR response (or gain, gain = eye velocity/head velocity) must increase to compensate for the relatively large translation of the eyes with respect to the target during head rotations. Retinal image movement is the likely feedback signal that drives VOR adaptation. However, it is not clear whether a retinal image position or velocity error is used primarily as the feedback signal. Several recent studies examining the likely feedback signal were limited because the drive they used to modify the VOR was near viewing and it is not known whether near viewing drives VOR adaptation or is a pre-programmed contextual cue that modifies the VOR. Thus, our study is based on analysis of the VOR evoked by horizontal head impulses during a well-established adaptation task. Eleven human subjects underwent incremental unilateral VOR adaptation training and were tested using the scleral search coil technique over 3 separate sessions. The update rate of the laser target (source of the retinal image error signal) used to drive VOR adaptation was different for each session (50 Hz [once every 20 ms], 20 Hz and 15/35 Hz). Our results showed unilateral VOR adaptation at 50 Hz (mean gain pre-adaptation: 0.98 $\pm$ 0.05 to mean gain post-adaptation: 1.20 $\pm$ 0.08, $P < 0.001$) and 20 Hz (0.99 $\pm$ 0.06 to 1.11 $\pm$ 0.07, $P < 0.001$). At 15 Hz, only half of the subjects adapted (0.93 $\pm$ 0.29 to 1.03 $\pm$ 0.26, $P = 0.55$). Our findings suggest that 1–2 retinal image position error signals (i.e., update rate $\sim$ 15–20 Hz) every 100 ms are sufficient to drive VOR adaptation.

C-5
IS THERE A CIRCADIAN RHYTHM OF THE VESTIBULAR FUNCTION?

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Background: It is well established that various physiological functions fluctuate according to a circadian rhythm, a periodical phenomenon repeated at a constant rate over a period of 24 hours. This is the case for body temperature, heart rate, muscular strength and metabolic functions. In animals, some elements of the literature demonstrate the existence of anatomical and functional links between vestibular system and biological rhythms. From a neuroanatomical aspect, multiple neural pathways have been demonstrated between the vestibular nuclei and the hypothalamus including the brain structure responsible for the generation of circadian rhythms ie the suprachiasmatic nucleus. The vestibular system is continuously involved in spatial orientation and equilibration reaction but only one study has tried to identify the circadian rhythmicity of the vestibular system (Wolf et al.,1990) using caloric stimulation and showed a maximum velocity of the vestibular nystagmus obtained in the morning.

Objectives: The goal of this study was to evaluate the effect of time of day on vestibular function.
Methods: The vestibulo-ocular reflex was measured at different times of the day: 6 points over 24 hours. This experimental protocol was applied on a young male adult population ($n = 11$, 22.4 ± 1.5 yrs) and on an aged population (7 women and 1 man, 70.7 ± 4.7 yrs). Horizontal eye movements were recorded by video-oculography in darkness. The canal-ocular response was evaluated by submitting the subject to an earth vertical axis rotation (EVAR) with clockwise and conterclockwise velocity steps of 60°/s (acceleration 100°/S2) delivered in a counterbalanced order. Quantified EVAR response parameters were the maximal initial velocity of nystagmus (Vi) and the time constant (TC).
Results: Young adult population There is no time of day effect on Vi ($F = 0.73$, $P = 0.59$). However, the TC shows a significant difference depending on the time of day ($F = 4.71$, $P < 0.005$). The highest values were recorded at 06:00 h (13.01 ± 3.40 s), while the lowest values were measured at 02:00 h (11.26 ± 3.05 s). Post hoc analysis indicates that the TC at 02:00 am was significantly lower than that at 06:00 am Aged population The results show a significant difference in Vi according to time of day ($F = 4.17$, $p < 0.005$). The post hoc analysis indicates that the Vi at 02:00 am was significantly lower than that recorded at 06:00 am, 10:00 am and 02:00 pm. In addition, TC presents a significant difference ($F = 2.67$, $p < 0.05$) according to the time of the day. The highest values are recorded at 06:00 am (10.86 ± 1.09 s), while low values are collected at 02:00 am (8.83 ± 3.05 s). Post hoc analysis indicates that the CT at 02:00 am was significantly lower than that at 06:00 am.
Conclusion: Our study demonstrated that there is an effect of the time of the day on the vestibular function in young and old subjects. These results should be taken into account in the context of studies on the vestibular function but also in the context of rehabilitation protocols.
Reference: Wolf M, Ashkenazi IE, Leventon G. Circadian variation of nystagmus in healthy and sick subjects. Arch Otolaryngol Head Neck Surg. 1990 Feb; 116(2):221-3

C-6
FUNCTIONAL MAGNETIC RESONANCE IMAGING OF VISUAL-VESTIBULAR INTERACTION

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Background: The information provided by the visual and vestibular systems is used by the brain to distinguish between self- and world-motion and maintain an accurate position of the body in space. Although the cortical response to either vestibular or visual processing has been investigated using neuroimaging, brain activation as a result of concurrent visual and vestibular activity has not been investigated.
Methods: Ten right handed healthy volunteers participated in this study. Vestibular stimulation was performed by irrigating the right ear canal for 50 s with 250 ml of cold (30°C) or warm (44°C) water. Each volunteer received two cold and two warm irrigations of the right ear in a counterbalanced order. The visual stimuli were vertical black and white stripes, which were either static or moving horizontally (8 degree/s). Overlaid on the stripes was a red central fixation dot. Prior to the vestibular stimulation in each run there were three 10 s periods of alternating static or visual motion (baseline). During the irrigation the participants kept their eyes open and under low lighting conditions. At the end of the irrigation the visual stimulation resumed for a further 120 s. The direction of the visual motion was either congruent or incongruent to the direction of the slow phase eye movements induced by the vestibular stimulation. At the end of each run participants were asked to rate their subjective experience of dizziness on a Likert scale with reference to the intensity of the standard caloric they received as part of the screening process. Eye movements were recorded with an infrared MRI compatible eye tracking system.
Results: In the static visual stimulus condition there was significant deactivation bilaterally in superior temporal gyrus, middle frontal gyrus and post central gyrus ($p < 0.001$, uncorrected) compared to baseline. In the condition where visual motion was congruent with the slow phase, there was widespread deactivation in parietal somatosensory areas including somatosensory association cortex, supramarginal gyrus, insular cortex and premotor regions. However, when the visual motion was incongruent, there was reduced deactivation, with bilateral insular cortex, premotor and dorsal posterior cingulate areas showing the most significant effects, with a preponderance for more deactivation in the right hemisphere. There was also evidence of increased activation during incongruent motion in the left frontal eye fields and cerebellum. The brain regions that were differentially activated in the congru-

ent and incongruent conditions included the posterior cingulate and cingulate cortex areas.
Conclusions: These preliminary findings suggest that concurrent vestibular and visual stimulation can result in suppression of activity in parietal, somatosensory and insular cortex regions, with the pattern of activation modulated by the direction of visual motion with respect to the direction of the caloric nystagmus. The suppression observed in the incongruent condition also appeared to be more unilateral and also included brain regions that have previously been associated with cognitive control conflict paradigms and internally guided allocation of attention. Identifying how the brain responds to situations where the visual and vestibular stimuli are in conflict may further our understanding of the neural basis of dizziness in both healthy individuals and patient populations.

C-7
SMALL STROKES CAUSING SEVERE VERTIGO-FREQUENCY OF FALSE-NEGATIVE MRIS AND NON-LACUNAR MECHANISMS

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Introduction: Posterior fossa strokes often present with vertigo or dizziness. Differentiating acute strokes from peripheral vestibular disorders in patients who present acute, continuous, prolonged vertigo or dizziness (i.e., the 'acute vestibular syndrome' [AVS])can be challenging.
Objective: Describe characteristics of small strokes causing AVS.
Methods: Ambispective cross-sectional study of AVS patients (acute vertigo or dizziness, nystagmus, nausea/vomiting, head-motion intolerance, unsteady gait) with at least one stroke risk factor from 1999–2011 at a single stroke referral center. Patients underwent non-quantitative HINTS 'plus' exam (Head Impulse, Nystagmus, Test-of-Skew plus hearing), neuroimaging to confirm diagnoses (97% by MRI), and repeat MRI in those with initially normal imaging but clinical signs of a central lesion. We identified patients with diffusion weighted imaging (DWI) strokes 10 mm in axial diameter.
Results: Of 190 high-risk AVS presentations (105 strokes), we found small strokes in 15 patients (median age 64, range 41–85). The most common vestibular structure infarcted was the inferior cerebellar peduncle (73%); the most common stroke location was the lateral medulla (60%). Focal neurologic signs were present in just 27%. The HINTS 'plus' battery identified small strokes with greater sensitivity than early MRI-DWI (100% vs. 47%, $p < 0.001$). False negative initial MRIs (6–48 hrs) were more common with small strokes than large strokes (53% [n = 8/15] vs. 7.8% [n = 7/90], $p < 0.001$). Non-lacunar stroke mechanisms were responsible in 47%, including six vertebral artery occlusions or dissections.
Conclusions: Small strokes affecting central vestibular projections can present with isolated AVS. The HINTS 'plus' hearing battery identifies these patients with greater accuracy than early MRI-DWI, which is falsely negative in half, up to 48 hours after onset. We found non-lacunar mechanisms in half, suggesting greater risk than might otherwise be assumed for patients with such small infarctions.

C-8
FEASIBILITY OF TRAINING TECHNICIANS TO PERFORM VESTIBULO-OCULAR REFLEX HEAD IMPULSE TESTING BY VIDEO-OCULOGRAPHY

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Introduction: Posterior fossa strokes often present with vertigo or dizziness. Bedside methods are critical to differentate acute strokes from peripheral vestibular disorders in patients who present acute, continuous, prolonged vertigo or dizziness (i.e., the 'acute vestibular syndrome' [AVS]). Diagnosis of central vs. peripheral disorders in AVS by bedside oculomotor physiology tests, known as the HINTS (Head Impulse, Nystagmus, Test of Skew) battery, is more accurate than MRI brain. However, a major barrier to widespread use of this approach is lack of expertise performing the head impulse test (HIT). This barrier might be overcome by using video-oculography (VOG)-based HIT testing, which provides the user with immediate feedback on technique by discarding improperly performed HIT maneuvers and accepting correct ones.

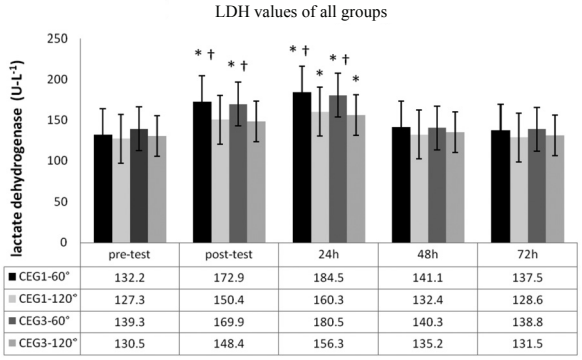
Objectives: It remains unknown whether novices can readily learn to correctly perform the HIT within a reasonable time frame, even using the VOG device. We sought to estimate how much training is required to competently perform the HIT maneuver when using the VOG device.

Methods: Observational study of new examiners performing the VOG HIT to estimate training time required to achieve competent performance at the level of an expert in HIT testing. Trainee examiners performed HIT using a commercially-available VOG device (ICS Impulse, GN Otometrics, Taastrup, Denmark). Testing was conducted on patients as part of an ongoing, IRB-approved research study of balance function in the elderly. This study examined non-acute outpatients over several test sessions. During each session, we measured the number of HITs (valid and invalid) needed by each examiner to record 20 valid HITs, as determined by the device. We compare these results to historical controls using results obtained by two experienced VOG HIT technicians. We report the cumulative number of HITs for new examiners to achieve the target ratio of fewer than 10 inadequate HITs to obtain 20 valid HITs in a single session.

Results: Three trainee examiners included two novices and one ENT resident that had not worked with VOG prior to the study. The two experienced technicians were research fellows (one a neuro-otologist, the other a post-doctoral medical graduate) who had conducted thousands of head impulses using the VOG device. The two novice trainees reached the target of fewer than 10 inadequate HITs to record 20 valid HITs after 148 and 187 cumulative HITs respectively. The ENT resident reached the same target after 89 HITs. The expert technicians' performance consistently exceeded the designated target ratio (Figure). The cumulative time for novices to learn correct HIT technique was less than one hour using the VOG device.

Conclusions: Training to perform HIT using VOG is feasible, does not require special baseline skills, and takes only a short time. Technicians, nurses, or emergency physicians could likely be trained to use the device, potentially enabling dissemination of the HIT technique. Prior to widespread implementation of HINTS by VOG, further studies should characterize the range and variation in training required using a larger sample of novice examiners. These studies would most sensibly be conducted in emergency department patients experiencing vertigo or dizziness and assess novice examiner emergency care providerslikely to use the device in clinical practice.

FIG. Novices can learn correct HIT technique in less than one hour using a VOG device.



	pre-test	post-test	24h	48h	72h
CEG1-60°	132.2	172.9	184.5	141.1	137.5
CEG1-120°	127.3	150.4	160.3	132.4	128.6
CEG3-60°	139.3	169.9	180.5	140.3	138.8
CEG3-120°	130.5	148.4	156.3	135.2	131.5

Oral Presentations D. Vestibular Testing

D-1
COMPARISON OF TRADITIONAL OCULAR MOTOR TESTING WITH A COMPACT, PORTABLE GOGGLE BASED SYSTEM INCORPORATING BOTH STIMULUS GENERATION AND EYE MOVEMENT CAPTURE AND ANALYSIS

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Introduction: The clinical battery for evaluation of vestibular function includes the assessment of ocular motility. Inclusion of these measures allows the clinician to determine the integrity of the ocular motor system and whether or not it is impacting vestibular test results. The assessment of ocular motor function has traditionally involved specialized equipment (e.g., ENG or VNG) located in a dedicated clinical environment. The need for a dedicated testing location may preclude testing of ocular motor function in other areas. A compact, portable ocular motor testing system may help to lower the overall cost of testing without significant compromise in data integrity.

Objectives: This study was conducted to assess the effectiveness of a compact, portable goggle based system incorporating both stimulus generation and eye movement capture and analysis. This Portable Assessment System (PAS),developed by Neuro Kinetics, Inc. (NKI) Pittsburgh, PA USA, integrates technology that allows for both stimulus displays and measurements of ocular motility. The study compared ocular motor

results obtained by PAS to those obtained by more traditional ocular motor systems, such as NKI's I-Portal®technology with its Neuro-Otologic Test Center (NOTC) and videonystagmography (VNG) systems.

Methods: Thirty three (33) adults between the ages of 18 and 47 years (mean: 24.12, SD: 5.98) completed a battery of ocular motor tests, including horizontal gaze, horizontal and vertical saccades, horizontal and vertical smooth pursuit, and optokinetics (OKN), as well as the vestibular tests of subjective visual vertical (SVV) and subjective visual horizontal (SVH) in all three modalities. Each participant completed these tests using PAS and the NOTC while ten (10) of the participants also completed the ocular motor tests in using the VNG system. Traditional variables for each of the ocular motor tests were collected. These included saccadic latencies, accuracies, and velocities; and pursuit and optokinetic gains. The mean SVV and SVH angles were compared between test devices.

Results: Results from the test methods were compared for test-retest reliability, internal consistency, and multiple comparisons. Statistical analyses were performed using SPSS 21. Overall, the analyses revealed no significant differences between PAS system and the traditional NOTC (rotation chair) and VNG measurement techniques for the majority of the tests of the ocular motor battery, specifically, the saccades, smooth pursuit and OKN tests. In contrast, differences were found between the test modalities for four tests; gaze, SVV and SVH and high frequency smooth pursuit. The results for these four tests had weaker reliability and internal consistency in the PAS modality.

Conclusions: These results demonstrate that a portable system for measuring ocular motor function is clinically viable and provides similar results to traditional assessment techniques. Clinical implications of these data and the current and future utility of tests delivered via the PAS system for vestibular and other types of assessments will be discussed.

D-2

THE EFFECT OF TRANSLATION DIRECTION BETWEEN ECCENTRIC AND CENTRIC ROTATIONS ON DYNAMIC SUBJECTIVE VISUAL VERTICAL (DSVV) DURING UNILATERAL CENTRIFUGATION TESTING

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Introduction: Unilateral centrifugation (UC) involves the eccentric displacement of an individual with high velocity rotation around a central axis. This off-center placement permits discrete stimulation of each utricle, allowing individualized evaluation of utricles. One UC paradigm involves the displacement of the individual to both eccentric positions after the maximum rotational velocity has been achieved (Clarke, et al. 1996; Wuyts, et al. 2003). Additionally, a series of subjective visual vertical assessments are made in each eccentric position as well as the centered position. These estimates of verticality we will term dynamic subjective visual vertical (dSVV). We previously have found a tendency for some participants and patients seen in the clinical setting to orient the dSVV to the left upon returning to the center position from right ear out eccentric rotation when using this UC protocol.

Objectives: This study examined the effects of starting eccentric position on dSVV angle in the center position by comparing center dSVV responses for leftward and rightward translations in adults with normal vestibular function. UC was performed on a Neuro-Kinetics, Inc. (Pittsburgh, PA USA) Neuro-Otologic Test Center (NOTC) rotational chair with high speed binocular infrared goggles at the Bloomsburg University of Pennsylvania Vestibular Clinic (PA, USA).

Methods: Each participant underwent repeated UC trials with randomized starting positions: center, eccentric left, and eccentric right. The eccentric positions were defined as lateral displacements of 4 cm to the right or left, respectively. Directions of rotation were clockwise (to participant's right) for the left eccentric (LE) condition and counterclockwise (to the participant's left) for the right eccentric (RE) condition. The centric position was tested twice, once in each direction of rotation. Participants were initially accelerated at 5°/s2 over 60 seconds until the maximum rotational velocity of 300°/s was reached and maintained for 90 seconds, following which SVV testing was performed in the starting position every ten seconds for sixty seconds. If the initial position was eccentric, the chair was then moved to the center position with a 15 second translation time, a five second period was permitted prior to repeating the SVV task. Each trial concluded by decelerating subjects at a rate of 3°/s2.

Results: Preliminary analysis from fourteen subjects found significant differences between the dSVV in the RE and LE conditions. Significant differences were found between the different eccentric conditions and the dSVV obtained after each respective translation to center. No significant difference was found when

comparing the centric dSVV post translation to centric dSVV when the direction of rotation was the same, however, there was a difference between these conditions when directions of rotation were opposite.
Conclusions: Based upon these results, two conclusions can be made. First, the direction of translation from eccentric position does have an effect on dSVV when moving to center. Second, the direction of rotation should be considered when comparing eccentric versus centric dSVV. Additional participants are currently being evaluated under these conditions and will be presented.

D-3
VESTIBULAR INVOLVEMENT IN ADULTS WITH HIV/AIDS 2. DOES THE HUMAN IMMUNODEFICIENCY VIRUS INFLUENCE THE VESTIBULOCOLLIC REFLEX PATHWAYS? A COMPARATIVE STUDY
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1. Introduction: HIV/AIDS is responsible for widespread clinical manifestations involving the head and neck. The prevalence and nature of vestibular involvement is still largely unknown.
Objectives: This study aimed to describe and compare the occurrence and nature of vestibular involvement among a group of adults infected with HIV compared to a control group. It also aimed to compare the vestibular function of symptomatic and asymptomatic HIV positive adults who receive antiretroviral (ARV) therapies to subjects not receiving ARV.
Methods: A cross-sectional study was conducted on 53 adults (29 male, 24 female, aged 23–49 years, mean = 38.5, SD = 4.4) infected with HIV, compared to a control group of 38 HIV negative adults (18 male, 20 female, aged 20–49 years, mean = 36.9, SD = 8.2). A structured interview probed the subjective perception of vestibular symptoms. Medical records were reviewed for CD4+ cell counts and the use of ARV medication. An otologic assessment and a comprehensive vestibular assessment (bedside assessments, vestibular evoked myogenic potentials, ocular motor and positional tests and bithermal caloric irrigation) were conducted.
Results: Vestibular involvement occurred in 79.2% of subjects with HIV in all categories of disease progression, compared to 18.4% in those without HIV. Vestibular involvement increased from 18.9% in CDC category 1 to 30.2% in category 2. Vestibular involvement was 30.1% in category 3. There were vestibular involvement in 35.9% of symptomatic HIV positive subjects, and 41.5% in asymptomatic HIV positive subjects. There was no significant difference in the occurrence of vestibular involvement in subjects receiving ARV therapies compared to those not receiving ARV therapies ($p = 0.914$; chi-square test). The odds ratio indicates that individuals with HIV have a 16.61 times higher risk of developing vestibular involvement during their lifetime of living with the disease and that it may occur despite being asymptomatic.
Conclusion: Vestibular involvement was significantly more common in subjects with HIV, especially peripheral vestibular involvement and should be examined and monitored throughout progression of the disease.
2. Introduction: HIV is a multifaceted disease involving the head and neck area. Objectives: This study compared VCR and VOR functioning in subjects with and without HIV. It also described test results throughout progression of the disease and compared it in HIV positive subjects with and without antiretroviral (ARV) therapies.
Methods: Subjects comprised 53 adults with HIV (mean age 38.5 $\pm$ 4.4) and 38 without HIV (mean age 36.9 $\pm$ 8.2). Clinical examinations included cVEMP and bithermal caloric tests.
Results: Abnormal cVEMP and caloric results were significantly higher in the HIV positive group ($p = 0.001$), with an odds ratio of 10.2. VCR and VOR involvement increased with progression of the disease. There were more abnormal test results in subjects using ARV therapies (66.7%) compared to those not using ARV therapies (63.6%), but this difference was insignificant.
Conclusion: HIV seems to influence VCR pathways. Combining cVEMP and caloric tests may be useful to detect early neurologic involvement in HIV positive subjects.

D-4
A COMPARISON OF VISUAL AND VESTIBULAR PRECISION USING PERCEPTUAL THRESHOLDS SHOWS THAT EACH DEMONSTRATE BETTER PRECISION AT SPECIFIC FREQUENCIES
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Introduction: We perceive motion with exquisite precision. Prior studies show that vestibular perception is

less precise than visual perception, but it is unclear whether these findings are the result of specific experimental conditions (e.g. the motion temporal frequency). To investigate this question, we characterized the frequency response of the perceptual systems that discriminate leftward from rightward roll tilt. We tested three conditions: "visual" (stationary subjects watched a rotating visual scene), "vestibular" (subjects rotated in the dark) and "visual-vestibular" (subjects rotated in the light while viewing an earth-stationary scene). We used thresholds to measure precision in roll tilt, which we have previously used to find enhanced precision in sensory integration in Vestibular Migraine patients.

Objectives: This study combined two classic approaches – measuring thresholds and assessing dynamics – to 1) compare the precision of sensory modalities, 2) investigate sensory integration, and 3) study dynamic neuroperception.

Methods: All subject (11) were tested using in each of three conditions – vestibular, visual or visual-vestibular – during separate sessions. To allow direct comparisons, we used similar perceptual threshold techniques and roll-tilt motion for all the conditions, across a range of frequencies (0.05, 0.1, 0.2, 0.5, 1, 2, 5 Hz). We used standard forced-choice direction recognition procedures that used adaptive 3-down/1-up staircases to adjust the stimulus level (sometimes supplemented with non-adaptive constant amplitude trials). Data were fit with a standard psychophysical "probit" model that assumes that the underlying perceptual noise is Gaussian. To measure thresholds that were relevant to physiologic situations, we chose a visual scene that was a large (63° field of view) photo print of a typical laboratory scene, rather than a computer-displayed view.

Results: We examined the dynamics of vestibular and visual thresholds and found that: 1) vestibular and visual thresholds are very close at 0.05 Hz, 2) there is a cross-over at 2 Hz where vestibular and visual thresholds are very close, 3) vestibular thresholds were lower than visual thresholds above the 2 Hz cross-over (ANOVA, $p = 0.0013$), 4) visual thresholds were lower than vestibular thresholds for frequencies ranging from 0.1 Hz to 1 Hz (ANOVA, $p < 0.001$). We also found that there was little change in visual threshold when field of view changed between 20° and 63°. Finally, we found that visual-vestibular thresholds are consistent with an optimal integration of visual and vestibular cues.

Conclusions: This is the first comparison, to our knowledge, of vestibular and visual motion perception thresholds across a broad range of frequencies. We found that vestibular thresholds were lower than visual thresholds at some frequencies, demonstrating that visual precision is not universally better than vestibular precision.

D-5
ASSOCIATION BETWEEN VESTIBULAR FINDINGS AND THE MOTOR PERFORMANCE IN HEARING IMPAIRED CHILDREN

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Introduction: The growing interest in vestibular and motor testing in hearing impaired children (HI) has corroborated the higher risk of vestibular impairment as well as motor and balance deficits in this population. The literature indicates that 20 to 85 % of children with sensorineural hearing loss demonstrate some type of vestibular dysfunction (Arnvig 1955; Brookhouser et al. 1982; Selz et al. 1996; Angeli 2003; Tribukait et al. 2004; Shinjo et al. 2007; Cushing et al. 2008; Kaga et al. 2008; O'Reilly et al. 2010, 2011; Maes et al. 2014), and tend to display higher percentages of motor and more specifically balance deficits (Horak et al. 1988; Siegel et al. 1991; Goodman and Hopper 1992; Cushing et al. 2008; Gheysen et al. 2008; An et al. 2009; Hartman et al. 2011; Livingstone et al. 2011). Because adequate balance control requires tuning and integration of different sensory input systems, such as the vestibular system, it is reasonable to assume that there is a connection between vestibular function and motor performance.

Objectives: The current study aimed to identify the association between vestibular findings and the motor performance by comparing the clinical balance performance of normal hearing children with those of hearing impaired children with and without vestibular dysfunction.

Methods: Thirty-six children (19 girls, 17 boys, mean age 7y5m, range: 3y8m–12y11m) were divided in 3 different groups. The first group (6 girls, 6 boys, mean age 7y5m) consisted of normal hearing children with normal vestibular responses; a second group (6 girls, 6 boys, mean age 7y6m) entailed hearing impaired children with normal vestibular responses, whereas the third group (7 girls, 5 boys, mean age 7y5m) comprised hearing impaired children with abnormal vestibular function. The two groups of hearing impaired children had a bilateral sensorineural hearing loss and were se-

lected so to that the mean auditory thresholds as well as the distribution of degree of hearing loss, etiology of hearing loss and type of hearing device was comparable for both groups. All children were examined with a vestibular test protocol consisting of three sinusoidal rotational tests (0.01 Hz; 0.05 Hz; 0.1 Hz at 50°/s) and collic vestibular evoked myogenic potential (cVEMP) measurements in combination with three clinical balance tests (balance beam walking, one-leg hopping, one-leg stance).

Results: Normal hearing children with normal vestibular responses demonstrated normal balance performance. Hearing impaired children with abnormal vestibular test results, obtained the lowest quotients of motor performance which were significantly lower compared to the normal hearing group ($p < 0.001$ for balance beam walking and one-leg stance; $p < 0.05$ for one-leg hopping). The balance performance of the hearing impaired group with normal vestibular responses was better in comparison with the vestibular impaired group, but still significantly lower compared to the normal hearing group ($p \leqslant 0.01$ for balance beam walking and one-leg stance; not significant for one-leg hopping).

Conclusion: These results indicate an association between vestibular function and motor performance in hearing impaired children, with a more distinct motor deterioration if a vestibular impairment is superimposed to the auditory dysfunction. These findings underscore the importance of vestibular and motor testing in hearing impaired children in order to start appropriate rehabilitation programs at an ear.

D-6
VESTIBULAR DAMAGE FROM CERVICAL SPINE INJURY – WHAT IS THE DIFFERENCE BETWEEN REAR END COLLISIONS AND HEAD ON COLLISIONS?

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Introduction: When whiplash was originally described, injuries were attributed to shearing of brain pathways as a result of extreme extension-flexion of the neck. With the advent of headrests and proper restraints (preventing the angular neck movement) the mechanism of whiplash has changed to a more linear deceleration of the head in a rear end type collision. The most common otolithic disorder is benign paroxysmal positional vertigo (BPPV). The most common cause in people under age 50 is head injury. BPPV is by definition a reflection of some type of structural otolithic disruption. For some time we have hypothesized "concussion" types of injuries in whiplash may involve a decelerative injury (whether or not a head impact actually occurred), and that otolithic trauma can result. We showed that patients who had suffered whiplash injures without hitting their head suffered similar symptoms to patients who had hit their head. These symptoms were also reported by patients who had more traditional inner ear disease, suggesting to us that the inner ear was possible the structure that had suffered the trauma.

Objectives: With the advent of airbags, head on collisions are now often survivable events. Patients often present to neuro-otology units with post traumatic symptom sets similar to those voiced by our rear end decelerative injury patients. The common factor in these two types of accidents is a rapid deceleration of the head. The initial trauma in head on collisions is also a rapid deceleration, the accelerative forces are increased by restraint systems, and this is further enhanced by air bag deployment (as less travel of the body will result in better survival potential, but will impart greater decelerative forces). Given that the otoconia of the ear (CaCO3) have roughly triple the specific gravity of the surrounding milieu, we have aimed to demonstrate that these decelerative forces will be imparted preferentially on these structures, in a similar manner in both groups .

Methods: With the advent of new tests capable of assessing otolithic structures, we looked at groups of patients to see what the differences were between patients involved in head on and rear end accidents. We looked at twenty patients who had been involved in head on collisions and referred to us for assessment in our clinic. They were compared with twenty patients sequentially referred who had suffered rear end collisions. Extensive histories were taken and all patients were assessed with a full vestibular test battery (CDP, SVV, OVEMPs, CVEMPs and calorics). The groups were both analyzed "subjectively" (to look for any differences in presenting symptoms) and also objectively to look for abnormality patterns in test assessments. We wondered if the two groups of patients were similar (both had suffered acute decelerative injuries) or were two different groups.

Results: The similarities and differences between these two groups of patents will be discussed with respect to presenting symptoms and test results.

Conclusions: We hypothesize that both these groups who have suffered decelerative injuries have under-

gone similar trauma to the vestibular structures of the inner ear. We will discuss our findings and how they suggest similarities and differences in these two patient groups.

D-7

QUANTIFYING THE VESTIBULO-OCULAR REFLEX WITH VIDEO-OCULOGRAPHY: NATURE AND FREQUENCY OF ARTIFACTS

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Objective: Video-oculography (VOG) devices are increasingly used to quantify the vestibulo-ocular reflex (VOR) at the bedside using the head impulse test (HIT). Little is known about the impact of disruptive phenomena (e.g., corrective saccades, nystagmus, fixation losses, eye-blink artifacts) on quantitative VOR assessment in patients with acute vertigo. This study systematically characterizes the frequency, nature, and impact of abnormal physiologic findings and artifacts on HIT VOR measures.
Methods: Detailed analysis of VOG-derived horizontal HIT results from a prospective study of 26 patients with acute vestibular syndrome (16 vestibular neuritis, 10 stroke). We created a structured coding manual and used it to assess 1358 HIT physiologic traces. All disruptive findings were coded based on morphologic similarity to known physiologic patterns or artifact types induced experimentally and reproduced in a laboratory setting. HIT traces were presented in random order and classified by a single, trained, masked rater. A second, independent rater re-coded a 10% subsample to assess inter-rater reliability. Outcomes were the presence and type of disruptive eye movement or artifact, whether the intrusion rendered the trace difficult to interpret, and whether these disruptive phenomena varied based on the underlying disease state. We report descriptive statistics, Cohen's kappa (inter-rater reliability), and Chi2 p-values (comparisons across disease states).
Results: According to structured, pre-defined criteria, 72% of HIT traces had abnormal (but pathophysiologically-appropriate) disruptive saccades, 44% of traces had at least one artifact and 42% of traces were uninterpretable. The most common intrusions limiting VOR interpretation were fast-phase eye movements (saccades or nystagmus) occurring during the VOR response. Inter-rater agreement on attributes varied (0.27–0.79) but was excellent for the presence of a normal VOR (0.78) and very good for the presence of one or more artifacts (0.64) or an uninterpretable trace (0.66). Abnormal head impulses in patients with vestibular neuritis were more susceptible to artifacts (57% of ipsilesional neuritis traces uninterpretable vs. 31–34% of contralesional neuritis traces and stroke traces, Chi2 $p < 0.001$).
Conclusions: Physicians using quantitative recording devices to measure responses to head impulses for clinical diagnosis should be aware of the potential impact of disruptive eye movements and measurement artifacts, especially in patients with an acutely abnormal HIT.

D-8

AUTOMATED COMPUTERIZED DYNAMIC VISUAL ACUITY TESTING: VALIDATION OF A NEW MEDICAL DEVICE

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Introduction: Apart from its role in balance, the vestibular system has a key role in maintaining visual fixation through the vestibulo-ocular reflex (VOR). Lesions of the vestibular system, particularly those caused by vestibulotoxicity, can often be detected by abnormalities of the VOR that manifest as reduced dynamic visual acuity (DVA). This allows for screening for vestibular lesions by testing DVA. Currently, computerized DVA tests are expensive and require training to administer successfully.
Objective: We set out to design a simple, sensitive test of DVA that could be self-administered
Methods: A series of 'Illegible-E' optotype characters are displayed in random orientations on a laptop computer screen that cycle in successively decreasing LogMAR sizes. These orientations are identified by the patient, using a wireless controller, to produce the static score. The same series is then presented in a different random order and identified during head oscillations at between 140° and 180°/second. This is achieved by instructing the patient to undertake headshakes while wearing a Bluetooth-controlled, head-mounted gyroscopic inertia measurement unit that only allows the

characters to be displayed when the head is moving at an angular velocity within the specified range. From these scores a ratio is produced. Normal DVA should closely approximate visual acuity at rest with a ratio of near 1.0.
Results: Ratio scores of 100 volunteers with normal vestibular function were compared to 100 subjects with either a unilateral or bilateral vestibular loss. A ratio of less than 0.85 was positive for vestibular dysfunction with a sensitivity of 96% and a specificity of 95%, as compared to results of VOR testing using a magnetic scleral search coil. A ratio of less than 0.6 was strongly predictive of bilateral vestibular lesions.
Conclusions: A computerized DVA test device can accurately detect vestibular lesions that can then be further investigated. The test can be used as part of a balance clinic, requiring less than five minutes to administer and has the potential to be used to screen for vestibular co-morbidities. This system is being incorporated into a pilot scheme to monitor vestibular function in patients who are receiving vestibulotoxic treatments at our institution.

D-9
INCONSISTENCIES IN CALORIC TESTING: TIME FOR A RETHINK?
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Introduction: It has been 100 years since Bárány was awarded the Nobel Prize for his work on the caloric effects on the vestibular apparatus. Since the development of caloric testing of vestibular function, caloric testing has become the mainstay of vestibular function testing in many units throughout the world, with great reliance being placed on the validity of the results. The exact mechanism of action of the caloric response was thought to be well known, but recent research has cast doubt upon the theories that underpinned the mechanism of caloric stimulation of the inner ear.
Objective: Part 1: To determine the response to irrigation with symmetrical pairs of water temperatures set at arbitrary levels. Part 2: To determine the correlation between caloric responses and magnetic scleral coil measurements of the vestibulocular reflex (VOR) in the context of the diagnosis of cerebellar ataxia with bilateral vestibulopathy (CABV/CANVAS).
Methods: Part 1: Seven normal subjects underwent caloric irrigations to both ears at temperatures of 44°C, 37°C, 30°C, 23°C, 16°C, 9°C and with iced water. Jonkee's formula was used to calculate the symmetry of caloric responses as measured by video nystagmography. Combinations of pairs of temperatures were used in a symmetrical fashion to determine the canal paresis, if present. Part 2: 34 patients with CABV/CANVAS underwent caloric testing using VNG/ENG and magnetic scleral search coil (MSSC) testing. Results were compared.
Results: Part 1: Of the seven normal subjects, the extent of caloric weakness was least variable at a difference of 6% between pairs of temperatures; the greatest difference was in a single subject who displayed a 33% caloric reduction on the right when standard 44°C/30°C temperatures were used, but this changed to a caloric weakness on the left of 21% when a combination of 30°C/37°C was used. In five of the seven subjects the caloric asymmetry changed sides when other pairs of temperatures were used in place of the standard 44°C/30°C combination. Part 2: 75% of the CABV/CANVAS cohort were found to have normal caloric function, but all had dramatically reduced gains as measured by MSSC (mean = 0.21, SD = 0.11). These abnormalities of the VOR were also clearly demonstrated by positive heat thrusts and abnormal LogMAR-based oscillopsia testing.
Conclusions: The value of results derived from the relatively arbitrary of the pairing of 44°C/30°C temperatures used in calorics is questionable if other temperature pairs can cause such drastic changes in caloric responses, sometimes sufficient to change the side of the weakness. The mechanism of action of the caloric response if often found to be normal in certain conditions in which the VOR is dramatically reduced; this suggests.

D-10
CAPTURING EPISODIC VERTIGO
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Objective: To enable ictal capture of acute vertigo in patients' homes.
Background: Opportunities of recording the ictal nystagmus that accompanies acute vertigo are rare and valuable; nystagmus characteristics could point to the underlying vestibular disorder.
Design/methods: Fifty consecutive patients presenting to a neuro-otology clinic with episodic vertigo

were taught to record spontaneous, gaze-evoked and positional nystagmus in their own home environment, using a custom-made lightweight pair of video-goggles. Monocular video data were collected at 30 Hz using infrared cameras. Portable audiometry was also recorded when aural symptoms were present.

Results: Four subjects had short-lived paroxysmal positional nystagmus consistent with posterior ($n = 3$) or horizontal ($n = 1$) canal BPV. The slow phase velocities (SPV) plotted as a function of time, had a crescendo-decrescendo profile which peaked at 3–10 s and could be fitted into a 5th–8th order polynomial curve. The peak SPV ranged from 5–95°/s. SPV had declined to 0 by 60 seconds. Ten subjects who fulfilled criteria for clinically definite Meniere's Disease and three with a diagnosis of delayed endolymphatic hydrops had episodic vertigo associated with horizontal/torsional nystagmus; three demonstrated ictal fluctuation in hearing threshold (15–60 dB). Their horizontal slow phase velocities (SPV) ranged between 10–52°/s and the SPV profile was flat over a 60 s recording interval. Two undertook consecutive recordings over 10–15 min intervals and demonstrated irritative, paretic and recovery nystagmus. Twenty-seven subjects fulfilled criteria for clinically definite (10) or probable (17) vestibular migraine. Their ictal nystagmus was characterized by spontaneous horizontal (10) vertical upbeating (5) or downbeating (6) or torsional (6)nystagmus with a flat SPV profile (SPV range: 5–25°/s) and enhancement during positional testing. Six subjects were unable to record ictal nystagmus at home.

Conclusions: Home-video nystagmography is feasible, enables detailed study of the ictal profiles of central and peripheral vestibulopathies and facilitates differentiation between common causes of episodic vertigo.

Oral Presentations E. Posturography

E-1
REPEATED ROMBERG RATIO IN QUIET STANCE POSTUROGRAPHY

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The Romberg test is the most widely used test for balance. The Romberg ratio, i.e. comparison of postural control parameters during stance with closed and open eyes, is sometimes in posturography used to assess visual influence on postural control. The aim for the study was to examine the stability of the ratio in healthy subjects. Thirty-six healthy subjects (17 males, 19 females aged 15–38 years old) were examined with posturography on 5 repeated occasions and once again after 3 months. Torque variance was measured and analyzed both in total and in frequency ranges below and above 0.1 Hz. Each subject on each test could be labeled as either visual dependent or independent according to the Romberg ratio. Twenty-eight subjects changed their ratio in visual dependence between the tests, and up to 50% of the subjects changed rated visual dependency between two consecutive test occasions. This suggests that Romberg ratios in quiet stance posturography, at least in healthy subjects, yield arbitrary results and the interpretation must be that the ratio is neither an accurate appreciation of sensory weighting in the postural control system nor consistent when repeatedly measured. The explanation could be that human postural control system has a redundancy of sensory feedback in quiet stance and that there is too much inter and intra individual variation for consistent and reliable results. There seems to be a risk for misinterpretation of results if ratios are calculated using quiet stance data, either with eyes open or closed. It appears thus that some sort of perturbation in the postural task is required for a proper assessment of the weighting of individual sensory components.

Oral Presentations F. Utricular and Saccular Testing with VEMP

F-1
THE EFFECT OF STIMULUS RISE-TIME ON THE OCULAR VESTIBULAR-EVOKED MYOGENIC POTENTIAL (OVEMP) TO BONE CONDUCTED VIBRATION (BCV)

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Introduction: The negative potential at 10 ms of the ocular vestibular-evoked myogenic potential (oVEMP n10) in response to bone-conducted vibration (BCV) delivered to the head at the midline in the hairline (Fz) is a new indicator of predominantly utricular function.

The usual stimulus is a 6 or 7 ms burst of 500 Hz including a 2 ms rise and fall time, but it is not known if these stimulus parameters are ideal.
Objective: We sought to find the combination of frequency and rise time for BCV stimulation which generates the largest oVEMP n10.
Methods: We tested 10 healthy subjects using tone bursts of BCV of 6ms duration at three stimulus frequencies, 250, 500 and 750 Hz, at rise times ranging between 0 and 2 ms. The BCV was delivered to Fz and the oVEMP was measured by surface emg electrodes beneath the eyes as the subject looked up. In addition we examined the effect of stimulus frequency in these same subjects by delivering 6 ms tone bursts with a zero rise time at a range of frequencies from 50 Hz to 1200 Hz.
Results: For 250 and 500 Hz the n10 response was significantly larger at the shorter rise times, being largest at zero rise time. With 0 ms rise time the n10 component was approximately uniform at frequencies from 100–750 Hz.
Discussion: We reasoned that given the neural evidence that otolith irregular afferents respond strongly to changes in linear acceleration (jerk), but only weakly to maintained linear acceleration (Fernandez and Goldberg, 1976) that it is probably jerk which is the key stimulus parameter and so the rapid change in linear acceleration at short rise times should result in larger oVEMP n10s in human subjects. That is what we found. For frequencies of 500 Hz and 750 Hz the largest n10 is found at the shortest rise time. We showed that there was no enhancement of n10 at 100 Hz, counter to the report by Todd et al. (2009). How then can we explain the "low frequency tuning" reported by Todd et al. (2009)? Todd et al. assumed that linear acceleration is the stimulus for oVEMP so in their study of frequency effects they attenuated the stimulus at higher frequencies in order to equate "constant acceleration" across frequencies. Furthermore they used the extremely long rise time of 5 ms in order to reduce "onset effects" for their analyses. Unfortunately this very long rise time will reduce or eliminate the very earliest part of the stimulus which we maintain is crucial for generating n10. We do so because the latency from stimulus onset to the foot of n10 is only 6 ms, so it must be that only events at the very earliest part of the stimulus (i.e. within about the first 3 ms) which can be responsible for triggering oVEMP n10. The combination of these two factors acts to reduce the size of n10 more at higher frequencies than at low frequencies and so give the appearance of a "low frequency tuning". On the basis of neural evidence we contend that it is change in linear acceleration (jerk) which is the stimulus for n10. When appropriate stimuli are used – short rise times, with approximately equal initial jerk at all frequencies – there is no evidence of the enhancement of n10 amplitude to 100 Hz stimulus. Finally recordings of the frequency response of single primary utricular irregular afferents in guinea pigs do not show the enhanced response to low frequency BCV stimuli postulated by Todd et al. (2009) either in terms of threshold or sensitivity.
Conclusion: oVEMP n10 is largest with 0 rise time.

F-2
THE FREQUENCY RESPONSES OF IRREGULAR PRIMARY UTRICULAR AFFERENT NEURONS TO BONE – CONDUCTED VIBRATION (BCV) AND AIR – CONDUCTED SOUND (ACS)
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Introduction: Bone conducted vibration (BCV) and air-conducted sound (ACS) are now being widely used to test otolith function. However it is not known how otolithic afferent neurons respond to different frequencies – their thresholds and sensitivites etc. It has been suggested that utricular mechanics causes an enhanced neural response to low frequencies ($\sim$ 100 Hz).
Objective: We sought to measure the frequency responses of irregularly firing utricular afferents activated by these stimuli (BCV and ACS) for frequencies from 100 Hz to 2000 Hz for BCV and 500 Hz–3000 Hz for ACS.
Methods: Single primary utricular neurons were recorded extracellularly in guinea pigs anesthetized with Ketamine and Xylazine. BCV stimulation was delivered either by a Radioear B-71 bone oscillator cemented to the skull or a Bruel and Kjaer 4810 Minishaker vibrating the stereotaxic frame. Air-conducted sound was delivered by a TDH 49 Headphone via a speculum. Thresholds were determined from extrapolation of a linear fit of increased firing to increased intensity at each frequency.
Results: Neurobiotin labelling showed that the recorded neurons originated from type I receptors at the striola of the utricular macula. For BCV utricular afferents have very low thresholds fairly uniformly across frequencies from 100 Hz up to 800–1000 Hz. For ACS the neurons have a V-shaped tuning curve with lowest thresholds at 1000–2000 Hz. Utricular neurons show

phase locking: for BCV up to 1500 Hz and for ACS up to 3000 Hz. An important consequence is that phase-locking limits the maximum firing rate of the neuron. Therefore to a stimulus of 100 Hz, the maximum firing rate is just 100 spikes/s, even though testing with higher frequencies shows the cell can fire at much higher firing rates.

Discussion: The thresholds for utricular neurons to 100 Hz are very similar to those for 500 Hz and even 750 Hz. The suprathreshold sensitivity functions are similar at all these low frequencies. There is no evidence of the "low frequency tuning" of utricular afferents postulated by Todd et al. (2009). Phase locking up to such high frequencies is probably due to the receptor hair cell being deflected once on each stimulus cycle and at low frequencies (<500 Hz), phase locking imposes a frequency-dependent limit on the maximum firing rate of the neuron. For these neurons each cycle is the effective stimulus. Phase locking raises a fundamental question: What aspect of the stimulus is the neuron locked on to? Is it linear acceleration? or change in linear accleration (jerk)? This is a major question for the interpretation of clinical results. Our preliminary evidence indicates that it is not linear acceleration but jerk which is the key parameter of the stimulus, in accord with the conclusion of TA Jones et al. (2011) for otolithic evoked potentials.

Conclusion: Utricular afferents originating from the striola have uniformly low thresholds for low frequency ($<$ 1000 Hz) vibration. In contrast their lowest thresholds for ACS are from 1000–2000 Hz. When activated, these neurons show phase locking up to high frequencies indicating that these utricular afferents are activated by each cycle of the stimulating frequency.

F-3
ACUTE PROBABLE SELECTIVE UTRICULAR MACULA IMPAIRMENT, OBJECTIVELY IDENTIFIED

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Introduction: The presence of spontaneous nystagmus in darkness with a strong horizontal component has been taken to indicate that there is asymmetrical function of the horizontal semicircular canals. If this horizontal spontaneous nystagmus can be suppressed by vision then it is regarded as due to peripheral horizontal canal dysfunction.

Material and methods: However we report evidence from 30 patients (8 male), who came to the MSA ENT Clinic, Cassino (FR) Italy, reporting acute, severe vertigo, postural unsteadiness, nausea and vomiting. In addition 50 healthy subjects were tested as controls. Patients and healthy subjects were submitted to instrumental audiovestibular tests to obtain objective measurements of their inner ear receptors.

Results: At the time of the attack all patients showed spontaneous nystagmus mainly with horizontal and vertical components (3D infrared video-oculography). Tests of dynamic horizontal canal function in normals and patients, using the video head impulse test (vHIT), showed that the functional status of both horizontal canals was within the normal range. Both patients and normals were tested with bone conducted 500 Hz Fz ocular and cervical VEMPs. All patients showed normal symmetrical results to cVEMPs while to oVEMPs they revealed asymmetrical function with an asymmetry ratio $> 40\%$. For this reason they were diagnosed as having unilateral selective utricular macula lesion.

Conclusion: Here we have presented patients who came to the Cassino (Italy) clinic, MSA ENT ACADEMY Center, with acute vertigo, postural unsteadiness and autonomic symptoms. In these subjects, spontaneous nystagmus gave every indication of having a superior or inferior or vestibular neuritis in toto; but objective tests of horizontal semicircular canal function using angular acceleration stimulation in the video head impulse test (vHIT), show that the horizontal canals have normal function. All of the patients reported here presented with those symptoms, and all were demonstrated to have normal horizontal canal dynamic function but to have a selective deficit of one or both otolith utricular maculae. This evidence, together with evidence from earlier studies, is establishing the case for new clinical entities – selective unilateral loss of utricular function.

F-4
SINGLE MOTOR UNIT ACTIVITY UNDERLYING CVEMPS: COMPARISON OF DIFFERENT STIMULI AND RECORDING SITES

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Introduction: Cervical vestibular evoked myogenic potentials (cVEMPs) are vestibular-dependent muscle reflexes recorded from the sternocleidomastoid (SCM) muscles. While commonly evoked by air-conducted

(AC) sound, interest is growing in cVEMPs evoked by vibration, however little is known about vibration-cVEMP properties.
Objective: We therefore investigated cVEMPs evoked by different forms of skull vibration. We also compared 3 recording sites in the SCM muscle. We used single motor unit recordings as they unambiguously show the behaviour of the target muscle, whereas surface potentials may depend upon electrode placement and activity of nearby muscles.
Methods: In 8 normal subjects we compared AC stimulation with 4 types of vibration (500 Hz sine waves at the mastoid or forehead, and minishaker taps at the mastoid directed inward or outward). In 5 subjects we recorded AC-cVEMPs at the upper, middle or lower sections of the SCM muscle. Motor units were recorded with concentric needle electrodes and cVEMPs were recorded simultaneously with standard surface electrodes. Single motor units were extracted from multi-unit recordings and quantified in peri-stimulus histograms.
Results: An inhibition (i.e. initial decrease in motor unit activity) and positive surface potential (i.e. p13) were seen in the ipsilateral SCM in response to stimulation with AC sound, both sine wave stimuli and inward taps, while an excitation (initial increase in activity) and negative surface potential were produced by outward taps. At each site in the SCM muscle the motor unit response recorded to AC sound was an inhibition, while the surface responses recorded over the upper and lower portions of the muscle were inverted.
Conclusions: cVEMPs evoked by vibration are often, but not exclusively, inhibitory in nature. Excitatory responses may be evoked when the direction of initial tap stimulation is reversed. The cVEMP projection has uniform polarity along the length of the SCM muscle. The earliest cVEMP surface response is a reliable indicator of the polarity of the reflex in SCM only when the traditional belly-tendon electrode montage is used and the recording electrode is near the motor point.

F-5
HOW IMPORTANT IS THE EFFECT OF STERNOCLEIDOMASTOID MUSCLE CONTRACTION STRENGTH ON CVEMP AMPLITUDE AND SYMMETRY?

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Introduction: Cervical vestibular evoked myogenic potentials (cVEMPs) are vestibular-dependent muscle reflexes recorded from the sternocleidomastoid (SCM) muscles. They are used clinically to test the function of the saccule and the main test metric is reflex symmetry. To ensure a fair left-right comparison, confounding factors need to be minimised. One potentially important variable is SCM muscle contraction strength, the effects of which are not well-understood. Objective: We therefore tested the impact of contraction strength on cVEMP amplitude, symmetry and clinical outcome.
Methods: 20 normal subjects and 36 patients with suspected vestibular migraine were tested. In normal subjects, cVEMPs were recorded at different intensities with constant SCM contraction and at different contraction levels with constant stimulus intensity. In the patients, cVEMPs were recorded with constant intensity at 3 contraction levels on both sides.
Results: In normal subjects, the effect of muscle contraction was linear for most of the range (mean R2 = 0.95), with some nonlinearities when the contraction was very weak or strong. Comparison of the contraction and intensity regression equations showed that a 50 μV change in SCM muscle contraction produced on average the same change in cVEMP amplitude as a 20 dB change of stimulus intensity. The right-left SCM contraction differences were similar in both groups and were usually low (mean difference 15 μV; mean asymmetry 10%), but some subjects showed large differences (up to 90 μV and 33% asymmetry). When raw p13–n23 amplitudes were used to calculate asymmetry, 11% of patients had false-positive cVEMP test results due to the hidden influence of asymmetric SCM contractions. These became normal once a ratio of raw amplitude to contraction strength was used.
Conclusions: Contraction strength is a critical factor in cVEMP testing and has as much influence on reflex size as changes in stimulus intensity. Uncontrolled differences in contraction strength can easily change a result from normal to abnormal and vice versa. Our data demonstrate the importance of measuring SCM contraction strength when recording cVEMPs.

F-6
NORMALIZING CVEMPS: WHICH METHOD IS THE MOST EFFECTIVE?

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Introduction: Normalization is a common method to reduce the high intersubject peak-to-peak (PP) amplitude variability in cervical vestibular evoked poten-

tials (cVEMPs). This variability comes about largely because the VEMP signal modulates a noisy muscle EMG, and the stronger the muscle contraction the larger the resulting PP VEMP. Normalization is used to control for individual muscle activation. The cVEMP response is obtained as the average of multiple – usually around 200 – individual traces each taken during roughly 35 ms after an acoustic stimulus. Normalization is accomplished by dividing the cVEMP waveform by a normalization constant that varies in amplitude with the individual muscle activity. By correcting for the muscle activation, the normalized-cVEMP amplitude is less variable between subjects and more representative of the vestibular signal that modulates the EMG, which makes it easier to distinguish between healthy and pathological responses. In the recent literature there are several different methods described to normalize cVEMP responses. Grossly, these methods differ in three ways in how the normalization constant is obtained or used. The three normalization alternatives are: (1) get the normalization constant from the root mean square (RMS) EMG, or from the rectified EMG; (2) get the normalization constant from the EMG in a pre-stimulus recording period, or from the entire recording period; and (3) obtain and apply the normalization constant on each individual VEMP trace, or after averaging all the traces. In order to find the most effective way of normalizing cVEMPs, we used all 8 combinations of the three alternative methods and evaluated which combination had the lowest intersubject variability. Objective: To assess which normalization method yields normalized cVEMP PP amplitudes that are the least variable across subjects.
Methods: cVEMPs for 250, 500, 750 and 1000 Hz tone bursts were obtained from 20 healthy subjects (40 ears) by our standard methods. For each ear and frequency, the PP amplitudes of the un-normalized (raw) VEMP and the 8 normalized VEMPs were obtained. For each measurement combination, the mean and standard deviation (SD) across ears were calculated. The coefficient of variation (CoV, i.e. SD divided by the mean) was used to assess the variability of the results from each method.
Results: The results were similar for all frequencies. Two normalization combinations yielded the lowest CoV's, the other six normalizations yielded less good CoV's and un-normalized cVEMPs yielded worst CoV's. The lowest CoV's were obtained by dividing the raw cVEMP by a normalizing constant from the entire averaged VEMP waveform, with normalization by RMS yielding slightly lower CoV's than normalization by the rectified waveform average. That the highest CoV's were for the raw cVEMP PP amplitude is similar to the result obtained in a previous study using same data. Interestingly, the left-right difference was relatively large in the raw results but was relatively small in the normalized results (regardless of the method).
Conclusions: The normalization method that yields PP cVEMP values with the least variation across subjects is to divide the average waveform by a normalization constant equal to the RMS EMG of the entire waveform.

F-7
ASSESSING OTOTOXICITY OF TERBINAFINE EARDROPS IN GUINEA PIGS USING CALORIC, OVEMP AND CVEMP TESTS

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Commercially available terbinafine solution (10 mg/ml) is a potential candidate for treating fungal infections of the ear (otomycosis). Before terbinafine eardrops can be utilized to treat otomycosis clinically, its toxicity to the inner ear must be determined. Guinea pigs were treated with 100 £gl saline and 100 £gl terbinafine at multiple doses on the right and left round window membranes, respectively. Those treated with terbinafine at the concentration of 50 and 100 mg/ml had solvent-induced dermatitis and were excluded from this study. Another 10 guinea pigs treated with100 £gl neomycin solution (100 mg/ml) were also included in this study for a positive control. At 2 weeks after treatment, each animal underwent an inner ear test battery including auditory brainstem response (ABR), and caloric, ocular vestibular-evoked myogenic potential (oVEMP) and cervical VEMP (cVEMP) tests for assessing the function of the cochlea, semicircular canals, utricle and saccule, respectively. All terbinafine-treated ears showed normal results in ABR, and caloric, oVEMP and cVEMP tests. Morphologically, the cochlear and vestibular explants harvested from all terbinafine-treated ears demonstrated normal morphology in the inner ear endorgans. In contrast, neomycin-treated ears showed significantly higher percentages of abnormal ABR and cVEMP test results when compared with those in terbinafine-treated ears. In conclusion, topical application of terbinafine eardrops may be a potential treatment for otomycosis without inducing ototoxicity in experimental animals. This study sets the stage to study the ototoxicity information of any drug using the inner ear test battery in both humans and animals.

F-8

DEVELOPMENT OF THE OVEMPS AND CVEMPS IN GROWING CHILDREN: A REVIEW

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Introduction: Conventionally, the caloric test, rotational test, and posturography have been used to investigate balance function in children. The former two tests can be performed in newborns to examine the semicircular canal function, while the latter one is utilized for assessment of balance function in children aged $>$ 3 years old. As for the otolithic function, recently emerging cervical vestibular-evoked myogenic potential (cVEMP) and ocular VEMP (oVEMP) tests have been widely adopted in clinical practice for evaluating the saccular and utricular functions, respectively.
Objective: This paper reviewed our experience in assessing the development of oVEMPs and cVEMPs in growing children.
Methods: Children from newborns to 15-year-old underwent cVEMP and oVEMP tests via air-conducted sound or bone-conducted vibration stimuli. Foam posturography was also performed in children after 3-year-old.
Results: The cVEMPs can be elicited in newborns at day 5, while the oVEMPs are absent in neonatal period. When children grow to 2 years old, the oVEMP test can be performed with eyes closed condition, while the oVEMP test with eyes up condition can be conducted in children aged $>$ 3 years old. Additionally, foam posturography indicated by the Romberg quotient of the sway velocity/area on foam pad is considered to reflect the otolithic function, which reached adult levels when the children at 12 years old.
Conclusion: For the functional development of the otolithic system in growing children to approach adult levels, the earliest occurrence is the oVEMP test, followed by the foam posturography, and cVEMP test.

Oral Presentations G. Head Impulse

G-1

VESTIBULAR AND VISUAL DEFECTS IN INTERNUCLEAR OPHTHALMOPLEGIA FROM MULTIPLE SCLEROSIS

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Introduction: Internuclear ophthalmoplegia (INO), caused by medial longitudinal fasciculus lesions, is characterized by ipsilesional eye adduction paresis with contralesional eye abduction nystagmus during horizontal saccades. Our study aimed to determine the vestibulo-ocular reflex (VOR) and compensatory saccade defects in INO to the head impulse test (HIT).
Materials and methods: We studied 28 (18 bilateral, 10 unilateral) INOs with the 3D HIT to examine their individual semicircular canal function and compensatory saccades. Binocular eye rotations were recorded with dual-search coils in response to high-acceleration head impulses delivered in individual canal planes. INO was defined as versional disconjugacy index (VDI) of $>$ 1.2 from volitional saccade testing to 20° horizontal eccentric targets. Their results were compared to normal subjects.
Results: In bilateral INOs, HIT showed bilateral reduction in horizontal canal function (gain: ipsilesional eye $=$ 0.42, contralesional eye $=$ 0.58) with severe reduction in posterior canal function (gain $=$ 0.08), but relative sparing of anterior canal function (gain $=$ 0.36). Horizontal HIT showed a difference in peak slow phase velocity between the abducting to adducting eye (ratio: left HIT $=$ 2.0, right HIT $=$ 1.4) There was a paucity of horizontal compensatory saccades in the adducting eye compared to the adducting eye with VDI of $\sim$ 4.0. In unilateral INO, the contralesional vertical canal VOR deficits were comparable to bilateral INOs. However, the ipsilesional horizontal canal VOR deficit of the abducting eye was minimal in contrast to the deficit from the adducting eye.
Conclusion: INO in multiple sclerosis is associated with significant vestibular dysfunction accounting for the oscillopsia during head motion. Gaze instability is due both to VOR gain deficits and horizontal disconjugacy in VOR velocity and compensatory saccades.

G-2

HORIZONTAL HEAD IMPULSE TEST GAIN AND SACCADE ANALYSIS DIFFERENTIATES ACUTE CEREBELLAR STROKE FROM VESTIBULAR NEURITIS

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Background: Clinical head impulse test (HIT) predicts acute cerebellar stroke (CS) but its interpretation is subjective.
Objective: We characterized the angular vestibulo-ocular reflex (aVOR) gain and compensatory overt saccade properties in HIT to differentiate acute CS from vestibular neuritis (VN).
Methods: Horizontal HIT was recorded <7 days from vertigo onset with dual-search coils in 31 CS involving anterior inferior, posterior inferior and superior cerebellar artery (11 AICA, 17 PICA, 3 SCA) confirmed by MRI and 19 VN. We determined the aVOR gain (ratio of eye to head velocity) and asymmetry (Gs), and saccade characteristics including cumulative amplitude (Am), amplitude asymmetry (As), and frequency of saccade $>5^\circ$.
Results: In CS, aVOR gain was symmetrically reduced in AICA (gain: ipsi $= 0.40$, contra $= 0.60$; Gs $=$ 20.0%), but largely preserved in PICA/SCA (gain: ipsi $= 0.75$, contra $= 0.74$; Gs $= -1.7\%$) stroke in contrast to VN (gain: ipsi $= 0.22$, contra $= 0.76$; Gs $=$ 54%). Saccades were smaller and occurred less frequently in AICA (Am: ipsi $= 3.95^\circ$, contra $= 3.08^\circ$; As $= 19.4\%$; saccade $> 5^\circ$: ipsi $= 16\%$, contra $=$ 7%) and in PICA/SCA (Am: ipsi $= 1.96^\circ$, contra $=$ 2.68°; As $= -12.8\%$; saccade$>5^\circ$: ipsi $= 5.4\%$, contra $= 7.4\%$) stroke, when compared to VN (Am: ipsi $= 8.55^\circ$, contra $= 1.03^\circ$; As $= 84.2\%$, saccade $> 5^\circ$: ipsi $= 49.2\%$, contra $= 0\%$). Consequently saccades were less asymmetrical in AICA stroke and often favored the contralesional side in PICA/SCA stroke, but skewed ipsilesionally in VN. For the diagnosis of CS, saccade analysis was more robust (As: 97% sensitive, 100% specific; Am: 90% sensitive, 100% specific) than aVOR gain asymmetry (87% sensitive, 100% specific).
Conclusion: HIT aVOR and saccade analysis differentiates CS subgroups from VN and complements clinical HIT.

G-3
VESTIBULAR SIGNS OF THIAMINE DEFICIENCY DURING THE EARLY PHASE OF SUSPECTED WERNICKE'S ENCEPHALOPATHY

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Background: Non-encephalopathic presentations of central nervous system thiamine deficiency may be difficult to diagnose. Vestibular findings in the pre-encephalopathy phase, despite their potential value to assist early diagnosis and enable early treatment before severe neurologic morbidity occurs, are not widely known. We describe neuro-otologic findings of Wernicke's syndrome in five patients with vestibular manifestations.
Objectives: To study vestibular function in patients reporting progressive imbalance, falls and oscillopsia in the context of chronic alcoholism or status post-gastric bypass.
Methods: We conducted a retrospective chart review of five cases of thiamine deficiency presenting with vestibular findings to a single center (07/2008-10/2011). All patients underwent clinical neurologic, neuro-ophthalmologic, and neuro-vestibular evaluation. Vestibulo-ocular reflex (VOR) testing was performed by clinical head impulse testing in all five, video-nystagmography in two, and by video head impulse testing in one. Diagnosis was confirmed by low serum levels of thiamine, response to replacement, and brain MRI to exclude other causes.
Results: One of the patients presented with an acute vestibular syndrome characterized by acute, persistent, vertigo, with severe vomiting and gait ataxia for 48 hours, mimicking vestibular neuritis or stroke. The others presented with subacute, progressive imbalance, unsteadiness, falls and oscillopsia. All 5 patients had bilaterally abnormal horizontal head impulse VOR responses and pathologic gaze-evoked nystagmus, without encephalopathy. In three where vertical-VOR responses were tested, two had dissociated loss of horizontal-VOR function with spared vertical-VOR function. After thiamine replacement, four had total resolution of vestibular and oculomotor findings. Novel findings included two patients whose VOR function improved within minutes of intravenous repletion and one whose recovery was documented by serial quantitative recordings.
Conclusions: Patients with thiamine-deficiency may present with predominantly vestibular symptoms and signs without encephalopathy. Head impulse VOR responses in these patients could be an important bedside marker for diagnosis, response to therapy, or prognosis. Early diagnosis of Wernicke's by examining vestibular reflexes and prompt intravenous treatment might prevent encephalopathy and other neurologic or systemic complications of thiamine depletion.

G-4
THE VIDEO HEAD IMPULSE TEST (VHIT) – PAST, PRESENT AND FUTURE

MacDougall, Hamish[1]; Holden, John[1]; McGarvie, Leigh[2]; Halmagyi, Michael[2]; Weber, Konrad[3]; Curthoys, Ian[1]
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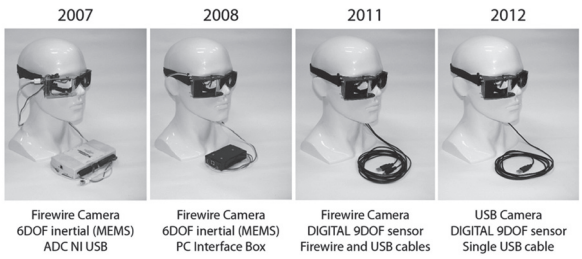
Past: After $\sim$ 20 years of developing video eye movement measurement techniques and equipment, in 2007 we made the first viable video head impulse testing (vHIT) glasses. The head impulse test (Halmagyi and Curthoys 1988) was previously performed using subjective assessment by the clinician or measured objectively using scleral search coils systems that are complex, bulky, expensive and uncomfortable (invasive). Previous video goggles such as those we had developed for measuring 3D binocular eye movements at up to 60 Hz were not suitable for vHIT because their sample rate is too low for brief VOR responses lasting $\sim$ 100 msec and they are so heavy ($\sim$ 500 g) that they resist rapid head accelerations (inertia), causing slip of the goggles vs the skull and measurement artefacts. In December 2007 we solved these issues by removing everything that was superfluous to requirement (binocular cameras, torsion measurement, mechanical adjustments) and developing a new specialised pair of vHIT glasses based on lightweight and tight fitting motorcycle sunglasses, with one high speed camera (250 fps) and inertial head movement sensors (MEMS), for a total weight of $\sim$ 60 g. vHIT glasses minimise measurement artefact by keeping all mass as close to the centre of head rotation as possible (low torque), and have a stiff housing to prevent any movement of the camera, hot-mirror, or IR LEDs. In January 2008 we were getting the first video head impulse data, and simultaneous search coil validation comparisons in May 2008. In June 2008 we tested normals and vestibular patients for: Impulsive testing of semicircular canal function using video-oculography. (Ann. N.Y. Acad. Sci. 1164: 486–491 (2009) accepted 5 August 2008); and The Video Head Impulse Test: Diagnostic Accuracy in Peripheral Vestibulopathy. (Neurology – Oct 2009; 73: 1134–1141).

Present: More recently we have improved and validated our algorithms for calculating the VOR gain during head impulses. These new methods have been particularly useful for vertical head impulse testing described and validated in the: Application of the video head impulse test to detect vertical semicircular canal dysfunction Otology & Neurotology, 34 (6): 974–979; and The video head impulse test (vHIT) detects vertical semicircular canal dysfunction (PLoS One 8 (4): e61488). The video head impulse test has been adopted by scientists and clinicians worldwide, and has demonstrated many compelling advantages over other vestibular tests such as caloric irrigation, and rotation testing.

Future: We are convinced that vHIT has a huge potential to revolutionise vestibular diagnosis but we also recognise that there are some potential challenges and obstacles to it reaching its full potential as quickly as possible. vHIT is a powerful tool which requires operator skill and understanding so we are investing significant effort in training and education. vHIT is also (arguable) the most difficult test for video systems to do well so we are concerned that some of the many commercial systems that now claim to do vHIT use old, slow, and heavy goggles, which probably still suffer from goggle slip and measurement artefacts. Other systems claim to do various different tests using the same goggles which might compromise the quality of vHIT results. Poor skill and equipment should not be attributed to vHIT, which, when performed well, offers a huge improvement over traditional vestibular diagnosis and to many other applications.



G-5
REFIXATION SACCADES IN A NORMAL POPULATION. sANT CUGAT DEL VALLES (BARCELONA, sPAIN)

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Introduction: Refixation saccades (RS) occur as a way to minimize retinal slip when patients with a vestibular deficit perform head impulses as part of their

daily life activities that include rapid head movements. RS can be better evaluated while the head impulse test is is performed at bedside, however some of them can go unnoticed. In recent years new technology to register the vestibulo-ocular reflex has emerged that allows a very precise registration of head and eye velocity. In this way RS can be better characterized. We were interesed in this issue in a a large puplation o f normal subjects.

Matherial and methods: In this study we selected normal subjects. They were family related or companions of patients seen at our department. They all had no history of vestibular impairment, vertigo or dizziness, posture and gait abnormalities, abnormal hearing impairment neither visual problems. Eye movements (gaze stability, saccades and smooth-pursuit) were normal and head and neck mobility was not restricted. There was no spontaneous nystagmus with or without visual fixation. We have used e video head-impulse test system (vHIT, GN Otometrics, Denmark) for the eavluation of the VOR. We have considered eye movements that occur once the head stops after the thrust imposed and when their velocity was $>50°$/s.

Results: The number of subject included was 211. Mean gain of the VOR was 1.06 ± 0.07. RS were detected in 52 subjects of which in 30 they occur after head impulses to both sides. There is signifcant increase in the number of subjects with RS when $>$ 71 years, but the number of RS by head impulses performed was significant higher in subjects $>$ 60 years. Mean velocty of the RS was $65 \pm 19.5°$/seg but this was not different according to age.

Conclusion: For RS assessment there is a correlation between clinical and video head-impulse testing in normal subjects. This finding must be taken into account when $>$61 years old patients are under evaluation. Not only gain of the VOR but also number of RS and their velocity should be taken into account.

G-6
VIDEO HEAD IMPULSE TESTING – AGE DEPENDENT NORMATIVE VALUES IN HEALTHY SUBJECTS

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Introduction: The recent development of practical and effective video Head Impulse Testing (vHIT) has presented the balance field with a robust technique to determine the function of all 6 semi-circular canals provided it is carried out correctly. Five years of experience with video head impulse testing in our clinic has allowed us to develop the skills and to recognize the procedural artifacts which can introduce errors into the data.

Objective: To determine the aged-matched control range of responses across the velocity range for all six canals.

Methods: vHIT tests were all carried out with prototype video goggles, and a minimum camera speed of 250 frames per sec recording the right eye. Subjects were tested while sitting upright in a lighted room with an eye level target at 1 m in front of them. Horizontal eye movement calibration was carried out and the calibration then checked prior to testing in each stimulus plane by moving the subject's head sinusoidally back and forth within the test plane at low speed to ensure that head and eye traces overlaid. The impulse stimulus consisted of passive short, sharp head rotations, delivered in unpredictable direction and magnitude. vHIT results were deemed acceptable when a maximum peak head velocity of at least 150 deg/sec in the vertical planes and 200 deg/sec in the horizontal plane were achieved. Impulses with overshoot greater than 30% on the head velocity or with any obvious artifacts or eye blinks were culled prior to data analysis. The gain was calculated for each stimulus as the ratio of the area under the desaccaded eye velocity to the area under the head velocity, across the time of the unilateral impulse. A minimum of 10 subjects in each age decade without any prior known or reported balance problems were recruited and tested. They provided informed consent.

Results: The gain results obtained indicate that, rather than use a single value, it would be better to discuss gain value at a given velocity in each plane. Horizontal gain displays a tight cluster around unity at low speeds, with a small drop off as velocity increases. Variability is much greater in the vertical planes, with a more rapid drop-off as speed increases. Results, however, vary less with age than the balance patient data would suggest.

Conclusion: vHIT, if carried out correctly, is a simple, fast, robust and reliable method of assessing semicircular canal function at all ages using the physiological stimulus of rotation.

G-7
VESTIBULO-OCULAR REFLEX IN PATIENTS WITH MENIERE'S DISEASE: ALL SEMICIRCULAR CANALS EVALUATION

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Objective: To examine the vestibulo-ocular reflex in the plane of all the semicircular canals in patients with unilateral definite Menière's disease.
Methods: We have studied the vestibulo-ocular reflex in 50 patients. The reflex was evoked by rapid head-impulses in the plane of the three semicircular canals in the affected and in the unaffected ear. The reflex was evaluated with a video system that analyzes the head and eye velocity: the gain (the relation between both magnitudes) was the objective measure.
Results: In 33% of the patients the examination of both ears was normal for all the semicircular canals, in 33% of patients the results from the affected ear were abnormal in at least one of the semicircular canals, in 30.5% patients the results were abnormal in at least one of the semicircular canals in both the affected and unaffected ears, and in 2.9% patient the results were abnormal only in the unaffected ear.
Conclusion: The assessment of the function of all the semicircular canals in patients unilateral Menière's disease shows that the most frequent abnormal result is obtained from the posterior canal of the affected ear and from the coupled superior canal of the unaffected ear; no correlation was found between abnormal findings and disease duration, time passed since the last vertigo crisis and pure-tone average.

Oral Presentations H. Vestibular Evoked Responses

H-1
THE TULLIO PHENOMENON – INVESTIGATED FROM A FLUID-DYNAMICAL POINT OF VIEW

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Introduction: A dehiscence (SCD) in the bony roof of the superior semicircular canal (SSC) can lead to sound-induced vertigo, also known as Tullio Phenomenon. It has been shown that a SCD in the right (left) ear leads to an upward-counterclockwise (upward-clockwise) beating nystagmus of constant slow-phase velocity (usually $< 10°$/s) when exposed to sound (usually 0.5 kHz–2 kHz, > 90 dB SPL). This eye motion is believed to be triggered by the vestibulo-ocular reflex (VOR) since it can be related directly to the ampullofugally deflected cupula in the SSC. However, the underlying mechanism which links a continuous sound input to a constant cupula deflection has not been explained yet.
Hypothesis: Approaching the medical problem from a fluid-dynamical point of view, we investigate a system of two incompressible fluids (endolymph and perilymph) that are separated by an elastic structure (membranous labyrinth, ML) and surrounded by a rigid structure (temporal bone, TB). The pathologic TB features two holes in the vestibular apparatus – oval window (OW) and SCD – such that we can regard the perilymph as an oscillating fluid column, driven by the stapes motion (analogous to the cochlea with the oval and round windows). Although the lymphatic fluids are nearly incompressible, the displacements in the *coupled* system of perilymph and ML will propagate with *finite* wave speed along the membrane due to fluid-structure interaction. We hypothesize that these traveling waves – damped by the fluid viscosity – lead to non-linear phenomena in the endolymph flow of the SSC and ultimately generate a non-zero, ampullofugal mean flow (*steady streaming*) that deflects the cupula towards the SCD. As the cupula counteracts its deformation, a constant equilibrium position will be reached quickly where forces due to the steady streaming are balanced by cupula forces.
Methods: The Navier-Stokes equations are solved numerically with the Finite-Volume Method (FVM) in an Arbitrary Lagrangian Eulerian (ALE) formulation on a straightened section of the deforming endolymph domain. The moving ML is simplified as a system of mass-damper-spring elements. This is solved in monolithic conjunction with the perilymph, yielding a dynamic boundary condition for the endolymph motion. The perilymph pressure at the location of the SCD is assumed to be equal to the reference pressure in the cranial cavity, and the stapes oscillations are modeled as a sinusoidal inflow/outflow at the OW.
Results and conclusions: Our numerical results show the propagation of a pressure wave along the ML from the OW towards the SCD. The local transmural pressure differences deflect the elastic membranous wall and thus induce an oscillating flow in the endolymph. An evaluation of the endolymph bulk velocities at two different cross-sections reveals a non-zero and unidirectional mean flow. By integrating the streaming component in time we get the accumulated fluid vol-

ume under the deformed cupula which relates directly to the slow-phase velocity of the eye response.
Because of idealizations on the canal geometry, the material behavior and the boundary conditions, the results are qualitative. By conducting a sensitivity analysis with respect to the unknown parameter values (e.g. for ML elasticity and density, stapes velocity, cupula stiffness), we find evidence that supports our hypothesis. Hence our numerical setup is able to capture the second-order effect of sound-induced endolymph streaming due to traveling waves on the membranous labyrinth.

H-2
OCULAR AND CERVICAL VESTIBULAR-EVOKED MYOGENIC POTENTIALS TO AIR CONDUCTED SOUND AND BONE CONDUCTED VIBRATION IN MÉNIÈRE'S DISEASE
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[1]MSA ENT ACADEMY CENTER; [2]Vestibular Research Laboratory, School of Psychology, the University of Sydney

Introduction: The changes which occur in the labyrinth during Meniere's Disease (MD), are still poorly understood. In this study we sought to test otolith function by using a relatively new technique in MD patients even during the acute MD attack. Air Conducted Sound (ACS) and Bone Conducted Vibration (BCV) delivered at the midline of the forehead at the hairline (Fz) (causing simultaneous and approximately equal amplitude linear acceleration stimulation at both mastoids) results in cervical evoked myogenic potentials (cVEMPs) recorded over contracted SCM and ocular evoked myogenic potentials (oVEMPs) recorded beneath both eyes while the subjects is looking up.
Methods: 30 patients with definite Meniere's Disease during quiescence, meeting guidelines set by the AAO-HNS criteria, were tested at MSA ENT clinic in Cassino (Italy) with ACS (500, 750 and 1000 Hz) and Fz BCV 500 Hz oVEMPs and cVEMPs, in the same session, on two occasion always during quiescence. 13 subjects with definite Meniere's Disease were tested during quiescence and at the time of attack with ACS (500, 750 and 1000 Hz) and Fz BCV 500 Hz oVEMPs and cVEMPs, in the same session. 16 healthy control subjects were tested at comparable intervals in the same paradigm.
Results: Responses to Fz BCV short tone burst stimuli in MDs tested during quiescence on two occasion, have confirmed results obtained by Manzari et al. 2010, showing significant asymmetry of n10 of the oVEMP to Fz BCV 500 Hz STB during the attack compared to quiescence but with no detectable change in the symmetry of the BCV cVEMP during the attack compared to quiescence. Healthy control subjects tested on two occasions showed no detectable change in the symmetry of oVEMPs or cVEMPs to Fz BCV 500 Hz STB. Responses to ACS showed different results . In patients tested on two occasions at the time of quiescence p13–n23 to ACS cVEMPs and n10 to oVEMPs revelead different tuning or sometimes p13-n23 to ACS cVEMPs potentials is present while n10 to ACS oVEMPs is absent and viceversa. At the time of attack ACS cVEMPs in MD subjects show quite same results obtained with BCV while n10 to ACS oVEMPs in attack is enhanced. When applying tone bursts in normal, there is a frequency tuning with lowest thresholds at 500–1000 Hz and best responses at 500 Hz for cVEMPs in normals confirming Rauch et al. 2006. Air-conducted sound oVEMP exhibited a dominant peak located at 750 or 1000 confirming Lewis et al. 2010.
Conclusion: In Meniere's Disease patients during quiescence air conducted sound short tone burst stimuli showed not reliable results. These results are to signify that ACS in MD patients is not symmetrically delivered to the otolithic regions (utricular macula and saccular macula), probably due to the endolymphatic hydrops that hinders the arrival of the stimulus to these inner ear regions. In other words, a mechanical process rather than an ionic change in endolymph may be responsible for this vestibular potentials behavior in MD patients.

Oral Presentations I. Vestibular Neurophysiology Morphology and Pathology

I-1
DIFFERENT CORTICAL NETWORKS ARE ACTIVATED DURING LATERAL AND ANTERO-POSTERIOR GALVANIC VESTIBULAR STIMULATION IN HUMANS
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Centre de Recherche Cerveau et Cognition, Toulouse, France

Vestibular signals are crucial to navigate through our environment. So far little is known about the cortical areas involved in the processing of vestibular in-

formation. A recent work has identified 2 cortical areas that show vestibular activity during lateral-galvanic vestibular stimulation (GVS): the human medial superior temporal cortex and the cingulate sulcus visual area (Smith AT et al, 2012). Nevertheless, there is no investigation on the cortical networks involved in the processing of vestibular information in the anteroposterior axis. GVS evokes anteroposterior or lateral sway of similar spatio-temporal features according to the stimulation configuration: equivalent afferent flows would result in an anteroposterior body response whereas lateral sway towards the anode is obtained with discrepant ones (Séverac Cauquil A et al, 1998). Taking advantage of this methodology, the objective of this work was to study the difference in the cortical activations during GVS in the lateral and anteroposterior axes. To this purpose, we ran a protocol in 4 healthy subjects where we randomly applied GVS in the four different configurations (front,back,left,right) with 1mA current during 2 seconds at 8 seconds intervals. Every condition was repeated 56 times in a randomized way including a fifth condition with no stimulation (baseline). The fMRI BOLD oxygen dependent measures were recorded during the experiment. Each recording session included an anatomical MRI data acquisition for the localization of the BOLD activity. Our results showed that contrasting the BOLD activity elicited by the stimulation in the anteroposteior axis against the baseline a significant increase in the BOLD signal was found in the inferior frontal gyrus, anterior insula, posterior cingulate cortex and middle occipital gyrus. On the other hand when we contrasted lateral axis stimulation against baseline we found a significant increase in the superior parietal lobe, anterior insula, posterior cingulate cortex, inferior and superior frontal gyrus and right frontal lobe. When these two contrasts were compared, we found that only two areas showed an overlapping increase in the BOLD activity: the inferior frontal gyrus and the anterior insula. Not surprisingly, both areas are part of the associative cortex and involved in high cognitive functions. Based on these results, we hypothesize that vestibular information from the anteroposterior and lateral axes are mainly processed by different networks.

I-2
PERCEIVED DISTANCE DURING OSCILLATORY LINEAR MOTION

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When oscillating linearly in the dark, humans perceive tilt at low frequencies and translation at high frequencies. The majority of information is available on tilt perception. We therefore asked seventeen subjects for their perceived distance between the turning points during sinusoidal lateral motion over fixed peak-to-peak distances of 1 and 2 m, both at frequencies of 0.1, 0.2 and 0.3 Hz. Larger distance resulted in larger estimates in all subjects. However, perceived distance only increased with frequency in twelve subjects, while it showed to decrease with frequency in four. One subject showed no frequency effect. We conclude that in some subjects the central nervous system uses high-pass filtering of otolith afferents, typically coding for inertial and gravitational acceleration to obtain an estimate of acceleration due to motion only, and integrates this estimate of inertial acceleration over time to get an estimate of distance. In other subjects, however, higher order cognitive processing seems to be at issue, possibly taking prior knowledge into account.

I-3
UTRICULAR HAIR CELLS AND TRANSITIONAL CELLS RECIPROCALLY REGULATE ENDOLYMPHATIC CATION MOVEMENT VIA PURINERGIC STIMULATION

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Yonsei University College of Medicine

Introduction: The main function of the dark cell in the utricle is K+ secretion to provide ionic milieu of endolymph to maintain normal balance function. Vestibular ampullary transitional cells were known to absorb cation via purinergic stimulation. However, the function of the transitional cell of the utricle and their role in the protection of hair cell were unknown.
Objectives: This study was performed to identify how the utricular transitional cells and hair cells reciprocally act to regulate inner ear cation movement to protect vestibular hair cells via purinergic regulation.
Method: The temporal bone of C57BL/6 mouse was dissected and the transitional cell and hair cell area of utricle was exposed. Vibrating probe was used to measure transepithelial current from the area and purinergic agonist, antagonist and various cation absorbing channel inhibitors were used to identify the function of the area.
Results: Minimal cation absorption current (5.0 ¡3/3 1.5 ěìA/cm2) was detected in the transitional cell

area and large cation absorption current (20.5 ¡3/3 3.4 ěìA/cm2) was detected in the hair cell area of the utricle. The cation absorption current of utricular transitional cell area was transiently increased with the application of ATP (100 ěìM). However, cation absorption current was changed to large cation secretion current with the application of ATP (100 ěìM) in the utricular hair cell area. The current in the both area was not changed with the application of 100 ěìM ADP, UTP, and UDP. The ATP induced current was blocked by Gd (10 ěìM). The each EC50 value of the current from the both area was 15 ěìM and 18 ěìM respectively and the current was inhibited by suramin (100 ěìM), PPADS (10 ěìM), and 5-BDBD(5 ěìM).
Conclusion: This result implies that utricular hair cells secret cation and transitional cell absorb cation via P2X2 and P2X4 receptor mediated purinergic stimulation. This is likely to happen to protect utricular hair cells in the stressful condition by providing a shunt for cation from hair cells to transitional cells.

I-4
RELATIONSHIP OF SUBJECTIVE VISUAL VERTICAL (SVV), STRAIGHT AHEAD (VSA), AND PERCEIVED EYE LEVEL (VPEL) IN PATIENTS WITH CENTRAL VS. PERIPHERAL VESTIBULAR DISORDERS WITH/WITHOUT SPONTANEOUS NYSTAGMUS

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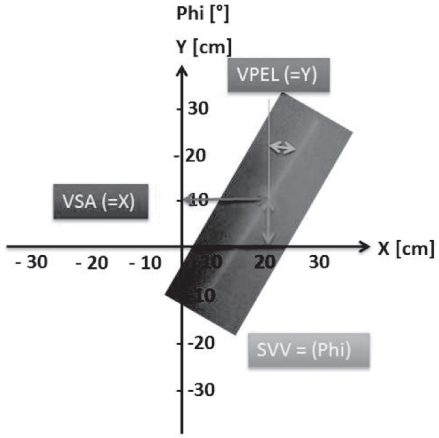
Introduction: Alterations of the subjective visual vertical (SVV) are a core feature of both central and peripheral vestibular disorders. Less is known about the effects of vestibular disorders on visual straight ahead (VSA) and visually perceived eye level (VPEL), and the interdependencies of these 3 degrees of perception.
Objectives: Here we aimed to characterize the relationship between SVV, VSA, and VPEL and their respective variations in different vestibular disorders. Moreover we analyzed these perceptions as a function of external cues such as initial target location or amount of backlight.
Methods: We evaluated 4 groups of patients (peripheral and central vestibular disorders with or without manifest spontaneous nystagmus), with central or peripheral pathologies in the caloric test. The findings of these patients were compared to those of an age-matched healthy control group. Patients were instructed to orient a line with a central marker via a custom-made joystick i) vertical, ii) straight ahead, and iii) at eye level. We took measurements during both darkness and dim backlight, which allowed for a moderate visual orientation.



Results: We demonstrate patients' profiles of perception depending on the type of vestibular disorder. Interestingly, the 3 degrees of perception, their interdependencies, and the influence of external cues vary specifically across the different vestibular disorders.
Conclusions: We were able to identify specific features of pathological perception as a function of the type of vestibular disorder. We interpret these findings in light of (pathological) sensor fusion mechanisms. In future, we aim to use these individual perception profiles of patients and the effect of treatments on these profiles to tailor therapeutic interventions more precisely.

I-5
PROLONGED ROLL-TILT LOCALLY DISTORTS THE INTERNAL ESTIMATE OF DIRECTION OF GRAVITY

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The subjective visual vertical (SVV) indicates perceived direction of gravity. Roll-angle dependent physiological misestimations – A-effect ($> 60°$ and $< 135°$) and E-effect ($< 60°$) – are known. Previously, we addressed another systematic bias in verticality perception, showing that after prolonged roll-tilt SVV estimates in upright position are biased towards the pre-

vious roll position. This suggests a shift in estimated vertical by the prior tilt. Potentially, after prolonged roll-tilt, the perceived vertical in any subsequent roll position is biased. Here we assessed whether such a "global" bias can be found or whether the bias is restricted ("local") to nearby roll angles. We measured the SVV in nine roll positions ($-120°$ to $+120°$, steps $= 30°$) after 5 minutes of roll-tilt in one of four "adapting" positions ($\pm$ 45°, $\pm$ 90°) and compared results with control trials without adaptation. After adapting at $\pm$ 90° adjustments were shifted significantly ($p < 0.05$) towards the previous adapting position for nearby roll-tilted positions (30, 60°) and upright only. After adapting at $\pm$ 45° significant ($p < 0.01$) shifts towards earth-vertical were noted for nearby roll-tilted positions (60, 90°) and upright. We simulated errors based on the sum of two functions reflecting A- and E-effects. By shifting the function representing the E-effect towards the adapting position, experimental data could be fitted successfully. We conclude that prolonged roll-tilt rather locally distorts verticality perception than globally shifting it. Short-term adaptation of the E-effect may explain these shifts and could reflect the brain's strategy to optimize estimates around recent roll positions – assuming that the body is usually (almost) parallel to gravity.

I-6
HIPPOCAMPAL STRUCTURES AND VESTIBULAR FUNCTION IN EPILEPTIC HUMAN

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Hôpital BEAUJON- University Paris VII

Introduction: Functional connexions between hippocampus (and adjacent structures) and vestibular formation are documented in animals and in healthy human. Hippocampal sclerosis is a specific epileptogenic brain injury. It may therefore affect hippocampo-vestibular connexions. Further, since most patients are treated by a surgical resection of the antero-mesial part of the temporal lobe, the influence of a loss of hippocampal projections on vestibular structures should be studied.
Objectives: To test the vestibular function of patients before and after resection of the antero-mesial part of the temporal lobe for intractable temporal epilepsy associated with hippocampal sclerosis.
Methods: Vestibular function (caloric test, HIT, VEMPs) was studied on 10 patients before and 6 months after temporal lobe surgery.
Results: Before surgery, vestibular function was normal in all patients with right temporal lobe epilepsy while patients with left injury had impaired vestibular functions contrasting with the absence of complain. After surgery, vestibular functions were altered in 7 cases, but in all patients, once again without any subjective symptom.
Conclusion: This study suggests an asymmetry of the connexions between left and right hippocampal structures and vestibule, with a pronounced basal alteration reinforced after surgery.

Oral Presentations J. New Examinations of Vestibular Dysfunction

J-1
VISUAL AND PROPRIOCEPTIVE FUNCTIONAL MRI INTERACTION IN BILATERAL VESTIBULAR LOSS IMPERIAL COLLEGE, LONDON

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Following bilateral vestibular loss (BVL) patients gradually adapt to the loss of vestibular input and rely more on other sensory inputs. Here we examine changes in the way proprioceptive and visual inputs interact. We used functional magnetic resonance imaging (fMRI) to investigate visual responses in the context of varying levels of proprioceptive input in 12 BVL subjects and 15 normal controls. A metal-free vibrator was developed to allow vibrotactile neck proprioceptive input to be delivered in the MRI system. A high level (100 Hz) and low level (30 Hz) control stimulus was applied over the left splenius capitis; only the high frequency stimulus generates a significant proprioceptive stimulus. The neck stimulus was applied in combination with static and moving (optokinetic) visual stimuli, in a factorial fMRI experimental design. We found that high level neck proprioceptive input had more cortical effect on brain activity in the BVL patients. This included a reduction in visual motion responses during high levels of proprioceptive input and differential activation in the midline cerebellum. In early visual cortical areas, the effect of high proprioceptive input was present for both visual conditions but in lateral visual areas, including V5/MT, the effect was only seen in the context of visual motion stimulation. The finding of a cortical visuo-proprioceptive interaction in BVL patients is consistent with behavioural data indi-

cating that, in BVL patients, neck afferents partly replace vestibular input during the CNS-mediated compensatory process. An fMRI cervico-visual interaction may thus substitute the known visuo-vestibular interaction reported in normal subject fMRI studies. The results provide evidence for a cortical mechanism of adaptation to vestibular failure, in the form of an enhanced proprioceptive influence on visual processing. The results may provide the basis for a cortical mechanism involved in proprioceptive substitution of vestibular function in BVL patients. Neuroimage Clinical 2014, 4, 274–282.

J-2
CONTRALATERAL SUPPRESSION OF DISTORTION-PRODUCT OTOACOUSTIC EMISSIONS: A POTENTIAL DIAGNOSTIC TOOL TO EVALUATE THE VESTIBULAR NERVE

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Contralateral suppression of distortion-product otoacoustic emission (DPOAE) is the phenomenon in which the DPOAE amplitude is suppressed in one ear when the contralateral ear is subjected to noise stimulation, compared with measurement without noise. The medial olivocochlear bundle (MOCB) and inferior vestibular nerve are suggested to be the origin of DPOAE contralateral suppression. Therefore, it can be inferred that DPOAE contralateral suppression is impeded in patients with lesions of the MOCB or inferior vestibular nerve. We thus hypothesized that DPOAE contralateral suppression shows a reduced response in patients with vestibular neuritis. DPOAE contralateral suppression was performed in normal subjects and patients with vestibular neuritis. DPOAE contralateral suppression showed a significantly reduced response in patients with vestibular neuritis at the f2 frequencies of 1257, 1587, and 2002 Hz, at which the DPOAE amplitude was significantly suppressed in normal subjects. We propose DPOAE contralateral suppression as a potential diagnostic tool to evaluate the functional integrity of the vestibular nerve.

J-3
FUNCTIONAL TESTING OF THE VOR IN VESTIBULAR NEURITIS

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The head impulse test is nowadays recognized as the gold standard for clinical testing of the angular VOR. By imposing unpredictable, abrupt head rotations in the planes of canals pairs it aims at unveiling the dysfunction of the semicircular canal towards which the head is rotated on the basis of Ewald's II law. Functional testing of the VOR aims at assessing the ability of the reflex to stabilize gaze in space and thus allow clear vision during head movements. The HITD approach to functional testing requires subjects to identify optotypes briefly displayed on a screen while an examiner manually imposes a set of head impulses involving a range of angular accelerations. Subjects are then classified based on the percentage of correct answers with respect to a population of controls. Here we used the HITD coupled to a video-oculography system to study XX patients suffering from vestibular neuritis and XX of those were re-tested after three months. We found that the HITD was able to unveil the ipsilesional deficit and the contralesional impairment, together with the improvement in the follow-up test. At the same time, VOG allowed us to gain insights on the role of covert saccades and the dynamics of functional testing.

J-4
BLAST EXPOSURE IS ASSOCIATED WITH UNILATERAL VESTIBULAR DAMAGE IN US VETERANS

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Blast exposMild traumatic brain injury (mTBI) is a significant problem for returning veterans from the recent conflicts. There is an increasing body of data that suggests that vestibular damage may be common in $\sim$ 30% of those with mTBI. In addition there is still a lack of data of the effects of a blast wave on vestibular function in this group. The goal of this work was to determine if veterans with a blast exposure or mTBI demonstrate impaired vestibular function. Twenty five veterans (males, 39.9 $\pm$ 9.6 years, 17 endorsed blast exposure, 12 had history of mTBI) participated. Ocular counter-roll was measured during two different protocols. To assess bilateral response, subjects were tilted $\pm$ 20 degrees at 0.03125 Hz (32 sec cycle) in the dark. To assess unilateral response subjects were rotated in the dark at 400 deg/sec for 5 min after which there

were translated 5 cm off center to the right and left for 30 sec, repeated 3 times. Infrared images of eyes were recorded continuously and analyzed using commercial software (SMI). Translation was not performed until subjects reported no sense of rotation.
Results found that there was no difference between bilateral ocular counter-roll between either the Controls (0.122 ± 0.016), those with just Blast exposure (0.184 ± 0.035) and those with mTBI + Blast (0.152 ± 0.023). In contrast, there was a greater difference when looking at unilateral differences in ocular counter-roll between groups with much greater percentage differences between sides in those with mTBI + Blast (Controls: $89.1 \pm 52.0\%$; Blast: $18.7 \pm 5.6\%$; mTBI + Blast: $248.1 \pm 120.9\%$). Interestingly, while those with mTBI + Blast showed greater unilateral differences, they did not show decrements in their equilibrium scores during posturography suggesting their postural control remains intact. These data indicate that veterans with blast exposure that was associated with a mTBI have increased risk of unilateral otolith damage. In addition, this unilateral damage is masked when using tests of bilateral function since the side with intact otolith function appears to compensate. The functional implications of this unilateral damage needs to be further explored. Supported by the War Related Illness and Injury Study Center, Veterans Administration and NIH grant R21DC009900 (Serrador).

J-5
EFFECTS OF BACKGROUND COMPOSITION, TILT, AND ROTATION ON ACCURACY OF THE SUBJECTIVE VISUAL VERTICAL AND PERCEPTION OF MOTION*

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Background: Visual dependence is the extent to which a person's spatial orientation and motion perception are affected by visual stimuli. One measure of visual dependence is the subjective visual vertical (SVV) on Rod and Frame/Disk Tests. Visual dependence may be seen clinically in patients with visually induced dizziness (VID), also known as visual vertigo. VID is a sensation of vertigo, unsteadiness or dizziness on exposure to complex or moving visual stimuli. VID usually is triggered by acute or episodic vestibular disorders, but may persist for years. One theory holds that persistent VID arises from pathological visual dependence that develops during acute illnesses, and then causes chronic sensitivity to provocative visual stimuli such grocery stores, traffic flow, and patterned décor. The features of visual stimuli that most affect space-motion perception are unknown. To investigate this, we piloted the use of a Rod and Frame/Disk paradigm with backgrounds of differing complexity and emotional valence.
Methods: 11 normal individuals and 5 patients with vestibular disorders (4 without VID, 1 with persistent VID) took part. Normal subjects had no dizziness (Dizziness Handicap Inventory [DHI] scores = 0). Patients without VID had minor symptoms (DHI = 8–14). The one with VID had major symptoms (DHI = 76) when tested. The Rod and Frame/Disk Test was administered on a laptop computer with a viewing cone over the screen to exclude extraneous stimuli. The experimental visual field consisted of a light pink rod in a central black circle superimposed on 8 test backgrounds: 2 stationary controls (plain black, 12 pink ovals), 3 of varying spatial complexity with 10 deg static tilt [plain pink frame (Frame), country road through a cornfield lined with utility poles (Country), bustling city street lined with skyscrapers (City)], and 3 of varying emotional valence with 20 deg/s circular rotation (12 pink ovals (rOvals), 12 neutral human faces (nFaces), 12 fearful/angry human faces (eFaces)]. Control backgrounds were presented twice, tilted and rotating backgrounds once each in clockwise and anticlockwise directions. Subjects completed 6 trials of each condition in sequences counterbalanced for stimulus direction and type.
Results: City caused significantly larger SVV errors than other condition in 10 subjects, and was among the largest in 5 others. For the cohort, City (3.9 deg) caused a larger mean error than Country (3.0 deg; $p < 0.007$), which gave a larger error than Frame (1.8 deg, $p < 0.002$). eFaces caused among the largest errors in 3 subjects. For the cohort, eFaces and nFaces caused the same error (2.0 deg), which trended larger than rOvals (1.7 deg, $p < 0.09$). 14 subjects reported vection during or after rotating conditions; 7 cited the face conditions as most compelling; 1 reported a tilt illusion with Country. Patients without VID had higher SVV errors than normal subjects on City, Country, and Frame (all $p < 0.05$), but not other conditions. The patient with VID had the highest SVV errors on all conditions but City.
Conclusions: Content of visual backgrounds significantly affected space-motion perception in all subjects, in general patients more than controls. Complexity of tilted backgrounds affected spatial orientation (SVV), whereas rotational content affected motion per-

ception. These preliminary findings suggest that spatial and emotional content of visual backgrounds may play a part in visual space-motion perception and VID symptoms.

*This abstract is an invited status report related to the International Classification of Vestibular Disorders and was not reviewed by the scientific committee.

J-6
ELECTRICAL VESTIBULAR STIMULATION AFTER VESTIBULAR NEURITIS

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Introduction: Vestibular neuritis is a clinical syndrome of vertigo, nystagmus, postural imbalance, nausea, and vomiting due to sudden unilateral loss of vestibular function. Our study aimed to determine the electrically-evoked vestibulo-ocular reflex (eVOR) deficits after vestibular neuritis to electrical vestibular stimulation (EVS).
Materials and methods: The eVORs were recorded as binocular 3D eye rotations evoked by bipolar, 100 ms current-step at [0.9, 2.5, 5.0, 7.5,10.0] mA with dual-search coils from 18 (9 left, 9 right) vestibular neuritis patients confirmed by caloric, head impulse, cervical VEMP and audiometry tests. In addition, a train of five 9 ms–5.0 mA current-pulses were also tested.
Results: In complete vestibular neuritis involving the superior and inferior vestibular nerves, eVOR latency was prolonged ipsilesionally from normal 8.8 ms to 11.5 ms. However eVOR latencies in superior and inferior vestibular neuritis were similar to normal at 8.9 ms. Tonic and phasic eVOR showed onset abnormality oscillations with reduced phasic initiation of the contralesion side and a reduction in tonic phasic response by about 20%. The horizontal eVOR response to the train stimulus showed a disconjugacy, which was not observed in normal responses.
Conclusion: The eVOR demonstrated distinctive characteristics related to the different parts of the vestibular labyrinth affected by vestibular neuritis. Due to EVS's instantaneous onset, this stimulus is well suited to demonstrating latency differences in the vestibular pathway.

J-7
PERCEPTUAL THRESHOLDS CAN HELP ASSAY PERIPHERAL VESTIBULAR FUNCTION AND MAY HELP ISOLATE PERIPHERAL DEFICITS

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Introduction: Clinical vestibular testing primarily measures reflexive responses, and although perceptual threshold measurements are a standard part of auditory and visual testing, they have not been used to evaluate vestibular disorders during dynamic motion. Because thresholds as a function of frequency (i.e., audiogram) have proven to provide a sensitive assay of peripheral function, we measured vestibular thresholds as a function of frequency in patients suffering severe bilateral peripheral loss and compared their thresholds to those recorded from normal subjects.
Objectives: Assess thresholds as a function of frequency in normal subjects, patients with total bilateral vestibular loss, and patients with idiopathic bilateral vestibular hypofunction (iBVH) to help assay the distribution of peripheral vestibular damage.
Methods: To facilitate direct comparison of various forms of peripheral dysfunction, we used identical perceptual threshold techniques to measure otolith function, canal function, and canal-otolith integration. Motion paradigms included yaw rotation (testing the lateral canals between 0.5 to 5 Hz), inter-aural translation (primarily testing the utricles between 0.3 to 5 Hz), superior-inferior translation (primarily testing the saccules between 0.3 to 5 Hz), and roll tilt (testing the vertical semicircular canals and the otolith organs between 0.05 and 5 Hz). For each motion direction, we used standard forced-choice direction recognition procedures that used adaptive 3-down/1-up staircases to adjust the stimulus level. Data were fit with a standard psychophysical "probit" model that assumes that the underlying perceptual noise is gaussian. Thresholds were measured with these standard psychometric techniques in 4 patients suffering severe idiopathic bilateral vestibulopathy; these thresholds were compared with thresholds measured in 14 normal subjects and 3 patients with completely absent peripheral vestibular function.
Results: We found that patients suffering total bilateral ablation had significantly high thresholds for all motion paradigms, but that the deficits were particu-

larly evident for superior-inferior (z-axis) translation and yaw rotation. We found that perceptual thresholds were abnormally elevated in the patients with idiopathic bilateral vestibulopathy for yaw rotation at all frequencies and for inter-aural translation at only the lower frequencies. Thresholds were not different from normal for the other two motion paradigms.
Conclusions: The results from patients suffering total bilateral vestibular ablation clearly show the vestibular system's contributions to perceptual thresholds. These threshold data clearly show that threshold testing can help assay peripheral deficits. The thresholds measured in patients suffering iBVH show that the distribution of vestibular dysfunction in this disorder is not uniform, but rather can affect lateral canal and possibly low-frequency utricular thresholds, while relatively sparing vertical canal and saccular function.

J-8
CROSS-CULTURAL VALIDITY OF THE VESTIBULAR ACTIVITIES AND PARTICIPATION (VAP) QUESTIONNAIRE: A CROSS-SECTIONAL STUDY

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The World Health Organization developed the International Classification of Functioning, Disability and Health (ICF) as a conceptual framework to evaluate health and disability across cultures. The VAP was previously developed using the ICF model to examine activities and participation abilities in persons with vestibular disorders. The purpose of this study was to examine the psychometric properties of the VAP in four different countries [the United States (Pittsburgh), Germany (Munich), Jordan (Amman), and Saudi Arabia (Riyadh)] in order to determine the objectivity, cross-cultural validity, and convergent construct validity of the instrument. Subjects: Individuals with vestibular disorders aged 18 and over. Data analyses: Rasch analysis was performed in an attempt to shorten the scale and remove redundant items. Unidimensionality by means of person-item deviation residuals was examined via a residual principal component analysis (PCA). Goodness of fit of the subscales was then determined and the differential item functioning across study centers was calculated. To examine convergent construct validity, the VAP was compared to the Dizziness Handicap Inventory (DHI). Results: 453 subjects consented and completed the VAP and the DHI during the same session. For the Rasch analysis, 50 people each from Pittsburgh and Munich were used and the data were pooled from Amman and Riyadh (total $n = 159$). The Rasch analysis revealed two separate subscales. Six items showed good fit for subscale 1 and six for subscale 2. Subscale 1 items included focusing attention, lying down, standing, bending, lifting and carrying objects, and sports. Subscale 2 items included walking long distances, climbing, running, moving around within buildings other than home, using transportation, and driving. The Pearson Product Moment Correlation between the DHI and subscale 1 was 0.66 and subscale 2 was 0.64. Discussion: The subscale items appear appropriate for use in at least 4 different centers around the world on three continents. The revised VAP consists of 12 items, essentially shortening the test by more than 50%. Conclusion: The new shortened version of the VAP allows a comparison of the impact of vertigo and dizziness on activity limitation and participation restrictions between different individuals as well as monitoring change over time within the same individual and is valid across countries and cultures.

Oral Presentations K. Central and Peripheral Disorders

K-1
INCREASED VISUAL DEPENDENCE IN DIABETIC PATIENTS ON THE COMPUTERIZED ROD AND FRAME TEST

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Introduction: A fundamental spatial reference for spatial orientation and maintaining an erect bipedal posture stance and balance on Earth is subjective visual vertical (SVV). The central representation of this SVV is based on the integration of vestibular, visual and somatosensory cues. Perceptual preferences for spatial orientation vary within the normal population with some individuals relying more on vision, hence

categorized visual field dependent (FD) and others on vestibular-proprioceptive cues and are known as visual field independent (FI). Some factors that affect reliance to visual cues include old age and vestibular dysfunction. Recent studies have found that diabetes increases the risk of vestibular dysfunction, a known risk factor for falls especially in the elderly, as measured by performance on postural testing. This study aims to determine whether differences in vestibular function exist at the perceptual level and can be detected on the Rod and Frame Test (RFT), which provides an indirect measurement of vestibular function, between normal subjects ($n = 27$, mean age: 56.5 ± 5.53 years) and diabetic patients ($n = 39$; mean age: 57.38 ± 6.52 years) without neuropathy or visual disturbance.

Methods: A computerized version of the Rod and Frame test (RFT) was used in this study. Subjects were tested in the upright position and they viewed the computer screen using head mounted video eye glasses (VUSIX iWEAR, VR920 Video Eyewear), which restricted the field of vision and gave the impression of viewing a large screen from a distance of 2 m. The subject was presented with a square white frame on a plain black background. Within the frame, the ends of a virtual line were marked by two white dots (which could be rotated around its center in either clockwise or anticlockwise directions using the mouse buttons). The starting position of the rod was $\pm$ 20° away from the vertical, and it could be moved in 0.5° increments. SVV judgment was performed in different visual contexts: SVV without a frame, (SVV), within a clockwise (CW; $+18°$Frame) or counterclockwise (CCW; $-18°$Frame) tilted frame. Four trials were carried out for each visual context in a random order. Absolute deviation errors in aligning the rod to the true vertical were measured in degrees.

Data analysis: Data was analyzed using the GraphPad InStat3 software. All data passed normality by the Kolmogorov and Smirnov test. Normal subjects and diabetic patients were compared for the SVV estimates using the unpaired t-test. Welch's correction applied was used when assuming that the two populations of data have different standard deviations (SDs). For all tests, the significance level was fixed at 0.05.

Results: There was no difference between absolute errors in the frameless SVV between controls and diabetic patients (controls: $0.93° \pm 0.45°$; diabetics: $1.08° \pm 0.58°$, $P = 0.26$). As for SVV with tilted frame, diabetic patients displayed very significantly higher errors than normal subjects (controls: $1.67° \pm 0.82°$; diabetics: $2.42° \pm 1.39°$, $P = 0.008$). In diabetic patients, there was a significant correlation between HBA1c levels and duration of diabetes exposure ($R = 0.37$, $P = 0.02$), however correlations between HBA1c levels or duration of disease with SVV were not significant.

Conclusion: The increased visual dependence in diabetic patients without neuropathy or visual disturbance indicates vestibular dysfunction at the perceptual level as measured by performance on the CRFT.

K-2
GAZE HOLDING IN PATIENTS WITH NEURODEGENERATIVE CEREBELLAR DISEASE

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Various neurodegenerative cerebellar diseases cause deficits in gaze holding, leading to centrifugal gaze-evoked nystagmus (GEN). In healthy subjects a weak centripetal eye drift can also be observed, which leads to physiological end-point nystagmus only at large gaze angles. Such drift is due to the imperfect memory of the neural network generating the eye position command. This network is usually modeled with a single-time-constant leaky integrator, implying a linear relation between drift velocity and eye eccentricity. The emergence of GEN is commonly explained by impaired cerebellar control that causes an increase of the slope of this linear relation compared to healthy subjects. However, a detailed analysis of gaze-dependent eye drift is missing. We recorded horizontal eye positions in 18 healthy subjects and 20 patients with degenerative cerebellar disease. They were asked to fixate on a flashing dot (50 ms every 2 s) slowly displacing (0.5 deg/s) between $\pm$ 40 deg of horizontal gaze eccentricity. The relation between eye drift velocity and gaze eccentricity was noticeably nonlinear. We fitted the smoothed eye velocity with a tangent function velocity = A*tan(B*position) (healthy-r2 = 0.85 ± 0.13, patient-r2 = 0.89 ± 0.12). Although not reflecting any physiological modeling, the chosen function is particularly convenient, since parameter A uniformly scales the output, while parameter B describes the emergence of nonlinearity with gaze eccentricity. Based on the parameter values obtained by single-subject fitting, we

propose a classification of the patients separating those exceeding the healthy subjects' mean + 1 standard deviation in the estimates of A-parameter only, B-parameter-only or A- and B-parameters. Our classification has the potential to reveal significant differences in the development of GEN in patients with cerebellar diseases. Specifically our methods identified: 1) a subgroup of patients showing a faster increase of the drift velocity with gaze eccentricity, but a nonlinear behavior similar to healthy subjects (change in A-parameter only); 2) a subgroup characterized by an earlier emergence of nonlinearity but no overall increase of the slope of drift velocity as a function of gaze eccentricity (change in B-parameter only); 3) a subgroup of patients showing both pathological behaviors (changes in both parameters). In conclusion, when the cerebellum no longer efficiently reinforces the brainstem contribution to gaze-holding, different centripetal drift behaviors can emerge, which show either an homogeneous decrease of eye drift compensation or a manifestation of the intrinsic non-linearity of the eye drift velocity at smaller gaze angles. We speculate that the two behaviors could result from different deficiencies of the neurons in the integrating network. Supported by the SNSF, Koetser Foundation, ZIHP University of Zurich.

K-3
HORIZONTAL CANAL OCCLUSION SYNDROME – HEAD JOLTING-INDUCED VERTIGO AND NYSTAGMUS

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Introduction: We report a new vestibular syndrome in two patients with intense vertigo and nystagmus following violent horizontal head jolting Objectives: To clarify the origin of a new paroxysmal vestibular syndrome induced by violent head-shaking (head jolting).
Methods: Case studies in two male patients (62 yrs and 58 yrs), with detailed vestibular testing and neuroimaging.
Results: The cardinal symptom is rotational vertigo after violent and brief oscillations of the head. This triggered intense horizontal nystagmus, with peak eye velocities above 100 deg/s, lasting 45 s. Horizontal angular velocities of the head required to induce these episodes could only be achieved actively by the patients themselves (ca.700 deg/s). Positional manoeuvres for horizontal/vertical canals were negative. In Patient 2 there appeared to be a filling defect in the left horizontal semicircular canal shifting after the head jolting stimulus. This patient underwent canal plugging with complete and immediate symptom resolution. Patient 1 was managed conservatively and, over a period of 6 years, the episodes gradually disappeared.
Conclusions: This new syndrome cannot be explained as positional vertigo, head-shaking nystagmus or vestibular paroxysmia. We attribute the 'head jolting' nystagmus in our two patients to mechanically dislodged material within the horizontal semicircular canal causing cupular deflection and excitation. Clinical examination, rather than imaging or vestibular testing established the diagnosis. Surgical or conservative treatment appears successful long term but canal plugging can resolve the problem rapidly.

K-4
VERTIGO AND NYSTAGMUS IN ORTHOSTATIC HYPOTENSION: PATTERNS AND POSSIBLE MECHANISM

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Introduction: Generalized cerebral ischemia from cardiovascular dysfunction usually lead to presyncopal dizziness, but several studies reported higher frequency of rotatory vertigo in cardiovascular patients.
Objectives: We sought to determine whether generalized cerebral ischemia due to cardiovascular disorders may produce objective vestibular dysfunction. Materials and Methods: We recruited 33 patients with orthostatic dizziness/vertigo due to profound orthostatic hypotension (OH) and 30 controls. All participants underwent recording of eye movements during two orthostatic challenging tests: Schellong and squatting-standing tests. Most patients had neuroimaging, and patients with abnormal eye movements were subjected to follow-up evaluations for 6 months.
Results: Symptoms associated with orthostatic dizziness/vertigo included blurred vision, fainting, and tinnitus. Ten (30%) of 33 patients developed rotatory vertigo and nystagmus during Schellong ($n = 5$) or squatting-standing test ($n = 5$). Four of them showed pure downbeat nystagmus while five had downbeat and

horizontal nystagmus with or without torsional component. Patients with orthostatic nystagmus had shorter duration of orthostatic intolerance than those without nystagmus ($1.0_{¡}{}^{3}\!/_{3}1.6$ vs $11.0_{¡}{}^{3}\!/_{3}9.7$ months, $p < 0.001$). In two patients, orthostatic nystagmus disappeared during follow-up despite the persistence of profound OH.

Conclusions: Generalized cerebral ischemia due to OH may induce vestibular dysfunction, which may be ascribed to cerebellar dysfunction due to hypoperfusion, or asymmetrical excitation of both labyrinth due to transient ischemia and/or disinhibition from inferior cerebellar hypoperfusion. Given the longer duration of orthostatic intolerance in patients without nystagmus, and resolution of orthostatic nystagmus during follow-up in presence of persistent OH, orthostatic vertigo and nystagmus may not be observed in longstanding OH due to adaptive mechanisms.

K-5
ISOLATED VESTIBULAR SYNDROME IN POSTERIOR CIRCULATION STROKE: FREQUENCY AND INVOLVED STRUCTURES

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Introduction: Dizziness/vertigo is one of the most common symptoms of posterior circulation stroke, and usually accompanies other neurological symptoms and signs. However, brainstem and cerebellar strokes may present with isolated vestibular syndrome including isolated vertigo or imbalance.

Objectives: This study aimed to determine the frequency and involved structures of acute isolated vascular vertigo by analyzing the data of prospectively recruited patients with posterior circulation infarctions in a referral Stroke Center.

Materials and Methods: We had consecutively recruited 132 adult patients with acute to subacute posterior circulation infarctions at the Stroke Center of Pusan National University Hospital between July 2011 and August 2012. We determined the frequency of isolated vestibular syndrome, and analyzed the involved neural structures. We also investigated any correlation between the frequency of isolated vestibular syndrome and separate vascular territories of the posterior circulation involved.

Results: Out of the 134 patients with posterior circulation infarctions, we identified 34 (25.8%) with isolated vestibular syndrome. The frequency of isolated vestibular syndrome was significantly higher in infarctions involving the proximal (61%) than in the middle (3%) or distal intracranial posterior circulation territory (6%) ($p < 0.01$). Common areas involved in isolated vestibular syndrome included the cerebellum ($n = 23$, 67.6%), inferior ($n = 3$, 8.8%) or superior ($n = 2$, 5.9%) cerebellar peduncles, and caudal lateral ($n = 4$, 11.8%) or rostral dorsolateral medulla ($n = 2$, 5.9%). Most (32/34, 94.1%) patients with isolated vestibular syndrome showed positive HINTS (negative head impulse, direction-changing nystagmus, and skew deviation). Initial neuroimaging including diffusion-weighted MRIs was negative in 17.6% (6/34) of patients with isolated vestibular syndrome.

Conclusions: Isolated vestibular syndrome occurs in approximately 25% of the patients with acute posterior circulation infarctions, and mostly involves the cerebellum, inferior or superior cerebellar peduncles, and caudal lateral or rostral dorsolateral medulla. The occasional negative neuroimaging in patients with acute isolated vascular vertigo highlights the significance of appropriate bedside evaluation in acute vestibular syndrome.

K-6
A STRUCTURED MONITORING PROGRAM FOR GENTAMICIN VESTIBULOTOXICITY

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Introduction: Aminoglycosides are routinely used to treat complex infections, however awareness of their potential vestibulotoxic effects has been shown to be poor. Gentamicin is the drug most commonly associated with vestibular toxicity; it is standard practice to monitor for renal toxicity, but there are limited data on monitoring of its vestibular side effects.

Objectives: To develop a pilot program to monitor vestibulotoxicity in patients undergoing intravenous gentamicin therapy. To determine the potential for recovery from vestibulotoxicity identified early in gentamicin therapy after the drug has been suspended.

Methods: A monitoring plan was implemented in partnership with the Dept. of Infectious Diseases at our site. The monitoring involved an assessment of dynamic visual acuity (DVA) using both LogMAR and computerized DVA testing along with portable static posturography. Clinical examination focused on the

VOR. Specific symptoms suggestive of vestibulotoxicity were recorded. Patients were assessed a mean of 3 times per week. Any reduction in vestibular function was reported to both the Otology and Infectious Diseases service. Patients identified to be developing vestibulotoxicity were also sent for further investigation that included magnetic scleral search coil, vHIT and VNG testing.

Results: 4 out of 14 patients enrolled in the study were identified to be developing vestibulotoxicity during monitoring. Key objective findings were in an increase in postural sway and a decrease of the standardized cDVA ratio. Mean cDVA ratio was 0.84 at the beginning of gentamicin treatment, but in affected individuals dropped to a mean value of 0.74 during therapy. The decrease correlated with increasing values of root mean square measurements of center of pressure in static posturography. Gentamicin treatment was suspended where possible. In 3 out of 4 patients in whom gentamicin was withheld, there was a substantial improvement of their cDVA ratio over the course of one week, suggesting that the early vestibulotoxicity was reversible in these patients.

Conclusion: Monitoring of Gentamicin therapy is important in preventing the possible permanent and often devastating effects of vestibulotoxicity. Our early results suggest that there is a role for the monitoring of vestibular function in patients undergoing IV gentamicin therapy. Ongoing research in this area concerning the process of implementation will be outlined.

K-7
INTERNATIONAL CLASSIFICATION OF VESTIBULAR SIGNS AND EXAMINATION TECHNIQUES, PART 1: NYSTAGMUS AND SACCADIC INTRUSIONS*

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Introduction: Vestibular research and patient care have been hindered by the lack of standardized terminology and a formal disease classification system. The International Classification of Vestibular Disorders (ICVD) has adopted a multi-layered structure: (I) Symptoms and Signs; (II) Syndromes; (III) Diseases and Disorders; and (IV) Mechanisms. As a first step in 2009, the Classification Committee of the Bárány Society (CCBS) published a consensus classification and definitions of vestibular symptoms. Subsequently the CCBS has commissioned a working group to develop a classification system and definitions for vestibular examination signs and techniques, with the goal of establishing a consistent universal nomenclature.

Objective: To develop international consensus definitions and a classification system for vestibular examination signs and office examination techniques used frequently in the assessment of patients with vestibular symptoms, as part of the ongoing efforts of the CCBS.

Methods: This work forms part of an ongoing multiyear project to develop the first edition of the ICVD, which uses a structured process for developing international consensus definitions for vestibular symptoms, signs, syndromes, disorders and diseases. This process, overseen by the CCBS, is based on expert, multidisciplinary committees with international representation developing diagnostic criteria for subsequent comment and refinement prior to publication. These criteria are based on a critical appraisal of current best scientific evidence. All definitions are supported by notes, comments, and written discussion according to a template established by the CCBS for ICVD consensus criteria.

Results: Classification and definitions were developed iteratively over a two-year period through discussion, presentation, and refinement. Initial discussion encompassed the entire spectrum of examination signs and techniques. Proper characterization of nystagmus was recognized as vital to the vestibular examination. Given their complexity and lack of universal nomenclature, the group elected to initially address only nystagmus and other oscillatory eye movements in this Part 1 document. First, nystagmus was defined and differentiated from saccadic intrusions and other nystagmus-like movements. Attributes necessary for a complete description of nystagmus were elaborated. A classification was developed based upon whether nystagmus is spontaneous, gaze-evoked, triggered by a specific trigger, or physiologic, following the ICVD symptom classification where possible. Common forms of nystagmus relevant to the evaluation of patients with vestibular disorders were prioritized. Features differentiating peripheral from central causes of nystagmus were highlighted. Definitions were created to be as purely phenomenological as possible, while also categorizing terms that imply etiol-

ogy or pathophysiology. When existing nomenclature was confusing, preferred, alternative, and rejected terminology were suggested.
Conclusions: Establishing a consensus classification and definitions of vestibular examination signs and techniques, beginning with nystagmus and saccadic intrusions, should facilitate the Bárány Society's effort to define diseases and disorders in its development of an International Classification of Vestibular Disorders.

*This abstract is an invited status report related to the International Classification of Vestibular Disorders and was not reviewed by the scientific committee.

K-8
VESTIBULAR OCULAR REFLEX (VOR) IN PRE-SYMPTOMATIC SPINOCEREBELLAR ATAXIA TYPE 3: A POSSIBLE BIOMARKER OF THE DISEASE

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Background: Spinocerebellar Ataxia Type 3 (SCA-3), also known as Machado-Joseph Disease (MJD), is an autosomal dominant neurodegenerative disorder for which genetic testing can reveal those at risk for developing the disease. The time at which a given individual begins to show symptoms is highly variable, with clinical diagnosis dependent on motor-ataxic symptoms. Quantitative measures that would identify pre-symptomatic gene carriers at the threshold of clinical diagnosis would be extremely valuable in early diagnosis, tracking disease progression, and assessing treatment.
Objective: To investigate if eye movements can be used as biomarkers to quantify the appearance and progress of the disease even pre-symptomatically. Methods: Using the magnetic search coil technique we recorded saccades, smooth pursuit, and vestibular-ocular reflex (VOR) of 10 symptomatic SCA-3 patients and 4 subjects at risk for developing SCA-3. Three of at risk subjects were genetically tested and found to have expanded "CAG" repeats in the ATXN3 gene i.e. they will develop the disease at some point. The fourth is a sibling of a symptomatic MJD patient who has declined genetic testing. The ataxia score of each patient was determined by the Scale for the Assessment and Rating of Ataxia (SARA).
Results: We found that the four at risk subjects have a reduction in the gain of the VOR as measured using the head impulse test. Nonetheless, we did not find any deficit in either their saccades or smooth pursuit. In contrast, all of the symptomatic patients had saccadic and smooth pursuit deficits in addition to impaired VOR. There was a trend of a negative correlation between VOR gain and SARA score (the lower the gain, the higher the SARA score) but the result did not reach statistical significance (r: -0.48, $p = 0.16$).
Conclusions: Individuals at risk for developing SCA-3 can be asymptomatic for years before receiving formal diagnosis. Our findings raise the possibility of using VOR gain as a neurophysiologic biomarker of the disease.

K-9
NORMATIVE VOR GAIN DATA FOR DIFFERENTIATING ACUTE VESTIBULAR NEURITIS AND STROKE BY HEAD IMPULSE VIDEO-OCULOGRAPHY

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Objective: Vestibular neuritis is often mimicked by stroke (pseudo-neuritis). Vestibular eye movements help discriminate the two conditions. We report normative vestibulo-ocular reflex (VOR) gain measures in neuritis and stroke presenting acute vestibular syndrome (AVS).
Methods: Prospective, cross-sectional study of AVS (acute, continuous vertigo/dizziness lasting $>$ 24 hrs) at two academic centers. We measured horizontal head impulse test (h-HIT) VOR gains in 26 AVS patients using a video h-HIT device (ICS Impulse™). All patients were assessed within one week of symptom onset. Diagnoses were confirmed by clinical exams, brain magnetic resonance imaging with diffusion-weighted images (MRI-DWI), and follow-up. Brainstem and cerebellar strokes were classified by vascular territory – osterior inferior cerebellar artery (PICA) or anterior inferior cerebellar artery (AICA).

Results: Diagnoses were vestibular neuritis ($n = 16$) and posterior fossa stroke (PICA $n = 7$; AICA $n = 3$). Mean h-HIT VOR gains (ipsilesional [SEM], contralesional [SEM]) were as follows: vestibular neuritis (0.52 [0.04], 0.87 [0.04]); PICA stroke (0.94 [0.04], 0.93 [0.04]); AICA stroke (0.84 [0.10], 0.74 [0.10]). VOR gains in neuritis (unilateral vestibulopathy) and PICA stroke (bilaterally normal VOR) were homogeneous, while AICA stroke gains were heterogeneous. In vestibular neuritis, borderline gains ranged from 0.62 to 0.73. Classifying AVS patients with bilateral VOR mean gains $\geqslant 0.70$ as suspected strokes yielded a total diagnostic accuracy of 90%, with stroke sensitivity of 88% and specificity of 92%.
Conclusions: Video h-HIT VOR gains differ between peripheral and central causes of AVS. PICA strokes are readily separated from neuritis using gain measures. Differentiating AICA strokes requires additional oculomotor and auditory findings in some patients.

K-10
VESTIBULAR SYNDROME DEFINITIONS FOR THE INTERNATIONAL CLASSIFICATION OF VESTIBULAR DISORDERS*

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Introduction: Progress in vestibular research has been hampered by a lack of standardization in clinical terminology and inconsistent diagnostic criteria for vestibular disorders. The International Classification of Vestibular Disorders (ICVD) has adopted a multilayered structure: (I) Symptoms & Signs; (II) Syndromes; (III) Diseases & Disorders; and (IV) Mechanisms. The second layer organizes Symptoms & Signs into recognizable Syndromes with an orderly differential diagnosis of Diseases & Disorders. For example, "acute vestibular syndrome" links the constellation of sudden onset vertigo, nausea, vomiting, head motion intolerance, gait unsteadiness, with underlying causes such as vestibular neuritis or acute cerebellar infarction. The purpose of this layer is primarily to define structured criteria for vestibular cohorts used in diagnostic research.
Objectives: To develop international consensus criteria defining the major vestibular syndromes, as part of the ongoing efforts of the Classification Committee of the Bárány Society (CCBS). Syndromes were defined to identify clinically-meaningful populations with specific anticipated underlying etiologies (and corresponding targeted diagnostic workups), but criteria were chosen to facilitate prospective classification prior to diagnosis, rather than post-hoc.
Methods: This work is part of the ICVD project, which uses a structured process to develop consensus definitions for vestibular symptoms, syndromes, and diseases. The process, overseen by the CCBS, uses critical appraisal of best scientific evidence by expert, multi-disciplinary working groups with international representation. Working groups develop draft definitions for comment and refinement prior to publication and dissemination. Definitions are supported by notes, comments, and written discussion using a template created for the ICVD.
Results: Syndrome criteria were developed iteratively over a four-year period through discussion, presentation, and refinement. Initial questions included whether positional disorders should be grouped with episodic spontaneous disorders. Later discussions focused on 100-word definitions for ICD-11 and syndrome subtypes. Three primary vestibular syndromes are defined – acute, episodic, and chronic (Table). Each represents an archetypal presentation for a class of vestibular disorders routinely encountered in clinical practice. Acute vestibular syndrome may be further sub-classified as occurring post-trauma, post-exposure (i.e., medication, illicit substance, toxin), or in the context of known relapsing multiple sclerosis. Episodic vestibular syndrome is divided into spontaneous and triggered forms, and, in the latter case, denoted by the

Table. Definitions for the three primary vestibular syndromes

Syndrome	Definition
Acute Vestibular Syndrome (AVS)	A clinical syndrome of acute-onset, continuous vertigo, dizziness, or unsteadiness lasting days to weeks, and generally including features suggestive of new, ongoing vestibular system dysfunction (e.g., vomiting, nystagmus, severe postural instability). There may also be symptoms or signs suggesting cochlear or central nervous system dysfunction. Acute vestibular syndrome usually connotes a single, monophasic event, often caused by a one-time disorder, but it may instead punctuate a relapsing-and-remitting or stepwise, progressive illness course. Disorders typically presenting this syndrome include vestibular neuritis, acute labyrinthitis, traumatic vestibulopathy, demyelinating disease with vestibular involvement, and strokes affecting central or peripheral vestibular structures.
Episodic Vestibular Syndrome (EVS)	A clinical syndrome of transient vertigo, dizziness, or unsteadiness lasting seconds to hours, occasionally days, and generally including features suggestive of temporary, short-lived vestibular system dysfunction (e.g., nausea, nystagmus, sudden falls). There may also be symptoms or signs suggesting cochlear or central nervous system dysfunction. Episodic vestibular syndrome usually connotes multiple, recurrent events caused by an episodic disorder with repeated spells (triggered or spontaneous), but may initially present after the first event. Disorders typically presenting this syndrome include benign paroxysmal positional vertigo, Menière's disease, vestibular migraine, panic attacks, hypoglycemia, and transient ischemic attacks affecting central or peripheral vestibular structures.
Chronic Vestibular Syndrome (CVS)	A clinical syndrome of chronic vertigo, dizziness, or unsteadiness lasting months to years and generally including features suggestive of persistent vestibular system dysfunction (e.g., oscillopsia, nystagmus, gait unsteadiness). There may also be symptoms or signs suggesting cochlear or central nervous system dysfunction. Chronic vestibular syndrome often connotes a progressive, deteriorating course, but sometimes instead reflects a stable, incomplete recovery after an acute vestibular event, or persistent, lingering symptoms between episodic vestibular events. Disorders typically presenting this syndrome include poorly-compensated unilateral vestibulopathy, chronic bilateral vestibulopathy, cerebellar degeneration, posterior cranial fossa neoplasms, and chronic psychological or behavioral conditions manifesting prominent vestibular symptoms.

specific trigger(s). Chronic vestibular syndrome may be further sub-classified as primary or occurring in secondary progression from another vestibular syndrome phenotype (i.e., post-AVS or post-EVS). Each form should also be classified as associated (or not) with auditory symptoms/signs or neurologic symptoms/signs.
Conclusions: Diagnostic studies focused on differential diagnosis, clinical decision rules, and diagnostic test accuracy require standardized inclusion criteria to define rigorous symptom-based cohorts. We believe these novel consensus definitions for the three primary vestibular syndromes will support the conduct of high-quality, multicenter clinical research studies focused on vestibular disorders diagnosis.
*This abstract is an invited status report related to the International Classification of Vestibular Disorders and was not reviewed by the scientific committee.

K-11
PROGRESS REPORT OF THE BEHAVIORAL SUBCOMMITTEE OF THE COMMITTEE ON CLASSIFICATION OF THE BARANY SOCIETY*

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Introduction: Progress in vestibular research has been hampered by lack of a standardized nomenclature. To address this problem the Barany Society established a Classification Committee in 2006 to develop the first International Classification of Vestibular Disorders (ICVD). The Classification Committee appointed several subcommittees to work on specific components of the ICVD. The Behavioral Subcommittee convened in 2010 to develop definitions of behaviorally mediated vestibular disorders, which are commonly encountered in clinical practice. The subcommittee presented definitions of anxiety- and depression-related vestibular disorders in 2012. This presentation will review the subcommittee's work over the last two years.
Methods: The Behavioral Subcommittee concentrated on three tasks between 2012 and 2014: (1) Ensuring that previously defined anxiety- and depression-related vestibular disorders were compatible with the nomenclature of the latest versions of the International Classification of Diseases (ICD) and Diagnostic and Statistical Manual of Mental Disorders (DSM). The 11th edition of the ICD is currently under development. The beta version may be perused online at http://apps.who.int/classifications/icd11/browse. The 5th edition of the DSM was published in May 2013. (2) Developing a consensus definition of the syndrome known as phobic postural vertigo (PPV) or chronic subjective dizziness (CSD) and defining its relationship to the concepts of space-motion discomfort and visual vertigo. (3) Beginning to define various functional vestibular syndromes (e.g., voluntary nystagmus).
Results: (1) Previously-defined anxiety- and depression-related vestibular syndromes were given minor updates to conform to new developments in ICD-11 and final definitions of DSM-5. These syndromes more clearly capture the existence of primary and secondary anxiety and depressive disorders that manifest vestibular syndromes. They are now termed: Episodic Vestibular Syndrome Due to Anxiety, Chronic Vestibular Syndrome Due to Anxiety, Vestibular Symptoms Due to Depression, Anxiety Complicating Episodic Vestibular Syndrome, Anxiety Complicating Chronic Vestibular Syndrome, Depression Complicating Vestibular Syndrome, and Fear of Falling. The previously defined Vestibular Illness Anxiety has been placed on hold because of unresolved nomenclature differences between ICD-11 beta and DSM-5. (2) Working with prominent outside experts, the subcommittee defined the syndrome of Persistent Postural and Perceptual Dizziness (PPPD), which consolidated the key features of PPV and CSD. Space-motion discomfort and visual vertigo were considered to be symptoms that can be seen with various peripheral, central, and behavioral vestibular disorders, including PPPD. They were not

considered to be independent diagnosis of their own. (3) Limited progress was made in defining functional vestibular syndromes. Nomenclature differences between ICD-11 beta and DSM-5 still loom large. Additional work must be undertaken with the ICVD Symptoms and Signs Subcommittee to refine symptom descriptions for these syndromes.
Conclusions: The ICVD anxiety- and depression- related vestibular disorders were updated and defined in final form. A consensus definition that reconciles PPV and CSD was developed. Additional work will be needed to define the functional vestibular disorders, but this being slowed by ongoing differences between ICD-11 beta and DSM-5.

*This abstract is an invited status report related to the International Classification of Vestibular Disorders and was not reviewed by the scientific committee.

K-12
BILATERAL VESTIBULOPATHY: DIZZINESS AND POSTURAL IMBALANCE*

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Bilateral vestibulopathy (BVP) is characterized by postural imbalance and unsteadiness of gait that worsens in darkness and on uneven ground, head or body movement-induced oscillopsia, and impaired spatial memory and navigation. Impaired function of the semicircular canals is diagnosed by a pathological bedside head impulse test (HIT) and/or bithermal caloric testing (sum of the mean peak velocities of the slow phase caloric-induced nystagmus for stimulation with warm and cold water on each side < 10 deg/s is pathological). If the HIT is unclear, it can be quantified by a video-oculography system with a combined recording of eye and head movements (VOR gain < 0.7 is pathological). A complementary test is dynamic visual acuity (a decrease of 0.2 or more is pathological). Cervical and ocular vestibular-evoked myogenic potentials (c/oVEMP) can be applied to evaluate the function of the otolith organs. There are the following subtypes of BVP depending on the affected anatomical structure and frequency range: impaired canal function in the low- or high-frequency range only and/or otolith function only. Synonyms are bilateral vestibular failure, bilateral vestibular loss. If known, the etiology (for instance, due to ototoxicity, bilateral Meniere's disease, bilateral vestibular schwannoma) should be added to the diagnosis.

*This abstract is an invited status report related to the International Classification of Vestibular Disorders and was not reviewed by the scientific committee.

K-13
VESTIBULAR PAROXYSMIA: RECURRENT SHORT ATTACKS OF VERTIGO*

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Vestibular paroxysmia (VP) is characterized by recurrent spells of vertigo or dizziness, lasting seconds to a few minutes, rarely longer. Attacks most often occur spontaneously but can also be induced by changes of head position that differ from those of benign paroxysmal positional vertigo, for instance, turning the head to the right or left in upright position. Possible accompanying symptoms are short attacks of tinnitus or changes in hearing. In the attack-free interval impaired vestibular or audiological function (mild to moderate) can be found. Neurovascular cross-compression of the eighth nerve in the root-entry zone is the assumed mechanism. MRI findings of vascular compression are not predictive of the disease or the affected side because this is also found in about 30% of healthy subjects. Important differential diagnoses are vestibular migraine, Menière's disease, benign paroxysmal positional vertigo and panic attacks. Response to treatment with carbamazepine supports the diagnosis.

*This abstract is an invited status report related to the International Classification of Vestibular Disorders and was not reviewed by the scientific committee.

K-14

NEUROPHYSIOLOGICAL EVIDENCE FOR GENERALIZED SENSORY NEURONOPATHY IN CEREBELLAR ATAXIA WITH NEUROPATHY AND BILATERAL VESTIBULAR AREFLEXIA SYNDROME (CANVAS)

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Introduction: Cerebellar Ataxia with Neuropathy and bilateral Vestibular Areflexia Syndrome (CANVAS) is a recently described vestibulo-cerebellar ataxia defined by the presence of cerebellar ataxia, a bilateral vestibulopathy and a somatic sensory deficit. The characteristic clinical sign is an abnormal visually enhanced vestibulo-ocular reflex. The somatic sensory deficit contributes to the significant level of disability in CANVAS.
Objective: To investigate whether the sensory deficit in CANVAS can be neurophysiologically characterised.
Methods: 15 CANVAS patients underwent four limb nerve conduction studies, blink reflexes with supraorbital, infraorbital and mental nerve stimulation, mechanically activated masseter reflex, somatosensory evoked potentials (SSEP), brainstem evoked response audiometry (BERA) and cutaneous silent period (CSP) testing.
Results: Neurophysiological investigation in 15 patients revealed uniformly absent sensory nerve action potentials in all four limbs, abnormal blink reflexes in 13/15, abnormal masseter reflexes in 7/12. Tibial H reflexes were absent in 12/15. Somatosensory evoked potentials were absent in 8/9 tested and brainstem evoked response audiometry abnormal in 4/9. Cutaneous silent period responses were abnormal in 7/15.
Conclusion: Whilst our initial description of CANVAS suggested the sensory deficit was most likely a length dependent process, we subsequently demonstrated neuropathologically that CANVAS involves cranial nerve and dorsal root ganglia pathology. This neuronopathy can now be clinically demonstrated with a non-invasive battery of neurophysiological tests. A sensory neuronopathy should be suspected in cerebellar and/or vestibular ataxias, particularly where the degree of ataxia is disproportionate to any clinically identified vestibular and/or cerebellar pathology.

K-15

NEW STRUCTURES OF PATIENT MANAGEMENT AND TRANSLATIONAL RESEARCH IN THE GERMAN CENTER FOR VERTIGO AND BALANCE DISORDERS

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Introduction: Vertigo is one of the most common complaints in medicine. Despite its high prevalence, patients with vertigo often receive either inappropriate or inadequate treatment. This deplorable situation is internationally well known and its causes are multiple: insufficient interdisciplinary cooperation, no standardized diagnostics and therapy, the failure to translate findings of basic science into clinical applications, and the scarcity of clinical multicenter studies. Five years ago the German Center for Vertigo and Balance Disorders (DSGZ) was constituted to build a suitable infrastructure with which these structural, clinical, and scientific deficits can be overcome.
Methods: We here review the previous developments in patient management and translational research at the DSGZ and discuss the future perspectives.
Results: Over the last years, the DSGZ has created a transverse and longitudinal care network which meets the needs of patients with vertigo and balance disorders and public demands for high-quality care at one specialized place: it is organized as a fully integrated chain of care with a multidisciplinary structure. A central outpatient clinic has been established as the core of the care network. It is operated by the different disciplines engaged in these disorders (neurology, otolaryngology, psychiatry, psychosomatic medicine, pediatrics) on one site. Common standards of practice have been established. This concept has overcome the division of disciplines and now serves as a prototype for other interdisciplinary clusters. Treatment of more than 3,500 selected patients per year proves the success of this innovative concept. A translational research infrastructure has been successfully promoted to increase advances in the scientific field of the DSGZ. Translational full research projects bundled interdisciplinary expertise by means of a combination of principle investigators from different institutions; young scientist groups helped to establish and standardize innovative methods and ideas; start-up projects enabled new diagnostic and therapeutic principles to be tested, which are now applied in clinical practice; and prospective con-

trolled clinical studies were initiated and extended to a multicenter setting.
Conclusions: The German Center for Vertigo and Balance Disorders has been established in Munich as an independent patient-oriented clinical interdisciplinary research and treatment center, which focuses on the transfer of basic knowledge to patient care. For the future, DSGZ aims to extend international networking in science, teaching and patient management in the field of vertigo and balance disorders.

Oral Presentations L. Cochlear-Vestibular Testing

L-1
LABORATORY TESTING OF THE VESTIBULAR FUNCTION*

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Laboratory testing of the vestibular function: report of the Barany Society standardisation subcommittee.

Introduction: Many diagnostic tests are performed world wide to quantify vestibular function. However, the clinical relevance of many of these tests are still under dispute and limited consensus exists about the precise measuring procedures and relevant input and output parameters.
Objective: In order to support the Standardization Committee of the Barany Society, many laboratory tests that might contribute to an unambiguous definition of vestibular syndromes were listed and reviewed.
Methods: Based on the international literature and practical experience of the authors, the following test were considered: caloric test (several variants with water and air irrigations), positional nystagmus tests (with VOG), rotatory tests (on and off-vertical axis, concentric and eccentric, fixation suppression test, many stimulus profiles), quantitative oculomotor tests (search for spontaneous and fixation nystagmus or abnormal eye movements, saccades, smooth pursuit and optokinetics), linear translation or tilt tests (using hexapods or sleds, many stimulus profiles), head impulse tests (3D, passive and active), dynamic visual acuity, vestibular evoked myogenic potentials (ocular, cervical, many stimulus profiles and modalities), subjective visual and haptic horizontal and vertical, galvanic/vibration/head shaking/sound induced nystagmus, static and dynamic posturography (including many sensory conditions).
Results: The large variety of available and applied vestibular tests is partly due to the attempt to assess the functionality of the 5 different sensor systems in each labyrinth and the function of the vestibular system per se or in comparison to other sensory systems (image stabilisation, balance and postural control, perception of the orientation and movement in space, interaction with several autonomic functions). The tests will be discussed based on an estimate of the sensitivity and specificity, clinical applicability, the impact on patient management, cost effectiveness and worldwide existing or lacking consensus regarding the input and output parameters, measuring devices and conditions, analysis techniques and procedures.
Conclusions: Based on these considerations we suggest that the standard vestibular test battery should be composed of: the head impulse test, caloric test, dynamic visual acuity test, VOG positional nystagmus tests, on-vertical axis rotatory chair tests (including fixation suppression test) and VEMP's. However, by following a specific sequence of testing the number of tests can be limited. In many patients a careful clinical qualitative examination of oculomotor function will make a quantitative oculomotor function assessment superfluous unless documentation and quantification is required. An evaluation of the on indication required additional tests as imaging techniques (MRI and CT), audiometry and laboratory testing (immune, infections etc.) will follow in a later stadium.

*This abstract is an invited status report related to the International Classification of Vestibular Disorders and was not reviewed by the scientific committee.

L-2
NEUROGENESIS IN THE COCHLEAR NUCLEUS FOLLOWING ACOUSTIC TRAUMA

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Introduction: Our previous studies have suggested that surgical lesions of the rat cochlea induce cell proliferation in the cochlear nucleus (CN) that may be related to neurogenesis.
Objectives: The aim of the present study was to further investigate the nature of cell proliferation in the CN,

following our initial result showing that it significantly increased at 72 h following acoustic trauma.
Methods: Rats were subjected either to an acoustic trauma (unilateral 16 kHz pure tone, 115 dB for 1 h under anaesthesia) that has previously been shown to induce tinnitus; sham animals were treated in exactly the same way but without acoustic trauma. BrdU immunohistochemistry was used to measure cell proliferation; an antibody to interleukin-6 was used to investigate inflammatory responses; and triple immunolabelling for BrdU and Ki-67, BrdU and CD-11b, and BrdU and doublecortin (DCX), was used to investigate cell division, microglial activation and neurogenesis (respectively).
Results: There was an increase in BrdU+ve cells in the CN following acoustic trauma with the cell count peaking at 72 h. This is unlikely to be proliferating inflammatory cells as a result of an trauma-induced inflammatory response as the IL-6 expression level was comparable between the sham and exposed groups. Immunolabelling revealed the BrdU+ve cells to co-express Ki-67 and DCX, but not CD-11b. However, acoustic trauma was not found to affect the DCX level in the CN. The number of BrdU+ve cells in the exposed animals was comparable to that of control at 4 weeks post-trauma.
Conclusions: Acoustic trauma induced proliferation of non-inflammatory cells in the CN. Most of the BrdU+ve cells co-labelled with DCX, but there was no difference in DCX expression between sham and exposed animals. There was also no difference in newborn cell survival between the groups. Neurogenesis may occur in the CN under physiological conditions; however, acoustic trauma may not alter the level of neurogenesis, if indeed it does occur

Oral Presentations M. Inner Ear Morphology, Imaging

M-1
VISUALIZATION OF INNER EAR STRUCTURE USING OPTICAL COHERENCE TOMOGRAPHY (OCT)

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Introduction: Recent advancements of inner ear researches, especially regeneration and protection of inner ear cells, have provided the basis of new treatment strategies of inner ear disorders. However, it is still difficult to apply those new technologies to clinics due to lack of accurate diagnosis of inner ear disorders. Optical coherence tomography (OCT) is a non-destructive cross-sectional imaging modality which utilizes near infra-red light. OCT has been applied to clinic in the field of ophthalmology and other clinics. OCT is expected to visualize internal structures of inner ear and provide diagnostic information.
Methods and results: Using animals internal structures of inner ears were investigated. Part of Reissner's membrane, part of basal membrane, and the soft tissue of scala media were identified. Helicotrema of cochlea was also observed. Saccular and utricular maculae were identified. Part of endolymphatic sac and duct were also observed. For clinical application we fabricated a prototype fiber-type OCT system. The scanner tip was inserted into the cochlea via cochleostomy in human temporal bone specimen and the OCT images were successfully obtained. Clinical data will also be presented.
Conclusion: OCT is a promising tool for visualize the inner ear fine structures.

M-2
THICKNESS OF THE BONY OTIC CAPSULE: ETIOPATHOGENETIC PERSPECTIVES ON SUPERIOR CANAL DEHISCENCE SYNDROME

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Objectives: The etiology of superior canal dehiscence (SCD) is controversial. An embryological perspective suggests that SCD may occur through failure of postnatal bone formation over the superior semicircular canal (SC), whereas a developmental theory suggests that trauma or pressure from the overlying temporal lobe could gradually thin the SC. In this study, we infer the etiology of SCD by comparing thickness of the bony otic capsule in SCD and non-SCD participants.
Methods: Twelve SCD patients (13 SCD ears and 11 normal ears) and 34 age-matched controls (68 ears) were included. The control group was subdivided into an aerated group (49 ears) and a non-aerated group (19 ears), as defined by the presence of air cells above the SC. Computed tomography (CT) of the temporal bone was performed on all participants. The thickness of the SC and horizontal canal (HC) were compared between the unaffected side in SCD patients and the controls. SC and HC thickness were also compared between aerated vs. non-aerated ears within the control group.

Results: The SC was thinner on the unaffected side in the SCD group ($n = 11$, 0.41 ¡3/3 0.23 mm) than in the control group ($n = 68$, 0.64 ¡3/3 0.21 mm; $p = 0.002$). The HC was also thinner in the SCD group ($n = 24$, 0.58 ¡3/3 0.11 mm) than in the control (0.70 ¡3/3 0.08 mm; $p < 0.0001$). Within the control group, the SC was significantly thicker in the aerated group (0.72 ¡3/3 0.07 mm) than in the non-aerated group (0.70 ¡3/3 0.09; p = 0.046); however, no significant difference was observed for HC thickness (aerated group, n = 49, 0.73 ¡3/3 0.14 mm; non-aerated group, $n = 19$, 0.60 ¡3/3 0.23 mm; $p = 0.350$).
Conclusion: The bony otic capsule is significantly thinner in SCD patients than in age-matched controls. However, even within unaffected individuals, SCs lacking overlying air cells are also thinner than those with overlying air cells. These results suggest that both embryological and developmental factors affect the occurrence of SCD.

M-3
SODIUM AND POTASSIUM ION CHANNEL DISTRIBUTION IN VESTIBULAR AFFERENTS – AN UPDATE

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Background: We have been investigating Na channel distribution with various Pan-Nav and Nav isoform-specific antibodies in vestibular afferents to determine the isoforms present at the AIS region of different classes of vestibular afferents. The sodium channel isoform Nav1.6 is the canonical sodium channel at the node of Ranvier and the axon initial segment, but we have previously found that this isoform is not present at pure calyx afferents (Lysakowski et al., JNS, 2011; Lysakowski and Price, ARO, 2013).
Methods: Methods used were similar to those used in our recent publication (Lysakowski et al., JNS, 2011), with the exception that most tissue was vibratome-sectioned rather than frozen-sectioned and lower concentrations (0.05%) of Triton X-100 were used.
Results: Nav1.6 and Navβ4 present at the heminode of dimorphic vestibular afferents, but not at pure calyx afferent heminodes. The afferent class and location of the heminode were determined by co-labeling with calretinin (a calyx afferent marker) and nodal marker antibodies, such as ezrin, Caspr1, and myelin basic protein. We have continued our search for the Nav isoforms in calyx afferents and now have new results from other isoforms, including Nav 1.3, 1.8, and 1.9, in addition to various Pan-NaV and beta subunit antibodies. Pan-Nav and Nav1.9 label the apical end of the calyx more intensely than expected in most afferents, and the label continues down to the heminode. Based on heminodal markers, the majority of calyx afferent heminodes are located above and the majority of dimorphic afferent heminodes below the basement membrane.
Conclusions: We conclude that while Nav1.6 has a role as the major player at the vestibular dimorphic afferent heminodes, other isoforms, such as Nav1.3, 1.8, 1.9 and Navβ4, are more prominent in pure calyx afferents and/or have supporting roles in dimorphic afferents.
Funding: Supported by NIH R01-02058 (AL and JMG).

M-4
3-D IMAGES OF THE VESTIBULAR MEMBRANOUS LABYRINTH RECONSTRUCTED FROM MICRO-CT SCANS OF FIXED TEMPORAL BONES

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Introduction: The spatial organization of the complex interconnected ducts and sacs of the inner ear is still poorly understood and we sought to extend the use of our new method (Uzun et al. 2007) of using osmium to stain the membranous labyrinth to show this spatial organization.
Objective: The present study set out to use high resolution microCT scans of human and guinea pig temporal boes to visualize exactly how the membranous structures are organized, with a focus on ductus reuniens, the utriculo-saccular duct and membrana limitans.
Methods: The methods have been described in detail. Guinea pig or human temporal bones were fixed with 3–5% paraformaldehyde and glutaraldehyde or just paraformaldehyde and then en bloc stained in 2% osmium tetroxide which attaches to the membranes of the inner ear and in microCT allows visualization of the spatial organization of these structures and their 3-d spatial relationships. The specimens were scanned by an XRadia high resolution microCT scanner at very high resolution down to 2 microns to visualize these very thin membranes and their interconnections. Other stains do not show inner ear membranes as well. The data were reconstructed using Aviso or VGstudio Max.

Results: Movies of the reconstructions will show the spatial characteristics of ductus reuniens, the utriculosaccular duct and membrana limitans as well as the different character of the perilymphatic space around the utricle, compared to the space around the saccule. The membrane limitans supports the utricular macula and in one human specimen was attached to the footplate of the stapes.
Conclusion: The use of osmium stained specimens with very high resolution Xray microCT allowed us to visualize the spatial relationships of membranous structures vital to inner ear functioning.

Oral Presentations N. Vestibular Loss

N-1
VESTIBULAR NEURITIS OR VESTIBULOPATHY – ARE THE MEASUREMENTS WRONG OR THE DIAGNOSES?

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Since about 2008 measurements of all 5 vestibular receptors are possible even in private practice. In 25 patients with a clinical diagnosis of acute peripheral unilateral vestibular deficit (UVD) we performed the complete vestibular test battery within 3 days after onset of symptoms. Results of each test were categorized into 0 = no hypofunction, 1 = slight or borderline hypofunction, 2 = definite hypofunction and 3 = severe hypofunction or total loss. If all receptors innervated by one nerve were lesioned and the maximum difference in score was one point, the pattern was assigned to a definite vestibular neuritis (VN). With differences of more than one point, VN was assumed rather unlikely and assigned as possible VN. Lesions of only one receptor or a difference of 2 or more points were assumed to be an improbable VN but rather an intralabyrinthic lesion pattern (ILP) and one single receptor lesion of 2 points or more or differences of 3 points in equally innervated receptors were assigned to a definite ILP. We found only 2 patients (8%) with a definite VN and 2 with a possible VN. Six (24%) had an improbable VN/probable ILP and 15 (60%) a definite ILP. Our results indicate that most patients (84%) with a UVD do not have VN but a lesion pattern better explained by ILP. Another explanation would be that the test methods are in to many cases false negative or positive. We suggest changing the diagnosis of acute UVD to vestibulopathy instead of VN, because this term is not restricted to the nerve. If VN is rather unlikely, intratympanic dexamethasone could be a better therapy for vestibulopathy than the common oral therapy, which has to be scientifically proven.

N-2
ALTERATIONS OF SUPRASPINAL LOCOMOTOR CONTROL IN BILATERAL VESTIBULOPATHY

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Introduction: Bilateral vestibulopathy (BVP) induces characteristic changes in the gait pattern. The lack of vestibular information may impair rhythm and feedback control mechanisms of gait. In the present study, we investigated the supraspinal locomotor network in patients with BVP by [18F]-FDG-PET in comparison to healthy controls.
Methods: Eight patients with BVP due to bilateral vestibular neurectomy and 8 age-matched healthy controls were included in the study. All subjects underwent an intense neurophysiological and -ophthalmological testing for vestibular deficits. Gait was assessed by video analysis. Furthermore, all subjects performed a [18F]-FDG-PET paradigm during real locomotion at self-selected comfortable speed. Brain activation patterns during locomotion were calculated by SPM analysis and compared between groups and in correlation to individual gait performance.
Results: Mean gait velocity was not significantly different between the groups, but gait variability was increased in BVP. In [18F]-FDG-PET during locomotion, regional cerebral glucose metabolism was relatively decreased in the vestibular nuclei, cerebellar vermis, insula and multisensory vestibular cortex as well as anterior hippocampus in the BVP group as compared to the control group.
Conclusions: Bilateral vestibular deafferentation functionally alters supraspinal locomotor control by the following mechanisms: 1) a reduced activation of the cerebellar locomotor region, which may impair the rhythm control of gait; 2) a decreased cortical multisensory activation, which may disturb feedback mechanisms during gait; 3) a reduced hippocampal activation, which may alter spatial orientation performance.

Oral Presentations O. BPPV

O-1
POLYMORPHISMS IN THE VITAMIN D RECEPTOR GENE IN BENIGN PAROXYSMAL POSITIONAL VERTIGO

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Introduction: Previous study showed decreased serum vitamin D in patients with benign paroxysmal positional vertigo (BPPV). The effects of vitamin D are exerted by interaction with the vitamin D receptor (VDR) and may be influenced by polymorphism in the VDR gene.
Objectives: Since there is no information on VDR genotypes in relation to BPPV, we tried to study the relationship between VDR alleles and BPPV in a group of patients from Korea.
Methods: The genotypes for 5 SNPs of the VDR gene were determined by the digestion pattern of the amplified DNA fragments using the restriction enzyme Apa I, Taq I, Bsm I, Fok I, and Cdx 2 in 72 BPPV patients of dizziness clinic of Chungnam National University Hospital. Differences in the VDR genotype frequency were compared between BPPV patients and controls by significance test between percentages. Haplotype analysis was done using haplo.stats in R library, one of statistical package for genetics. The Asian population from Hapmap and 1000 genomes projects were used as control group.
Results: Of 5 polymorphisms evaluated, the genotype proportions of 3 BsmI, ApaI, and TaqI of patients were different from those of controls. In logistic regression analysis, the genotype "GG" frequency in BsmI SNP, genotype AC in ApaI SNP and genotype CT in TaqI were lower in patients than in controls ($p < 0.05$). Between 2 groups, the frequency of subjects carrying the CTGTG haplotype (for markers rs7975232-rs731236-rs1544410-rs2228570/rs10735810-rs11568820), was significantly higher in the patients group, (0.83%; OR = 38.1, 95% CI: 7.80–186.50, $p < 0.001$) which was associated with an increased risk of BPPV patients group (25.61%). In contrast, the frequency of the CTGTA (9.33% vs. 24.60%, OR = 0.19, 95% CI: 0.07–0.50, $p < 0.001$), ATGCG (4.63% vs. 18.5%, OR = 0.24, 95% CI: 0.09–0.65, $p < 0.001$), CCATA (0 % vs. 4.35%, $p < 0.001$), CTATA (0% vs. 3.91%, $p < 0.001$) haplotypes (for markers rs7975232-rs731236-rs1544410-rs2228570/rs10735810-rs11568820) were significantly lower in the patient group than in the controls, suggesting a significant protective effect against BPPV.
Conclusion: In this study, genetic variation in the VDR for Apa I, Taq I, and Bsm I was associated with BPPV. This genetic risk factor, if confirmed, could be one among the risk factors identified for BPPV.

O-2
PERSISTENT GEOTROPIC DIRECTION-CHANGING POSITIONAL NYSTAGMUS – THE LIGHT CUPULA

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Introduction: Sometimes, we encountered geotropic positional nystagmus which is persistent, does not show latency, and sustains the intensity over repetitive examinations. Recently, persistent geotropic directional chaniging positional nystagmus (DCPN) has been reported, which is thought to be due to the light cupula of horizontal canal.
Objective: To characterize the clinical features and typical positional nystagmus in patients with persistent geotropic DCPN, and address the possible pathophysiology of the disease.
Methods: Twenty one patients (M:F = 6:15; 35 $\sim$ 75 yr) with persistent geotropic DCPN were included.Positional nystagmus was observed and analyzed using videonystagmography. 'Bow and lean test' and 'supine head roll test' were performed, and the 'null point' in which the nystagmus ceases was sought by turning the head to the right or left in the supine position in all patients. The affected side was determined by considering the side of the null point and the direction and intensity of the positional nystagmus.
Results: All of 21 patients showed persistent geotropic DCPN without latency. Of 21 patients, the null point was identified in 19 patients (90%). On supine head roll test, the intensity of nystagmus was stronger on one side in14 patients (67%) in which 13 were on the right and 1 was on the left. Both bowing and leaning nystagmus were shown in 17 patients in which 16 exhibited bowing and leaning nystagmus with opposite

direction. Overall, the affected side could be identified in 19 patients (90%). In most patients, the symptom and sign improved in a week or less without any specific treatment.

Conclusions: The patients with light cupula show persistent geotropic DCPN without latency. Affected side(s) can be determined by the direction and intensity of the characteristic positional nystagmus, and the side of the null point. The pathophysiology and treatment of light cupula still need further investigation.

O-3

CAUSES AND CHARACTERISTICS OF HORIZONTAL POSITIONAL NYSTAGMUS

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Introduction: Direction changing horizontal positional nystagmus is commonly observed in the context of horizontal canalithiasis, cupulolithiasis and central vestibular disorders.

Objectives: Our aim was to describe the spatio-temporal characteristics of 60 consecutive patients with symptomatic horizontal positional nystagmus.

Materials and Methods: All patients underwent clinical examination, vestibular testing and positional testing on the Epley Omniax Rotator with left and right ears down. Monocular video data was collected at 30 Hz and analysed offline. Nystagmus Slow Phase Velocity (SPV) was plotted as a function of time.

Results: Thirty-one subjects diagnosed with horizontal canalithiasis showed bursts of horizontal geotropic nystagmus with the affected ear down (onset: 0.8 $\pm$ 1 s range 0–4.9 s, duration: 11.7–47.9 s, peak SPV 79 $\pm$ 67°/s). The SPV peaked at 5–20 s and dropped to 1.8% of the peak value by 40 s. Nine subjects diagnosed with horizontal cupulolithiasis showed persistent apogeotropic horizontal nystagmus (onset: 0.7 $\pm$ 1.4 s range: 0–4.3 s, peak SPV 54.21 $\pm$ 31.82°/s and 26.62 $\pm$ 12.22°/s with unaffected and affected ears down). At 40 seconds, nystagmus SPV had decayed to only 81% and 65% of the peak for unaffected and affected ear down positions. Horizontal direction changing nystagmus was observed in 20 further subjects. Thirteen subjects were diagnosed with Vestibular Migraine; in these patients persistent geotropic or apogeotropic nystagmus was recorded. Unlike the subjects with BPV, migraineurs had symmetrical peak SPVs (Left: 13.0 $\pm$ 8.1°/s and Right 14.6 $\pm$ 10.9°/s). At 40 seconds from onset, average SPV was 61% of the peak value. Two subjects with Meniere's Disease had persistant apogeotropic nystagmus. Of the five remaining patients, one was found to have a vestibular schwannoma; two subjects had vestibular function tests indicative of unilateral peripheral vestibulopathies, one subject had otosclerosis and one subject had bilateral vestibular failure.

Conclusion: Symptomatic direction changing horizontal positional nystagmus can be found in various central and peripheral vestibulopathies. Plotting the SPV profile of horizontal positional nystagmus can be useful in the separation of canalithiasis, cupulolithiasis and diverse central and peripheral vestibulopathies.

O-4

A MULTICENTER RANDOMIZED DOUBLE-BLIND STUDY ON COMPARISON OF THE EPLEY, SEMONT, AND SHAM MANEUVERS FOR THE TREATMENT OF POSTERIOR CANAL BENIGN PAROXYSMAL POSITIONAL VERTIGO

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Introduction: A canalith repositioning procedure, known as the Epley maneuver, has been established as a recommended treatment for posterior canal BPPV. However, only a few studies to date have compared the effectiveness of the Epley and Semont maneuvers in patients with posterior canal BPPV.

Objectives: To evaluate the short-term efficacy of Epley, Semont, and sham maneuvers for resolving posterior canal benign paroxysmal positional vertigo (BPPV) in a prospective multicenter randomized double-blind controlled study.

Methods: Subjects were randomly divided into three groups and treated with the Epley (36 patients), Semont (32 patients), or sham (Epley maneuver for the unaffected side, 31 patients) maneuvers. The maneuver was repeated twice in total if there was still positional vertigo or nystagmus at day 0, and the presence of nystagmus and vertigo on positional testing were evaluated immediately, 1 day, and 1 week after treatment.

Results: After the first maneuver, the Epley group showed a significantly higher resolution rate of po-

sitional nystagmus than the Semont or sham groups (63.9%, 37.5%, and 38.7%, respectively). After the second maneuver, the resolution rate (83.3%) of positional nystagmus in the Epley group was significantly higher than that (51.6%) of the sham group. At 1 day and 1 week after treatment, the resolution rate of positional nystagmus in the Epley group was significantly higher than those of the Semont and sham groups. Similar results were seen for the resolution of positional vertigo.

Conclusions: The Epley maneuver showed persistent resolution rates of positional vertigo and nystagmus without a fatigue phenomenon. The Epley maneuver was significantly more effective per maneuver than the Semont or sham maneuvers for the short-term treatment of posterior canal BPPV. The Semont group showed a higher success rate than the sham group, but the Semont maneuver was not significantly superior to the sham maneuver.

O-5
EXPERIMENTAL STUDY ON THE ETIOLOGY OF BPPV-VIBRATION APPLIED TO THE LABYRINTHS WITH AND WITHOUT VESTIBULAR DYSFUNCTION-

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Introduction: BPPV sometimes develops after mechanical stimulation to the temporal bone, such as ear or dental surgery and physical exercise using a vibration device. It is suspected that the vibration to the ear is one of the causes of BPPV. Moreover, inner ear diseases or aging can also be a predisposed factor of BPPV. We investigated if mechanical vibration to the ear could induce otoconial dislodge. The isolated labyrinthine models of the bullfrog with and without vestibular dysfunction models were used.

Method: The vestibular dysfunction was created by injecting gentamicin into the perilymphatic space. In experiment 1, vibration was applied to the isolated labyrinthine models by using a surgical drill for 10 minutes. The time required for otoconial dislodge was measured. In experiment 2, vibration was applied to the models by using a rotary shaker. The otoconial disloged was checked after 30 minutes.

Result: Exp.1: in the normal models ($n = 21$), average time for otoconial dislodge was 7 minutes and 35.7 seconds. In the vestibular dysfunction models ($n = 14$), it was 2 minutes and 11.2 seconds. Exp.2: in the normal models ($n = 16$), the otoconial mass was detached in none of the labyrinth preparations. In the vestibular dysfunction models ($n = 15$), the otoconial mass was detached in 6 out of 15 labyrinth preparations. In both experiments, the sensory hairs are found to be reduced in the vestibular dysfunction models.

Discussion: The Exp. 1 demonstrated that the utricular otoconia were dislodged into the semicircular canal by vibration. In the vestibular dysfunction models, the time to dislodge was significantly shorter than normal models ($P = 0.0005$). The stimulus of the Exp. 2 was weaker than the Exp.1. None of the otoconia disloged in the normal models, but the otoconia disloged in 40% of the vestibular dysfunction models. In the vestibular dysfunction models, the utricular macula sustained morphological damage. Other insults, such as ischemia, endolymphatic hydrops, or aging, potentially change the utricular macula, thus leading to easy dislodge of the otoconia from the macula.

O-6
DCRM (DYNAMIC CANALITHS REPOSITIONING MANEUVER): A NEW MANEUVER TO TREAT BOTH PC AND LC-BPPV IN THE SAME SESSION. MARIGNANE-FRANCE

Richard-Vitton, Thomas
Clinique

Introduction: Canaliths involving both posterior and horizontal canals could be under-reported. Benign Paroxysmal Positional Vertigo (BPPV) of two canals from the same side actually represents about (25%) of the PC-BPPV and often needs several therapeutic sessions to be cured.

Objectives: The aim of this study is to propose a new therapeutic maneuver using a mechanical assistance and permitting to treat both canals during the same session.

Methods: This prospective study selected 120 subjects from 1100 patients who presented with some positional vertigo. These dizzy patients, who presented with positional nystagmus typical from both posterior and horizontal canalithiasis, were included: seventy two women and 48 men, ranged from 15 to 96 years old with an average of 56. Their history began from 2 days to 6 months ago, with an average of 45 days, before the therapeutic session. The TRV armchair allows rotation of patients wearing infrared video goggles, with both eyes hidden, in all semi-circular planes for 360° or more. An abutment with shocks absorber permits to

briskly smoothly stop the rotation of the horizontal rotation (pitch plane equivalent) of the chair 45° under the horizontal plane. The analysis of the positional nystagmus in the total darkness permits to have a better detection of the horizontal component that is very sensitive to the fixation. When the horizontal component is apogeotropic, the maneuver consists to make 6 series of 5 smooth shocks on the shocks absorbers placing prior the involved ear toward the floor, nose turned at 90° from the roof, with a position of the head 45° under the horizontal plane. Each series is made with a 45° more rotation toward the safe side to make the sixth position 45° nose down the floor to the safe side. It will permit a 225° rotation that will place progressively the lateral canal from the cuppula toward the floor to stoma of the canal toward the floor in six steps. If the horizontal component is geotropic, then the first step is beginning 45° toward the involved side, like a Dix Hallpike maneuver and there will be 5 steps in place of 6. These series of shocks permit to give to the very little particles, that are to light to progress thanks to the gravity, some hypergravity that helps its to move toward the exit of the canal.

The patient was considered as cured if there was an absence of symptoms or findings 7 days later. In case of residual dizziness, repeat therapeutic sessions were performed or patients benefit further vestibular examination and sometime MRI.

Results: One hundred five of the 120 patients were totally freed of symptoms with one session. The horizontal component of the mixt involvement was apogeotropic in 85 patients (70.8%). The apogeotropic form didn't need more session than geotropic form. The dynamic therapeutic maneuvers seem to improve the therapeutics' success of apogeotropic horizontal BPPV and permit to manage promptly combined BPPV.

Conclusion: The misdiagnosis of the horizontal involvement of a mixt BPPV could produce some persistent unsteadiness or drunkenness sensations after a therapeutic maneuver for PC-BPPV. Often considered as a post-BPPV otolithic syndrome, this could be a residual horizontal canalithiasis linked to a very few otoliths in the lateral canal and could be successfully treated with this new maneuver. This technic permits to improve the management of canalithiasis, especially that involving the horizontal canals.

O-7
POLYSOMNOGRAPHY DETECTS BENIGN PAROXYSMAL POSITIONAL VERTIGO

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Background: Benign paroxysmal positional vertigo (BPPV) is one of the most common causes of dizziness and is well known for being elicited with changes of head position in bed. Nevertheless, video-polysomnography (PSG) has not yet been considered as a tool to detect BPPV.

Case report: A 59-year-old woman was admitted to our emergency department because of repeated attacks of rotational vertigo, triggered by head movements while in bed. Barbecue maneuver to the left revealed delayed apogeotropic horizontal nystagmus. Barbecue maneuver to the right caused even stronger persisting apogeotropic nystagmus, establishing the diagnosis of left lateral canal cupulolithiasis. Since the attacks were often precipitated by changes of body position at night and thus interfering with sleep quality, PSG including electrooculography (EOG) was performed. While the patient was awake during the night, six episodes of apogeotropic positional nystagmus were observed with change of body position. Several episodes with changes of head position but unaltered body position also triggered positional nystagmus. The patient subsequently underwent several therapeutic repositioning maneuvers on our 3D turntable, which relieved her symptoms.

Conclusions: This case provides the first evidence that PSG can detect BPPV in the sleep laboratory. The typical EOG pattern of positional nystagmus should therefore be brought to the attention of sleep specialists, because this cumbersome condition is highly prevalent yet often overlooked, while the diagnosis is easy and treatment is safe, inexpensive and highly effective.

O-8
OTOLITH FUNCTION IN PATIENTS WITH RECURRENT BENIGN PAROXYSMAL POSITIONAL VERTIGO EVALUATED BY VEMP

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Introduction: Benign paroxysmal positional vertigo (BPPV) is one of the most common causes of vertigo caused by the detachment of otoconia in otolith organs floating in the semicircular canals. BPPV may be recurrent, but the cause and risk factors of recurrence are still not clear.
Objective: To explore the roles of otolith functions in the recurrence of benign paroxysmal positional vertigo (BPPV) by the detection of cervical vestibular evoked myogenic potential (cVEMP) and ocular vestibular evoked myogenic potential(oVEMP).
Methods: Tweenty-six recurrent posterior canal BPPV (PC-BPPV) patients and 60 non-recurrent PC-BPPV patients who referred to vertigo clinic of our hospital between November 2012 and April 2013 were enrolled in this study. All patients underwent cVEMP and oVEMP tests using 500 Hz tone-burst stimuli. cVEMP and oVEMP tests were also performed on 40 age- and gender-matched normal subjects. All the data underwent statistical analysis by SPSS 17.0.
Results: No significant differences were found in gender, age, bilateral rate between 26 recurrent patients and 60 non-recurrent patients ($P > 0.05$). Abnormal cVEMP responses were detected in 10 of 26 (38.46%) subjects in the recurrent BPPV group and abnormal oVMEP responses were detected in 16 of 26 (61.54%) subjects in the recurrent BPPV group.While in the non-recurrent group, abnormal rates of cVEMP and oVMEP were 21.67% and 31.67% respectively. Abnormal rate of oVMEP in recurrent BPPV group was significantly higher than that in non-recurrent group ($f\acute{O}2 = 6.707$, $P < 0.01$). No significant difference of abnormal rate of cVEMP was found between recurrent BPPV group and non-recurrent group ($f\acute{O}2 = 2.612$, $P > 0.05$). In 86 BPPV patients, the abnormal rates of cVEMP and oVEMP were 6.74%, and 40.70% respectively, while in normal control group, the abnormal rates of cVEMP and oVEMP were 10.00% and 12.50% respectively. Significant difference could be found in abnormal rate of cVEMP and oVEMP between BPPV patients and normal subjects ($f\acute{O}2 = 4.546$, $P < 0.05$; $f\acute{O}2 = 10.018$, $P < 0.01$).
Conclusion: The abnormal rate of oVEMP in recurrent BPPV patients is significantly higher than that of non-recurrent patients, which indicated that dysfunction of utricle might play a role in recurrence of BPPV. Our data showed that cVEMP or oVEMP abnormalities in the BPPV group were significantly higher than those in the normal control group, which implyed that VEMP abnormality might be one of cause for BPPV occurrence.

Oral Presentations P. Whiplash Injuries, Neck Disorders

P-1
ARE NAUSEA AND VISUAL VESTIBULAR MISMATCH SUGGESTIVE OF FAILURE TO COMPENSATE BECAUSE OF BILATERAL PATHOLOGY?

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Introduction: We suspect that bilateral vestibular pathology may be more common than previously thought. Traditional vestibular testing (the caloric test) measures one parameter (slow phase velocity) so that an abnormal caloric result will imply a “normal side” and a “pathological side”. The patient is told that any permanent damage will be compensated for, because it is assumed that there is a normal template which must exist for the damaged side to be compared to (Rutka 1995). Otolithic tests such as VEMP testing, enable us to measure more than one parameter of dysfunction. Studies by us and others suggest that bilateral pathology may be more common than previously suspected. This should raise concerns, as it has been stated that if the labyrinth on the presumed ‘normal’ side is also affected or diseased this could possibly disrupt the “normally expected” compensation process (Halmagyi and Curthoys, 1999). The same authors stated in 2013 that “the functional status of the ‘healthy’ vestibular labyrinth is of crucial importance in determining the final outcome of the compensation process”.
Objectives: We classify patients who have been symptomatic for a year as “having failed to compensate”. Quite often they voice complaints of the symptom set of “visual vestibular mismatch” (VVM), or “visually

induced dizziness". This is a validated symptom set suggesting otolithic pathology. Many patients have bilateral abnormalities on VEMP testing. We regard the development of VVM as being suggestive of ineffective compensation for vestibular pathology. The symptom set of VVM and the complaint of nausea results from an inappropriate dependence on visual cues for balance maintenance. We hypothesize that the presence of bilateral pathology is a risk factor for effective compensation, as these patients no longer have a healthy side to use. In our experience, some patients are left with subtle signs of vestibular pathology (imbalance), and some with autonomic symptoms of their deficit (e.g. nausea, VVM). We feel that the persistence of these autonomic symptoms suggests a less than effective compensation and the rate of VVM would be higher in our bilateral patients than in those with unilateral pathology. We also hypothesize that presenting signs of nausea would be higher in bilateral patients.
Methods: A retrospective chart review of patients referred to our neuro-otology unit was carried out. All patients underwent a full battery of tests and also completed our visual vestibular mismatch questionnaire, which we have validated as a technique of documenting vestibular disease. Prior to assessment, patients were grouped into "VVM negatives" and VVM positives" based on their answers to 5 questions. In a corollary experiment, patients were grouped into two groups in a separate fashion. Patients were classified with either a primary complaint of imbalance or a primary complaint of nausea.
Results: We will be discussing the results of these two experiments, to determine if the persistence of nausea or the development of the symptom set known as VVM, was correlated to the presence of bilateral pathology.
Conclusions: We will be discussing the hypothesis that nausea and VVM are signposts of poorly compensated vestibular disease, related to bilateral pathology, which prevents effective compensation.

Oral Presentations Q. Hydrops-Meniere

Q-1
REGULATORY VARIANTS IN THE NFKB1 GENE INFLUENCE THE AUDITORY PROGNOSIS IN UNILATERAL MENIERE'S DISEASE*

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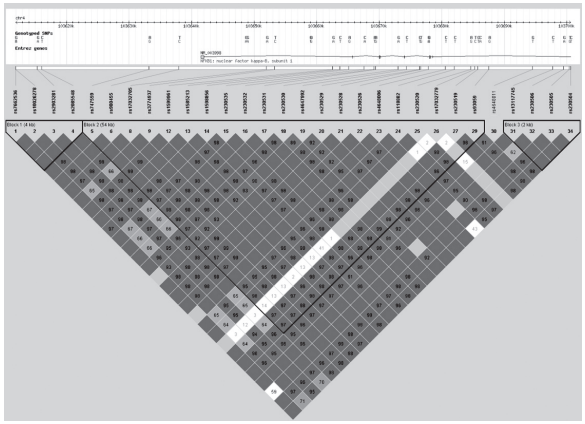
Introduction: Patients with Meniere's disease (MD) have an elevated prevalence of several autoimmune diseases (rheumatoid arthritis, systemic lupus erythematosus, ankylosing spondylitis and psoriasis), suggesting a shared autoimmune background. Functional variants of several genes involved in the NF-κB pathway have been associated with two or more immune-mediated diseases and allelic variations in the TLR10 gene may influence bilateral involvement and clinical course in MD.
Methods: We have genotyped 716 cases of MD and 1628 controls by using the ImmunoChip, a high-density genotyping array containing 186 autoimmune loci, to explore the association of immune system related-loci with sporadic MD. We selected allelic variants in the NF-kB pathway (REL, TNFAIP3, REL, NF-κB 1 and TNIP1 genes) for further analyses to evaluate the impact of these SNPs in the clinical outcome of MD in our cohort by Kaplan-Meier curves and log-rank test. Hearing loss progression was estimated as the mean time to reach hearing stage 3 (>40 dB HL). Functional evaluation of regulatory variants was perfomed in silico by using the bioinformatics tools HaploReg, seeQTL and RegulomeDB.
Results: We identified two potential regulatory variants in the NFKB1 gene (rs3774937, T>C) and rs464

8011, G>T) that were associated with a faster hearing loss progression in patients with unilateral MD (log-rank test for each allele, $p = 0.001$). The allelic frequencies of rs3774937-C and rs4648011-G in patients with unilateral MD were 0.31 and 0.37, respectively. These variants showed a high linkage disequilibrium (r2 $= 0.67$, D' $= -0.95$), despite they were in different haploblocks (Fig. 1). The haplotype CG has a frequency of 32% in patients and carriers of this haplotype reached 40 dB 30 months earlier than the rest of the haplotypes ($p = 0.006$). Interestingly, these variants did not influence hearing in bilateral MD. Bioinformatics tools predicted that these variants changed the interaction with the following transcription factors: DMRT1, LUN-1, YY1 for rs3774937 and Foxc1, Zfx for rs4648011. NF-kB pathway regulates proinflammatory cytokine production and cell survival and it mediates the duration of the inflammatory response and these variants probably influence gene expression and inflammation in MD. However, multiple interactions are possible in the NF-kB network and the molecular mechanism remains unknown.



Conclusions: Regulatory variants in the NFKB1 can be used as genetic markers to predict a worse hearing outcome in patients with unilateral MD.

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*This abstract is an invited status report related to the International Classification of Vestibular Disorders and was not reviewed by the scientific committee.

Q-2
DURATION OF MENIERE'S DISEASE IS NOT RELATED WITH ECOG AND VESTIBULAR LOSS EXCEPT HEARING OUTCOMES

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Backgrounds: In Meniere's disease (MD), the natural courses regarding the degree of vestibular and hearing loss is hard to predict. If it is possible, it would be very helpful to better counsel the patients for functional disability such as vertigo severity and auditory symptoms.
Objectives: The aims of this study were to evaluate degree of vestibular and hearing loss according to the disease duration. In addition, the correlation between these objective measures and the subjective functional disability was assessed.
Methods: In this retrospective study, 47 patients with unilateral definite MD were enrolled. The pure tone audiogram (PTA), ECoG and caloric response were measured at initial visit. Frequency of vertigo (FV, true vertigo lasting over 20 minutes), DHI and MSQ were also evaluated for subjective measures. Disease duration was the period from the first attack of true vertigo to the initial visit.
Results: The patients were divided into three subgroups according to the disease duration: Group 1 (less than 12 months of duration, $n = 27$), group 2 (between 12 months to 60 months, $n = 12$) and group 3 (above 60 months, $n = 8$). DHI, MSQ scores and FV were not significantly different between three groups ($p > 0.05$). Regarding hearing stage by AAO-HNS criteria, in group 3, the incidence of stage 3 and 4 was higher than other groups ($p < 0.05$). Incidence of canal paresis by the caloric response were 37% (7/19), 67% (6/9) and 33% (2/6) respectively ($p > 0.05$). Incidence of abnormal SP/AP ratio (> 0.34) were not different in each group: 72% (18/25), 89% (8/9) and 86% (6/7) respectively, but it could predict the hearing outcomes (poorer outcomes).
Conclusions: Duration of disease in MD was not related with frequency of dizzy attack and functional disability. However, hearing loss was getting worse with disease duration. Also, high SP/AP ratio on ECoG was proved to be related with poorer hearing outcomes.

Q-3
LONG-TERM EFFICACY OF ENDOLYMPHATIC SAC-MASTOID SHUNT SURGERY FOR INTRACTABLE MENIERE DISEASE OF DIFFERENT STAGES

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Introduction: Although the effectiveness of endolymphatic sac surgery in the treatment of patients with Meniere's disease is still open for debate, endolymphatic sac surgery is the most frequently employed conservative surgical approach for patients with MD when hearing is still serviceable. Endolymphatic sac decompression and endolymphatic sac-mastoid shunt surgery are two common types of endolymphatic sac surgery. The study of the effectiveness of endolymphatic sac-mastoid shunt surgery for intractable meniere disease of different stages is scarce.
Objective: To investigate the long-term effect of endolymphatic sac-mastoid shunt surgery for intractable meniere disease of different stages according to hearing level.
Methods: Data from 240 patients diagnosed with unilateral MD strictly meeting the Hearing and Equilibrium criteria issued by American Academy of Otolaryngology-Head and Neck Surgery Committee (1995) from January 1983 to January 2012 were analyzed in this study. Endolymphatic sac-mastoid shunt surgery was performed in pathological ear for each patient. The evaluation of therapy followed the guidelines for diagnosis and evaluation of therapy in MD(1995).Vertigo control and auditory function were measured in two-years follow-up.
Results: According to the preoperative staging of hearing, among these 240 patients, there were 12 cases in stage¢ñ (with an average hearing threshold $<$ 25 dB), 130 cases in stage¢ò (with an average hearing threshold of 25 $\sim$ 40 dB), 85 in stage ¢ó (41 $\sim$ 70 dB) and 13 cases in stage ¢ô(with an average hearing threshold $>$ 70 dB). Control rate of vertigo was 77.9%(187/240) in two-years follow-up,with total control 49.2% (118/240)and substantial control 28.7%(69/240). The hearing was improved in 25.0% (60/240)cases, no change in 59.2% (142/240)of cases, worse in 15.8%(38/240) cases. According to different stages, vertigo control rate was 83.3% (10/12)in stage¢ñ, 82.3% (107/130)in stage ¢ò, 75.3%(64/85) in stage ¢ó and 46.2%(6/13) in stage ¢ô. Vertigo control rate of stage ¢ôpatients was significantly lower than that of other stage patients ($P < 0.05$), while vertigo control rate of stage I, II, III patients had no significant difference with each other ($P > 0.05$).
Conclusion: Endolymphatic sac-mastoid shunt operation is an effective method in the treatment of intractable Meniere's disease of stage ¢ñto ¢ó. The effect was poor in stage ¢ô patients.

Q-4
SEEING IS BELIEVING? MRI INNER EAR IMAGING FOR MENIERE'S DISEASE CORRELATED WITH TONE BURST ELECTROCOCHLEOGRAPHY

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Introduction: In the twenty-first century Meniere's disease is almost unique as being a relatively common condition whose "certain" diagnosis is based on symptoms supported by a post-mortem. The current AAO-HNS Guidelines for the diagnosis and evaluation of therapy in Meniere's disease do not recognise the validity let alone the existence of any in vivo test that can confirm endolymphatic hydrops. The claim that a click stimulus tone burst response from transtympanic electrocochleography (EcochG) is a reliable test to indicate endolymphatic hydrops has been disproved, which led to disillusionment and abandonment of the test in the United States. Subsequently Gibson, in numerous publications, has shown that a tone burst stimulus dramatically increases the reliability and sensitivity of the test. In his department a combination of responses (based on longstanding published voltage criteria) to a combination 0.5 kHz, 1 kHz and 2 kHz tone bursts achieves an 88% sensitivity for diagnosing hydrops based on symptom score indicating the likelihood of Meniere's disease. In our department (unpublished) a combination of click (SP/AP ratio of 0.5), or 0.5 kHz, 1 Kz or 2 kHz tone burst responses gave a sensitivity of 80%. In 2007 Nakashima et al used intratympanic gadolinium to produce clear images of endolympahtic hydrops in Meniere's disease inner ear using a 3 Tesla scanner. The dose and timing of gadolinium administration and the safety have been established and a hydrops grading system proposed. There has been intense interest in this technique, raising hopes that visusalisation of the hydrops on a scan might be the gold standard test for

Meniere's disease and the basis of comparison for any competing test. Following a small pilot study in our department it was decided to test a large number of subjects with different inner ear symptoms to compare the sensitivity of MRI inner ear imaging with tone burst EcochG.

Methods: Ninety-three subjects have been tested, comprising (1) 48 with likely Meniere's disease (2) 17 with sudden unilateral hearing loss (3) 26 with unilateral hearing loss and (4) 2 with unilateral tinnitus. Twenty-four hours prior to scanning each had a pure tone audiogram and a trans-tympanic tone burst and click stimulus EcochG test in the affected ear, followed by instillation of dilute (1/8) 'Multihance' gadolinium in the ear over 30 minutes. Subjects with recurrent vertigo were given a definite, probable or possible likelihood for having Meniere's disease. The EcochG criteria for hydrops were as per Gibson. The MRI scans were reported by two radiologists as none, mild or significant hydrops in the cochlea and in the vestibule.

Results: In 9 out of 93 patients (10%) gadolinium entry was insufficient to assess for hydrops. 27 out of 93 (29%) had had suboptimal Gad entry and 57 (61%) had good Gad entry. Of 25 subjects with definite Meniere's disease 20 (80%) had "positive" EcochGs and 9 (36%) had positive MRIs, so 21 (84%) had a positive EcochG and/or positive MRI.

Conclusion: In patients with a symptomatic diagnosis of Meniere's disease tone burst EcochG has an at least 80% sensitivity for implying hydrops compared with 36% visualisation on MRI. This is due to the variability of gadolinium entry and that in visually assessing a relatively coarse image inside such a small structure a very significant degree of hydrops must be present.

Q-5
JOINT CONSENSUS DIAGNOSTIC CRITERIA FOR MÉNIÈRE'S DISEASE*

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Introduction: Different prior efforts have sought to define a diagnosis for Ménière's disease (MD). The Japanese Society for Equilibrium Research proposed clinical criteria for diagnosis of MD in 1974. The American Academy of Otolaryngology-Head and Neck Surgery (AAO-HNS) developed the guidelines for the diagnosis and therapy in MD originally in 1972 and revised them in 1985 and 1995. Despite the great contribution of these guidelines to clinical research evaluating the effectiveness of medical and surgical treatments for MD, no biological marker for diagnosis or prognosis has been identified for MD, but an evolving understanding of MD and vestibular migraine make it essential to update these criteria to match current best scientific evidence.

Objectives: To develop international consensus diagnostic criteria for MD as part of the ongoing efforts of the Classification Committee of the Bárány Society (CCBS), in conjunction with the Equilibrium Committee of the AAO-HNS, the Vertigo Committee of the European Academy of Otology and Neurotology (EAONO), and the Japan Society for Equilibrium Research.

Methods: This work forms part of an ongoing multi-year project to develop an International Classification of Vestibular Disorders (ICVD), which uses a structured process for developing international consensus definitions for vestibular symptoms, syndromes, disorders, and diseases. This process, overseen by the CCBS, is based on expert, multi-disciplinary committees with international representation developing diagnostic criteria for subsequent comment and refinement prior to publication. These criteria are based on a critical appraisal of current best scientific evidence. When appropriate, collaborations with other key societies are established for joint development of criteria, as in this case. All definitions are supported by notes, comments, and written discussion according to a template established by the CCBS for ICVD consensus criteria.

Results: MD criteria were developed iteratively over a four-year period through discussion, presentation, and refinement. Two diagnostic categories were considered: definite and probable MD. The primary adjustments to prior criteria were to clarify the nature of auditory symptoms and signs present for definite MD. Definite MD is defined by (A) two or more spontaneous episodes of vertigo, each lasting 20 minutes to 12 hours; (B) audiometrically documented low- to medium-frequency sensorineural hearing loss in the affected ear on at least one occasion before, during or after one of the episodes of vertigo; (C) fluctuating aural symptoms (hearing, tinnitus or fullness) in the affected ear and (D) other causes excluded. Probable MD is defined by (A) two or more episodes of vertigo or dizziness, each lasting 20 minutes to 12 hours; (B) fluctu-

ating aural symptoms (hearing, tinnitus or fullness) in the affected ear; (C)other causes excluded.
Conclusions: Recently-defined disorders that may mimic MD (e.g., vestibular migraine, superior canal dehiscence syndrome, audio-vestibular transient ischemic attack) have increased the need for refinements and clarifications to well-established MD definitions. In addition, clinical variability combined with genetic heterogeneity underlying MD makes well-defined phenotyping essential to define genotype-phenotype correlation in patients with a history of episodic vertigo and hearing loss. These updated consensus diagnostic criteria for MD will support the conduct of high-quality, multicenter clinical research studies through correct identification and recruitment of more homogeneous cohorts of MD patients.
Fundings: The Barany Society, the EAONO and Neuro+ have funded the working meetings to develop a consensus definition for MD.

*This abstract is an invited status report related to the International Classification of Vestibular Disorders and was not reviewed by the scientific committee.

Q-6
OVAL WINDOW APPLICATION OF GENTAMICIN IN PATIENTS WITH MENIERE'S DISEASE A VESTIBULAR ABLATION SPARING THE COCHLEA, WHEN TRANSTYMPANIC TREATMENTS FAIL*

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The present approach was made to develop a minor surgical procedure to ablate vestibular function whilst sparing the cochlea in patients with incapacitating Meniere's disease that failed to respond to transtympanic gentamicin. Preferably to those who still had some useful residual hearing.
The patients have been studied for at least six months and up to 10 years from the procedure No control group was used. We report 11 patients patients with incapacitating Meniere's disease not responding to conservative or transtympanic gentamicin treatment. Patients were operated on with tympanotomy with shielding of round window and placement of gelfoam soaked with gentamicin in the oval window niche. They were then followed 2–5 year postoperatively and a final check up by means of registered data was made at the end of 2013. In nine out of ten patients, vestibular function was ablated and vertigo attacks disrupted without further deterioration on hearing. The last patient, who before surgery did have PTA $>$90 dB, did not respond to the procedure and underwent a labyrinthectomy, which did not cure his symptoms, either. He ended up with having postural phobic vertigo as a complementary diagnosis, which was than treated.
Conclusion: Although a small materiel, this procedure of 'specific oval window gentamicin application' offers a possible option to ablate vestibular function, while saving hearing in those patients that do not respond to transtympanic gentamicin.

*This abstract is an invited status report related to the International Classification of Vestibular Disorders and was not reviewed by the scientific committee.

Q-7
MÉNIÈRE'S DISEASE – A REAPPRAISAL SUPPORTED BY A VARIABLE LATENCY OF SYMPTOMS AND THE MRI VISUALIZATION OF ENDOLYMPHATIC HYDROPS

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The aim was to evaluate the onset of vertigo, hearing loss and tinnitus in Ménière's disease and the associated endolymphatic hydrops (EH) of the inner ear. Disease specific symptoms were reviewed among referred patients in a tertiary referral hospital in Finland and in members of a Finish Ménière Association in. The MRI of a separate group of patients was undertaken in a tertiary referral centre in Japan. Multicentre evaluation of three patient groups. 350 patients were reviewed in the referral hospital along with 740 members of the Ménière Association. MRI was undertaken in 224 patients. Latency and symptom development in Ménière's disease, and the appearance of endolymphatic hydrops of the inner ear in monosymptomatic patients and in Ménière's disease. The mean age of the first symptom was 43.8 years, with 10% of the patients being older than 65 years. The time

delay between hearing loss and vertigo was more than 5 years in 20% of members and of patients. Gadolinium contrasted MRI demonstrated EH in 90% of patients with Ménière's disease, in which 75% was bilateral among patients with unilateral symptoms. In mono-symptomatic patients with vertigo, tinnitus or hearing loss; EH was demonstrated in 55–90% of the patients either in the cochlea and/or the vestibulum of the symptomatic ear. Ménière's disease shows often bilateral EH and comprises a continuum from a mono-symptomatic disease to the typical symptom complex of the disease. We suggest that a 3T-MRI measurement should be carried out in patients with sensory-neural hearing loss, vertigo, and tinnitus, 4 hours after the intravenous injection of a gadolinium contrast agent to verify the inner ear pathology. This may lead to a better management of the condition.

Q-8
IDENTIFICATION OF A NOVEL MUTATIONS IN FAM136A AND DTNA GENES IN AUTOSOMAL DOMINANT FAMILIAL MENIERE'S DISEASE*

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Introduction: Meniere's disease (MD) is a complex disorder characterized by sensorineural hearing loss, episodic vertigo and tinnitus. Familial MD is found in 8-10% of cases in European population. Although genetic heterogeneity is observed, most of the families have an autosomal dominant (AD) pattern of inheritance with incomplete penetrance. We have used whole-exome sequencing (WES) in a family from the southeast of Spain with three affected women in consecutive generations to identify rare variants and functional analysis to assess their pathogenicity.
Methods: DNA was isolated from peripheral blood of patients with MD and a healthy man of the second generation. The libraries were prepared with the Agilent's All Exon 50MB capture kit and WES of genomic and mitochondrial DNA was carried out in a SOLiD 5500xl platform. Bioinformatics analyses were performed by using the Bioscope software, SAMtools and MAQtools, obtaining $\sim$ 50.000 single nucleotide variants (SNV) per exome. Functional annotation software (ANNOVAR) and minor allelic frequency (MAF) < 0.01 were used to prioritize non-synonymous SNV according to: a) the effect in protein structure and phylogenetic conservation by using a seven points scoring system (SIFT, PolyPhen2, Graham's Matrix, GERP+, Mutation taster, PhastCons and PhyloP); b) cross species phenotype comparison according to the inheritance pattern and mouse as model organism phenotype by the Exomizer software and c) genomic data fusion combining deleteriousness of the variant, haploinsufficiency prediction and similarity of the given gene to known genes associated with the phenotype by the eXtasy suite.
Results: We have identified and validated by Sanger sequencing two novel heterozygous SNV FAM136A and DTNA genes in all affected cases of this family. FAM136A is a protein located in the mitochondria and its function is unknown. The variant (chr2:70527974 G>A) leads to a novel stop codon which was not found in 1000 sporadic MD patients. FAM136A expression was evaluated by qPCR in lymphoblastoid cell lines of patients and controls. Two mRNA transcripts of 1810 and 936 bps length were identified, but only the larger transcript harbors the mutation. Of note, the mutant mRNA has a significant reduced expression in patient lymphoblasts when they were compared with controls ($p = 0.002$). Immunoblotting confirmed the presence of two wild-type proteins isoforms (138 and 105 AAs, respectively) in patient lymphoblasts. However, we were not able to detect the mutant predicted protein resulting from the novel SNV (76 AAs, 8 kD) in either patients or control immunoblots, and it is possible that this short fragment is processed in the proteosome. DTNA gene encodes á-dystrobrevin (ADB), a protein expressed in the utricle hair cells, found in the dystrophin-associated protein complex in plasma membrane that connects the cytoskeleton to the extracellular matrix. Absence of glial ADB causes loss of function in aquaporin 4 channel, abnormalities in the blood-brain barrier and progressive brain edema. The SNV (chr18:32462094G>T) leads to a missense mutation which was not found in 290 controls.
Conclusions: FAM136A and DTNA are the first two genes associated with familial MD. We hypothesize a multi-hit model with mutations in FAM136A and DTNA genes, both being required to produce the phenotype. Further studies are required to evaluate the functional impact of these mutations in neural and otic progenitors generated from carriers of these mutations.
Funding: This study was funded by Grants from CSBS-2012-0242 and Meniere's Society, UK.

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Q-9
ALTERED N-TERMINAL CHROMOGRANIN A PROCESSING IN MENIERE'S DISEASE

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Objectives: Normally vertigo spells in Menière's Disease (MD) cluster in specific periods, followed by long asymptomatic periods. The aim of our work was to assess a possible role of chromogranin A (CgA), a protein released in circulation by the neuroendocrine system and which is capable to preserve the quiescence of the endothelial lining of vessels, in clustering of MD attacks. We have analysed in normal subjects and MD patients the circulating levels of full-length CgA and its N-terminal fragment (called vasostatin-1), the latter known to preserve the endothelial barrier function, inhibit pro-inflammatory cytokines, and inhibit vasoconstriction.
Methods: Sera levels of CgA and proteolytic fragments have been assessed in 36 MD patients and 35 controls by using various ELISAs to assess full-length CgA and its N-terminal fragmentation. Two assays have been performed: a. Assay 1: detects full-length CgA and fragments lacking the C-terminal region (FRs), but not CgA 1-76 b. Assay 2: detects CgA1-76, mainly vasostatin 1. Moreover, fragmentation index of N terminal regions have been established according to the following formula: N-terminal fragmentation index (N-term) = assay2/assay1.
Results: The circulating levels of full-length CgA were higher in patients compared to controls (1.18 ± 1.33 nM vs 0.73 ± 0.38 nM; $p = 0.05$); the N-terminal fragmentation index, corresponding to the percentage of vasostatin-1 over the total CgA, was 58% in normals and 34% in patients. A positive correlation has been found between total Cga levels and number of vertigo spells in the last 3 months and days from the last vertigo attack; a negative correlation has been found between N-term values and number of vertigo spells in the last 3 months.
Conclusion: MD patients showed altered proteolytic processing of circulating CgA. The reduced levels of vasostatin-1 might contribute to promote endothelial activation in MD, with potentially important pathophysiological implications.

Q-10
LONG-TERM EFFICACY OF SEMICIRCULAR CANAL OCCLUSION IN THE TREATMENT OF INTRACTABLE MENIERE'S DISEASE

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Introduction: Meniere's disease is a common chronic inner ear disease which is characterised by intermittent episodes of vertigo, fluctuating sensorineural hearing loss, tinnitus and aural pressure. Because the definitive pathogenesis is still unknown, there is currently no cure. Operative measures are considered when medical treatment failed to control the vertigo. Semicircular canal occlusion was firstly reported using for the treatment of intractable benign paroxysmal positional vertigo. Our study aimed to explore whether triple semicircular canal occlusion could be used for the treatment of intractable Meniere's disease.
Objective: To explore the long-term efficacy and safety of triple semicircular canal occlusion (TSCO) in the treatment of intractable Meniere's disease (MD) so as to provide a alternative surgical procedure for treating this disorder.
Methods: Thirty-two patients diagnosed with unilateral MD strictly meeting the Hearing and Equilibrium criteria issued by American Academy of Otolaryngology-Head and Neck Surgery Committee (1995) who referred to vertigo clinic of our hospital between Dec.2010 and Dec.2011 were enrolled in this study. Triple semicircular canal occlusion (TSCO) was performed in pathological ear for each patient.Vertigo control and auditory function were measured before and 2 years after surgery. Pure tone audiometry, caloric test, and vestibular evoked myogenic potential (VEMP) were performed for evaluation of audiological and vestibular function in two-years follow-up. Magnetic resonance imaging of the inner ear fluid water was performed after 2 years for the morphology of membranous labyrinth in the imaging of TSCO.
Results: Control rate of vertigo was 100% in two-years follow-up,with total control 81.7% and substantial control 18.3%. The hearing was preserved in 71.9% of cases, with 28.1% of hearing loss rate. Twenty-four months after treatment, canal paresis was found in the operation side of all patients by caloric test. All patients had no facial paralysis, cerebrospinal fluid leakage, and other complications.

Conclusions: TSCO, which can reduce vertiginous symptoms in patients with intractable MD, represents an effective and safe therapy for this disorder. TSCO is expected to be used as an alternative procedure for the treatment of MD in selected patients suffering from moderate to severe hearing loss.

Q-11

VISUALIZATION OF ENDOLYMPHATIC HYDROPS IN 3D-FLAIR MRI AFTER INTRATYMPANIC GD-DTPA ADMINISTRATION IN MENIERE'S DISEASE PATIENTS

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Introduction: Although the pathogenesis of Meniere's disease (MD) is still unknown, endolymphatic hydrops (EH) is known as a typical pathological mark which has been confirmed in autoptic specimens. Recent studies in imaging EH by three-dimensional, fluid-attenuated inversion recovery (3D-FLAIR) of magnetic resonance imaging (MRI), after intratympanic gadolinium administration, enables visualization of endolymphatic hydrops in patients with MD. However, there was still an absence in the standard and optimal objective indicators of MRI to diagnose "endolymphatic hydrops"and the correlation between the degree of hydrops and otoneurological tests is still lack.
Objectives: To study the feasibility of endolymphatic visualization and the diagnosis of Meniere's disease by applying intratympanic gadolinium adminstration through the tympanic membrance and 3D-FLAIR MRI. To study the relationship between the endolymphatic hydrops visualized by MRI and audio-vestibular functional tests, such as pure tone audiometry (PTA), electrocochleography (EcoG), caloric test and vestibular evoked myogenic potential (VEMP).
Methods: With a 3 Tesla MRI unit, 3D-FLAIR imaging was performed 24 hours after intratympanic gadolinium through the tympanic membrance in 32 patients with clinically diagnosed unilateral Meniere's Disease. We visualized the enhanced imaging of perilymphatic space in bilateral cochlea, vestibular and (or) canal, scoring scala tympani and scala vestibule of bilateral cochlear basal turn respectively and measuring the developing area of bilateral vestibule. The enhanced imaging of perilymphatic space in bilateral cochlea, vestibular and canal on 3D-FLAIR imaging were observed by two radiologists independently. PTA, EcoG, caloric test and VEMP were performed. The relationship between the endolymphatic hydrops visualized by MRI and audio-vestibular functional tests were studied. Statistical methods include Wilcoxon tests, t tests and ANOVA.
Results: The gadolinium appeared in almost all parts of the perilymph in cochlea, vestibular and (or) canal in all 41 patients' inner ears, so the endolymphatic space was clearly shown on 3D-FLAIR imaging. The score of scala tympani between the affected side and the healthy side were no statistically significant different ($Z = 1.165$, $P > 0.05$). The score of scala vestibuli between the affected side and the healthy side were statistically significant different ($Z = 4.586$£¬ $P < 0.05$). The developing vestibulear area[(5.61¡À2.77) mm2, £¨8.70¡À2.88)mm2] between the affected side and the healthy side were statistically significant£¨t $= 5.28$£¬ $P < 0.05$£©. Abnormal vestibular evoked myogenic potentials were significantly correlated with the developing vestibular area of the affectedside£¨ F $= 18.066$£¬ $P < 0.05$£©. Abnormal electrocochleography were significantly correlated with scala vestibuli score value of cochlear basal turn in the affected side£¨ $Z = 2.96$£¬ $P < 0.05$£©. No significant correlation between the scala vestibuli score value or the developing vestibular area and caloric test or PTA findings.
Conclusions: 3D-FLAIR MRI with intratympanic gadolinium injection through the tympanic membrance can discriminate the border between the perilymph and the endolymph and show endolymphatic hydrops. This method may provide radiographic reference for diagnosis of Meniere's disease. The results of VEMP and electrocochleography might have appropriate correlation with degree of vestibular and cochlear hydrops.

Oral Presentations R. Acoustic Neuromas/Otoneurosurgery

R-1

PREHAB VS. REHAB – PRESURGICAL TREATMENT IN VESTIBULAR SCHWANNOMA SURGERY ENHANCES RECOVERY OF POSTURAL CONTROL BETTER THAN POSTOPERATIVE REHABILITATION

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Objective: To evaluate post-surgical postural stability.
Design: Retrospective study on consecutive patients Patients: 44 patients with intact vestibular function. 20 were medically deafferented with intratympanic gentamicin before surgery, whilst performing vestibular rehabilitation exercises before and after the injections (PREHAB).
Method: Postural stability measured as energy expenditure while subjected to vibratory stimulation of the calf muscles, measured prior to surgery (or gentamicin treatment) and 6 months after surgery.
Results: Patients pretreated with gentamicin had significantly better postural stability at the time for follow-up ($p < 0.05$) and displayed a better adaptive capacity when faced with a postural challenge ($p < 0.01$). They were also able to use vision more efficiently to control their stability ($p < 0.05$).
Conclusions: By separating the sensory loss from the intracranial surgical trauma does the postural control system benefit from a better rehabilitation both in long-term (habituation) and short-term (adaptation) performance, when experiencing a postural challenge or resolving a sensory conflict. The benefits could be attributed to; active motor learning as the vestibular function slowly attenuates and completion of sensory reweighting prior to surgery. In contrast, immobilization from nausea after surgery, stress and cognitive dysfunction from the combination of surgical and abrupt sensory trauma could explain the worse compensation.

Oral Presentations S. Migraine Including Vestibular Migraine

S-1
POPULATION-BASED STUDY OF VESTIBULAR SYMPTOMS IN MIGRAINEURS

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Objective: To assess the frequency of vestibular symptoms in a group of 871 migraineurs from a nation-wide population-based study of migraine and tension-type headache in 5323 individuals
Methods: Data was gathered at face-to-face interview by general practitioners using a structured questionnaire to diagnose and characterize migraine. Here we consider only two questions: (1) have you had vertigo with or apart from your headaches? (2) have you experienced motion sickness (MS) all your life? The target group was defined as: (a) migraineurs with either vertigo or MS – "Migraine with Vestibular Symptoms" (MwVS) their control group being migraineurs with neither vertigo or MS (MwoVS); (b) migraineurs who reported vertigo – 'Migraine with Vertigo' group (MwV); their control group being migraineurs without vertigo (MwoV). Data from these 2 subgroups was analysed regarding headache characteristics, headache-associated symptom and previous medical history.
Results: Amongst the 871 definite migraineurs 534 had MwV, 337 had MwoV, 663 had MwVS, 208 had MwoVS. MwVS patients had significantly more headache, aura, nausea, vomiting, osmophobia, allergy, allodynia, headache increasing with head motion, noise as trigger for headache, days needing analgesics than MwoVS patients and also higher migraine disability scores (MIDAS) apart from which the clinical pattern was the same in MwV patients as in MwVS patients.
Conclusion: There are significant differences in the clinical profiles of migraineurs with either vertigo or with MS or with both, and migraineurs with neither vertigo nor MS. These differences might reflect differences in the pathophysiology of migraineurs with vertigo or MS.

S-2
DO VESTIBULAR MIGRAINE PATIENTS DIFFER FROM MIGRAINE PATIENTS WITHOUT HISTORY OF VERTIGO IN ANXIETY?

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Background: Studies showed that anxiety and mood disorder were more common in migraine patients than healthy controls
Objective: Aim was to compare vestibular migraine patients, migraine patients without history of vertigo (migraine only) and healthy controls according to their anxiety and depression scores.
Patients and methods: 35 definite vestibular migraine patients according to Neuhauser criteria, 30 migraine only patients and 30 healthy controls were included in the study. Hamilton Anxiety Rating Scale (HAMA), The State-Trait Anxiety Inventory (STAI-X1 and STAI-X2), Beck Depression Inventory (BDI), Anxiety Sensitivity Inventory-3 (ASI-3), Panic-Agoraphobic Scale (PAS; assessing panic like symptoms, stress sensitivity, anxious expectation, illness phobia and hypochondriasis, and reassurance seeking) and Penn State Worry Questionnaire (PENN) were used for assessment. ANOVA test was used in between group comparisons and BONFERRONÝ test was used for post-hoc analysis.
Results: We found that there were significant differences in HAMA ($p = 0.050$), PENN ($p = 0.43$), STAI-X2 ($p = 0.003$) and panic like symptoms ($p = 0.001$), agoraphobia ($p = 0.012$) subscales of PAS scores also general score (0.005) between vestibular migraine and control group. There was also significant difference in HAMA ($p = 0.016$) between migraine only patients and control group. Migraine only and vestibular migraine patients differed in reassurance orientation ($p = 0.04$) and agoraphobia ($p = 0.030$) in subscales of PAS.
Conclusion: Our results showed that migraine only was related to higher levels of anxiety whereas vestibular migraine was related to both to anxiety and depression symptoms. Psychiatric symptoms may contribute to severity and disability related to migraine only.

S-3
MIGRAINE AND SUDDEN DEAFNESS

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Introduction: Sudden deafness is defined as hearing loss over a period of time of up to 72 hours, with a sensorineural hearing loss of at least 30 db in three consecutive frequencies, of uncertain etiology. Its diagnosis and treatment are a challenge. First described in 1944 by De Kleyn A.; it has an incidence of 5–20 per 100000; With 32–65% of spontaneous recovery. It can appear at any age, though it is more frequent between the 3rd and 7th decades of life, with two frequency peaks: one between 30–40 y.o. (usually viral) and 55–70 y.o. (usually vascular) and with a higher female prevalence at an early age and male prevalence at an older age. In previous papers (Carmona et al. 2008, 2009, 2012) we suggested that vestibular migraine, mainly with auditory symptoms, is a risk factor for sudden deafness. We decided to carry out a retrospective study on the 49 patients who consulted a general ORL due to sudden deafness over a 36 month period.
Material and methods: We studied 49 patients who suffered from sudden deafness, 23 women and 26 men. We performed a clinical exam, Audiogram with speech discrimination upon diagnosis 10 days later. Additionally, all patients were studied with Echo-G and ABR and MRI to rule out brain tumors. All patients were retrospectively questioned by an expert and the history of migraine was collected according to the current IHS (International Headache Society) criteria.
Results: In this group of patients 39% of the women (13%) suffered from migraine and only 15% of the 26 men. The age mean was 45 y.o. If the general population proportion "20/100000" is compared against the proportion of patients in the sample which is 13/49 a comparison test of the sample proportion was performed. The hypothesis to evaluate were: H0) The proportion of patients with migraine in the sudden deafness Group is 20/100000. H1) The proportion of patients with migraine is higher among those with sudden deafness than in the general population. The resulting statistic would be: $z = 131, 23$. and the probability associated to this test would be $p < 0.0001$. Thus the sample proportion and the general population proportion are not equal. The proportion of patients with migraine is higher among those with sudden deafness as compared to the general population ($p < 0.0001$). Migraine Relative Risk in the women's group as compared to the men's is: RR = 3. This is interpreted as the proportion of patients with migraine in the women's group as compared to the same proportion in the men's. Odds Ratio = 4. It is interpreted as: Women have a 4 time higher change of suffering from migraine than men.
Conclusions: Migraine seems to be a risk factor, al least in women, where its prevalence was twice that of the general population.

S-4

ABNORMALITIES IN VESTIBULO-SPINAL PATHWAYS ARE INDICATORS OF A POOR PROGNOSIS FOR MIGRAINOUS VERTIGO

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We evaluated abnormal vestibular function test results in migrainous vertigo patients and assessed their association with treatment responses. We investigated a cohort of 116 patients who had suffered recurrent vertigo attacks for more than 6 months. A combination of life style modifications and medications were used to treat these subjects. The patients were asked to score the treatment success by ranking symptom score from 0 to 100%, the improvement in overall severity of headache and vertigo. Patients were then classified as complete remission (CR), symptomatic improvement ¡Ã 50% (GR, good response), or $<$ 50% improvement (PR, poor response) after 6 months of treatment. The responsiveness to medications and the vestibular test result metrics were analyzed to identify clinical outcome predictors. A symptomatic improvement of ¡Ã 50% in vertigo and headache was observed in 72 % and 78%, over mean periods of 2.4 and 2.3 months, respectively. Abnormal caloric, VEMP, and vestibular ratio measurements were found in 27%, 30%, and 55%, respectively. Abnormal vestibular ratios on posturography showed significant correlation with PR of vertigo and a normal VEMP was significantly related to GR from headache, though abnormal caloric results showed no significant difference among our three groups. PR of vertigo symptoms was observed in 7% of patients with a normal vestibular ratio and 35% of patients with abnormal vestibular ratio. CR from headache was observed in 62% of patients with a normal VEMP and 30% in patients with an abnormal VEMP. In summary, over 70% of the patients with migrainous vertigo experienced improvements in both headache and vertigo through a combination of life-style changes and prophylactic medications. Abnormal vestibular ratios on posturography and abnormal VEMP responses were frequent findings in our cohort and were indicators of a poor prognosis. The pathophysiology of migrainous vertigo appears to be closely related to vestibular abnormalities, especially in vestibule-spinal pathways.

S-5

VESTIBULAR FINDINGS IN PATIENTS WITH PERSISTENT GEOTROPIC POSITIONAL NYSTAGMUS

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Introduction: Beginning in 2004, we analyzed spontaneous and position-induced horizontal nystagmus in patients with geotropic persistent direction changing nystagmus (g-PDCN) during acute vestibular disability.
Objectives: We have examined subjective symptoms and characteristics of nystagmus in patients with persistent geotropic nystagmus using vestibular tests, as well as possible correlations to migraine in this group.
Methods: We enrolled 20 patients with a mean age of 53 years. The slow phase velocity (SPV) of the geotropic nystagmus and the nystagmus with the patient's head in the supine (S) and prone (P) positions was recorded. All patients completed caloric tests, SVH and VEMP. All tests were repeated at follow-up (FU).
Results: SPV of the geotropic nystagmus directed to the left was 5.5°/s and 3.5°/s to the right. In 72% of patients, nystagmus in the P position was opposite to that in the S position. The vestibular tests were pathologic in about 60%. At FU geotropic nystagmus was found in 40%, but was significantly less intense. The vestibular test results remained at the same level at FU. Recurrent vertigo was reported in 78% of the patients. Forty percent of the patients suffered from migraine.
Conclusion: Persistent geotropic nystagmus indicates a condition of a light cupula, which is accompanied by vestibular disability and a high incidence of pathological findings in the vestibular tests.

Oral Presentations U. Central Aspects of Vertigo

U-1

CEREBELLAR METABOLIC INVOLVEMENT AND ITS CORRELATIONS WITH CLINICAL PARAMETERS IN VESTIBULAR NEURITIS: "TOR VERGATA" UNIVERSITY EXPERIENCE

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Vestibular Neuritis (VN) is sudden, usually partial, unilateral damage of the vestibular system which constitutes a model of unilateral vestibular failure in order to study its effects on brain activation/deactivation changes. As cortical worked out models are seldom described in literature, a lack of knowledge regarding the exclusive cerebellar involvement is still present. The aim of the present study was to analyze the regional cerebellar glucose metabolism pattern (rCGM) during the first few days from the onset of VN and after one month by using a [18F] fluorodeoxyglucose positron emission tomography (FDG-PET)/Computer Tomography (CT) approach. Eight right handed patients (five females; three males; mean age 48 $\pm$ 7 years) presenting with the first and sole episode of right-sided VN underwent a neurological and otoneurological examination, including electrooculography and Bucket test, and a PET/CT brain scan during the early phase of VN (2 days) (PET0) and after 1 month (PET1). 26 Cerebellar Volumes of Interest (VOI) were extracted from the Automated Anatomical Labeling library. VOIs were converted to analyze format and normalized to thalamus using an in-house Matlab script. Mean intensity within VOIs was calculated in both phases and processed with a within-subjects ANOVA. The Bonferroni method was used to test post hoc of significant main effects and interactions and Spearman's rank correlation was performed between significant values and neurological and otoneurological scores. A significant ($p < 0.005$) rCGM decrease was found in bilateral Lobules III, VI and X and in Vermis 1–2, 3, 6 (Anterior Cerebellar Lobe – ACL) and 10 at PET0 as compared to PET1. Moreover, at PET1 a significant positive correlation ($r = 0.78$) was found between Bucket test and values of metabolism in Vermis 10 (nodulus). At PET0 a significant negative correlation ($r = -0.60$) was found between nystagmus slow phase velocity (SPV) scores and values of metabolism in right Lobule X (flocculus). These data suggest an interesting cerebellar behaviour for which deactivation pattern in ACL could be supposed in subserving and bottom-up regulating bilateral cortical devoid of sensory modality conflict during the acute VN-related controversial inflow between optical and vestibular input. Furthermore, the present findings reinforce the idea of nodulus involvement in higher order functions, suggesting its possible role in postural arrangement after the phasic loss of the vestibular sensory modality. On the other side, the negative correlation found between the right flocculus rCGM and SPV scores could highlight its specific pivotal role in controlling nystagmus parameters and in adapting vestibulo-ocular reflex by superimposing its function between vestibular inputs and eye movement network. In conclusion, for the first time, by using a PET/CT and automated anatomical labeling approach, it was possible to find those metabolic cerebellar changes that, in accordance with otoneurological scores, could unravel additional central aspects of early and late VN.

U-2
PREDICTING RECOVERY IN ACUTE VESTIBULAR NEURITIS

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Introduction: Long term clinical outcome in patients with acute vestibular neuritis (VN) is poorly predicted by vestibular-ocular reflex assessments. Accordingly, we prospectively assessed higher order visuovestibular compensatory mechanisms in 31 patients with acute VN.
Methods: Patients were studied in the acute and recovery phases of vestibular neuritis (median 2 days and 10 weeks, respectively) with vestibulo-ocular (VO) and vestibular-perceptual (VP) responses both at threshold and supra-threshold levels. Supra-threshold stimuli (90°/s velocity step rotations) allowed quantification of VO and VP time constants (Okada et al Brain; 1999;122:1293). Additional measures of visual dependency (rod-and-disc test), dizziness symptom load (Dizziness Handicap Inventory) and psychological factors (HADS, BSQ, VSS-Autonomic Arousal) were obtained.
Results: Particularly in the acute phase, VO and VP thresholds increased, more so ipsilesionally but without VO-VP dissociation. In contrast, suprathreshold VO-VP time constants were dissociated acutely – VP responses were reduced symmetrically whereas VO responses were less reduced and asymmetric. Visual dependency was significantly elevated acutely but, like all other measurements, improved at recovery phase.

Clinical outcome (Dizziness Handicap Inventory) was correlated with levels of visual dependency ($p = 0.001$), autonomic anxiety ($p = 0.001$), anxiety and depression ($p < 0.001$), fear of body sensations ($p = 0.001$) and, to a lesser degree, by vestibular perceptual thresholds ($p = 0.011$) and caloric canal paresis ($p = 0.012$). Factor Analysis revealed a strong association between clinical outcome, visual dependency and psychological factors, all loading on a single component accounting for 59.4% of the variance. Canal paresis loaded separately on a second component accounting for only 12.9% of variance and not including clinical outcome.

Conclusions: The bilateral suppression of supra-threshold vestibular perception observed acutely represents a recently recognised central adaptive 'anti-vertiginous' mechanism (Cousins et al. PLoS One; 2013;8: e61862. However, poor symptomatic recovery is best predicted by increased visual dependency and psychological factors. The findings show that recovery from unilateral vestibular deficit is mediated by higher order central mechanisms, combining multisensory integration and psychological processing. The findings pave the way for early identification and treatment of patients with poor clinical outcome in acute VN.

U-3
VASCULAR VERTIGO: NEURO-OTOLOGICAL FINDINGS*

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Introduction: Dizziness and vertigo are the most common symptoms of cerebrovascular events involving the vertebrobasilar artery territory. Isolated vestibular symptoms can be the first manifestations of progressive vertebrobasilar ischemia, and may herald major posterior fossa stroke or be harbingers of future stroke. They may also occur with hemispheric stroke syndromes.

Objectives: The Committee for Classification of Vestibular Disorders of the Barany Society formed a Subcommittee for Vascular Vertigo to define neuro-otological findings in key cerebrovascular syndromes for the International Classification of Vestibular Disorders.

Methods: The Subcommittee reviewed previous reports on neuro-otology in strokes and summarized the important vestibular findings by vascular territory. Major ischemic stroke syndromes were defined by the vascular territory affected (vertebral artery [VA], basilar artery [BA], anterior inferior cerebellar artery [AICA], posterior inferior cerebellar artery [PICA], superior cerebellar artery [SCA], internal auditory artery [IAA], internal carotid artery [ICA]), which determines the structures involved and the resulting clinical signs. Isolated vestibular presentations with normal vestibulo-ocular reflexes are typical of VA, PICA, and SCA syndromes, and may sometimes be seen with BA, AICA, IAA, or ICA strokes. The diagnostic and therapeutic aspects of vascular vertigo are provided for key vascular syndromes only when considered necessary.

Results: With recent developments in clinical neuro-otology and neuroimaging, neuro-otological findings have expanded in each stroke syndrome, and diagnosis of isolated vertigo from brainstem and cerebellar strokes has increased markedly. Vestibular presentations with unilaterally or bilaterally impaired vestibulo-ocular reflexes, with or without comorbid auditory symptoms or signs are typical of AICA and IAA infarctions, and may also be seen with BA and, rarely, VA, PICA, or SCA ischemic strokes. In a study of a population of acute vestibular syndrome patients from a single center, a detailed bedside examination focused on vestibulo-ocular reflex assessment by head impulse testing, nystagmus features, and ocular alignment was superior to neuroimaging (even by MRI) for detecting strokes. Although transient vertigo, dizziness, or unsteadiness (spontaneous episodic vestibular syndrome) is the most common initial presentation of vertebrobasilar ischemia, and patients with isolated vertigo appear to have a higher risk of stroke than the general population, the optimal diagnostic and therapeutic approaches to transient vestibular symptoms of vascular origin remain unknown.

Conclusions: There has been marked progress in the diagnosis of strokes presenting with acute continuous vertigo, but future studies are required to define correct diagnosis and therapy of transient vertigo of vascular origin.

*This abstract is an invited status report related to the International Classification of Vestibular Disorders and was not reviewed by the scientific committee.

U-4

EPILEPTIC VERTIGO AND DIZZINESS – A SYSTEMATIC REVIEW OF THE LITERATURE

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Introduction: Little is known about the frequency and clinical characteristics of epileptic vertigo and dizziness (EVD). Dizziness as part of a larger seizurelike presentation (non-isolated EVD) is readily identified as epileptogenic, but when vestibular symptoms are the only manifestation (isolated EVD), differentiation from otologic causes may be difficult.

Objectives: Characterize vestibular symptoms due to seizures using systematic literature review.

Methods: Electronic (MEDLINE) and manual search for English-language studies (1966–2012) of vertigo or dizziness due to seizures. Two independent reviewers selected studies. Study characteristics and clinical features were abstracted. We defined three article types based on the population studied: (1) seizures, some experiencing dizziness/vertigo (disease cohort); (2) vertigo/dizziness, some due to seizures (symptom cohort); and (3) seizures and vertigo/dizziness in all patients described (combined cohort).

Results: We identified 75 studies describing 10,227 patients (disease cohort = 7,924; symptom cohort = 2,058; combined cohort = 245). Thorough diagnostic workups (brain MRI plus vestibular testing plus ictal EEG) was rare ($< 0.1\%$). Confirmatory (ictal) EEG was reported in 409 (4.0%). Complete neuro-otologic assessment was reported in 1,106 (10.8%). Non-isolated EVD was diagnosed in 919 patients (9.0%); isolated EVD was identified in 84 patients (0.8%). Localized EEG abnormalities (observed in 321 EVD cases) were most frequently temporal (87.2%); parietal involvement was noted in just 5.6%. Duration of episodic vestibular symptoms varied, but was very brief (< 30 sec) in 71.1% of isolated EVD vs. 6.9% of non-isolated EVD.

Conclusions: Non-isolated EVD may be fairly common, but isolated EVD appears to be rare. EVD is primarily associated with temporal lobe seizures; whether this reflects greater epidemiologic prevalence of temporal lobe seizure or a tighter clinical association with dizziness and vertigo than other brain regions remains unknown. Consistent with clinical wisdom, isolated EVD spells often last just seconds, although many patients have longer spells. A preponderance of lower-quality studies suggests further research is needed.

Oral Presentations V. Psychiatric/Physiological Aspects of Vertigo

V-1

ACROBATIC TRAINING REDUCES ANXIETY IN A MUTANT MICE MODEL OF PROGRESSIVE PERIPHERAL VESTIBULAR LOSS

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Background: Anxiety disorders are among the most common mental disorders, and are co-morbid with balance disorders in a significant proportion of cases. Presently, it is unclear whether anxiety and balance disorders are causally related, and what direction this causality may take. In a previous study we demonstrated anxiety-like behavior in a mice model of progressive peripheral vestibular loss, suggesting that progressive vestibular deficit leads to anxiety.

Objectives: To investigate the effect of an acrobatic training on both balance and anxiety in the mice model of progressive peripheral vestibular loss.

Methods: We studied 4 groups of mice defined by Genotype x Training: 31 head-banger (Hdb) mutant mice in which the balance disorder is due to progressive elongation of stereocilia in vestibular peripheral organs, and 31 wild-type (Wt) mice. Mice of each genotype were kept in either normal or in acrobatic-treatment cages from birth. The effect of such exposure

on balance and anxiety were tested in adulthood. Balance was assessed by swim, tail-hang, elevated platform and rotarod tests. Anxiety was assessed by open-field and elevated plus-maze tests.
Results: Vestibular Hdb mice without balance training showed the lowest behavioral balance performance and the highest behavioral anxiety scores as compared to the other three groups. Early and continuous acrobatic training improved the balance of both Wt and Hdb mice to the extent that trained members of both genotype groups were indistinguishable on balance tests. In parallel to the improved balance in trained Hdb mice, they demonstrated a significant decrease in anxiety scores.
Conclusions: These findings show that rescued balance ameliorates anxiety in vestibular-deficient mice. Further studies are required to reveal whether the improved balance is associated with plasticity of the vestibular-deficient system.

V-2
PERSONALITY TRAITS MODULATE SUBCORTICAL ANDCORTICAL VESTIBULAR AND ANXIETY RESPONSES TO SOUND-EVOKED OTOLITHIC RECEPTOR STIMULATION
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Background: Strong links between anxiety and vestibular symptoms have been recognized for decades. Anxiety-related personality traits such as neuroticism and introversion may also affect vestibular function. Recently, the combination of neuroticism and introversion was identified as a risk factor for chronic subjective dizziness (CSD), a common neurotologic syndrome similar to phobic postural vertigo. In contrast, positive traits such as resilience were found to reduce the risk of chronic vestibular symptoms. However, the relationship between personality traits and activity in brain vestibular networks has not been investigated yet.
Methods: Twenty-six right-handed, drug-free, medically and psychiatrically healthy individuals underwent functional magnetic resonance imaging (fMRI) during sound-evoked vestibular stimulation. Regional brain activity and functional connectivity were measured by fMRI in response to short tone bursts (STB) at 100 dB. This stimulus is known to activate receptors in the saccules and areas of the vestibular cortex. Comparison stimuli consisting of STBs at 65 dB and white noise at 100 dB, which do not activate peripheral or central vestibular structures, were used to control for sound intensity and non-specific responses to noise. Personality traits of the Five Factor Model (neuroticism, extraversion, openness, agreeableness, consciousness) were measured with a standardized inventory (the NEO-PI-R) and correlated to brain activity and connectivity in regions of interest selected a priori for their association with cortical and subcortical vestibular and anxiety systems.
Results: Neuroticism and extraversion correlated with activity and connectivity in vestibular, visual, and anxiety systems during vestibular stimulation. Neuroticism correlated positively with activity in the pons, vestibulocerebellum, and para-striate cortex (V2), and negatively with activity in the supra-marginal gyrus (SMg). Neuroticism also correlated positively with increased connectivity between pons-amygdala, cerebellum-amygdala, inferior frontal gyrus (IFg)-SMg, and IFg-V2. This suggests that neuroticism was associated with increased activity of subcortical vestibular and vestibulo-cerebellar structures, increased activity of vestibular-anxiety system connections, and a bias toward visual versus vestibular activation in the cortex. Extraversion correlated negatively with amygdala activity and positively with amygdala-cortical connectivity (amygdala-IFg). In other words, higher introversion was associated with greater amygdala reactivity and lesser connectivity between the amygdala and IFg, a circuit known to affect fear conditioning that also has poorer connectivity in social and generalized anxiety disorders.
Conclusions: Neuroticism was associated with increased vestibular system responses to vestibular stimuli and greater vestibular-anxiety system connectivity. Introversion was associated with increased anxiety system responses to vestibular stimuli and poorer connectivity in cortical-subcortical circuits that modulate anxiety. These personality-related changes in brain activity may mediate hypersensitivity to motion stimuli in neurotic individuals and potentiated fear conditioning to postural threat in introverted individuals, and are possible brain mechanisms underlying high rates of vestibular-anxiety comorbidity. They also may be the brain correlates of observed links between neuroticism/introversion and CSD.

V-3
CATASTROPHIZATION IN DIZZINESS. HAVE WE FOUND THE MISSING LINK?
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Introduction: Vertigo and chronic imbalance are complex problems that cause a very substantial reduction in quality of life for patients and a considerable disease burden on society. Often patients with identical vestibular function tests and ostensibly similar attacks describe very different levels of symptoms. Neurotologic investigation often yields no explanation for this discrepancy. Any symptom can be magnified by perception problems and the concept of 'catastrophization', a personality-based trait, which has been studied in detail in the pain literature, but has not been studied in the context of balance disorders. The entity of catastrophization is distinct from anxiety and other neuroses and may have much to offer in the explanation of these differences in symptom load.
Objectives: To construct and validate a scale to measure levels of catastrophization in dizziness.
Methods: Two hundred patients completed a version of the Pain Catastrophization Scale, modified for use in balance, the TDCS. This scale was measured alongside measures of mood (PANAS), dizziness handicap (DHI), and confidence with balance (ABC) as well as a visual analogue scale of symptom severity. These data were used to validate the scale and investigate the role of catastrophization in chronic imbalance. Domains of 'rumination', 'magnification' and 'helplessness' were assessed alongside reliability, internal, external and construct validity.
Results: TDCS scores were found to be reproducible over time with a Cronbach's alpha of 0.92 across two successive visits. Catastrophization was found to be independent of psychiatric symptoms, such as depression or anxiety, but correlated strongly with the overall VAS of severity of symptoms, the DHI ($r = 0.596$, $p = 0.001$) and ABC ($r = -0.632$, $p = 0.001$). Importantly, it was the only metric to predict improvement in the DHI with treatment ($p = 0.048$). It correlated strongly with the BCS, a measure of general catastrophization of normal bodily functions, suggesting an overall validity even more robust than the pain scale on which it was based.
Conclusions: The TDCS, a measurement of catastrophization in balance, will allow the role of psychological overlay in balance symptoms to be measured accurately and treated appropriately. In clinical practice this will give the clinician the opportunity to direct resources and clinical focus towards the source of symptoms of imbalance, be they predominantly organic or somatoform in origin. Early cognitive behavioral therapy (CBT) is very effective in this area if patients can be appropriately and timeously referred. This is the first attempt to quantify this previously poorly recognized but important aspect of the diagnosis and treatment of balance disorders.

Oral Presentations W. Cognitive/Cortical Aspects of Vertigo

W-1
ESTIMATION OF PASSIVELY TRAVELLED ROTATIONS IN DARKNESS BY VESTIBULAR PATIENTS

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Introduction: In the present study, we required patients with vestibular disorder and control subjects to estimate verbally their passively travelled rotation angles in complete darkness, rotations imposed with a motorized Barany chair. The Vestibulo-Ocular Reflex (VOR) was also measured. The aim of this study was to establish the role of vestibular input in spatial orientation, to get a better understanding of the disability of these patients, and possibly to add a new tool for vestibular rehabilitation program.
Material and methods: We compared four groups, Control Group (CG), Acute Unilateral Canal Paresis (AcUCP), Chronic Unilateral Canal Paresis (ChUCP), and Bilateral Canal Paresis (BilCP). The stimulus was a sequence of eight successive passive rotations, with four amplitudes (90°, 180°, 270°, 360°) in two directions (CW and CCW).
Results: We found great underestimates of passive rotations in patients with bilateral hyporeflexia on both sides, whereas the performance in the estimation of the travelled angles was good in the Control Group. The performance was slightly lower in unilateral groups in both sides. Surprisingly, there was no clear underestimation in lesion side of unilateral canal paresis while the VOR gain was low. This point will be discussed. This study allowed us also to describe two remarkable findings: – a mechanism of vestibular compensation after acute unilateral neuritis: an increase of the VOR

gain in lesion side and a decrease in healthy side, resulting in a similar gain in both sides. – the correlation between VOR gain and perception was surprisingly not significant in CG and neither in unilateral groups.
Conclusion: We found great underestimates of passive rotations only in patients with bilateral hyporeflexia on both sides. The estimation of passively travelled rotations in darkness could be used to confirm a bilateral canal paresis. There was no clear underestimation in lesion side of unilateral canal paresis while the VOR gain was low. The correlation between VOR gain and perception was surprisingly not significant in CG and neither in unilateral groups. This study shows the complex relationship between perception and VOR and could contribute to another assessment of the spatial handicap in vestibular patients.

W-2
LOCOMOTOR ADAPTATION IN MENIERE'S DISEASE AND VESTIBULAR NEURITIS PATIENTS

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Imperial College London

Introduction: Patients with a unilateral vestibulopathy undergo a process of central adaptation to compensate for the imbalance in vestibular tone that is ultimately responsible for symptoms of dizziness and unsteadiness.
Objectives: We explored whether these adaptive abilities extend to other types of adaptation, specifically locomotor adaptation. If so, given that the ability to adapt correlates with symptomatic compensation, poorly compensated patients should have reduced locomotor adaptation to balance perturbations.
Methods: Twelve patients with unilateral "recovered" vestibular neuritis (VN), twelve with unilateral "active" Meniere's disease and twelve age-matched controls were recruited to this study. Locomotor adaptation was assessed using the broken escalator paradigm that induces a recordable increase in trunk displacement and gait velocity, termed the locomotor after-effect (LAE). We recorded baseline levels of dizziness using the Dizziness Handicap Inventory. All groups performed 5 baseline trials stepping onto a stationary sled (BEFORE trials), 5 with the sled moving (MOVING or adaptation trials) and 5 with the sled stationary again (AFTER trials).
Results: Dizziness scores were twice as high in MD compared to VN ($P = 0.037$), and caloric paresis twice as large ($P = 0.040$). During the MOVING trials, MD patients had larger levels of trunk sway compared to VN ($P < 0.01$) and controls ($P < 0.001$). The MD patients had a significantly larger LAE compared to VN and controls ($P < 0.05$), but there was no difference in LAE size between VN patients and controls. Increased dizziness scores predicted increased sway in the MOVING trials that in turn predicted an increased LAE size. Gait velocity was slower in patients compared to controls in all trial phases.
Conclusions: The increase in the size of trunk sway during balance perturbations shows reduced locomotor adaptation but the increased after-effect size is probably associated with an impaired risk assessment of sled movement in AFTER trial 1. From a clinical perspective, this is presumably an indication of how dizziness in poorly compensated vestibular patients interferes with their own motor activities.

W-3
HUMAN ANGULAR PATH INTEGRATION, TIMING AND THE TEMPOROPARIETAL JUNCTION

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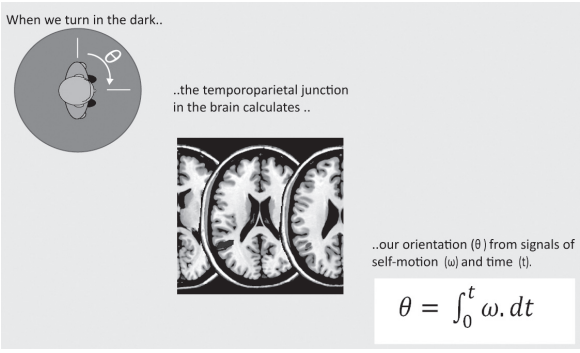
Path integration is the process of updating ones travelled distance from motion cues. For linear path integration optic flow, motor efference copy, kinaesthetic, haptic, and vestibular cues contribute whereas vestibular cues predominate for angular path integration. Theoretically, path integration could involve a temporal integration of motion cues, requiring a timing mechanism inherent to this mathematical function. In support we found that in healthy subjects, when vestibular-derived angular position was updated by masked imperceptible visual landmarks, motion du-



ration estimates were congruently updated. The link between timing and path integration was further explored in brain lesion patients demonstrating that angular path integration was severely disrupted by right temporoparietal junction (TPJ) lesions for leftward (not rightward) whole-body turns. TPJ patients displayed a timing bias, perceiving leftward rotations as briefer than rightward. The navigational deficit was however unrelated to neglect or self-motion velocity perception. These data suggest an intimate relationship between human angular path integration and an explicit representation of timing duration, that is relevant to the understanding of human spatial navigation and sheds light on the neural mechanism of timing perception.

W-4
VESTIBULAR CONTRIBUTIONS TO BODILY SELF-CONSCIOUSNESS

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Introduction: A minimal sense of self relies on various bodily signals. While a strong emphasis has been traditionally put on visual, tactile and interoceptive processes, recent research has noted that vestibular signals should also be important for a sense of self (e.g. Lopez (2013) Front Integr Neurosci, 7:91, "A neuroscientific account of how vestibular disorders impair bodily self-consciousness"). For example, patients with vestibular disorders may experience deformations of their body, lose connection with their body, or experience disembodiment. Yet, the influence of vestibular misintegration on bodily distortions had until recently not been quantified using well-controlled psychophysical procedures.
Objectives: Here, I present several lines of evidence showing that vestibular signals contribute to the sense of self by combing approaches from neurology and neuropsychology in epileptic patients and psychophysics in healthy participants receiving caloric vestibular stimulation (CVS).
Methods: Vestibular sensations and sensations of bodily distortions were analyzed during epileptic seizures in the temporo-parietal and frontal cortex (Lopez et al. 2010, Epilepsy and Behavior, 17: 289–292; Heydrich et al., 2011, Epilepsy and Behavior, 20: 583–586). In healthy participants, we measured how CVS (warm air in the right ear and cold air in the left ear) influenced internal models of the left hand (Lopez et al. 2012, Neuropsychologia, 50: 1830–1837). CVS was compared to a control thermal stimulation, that is injection of air at body temperature in both ears. In a first experiment (18 participants) we used a tactile distance comparison task between two body segments (left hand and forehead) to measure how participants judged the size of objects touching the skin. In a second experiment, 17 participants located four anatomical landmarks (proprioceptive judgments) on their left hand by pointing with a stylus hold in their right hand on a digitizing tablet.
Results: Analyses of seizures in epileptic patients showed that vestibular illusions were often associated with distortions of the body schema as well as with the experience of a disembodied self-location (i.e. the experience that the self is located outside the physical body). In healthy participants, CVS modified the internal model of the body. In the tactile distance comparison task, objects contacting the left hand were judged as longer during CVS as compared to the control thermal stimulation. In addition, the pointing task towards anatomical landmarks indicated that the internal model was also modified, since the left hand was perceived as significantly longer and wider.
Conclusions: The results indicate that internal models of the body adjust as a function of vestibular signals, modifying the experience of self-location as well as representations of hand size. The data provide clinical and experimental evidence that vestibular functions are not limited to postural and oculomotor control, and extend the contribution of the vestibular system to bodily cognition. The findings further suggest the inclusion of vestibular signals into current models of body representations and bodily self-consciousness (see Lopez (2013) Front Integr Neurosci, 7:91).

W-5
THE CORTICAL MECHANISMS OF OSCILLOPSIA AND ITS SUPPRESSION

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Patients with an acquired involuntary eye oscillation (nystagmus) complain of perceived visual world motion (oscillopsia) concomitant with retinal slip of the visual world. In contrast humans with early onset infantile nystagmus typically report no oscillopsia. There are two contending hypotheses regarding the brain mechanisms that render infantile nystagmus individuals asymptomatic, i.e. visual cortex spatial updating

of eye position versus suppression of visual motion cortical activity. Animal models of infantile nystagmus with single neurone studies could theoretically provide further insight however probing perception in animals is problematic. Since human studies thus far have been purely psychophysical, we combined psychophysics, eye movement recording and neurophysiology in six healthy volunteers with normal eye movements and four healthy individuals with infantile nystagmus without oscillopsia. First we measured visual cortical spatial updating by applying transcranial magnetic stimulation (TMS) to area V5/MT during gaze fixation. Visual cortex TMS evokes a percept of light or 'phosphene'. Phosphenes are fixed in space for a given gaze direction and stimulus cortical location but move in tandem with voluntary eye movements (phosphenes are retinotopic). We provoked an involuntary nystagmus and oscillopsia in the healthy individuals via a cold caloric irrigation. Subjects indicated their perceived phosphene location by means of a mouse click on a screen at baseline and then again during the caloric-evoked nystagmus. During a caloric-evoked nystagmus, subjects' phosphene location remained fixed in external space, i.e. there was no updating of phosphene location with eye position ($r2 = 0.05$; $P > 0.05$ for horizontal eye vs. phosphene position). In contrast when infantile nystagmus subjects fixated upon a perceptually stable central fixation target, eye and phosphene position were correlated ($r2 = 0.43$; $P = 0.006$). We then probed V5/MT excitability with TMS. We found a continuous modulation of brain excitability across the nystagmus cycle in 4 infantile nystagmus subjects. The range of this excitability modulation was well outside the 95% confidence intervals for the variability in V5/MT excitability seen in normal volunteers (across slow and quick phases) during an acute vestibular-nystagmus evoked by caloric irrigation. In summary, we demonstrate for the first time, a direct link between visual spatial updating and visual-perceptual stability. Secondly we show that some infantile nystagmus subjects may utilise a second oscillopsia suppression mechanism via a phasic modulation of area V5/MT excitability.

W-6

THE NEUROANATOMICAL CORRELATES OF TRAINING-RELATED PERCEPTUO-REFLEX UNCOUPLING IN DANCERS

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Sensory input evokes low-order reflexes and higher-order perceptual responses. Vestibular stimulation elicits vestibular-ocular reflex (VOR) and self-motion perception (e.g., vertigo) whose response durations are normally equal. Adaptation to repeated whole-body rotations, for example, ballet training, is known to reduce vestibular responses. We investigated the neuroanatomical correlates of vestibular perceptuo-reflex adaptation in 29 female ballet dancers (average age 21.9 years and all right handed) and a matched group of 20 female controls (high level rowers of average age 21.2 years and all right handed). Dancers' vestibular-reflex and perceptual responses to whole-body yaw-plane step rotations were: (1) Briefer and (2) uncorrelated (controls'reflex and perception were correlated). Voxel-based morphometry showed a selective gray matter (GM) reduction in dancers' vestibular cerebellum correlating with ballet experience. Dancers' vestibular cerebellar GM density reduction was related to shorter perceptual responses (i.e. positively correlated) but longer VOR duration (negatively correlated). Contrastingly, controls' vestibular cerebellar GM density negatively correlated with perception and VOR. Diffusion-tensor imaging showed that cerebral cortex white matter (WM) microstructure correlated with vestibular perception but only in controls. In summary, dancers display vestibular perceptuo-reflex dissociation with the neuronatomical correlate localized to the vestibular cerebellum. Controls' robust vestibular perception correlated with a cortical WM network conspicuously absent in dancers. Since primary vestibular afferents synapse in the vestibular cerebellum, we speculate that a cerebellar gating of perceptual signals to cortical regions mediates the training-related attenuation of vestibular perception and perceptuo-reflex uncoupling.

W-7

THE STATE DEPENDENCY OF V5/MT AND V1/V2 EXCITABILITY IN RESPONSE TO ADAPTATION TO VARYING VISUAL MOTION COHERENCE

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Repetitive exposure to visual motion stimuli is used to reduce symptoms in patients with visually-induced dizziness. We previously explored the brain responses to visual motion, showing that adapting to random vi-

sual motion increases the excitability of human visual motion cortex area V5/MT. This was probed by assessing the change in phosphene induction following adaptation using transcranial magnetic stimulation (TMS) at threshold intensity, i.e. at a level which yielded a 50% phosphene report rate at baseline. Given the state-dependency of visual cortical responses to TMS we asked whether post-adaptation visual cortical excitability could be influenced by (a) the probe TMS intensity as calibrated to baseline % phosphene reports (b) the degree of coherence of the adapting visual motion stimulus (c) the brain area tested, i.e. V5/MT vs. V1/V2 (early visual cortex). The TMS intensity was first calibrated to achieve a baseline phosphene rate of 50% (TMS50), 70% (TMS70) or 90% (TMS90) in the left hemisphere (V5/MT or left V1/V2). For each trial, 20 TMS pulses were applied at the desired titrated intensity with a 6s inter-stimulus interval and the average phosphene rate recorded. The subjects were then adapted to visual motion for 2 minutes. We tested four different visual motion coherences presented in randomised order ranging from near 100% coherence to near totally random. Finally, for each trial, 20 TMS pulses at the baseline intensity were applied post-adaptation and the average phosphene rate obtained. For Area V5/MT, a repeated measures ANOVA showed a significant effect of TMS intensity ($P = 0.002$) whereby TMS at threshold intensity (TMS50) was associated with a post-adaptation increase in excitability whereas supra-threshold intensities (TMS50 & TMS90) were associated with a reduction in post-adaptation excitability. Although there was no main effect of visual motion stimulus coherence, this factor showed a significant interaction with TMS intensity ($P = 0.017$). Testing with TMS50 intensity yielded a post-adaption to random visual motion increase in excitability whereas adapting to coherent visual motion did not show much increase in V5/MT excitability above baseline. In contrast TMS90 and TMS90 intensities showed little modulation with visual motion coherence change. For early visual cortex (V1/V2), the same pattern in response was observed as that seen for V5/MT in response to escalating the probe TMS intensity – a repeated measures ANOVA showing a significant effect of TMS intensity ($P < 0.001$) but, unlike for V5/MT, for V1/V2 there was no interaction between visual motion stimulus coherence and TMS intensity. Our data show that the baseline TMS intensity used to the probe brain excitability post-intervention is critically important in determining the direction of the observed excitability change. Secondly, the degree of visual motion coherence that is used in assessing the adaptation to visual motion also affects the magnitude of the change in excitability for V5/MT but not V1/V2. We explain these data on the basis of the known differences in neuronal receptive fields to visual motion between V5/MT and V1/V2. Our data also argue for the need to investigate the impact of random motion stimuli in dizzy patients as opposed to traditional optokinetic stripes. Indeed many patients complain of dizziness when faced with Brownian-type motion such as crowds in shopping mall.

W-8
GALVANIC VESTIBULAR STIMULATION IMPAIRS CELL PROLIFERATION AND NEUROGENESIS IN THE RAT HIPPOCAMPUS BUT NOT SPATIAL MEMORY

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Introduction and objectives: Since movement is recognized to stimulate hippocampal neurogenesis and movement is impossible without activation of the vestibular system, we speculated that activating the vestibular system in rats while minimizing movement, by delivering galvanic vestibular stimulation (GVS) under anaesthesia, would affect hippocampal cell proliferation, neurogenesis, and spatial memory.
Methods: Cell proliferation was measured in animals receiving GVS or sham treatment for 1 h under anaesthesia using the DNA replication marker, bromodeoxyuridine (BrdU), and triple immunolabelling was used to identify the phenotype of the newborn cells. In a separate group of animals, the effects of GVS or sham treatment on performance in memory tasks was studied.
Results: Compared to the sham control group, the number of cells incorporating BrdU was significantly reduced in the bilateral hippocampi in both the cathode left-anode right and cathode right-anode left stimulation groups (P ¡Ü 0.0001). The majority of the BrdU+ve cells co-expressed Ki-67, a marker for cell division, suggesting that these BrdU+ve cells were still in the cell cycle; however, there was no significant difference in the degree of co-labelling between the two stimulation groups. Single labelling for doublecortin (DCX), a marker of immature neurons, showed that while there was no significant difference between the different groups in the number of DCX+ve cells in the right dentate gryus, in the left dentate gyrus

there was a significant decrease in the cathode left-anode right group compared to the sham controls (P ¡Ü 0.03). Nonetheless, when animals were tested in place recognition, object exploration and Morris water maze tasks, there were no significant differences between the GVS groups and the sham controls.
Conclusions: These results suggest that GVS can have striking effects on cell proliferation and possibly neurogenesis in the hippocampus, without affecting spatial memory.

Oral Presentations X. Aging and Balance

X-1
AGE-RELATED VESTIBULAR LOSS AND FRAILTY IN OLDER INDIVIDUALS

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Background: Age-related vestibular loss (ARVL) is the reduction in vestibular function associated with the aging process. ARVL appears to be a prevalent condition among community-dwelling older adults; however, the functional implications of ARVL have not been rigorously established. In this study, we assessed the association between ARVL and frailty, an important geriatric syndrome characterized by global functional decline and decreased resilience to homeostatic disturbances.
Methods: We enrolled a "normative" sample of 50 community-dwelling participants age 70 and older. Vestibular function was measured using the head impulse test (HIT), a qualitative measure of the vestibulo-ocular reflex (VOR). The five components of the frailty assessment were administered, specifically 1) grip strength; 2) gait speed; 3) weight loss in the previous year; 4) exhaustion; 5) and physical activity, and a composite frailty score was computed. Participants were also evaluated for other factors influencing functional status including visual acuity, somatosensory function and muscle strength.
Results: The participants' mean age was 77 years (range 70–95); 48% were male and 52% female. Fifty percent of participants had an abnormal HIT, and 58% were frail. Vestibular dysfunction (i.e. an abnormal HIT) significantly increased the odds of frailty 10-fold in multivariate analyses adjusted for age, gender, and other potential risk factors.
Conclusions: We observed a significant association between vestibular dysfunction and frailty. Vestibular dysfunction and specifically VOR impairment fundamentally destabilize an individual's interaction with their environment, possibly leading to activity curtailment and consequent muscle weakness which are hallmarks of the frailty phenotype. Screening for ARVL in older individuals and directing appropriate therapy may be critical to preventing this highly morbid outcome.

X-2
A "BALANCING SHOE" TO PREVENT BACKWARD FALLS

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Background: A protective postural response with the execution of a compensatory "extra step" is commonly applied by physical therapists in neurological patients and elderly persons in order to regain balance and prevent falls. Very often, this response is too slow and subjects do not success to make the step before falling. A "Balancing shoe" (BS) prototype with an embedded electro mechanic mechanism has been recently designed in an attempt to replace the extra step by providing the needed foot displacement to regain balance.
Objective: To test the feasibility of a BS prototype to prevent backward falls.
Methods: We tested six healthy elderly subjects standing on a computerized platform under two provoking postural instability conditions: 1) Sudden and brisk forward movement of the platform; 2) Pulling subject backward. Postural reactions were measured by pressure sensors of the computerized platform and by cameras detecting the displacement of markers mounted over the subject's body. All tests were also videotaped.
Results: In most trials, when platform or pull perturbations were enough to produce significant imbalance, BS rolled back preventing backward falls. In some cases, BS operated concomitantly with the subject who was doing a step backward. In these cases, subject and BS "worked together" and complemented each other. There were no reports of discomfort or any complaint that shoes disturbed normal reactions.
Conclusions: BS seems to be a feasible mean for preventing backward falls.
Disclosures: YM and AS are co-founders of B-Shoe technologies. Supported by a fund of The Ministry of Industry, Trade and Labor, Office of the Chief Scientist, Technological Incubators Program, Israel.

X-3
DIMINISHED TACTILE AND VIBRATION SENSATION IN THE FEET DOES NOT IMPEDE IMPROVEMENTS IN POSTURAL CONTROL FOR RELATIVELY HEALTHY ELDERLY AFTER HAVING PERFORMED SELF ADMINISTERED BALANCE ENHANCING EXERCISES IN THE HOME ENVIRONMENT FOR SIX WEEKS

Hafstrom, Anna; Terdén, Josefine; Malmström, Eva-Maj; Fransson, Per-Anders; Magnusson, Måns
Department of Otorhinolaryngology, Head and Neck Surgery, Clinical Sciences

Introduction: Preventing falls in the elderly is important as about 30% of community-dwelling people over 65 years of age fall each year. Objectives: To assess if proprioception in the lower extremities influences the effectiveness of prescribing a six week self administered balance enhancing exercise program (BEEP) for static and dynamic balance control in elderly 60 years and older.
Methods: The study was conducted as a randomized controlled crossover trial. 40 relatively healthy community-dwelling elderly (70 $\pm$ 5 years old, 22 women and 18 men) were evaluated using visual, vestibular, balance, and gait function tests. Vibration sensation of the first and fifth metatarsal heads, and the plantar surfaces of the heel, first and fifth toe was measured with a Bio-Thesiometer. Plantar tactile sensation was evaluated for the heel, first and fifth toe pads with the Semmes-Weinstein Monofilament test. All subjects were evaluated before and after performing a six week BEEP which included balance, strength, and VOR challenging exercises self administered in the home environment. The primary outcome measures included one-legged stance time (OLST) on firm or compliant surfaces and with eyes open (EO) or eyes closed (EC).
Results: As presented in the abstract "Six Weeks of Unsupervised Balance Exercises Performed in the Home Environment Improves Balance Control in Relatively Healthy Elderly" the OLST improved significantly after performing the BEEP for six weeks. The OSLT on solid surface with EO improved $\geqslant 35\%$ for both feet ($p < 0.001$). The ipsilateral vibration sensation of the metatarsal heads correlated significantly with the OLST both before and after performing the BEEP ($p < 0.010$). The ipsilateral tactile sensation correlated with OLST only before the BEEP, more with the right ($p < 0.004$) than the left foot ($p < 0.039$). The improvement in OLST after 6 weeks was not correlated to the ipsilateral tactile nor to vibration sensation. The OLST with EC on solid surface improved $\geqslant 300\%$ ($p < 0.001$).The ipsilateral vibration sensation of the right metatarsal heads and first toe correlated significantly with the OLST before performing the BEEP ($p < 0.006$). The ipsilateral tactile sensation of the right foot correlated with OLST before the BEEP ($p < 0.011$). The improvement in OLST after six weeks was not correlated to ipsilateral tactile nor to vibration sensation. On compliant surface with EO the OLST improved 71% for the right and 55% for the left foot ($p < 0.001$). No significant correlations were found for ipsilateral vibration sensation and OLST before the BEEP. Only the ipsilateral vibration sensation of the right metatarsal head correlated with OLST ($p = 0.009$) after the BEEP. The ipsilateral tactile sensation of the right foot, however, correlated with OLST both before and after the BEEP ($p < 0.0116$). The improvement in OLST after six weeks was not correlated to ipsilateral tactile nor to vibration sensation.
Conclusions: The present results indicates that relatively healthy elderly, despite poor vibration proprioception and tactile sensation in the feet, can improve their balance control by performing the self administered BEEP. Thus, it seems like elderly with potentially balance-impairing diminished tactile and vibration sensation in the feet can improve postural balance by compensating with other balance controlling strategies, possibly by strengthening other body segments and improving body segment coordination and interdependency.

X-4
SIX WEEKS OF UNSUPERVISED BALANCE EXERCISES PREFORMED IN THE HOME ENVIRONMENT IMPROVES BALANCE CONTROL FOR RELATIVELY HEALTHY ELDERLY

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Introduction: Fall prevention is an important part of health care for the elderly since approximately 30% of community-dwelling people over 65 years of age fall each year. Elderly and society would greatly benefit if balance exercises performed unsupervised in the home environment could increase balance control and thus reduce the risk of falling.
Objectives: To assess the effectiveness of prescribing a six week balance enhancing exercise program

(BEEP) in static and dynamic balance control in healthy elderly 60 years and older.
Methods: The study was conducted as a randomized controlled crossover trial. 40 relatively healthy community dwelling elderly (70 $\pm$ 5 years old, 22 women and 18 men) were evaluated at the Lund Balance Laboratory where visual, vestibular, proprioceptive, balance, and gait functions were tested. Subjects were randomized to either a balance exercise group (BEG) or an initial control group (CG. The BEG subjects were instructed to perform the BEEP daily during six weeks, whereas the CG subjects were instructed to maintain their routine daily activities. Both groups returned for reevaluation after six weeks. The CG were then asked to perform the BEEP for six weeks and returned for a new evaluation. The BEEP included balance, strength and VOR challenging exercises and was performed for about 15–20 minutes daily without supervision in the home environment. The primary outcome measures included standing ability on one foot (one-legged stance time: OLST) and two feet (posturography) on firm or compliant surfaces and with eyes open (EO) or eyes closed (EC). Other outcome measures were speed and cadency when walking 30 meters, the time up to go (TUG) test, Berg Balance Scale and a modified step stool test.
Results: After performing the BEEP, the OLST on solid surface with EO improved from 37 to 51 s (38%) on the right and from 37 to 50 s (35%) on the left foot ($p < 0.001$). With EC on solid surface the OLST increased threefold on both feet ($p < 0.001$); from 4 to 15 s on the right and from 5 to 16 s on the left foot. With EO on the compliant surface the OLST also improved; from 28 to 48 s (71%) on the right and from 29 to 45 s (55%) on the left foot ($p < 0.001$). Improvements were also made in walking speed ($p < 0.001$), the TUG test ($p = 0.001$), in Berg Balance Scale ($p = 0.018$), as well as the time performing the modified step stool test ($p = 0.001$). The improvements in postural control after the BEEP were confirmed in the posturography tests. Balance had improved significantly when subjects were perturbed standing on solid surface with EO ($p < 0.001$), with EC ($p = 0.001$), and when standing on compliant surface with EO ($p = 0.012$), but not with EC. In the test-re-test evaluation, the CG subjects did not improve their ability to stand on one foot in any of the test conditions nor in any of the posturography tests or other outcome measures, except for a small improvement in walking speed (1.4 to 1.5 m/s; $p = 0.019$).
Conclusions: Performing unsupervised balance exercises for six weeks in the home environment can significantly improve balance control in healthy elderly. We plan to investigate if performing these balance enhancing exercises regularly will prevent future fall accidents for healthy elderly in a follow up study.

X-5
ABNORMALITIES OF FIXATION, SACCADE AND PURSUIT IN POSTERIOR CORTICAL ATROPHY

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Introduction: Patients with posterior cortical atrophy have impairments in visuo-perceptual and visuospatial processing, spelling and calculation, associated with atrophy of the parietal and occipital lobes. Patients are often noted to have clinical features of Balints syndrome – in particular oculomotor apraxia – however the proportion of patients with this symptom varies widely across studies.
Objectives: To systematically record oculomotor function in this patient group, describing the particular characteristics of oculomotor abnormalities in posterior cortical atrophy.
Methods: We recorded fixation, saccade and smooth pursuit eye movements in 20 patients with posterior cortical atrophy (eight male, mean age 63.2 years) using an infrared pupil tracking system. Their performance was compared to that of 22 healthy controls (seven male, mean age 63.3 years) and 12 patients with typical Alzheimer's disease (in whom recent episodic memory was the most prominent symptom; seven male, mean age 69.7). Patient groups were matched for disease duration and MMSE but not age (posterior cortical atrophy patients tend to have an earlier age at onset than typical Alzheimer's patients).
Results: Posterior cortical atrophy patients showed a higher frequency of large saccadic intrusions during fixation compared to both healthy controls and typical Alzheimer's patients. Saccades were hypometric, significantly shorter than those of healthy controls and typical Alzheimer's patients. Both patient groups were impaired compared to healthy controls in the smooth pursuit task. The proportion of posterior cortical atrophy patients falling outside normal levels of control performance (defined as two standard deviations from control mean) was higher than anticipated from previous reports of oculomotor apraxia in this patient group.
Conclusions: This study establishes the oculomotor abnormalities present in posterior cortical atrophy for

the first time, describing features unique to this condition and features in common with typical Alzheimer's disease. The detailed and sensitive tests in this study revealed that such deficits are more common than previously appreciated with a standard clinical examination. The cognitive mechanisms and neurological basis for this impairment are discussed, with the features observed suggesting that both visual cognition and automatic oculomotor mechanisms can be impaired in this patient group.

X-6
AGEING REDUCES VESTIBULO-OCULAR REFLEX ADAPTATION IN MICE

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Introduction: Ageing of the vestibular system is associated with neurodegenerative processes such as loss and functional decrease of vestibular hair cells, vestibular afferents and cells in the central vestibular nuclei. Disequilibrium in the aged is almost three times more prevalent than in the young, and symptoms like dizziness, vertigo and imbalance affect people most during their later years in life. There may be a link between these symptoms and a functional decrease in the vestibulo-ocular reflex (VOR) due to ageing. The VOR is our main vision stabilising system during head movements, and has direct input from the vestibular organs. It is possible that the VOR compensates for neurodegenerative losses via adaptation mechanisms; however, this could result in reduced adaptation capacity available for non-ageing related changes demanded of the VOR.
Objectives: To study age-related changes in VOR function and VOR adaptation using young (3 months old – equivalent to a $\sim$ 10 year old human) and aged (30 months old – equivalent to a $\sim$ 80 year old human) C57BL/6 mice. Methods: We determined the VOR gain (eye velocity/head velocity) in darkness by measuring 3D eye movements in response to whole-body sinusoidal rotations (0.1–10 Hz, at peak velocities 20, 50 and 100°/s). Data was collected from 16 C57BL/6 wild type mice (male and female; 8 young and 8 aged), each contributing to three groups: no training (baseline VOR, ideally gain = 1), gain-increase (x1.5) training, and gain-decrease (x0.5) training in randomised order. VOR adaptation training consisted of whole-body sinusoidal rotations (0.5 Hz, peak-velocity 20°/s, duration 40 minutes) in the horizontal plane synchronised to horizontal rotations of a visual projection (random pattern of light spots projected onto a dome surrounding the animal) in the opposite direction with x0.5 or x1.5 velocity of the vestibular stimulus. The VOR response in darkness was measured immediately after adaptation training.
Results: Our study showed a small, but non-statistically significant, effect of ageing on the baseline VOR response during low-acceleration vestibular stimuli. However, averaged across stimulus velocities and frequencies the VOR gains were similar at $\sim$ 0.80 in both young and aged mice. In contrast, age significantly affected the capacity for VOR adaptation, which was measured as the difference in horizontal VOR gain after gain-increase versus gain-decrease adaptation. In young mice the VOR gain measured at 20°/s (the same velocity used during training) after adaptation training, and averaged across frequencies, was 0.90 for gain-increase and 0.57 for gain-decrease adaptation (a difference of 0.33). In contrast, in aged mice the VOR gain was 0.82 for gain-increase and 0.73 for gain-degrease adaptation (a difference of 0.09). This $\sim$ 72% decrease in adaptation capacity was statistically significant. Comparison of post-adaptation and baseline VOR responses at 20°/s indicated that gain-decrease adaptation was more effected by ageing compared to gain-increase adaptation.
Conclusions: This study shows that ageing minimally affects baseline VOR function, but severely decreases the capacity for VOR adaptation. Our results suggest that the vestibular tonic pathways that predominantly mediate the low-velocity/low-frequency (i.e., low-acceleration) VOR and play a greater role in VOR gain-decrease (compared to gain-increase) adaptation are most affected by ageing.

X-7
FALLS, PRESBYEQUILIBRIUM AND QUALITY OF LIFE AMONG OLDER ADULTS RESIDING IN AN INSTITUTIONAL SETTING AND EFFICACY OF GUIDED AND SELF-TRAINING

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And quality of life, and whether self-administered training is comparable with guided training among older adults residing in an institutional setting. Careful case histories were taken among 72 elderly that

initially participated in the study. In part of the elderly VOG testing were made. A randomized, prospective intervention study among 55 elderly was undertaken. Three intervention groups were evaluated: Muscle force training, balance and muscle force training and self-administered training. Each group underwent one hour's training twice a week for 3 months. Postural stability was measured at onset, after 3 months and after 6 months. Time domain dependent body sway variables were calculated. The fall rate was evaluated for 3 years. General health related quality of life (QoL) was measured with a 15D instrument. Postural stability was used as a primary outcome, with quality of life and falls used as secondary outcomes.

Results: Dizziness, vertigo, poor maintenance of posture, and black-outs were reported by 54 % of the 72 elderly and make them at risk for falls, and reduced quality of life. The most common complaint was postural instability, with a tendency to fall. "Spinning" vertigo and "floating" sensation had a strong inter-correlation and correlated with habitual falls. The various dizziness symptoms often occurred in combinations. Attacks of self-experienced syncope never occurred alone but always in combination with "spinning vertigo" or "tendency to fall". In factorial analysis, presbyequilibrium could be divided into six categories. Two of these categories correlated with falls. In the majority of the elderly, vestibular abnormalities were found, as reduced vestibulo-ocular reflex gain 6/38, spontaneous nystagmus 5/38, gaze deviation nystagmus 5/38, head shaking nystagmus 9/38, pathologic head thrust test 10/38 and positional nystagmus in 17/38. Muscle force trainees were able to undertake training, progressing towards more strenuous exercises. In posturography, after training the number of spiky oscillations was reduced and stationary fields of torque moments of the ankle increased, providing better postural stability in all groups. Especially, the zero crossing rate of weight signal and the number of low variability episodes in the stabilogram were improved after training. No difference was found between different training groups in posturography outcomes, however, a reduction of fall rate was significant only in the guided training groups. A significant part of the variability of the QoL could be explained by the posturography outcome (46%). However, the outcome of training was associated with a reduced QoL.

Conclusions: Even moderate or severely demented residents could do exercises in five person groups under the supervision of a physiotherapist. An improvement in postural stability was observed in all training groups, indicating that even self-administered training could be beneficial. Posturography outcome indicated that training alters the postural strategy by reducing the oscillatory fluctuations of body sway signal. However, only guided training tended to reduce falls. Short training intervention programs may decrease QoL by changing the elderly's daily routine to one which is more active and exhausting.

Oral Presentations Y. Intratympanic Treatment

Y-1
NANOTECHNOLOGY AS IN INNER EAR REGENERATION

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Several novel, multifunctional nanoparticles have been developed, which are targetable to selected tissue, biodegradable, traceable in-vivo, and equipped with controlled payload release. They can be used to transport therapeutic agents, such as drugs, genes, small interfering RNAs (siRNAs) and growth factors into the inner ear. To visualise the targetability and accuracy of the delivery, the nanoparticles can be traced with magnetic resonance imaging (MRI). The NPs are coated with a 'stealth' layer, and decorated with targeting ligands, markers, transfection agents and endosomal escape peptides. As payloads, we have used genes such as the BDNF-gene, Math1-gene and Prestin-gene that we have constructed and delivered in-vitro. shRNA has been used in-vitro to silence the negative regulator of Math1, the inhibitors of differentiation and DNA binding. In order to facilitate the passage of cargo from the middle ear to the inner ear, the oval window transports gadolinium chelate more efficiently than the round window and is the key element in introducing therapeutic agents into the vestibule and cochlea. Depending upon the type of NPs, different migration and cellular internalization pathways are employed, and optimal carriers should be designed depending on the cargo. The use of NPs as drug/gene/siRNA carriers is fascinating and can also be used as an intraoperative adjunct to cochlear implantation to attract the peripheral processes of the cochlear nerve. It is hoped that this technology will come to be used as an alternative carrier to viral vectors traditionally used in gene delivery, but without the severe adverse effect.

Oral Presentations Z. Vestibular Compensation, Rehabilitation, New Treatments

Z-1
TREATMENT OF VESTIBULAR/BALANCE DYSFUNCTION VIA MULTIMODAL VIBROTACTILE, VISUAL, AND AUDITORY FEEDBACK CELEBRATION, FL USA

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Introduction: Military and civilian programs are interested in properly caring for patients with TBI. In the military, signs and symptoms of mTBI include vestibular injury resulting in dysequilibrium, dizziness, and imbalance. Likewise, older populations with vestibular deficit dizziness, imbalance, and resultant falls are significant burdens of care worldwide. Multimodal Sensory Enrichment Device (SEMD) is a medical device system for assessment and rehabilitation of patients with dizziness, balance deficit, and/or movement disorders. SEMD provides vibrotactile, visual, and audio cueing within a hierarchy of skill set protocols. Objectives: A prospective, case control, multi-site, clinical trial Clinical Trial Evaluation of a Sensory Enrichment Multimodal Device (SEMD) on Physical Therapy Patients with Dysequilibrium investigated the relationship between specialized vestibular-balance physical therapy intervention and specialized vestibular-balance physical therapy plus SEMD.
Methods: Twenty-five civilian subjects, controls 8 males/7 females and device 4 male/10 females, ages 51 to 84 years, at three investigational sites, completed up to 12 physical therapy sessions with outcome data collected.
Results: A strong trend supporting SEMD as a device that improves restoration of vestibular input was found by treatment session 2. In addition, a beneficial effect reducing fall risk measured by Berg Balance Score, and increasing number of No-falls on Condition 5 Sensory Organization Test and Self-report Falls in the physical therapy plus SEMD group by treatment session 4 was found. The physical therapy only group achieved these results after treatment session 12.
Conclusions: This study demonstrates SEMD efficiency in decreasing number of physical therapy visits and improving early on outcomes in vestibular function, fall risk and actual falls in physical therapy patients with vestibular and balance deficits.

Z-2
VESTIBULAR REHABILITATION: ASSESSMENT AND RESULTS

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Introduction: Vestibular rehabilitation is indicated when medication, liberatory manoeuvres or natural exercises of daily life are not enough to completely cure or completely compensate vestibular diseases. The aim of this study is to situate which factors prevent natural vestibular compensation and to present our vestibular techniques' in order to build specific program for each. 250 patients underwent vestibular rehabilitation in our center. Three general principles guide us: – we tried to discover if the subject has changed the relative weight of visual and proprioceptive inputs since his vestibular pathology. The goal is to highlight a proprioceptive, vestibular or visual dependency with questionnaires and physical exercises. – we looked for the factors that could prevent the subject to compensate naturally or spontaneously: co-morbidity, the intensity of feeling of the vertigo crisis and or the psychosocial context during the vertigo crisis and the compensation period – rebuild balance with exercises which increase the weight of the vestibular input and improve the quality and weight of the other inputs.
Material and methods: We performed a battery of tests to analyse the balance and sensations of the patient. For each exercise, we appreciate the performance and the feeling during minimum one minute. The aim is to discover which exercises triggers symptoms of the patient in order to guess the compensation mechanisms of the patient. We use mainly exercises, eyes open and closed, on foams or wide slow optokinetic stimulations. We will present our original exercise on the visual input through simple exercises for highlighting a gaze avoidance behaviour and to teach them how to use and to tolerate the "automatic" system of stabilisation of visual surrounding during self-motion (walking, during a slow rotation on moving chair, and during wide optokinetic stimulation. The hypothesis is that the vertigo chronic patient has a tendency to control eye movements voluntary rather than to use the "automatic" physiological spontaneous eye movement because he/she try to avoid the perception of apparent visual surrounding motion during self-moving.
Results: Meniere disease (20%), unilateral canal paresis (19%) unsteadiness (12%) are the most frequent aetiologies of all patients (group P). Two sub-groups

are distinguished; group A with patients who underwent only 1–4 sessions (36.8%) and group B who underwent more than 4 sessions (63.2%). Mean numbers of sessions in group B is 10. In group A, the patients with neuroma or bilateral vestibular areflexia are the most frequent aetiologies. Patients in this group stopped early the rehabilitation because they feel cured (35%), non motivated (19%), satisfied (7%). In group B, abnomalities in otoneurologic examination is found in 31% of cases. Main symptom of patients was unsteadiness (75%), vertigo (28%), isolated visual dependence, depression (38%). On foam, 63% of patients were disturbed and foam triggered the main symptom of 32% of patients. On rotating chair, 42% were disturbed at least once and 8% were disturbed only in one condition. Global results of rehabilitation: improvement in 41%; satisfaction in 52%; and failure in 7% (mainly bilateral areflexia and pseudo neuritis).

Z-3
CENTRAL NEURON RESPONSES INDUCED BY VESTIBULAR PROSTHESIS STIMULATION: IMPLICATIONS FOR VESTIBULAR FUNCTION

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Loss of vestibular function is relatively common in humans, and can cause gaze and balance instability. We have focused on the development of a chronically implanted vestibular prosthesis to improve functional outcomes in patients suffering from bilateral vestibular deficiency. This device consists of a gyroscope, which senses the movement of the head, and electrode arrays implanted in each semicircular canal, which stimulate the vestibular nerve to send head motion information to the brainstem. Recent studies by us and others have shown that vestibular prostheses stimulation can elicit vestibulo-ocular reflex (VOR) responses. However, the gain and time constant values of the evoked VOR eye movements are lower than those observed in response to natural stimulation. To improve behavioral performance it is essential to understand how the brain responds to this type of stimulation. Accordingly, here we sought to first determine whether prosthetic stimulation could evoke other vestibular reflexive responses such as vestibulo-collic reflexes (i.e., VCR; reflexive head movements). Next we determined how neurons mediating reflexive movements (i.e., VOR and VCR) respond to prosthetic stimulation.
Each monkey was chronically implanted with an array of electrodes located near the crista termination of each semicircular canal ampullary nerve. Maximum current amplitudes were set to 80% of the value at which facial muscle activation was visible using biphasic pulses (200 μs/phase). Thirty stimulation pulse trains lasting 100ms were delivered via the horizontal canal electrode for each current amplitude (12.5, 25, 50, 75 and 100% of the maximum current) and pulse rate (50, 100, 200 and 300 pps). We found that stimulation consistently evoked significant head as well as eye movements in the direction contraversive to the stimulated nerve. Additionally, although the evoked head movements were significantly smaller than the evoked eye movements, they substantially contributed to gaze stabilization after 75 ms (20–30%). Interestingly, head movement latencies were considerably longer than those of the eye (40 versus 5 ms), suggesting the vestibulo-collic reflex pathways play a less dominant role than direct VOR pathways in gaze stabilization.
Next, we identified central vestibular neurons that receive direct input from the vestibular nerve, and determined the stimulation current amplitude for each unit by gradually increasing the current amplitude of biphasic pulses (200ìs/phase) delivered at 100 pps until spikes were reliably evoked at monosynaptic latencies (0.7–1.3 ms). Next, we applied pulse trains of 50pps-300pps to determine how neurons responded to sustained stimulation. We found that each neuron's spiking activity was highly time locked to pulses delivered through the prosthesis providing evidence that the vestibular afferent population was synchronously activated by prosthetic stimulation, which in turn drove synchronous central responses. We hypothesize that this synchronicity is in part the cause for the differences in vestibular reflex efficacy and dynamics induced by vestibular prosthesis thus far (as compared to natural head-motion stimulation), and predict that desynchronizing afferent inputs will enhance the response of central vestibular neurons to prosthetic stimulation thereby improving behavioral performance.

Z-4
BALANCE: HEAD REFERENCED COCHLEAR IMPLANT STIMULATION IMPROVES BALANCE IN CHILDREN WITH COCHLEOVESTIBULAR LOSS

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Objective: To improve balance in children with cochleovestibular loss by providing head referenced stimulation through bilateral cochlear implants (CI).
Method: Balance was assessed in 10 children with known vestibular dysfunction in two conditions presented randomly: with and without CI stimulation being linked to head referenced deviations from center of gravity. Balance was tested using the Bruininks-Oseretsky Test (BOT-2) in a "real-world" virtual-environment at the Challenging Environmental Assessment lab. Light-emitting markers measured angular movements of the head and trunk and center of pressure was measured using forceplates lining the floor.
Results: Head reference CI stimulation significantly improved static and dynamic balance in CI users as measured by the BOT-2 ($p = 0.0003$). Time to fall improved significantly in tasks of moderate difficulty ($p = 0.02$) but both the easiest and most difficult tasks yielded less prominent improvements. Angular deviations of the head and trunk were significantly reduced in tasks where vision (eyes closed) and proprioceptive (balance beam) inputs were limited ($p = 0.04$ and 0.05, respectively). Overall postural stability also improved with head-referenced stimulation as demonstrated by a reduction in center of pressure path length ($p = 0.018$).
Conclusion: Remaining upright requires careful integration of visual, proprioceptive and vestibular information and is significantly impaired in children with cochleovestibular loss. Head referenced stimulation delivered via bilateral CI improved static and dynamic balance and improved postural control in children with cochleovestibular loss thus providing a potential therapeutic intervention for this functional challenge.

Z-5
THE GENEVA-MAASTRICHT VESTIBULAR NEUROPROSTHESIS PROTOTYPE: IMPROVED DYNAMIC VISUAL ACUITY IN 5 PATIENTS WITH A BILATERAL VESTIBULAR LOSS

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Introduction: We have previously demonstrated that over 80% of patients with a bilateral loss of the vestibular function (BVL) have abnormal visual acuity (VA) loss when walking, which correlated with the presence of handicapping oscillopsia.
Objectives: In this study we aimed to significantly improve the dynamic VA using the Geneva-Maastricht vestibular implant prototype.
Methods: Five BVL patients, unilaterally or bilaterally deaf, were fitted with the Geneva-Maastricht vestibular implant (GM-VI), which is a modified cochlear implant (MED-EL) with "vestibular" electrodes. Motion sensors fixed to the patient's head, provided motion information to a regular cochlear implant processor, which controlled the electrical stimulation delivered through the "vestibular" electrodes. For this experiment, only the electrode in contact with the posterior ampullary nerve was active. VA was determined using Sloan letters displayed on a computer screen (Logarithm of the Minimum Angle of Resolution [logMAR] units), in four conditions: (1) with the patient standing still without moving (static), (2) while the patient was walking on a treadmill at constant speed with the GM-VI turned off (system OFF), (3) while the patient was walking on a treadmill at constant speed with the GM-VI turned on providing coherent motion information (system ONmotion), and (4) while the patient was walking on a treadmill at constant speed with the GM-VI turned on but providing aberrant (e.g., out-of-phase) motion information (system ONnoise). The dynamic VA loss (static VA – VA while walking) in the system OFF and ON conditions was computed and compared.
Results: The mean dynamic VA loss in the system OFF condition was 0.14 logMAR (standard error of the mean, SEM = 0.01). In the system ONmotion condition, the dynamic VA loss improved to an average of 0.03 logMAR (SEM = 0.01), a minimal loss close to that observed in subjects with normal vestibular function. On the contrary, no improvement was observed in the system ONnoise condition (mean = 0.13, SEM = 0.02). The significant differences between conditions were clinically (> 0.1 logMAR) and statistically significant (One way repeated measures analysis of variance: $F(2,8) = 30.11$, $p < 0.001$; Post-hoc Tukey tests: system OFF vs system ONmotion $p < 0.001$, system ONmotion vs system ONnoise $p < 0.001$; system OFF vs system ONnoise $p = 0.84$).
Conclusions: By selectively delivering motion information to the vestibular nerve, it is possible to significantly improve or even normalize the dynamic VA during walking in BVL patients. This clearly demonstrates the rehabilitation potential of the Geneva-Maastricht vestibular implant and opens new treatment perspectives for a patient population for whom no convincing therapeutic options exist today.

Z-6
N-ACETYL-L-LEUCINE ACCELERATES VESTIBULAR COMPENSATION BY ACTION IN THE CEREBELLUM AND THALAMUS

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Background and aim: An acute unilateral vestibular lesion leads to a vestibular tone imbalance with nystagmus, head roll tilt and postural imbalance. These deficits gradually decrease over days to weeks due to central vestibular compensation (VC). This study investigated the effects of i.v. N-acetyl-DL-leucine, N-acetyl-L-leucine and N-acetyl-D-leucine on VC using behavioural testing and serial [18F]-Fluoro-desoxyglucose ([18F]-FDG)-μPET in a rat model of acute unilateral chemical labyrinthectomy (UL).
Methods: Vestibular behavioural testing included measurements of nystagmus, head roll tilt and postural imbalance before and on days 1, 2, 3, 5, 7, 9, and 15 after UL. In addition, sequential whole-brain [18F]-FDG-μPET was performed before and on days 1, 3, 7, 15 after UL.
Results: A significant reduction of postural imbalance scores was identified on day 7 in the N-acetyl-DL-leucine ($p < 0.03$) and the N-acetyl-L-leucine groups ($p < 0.01$), compared to the control group, but not in the N-acetyl-D-leucine group (comparison for applied dose of 24 mg i.v. per rat, equivalent to 60 mg/kg body weight, in each group). The course of postural compensation in the DL- and L-group was accelerated by about 6 days relative to controls. The effect of N-acetyl-L-leucine on postural compensation depended on the dose: in contrast to 60 mg/kg, doses of 15 mg/kg and 3.75 mg/kg had no significant effect. Measurements of the regional cerebral metabolic rate for glucose (rCGMglc) by means of μPET revealed that only N-acetyl-L-leucine but not N-acetyl-D-leucine caused a significant increase of rCGMglc in the vestibulocerebellum and a decrease in the posterolateral thalamus and subthalamic region on days 3 and 7.
Conclusions: N-acetyl-L-leucine improves compensation of postural symptoms after UL in a dose-dependent manner, most likely by activating the vestibulocerebellum and deactivating the posterolateral thalamus.

Z-7
ATTENTION MODULATES ADAPTIVE MOTOR LEARNING IN THE "BROKEN ESCALATOR" PARADIGM LOCOMOTOR AFTER-EFFECT

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Introduction: The physical stumble caused by stepping onto a broken (stationary) escalator represents a locomotor after-effect (LAE) that attests to a process of adaptive motor learning.
Objective: To assess whether this adaptive learning process is primarily explicit (requiring attention resources) or implicit (independent of attention).
Methods: To address this question, we diverted attention in the MOVING and AFTER phases of the LAE by loading these phases with a secondary cognitive task (sequential naming of a vegetable, fruit, and a colour). Thirty-six healthy adults were randomly assigned to 3 equally sized groups. They performed 5 trials stepping onto a stationary sled (BEFORE trials), 5 with the sled moving (MOVING trials) and 5 with the sled stationary again (AFTER trials). A 'Dual-Task- MOVING (DTM)' group performed the dual-task in the MOVING phase and the 'Dual-Task-AFTER-EFFECT (DTAE)' group in the AFTER phase. The 'Control' group performed no dual-task. We recorded trunk displacement, gait velocity and gastrocnemius muscle EMG of the left (leading) leg.
Results: During the MOVING trials, the DTM, but not the DTAE group, had larger levels of trunk displacement compared to controls. An after-effect was seen in the first AFTER trial (AFTER trial 1) in all groups. The DTM group, however, had a significantly smaller trunk displacement after-effect compared to controls. There was no difference between the DTAE group and controls. Gait velocity was unaffected by performing the secondary cognitive task in both groups.
Conclusions: Locomotor skill adaptive learning involves explicit locomotor learning, whereas once acquired, its expression is automatic (implicit). Our findings suggest that the degree of automaticity is greater for motor skill execution than for its acquisition. Such explicit and implicit modes of learning offer flexibility to multi-task in day-to-day activities. In the clinical setting patients should be actively encouraged to maintain maximal attention when learning new or challenging locomotor tasks during rehabilitation.

Z-8
EFFECTIVENESS OF CONVENTIONAL VERSUS VIRTUAL REALITY-BASED VESTIBULAR REHABILITATION IN THE TREATMENT OF DIZZINESS, GAIT AND BALANCE IMPAIRMENT IN UNILATERAL PERIPHERAL VESTIBULAR HYPOFUNCTION

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Introduction: Unilateral peripheral vestibular disease results in gait and balance impairment, dizziness and oscillopsia. Vestibular rehabilitation is of benefit, but optimal treatment has not been elucidated. The Nintendo Wii Fit Plus is a low cost virtual reality system that challenges balance and provides visual and auditory feedback. It may improve motor re-learning of balance and patient satisfaction with treatment.
Objectives: The objective of this study was to compare the effectiveness of Nintendo Wii Fit Plus based vestibular rehabilitation to conventional vestibular rehabilitation, in patients with peripheral vestibular hypofunction.
Methods: In an assessor blind, two centre, randomised controlled trial, 71 patients with unilateral peripheral vestibular hypofunction were randomly allocated to either conventional ($n = 36$) or virtual reality based ($n = 35$) vestibular rehabilitation for 6 weeks. Patients in the virtual reality group received a Nintendo Wii Fit Plus to exercise with at home and patients in the conventional group received a foam balance mat. Treatment consisted of weekly visits to a physiotherapist and a progressive daily home exercise program. The primary outcome measure was gait speed (measured with three dimensional gait analysis). Secondary outcomes included computerised dynamic posturography, dynamic visual acuity, the Hospital Anxiety and Depression Score, the Vestibular Rehabilitation Benefits Questionnaire, and the Activities Balance Confidence Questionnaire. Outcomes were assessed post treatment and at 6 months. Ethical approval was obtained from both centres.
Results: There were no significant differences in gait speed between the groups post intervention (adjusted mean difference -0.03 m/sec; 95% CI -0.09¡æ0.02 m/sec). There were also no significant differences between the groups on computerised dynamic posturography (Composite Score of Sensory Organisation Test, adjusted mean difference; $+0.82\%$; 95% CI -5.00¡æ6.63%) or on any of the other secondary outcomes ($P > 0.05$). In both groups, adherence to exercise was high ($\sim 77\%$) but the Wii group reported significantly more enjoyment ($p = 0.001$), less difficulty with ($p = 0.03$), and tiredness after ($p = 0.03$) exercises. Similarly, at six months there were no significant differences in physical outcomes between the groups.
Conclusion: The study suggested that the Nintendo Wii Fit Plus¢â provided a more enjoyable method of retraining balance in patients with peripheral vestibular hypofunction, however it was not superior to conventional vestibular rehabilitation.

Z-9
CENTRAL ADAPTATION TO REPEATED GALVANIC VESTIBULAR STIMULATION: POTENTIAL FOR TREATMENT OF INTRACTABLE VERTIGO

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Introduction: GVS activates canal and otolith afferents of all directional preferences simultaneously, and the response is unlike any produced by natural motion. We studied adaptation to repeated GVS exposure over a period of 12 weeks.
Methods: Subjects (10) were exposed to a total of 10 min pseudorandom bilateral bipolar GVS per week (120 min total) whilst performing computerized dynamic posturography (CDP) and tandem (heel-toe) walking. In addition, 3D eye movements were acquired with video-oculography. Follow-up tests were performed at week 18 and 36.
Results: During GVS there was a significant decrease in the CDP vestibular index at week 1, which returned to baseline in an exponential manner over a period of weeks, and this improvement was maintained during follow-up testing on week 18 and 36. Similarly, no subject could perform the tandem walk with GVS at week 1, but by week 12 could walk an average of 9 steps without breaking stride. Low-level reflex responses, such as mediolateral sway and the ocular torsion response, were unchanged over the 12-week period of exposure to GVS (and at follow-up). In contrast, complex behavior that required central integration of vestibular, visual and somatosen-

sory input at the level of the cerebellum, such as CDP and tandem walking, returned to baseline during adaptation to repeat GVS exposures. This suggests that GVS adaptation did not occur at the vestibular end-organs or involve changes in low-level vestibulo-ocular or vestibulo-spinal reflexes. Faced with unreliable vestibular input, the CNS reweighted sensory input to emphasize veridical somatosensory and visual information to regain postural and locomotor function. After a period of recovery subjects exhibited dual adaption and the ability to rapidly switch between the perturbed and natural vestibular state for up to 6 months. In a subsequent experiment, GVS-adapted subjects performed significantly better than controls on a visual nulling task in the presence of random motion perturbations, which suggests that repeated exposure and adaption to pseudorandom GVS improved subsequent ability to ignore disruptive vestibular input and switch to more veridical modalities (vision, proprioception). We have begun to explore the possibility that adaptation to pseudorandom GVS may prove beneficial in patients with intractable vertigo. To date, five patients have undergone the GVS adaptation protocol, three of which have reported significant alleviation of symptoms post-treatment.

Conclusion: Although preliminary, these pilot results suggest a potential for GVS training to improve quality of life in this difficult to manage patient group.

Z-10
THE GENEVA-MAASTRICHT VESTIBULAR NEUROPROSTHESIS PROTOTYPE: UPDATE ON THE RESULTS OBTAINED IN THE FIRST 11 PATIENTS IMPLANTED BETWEEN 2007 AND 2013

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Introduction: For a decade our group has pioneered the field of electrical stimulation of the vestibular nerve in humans with a bilateral loss of the vestibular function (BVL). Our ambitious aim is to artificially restore vestibular function in this patient population using a concept similar to that of cochlear implants for the rehabilitation of profound deafness.

Objectives: Up-to-date report of unique data obtained in the first 11 patients fitted with our vestibular neuroprosthesis prototype.

Methods: Eleven patients with a BVL, unilaterally or bilaterally deaf, were fitted with a modified cochlear implant (MED-EL) providing 1 to 3 "vestibular" electrodes in addition to the "standard" cochlear array. Vestibular electrodes were implanted in the vicinity of the posterior (PAN), lateral (LAN), or superior (SAN) ampullary nerves. During testing sessions, steady-state electrical stimulation was delivered to each vestibular electrode (separately). Then, the amplitude of electrical stimulation was modulated in order to elicit controlled eye movements. We report our clinical experience with the device, as well as maximum amplitude, peak velocity, and axis of electrically evoked eye movements. We also verified the potential impact of the observed responses on vision by measuring visual acuity during electrical stimulation trials. Patients' perception was documented.

Results: At the time of writing of this abstract, the longest follow-up period was of 6 years 7 months (implantation July 2007), and the shortest was of 7 months (implantation July 2013). We observed no surgical/medical complications related to implantations. Electrically evoked eye movements were successfully evoked upon stimulation in 21 out of the total 24 implanted electrodes. The 3 non-responsive electrodes (in two patients) were out of position as revealed by CT imaging. The evolution of electrical thresholds and impedances was comparable to that of "cochlear" electrodes. The maximum eye movement amplitude recorded was of 2.9° for the PAN, of 4.9° for the LAN and of 2.7° for the SAN. Maximum observed peak velocities were 45°/s for the PAN, 85°/s for the LAN, and 48°/s for the SAN. The axis of the evoked eye movements was consistent with PAN stimulation in 8 out of 11 PAN electrodes (angle $>75°$), in 2 out of 6 LAN electrodes (angle $<25°$), and in 4 out of 6 SAN electrodes (angle $< -75°$). Electrically evoked eye movements resulted in a clinically significant loss of visual acuity (>0.1 logMAR) in 5 out of the 11 PAN/SAN electrodes. Sensations other than vestibular (e.g., auditory, somatosensory) were reported.

Conclusions: Chronic electrical stimulation of the ampullary nerves appears technically feasible using our vestibular neuroprosthesis prototype in humans with a BVL of different etiologies and substantially different disease durations. Amplitude modulated stimulation resulted in controlled eye movements with good directional sensitivity in more than 60% implanted electrodes. These eye movements were often within the range of natural compensatory eye movements generated in every-day dynamic conditions such as walk-

ing and large enough to significantly alter the patients' visual abilities. Perceptive findings suggest current spread to nearby neural structures.

Z-11
THE GENEVA-MAASTRICHT VESTIBULAR NEUROPROSTHESIS PROTOTYPE: CHALLENGING THE VOR IN PATIENTS WITH BILATERAL VESTIBULAR LOSS

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Introduction: The vestibulo-ocular reflex (VOR) allows optimal gaze stabilization during fast, high frequency head movements. It is a highly plastic reflex. The VOR is commonly assessed during whole body rotation around the vertical axis. Under those conditions, the expected VOR is predominantly horizontal as it results from activation of the horizontal canals. By performing such a test while selectively delivering motion information to the posterior ampullary nerve in a patient with a bilateral vestibular loss (BVL) using the Geneva-Maastricht vestibular neuroprosthesis, we measured an immediate, almost purely horizontal VOR. Our setup gave us the unique opportunity to compare VOR characteristics during real and virtual motion. Objective: To challenge the VOR plasticity in BVL patients by selectively delivering motion information to vertical canals while rotating around the vertical axis.
Material and methods: Three BVL patients, unilaterally or bilaterally deaf, were fitted with the Geneva-Maastricht vestibular implant (GM-VI). This is a modified cochlear implant (MED-EL) with "vestibular" electrodes. Motion sensors mounted on a rotatory chair allowed motion-induced modulation of the amplitude of a baseline electrical stimulation of the posterior (PAN) or superior (SAN) ampullary nerve. The motion stimulus was a sinusoidal rotation around the vertical axis (f = 1 Hz, ùmax = 30°/s). The VOR was measured in three conditions in dark: 1) Dynamic with the system OFF (patient sitting on the rotating chair with GM-VI OFF), 2) Dynamic with the system ON (patient sitting on the rotating chair with GM-VI ON), and 3) Static (patient sitting on a chair besides the rotating chair with the GM-VI ON).
Results: The same electrical stimuli evoked different VOR-responses. A predominantly vertical VOR was elicited in the static condition whereas a predominantly horizontal VOR was elicited in the dynamic conditions. The VOR obtained in the GM-VI ON condition was much more pronounced than the minimal (residual) VOR obtained in the GM-VI OFF condition.
Conclusion: The observation made in one patient is reproducible and consistent. Activation of vertical canals using the GM-VI generates predominantly vertical eye movements in static conditions. However in dynamic conditions, additional proprioceptive and possibly minimal residual vestibular input seem to be enough for adapting the VOR to the real motion. This is very promising, suggesting that a vestibular prosthesis may not have to perfectly mimic the natural system to improve the condition of patients with bilateral vestibular loss. No funding or other support received.

Z-12
EHEALTH IN MENIÈRE'S DISEASE: A WEB-BASED PEER-SUPPORT PROGRAM

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Aim: Web-based peer support has different challenges compared to personal peer support and the most demanding task is to be person-focused. In this paper we present a peer support programme for Menière's disorder (MD) that uses data base resources, applies artificial intelligence in decision making, and has a user centred approach in determining the impact of the disorder and in the patient empowering process.
Methods: Data was retrieved from 740 cases of MD to develop the program. The program uses pattern recognition in the diagnosis of MD. The impact of MD is assessed by ICF-based structured questions. Personal data on quality of life, personal traits, complaints, and attitude are collected interactively. The Norton-Kaplan model is applied to construct a strategic person-focused approach. By working on critical success factors, short term goals are then pursued.
Results: The peer-support program comprises the following elements: It first assesses the diagnosis and individual participant's disorder profile. Thereafter it interactively determines the impact caused by the disorder using ICF classification, evaluates personal traits and attitudes towards the disorder, and identifies positive aspects. The eligibility of the subject to enter the

program is based on their diagnosis and quality of life score. The inference engine uses a database to compare the impact of the complaints, personal traits and attitudes with 50 referents. In the therapeutic component, the participant defines vision, time frame, inspects confounding factors, determines goals, establishes a strategy and starts to work on the three most important ICF-based problems caused by the disorder. Interactively with the person, the program guides them to find solutions that minimise their restrictions. The program utilizes collaboration with significant others and enhances positive thinking. To assist the person to cope, reference data on coping strategy are retrieved from the database. In the outcome analysis, several measures including quality of life, post traumatic growth factor index and personal satisfaction are used. The program provides a hard copy of personal complaints, problems, strategy, attitude, goals and outcome measures. The information package contains pdf-files of major complaints, 240 animated slides and 12 video case histories.

Conclusions: We have created a web-based peer-support system that is user-centred, able to classify the characteristics, profile the impact of the disorder, assist in decision making, and interact with the individual participant. The programme contains a large database on the complaints and impact of MD. The modified Kaplan-Norton model is used to establish a personal strategy that empowers the participant and improves coping with the disorder.

Z-13
MULTIPLE TIMESCALES IN THE ADAPTATION OF THE ANGULAR VOR

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Motor learning in voluntary movements such as saccades and pointing was shown to rely on memory processes having multiple timescales. Learning affects the forward sensory model in the cerebellum through highly adaptable states which learn quickly from motor errors but have poor retention, and through more stable states that learn more slowly but have greater retention. We have investigated whether a similar learning mechanism holds also for adaptation of the vestibulo ocular reflex, exploiting retinal slip with transient head rotations as an adaptive stimulus. Eight healthy subjects were recorded in a paradigm comprising a set of incremental gain reduction trials followed by a shorter set of trials asking for an incremental gain increase, and a final set of catch trials in which the subject had no feedback on the performance of the VOR. The latter allowed assessing whether spontaneous recovery of the previously adapted low gain state occurred. Our results show that multiple timescales are present in short-term VOR adaptation and that these may act on the forward model of the ocular motor plant in the cerebellar flocculus. Such a finding could be of great relevance to the design of new vestibular rehabilitation approaches.

Z-14
ANTAGONISM OF ELECTRIC FIELD DISRUPTION OF VISUAL PERCEPTUAL PERFORMANCE IN HUMAN V5/MT BY DOPAMINE D1 RECEPTOR ACTIVATION

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We have previously shown that vestibular activation can selectively modulate visual cortex excitability, raising the possibility that approaches that modulate visual cortical may be used to promote vestibular rehabilitation. Clinical observations such as reports of visual hallucinations with dopa therapy in Parkinsons Disease, suggest that dopamine may enhance visual cortical responsivity and hence may be useful for vestibular therapy. Another aspect pertinent to symptoms in patients with sensory deficits is the increase in uncertainty of sensory estimates of events in the external world due to increased 'sensory noise'. Increased sensory 'noise' in the visual cortex can be modelled by applying TMS (transcranial magnetic stimulation) to the visual cortex. We thus applied TMS to left V5/MT when volunteers were required to determine the net direction of coherently moving dots embedded within a cloud of random dots (i.e. a random dot kinematogram – RDK). The RDK display lasted 200ms and could appear either in the right or left visual field. By varying the ratio of coherent to random dots within the RDK, we could modulate task difficulty of indicating the overall dot direction. Critically, stimulating left V5/MT evokes a phosphene in the right visual field that overlay the location of the RDK in that hemifield but not of a RDK in the left hemifield. When the TMS and right hemifield RDK onset was contemporaneous, subjects' discrimination of RDK dot direction was worse when compared to performance for RDK appearing in the left hemifield. We assessed the ef-

fect of placebo, pergolide (a dopamine D1/D2 agonist) and cabergoline (a D2 agonist) on modulating visual perceptual performance in visual motion discrimination of a random dot display. On each session, calibration of both the TMS intensity (titrated to 79% phosphene reports) and visual perceptual performance (titrated to 79% correct left-right responses) was obtained using an automated Bayesian algorithm. Twelve male volunteers were tested in a double-blinded fashion on 3 sessions separated by at least 10 days, using a William's balanced order design (to counteract carryover effects). We assessed the effect of dopamine absorption by measuring baseline and post-dose serum Prolactin levels. The TMS could be at the onset of the RDK or be 200 ms before or after the RDK onset. A 3×2 ANOVA (time: -200, 0, 200 ms and laterality: right vs left hemifield) showed a main effect of laterality ($P < 0.05$) for both placebo and cabergoline but not pergolide ($P = 0.8$). The main effect was seen at time $= 0$ ms condition (simultaneous TMS and RDK) whereby performance was worse for the right hemifield RDK compared to left for placebo and cabergoline but not for pergolide. Our data suggest that pergolide (dopamine D1 and D2 receptor agonist) but not cabergoline (D2 agonist) antagonises the disrupting effect of TMS upon visual perceptual performance. These data suggest that further work is required to assess the clinical merits of employing dopamine D1 activation in modulating visual perceptual performance and hence as an aid to vestibular rehabilitation.

Z-15
A NOVEL PARADIGM THAT RESTORES VESTIBULAR FUNCTION USING IMPERCEPTIBLE GVS STIMULATION

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Loss of vestibular function occurs with both disease and aging, but currently there are limited options to treat this loss. Recent evidence has demonstrated that the introduction of an imperceptible level of electrical noise stimulation is actually able to improve neural signals, rather than impair them. We tested the ability to improve vestibular function, specifically the vestibular ocular reflex of ocular counter-roll, a measure of otolith function, in a group of veterans.

To test this we applied imperceptible levels of electrical noise to electrodes located over the mastoid process during sinusoidal roll tilt of $\pm$ 25 degrees at 3 frequencies (0.03125, 0.125 & 0.25 Hz) in 20 veterans (48 $\pm$ 15 years). We examined ocular counter-roll (OCR) during tilt, a reflexive eye rotation in the opposite direction mediated through the vestibular system, specifically the otoliths (utricles). Stimulation levels during noise application were a mena of 0 mA with peak stim values of 0.30 $\pm$ 0.08 mA which could not be sensed by the participants. All testing was done in a double blind fashion with neither the experimenter nor participant knowing if it was stimulation or sham trial.

Using this stimulus we were able to significantly increase OCR at all 3 frequencies (0.03125: $+38 \pm 10\%$; 0.125: $+37 \pm 6\%$; $+85 \pm 41\%$; $P < 0.001$). What was even more impressive was that not only were we able to obtain an approximately 40% increase in OCR but we were able to demonstrate increases in 18/20 subjects at 0.03125 Hz, 19/20 subjects at 0.125 Hz, 17/20 subjects at 0.2 Hz. This increase was also linearly correlated with baseline OCR at all frequencies (0.03125: R $= -0.57$, $P = 0.008$; 0.125: R $= -0.667$, $P = 0.002$; 0.2: R $= -0.40$, $P = 0.081$). Thus, subjects with lower initial OCR were more likely to demonstrate greater increases in OCR during stimulation. Beyond the increase in OCR, stimulation improved balance. There was a significant increase in equilibrium scores during quiet standing on a foam block (Sham: 80.9 $\pm$ 2.5 to Stim: 82.9 $\pm$ 2.8) and quiet standing on foam block with eyes closed (Sham: 65.7 $\pm$ 3.3 to Stim: 71.6 $\pm$ 3.4, $P = 0.006$).

These findings demonstrate that vestibular function can enhanced in those that have lost vestibular function using a GVS stimulation paradigm that is imperceptible to the patient. This stimulation not only improves OCR but also produces a functional improvement in balance. This novel paradigm could provide a completely new treatment paradigm for vestibular loss. Future work to determine effectiveness of stimulation over long term periods are necessary to use this paradigm as a treatment. Supported by the War Related Illness & Injury Study Center, Veterans Administration and NIH grant R21DC009900 (Serrador).

Z-16
BILATERAL HIGH VELOCITY VESTIBULAR LOSS: VESTIBULAR REHABILITATION TREATMENT OUTCOMES

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Introduction: Dizziness with rapid head movement, oscillopsia and imbalance are a challenging collection

of symptoms, often causing patients significant disability. In the setting of these symptoms, testing will often reveal normal ENG calorics, but with a detailed clinical examination and laboratory testing with a magnetic scleral search coil (MSSC) and/or vestibular head impulse goggles (vHIT), a diagnosis of bilateral isolated high velocity vestibular loss (HVVL) can often be made. Although relatively recently described, HVVL has been shown to produce a substantial symptom burden. No treatment has been shown to be effective for this diagnosis.

Objectives: To determine if focused Vestibular Rehabilitation Therapy (VRT) improves the symptoms caused by reduction of the VOR at high velocities of angular head rotation and to determine the potential nature of this change.

Methods: 8 patients, identified as having normal caloric function but a diagnosis of HVVL (confirmed with MSSC and/or vHIT testing), were recruited. All patients underwent traditional VRT, which focused three main areas: adapting the gain of the VOR, centered around the higher velocities, as well as balance and gait retraining.

Results: All patients reported clinical improvement. Mean VOR gain at $>200°$/s prior to treatment was 0.70; following treatment, this improved to 0.91 ($p < 0.001$). Dynamic visual acuity improved from a mean of 5.4 lines lost on the LogMAR chart to 2.4 lines lost. The mean score on the Dizziness Handicap Inventory (DHI) improved from 46.75 to 38. Mean scores on the Activities Specific Balance Confidence Scale improved from 50 to 71.43%. Mean Dynamic Gait index scores improved from 18 to 23.34. Of the 8 patients, only one could complete condition 4 of the Modified Clinical Test of Sensory Interaction in Balance at the commencement of VRT (mean time to fall of 10.4 seconds (SD = 8.1)); this improved to 7 of 8 at the end of treatment ($p = 0.01$).

Conclusions: HVVL is under-diagnosed. Once identified it appears that a customized VRT program is a viable treatment option to improve the gains of the VOR and to make functional subjective and objective improvements, thus reducing the impact of the condition.

Z-17
CEREBELLAR ATAXIA WITH BILATERAL VESTIBULOPATHY: TREATMENT OPTIONS

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Introduction: Cerebellar Ataxia with Bilateral Vestibulopathy (CABV) is a recently described condition. Patients experience falls, gait and balance disturbances and become dizzy with rapid head movements. Historically, patients were given a poor prognosis, given their characteristically progressive symptoms. This often led to patients adopting behaviours that accelerated their functional decline.

Objective: To ascertain if patients with CABV could obtain benefit from a program of vestibular rehabilitation therapy to improve quality of life, reduce subjective complaints of dizziness/imbalance and to improve functional mobility.

Methods: An analysis was undertaken of eight sequential patients with CABV (mean age 51.3 years SD = 11.7) that had completed customized vestibular rehabilitation therapy (VRT) for 10–12 sessions over 5 months. All patients presented with normal ENG calorics, a bilateral high velocity vestibular impairment on magnetic scleral search coil testing and had typical central oculomotor abnormalities. In conjunction with the patients' goals, multifactorial interventions were designed within VRT. The treatment goals were centered around functional mobility and the activities of daily living. In addition, we challenged the patients' balance and gait in the clinical setting and through home exercises and, if dizziness was present, we used habituation training.

Results: Patients demonstrated significant improvements on subjective measures of dizziness handicap and balance confidence. Mean Dizziness Handicap Inventory score at onset of VRT was 62 (SD = 24.96); this score improved to 40.57 (SD = 26.70) ($p = 0.018$) at time of discharge. Mean score on the Activities Specific Balance Confidence Scale at onset was 53.10% (SD = 24.50) and improved to 63.91% (SD = 25.64) ($p = 0.012$). As expected, attempts to improve the vestibulo-ocular reflex (VOR) were unsuccessful, as measured by LogMAR scores ($p = 0.225$). Despite this, clinical measures including the Motion Sensitivity Quotient (MSQ), Modified Clinical test of Sensory Interaction in Balance and Dynamic Gait Index also all showed statistically significant improvements.

Conclusions: CABV is a progressive condition previously believed to be refractory to treatment. A comprehensive, personalized vestibular rehabilitation program can be a valuable tool to improve patients' symptoms of dizziness, improve balance and gait as well as to reduce patient's perceptions of dizziness handicap and increase balance confidence. These measured improvements in function resulted in patients reducing their self-imposed restrictions on their activities of daily liv-

ing and reduced reported frequency of falls associated with their imbalance. These preliminary results suggest that, at least in the near term, CABV has a prognosis that can be modified by customized rehabilitation of the vestibular system and by general conditioning.

Z-18
4-AMINOPYRIDINE IMPROVES POSTURAL IMBALANCE IN ACUTE VESTIBULAR SYNDROME, BUT IMPAIRS LONG-TERM COMPENSATION

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Background and aim: The aim of the present study was to investigate the effects of the potassium channel blocker 4-aminopyridine (4-AP) on ocular motor and postural symptoms in acute unilateral vestibulopathy and its long-term consequences for central vestibular compensation by behavioural testing and serial [18F]-Fluoro-desoxyglucose ([18F]-FDG)-μPET in a rat model of chemical unilateral labyrinthectomy (UL).
Methods: Twenty Sprague-Dawley rats underwent a left-sided UL by transtympanic injection of bupivacaine and arsenilate. Ten animals were treated with 4-AP p.o. (1 mg/kg once a day) for 3 days after UL. The other animals received a pure 0.9% NaCl-solution p.o. as a control group. Behavioural testing for symptoms of vestibular tone imbalance including registration of nystagmus and postural asymmetry was performed 1 day before and at days 1, 2, 3, 7, 9, 15, 21, 30 after UL. On days 1 to 3 additional behavioural testing was performed 2 h after each application of 4-AP or NaCl. For functional imaging, sequential whole-brain [18F]-FDG-μPET was performed before and on 1, 3, 7, 15, 30 day after UL.
Results: All rats showed clinical signs of an acute vestibular syndrome following bupivacaine/arsenilate injection with a maximum at 2 and 3 days. Administration of 4-AP at 1–3 days significantly improved postural imbalance 2 h after application as compared to the status prior (on average by 45% in the postural asymmetry scores); it did not have an effect on the intensity of the spontaneous nystagmus. However, the effect of 4-AP on postural imbalance was only transient and tended to fade out 6 h after administration. Remarkably, animals in the 4-AP group had a prolonged and impaired course of postural compensation as compared to the control group (on average 35% increase in postural asymmetry scores on days 21 and 30). μPET showed a significant increase of regional cerebral glucose metabolism (rCGM) in the ipsilesional vestibulocerebellum 2 h after administration of 4-AP. This effect was only transient. However, an asymmetry of rCGM developed after day 3 in the vestibular nuclei and posterolateral thalami in the 4-AP but not in the control group.
Conclusions: Early administration of 4-AP transiently improves postural imbalance in acute unilateral vestibulopathy. However, reduction of the symptom burden during the acute phase of the vestibular syndrome seems to hamper the course of vestibular compensation. This confirms two principles which are well established in the practical treatment of patients with acute vestibulopathy: 1) Pharmacological treatment for acute symptom relief should be given only on demand and as short as possible. 2) Early postural challenge may increase symptomatic pressure and thereby accelerate vestibular compensation.