

Symposiums

SP01-1

BPPV-Update & Controversies

“LIGHT CUPULA” – NEW PERSPECTIVE OF OTOLITH INDEPENDENT BENIGN PAROXYSMAL POSITIONAL VERTIGO

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Benign paroxysmal positional vertigo (BPPV) is one of the most common causes of recurrent vertigo and is characterized by transient vertigo and nystagmus elicited by change of head position. Direction-changing positional nystagmus (DCPN) is typically observed upon head turning to either side in supine position in patients with horizontal canal (HC) BPPV. The geotropic nystagmus of HC canalolithiasis is transient, has short latency, and is either weakened or lost after repetitive examination (fatigability). However, clinicians sometimes see patients with relatively long-duration geotropic DCPN without latency and fatigability. Recently, the concept of a “light cupula”, exhibiting persistent geotropic DCPN, has been introduced. The theory of light cupula indicates cupula with lower specific gravity than the surrounding endolymph. The characteristics of nystagmus in these patients are as follows: 1) a null plane at which nystagmus ceases can be found when the patient’s head is turned to the affected ear for some degrees, 2) horizontal nystagmus towards the affected side in bowing (nose-down) position, 3) horizontal nystagmus towards the healthy side in leaning or supine position, and 4) persistent geotropic DCPN without latency when the patient’s head is turned to the right or left in supine position. In this session, we would like to discuss about this phenomenon and its clinical implications.

SP01-2

BPPV-Update & Controversies

BENIGN PAROXYSMAL POSITIONAL VERTIGO (BPPV) – NEW DEFINITIONS

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In the last few years, attempts have been made to describe and explain new, atypical nystagmus patterns in peripheral positional vertigo, other than in the already well-accepted posterior canalolithiasis and horizontal canal/cupulolithiasis. Some of these patterns are paroxysmal, such as the paradoxically direction-changing horizontal nystagmus in lateral supine position, others more subtle and persistent as the peripheral downbeat nystagmus. Apart from the nystagmus types provoked by head-position changes, theories have been put forward to explain BPPV even without any nystagmus provocation at all. It has been even suggested that this variant may be more frequent than anticipated.

The aim of the presentation is to review currently accepted and newer, atypical nystagmus types in BPPV. Here it is suggested that it is possible to explain all these variants bearing in mind that otoconial debris may float into any canal, into its short arm or long arm, be attached onto any cupula and that sometimes in absence of free floating otoconia, cupular pathology may cause the symptoms, as in the ‘light cupula’ disorders. After defining the possible nystagmus directions, their temporal and intensity patterns and the necessary examination methods, a comprehensive classification of possible BPPV variants will be attempted and the underlying hypothetical pathologies will be described. As a first step to create this new all-inclusive framework, the term ‘peripheral positional vertigo and

dizziness' (PPVD) will be suggested to mirror the necessity to include more subtle nystagmus types and other forms without any nystagmus at all among the conspicuous paroxysmal BPPV variants.

SP01-3

BPPV-Update & Controversies

ANTERIOR CANAL BPPV

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Data on the frequency and therapeutic management of anterior-canal benign paroxysmal positional vertigo (AC-BPPV) are sparse. The AC-BPPV is a rare form characterized by a predominant positional down-beating nystagmus (pDBN) with a small torsional component, not always detectable, during Dix-Hallpike and straight head hanging position maneuvers. In patients without the torsional component, it is more difficult to determine the affected side. pDBN can also be observed in atypical forms of posterior canal-BPPV when the debris are located in the non-ampullar arm of the posterior canal and move in the opposite direction to that expected. The clinical characteristics of this disease, e.g. duration, latency, fatigability of the nystagmus, and resolution differ from posterior canal-BPPV. The pathophysiology and different clinical characteristics of AC-BPPV are not fully established at the present time. Furthermore, AC-BPPV main oculomotor finding, (pDBN), may be also a clinical sign of central nervous system abnormality. It occurs with lesions in the vestibulocerebellum (floccular and nodular lesions) and is often associated with other signs more typical of central abnormalities such as saccadic and smooth pursuit alterations.

Many physical procedures have been described for the treatment of AC-BPPV: some are variants of Epley and Semont maneuvers; Crevits and Yacovino et al. described original repositioning maneuvers while the Brandt Daroff exercises may be used in non-responding patients.

SP01-4

BPPV-Update & Controversies

LONG-TERM FOLLOW UP AND INNER EAR FINDINGS IN INTRACTABLE BPPV

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Objective: To investigate the occurrence rate, prognosis, and inner ear abnormality in intractable BPPV.

Patients: Intractable BPPV was defined in case of either a persistent nystagmus or a frequent relapse each lasting more than one year after the initial diagnosis.

Intervention: T2-weighted 3-dimensional fast imaging employing steady-state acquisition sequences of MRI were reconstructed 3-dimensionally for 13 intractable BPPV patients and 14 control volunteers.

Main Outcome Measure: Transition and relapse of nystagmus were monitored. Semicircular canals were evaluated for a stenosis or filling defect.

Results: Eighteen patients (four with posterior canal type, two with horizontal canal type with geotropic nystagmus, and 12 with apogeotropic nystagmus) fulfilled the above criteria for intractability among 495 BPPV patients. The occurrence rate of intractable BPPV was 3.6%. Also, the rate of nystagmus transition was significantly higher in patients with geotropic nystagmus and the posterior canal type (100%) compared with those with apogeotropic nystagmus (33.3%). Of the 13 intractable BPPV patients who underwent MRI, 11 (84.6%) had a total of 23 canals with abnormal appearance (29.5%), showing a significantly higher incidence compared with controls. There was no correlation between the affected canal diagnosed by MRI and the type of nystagmus.

Conclusions: The low incidence of nystagmus transition in patients with apogeotropic nystagmus suggests a difference in pathophysiology between apogeotropic nystagmus and other types of BPPV. Stenosis and filling defect of canals on MRI, which would indicate an innate narrowing and/or an otoconial jam of the semicircular canal, may account for the intractability of BPPV.

SP02-1

The Inner Ear Imaging

CLASSIFICATION OF MENIERE'S DISEASE WITH USE OF ENDOLYMPHATIC HYDROPS IMAGING**Tsutomu NAKASHIMA**^{1,2}, Ilmari PYYKKÖ³, Michihiko SONE¹, Masaaki TERANISHI¹, Tadao YOSHIDA¹, Takafumi NAKADA^{1,4}, Kyoko MORIMOTO¹, Shinji NAGANAWA⁵¹*Department of Otorhinolaryngology, Nagoya University Graduate School of Medicine, Japan*²*Department of Rehabilitation, Ichinomiya Medical Treatment & Habilitation Center, Japan*³*Department of Oto-laryngology, University of Tampere, Finland*⁴*Department of Otorhinolaryngology, Gifu Prefectural Tajimi Hospital, Japan*⁵*Department of Radiology, Nagoya University Graduate School of Medicine, Japan*

Background: A new criteria of Meniere's disease (MD) was published in Journal of Vestibular Research in 2015. The new criteria included definite MD and probable MD but excluded possible MD. Possible MD, borderline MD or initial stage of MD should be investigated.

Methods: Endolymphatic space size in the cochlea and the vestibule was evaluated with 3T MRI after intravenous or intratympanic injection of gadolinium contrast agents in 1,500 patients with typical MD, atypical MD or other diseases including migraine associated vertigo.

Results: Almost all ears with definite and probable MD defined by AAO-HNS had endolymphatic hydrops (EH) in both the cochlea and the vestibule. Either cochlear EH or vestibular EH was observed in all ears with definite MD. In contrast to vestibular MD that was defined by AAOO in 1972 had vestibular EH, no vestibular EH was observed in the majority of patients with migraine associated vertigo. Asymptomatic mild or significant EH was frequently observed on non-affected side in patients with unilateral definite MD.

Conclusion: When EH is not observed at all on MRI, diagnosis of MD should be reconsidered. Cochlear MD and vestibular MD should be included in the diagnosis of MD as EH has been observed in many atypical cases. Classification of MD (not criteria of MD) with use of EH imaging may be useful.

SP02-2

The Inner Ear Imaging

HYDROPIc EAR DISEASE: MENIÈRE AND FRIENDS**Robert GÜRKOV**¹, Eike KRAUSE¹¹*Department of Otorhinolaryngology, University of Munich, Germany*

Menière's disease is a chronic condition with a prevalence of 200–500 per 100,000 and characterized by episodic attacks of vertigo, fluctuating hearing loss, tinnitus, aural pressure and a progressive loss of audiovestibular functions. Over 150 years ago, Prosper Menière was the first to recognize the inner ear as the site of lesion for this clinical syndrome. Over 75 years ago, endolymphatic hydrops was discovered as the pathologic correlate of Menière's disease. However, this pathologic finding could be ascertained only in post-mortem histologic studies. Due to this diagnostic dilemma and the variable manifestation of the various audiovestibular symptoms, diagnostic classification systems based solely on clinical findings have been repeatedly modified and have not been uniformly used in scientific publications on Menière's disease. Recent developments of high resolution MR imaging of the inner ear have now enabled us to visualize in-vivo endolymphatic hydrops in patients with suspected Menière's disease. In this review, we summarize the existing knowledge on imaging based evaluation of patients with suspected Menière's disease. These indicate that endolymphatic hydrops not only is responsible for the full-blown clinical triad of simultaneous attacks of auditory and vestibular dysfunction, but also for other clinical presentations such as "vestibular" and "cochlear Menière's disease". As a consequence, we propose a new terminology of "Hydropic Ear Disease" which is based on both clinical and imaging characteristics of these disorders in order to clarify and simplify their diagnostic classification.

SP02-3

The Inner Ear Imaging

IMAGING OF INNER EAR STRUCTURE USING OPTICAL COHERENCE TOMOGRAPHY (OCT)**Juichi ITO**¹, Yosuke TONA², Tatsunori SAKAMOTO², Takayuki NAKAGAWA²¹*Department of Otolaryngology Head And Neck Surgery, Shiga Medical Center For Adults Research Institute, Japan*²*Department of Otolaryngology Head And Neck Surgery, Graduate School of Medicine, Kyoto University, Japan*

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. Inner ear structures have internal structures with thin membranous labyrinth surrounded by bony capsule. Optical coherence tomography (OCT) is a non-destructive cross-sectional imaging modality which utilizes near infra-red light. OCT has widely been applied to clinic in the field of ophthalmology, dermatology, and cardiovascular medicine. 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. We also evaluated potential of OCT for the visualization of the vestibular system including maculae, otolith of extracted mouse inner ears. Normal and Slc26a4 knockout mice, which are known to show severe endolymphatic hydrops, were used in this study and found the endolymphatic hydrops well by OCT

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.

Conclusion: OCT is a promising tool for visualize the inner ear fine structures.

SP03-1

Vascular Vertigo

PUBLIC HEALTH IMPACT OF MISSED STROKE IN PATIENTS PRESENTING SYMPTOMS OF ACUTE DIZZINESS AND VERTIGO**David E. NEWMAN-TOKER***Department of Neurology, The Johns Hopkins University School of Medicine, USA*

Vertigo and dizziness are responsible for 4.4 million emergency department (ED) visits in the US each year. Strokes account for 3–5% of all ED vertigo and dizziness presentations, and most of these are acute ischemic strokes in the brainstem, cerebellum, or both. After ruling out general medical causes, ED providers are tasked with differentiating common, benign peripheral vestibular causes from dangerous central ones (principally stroke). This is difficult because vertigo is the most common posterior circulation ischemic stroke symptom and is frequently unaccompanied by more obvious neurological symptoms or signs. As a result, patients often undergo lengthy, expensive, and sometimes risky diagnostic evaluations in the ED to 'rule out' stroke. Despite these evaluations, some ED patients are erroneously diagnosed with benign dizziness and discharged, only to return with new or worsening stroke symptoms in the subsequent days or weeks. Multiple population-based and prospective institutional studies have found the risk of subsequent hospital admission with stroke is 0.14–0.50% at 7 days, 0.18–0.70% at 30 days, and 0.41–1.8% at 365 days, after being released from the ED with a vestibular or symptom-only dizziness diagnosis. The high early risk of return (50-fold over propensity-score matched ED controls) is consonant with the pathobiology and natural history of major stroke following transient ischemic attack or minor stroke, where the greatest risk occurs in the days after the initial event. Best evidence suggests there may be 45,000–75,000 missed strokes presenting acute dizziness or vertigo each year in US EDs, and perhaps one million or more worldwide.

SP03-2

Vascular Vertigo

ORIGIN OF VERTIGO IN ROTATIONAL VERTEBRAL ARTERY SYNDROME**Kwang-Dong CHOI***Department of Neurology, Pusan National University Hospital, Pusan National University School of Medicine and Biomedical Research Institute, Korea*

Rotational vertebral artery occlusion (RVAO) is characterized by recurrent attacks of paroxysmal vertigo, nystagmus, and syncope induced by horizontal head rotation. Most patients with RVAO exhibit a stenosis or anomaly (eg, hypoplasia or termination in the posterior inferior cerebellar artery) of the vertebral artery (VA) on 1 side and the dominant VA is compressed at the C1-2 level during contraversive head rotation, which compromises the blood flow in the vertebrobasilar artery territory (typical RVAO). However, some patients may show atypical patterns, such as compression of VA at other cervical levels, simultaneous compression of both VAs, compression of the dominant VA during ipsilateral head rotation or tilt, and compression of the nondominant VA terminating in the posterior inferior cerebellar artery (PICA). Based on the side of tinnitus and patterns of nystagmus induced by head rotation, transient excitation of the inner ear in the compressed VA side has been proposed as a mechanism of vertigo and nystagmus in RVAO. In contrast, transient ischemia of the inferior cerebellum or lateral medulla rather than labyrinth may induce isolated vertigo and nystagmus in RVAO. A recent systematic study also suggested that the symptoms in most patients with RVAO may be ascribed to asymmetrical excitation of the bilateral labyrinth induced by transient ischemia or by disinhibition from inferior cerebellar hypoperfusion.

SP03-3

Vascular Vertigo

AUDIOVESTIBULAR LOSS IN AICA TERRITORY INFARCTION: PATTERN AND CLINICAL IMPLICATION**Hyung LEE**¹, Hyun-Ah KIM¹¹*Department of Neurology, Keimyung University School of Medicine, Daegu, Korea*

Acute audiovestibular loss is a common neurotological condition that is characterized by sudden onset of severe prolonged vertigo and hearing loss. Acute ischemic stroke in the distribution of the AICA is known to be associated with vertigo, hearing loss, nystagmus, facial weakness, gait ataxia, and hypalgesia. To date, at least eight subgroups of AICA infarction have been identified according to the pattern of neurotological presentations, among which the most common pattern of audiovestibular dysfunction is the combined loss of auditory and vestibular functions. Unlike inner ear dysfunction of a viral cause, which can commonly present as an isolated vestibular (i.e., vestibular neuritis) or cochlear loss (i.e., sudden deafness), labyrinthine dysfunction of a vascular cause rarely results in isolated loss of vestibular or auditory function. Because audiovestibular loss may occur in isolation before ponto-cerebellar infarction involving AICA distribution, audiovestibular loss may serve as a window to prevent the progression of acute audiovestibular loss into more widespread areas of infarction in posterior circulation (mainly in the AICA territory). Clinician should keep in mind that acute audiovestibular loss may herald impending AICA territory infarction, especially when patients had basilar artery occlusive disease presumably close to the origin of the AICA on brain MRA, even if other central signs are absent and MRI does not demonstrate acute infarction. This review aims to highlight recent advances on audiovestibular loss in the AICA territory infarction and to address their clinical significance.

SP03-4

Vascular Vertigo

CILOSTAZOL VERSUS ASPIRIN THERAPY IN PATIENTS WITH CHRONIC DIZZINESS AFTER ISCHEMIC STROKE**Ken JOHKURA***Department of Neurology, Yokohama Brain And Spine Center, Japan*

Background: Chronic dizziness is frequently reported by patients in the chronic stage after ischemic stroke. The aim of this study was to determine the efficacy of cilostazol versus that of aspirin for the chronic dizziness that follows ischemic stroke.

Methods: We performed a prospective, randomized, open-label, blinded endpoint trial. One hundred six patients who suffered supratentorial ischemic stroke within the previous 1–6 months and subsequently complained of persistent dizziness without other obvious sequelae were enrolled. Patients were randomly given cilostazol (200 mg/day) or aspirin (100 mg/day) for 6 months. Rates of improvement in the dizziness were then evaluated. Changes in fixation suppression of the vestibulo-ocular reflex (an indicator of cerebral control over the brainstem reflex related to balance), regional cerebral blood flow (CBF) in the cerebrum, cerebellum, and brainstem; and the Zung Self-Rating Depression Scale (SDS) were also evaluated.

Results: Dizziness was significantly improved in the cilostazol group vs. the aspirin group ($P < 0.0001$) after the 6-month therapy. The capacity for fixation suppression of the vestibulo-ocular reflex was improved ($P < 0.0001$), and regional CBF in the cerebrum (relative to that in the brainstem [$P = 0.003$] and to that in the cerebello-brainstem [$P = 0.012$]) was increased only in the cilostazol group. There was no statistical difference in the change in SDS scores between the two groups.

Conclusion: Cilostazol improves the chronic dizziness that follows ischemic stroke and increases supratentorial CBF and cerebral function for adaptation of the brainstem reflex related to the sense of balance.

SP04-1

VEMP (Clinical) – Clinical Application of VEMPs

INTERPRETATION OF VEMPs IN PERIPHERAL VESTIBULOPATHIES

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Vestibular-evoked myogenic potentials (VEMPs) are now established clinical tests of otolith function. Cervical VEMPs (cVEMPs) are used to assess inferior nerve otolith function (i.e. test mainly saccular function) and ocular VEMPs (oVEMPs) are used to assess superior nerve otolith function (i.e. test mainly utricular function). VEMPs can be abnormal in diseases that cause damage to the otoliths or their central pathways, such as vestibular neuritis or vestibular schwannoma, or those that alter the transmission of VEMP stimuli through the vestibule, such as superior canal dehiscence or Meniere's disease. This presentation will focus on interpretation of cVEMP and oVEMP test abnormalities in clinical contexts. Factors causing false positives, such as stimulus type (AC vs BC), age, conductive hearing loss, insufficient muscle contraction and electrode placement, will also be discussed.

SP04-2

VEMP (Clinical) – Clinical Application of VEMPs

CLINICAL APPLICATIONS OF VESTIBULAR-EVOKED MYOGENIC POTENTIALS

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The vestibular evoked myogenic potential is a short-latency surface potential evoked by activation of vestibular end-organs, using air-conducted (AC) sound or bone-conducted (BC) vibration. It is generated by the modulation of electromyographic signals either from the sternocleidomastoid muscle for the cervical-VEMP (cVEMP), the inferior oblique muscle for the ocular-VEMP (oVEMP).

In third window syndromes such as superior canal dehiscence, reflex thresholds to AC-stimuli are pathologically lowered, AC oVEMPs are enlarged and BC oVEMPs show significantly delayed peak-latencies.

In acute vestibular syndromes, VEMPs complement head impulses in the identification of vestibular neuritis where AC and BC oVEMPs show more frequent asymmetries than do AC cVEMPs, reflecting predominant superior nerve involvement. There are no VEMP abnormalities that are specific to posterior circulation strokes.

Ipsilesional reduction in AC cVEMP reflex-amplitude (35–55%) and altered tuning of both cVEMPs and oVEMPs has been reported in Menieres Disease (MD). ACoVEMP, ACcVEMP, BCcVEMP and BCoVEMP are abnormal in MD in a descending order of prevalence.

There are no significant differences in AC click- and BC tap-evoked cervical and ocular VEMPs between Vestibular Migraine and controls and tuning characteristics in VM do not differ significantly from age-matched controls. VM can be separated from MD with 90% sensitivity using cVEMP asymmetry-ratios to a 0.5 kHz tone, frequency peak amplitude ratios (0.5/1 kHz) and the caloric test.

Stimulus parameters and testing protocols can be manipulated to enhance the sensitivity of VEMPs in a given clinical setting. Demonstration of distinct patterns of saccular and utricular involvement enables differentiation of common vestibular disorders.

SP04-3

VEMP (Clinical) – Clinical Application of VEMPs

INNER EAR TEST BATTERY COMPRISING VEMP TESTING TO MAP THE AFFECTED TERRITORY OF INNER EAR DISORDERS

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Stimulation via loud sound or bone vibration enables recording of vestibular-evoked myogenic potential (VEMP) from cervical muscles (called cervical VEMP, cVEMP) and extraocular muscles (called ocular VEMP, oVEMP). These two emerging tests expand the test battery available to clinicians for exploring dynamic otolithic function. Coupled with audiometry and caloric test, the inner ear test battery is designed for comprehensive assessment of the inner ear function including the cochlea, saccule, utricle and semicircular canals.

Clinically, the inner ear test battery has been widely adopted in cases of peripheral vestibular diseases such as 1) chronic otitis media with vertigo; 2) radiation-induced otitis media with vertigo; 3) otosclerosis with vertigo; 4) acute acoustic trauma or noise-induced hearing loss; 5) vestibular inflammatory diseases i.e. vestibular neuritis, herpes zoster oticus; 6) sudden deafness; and 7) Meniere's disease. In central vestibular disorders, the inner ear test battery may help map the affected territory in cases of 8) vestibular migraine; 9) posterior fossa stroke; and 10) posterior fossa tumor.

In conclusion, complete assessment of the inner ear function via an inner ear test battery comprising audiometry, oVEMP, cVEMP and caloric tests may stimulate to elucidate the mechanism of inner ear disorders.

SP04-4

VEMP (Clinical) – Clinical Application of VEMPs

CURRENT ISSUES IN THE CLINICAL APPLICATION OF VEMPs

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VEMPs (vestibular evoked myogenic potentials), both cervical and ocular, are proving to be useful methods of assessing vestibular function and dysfunction. At present there is uncertainty on a number of issues related to the use of VEMPs. In this presentation I will attempt to address a number of these questions, such as: Which stimulus to use? Which reflex to study? Who should be tested? and the interpretation of abnormalities.

SP05-2

[The Won-Sang Lee Memorial Symposium] Meniere's Disease (Clinical) – Intratympanic Drug Application

INTRATYMPANIC DRUG APPLICATION IN MENIERE'S DISEASE

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The treatment in intractable Ménière's disease patients to medical treatment remains a challenge. Intratympanic gentamicin stands as a good alternative in the management of refractory vertigo patients by chemically ablating the vestibular function. Due to the ototoxic effect of gentamicin on hearing as well as vestibular function, low-dose intratympanic gentamicin therapy is gaining popularity with successful control of the symptoms of Ménière's

disease, while preserving hearing. Anatomic barriers to the round window membrane (adhesions, bone dust blocking the round window, or a thickened round window membrane) may be a significant cause of intratympanic gentamicin failure, and middle ear exploration with direct application of gentamicin to the round window can be considered before further ablative therapy.

Intratympanic steroid perfusion is also reported to control vertigo, though less effectively than intratympanic gentamicin, and improve functional activity in intractable Ménière's disease patients with good hearing preservation. Intratympanic (IT) dexamethasone can allow a large percentage of intractable Ménière's disease patients to avoid ablative therapies. It was reported that there were no possible systemic effects of intratympanic dexamethasone on the hypothalamic-pituitary-adrenal axis, inflammation, and bone metabolism. It may therefore be a viable alternative treatment for intractable Ménière's disease.

SP05-3

[The Won-Sang Lee Memorial Symposium] Meniere's Disease (Clinical) – Intratympanic Drug Application **EXPERIMENTALLY-INDUCED ENDOLYMPHATIC HYDROPS IN MICE EVALUATED AND FOLLOWED WITH 9.4 T MRI**

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There has long been a need for an experimental model of endolymphatic hydrops for studies of intervention. There have been some reports on induced hydrops in animals, however, the endpoint has generally been evaluation of histological findings. Thus it has not been possible to do interventions on a verified hydrops. Vasopressin (VP) may play a critical role in endolymph homeostasis according to previous studies. Here, we evaluate the effect of VP treatment in vivo on two mouse strains by chronic subcutaneous administration of VP via mini-osmotic pumps; using MRI as read-out. High resolution MRI at 9.4 T in combination with intraperitoneally delivered Gadolinium (Gd) contrast demonstrated the development of endolymphatic hydrops in both strains (C57BL6 mice – 5 mice, 5 weeks of administration and CBA/J mice (4 mice, 3 weeks administration; 6 mice, 3 and 4,5 weeks administration) induced. These results contribute to the future use of MRI as a tool in the diagnosis and treatment of inner ear diseases such as Meniere's disease and as a critical tool in evaluating inner ear homeostasis in mice, and hopefully will forward understanding human disease.

SP05-4

[The Won-Sang Lee Memorial Symposium] Meniere's Disease (Clinical) – Intratympanic Drug Application **TONE BURST ELECTROCOCHLEOGRAPHY AND MRI INNER EAR IMAGING IN THE DIAGNOSIS OF MENIERE'S DISEASE**

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Objective: To compare the sensitivity of gadolinium MRI inner imaging with tone burst electrocochleography (EcochG) for diagnosing endolymphatic hydrops.

Study Design: A prospective study on patients who were to have an MRI scan to exclude retrocochlear pathology. Setting: Tertiary care center.

Patients: One hundred and two patients: 57 patients with Possible, Probable, or Definite Meniere's disease, 25 with asymmetrical hearing loss, 18 with sudden sensorineural hearing loss, and 2 with unilateral tinnitus had additional MRI inner ear imaging and click and tone burst stimulus EcochG testing.

Intervention: Diagnostic.

Main Outcome Measure: To compare the sensitivity of the two techniques.

Results: In 30 patients with symptom-based Definite Meniere's disease, tone burst EcochG was positive in 25 (83%) and the click EcochG was positive in 9/30 (30%), and gadolinium MRI imaging diagnosed hydrops in 14 (47%). A positive result for either MRI imaging or tone burst EcochG was seen in 26 patients (87%). In 14 subjects with symptom-based Probable Meniere's disease, 10 (71%) had either a positive EcochG or MRI. In 13 with Possible Meniere's disease, four (31%) had a positive EcochG or MRI.

Conclusion: This study confirms the greatly enhanced diagnostic sensitivity of tone burst EcochG over click response in diagnosing endolymphatic hydrops in Meniere's disease.

Even though adequate MRI imaging was achieved in 90%, tone burst EcochG was a more sensitive test.

SP06-1

Vestibular Migraine

CLINICAL FEATURES AND DIAGNOSTIC CRITERIA IN VESTIBULAR MIGRAINE

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During the last three decades a new vestibular syndrome has emerged that is now termed vestibular migraine. Evidence for vestibular migraine is provided by epidemiologic data demonstrating a strong association between migraine and vestibular symptoms. In individual patients, the diagnosis is based on the temporal association of vestibular and migraine symptoms. Diagnostic criteria for vestibular migraine have been elaborated jointly by the International Headache Society and the Bárány Society and were published in 2012. Today, vestibular migraine is recognised as one of the most common causes of episodic vertigo. The clinical presentation of vestibular migraine is heterogeneous in terms of vestibular symptoms and duration of episodes. Symptoms include spontaneous and positional vertigo but also head motion-induced and visually-induced vertigo accompanied by migraine features such as headache, photo- and phonophobia or visual auras. Attacks may last between 5 minutes and 72 hours. Similar to migraine, there is no clinical or laboratory confirmation for vestibular migraine and the diagnosis relies on the history and the exclusion of other disorders.

SP06-2

Vestibular Migraine

COMORBIDITIES IN VESTIBULAR MIGRAINE

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Diagnosing vestibular migraine (VM) currently depends upon symptoms in two dimensions: episodic vestibular symptoms temporally related to migraine symptoms, according to recent consensus criteria. The characteristics of vestibular symptoms and headache that should be required for VM remains unsettled. Insufficient migraine features may prevent diagnosing VM in patients with longstanding episodic vertigo associated with headache who are otherwise identical to those meeting VM criteria. Furthermore, the frequent presence of comorbid conditions introduces a third dimension of diagnostic uncertainty that may confound clinical application and research validation of VM criteria. Several neurotologic conditions whose symptoms overlap with VM occur more frequently in migraineurs than controls, including benign paroxysmal positional vertigo, Ménière's disease, and motion sickness. VM patients also have high rates of persistent postural-perceptual dizziness (PPPD), which is characterized by chronic (often daily) non-vertiginous dizziness, unsteadiness, and sensitivity to motion. The type and maximal duration of vestibular symptoms attributable to VM versus a separate syndrome like PPPD is a key issue as diagnostic criteria and presumed pathophysiology of VM are refined. Our pharmacologic dissection trial of patients with comorbid VM and PPPD revealed improvement of PPPD-specific symptoms using sertraline, suggesting that chronic vestibular

symptoms in patients with VM represent co-existing PPPD, not a chronic form of VM. Broadly inclusive studies of well-characterized patients with wide-ranging vestibular, headache, and psychiatric symptoms are needed to fully understand how vestibular symptoms and migraine interact in order to truly validate vestibular migraine, distill its essential features, define its boundaries, and characterize overlapping comorbidities.

SP06-3

Vestibular Migraine

MAL DE DEBARQUEMENT SYNDROME: NEUROIMAGING AND NEUROMODULATION UPDATES

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Mal de Debarquement Syndrome has historically been considered a clinically definable but not diagnostically determinable disorder. However, in recent years, both functional imaging with fMRI and EEG and structural imaging studies have helped define a neural signature of MdDS. Neuromodulation methods such as transcranial magnetic stimulation and transcranial electrical stimulation have opened both therapeutic options for patients with MdDS as well as to function as tools to probe the underlying biology of MdDS. The iterative process of using imaging biomarkers to define MdDS and measure their changes as a function of symptom change after neuromodulation is allowing us to hone in on the core neurocircuitry that is relevant to the biology of this disorder which includes a derangement in self-motion perception but also has important cognitive and mood regulation aspects. The systematic study of MdDS as a neurological disorder also connects it to other disorders related to sensory processing and regulation of mood and affect. MdDS is the natural model for how the brain entrains to external oscillators in the environment and unfortunately become persistently changed by it. Though the syndrome is relatively less common than other forms of motion perception disorders, the basic processes involved in the development of MdDS are likely relevant to how our brains adapt to all kinds of environmental oscillators.

SP06-4

Vestibular Migraine

NEURO-OTOLOGICAL FEATURES IN VESTIBULAR MIGRAINE

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There is no specific testing abnormality in vestibular migraine (VM), neither in the acute episode nor in the interval. However, laboratory testing can be useful to exclude other diseases and to reassure the patient. It is important to bear in mind that minor signs of peripheral and central vestibular dysfunction are not uncommon in patients with VM in the symptom-free interval. Examination during an episode of VM usually yields spontaneous or positional nystagmus, indicating central vestibular dysfunction in most patients. In the interval, positional nystagmus of a central type is not uncommon and has been described in about 10–20% of patients. The most consistent laboratory finding in VM is a unilaterally reduced caloric response, occurring in about 10–20% of patients. Video-head impulse testing shows a mildly reduced unilateral gain in about 10% of patients with VM. Assessment of cervical and ocular vestibular-evoked myogenic potentials (cVEMPs and oVOMPs) in patients with VM has yielded conflicting results. VEMPs do not seem to be helpful for the differentiation of VM from Menière's disease, where similar results can be found. It is important to notice that clinical and laboratory findings of vestibular dysfunction are not specific to patients with VM but can also be found in migraine patients without a history of vestibular symptoms. Audiometry may reveal sensorineural hearing loss but low-frequency, progressive or fluctuating hearing loss, typical for Menière's disease, is a rare finding in VM.

SP07-1

Head Impulse Test

DIAGNOSING STROKE IN EMERGENCY DEPARTMENT VERTIGO BY VOG-HINTS-EXAMINING THE FUTURE OF THE “EYE ECG”**David E. NEWMAN-TOKER***Department of Neurology, The Johns Hopkins University School of Medicine, USA*

Patients who present to the emergency department with symptoms of acute vertigo or dizziness are frequently misdiagnosed. Missed opportunities to promptly treat dangerous strokes can result in poor clinical outcomes. Inappropriate testing and incorrect treatments for benign peripheral vestibular disorders lead to patient harms and unnecessary costs. Over the past decade, novel bedside approaches to diagnose patients with the acute vestibular syndrome have been developed and refined. A battery of three bedside tests of ocular motor physiology known as “HINTS” (head impulse, nystagmus, test of skew) has been shown to identify acute strokes more accurately than even magnetic resonance imaging with diffusion-weighted imaging (MRI-DWI) when applied in the early acute period by eye-movement specialists. Recent advances in lightweight, high-speed video-oculography (VOG) technology have made possible a future in which HINTS might be applied by non-specialists in frontline care settings using portable VOG. Use of technology to measure these eye movements (VOG-HINTS) to diagnose stroke in the acute vestibular syndrome is analogous to the use of electrocardiography (ECG) to diagnose myocardial infarction in acute chest pain. This “eye ECG” approach could transform care for patients with acute vertigo and dizziness around the world. In the United States alone, successful implementation would likely result in improved quality of emergency care for hundreds of thousands of peripheral vestibular patients and tens of thousands of stroke patients, saving roughly \$1 billion per year in the process. Internationally, this approach could potentially impact one million stroke victims and 20 million patients with peripheral vestibular disorders.

SP07-2

Head Impulse Test

HEAD IMPULSE TESTS IN CENTRAL VESTIBULAR DISORDERS**Jeong-Yoon CHOI¹, Ji-Soo KIM¹***¹Department of Neurology, Seoul National University College Medicine, Seoul National University Bundang Hospital, Seongnam, Korea*

The head impulse test (HIT) can evaluate the vestibulo-ocular reflex (VOR) during high acceleration and high frequency stimuli. The corrective “catch-up” saccades after a head impulse indicate a decreased vestibular response. While overt catch-up saccades are a diagnostic hallmark of acute peripheral vestibular disorders, HIT is known to be mostly normal in central vestibular disorders. A central pathology should therefore be suspected if a patient with acute vertigo and spontaneous nystagmus shows normal HIT. However, recent studies also have documented various patterns of abnormal HITs in central vestibulopathies. The head impulse gain may be decreased in both horizontal directions with corrective catch-up saccades in unilateral lesions involving the vestibular nucleus, nucleus prepositus hypoglossi (NPH), inferior cerebellar peduncle (ICP), or flocculus. Furthermore, lesions involving the NPH, ICP or flocculus may cause positive HITs in the presence of preserved caloric responses, indicating a selective impairment of the VOR during high acceleration and high velocity stimuli. In contrast, the head impulse VOR gain may be hyperactive with reversed corrective saccades in diffuse cerebellar lesions. A refixation saccade in the plane other than that being stimulated during HIT (perverted, i.e., downward catch-up saccades after head rotation in the yaw plane) also suggests a central lesion. Patients with central lesions may show a premature deceleration of the VOR likewise in some of the aged person. Patients with central vestibulopathy may show various patterns of abnormal HIT. Careful evaluation of HIT may disclose central as well as peripheral vestibular lesions in patients with dizziness and imbalance.

SP07-3

Head Impulse Test

VIDEO HEAD IMPULSE TEST, JAPAN EXPERIENCE**Tetsuo IKEZONO**¹, Susumu SHINDO^{1,2}, Kazuki SUGIZAKI^{1,2}, Tomoe INOUE¹, Akinori ITO²¹*Department of Otorhinolaryngology, Saitama Medical University, Japan*²*Department of Neurotology, Saitama Medical University, Japan*

vHIT provides objective measurements of the VOR gain, and detects both overt and covert CUS. Our institute imported ICS impulse in late 2012 and made a study group in Japan along with several other universities. There are about 12 ICS devices in total in Japan. We are trying to overcome “the device lag” between Japan and other countries. We have tested more than 450 cases in our institute and I will summarize our experiences by focusing 3 points below. 1. The relationship between the vestibular failure tested by both the caloric test and vHIT, and the presence of symptoms characteristic to bilateral vestibulopathy (BV). A total of 210 cases were included, the abnormal vHIT findings well correlated with BV symptoms, but not ice-water caloric test responses. The results indicated that suspected BV patients should be tested by the combination of 2 test batteries to make a proper diagnosis. 2. The diagnostic accuracy of vHIT compared to caloric test is still under discussion. In Japan, monothermal cool caloric testing (MCCT) is more common in daily practice in many institutes. The objective was to evaluate the performance of the vHIT and MCCT mutually. The results indicated that MCCT has good enough diagnostic accuracy compared to bithermal stimulation. 3. The association between morphology of the inner ear malformations and vestibular function was studied in 16 years from 234 cases screened by vHIT and MRI.

SP07-4

Head Impulse Test

VIDEO HEAD IMPULSE TEST: TECHNIQUES AND ARTIFACTS**Georgios MANTOKOUDIS**¹, Michael SCHUBERT², David E. NEWMAN-TOKER³¹*Department of Otorhinolaryngology, Head And Neck Surgery, Inselspital Bern, University of Bern, Switzerland*²*Department of Physical Medicine and Rehabilitation, Johns Hopkins University School of Medicine, Baltimore, USA*³*Department of Neurology, Johns Hopkins University School of Medicine, Baltimore, USA*

The video head impulse test (vHIT) is increasingly used to assess the vestibulo-ocular reflex (VOR) at the bedside, however, different techniques and potential artifacts might have an impact on VOR gain measures and saccade analysis. Our data show that predictable and unpredictable HITs involve unique metrics of saccades and VOR gain depending on whether the head is rotated towards or away from center. Specifically, we have found that saccade latencies for inward HITs were consistently shorter (mean 183.48 ms \pm 4.47 SE) than those generated during outward HITs in patients with acute vestibular syndrome. Acutely, there is a disparity between inward and outward head impulses, with more covert saccades seen when using more predictable (i.e. inward) rotations. This disparity disappears by 30 days, due to an increase in covert saccade frequency with less predictable (i.e. outward) rotations. There was no difference in the ipsilesional aVOR gain for inward or outward directed head impulse rotations, however, the contralesional aVOR gain was greater for outward directed head rotations (albeit of small magnitude). vHIT users should be aware of the impact of bedside HIT technique (examiner behind or in front of the patient, inward vs. outward rotations, holding the patients jaw or the head on the top) on the presence of artifacts that might influence test result interpretation.

SP08-1

Gait & Posture

CORTICAL AND SPINAL DESCENDING SIGNAL CONTRIBUTION TO BIPEDAL LOCOMOTION**Futoshi MORI***Department of Occupational Therapy, University Medical Center, Prefectural University of Hiroshima, Japan*

Despite its apparent simplicity, human bipedal (Bp) walking is a highly tuned motor behavior. To elucidate CNS control mechanisms of human Bp walking, SPECT and NIRS studies have been performed in the healthy and

morbid human subjects, walking on the still surface and the moving treadmill surface. Results of these studies have already demonstrated that neural activity of multiple cerebral cortical areas, including sensorimotor areas, was highly enhanced. However, because of limitation in the human subjects, further analytical studies of CNS neuronal mechanisms have not been done. For this reason, we have developed Bp walking monkey model, and even Bp walking rat model. PET monkey study showed that during its Bp walking, neural activation level was much higher in the motor areas (primary motor cortex, supplementary motor area and premotor area) than that at the rest period in the same monkey. Since pyramidal and extrapyramidal descending tracts originate from the motor-related cerebral cortex, it is possible that multiple descending tracts exert parallel and tuned activation of walking-related spinal cord mechanisms. We have also found that spinal motoneuronal activation level of Bp-walking rats are depressed than that in the control rats, and that after selective severance of the corticospinal tract, activation level of motor neuron returns to that in the control. All these results suggest that, for the elaboration of seamless Bp walking, selective yet multiple cortical and subcortical activations, and resultant simultaneous tuned activation of walking-related spinal cord mechanisms are necessary.

SP08-2

Gait & Posture

SENSORY AND REFLEXIVE HYPERSENSITIVITY TO ROTATIONAL STIMULI IN MAL DE DEBARQUEMENT SYNDROME

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Mal de Debarquement (MdD) is an imbalance syndrome presenting classically as persistent abnormal non-vertiginous motion sensations after a sea voyage. There is no consensus on pathogenesis other than it is probably not a primary vestibular disorder as clinical vestibular function tests are normal and it is unresponsive to vestibular treatments. This study aimed to determine if MdD patients are hypersensitive to vestibular signals of rotation with the hypothesis that they would show perceptual but not reflex hypersensitivity.

Patients and matched controls were studied. All had normal head impulse and caloric tests of VOR function. Perceptual sensitivity to whole-body yaw and lateral rocking stimulation, both real and illusory motion evoked by galvanic vestibular stimulation (GVS) were determined by psychophysical tests. Balance during standing was assessed by forceplate posturography while vestibulospinal reflexes were assessed by GVS-evoked medium-latency reflexes.

Posturographic measures from MdD patients were not different to control. MdD patients showed exaggerated senses of self-motion during real and virtual (GVS evoked) yaw. However, MdD thresholds for detecting small imposed yaw rotations were increased. MdD patients showed exaggerated senses of self-motion during real and virtual. Against our hypothesis, MdD showed markedly increased and delayed medium-latency GVS responses during standing.

We conclude that MdD is characterised by perceptual motion hypersensitivity and vestibulospinal hyper-reflexia, but normal VOR responses. The results indicate separation of perceptual, balance and ocular processing of vestibular afference. MdD could reflect disordered autoregulation of vestibular sensitivity or integration with somatosensory and visual afference as occurs in normal subjects.

SP08-3

Gait & Posture

DEVELOPMENT OF A SELF-PACED TREADMILL TRAINING INTERFACE FOR ENHANCING EFFECTIVENESS OF GAIT REHABILITATION

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Robotic exoskeletons and body-weight supported treadmill training (BWSTT) are widely used for gait rehabilitation after brain injury since they provide safe and convenient rehabilitation environment; however, treadmill based

training paradigms have not been shown to create superior results when compared with traditional physical therapy methods such as overground training. One explanation for this may be that walking at a constant, fixed speed requires little cognitive engagement from the user, which has been postulated as a key factor in the success of motor learning. To enhance the effectiveness of treadmill-based gait training, this study aims to develop a self-paced treadmill speed control interface that adjusts belt speed according to the user's intention to change walking speed that was detected by using depth sensors. A self-paced speed control algorithm was developed based on the pelvis position and swing foot speed measurement. To evaluate the effectiveness of new treadmill training interface, a clinical study was designed and conducted to compare brain activities during two different walking conditions – walking under constant treadmill speed and walking under user-driven treadmill speed. The EEG (electroencephalogram) data revealed that relative to the traditional constant speed treadmill, the user-driven (self-paced) walking resulted in statistically significant decreases in spectral power, i.e. desynchronization, in the anterior cingulate, sensorimotor cortices, and posterior parietal lobe of the cortex. These results indicate that user-driven treadmills more fully engage the motor cortex and therefore could facilitate better training outcomes than a traditional treadmill.

SP09-1

Video Head Impulse Test (Round Table)

DO TECHNOLOGY, TECHNIQUE OR CHOICE OF GAIN CALCULATION METHOD SIGNIFICANTLY IMPACT MEASURES OF VOR GAIN BY VIDEO HIT?

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The video head impulse test (vHIT) has revolutionized modern clinical vestibular testing. Rapid expansion and use of this technology in vestibular function test laboratories, subspecialty clinics, and even frontline care settings such as the emergency department (ED) has the potential to transform bedside vestibular diagnosis. However, rapid diversification of vHIT technologies and methods has led to proliferation of different technologies (head-mounted vs. free-standing; fixed-eye vs. alternating-eye), testing techniques (from the front vs. from behind; lateral-to-center [inward] vs. center-to-lateral [outward]), and vestibulo-ocular reflex (VOR) gain calculation methods (ratio of eye-to-head velocity at a fixed point in time [point-in-time gain] vs. ratio of velocity slopes over a time range [regression gain] vs. ratio of areas under the curves after de-saccading [position gain]). Technologies have not generally been studied head-to-head, but some have been compared to the 'gold standard' (dual magnetic scleral search coil-based VOR gain measures). 'Normal' ranges for VOR gains by vHIT appear to be lower than those measured by search coils, especially in the presence of artifacts. Head impulses performed from the front may be more artifact-prone. Inward impulses lead to more covert saccades, but have not been systematically studied for their impact on mean gain measures. Point-in-time VOR gain at 60 ms may be equivalent to position (area-under-the-curve) gain, but other gain calculation methods yield slightly different results. These differences and others (e.g., proprietary algorithms to filter artifacts or de-saccade eye velocity curves) should be systematically studied across a range of clinical problems to assess their impact on clinical diagnosis.

SP09-4

Video Head Impulse Test (Round Table)

THE VIDEO HEAD IMPULSE TEST (VHIT)

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A patient with zero vestibular input can generate slow compensatory eye movements to low frequency head turns, but cannot generate slow compensatory eye movements to brief high acceleration head turns ("head impulses" – HIMPs). Those results show 1) that vHIT is a valid test of vestibular function and 2) that low frequency head turns

are not. vHIT gives objective measures of the level of function of all semicircular canals and allows definite diagnosis of bilateral vestibular loss.

The caloric is a different test of canal function and some patients have normal responses to rotation in vHIT but reduced or absent responses to calorics. However the important question is the sensitivity and specificity of vHIT, not against calorics, but for detecting surgically verified absent horizontal canal function and the sensitivity and specificity of vHIT for detecting such known loss is 1.0.

Recently we have published 1) age-related norms for VOR gain in all canals with vHIT showing very little decrement in VOR gain with age; 2) A new variant of the vHIT protocol, called SHIMPs, which requires the subject to maintain fixation on a head-fixed rather than an earth-fixed target during the head impulse. The results are complementary: with SHIMPs healthy individuals make a corrective saccade because initially they do not suppress their VOR and so their gaze is driven off the head-fixed target. In contrast, in patients with vestibular loss, their inadequate VOR does not drive their eyes off the head-fixed target so they do not make corrective saccades.

SP10-1

Basic Physiology of Vestibular Compensation and Adaptation

THE VESTIBULAR CALYX ENDING AS AXON INITIAL SEGMENT: ION CHANNEL MOLECULES AND IMPLICATIONS FOR FUNCTION

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Background: Our investigations of Na channel distribution with various Pan-Nav and Nav isoform-specific antibodies in vestibular afferents aim to determine the Nav isoforms present in different vestibular afferent classes. We have examined their immuno-localization in the various microdomains of the calyx ending (Lysakowski et al., JNS, 2011). Recordings from calyx endings in different species have also reported the presence of an A-current and an h-current, so we have also searched for candidate molecules for these currents.

Results: Afferent class and heminodal location were determined by co-labeling with calretinin (Desai et al., 2005) and nodal and AIS marker antibodies, such as ezrin, Caspr1, beta-IV spectrin and myelin basic protein. The inner surface of both afferent types (Domain 1) contains Nav1.5, while the apical end (Domain 2) contains Nav1.9 in dimorphic afferents and is truncated in calyx afferents, and the outer calyx surface (Domain 3) labels with Nav1.2 in dimorphic and Nav1.3 in calyx afferents. Nav1.6 was present at the heminodes (Domain 4) of dimorphic vestibular afferents, but not at pure calyx afferent heminodes, while Nav1.1 is present in all afferents. Using various A-current candidate antibodies (Kv1.4, 4.2 and 4.3), we obtained light labeling of dimorphic calyces and intense labeling of dimorphic boutons with Kv4.3. Immunolabeling with h-current candidate antibodies (HCN1 and HCN2) produced moderate labeling with HCN2 in all calyx endings, albeit somewhat less in calyx afferents.

Conclusions: Calyx and dimorphic afferents appear to mostly vary in their ion channel composition and this likely has implications for their separate functions.

SP10-2

Basic Physiology of Vestibular Compensation and Adaptation

UNILATERAL LABYRINTHECTOMY IN LARVAL XENOPUS CAUSES PERMANENT POSTURAL ASYMMETRIES AND SCOLIOTIC DEFORMATIONS

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Adolescent idiopathic scoliosis is characterized by severe deformations of the skeleton and often associated with vestibular deficits. A clear vestibular origin of such deformations was confirmed in adult *Xenopus* frogs after a unilateral removal of labyrinthine endorgans (UL) at pre-metamorphic larval stages. In contrast to terrestrial vertebrates, including frogs, permanently aquatic *Xenopus* lack body weight-supporting limb proprioception that potentially as-

sist in vestibular compensation. Thus, the absence of relevant proprioceptive signals and a consequently restricted vestibular plasticity in this species might be the cause for the observed deformation of the skeleton after UL. The causality and sequence of events was evaluated in semi-intact preparations of *Xenopus* tadpoles in which swimming- and passive motion-induced motor activity was recorded. Following UL, spinal ventral roots and extraocular motor nerves on the contra- but not ipsilesional side remained permanently silenced and rendered unresponsive to motion stimulation. In contrast, rhythmic bursting of spinal ventral roots during spontaneous fictive swimming displayed a bilateral symmetry, indicating that the observed motion-related motor asymmetry derives from an imbalanced descending activity, compatible with the persistent loss of virtually all contralateral projecting vestibulo-spinal neurons on the ipsilesional side. Thus, the aquatic lifestyle and the absence of body weight-supporting limb proprioceptive signals in amphibian tadpoles as a potential sensory substitute for vestibular compensation after UL likely causes a permanent asymmetry in the descending drive to axial and limb muscles, a consequent asymmetric growth of cartilage and bone and thus scoliotic skeletal deformations.

SP10-3

Basic Physiology of Vestibular Compensation and Adaptation

HOW DOES THE BRAIN GENERATE COVERT SACCADES IN HIGH ACCELERATION PASSIVE HEAD IMPULSES.

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In response to passive high-acceleration head impulses patients with low vestibuloocular reflex (VOR) gains may produce corrective saccades (in the direction of deficient slow phases) that are covert, i.e., executed while the head is still moving.

During active, combined eye (saccade)-head movements that redirect gaze the brain may suppress the VOR slow phase response and the degree of suppression is correlated with the amplitude of the desired change in gaze. In these conditions any ongoing VOR opposes saccade velocity and thereby increases the time to complete the gaze shift. Consequently, when the VOR is inhibited the eyes reach their new target more quickly.

Here we examined 23 patients with acute vestibular neuritis using passive head impulses and found that corrective saccades of more than 10 deg amplitude also inhibit the VOR, though in this paradigm inhibition of the VOR could increase the time to refixate the target. In these testing conditions we found 1) saccades are faster and more accurate if the residual VOR is higher, 2) the amplitude-peak velocity relationship of the larger, corrective saccades deviates from that of head-fixed saccades, and 3) saccades compensate also for the head displacement occurring during their execution. We propose a mathematical model to account for these findings hypothesizing that covert saccades are driven by a desired gaze-position signal based on 1) a prediction of head displacement using vestibular and extra-vestibular signals, 2) a modulation of the VOR command dependent on predicted saccade amplitude, and 3) a gaze control feedback loop.

SP10-4

Basic Physiology of Vestibular Compensation and Adaptation

BASIC PHYSIOLOGY OF VESTIBULAR COMPENSATION AND ADAPTATION**Kathleen Elizabeth CULLEN***Department of Physiology, McGill University, Montreal, Quebec, Canada*

The vestibular system is essential for our perception of self-motion, as well as the generation of reflexes that ensure postural and gaze stability. Vestibular pathways show remarkable plasticity in response to the effects of ageing, disease and peripheral trauma. Previous studies have largely focused on compensation in the pathways that mediate the vestibulo-ocular reflex (VOR) after unilateral vestibular loss. In our recent work, we first demonstrated a strong relationship between the recovery of motor performance after lesion and the recovery of vestibular sensitivity in single neurons constituting the first central stage of the VOR. Notably, compensation was further characterized by the substitution of other self-motion inputs (i.e. proprioceptive and motor related) at the level of these same central neurons. Second, we found that dynamic reweighting of vestibular and extr vestibular inputs also drives behavioural recovery (i.e. postural reflexes) within vestibulospinal pathways after vestibular lesion. Third, we established that the mechanism underlying vestibular compensation is constrained by parallel changes in neuronal response sensitivity and variability. Nevertheless, the increased weighting of extr vestibular input can lead to beneficial and enduring changes in self-motion processing. Together, these findings support the proposal that rehabilitation approaches that engage this multimodal convergence are probably most effective in improving functional recovery. Finally, we have recently directly probed how vestibular neurons respond to restoration of vestibular function with a vestibular prosthesis – an exciting new technological advancement – and found rapid and coordinated plasticity within specific sites of both the VOR and vestibulo-spinal reflex pathways ensures robust performance.

SP11-1

The 3rd Joint Meeting of The Korean Balance Society and Japan Society for Equilibrium Research

VESTIBULAR FUNCTION CHANGE IN VASOPRESSIN-INDUCED HYDROPS MODEL**Minbum KIM**¹, **Kyu-Sung KIM**²¹*Department of Otorhinolaryngology, Catholic Kwandong University College of Medicine, Incheon, Korea*²*Department of Otorhinolaryngology, Inha University College of Medicine, Incheon, Korea*

Objectives: To evaluate the efficacy of a new treatment for hydrops, the traditional hydrops model is not appropriate since it represents only the chronic stage of disease. Recently, a new dynamic model was introduced for acute aggravation of hydrops using the vasopressin type-2-receptor agonist, desmopressin. The purpose of this study was to evaluate vestibular function change in vasopressin-induced hydrops model.

Methods: In two to four weeks after surgical ablation of endolymphatic sacs in guinea pigs, acute aggravation of hydrops was induced by desmopressin (100 ug/Kg, SC, VP). Auditory brainstem response (ABR) test and bidirectional sinusoidal harmonic acceleration (SHA) test with an animal rotator were performed before and after VP, respectively. Histologic sections parallel to the modiolar axis were made for observing changes in the Reissner's membrane and endolymphatic hydrops.

Results: In 60 to 90 min after VP, symmetry score on bidirectional SHA tests increased from 6.50 ± 7.60 to $25.23 \pm 9.84\%$ ($p = 0.04$). While some animals showed larger response during rotation at the direction of hydrops ear (irritating response), the other showed smaller response (paretic response). Symmetric response was recovered in 120 to 180 min. In all the animals, endolymphatic hydrops with the distension of Reissner's membrane were histologically observed after VP.

Conclusion: VP can transiently induce acute aggravation of hydrops and asymmetric vestibular dysfunction in guinea pigs. This model can be helpful to study a new treatment for the acute attack of hydrops. Furthermore, it might give some clues to explain the mechanism of bidirectional nystagmus in Meniere's disease.

SP11-2

The 3rd Joint Meeting of The Korean Balance Society and Japan Society for Equilibrium Research

VIDEO HEAD IMPULSE TESTS IN CEREBELLAR ATAXIAS AND INTERNUCLEAR OPHTHALMOPLEGIA

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Purpose: Video head impulse test (vHIT) allows objective and quantitative measurements of the vestibulo-ocular reflex (VOR) during high acceleration stimuli. HIT is mostly normal in central vestibular disorders, but various patterns of abnormalities have also been reported in diffuse or circumscribed lesions involving the central vestibular structures. We determined abnormalities of the VOR using vHIT in chronic cerebellar ataxias and internuclear ophthalmoplegia (INO).

Methods: We measured the horizontal and vertical HITs in 32 patients with chronic cerebellar ataxia [e.g., spinocerebellar ataxia (SCA) and cerebellar type of multiple system atrophy], 16 patients with INO, and 42 normal controls using a vHIT device. We measured the gains of the VOR and determined the presence of compensatory catch-up saccades.

Results: The patients with cerebellar ataxia showed a decrease of the head impulse VOR gain for the anterior and posterior canals on both sides, but normal gain for the horizontal canals. Some patients with SCA6 or other types of cerebellar ataxia with longer disease duration showed posterior canal-dominant VOR impairments. In unilateral INO, the mean VOR gain for the contralesional posterior canal was markedly impaired while that for the ipsilesional posterior canal was preserved. The VOR gains of both anterior canals were also mildly decreased. In bilateral INO, the VOR impairments were more severe for the posterior canals.

Conclusions: The patients with cerebellar ataxia or INO showed lower head impulse VOR gains for the vertical canals, but more the posterior ones. This posterior canal-dominant VOR impairment suggests that the anterior canal signals pass through the pathway other than the medial longitudinal fasciculus and disinhibition of the anterior canal pathway by the cerebellar lesions. Analysis of the VOR using vHIT may help differential diagnosis of cerebellar and brainstem disorders.

SP11-3

The 3rd Joint Meeting of The Korean Balance Society and Japan Society for Equilibrium Research

FACTORS PREDICTING PROGRESSION FROM UNILATERAL TO BILATERAL MENIERE'S DISEASE

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In the course of Meniere's disease (MD), approximately one third of patients progress from unilateral to bilateral MD. For optimal treatment, the potential risk for contralateral ear involvement should be properly assessed. This study aimed to explore factors predicting progression from unilateral to bilateral Meniere's disease.

Clinical records of 180 consecutive patients with definite MD were reviewed. Patients were classified into the following 3 groups: patients with unilateral MD (CEI-, contralateral ear involvement-), patients exhibiting progression from unilateral to bilateral MD (CEI+), and patients with bilateral MD at the time of first consultation (BL, bilateral). Age, gender, duration of symptoms, stage of disease, left-right difference on caloric test, results of vestibular-evoked myogenic potential (VEMP) recording, subjective visual horizontal, and time to remission of vertigo attacks were compared.

When stages 1 with 2 and 3 with 4 were combined, there were more cases of stage 3 or 4 disease in both the CEI+ and BL groups than in the CEI- group. On VEMP responses, the proportions of patients exhibiting normal responses

on both sides or absent responses on both sides in the CEI+ and BL groups were larger than those in the CEI- group. In regression analysis, stage 3 or 4 and lack of left-right difference in VEMP response were factors significantly associated with contralateral ear involvement.

In patients with unilateral MD, stage 3 or 4 disease and lack of left-right difference in VEMP responses at initial examination were risk factors for contralateral ear involvement.

SP11-4

The 3rd Joint Meeting of The Korean Balance Society and Japan Society for Equilibrium Research

MUTUAL EVALUATION OF CALORIC TEST AND VIDEO HEAD IMPULSE TEST

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Both head impulse test (HIT) and caloric test are the important tests for examining vestibular deficits. HIT has a moderate sensitivity (35–45%) and high specificity (90%) when compared to caloric test. In 2009, video Head Impulse Test (vHIT) was introduced. vHIT have better diagnostic accuracy with many advantages, such as detecting covert catch up saccades which can hardly be seen by naked eyes. However, few studies have been conducted to evaluate the performance of vHIT in Asian cephalic type which has more chance to have false data due to goggle slippages. The main purpose of the present study was to evaluate the performance of vHIT compared to caloric tests in Japanese population.

One unique point in this study is that we used monothermal cool stimulation for caloric test (MCCT) which is widely used throughout Japan. To my knowledge, in Korea, monothermal stimulation was once used previously, but now bithermal stimulation technique is more used as in other countries world wide.

We performed a retrospective chart review of the 366 cases who had undergone vestibular assessment during 2012 and 2014. The results showed that the sensitivity of vHIT was 62.6% and specificity was 86.2% when compared to MCCT. The area under the ROC curve in the MCCT was 0.892 using VOR gain as dependent variable, and 0.849 using CUS as dependent variable. Our study showed MCCT decreases test time and side effects without reducing sensitivity of caloric test in bithermal stimulation.

SP11-5

The 3rd Joint Meeting of The Korean Balance Society and Japan Society for Equilibrium Research

CLINICAL CHARACTERISTICS AND TREATMENT OUTCOME IN CASES OF NEUROVASCULAR CROSS COMPRESSION OF THE COCHLEAR NERVE

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Objectives: Neurovascular cross compression (NVCC) of the cochlear nerve is caused by aberrant or tortuous vessel that causes nerve compression with subsequent hyperexcitation and neuropathy. In most cases, carbamazepine may be of great help to alleviate typewriter tinnitus. The aim of this study was to investigate clinical characteristics and treatment outcome in patients with NVCC.

Methods: We reviewed medical records of 24 patients who were diagnosed with NVCC retrospectively. Patients who were diagnosed with NVCC based on the symptom underwent audiometric test, vestibular function tests, and internal auditory canal magnetic resonance imaging (IAC-MRI). For patients with suspicious NVCC, carbamazepine 200 mg 1T bid was prescribed as a start dose for 3 weeks.

Result: Among 24 patients, 7 were male and 17 were female with a mean age of 51.6 years. Fourteen of 16 patients who revisited after initial carbamazepine trial reported improvement of tinnitus and dizziness. All patients had symmetric pure tone threshold. In 8 patients, subjective dizziness was accompanied but only 1 patient shows canal paresis. On IAC-MRI, vascular contact to the vestibulocochlear nerve or vascular loop invagination into the IAC showed on statistical differences as compared with asymptomatic controls.

Conclusion: NVCC of the cochlear nerve can be characterized by typewriter tinnitus and recurrent vertigo with overall no changes in hearing thresholds or vestibular function. As audiologic, vestibular, or radiologic tests are

normal in the majority of cases, meticulous history taking especially focused on the characteristics of sound and responsiveness to meditation are important for proper diagnosis and management.

SP11-6

The 3rd Joint Meeting of The Korean Balance Society and Japan Society for Equilibrium Research

EFFECT OF ISCHEMIA ON THE VESTIBULAR APPARATUS: AN EXPERIMENT USING THE BULLFROG MODEL

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Inner ear disorder is one of the main causes of vertigo. Though it has not been proven, many of the inner ear disorders are probably induced by the ischemia or virus infection. It is not easy to evaluate the circulation of the vestibule because of its anatomical location.

The objectives are to establish the vestibular ischemia model using bullfrog, and to investigate changes of the vestibular apparatus in the ischemic condition.

Bullfrogs were used. Under the anesthesia with ether, the unilateral temporal bone was opened from the oral cavity. The vestibular artery on the nerve was cut (vestibular ischemia model). In some cases, the vestibular artery was not cut (sham surgery). The intact temporal bones served as control. Two to 7 days later, the semicircular canals and utriculi were removed. Cupula was stained with India ink and was investigated in frog Ringer solution. The ampullae and utricular maculae were fixed, cut in 4 μ m thickness, and were stained with hematoxylin-eosin. Neuroepithelia of ampullae and maculae were investigated under light microscope.

In vestibular ischemia model, 30–50% of cupula in semicircular canals and 33.3% of utricular otolithic membrane was damaged. In the sham surgery and control groups, no cupula and no otolithic membrane was damaged. Neuroepithelia were damaged in 50–80% of the ampulla and 66.7% of maculae in vestibular ischemia model.

When the damage of neuroepithelium was extensive, cupula and otolithic membrane were damaged easily. The vestibular ischemia damages the neuroepithelia first.

SP12-1

Vestibular Rehabilitation

AN EVIDENCE-BASED CLINICAL PRACTICE GUIDELINE FOR PERSONS WITH VESTIBULAR HYPOFUNCTION

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A systematic review of the literature was performed to determine if exercises are effective at enhancing recovery in persons with unilateral and bilateral vestibular hypofunction. Articles included meta-analyses, systematic reviews, randomized controlled trials, cohort studies, case control series, and case series for human subjects published in English. One hundred thirty-five articles were identified as potentially relevant to this clinical practice guideline. Based on strong evidence, clinicians should offer vestibular rehabilitation to persons with unilateral and bilateral vestibular hypofunction with impairments and functional limitations related to the vestibular deficit. Clinicians should not include voluntary saccadic or smooth-pursuit eye movements as specific exercises for gaze stability. Clinicians may offer specific exercise techniques to target identified impairments or functional limitations. Based on moderate evidence and in consideration of patient preference, clinicians may provide supervised vestibular rehabilitation. Based on expert opinion, clinicians may prescribe a minimum of three times per day for the performance of gaze stability exercises as one component of a home exercise program. Persons without significant comorbidities that affect mobility and with acute or sub-acute unilateral vestibular hypofunction may need 1x/week supervised sessions for 2–3 weeks; persons with chronic unilateral vestibular hypofunction may need 1x/week sessions for 4–6 weeks; persons with bilateral vestibular hypofunction may need 1x/week sessions for 8–12 weeks. In addition to supervised sessions, patients are provided a daily home exercise program. These recommendations are intended as a guide for physical therapists and clinicians to optimize rehabilitation outcomes for persons with peripheral vestibular hypofunction undergoing vestibular rehabilitation.

SP12-2

Vestibular Rehabilitation

NEUROPLASTICITY AND VESTIBULAR COMPENSATION

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The lecture questions the relationships between the plastic events responsible for the recovery of the vestibular functions following a unilateral vestibular loss, that is, vestibular compensation, and the procedures used by the physiotherapists to improve the functional recovery, that is, vestibular rehabilitation therapy (VR).

The main objective is to provide clinicians with an understandable view on When and How to perform VR, and to explain Why VR may benefit from basic knowledge collected in animal models, and How VR therapy may alter the recovery mechanisms.

There is a critical period after vestibular injury during which most of the plasticity mechanisms described in the developing brain are re-expressed. These early plastic events depend however of the real nature of the vestibular loss, with strong structural reorganizations of the neuronal networks after sudden and total loss, and more functional adaptations after progressive and partial loss. This early plastic window of opportunity varies therefore as a function of vestibular etiology, and the optimal timing of VR therapy and how VR therapy must be tailored depend on this cross-talk between retraining procedures and post-lesion vestibular plasticity mechanisms.

To get fast recovery and to ensure good quality of life of their vestibular loss patients, the physiotherapists have to respect some common sense principles (i.e., early active retraining), to improve and/or change their sensorimotor performances (i.e., gaze and postural stability, orienting), and to find why the patients show a poor functional recovery (i.e., anxiety, stress, maladapted or avoiding strategies, ...).

SP12-3

Vestibular Rehabilitation

THE EFFECT OF DUAL-TASK EXERCISES ON VESTIBULAR REHABILITATION OUTCOME IN PEOPLE WITH A VESTIBULAR DISORDER

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Background: A growing body of literature suggests a relationship between vestibular dysfunction and cognitive impairment while patients often report symptoms of memory loss, decreased attention and “brain fog”. However, no

studies to date have specifically investigated the effect of vestibular rehabilitation (VR) on cognitive function or the effect of dual-task exercises on VR outcome.

Design: Single-blinded parallel randomized control trial with baseline, 6- and 12-week comparisons.

Setting: Tertiary care clinic, London, UK

Participants: Fifty participants (age 18–80 years old) with chronic peripheral vestibular symptoms

Intervention: Customised vestibular rehabilitation with and without dual-task exercises. Individualised VR sessions occur once monthly for three months; a customised home programme is also provided for each participant.

Measurements: Treatment response is assessed with the Functional Gait Assessment with and without a dual-task (motor and cognitive) component; questionnaires for symptoms, symptom triggers, balance confidence, perceived dizziness handicap; and the CANTAB cognitive battery testing attention, memory and executive function domains.

Results: Preliminary data ($n = 11$) indicates no significant between-group differences either at baseline or at 6-week follow-up. Within-group data, however, indicates significant improvements for common vestibular symptoms ($Z = -2.02$; $P < 0.05$), perceived dizziness handicap ($Z = -2.20$; $P < 0.05$), Functional Gait Assessment ($Z = -2.03$; $P < 0.05$), memory ($Z = -2.21$; $P < 0.05$) and attention ($Z = -1.99$; $P < 0.05$) test scores ONLY for the VR plus dual-task exercise group. No significant within-group improvements were noted for the VR only group.

Conclusion: Preliminary data suggests that customized VR combined with dual-task exercises may provide better outcome at 6-weeks for subjective symptoms, perceived dizziness handicap, functional gait and particular cognitive domains compared to customized VR in isolation.

SP12-4

Vestibular Rehabilitation

SENSORIMOTOR RESULTS FROM A JOINT NASA AND RUSSIAN PILOT FIELD TEST

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Until recently assessing the full impact of sensorimotor decrements associated with long-duration spaceflight had not yet been achieved immediately following landing. To overcome this limitation and determine the crewmembers functionality, both the Russian and U.S. space programs have implemented crew testing at the Soyuz landing site with additional follow-up measurements within 24 hours. Identified as the Pilot Field Test (PFT), NASA's research included: (1) sit-to-stand tests, (2) a recovery from fall test where the crewmember begins in the prone position and then stands for 3.5 minutes while cardiovascular and postural ataxia data are acquired, and (3) a tandem heel-to-toe walk. Video, heart rate, blood pressure, body and limb position, and severity of postflight motion sickness were collected during each test session. Russian investigators made additional measurements associated with: (a) obstacle avoidance, (b) muscle compliance, (c) postural adjustments to perturbations (pushes) and (d) center of mass measurements made with insoles inserted into the crewmembers' shoes. Data from 18 subjects have been obtained. With the end of the PFT investigation additional sensorimotor tests are now being undertaken. Overall the increased level of functional deficits, not attributable to strength, observed in crewmembers has been substantially greater than previously observed when compared with measurements obtained after 24 hours. Full recovery requires 6 to 16 days. Measureable performance parameters such as those associated with functional behaviors are required to provide an evidence base for characterizing programmatic risks for undertaking exploration missions where crewmembers will be unassisted after landing.

SP12-5

Vestibular Rehabilitation

VESTIBULO-OCULAR REFLEX GAIN ADAPTATION RETENTION: THE EFFECTS OF PASSIVE VS. ACTIVE ROTATIONS AND REPETITION

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Incremental vestibulo-ocular reflex (VOR) gain (eye-velocity/head-velocity) adaptation training increases the VOR response by a larger amount in a shorter period of time compared to conventional training that relies on a constant, large retinal image error signal to drive adaptation.

We sought to determine the short-term time-course of VOR retention after incremental VOR adaptation training. We tested the effect of passive versus active adaptation training, testing time interval, repetition and incremental training protocol.

We tested 5 normal subjects over 7 separate sessions. For sessions 1-4, we compared active versus passive adaptation training lasting 15 minutes with the VOR gain challenged to increment by 0.1 every 90 seconds. We measured the VOR gain in darkness at 10 versus 20 minute intervals for 1 hour post-training ($2 \times 2 = 4$ conditions). For sessions 5-7, the training lasted 5 minutes every 20 minutes for 1 hour. We measured the VOR gain at 20 minute intervals for 1 hour post-training. The 5 minute training comprised either: 0.1 gain increments every 30 seconds, 0.1 gain increments every 60 seconds or 0.2 gain increments every 60 seconds.

Focusing on the results from session 1, the active and passive VOR gains both increased by $\sim 12\%$ after active training. The post-training active VOR gain at 20, 40 and 60 minutes was 13%, 12% and 16% higher than pre-training. Similarly, the passive VOR gain was 8%, 13% and 13% higher at the same time intervals.

Our data suggest that the VOR gain is completely retained for at least 1 hour after incremental adaptation training.

SP13-1

Vestibular Prosthesis

SEMICIRCULAR CANAL INDUCED EYE MOVEMENTS – THE FUNDAMENTAL BASIS OF THE VESTIBULO-OCULAR REFLEX (VOR)

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When Jun-Ichi Suzuki and I began to collaborate in 1962, the only studies that had been done on the Vestibulo-Ocular Reflex (VOR) had utilized caloric and rotational stimuli and central nervous system lesions. Single pulses and low frequencies of stimulation were ineffective. Suzuki implanted fine bipolar stainless steel wires next to the ampullary nerves of each of the semi-circular canals and I used trains of pulses at different frequencies to activate the canal nerves. These experiments performed on cervically-transected sleeping cats produced dramatic results. The first pulse of the train, raise the level of central excitability and the second pulse occurring at a relatively short latency, evoked monosynaptic excitation of the 3-neuron VOR, activating eye muscles in 2.5–3.1 msec, the transmission time between the labyrinths and the eye-muscles. This powerful activation enabled the eye muscles to follow stimulation frequencies up to 400/sec, revealing the true function of the VOR namely, to stabilize gaze in space during head movement. Lateral-canal stimulation also caused deviation of the head and extension of the ipsilateral and flexion of the contralateral forelimbs, in intact cats, to initiate a turn into the direction of the eye movement. Each canal activated all 12 eye muscles, 6 excited and 6 inhibited so that each canal caused eye movement in the plane of that activated canals, $\sim 30^\circ$ above the spatial horizontal, for the lateral canals and $\sim 45^\circ$ from the midline for the vertical canals. These findings, evolved 53 years ago essentially formed the basis for the development of vestibular prosthesis.

SP13-2

Vestibular Prosthesis

RESTORING VESTIBULAR SENSATION: SCIENTIFIC FOUNDATIONS, CURRENT STATUS AND OUTLOOK FOR THE FUTURE

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Research by Suzuki, Cohen et al. in the 1960's demonstrated that focal electrical stimulation can elicit directionally-specific reflexive eye movements. Numerous preclinical studies at the Massachusetts Eye & Ear Infirmary, Johns Hopkins, and University of Washington have since demonstrated the efficacy of this technology in animals. In

rodents and rhesus monkeys rendered bilaterally vestibular-deficient via treatment with gentamicin and/or plugging of semicircular canals, multichannel vestibular stimulation partially restores the 3D vestibulo-ocular reflex for head rotations about any axis, over a range of speeds typical of head movements in daily life. Response direction improves over time with adaptation to artificial input. Electrically-evoked compound action potentials generated by vestibular nerve branches correlate strongly with evoked eye movements, providing an alternate measure of performance that is robust under general anesthesia. More recently, studies involving electrical stimulation using modified cochlear implant stimulators by Phillips, Rubinstein et al. (for pacing to balance vestibular tone during vertigo attacks) and by Guyot, Perez-Fornos, Kingma et al. (delivering episodic stimulation to the labyrinth) have provided tantalizing data suggesting therapeutic potential in humans. No group has yet tested a vestibular implant system designed for chronic, continuous sensory restoration in humans; however, we recently garnered federal regulatory approval to start a first-in-human clinical trial of such a system (the Labyrinth Devices MVI Multichannel Vestibular Implant) at Johns Hopkins. This lecture will introduce the topic of prosthetic vestibular stimulation and briefly review the growing body of preclinical, clinical, epidemiologic and quality of life evidence that provide the foundation for this approach.

SP13-3

Vestibular Prosthesis

MULTI-SPECIES VESTIBULAR IMPLANT STUDIES

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We began developing vestibular implant technology about 20 years ago at Oregon Health Sciences University and used this technology in a series of studies performed there and at the Massachusetts Eye and Ear Infirmary in which we applied patterned chronic electrical stimulation to the vestibular periphery of animal models. We focused these first vestibular implant studies to investigate how the brain learns to use artificial information provided via electrical stimulation. Specifically, we measured eye movements in various animal models while providing patterned electrical stimulation. In this talk, we present published data that show:

- 1) That the brain acclimates to chronic resting-rate excitation in about one day. This is important because otherwise vestibular implants would yield chronic disequilibrium that would need to be overcome – either technically or via patient tolerance of disequilibrium.
- 2) That the brain learned to recognize – and rapidly adapt to – the baseline stimulation when repeatedly provided the same baseline stimulation. This was a crucial finding because, otherwise, patients would suffer prolonged disequilibrium every time their implant was turned on or off (e.g., for bathing, sleeping, etc.).
- 3) That the desired motion-modulated responses were maintained when the fore-mentioned acclimation to constant rate stimulation occurred. This was an important finding because acclimation could have resulted from total disregard of all signals carried by the stimulated neurons, which would yield an ineffective vestibular implant.

SP13-4

Vestibular Prosthesis

THE DISCHARGE OF VESTIBULAR NUCLEUS NEURONS DURING FUNCTIONAL STIMULATION WITH A VESTIBULAR PROSTHESIS

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Background: An implantable vestibular prosthesis has the promise of restoring natural vestibular function by activating vestibular neurons with modulated electrical stimulation of the vestibular nerve. In our experiments, we examined the characteristics of vestibular nucleus neuron discharge during electrical stimulation with one such device.

Methods: Two rhesus monkeys were implanted with a vestibular prosthesis identical to devices currently evaluated in human patients. The fully implantable device was activated to produce biphasic pulse trains that varied in current amplitude or pulse frequency. Vestibular nucleus neurons were recorded with tungsten microelectrodes during electrical stimulation and during natural behaviors. Eye movements were recorded with scleral coil.

Results: We sampled 180 neurons in the vestibular nucleus. Half of the neurons were phase locked to the electrical stimulus (spike probability ≥ 0.20). Other non-driven nearby vestibular neurons were recorded in the same tracks for comparison. The coefficient of variation and unit resting rates for both neuron groups were comparable, and unrelated to the probability of eliciting a spike with electrical stimulation. Putative vestibulo-ocular and vestibular only neurons were driven. The probability of an elicited spike increased with current amplitude, and decreased with current frequency, but often saturated below $p = 1.0$. The latency variability of the stimulus-evoked discharge was related to stimulation current.

Conclusions: Neural synchrony, firing frequency, and spike probability of driven vestibular nucleus neurons are all modulated by changes in stimulation current and stimulation pulse frequency, producing seemingly natural electrically elicited vestibulo-ocular reflex behavioral responses.

Funding: NIDCD, NCRR-ORIP, Cochlear Ltd., Wallace H. Coulter Foundation

SP13-5

Vestibular Prosthesis

PROGRESS AND CHALLENGES IN THE CLINICAL APPLICATION OF A VESTIBULAR PROSTHESIS

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Between October 2010 and August of 2012 we implanted four human subjects with a vestibular neurostimulator that has also been studied chronically in nonhuman primates. We have two year data in one of the subjects and greater than three year data in three of them. We have localized the electrodes with temporal bone CT scans in these same three subjects. Initially, stimulation of most implanted canals produces robust canal-plane electrically-evoked eye movements with some off-plane motion as well. Then decreased responsiveness and subsequent response fluctuation has been observed. We believe this fluctuation may be due to the subject's underlying Meniere's disease diagnosis but this remains to be proven. The dynamic range for electrically-evoked percepts, eye-movements, postural sway and vestibular compound action potentials varies across measure, canal, subject and time. Electrode placement appears variable on CT across canals and subjects and response measures are not robustly linked to electrode location relative to the ampulla. We believe some of this variability is due to the small surface area of our stimulating electrodes and have redesigned the device with larger ones. We will soon begin implanting nonhuman primates with the modified device and will be applying to the US FDA for a modification of our IDE so that we can begin human studies of this second generation vestibular neurostimulator. We believe the design changes will produce human results more consistent with what we have seen in nonhuman primates.

(Supported by NIDCD, Cochlear Ltd and gifts to the Virginia Merrill Bloedel Hearing Research Center)

SP13-6

Vestibular Prosthesis

VESTIBULAR IMPLANTS IN HUMANS: THE EXPECTED AND THE UNEXPECTED FINDINGS

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Our team has fulfilled several milestones in the development of vestibular implants in humans. Special surgical techniques have been developed. Modified cochlear implants providing extracochlear electrodes to be put in contact with vestibular structures have been developed in collaboration with MED-EL (Innsbruck, Austria). Twelve volunteer patients with a total bilateral vestibular loss have been implanted with prototype devices. Finally, specific methods of electrical stimulation as well as the necessary interfaces to capture the signal coming from a motion sensor and use it to modulate the stimulation signals delivered via the implanted vestibular electrodes were also developed.

Our results demonstrated that the artificial restoration of the Vestibulo-Ocular Reflex (VOR) is possible via electrical stimulation of semicircular canal afferents. This was an “expected” result. A more “unexpected” finding was that it is also possible to evoke an artificial Vestibulo-Collic Reflex in the same settings. Additional interesting results concern vestibular percepts evoked by electrical stimulation. Surprisingly, reported percepts were heterogeneous and only a minority of patients reported a rotatory sensation in response to electrical stimulation of the vestibular nerve. These findings indicate that multiple neural pathways, other than that of the VOR, were activated during our acute experiments.

In conclusion, chronic electrical stimulation of the vestibular nerves seems technically feasible in humans. These results do not only open the door to a novel therapeutic alternative for patients with a bilateral vestibular loss, but also offer an unprecedented opportunity to increase our fundamental understanding of the vestibular system.

SP14

Neurosensory Diagnosis and Prognosis of Mild Traumatic Brain Injury

NEUROSENSORY DIAGNOSIS AND PROGNOSIS OF MTBI

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Mild traumatic brain injury (Concussion) is an increasingly common public health issue that affects individuals in all aspects of life. Neurosensory effects are among the most common sequela seen after concussion, with balance-related findings being the most common among this group. This session examines how neurosensory consequences of concussion can be used to help diagnose the injury acutely and follow progress of this injury over time. This seminar examines what can be learned by examining presenting symptoms and OVRT test results in individuals with concussion. These neurosensory examines allow for diagnosis and provide prognostic implications for this common injury pattern. In particular the presenters will utilize data from basic and clinical studies to define the following: 1) Initial presenting symptoms of mTBI and how these symptoms progress over the acute time period, 2) The use of an objective and reliable non-invasive detection method, 3) How this work can inform us about the progress and prognosis of individuals suffering from concussion, and 4) translational insights from fundamental research to understand underlying biological events. After this examination we will address the treatment of these patients with an emphasis on neurosensory and vestibular rehabilitation. Participants in this session will gain a greater understanding of how vestibular disorders are an important tool in the diagnosis and treatment of this increasingly common and well-publicized disorder.

SP15-1

Genetics for Inner Ear/Vestibular Disorder

DISTINCT VESTIBULAR PHENOTYPES IN DFNA9 FAMILIES WITH COCH VARIANTS

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Mutations of COCH can cause hearing loss and less frequently vestibular symptoms. However, vestibular phenotypes, especially in terms of the location of specific variants are not well documented yet. In this study, a retrospective and prospective cohort survey was performed in two tertiary referral hospitals to demonstrate vestibular

phenotypes of DFNA9 subjects with a focus on the relationship with the location of COCH mutations. Two DFNA9 subjects were recruited from the previously collected cohort, each segregating p.G38D and p.C162Y of the COCH gene. Another two DFNA9 families were newly detected by targeted resequencing of known 129 deafness genes (TRS-129). These two families segregated the p.G38D variant of the COCH gene as the causative mutation, making p.G38D the most frequent COCH mutation in our Korean cohorts. Regarding the detailed clinical phenotype of the four DFNA9 families with documented vestibular phenotypes, we were able to classify them into two groups: one (p.C162Y variant) with a Meniere's disease (MD)-like phenotype and the other three (p.G38D variant) with significant bilateral vestibular loss without any definite MD symptoms. Distinct vestibular phenotypes depending on the location of COCH mutations were demonstrated, and this study correlates a genotype of p.G38D in COCH to the phenotype of bilateral total vestibular loss, therefore expanding the vestibular phenotypic spectrum of DFNA9 to range from bilateral vestibular loss without episodic vertigo to MD-like features with devastating episodic vertigo. In addition, the p.G38D variant of the COCH gene is suggested to be a frequent cause of progressive audiovestibular dysfunction in Koreans eventually requiring cochlear implantation (CI).

SP15-2

Genetics for Inner Ear/Vestibular Disorder

RESTORATION OF PENDRIN IN THE ENDOLYMPHATIC SAC RESTORES BALANCE IN A PENDRED SYNDROME MOUSE MODEL

Philine WANGEMANN

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Mutations of SLC26A4 are a common cause of hearing loss and vestibular dysfunction. SLC26A4 encodes pendrin, an anion exchanger expressed in a variety of epithelial cells in the cochlea, the vestibular labyrinth and the endolymphatic sac. Dysfunction of pendrin is associated with an enlargement of the inner ear including the cochlea and the vestibular labyrinth. Slc26a4 Δ/Δ mice recapitulate the enlargement, fail to acquire hearing and vestibular function, and thereby represent a model for the human phenotype. The enlargement of the inner ear in Slc26a4 Δ/Δ mice originates with fluid secretion in the utricle that occurs during the embryonic phase of development. Fluid secretion in the utricle of Slc26a4 Δ/Δ mice leads to swelling of the entire inner ear since it is unopposed by fluid absorption in the endolymphatic sac. We generated a transgenic mouse line that expresses human SLC26A4 controlled by the promoter of ATP6V1B1. Crossing this transgene into the Slc26a4 Δ/Δ line restored pendrin expression in the endolymphatic sac without inducing detectable expression in the cochlea or the vestibular sensory organs. The transgene prevented enlargement of the membranous labyrinth, restored normal otoconia formation in the utricle and saccule and normal sensory functions of hearing and balance. Our study demonstrates that restoration of pendrin expression in the endolymphatic sac is sufficient to restore both hearing and balance.

SP15-3

Genetics for Inner Ear/Vestibular Disorder

CHARACTERIZATION OF THE TRANSCRIPTOME OF VESTIBULAR DYSFUNCTION ASSOCIATED WITH SLC26A4 MUTATIONS

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Recessive mutations in SLC26A4 are responsible for non-syndromic enlarged vestibular aqueduct and Pendred syndrome, constituting a common cause of hearing impairment in humans. In addition to hearing loss, patients with SLC26A4 mutations also suffer from episodic vertiginous attacks. To date, several mouse models with Slc26a4 mutations have been established. Corresponding to the human counterpart, mice with defected Slc26a4 revealed both hearing loss and vestibular dysfunction. In contrast to hearing loss which has been exhaustively investigated in these Slc26a4-defected mice, the pathogenetic mechanisms underlying vestibular dysfunction associated with Slc26a4 mutations remain largely unexplored. In our recent studies, we performed RNA-seq analyses on the vestibular extracts obtained from three groups of mice: Slc26a4-defected mice with circling behavior, Slc26a4-defected mice without circling behavior, and wild-type mice. The expression data were then subjected to Ingenuity Pathways Anal-

ysis (IPA), and the differentially expressed genes were validated on real-time PCR and immunohistochemistry. Our results revealed that reactive oxygen species might play a pivotal role in the development of vestibular phenotypes in *Slc26a4*-defected mice. These findings provide insights into the molecular pathology of vestibular dysfunction related to *SLC26A4* mutations, and may inform future studies on the potential therapeutic implications of modulating the associated genes or pathways.

SP15-4

Genetics for Inner Ear/Vestibular Disorder

GENETICS IN VESTIBULAR MIGRAINE AND EPISODIC ATAXIA

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Many vestibular and cerebellar disorders have a strong genetic background, but clinical heterogeneity leads to the slow progression in the molecular genetics of dizziness. Vestibular migraine is the common cause of spontaneous recurrent vertigo. It consists of recurrent episodes of vestibular symptoms with a current or previous history of migraine according to the International Classification of Headache Disorders. The strong familial clustering has been reported with genetic heterogeneity. Some locus were found to have a correlation with vestibular migraine, but no mutation was identified in candidate genes. Episodic ataxias (EAs) are a clinically heterogeneous group characterized by recurrent spells of truncal ataxia and incoordination. There are several subtypes defined by clinical features and genetic characterizations. The most common subtypes are EA1 and EA2, caused by mutations in *KCNA1* and *CACNA1A*, respectively. They have well-defined clinical features and been reported in ethnically multiple families. The other genes, such as *CACNB4*, *SLC1A3*, *UBR4* are also known to cause EAs. However, many patients with EA-like clinical features still do not have mutations in a known EA gene. In the future, wide availability of whole-exome sequencing can help to define candidate genes and identify new mutations associated with EA.

SP16-1

Superior Canal Dehiscence Syndrome

STUDY OF SUPERIOR CANAL DEHISCENCE IN FRESH HUMAN SPECIMENS

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Superior canal dehiscence (SCD), a defect of the superior semicircular canal bony capsule, is considered a pathological “third window” of the inner ear (round and the oval windows being the first two). This results in abnormal inner-ear pressures and sound transmission, disrupting balance and hearing.

We studied SCD effects in response to ear-canal sound stimulation in fresh human specimens. Inner-ear fluid pressures in the vestibule (Pv) and scala tympani (Pst) near the round window were measured with micro-fiberoptic pressure sensors, while velocities of the stapes and round window (Vstap, Vrw) were measured with laser Doppler vibrometry.

Measurements enabled estimates of flow across the ampulla with SCD. Because the acoustic pressure at the SCD (Pscd) was nearly zero, SCD resulted in a differential pressure between Pv and Pscd, resulting in volume velocity towards the SCD through the ampulla.

To measure effects on hearing, the cochlear input drive ($\Delta P = P_v - P_{st}$) provided a mechanical audiogram. Pressures as well as Vrw were affected by SCD size but not location, and decreased with frequency at low frequencies. Vstap generally increased slightly or remained unchanged.

The effect on pressures and velocities were consistent with the SCD leakage-pathway impedance behaving as an acoustic mass plus a resistor, increasing at high frequencies due to the fluid mass in the canal. SCD decreased the overall impedance of the inner ear at low frequencies, resulting in reduction of pressures in both scalae.

SP16-3

Superior Canal Dehiscence Syndrome

SUPERIOR CANAL DEHISCENCE INDUCED VESTIBULO-OCULAR REFLEX**Swee T AW***Department of Neurology, Royal Prince Alfred Hospital, Australia*

Background: Superior canal dehiscence (SCD), a temporal bone defect of the superior semicircular canal, causes vestibular and cochlear receptor hypersensitivity to sound.

Objective: To determine the vestibulo-ocular reflex (VOR) in SCD patients to air-conducted clicks (AC-C) and (AC-T) tones, and bone-conducted vibrations (BC-V).

Methods: Three-dimensional eye rotations were evoked by: 1) AC-C (0.1 ms, 110 dB NHL) and AC-T (0.5 s, 105 dB NHL, 0.5/2.0 kHz) in 19 SCDs; 2) BC-V (7 ms, 110 dB NHL, 0.5 kHz) in 17 SCDs. Eye rotation axes of their VORs, computed by vector analysis, were then referenced to known semicircular canal planes. Their results were compared to normal responses and contrasted with responses from one posterior canal dehiscence (PCD). SCD and PCD patients were confirmed by CT imaging.

Results: Normal VOR evoked by clicks, tones or vibrations were miniscule. In SCDs, AC-C VOR comprised upward, contraversive torsional eye rotations at 9 ms latency with magnitude up to 92 deg/s and threshold 10–40 dB below normal. Its eye rotation axis aligned with the superior canal axis, suggesting activation of superior canal receptors. AC-T evoked vestibular nystagmus (Tullio phenomenon). BC-V VOR in unilateral SCD was similar to AC-C VOR, while bilateral SCDs exhibited torsional cancellation and vertical summation from concomitant contralateral stimulation, irrespective of any conductive hearing loss. PCD showed a downward instead of upward VOR component.

Conclusions: In SCDs, AC-C and AC-T evoke high-magnitude, low-threshold VORs indicating superior canal receptor hypersensitivity to sound. BC-V VOR help identifies SCD in conductive hearing loss. A downward instead of upward VOR component distinguishes PCD from SCD.

SP16-4

Superior Canal Dehiscence Syndrome

LABORATORY TESTS OF COCHLEOVESTIBULAR HYPER-RESPONSIVENESS IN SUPERIOR CANAL DEHISCENCE SYNDROME**Ja-Won KOO***Department of Otorhinolaryngology, Seoul National University College of Medicine, Seoul National University Bundang Hospital, Korea*

We reviewed the findings of audio-vestibular laboratory tests of patients with superior canal dehiscence (SCD) syndrome and determined their diagnostic values and relationships with clinical parameters. Thirteen symptomatic SCD patients (1 bilateral) confirmed by temporal bone computed tomography (TBCT) and cervical vestibular evoked myogenic potentials (cVEMP) were recruited. SCD sizes were measured on reformatted images in the plane of the superior canal (SC). Results of audiologic tests (audiometry, cVEMP, electrocochleography (ECoG)) for 14 affected and 12 contralateral unaffected ears were evaluated. Relationships between summing potential (SP) to action potential (AP) ratios, as measured by ECoG, and other audiometric parameters were evaluated. Sensitivity analysis of SP/AP ratios was performed by plotting receiver operating characteristic (ROC) curves for SCD syndrome patients and 19 age-matched healthy controls. Mean SP/AP ratio of SCD ears was significantly higher than that of unaffected ears (0.52 versus 0.25, $p < 0.001$) and SPs were significantly elevated in affected ears ($p = 0.011$), whereas APs were similar for affected and unaffected ears. SP/AP ratio showed a sensitivity of 92.3% and a specificity of 94.0% for distinguishing SCD syndrome patients given the inclusion criteria applied (symptoms, TBCT, cVEMP threshold) at a cutoff value of 0.34 ($p < 0.001$). SP/AP ratio was not correlated with SCD size or cVEMP threshold in affected ears. Negative absolute values of bone conduction at low frequency tended to increase with SP/AP ratio. Five out of 13 patients underwent surgical repair experienced symptomatic improvement with normalization of SP/AP ratios and VEMP threshold. ECoG and VEMP appears to be a valuable diagnostic adjunct for functional demonstration of the third window in the otic capsule with high sensitivity and specificity, and thus, can support a clinical diagnosis of SCD when used in conjunction with clinical and radiological findings.

SP17-1

Vestibular Brain and Functional Imaging

THE VESTIBULAR BRAIN AND FUNCTIONAL IMAGING**Marianne DIETERICH***Department of Neurology and German Center for Vertigo and Balance Disorders-IFB, Ludwig-Maximilians-University, Munich, Germany*

This review summarizes our current knowledge of multisensory vestibular network structures and their functions in humans. Most of it derives from brain activation studies with PET and fMRI conducted over the last decades. The patterns of activations and deactivations during caloric and galvanic vestibular stimulations in healthy subjects represent a cortical and subcortical vestibular network in the temporo-parieto-insular cortex of both hemispheres. These “normal” patterns have been compared with those in patients with acute and chronic peripheral and central vestibular disorders. Major findings were the following: (1) In patients with acute unilateral vestibular loss (e.g. vestibular neuritis) the central vestibular system exhibits a spontaneous visual-vestibular activation-deactivation pattern similar to that described in healthy volunteers during vestibular stimulation. (2) Patients with acute lesions of the vestibular nuclei due to infarctions (Wallenberg’s syndrome) showed no or significantly reduced activation in the contralateral cortical hemisphere but increased activations in ponto-cerebellar loops. (3) Patients with posterolateral thalamic infarctions exhibited significantly reduced activation of the multisensory vestibular cortex areas in the ipsilateral hemisphere, if the ear ipsilateral to the thalamic lesion was stimulated. Activation of similar areas in the contralateral hemisphere was also diminished but to a lesser extent, and the right hemispheric dominance in right-handers was preserved. These findings indicate that there are bilateral ascending vestibular pathways from the vestibular nuclei to vestibular cortex areas with the posterolateral thalamus as a vestibular gatekeeper. Furthermore, there is evidence for a dominance of the ipsilateral ascending pathways and a dominance of the right hemisphere in right-handedness.

SP17-2

Vestibular Brain and Functional Imaging

THE ROAD AHEAD: FROM THE HUMAN VESTIBULAR CORTEX TO VESTIBULAR CONNECTOMICS**Peter Zu EULENBURG**^{1,2}, Felix HOFFSTAEDTER³, Ria Maxine RUEHL^{1,2}¹*German Center for Vertigo and Balance Disorders, Ludwig-Maximilians University, Munich, Germany*²*Department of Neurology, Ludwig-Maximilians University, Munich, Germany*³*Institute of Clinical Neuroscience and Medical Psychology, Medical Faculty, Heinrich Heine University, Düsseldorf, Germany*

The search for the human homologues to established non-human primate regions for the cortical areas processing of vestibular information such as the parieto-vestibular insular cortex (PIVC), area 6, and the human medial superior temporal field (hMST) is still ongoing. Recently observed vestibular regions like the cingulate sulcus visual (CSv) on the other hand still have to be incorporated into our knowledge of the human cortical vestibular network. To achieve further progress and precise human anatomical landmarks with respect to the topology, methodological obstacles such as somatosensory confounders with the employed artificial vestibular stimuli have to be eliminated foremost. Advances in MRI sequences and the emergence of new analytical tools from machine learning will then allow for an increased spatiotemporal resolution as well as a higher signal detection sensitivity for the entire field of vestibular neuroimaging. To illustrate some of these advances and the ensuing prospects, the talk will focus on confounder-free galvanic vestibular stimulation experiments from our lab in combination with the analysis of publicly available large-scale repository data. Here, we used a hierarchical clustering algorithm on structural covariance and functional connectivity data to investigate the vestibular network. Differing baseline conditions, eyes open and closed, in combination with new developments in the denoising of resting state data were also applied to the repository data. This talk aims to give a short introduction of established and probable cortical vestibular regions in humans derived from functional neuroimaging whilst at the same time giving an outlook into the emerging field of vestibular connectomics.

SP17-3

Vestibular Brain and Functional Imaging

ALTERED VESTIBULAR CORTEX FUNCTIONAL CONNECTIVITY AT REST IN VESTIBULAR NEURITIS**Hyo-Jeong LEE¹**, Ja Hee KIM¹, Hyejin KANG^{2,3}, Eunkyung KIM^{2,4,5}, Sung Kwang HONG¹, Hyung-Jong KIM¹¹*Department of Otolaryngology, Hallym University College of Medicine, Korea*²*Department of Nuclear Medicine, Seoul National University College of Medicine, Korea*³*Department of Data Science For Knowledge Creation Research Center, Seoul National University, Korea*⁴*Department of Department of Data Science For Knowledge Creation Research Center, Seoul National University, Korea*⁵*Department of Department of Data Science For Knowledge Creation Research Center, Medical Research Center, Seoul National University, Korea*

Vestibular neuritis (VN) is a sudden failure of vestibular function, that occurs mostly unilaterally. In this study, we used resting state (RS-) fMRI to examine change of functional connectivity for functional recovery in sixteen unilateral VN patients (M:F = 9:7; mean age of 43.7 ± 16.8 , left:right-lesioned = 7:9). Brain MRI(T1 and RS-fMRI) and clinical observation were performed within 2 days of diagnosis of acute VN and repeated at 2–3 months later (follow-up). Caloric test results and Korean version of the dizziness handicap Inventory (K-DHI) was collected at the time of MRI. Functional MR data was preprocessed with SPM12 software and seed-based analysis was performed to identify changes of RS- functional connectivity during recovery period using REST toolbox. Areas OP2 from each hemisphere were selected as seed ROIs, as the area in the right side has been reported as a core region for vestibular processing in a meta-analysis. Statistical threshold was set at $p < 0.05$ (FDR-corrected). We observed significantly increased connectivity with LOP2 after 3 months in vestibular network including the bilateral cingulate cortex(CG), the right cerebellum, the right superior temporal gyrus (STG), the right OP3, the right precentral gyrus, the left insula and the visual cortices. K-DHI improvement was positively correlated with connectivity increase in the right STG, the right OP3, the right anterior/middle CG. The observed alterations of function connectivity of LOP2 might be related to the disturbed network of ROP2 due to acute peripheral vestibulopathy, leading to central compensation of homologous area for functional recovery.

SP18-1

Spatial Orientation

SPATIAL MEMORY AND NAVIGATION IN A 3-D ENVIRONMENT: ANISOTROPY FOR HORIZONTAL AND VERTICAL DIMENSIONS**Thomas BRANDT¹**, Marianne DIETERICH¹, Andreas ZWERGAL¹, Stefan GLASAUER¹¹*German Center for Vertigo and Balance Disorders, Ludwig-Maximilians-University, Munich, Germany*

Animal experiments report contradictory findings as to whether there is a behavioral and neuronal anisotropy exhibited in vertical and horizontal capabilities of spatial orientation and navigation, particularly with respect to the comparability of available reference frame cues. The vertical component may be less critical for survival in ground-based animals like dogs or rats. Psychophysical experiments provide first evidence that the internal representation of a familiar multilevel building is distorted compared to the dimensions of the true building: vertically taller and horizontally shorter. This was not only demonstrated in the mathematical reconstruction of a mental modal based on the analysis of pointing experiments but also by the participants drawing of the front view and the ground plan of the building. In the mental model both plans were altered in different directions: compressed for the horizontal floor plane and stretched for the vertical column plane. Spatial orientation was also tested with behavioral and PET correlates during a horizontal and vertical real navigation task in humans. Spatial navigation performance was significantly better during horizontal navigation with the glucose metabolism increased in the right hippocampus, bilateral retrosplenial cortex and the pontine tegmentum. In contrast, vertical navigation activated the bilateral hippocampus and insula. Visually guided landmark recognition seems to be more important for horizontal navigation, while distance estimation based on vestibular input might be more relevant for vertical navigation.

SP18-2

Spatial Orientation

AN INTERNAL MODEL OF GRAVITY AND ITS ROLE IN SPATIAL ORIENTATION**Dora E. ANGELAKI***Department of Neuroscience, Baylor College of Medicine, USA*

Whether running to catch a ball or turning to reach for a cup of coffee, the ability to navigate in the world and interact with the environment depends critically on knowing our current motion and allocentric orientation in the world. Motion sensors in the vestibular inner ear play a particularly important role in this process. However, moving in a gravitational environment complicates estimation of these signals. As pointed out by Einstein over a century ago, all acceleration sensors, including the otolith organs, also respond to the force of gravity. Although illusions can occur when there are insufficient sensory cues available, under most circumstances the brain can accurately distinguish between tilting relative to gravity and translating through space, even in the absence of vision. We have identified a network of neurons in the macaque vestibulo-cerebellum that appears to perform the required computations by using multimodal sensory information from both sets of vestibular sensors to compute an internal model of gravity. Gravity signals have also been found in anterior thalamus neurons that encode 3D head orientation. This tuning is gravity-anchored, and occurs during passive motion in both dark and light conditions. These gravity signals are used to estimate visual orientation in the allocentric world, and bilateral labyrinthectomy causes deficits in both allocentric visual orientation perception and vertical arm movement planning and execution.

SP18-3

Spatial Orientation

VESTIBULAR LOSS INFLUENCES SPATIAL NAVIGATION STRATEGY: FROM RODENT TO PATIENTS**Stephane BESNARD**¹, Alice BENOIT¹, Marie-Laure MACHADO¹, Bruno TRUCHET², Franck CHAILLAN², Bruno PHILOXENE¹, Marilynne GUILLAMIN³, Karim BOUMÉDIÈNE⁴, Paul SMITH⁵, Pierre DENISE¹¹*Department of Physiology, Normandie Univ, Unicaen, Inserm U 1075 Comete, Caen, 14032, France, France*²*Department of Laboratoire De Neurosciences Cognitives, Umr Cnrs 7291, Université Aix – Marseille, Fédération 3c, Marseille, France, France*³*Department of Ifr Icore, Normandie Univ, Unicaen, Ifr Icore, Caen, 14032, France, France*⁴*Department of Unité De Recherche Matrice Extra Cellulaire Et Pathologie (ea 3214), Normandie Univ, Unicaen, Unité De Recherche Matrice Extra Cellulaire Et Pathologie (ea 3214), Caen, 14032, France, France*⁵*Department of Pharmacology And Toxicology, Brain Health Research Centre, University of Otago, Dunedin, New Zealand, New Zealand*

Spatial declarative memory refers to a spatial strategy using numerous sources of sensory information, mainly visual and vestibular, integrated within the hippocampus. In contrast, procedural memory refers to a response strategy based on motor skills and gestures and involves the striatum. Since the vestibular system encodes motion and sends projections to the hippocampus and the striatum, we hypothesized that vestibular loss might impair both navigation strategy and learning processes, and that these impairments could be in part mediated through NMDA receptors and LTP modulation. In a rat model of bilateral vestibular loss, we have shown that during spatial orientation tasks animals switched to a procedural memory strategy associated with a modulation of the NMDA receptors expression decreased within the striatum and increased within the hippocampus combined with an increase of the hippocampal early phase of LTP. In humans, evaluated with the Virtual Human Maze[®], the control group preferred a procedural memory strategy while bilateral areflexic patients equally used a spatial or response strategy. Our results show that the loss of vestibular information crucially influences our ability in spatial navigation and depends on species. In rodent, our findings suggest that hippocampal integration and selective discrimination of sensory inputs were impaired after vestibular loss, then switching to a more striatal-related egocentric strategy of spatial navigation. In humans, we suggest that, in static conditions, bilateral areflexic patients counterbalance their vestibular loss with visual information and tend to use a strategy of spatial response.

SP18-4

Spatial Orientation

TWO SIGNALS FOR VERTICALITY**Elisa Raffaella FERRE***Department of Psychology, Royal Holloway University of London, United Kingdom*

Humans possess an internal model of gravity, which allows the accurate perception of what is up and what is down, or, in other words, what is vertical. The integration of vestibular-gravitational information with other somatic signals is essential for sensing verticality. Vestibular cues are known to influence verticality representation in visual domain. However, it remains unclear how we perceive verticality for stimuli applied to the skin surface. Theoretically, as bipedal animals, the neuraxis, as well as vestibular signals, might represent a proxy for verticality. To address this question, a psychophysical subjective tactile vertical task has been combined with galvanic vestibular stimulation (GVS) in healthy participants. Brief left anodal and right cathodal GVS, or right anodal and left cathodal GVS, or sham stimulation were delivered at random while participants judged the orientation of lines drawn on their forehead. Online vestibular signals induced by GVS did not produce misperceptions of tactile verticality. Conversely, asking participant to tilt the head induced a clear bias in verticality judgements toward the neuraxis. This bias was present also for stimuli not aligned with the body midline. Taking together, these results support the idea of two distinct representations of verticality: a vestibular representation, based on the direction of gravity, which is adopted as reference for visual verticality judgements, and a somatosensory representation which is not based on any online vestibular-gravitational signal, nor on the midline. The neuraxis is a critical reference for this representation.

SP18-5

Spatial Orientation

VESTIBULAR PROJECTIONS TO THE HIPPOCAMPUS**Paul SMITH**¹, Martin HITIER^{1,2}, Yanfeng ZHANG^{1,3}, Go SATO^{1,4}, Yiwen ZHENG^{1,5}, Stéphane BESNARD⁶¹*Department of Pharmacology And Toxicology, School of Medical Sciences, And the Brain Health Research Centre, University of Otago Medical School, Dunedin, New Zealand*²*Department of Otolaryngology-head And Neck Surgery And Anatomy, Chu De Caen, And Unicaen, Caen., France*³*Department of Physiology, Anatomy And Genetics, University of Oxford, Oxford, United Kingdom*⁴*Department of Otolaryngology, University of Tokushima School of Medicine, Japan*⁵*Department of Pharmacology And Toxicology, School of Medical Sciences, And the Brain Health Research Centre, University of Otago Medical School, Dunedin, New Zealand*⁶*Department of Inserm, U 1075 Comete Caen, France*

It has been established for some time that the peripheral vestibular system, via the vestibular nucleus and possibly the cerebellum, transmits vestibular information polysynaptically to the hippocampus, where it appears to be used in the development of spatial memories. Nonetheless, how different types of vestibular information are transmitted to different parts of the hippocampus, is less clear. We undertook selective electrical stimulation (< 400 microA, bipolar) of the vestibular labyrinth in anaesthetised rats and in the hippocampus performed c-Fos immunohistochemistry and local field potential (LFP) recording using a 16 channel electrode microarray. In stimulated ($n = 15$) compared to sham ($n = 5$) rats, we observed selective c-Fos activation in the dorsal hippocampus. Double immunofluorescence labelling with NeuN showed that the c-Fos labelling was in mature hippocampal neurons, whereas c-Fos did not co-label for doublecortin, a marker of immature neurons. Selective stimulation of different vestibular receptor groups resulted in long-latency LFPs in different parts of the hippocampus. For example, selective stimulation of the posterior canal ampulla caused a triphasic LFP in different hippocampal subregions, with a latency of approximately 21 ms, with the amplitudes higher and latencies shorter in the dorsal hippocampus. These studies suggest a complex projection of vestibular information to different hippocampal subregions that provides clues as to how the hippocampus might use different kinds of vestibular information in spatial orientation and memory.

SP19-1

Meniere's Disease (Basic) – Recent Progress in Revealing Pathologic Mechanism of Meniere's Disease

A LOCUS AT 6P21.33 ASSOCIATED WITH BILATERAL MENIERE DISEASE REGULATES CLASS II HLA GENES AND TWEAK/FN14 PATHWAY

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Purpose of the study: To define a genetic marker associated with autoimmune Meniere's disease.

Methods: We genotyped 899 patients with MD (379 bilaterally affected), and 1798 Iberian controls with the Immunochip. After defining the locus with candidate single nucleotide variants (SNV), we performed a conditional haplotype gene expression assay in peripheral blood mononuclear cells (PBMC). RNA expression levels were measured using the HumanHT-12 v4 Expression BeadChip. Limma R package was used for expression data analysis and normalization and for differential expression analysis. Differentially expressed genes in PBMC (adjusted $P < 0.001$) according to the conditional haplotype, were used to predict involved pathways.

Results: A locus at 6p21.33 is associated with bilateral MD (rs9380217; OR = 1.74 (1.41–2.20), ($P = 1.0 \times 10^{-6}$). Gene expression profile of homozygous haplotype-conditioned individuals demonstrates that this region is a trans expression quantitative trait locus (eQTL) for some class II HLA genes in PBMC, showing significant differences in 973 genes ($P < 0.001$). Signaling network analysis predicts several involved pathways, being the TWEAK/Fn14 pathway the top candidate ($P = 3.8 \times 10^{-8}$). Functional studies with haplotype-conditioned lymphoblastoid cells from patients with MD suggest that this eQTL may regulate cellular proliferation via the TWEAK/Fn14 pathway.

Conclusions: The SNV rs9380217 and rs4947296 could be used as predictors for bilateral SNHL in MD and the results support an immune dysfunction in the carriers of the risk haplotype.

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SP19-2

Meniere's Disease (Basic) – Recent Progress in Revealing Pathologic Mechanism of Meniere's Disease

AUTOIMMUNITY AND INNER EAR INFLAMMATION AS AN ETIOPATHOGENESIS OF MENIERE'S DISEASE

Sung Huhn KIM

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The pathologic mechanism of Meniere's disease is still unclear. In this study, we evaluated autoimmunity and inflammation in human endolymphatic sac as a potential cause of Meniere's disease. In addition we tried to find useful biomarker candidates for diagnosis. We investigated the protein composition of human inner ear fluid using liquid column mass spectrometry, the autoimmune reaction between circulating autoantibodies in patient serum and multiple antigens using the Protoarray system, the immune reaction between patient serum and mouse inner ear tissues using western blot analysis. The changes of ion transport in human endolymphatic sac epithelium after the exposure to the inflammatory cytokines were investigated using electrophysiological methods. Nine proteins, including immunoglobulin and its variants and interferon regulatory factor 7, were found only in the inner ear fluid of patients with Meniere's disease. Enhanced immune reactions with 18 candidate antigens were detected in patients with Meniere's disease in Protoarray analysis. Antigen-antibody reactions between mouse inner ear proteins with molecular weights of 23–48 kDa and 63–75 kDa and patient sera were detected in 8 patients. After the exposure of endolymphatic sac epithelium to inflammatory cytokines, sodium transport ability was significantly deteriorated in human endolymphatic sac epithelium. These findings suggest that autoimmunity could be one of the pathologic mechanisms behind Meniere's disease. Multiple autoantibodies and antigens may be involved in the autoimmune re-

action. Specific antigens that caused immune reactions with patient's serum in Protoarray analysis can be candidates for the diagnostic biomarkers of Meniere's disease.

SP19-3

Meniere's Disease (Basic) – Recent Progress in Revealing Pathologic Mechanism of Meniere's Disease

ROLE OF VASOPRESSIN-AQUAPORIN2 SYSTEM IN THE FORMATION OF ENDOLYMPHATIC HYDROPS

Akinobu KAKIGI

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Meniere's disease is histologically characterized by endolymphatic hydrops (EH) in the inner ear. The mechanisms underlying the over accumulation of endolymph still remain an enigma. There is considerable evidence that water homeostasis in the inner ear is regulated partly via the vasopressin-aquaporin2 (VP-AQP2) system, suggesting that EH, a morphological characteristic of Meniere's disease, reflects the mal-regulation of the VP-AQP2 system in inner ear fluid. Moreover, the poor development of the endolymphatic sac and duct and fibrosis of the endolymphatic sac (ES) have been reported in the temporal bones of Meniere patients. Based on these results, we hypothesized that a combination of ES dysfunction and dysregulation of endolymph might induce Meniere's attacks.

We have developed an animal model which is considered to be better suited for MD, because this model consists of a combination of ES dysfunction and dysregulation of endolymph induced. In contrast to previous animal models that very rarely showed episodes of imbalance, spontaneous nystagmus and vertiginous attacks are clearly evident in our model. Moreover, our model shows hearing impairment. Further, we have recently visualized the developing EH via OCT in live guinea pigs.

In this paper, experimental evidence to support the above-mentioned hypothesis will be presented mainly based on our recent studies.

SP19-4

Meniere's Disease (Basic) – Recent Progress in Revealing Pathologic Mechanism of Meniere's Disease

INTEREST OF 3D WIDEBAND TYMPANOMETRY IN MÉNIÈRE'S DISEASE

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Introduction: the abnormal regulations of intralabyrinthic pressures in Meniere's disease ears (MD) modify their sound transfer function (STF). STF could be studied by multifrequential acoustic immittance technics, using tonal stimuli or clicks (3D Wideband acoustic immittance: WAI). In this study, we wanted to verify if data provided by WAI could be useful in the diagnosis of MD.

Materials and methods: Immittance data were recorded in 25 normal ears (NE) and 43 MD ears, in the sitting and laying positions. RF were compared on the Tymstar V2- Interacoustics (tonal stimuli) and the Titan WB – Interacoustics (clicks). The spectral absorbance curves were studied at ambient pressure (Pa) and at the peak of maximal absorbance (Ppe) on the Titan WB. Statically significant results are presented.

Results: RF are lower and demonstrate larger postural changes in MD than NE only in the tymstar data. MD show increased absorbance than NE for the spectral band of 800–1000 Hz and 3000 Hz in all the positions and the tested pressures. The gaps between the Pa and the Ppe are larger in MD than NE in all the positions. The absorbance's postural changes are > 7% in MD, especially in the 800–1000 Hz and 3000 Hz spectral bands, with a sensitivity of 94% and a specificity of 85%.

Conclusions: The RF calculation paradigms of WB Titan should be improved. SFT of 2 spectral bands of interest are impacted by hydrops. Some data of 3D WB tympanometry are useful tools for the diagnosis of MD.

SP19-5

Meniere's Disease (Basic) – Recent Progress in Revealing Pathologic Mechanism of Meniere's Disease

EFFECT OF ROUND WINDOW PERFUSION OF ISOSORBIDE FOR ENDOLYMPHATIC HYDROPS IN VASOPRESSIN-INDUCED ANIMAL MODEL

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Isosorbide (ISB) reduces the volume of endolymph and its oral administration is clinically effective in patients with Ménière's disease. The purpose of this study was to evaluate the effect of ISB round window perfusion (RWP) on vestibular imbalance using a new acute attack endolymphatic hydrops model. A total of 70 male Hartley guinea pigs were used. Isosorbide was applied via RWP and PO. Perilymph of scala tympani was collected through round window membrane and intracochlear concentration was analyzed using HPLC-RI. Acute aggravation of hydrops was induced by desmopressin (VP). Auditory and vestibular functions were measured before and after ISB treatment using ABR test and the bidirectional sinusoidal harmonic acceleration (SHA) test with an animal rotator, respectively. The result showed that ISB of 25%, 50%, and 100% can pass the round window membrane after RWP, and RWP with 50% and 100% ISB showed higher intracochlear concentrations than 25% ISB. VP successfully induced temporary asymmetric vestibular function in guinea pigs with surgically ablated endolymphatic sacs. In the normal guinea pigs, transient vestibular imbalance was observed after RWP of 50% ISB, but not after RWP of 25% ISB. Especially, RWP of 25% ISB preserved symmetric vestibular function against VP at the acute attack hydrops model. In conclusion, ISB was able to pass the round window membrane into the perilymphatic space, and RWP of ISB preserved symmetric vestibular function in the acute hydrops model induced by VP. Thus, RWP such as intratympanic injection could be a candidate treatment for vertigo attack in Ménière's disease.

SP20-1

Visually Induced Dizziness; What Is It; Where Does It Come From; How Can We Deal With It?

VISUALLY INDUCED DIZZINESS – HISTORY TAKING IS CRUCIAL

Mallinson A¹, Longridge NS¹

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Visually induced dizziness or “visual vestibular mismatch” results from vestibular system deficit. In present day medical legal cases resulting from decelerative trauma, patients voice symptoms of VVM during detailed history taking. In nontrauma vestibular patients, this symptom set is often disregarded, or not even voiced at all, as history taking is often abbreviated after more “traditional” vestibular complaints (spinning) are voiced by the patient. This allows for a diagnosis of vestibular pathology. If complaints of VVM were voiced during a history taking, they were often dismissed as anxiety or stress.

These concerns caused us to look at a trauma group and a non trauma group of vestibular patients, and we took extensive histories in all patients. The histories of both groups of patients were virtually identical and the vestibular test results were also similar in both groups of patients. This suggests to us that both groups of patients were virtually identical and these patients' symptoms can only be understood by the taking of an in-depth history.

SP02-2

Visually Induced Dizziness; What Is It; Where Does It Come From; How Can We Deal With It?

INTRATYMPANIC GENTAMICIN CAUSING VISUALLY INDUCED DIZZINESS

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When perambulating the VOR allows maintenance of gaze on a fixed target unless a conscious decision is made to relocate the eyes to look at something else. Similar refocusing to another object occurs in emergency circumstances with a peripheral visual, auditory or olfactory threat, or even a touch or taste threat. Visually-induced dizziness is a change in sensitivity so that a lower threshold of threat results in need to urgently relocate vision; this urgency can

be stressful (?can cause stress). The question to determine is whether visually-induced dizziness seen in different specialties, otological, neurological and psychiatric is different disorders manifesting with the same complaints, evolutionary convergence, or is due to slightly different complaints causing referral to different specialties but arising from the same underlying disorder.

SP20-3

Visually Induced Dizziness; What Is It; Where Does It Come From; How Can We Deal With It?

EARLY PREDICTORS OF CLINICAL RECOVERY FROM ACUTE VESTIBULAR NEURITIS.

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In order to identify early predictors of poor symptomatic recovery in Vestibular Neuritis patients we followed up 40 vestibular neuritis (VN) patients in the acute (median 2 days), recovery (median 10 weeks) and long term (10 month) phases. Clinical outcome was assessed with the Dizziness Handicap Inventory (DHI) and measurements included vestibulo-ocular, visuo-vestibular psychophysical tests and psychological questionnaires.

Worse clinical outcome (DHI score at 10 weeks and 10 months) was predicted by greater visual dependency (rod and disc test), autonomic anxiety and fear of bodily sensations acutely. Factor Analysis revealed a strong association between clinical outcome, visual dependency and psychological factors, all loading on a single statistical component accounting for 59% of the variance. Canal paresis and vestibular-perceptual thresholds loaded separately on a second component accounting for only 12% of variance which, notably, did not include clinical outcome.

Recovery from VN can be predicted by a tightly coupled combination of psychological factors and visual dependency. The tight association between psycho-physical and psychological variables provides a model for psychosomatic research in the vestibular field. Early identification and treatment of these factors may prevent the development of chronic disability following VN.

SP20-4

Visually Induced Dizziness; What Is It; Where Does It Come From; How Can We Deal With It?

AGE RELATED CHANGES IN VISUAL DEPENDENCE AND VISUALLY INDUCED DIZZINESS

Philippe PERRIN

University of Lorraine, Nancy, France

Visual dependence or preference in balance maintenance becomes more prevalent as we age; both vestibular pathology and certain physical activities are factors involved in how we develop a preference. These factors also play a role in vestibular patients who experience newly developed motion sickness.

SP20-5

Visually Induced Dizziness; What Is It; Where Does It Come From; How Can We Deal With It?

NYSTAGMUS SLOW PHASE CLOCKS, SACCADE DWELL TIMES AND VISUAL STABILITY: A ROLE IN VISUALLY INDUCED DIZZINESS?

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Recent analyses show that durations of slow phases of human optokinetic nystagmus are consistent with a basic interval generator (200–250 ms Gaussian clock), with a random probability of generating an FP at the end of a clock cycle. Further, the probability of generating a fast phase at the end of each clock cycle decreases significantly during performance of a choice reaction task. These findings indicate that the alternation between slow and fast phases of

optokinetic status is not purely reflexive. Rather, the generation of the FP, at the conclusion of a clock cycle, shows a dual-task interference effect. These ‘slow phase dwell times’ are remarkably similar to the published findings for slow phases in congenital nystagmus, durations of saccadic intrusions, the timing of square wave jerks that intrude during fixation and the saccade dwell time for sequential saccades during scene scanning or reading (the ‘interval between saccades’) and are consistent with the approximately 200 ms sampled data period for control of eye movements, proposed in 1963 by Young and Stark. Hence, duration of an optokinetic nystagmus SP is a quantized sampling behavior that is specialized for visuospatial information processing and fast phase target selection. The ‘clock’ interval represents a temporal unit of data sampling for eye movement control, when eye velocity should match hypothetical visual motion. It is proposed that dysregulation of nystagmus clocking behavior may be associated with visually induced dizziness.

SP20-6

Visually Induced Dizziness; What Is It; Where Does It Come From; How Can We Deal With It?

EFFECTS OF CLINICAL STATE AND VISUAL BACKGROUND ON VISUAL DEPENDENCE MEASURED BY A MODIFIED ROD AND FRAME/DISK TEST

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Background: Patients who remain symptomatic following acute vestibular syndromes frequently report visually induced dizziness, which past research linked to visual dependence. This study assessed the effects of clinical state and composition of the visual environment on visual dependence using Rod and Frame/Disk Tests modified with tilted backgrounds of differing complexity and rotating backgrounds of differing emotional valence. Background composition was predicted to have a larger effect on visual dependence in patients with persistent dizziness than normal controls.

Methods: Thirty-five normal individuals, 13 patients with peripheral vestibular deficits or vestibular migraine, and 11 patients with persistent postural-perceptual dizziness (PPPD) participated. Rod and Frame/Disk backgrounds were plain black and stationary ovals; square frame, country road, and city street scenes tilted 10° right and left of vertical; and ovals and faces with neutral or emotional expressions rotated 20°/second in clockwise and counter-clockwise directions. Subjects completed the Dizziness Handicap Inventory (DHI).

Results: For all subjects, average subjective visual vertical (SVV) errors were higher for city (4.61°) and country (3.98°) scenes than frame (2.60°) and plain (0.99°) backgrounds (ANOVA, $p < 0.0001$). SVV errors were higher for rotating backgrounds (1.74°–1.98°) than stationary ovals (1.06°) ($p < 0.0001$), but did not differ among ovals and faces. Subjects with PPPD had larger SVV errors than controls with frame (4.07° vs. 2.14°, $p < 0.02$) and country (5.38° vs. 3.49°, $p < 0.02$) backgrounds. DHI scores differed significantly among groups (control: 0.71, vestibular: 21.4, PPPD: 49.5, $p < 0.0001$), and predicted SVV errors.

Conclusions: Clinical state and composition of visual backgrounds, particularly tilted backgrounds, independently influenced visual dependence.

SP20-7

Visually Induced Dizziness; What Is It; Where Does It Come From; How Can We Deal With It?

VISUALLY INDUCED DIZZINESS: HOW CAN WE DEAL WITH IT?

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Individuals with visually induced dizziness are believed to be overly reliant on visual input for balance (ie, visually dependent). Visually induced dizziness can significantly improve when customized vestibular rehabilitation exer-

cises are combined with exposure to optokinetic stimuli. However, the frequency of treatment sessions (once or twice weekly for an average of 8-weeks) and the equipment used (expensive and space consuming) can make it difficult to incorporate these techniques into everyday clinical practice where exercises may be practiced unsupervised. The aim of this presentation is to a) provide an overview of recent findings on “high-tech” vs. “low-tech” optokinetic stimuli including virtual reality and home exercise gaming and b) identify future areas of research for the management of visually induced dizziness symptoms.

SP21-1

Vestibular Disorder and Autonomic Interaction Symposium

VESTIBULAR INFLUENCES ON THE CONTROL OF BLOOD PRESSURE

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A bilateral labyrinthectomy (BL) attenuates the regional changes in vascular resistance that ordinarily occur during postural alterations, resulting in blood pressure lability. For example, acutely following BL, the increase in hindlimb vascular resistance that ordinarily occurs to prevent peripheral blood pooling was attenuated up to 30% during the first 10 seconds following the onset of a 60° head-up tilt. Vestibulosympathetic responses (VSR) have little physiological role during postural changes <20° that have negligible impact on the distribution of blood in the body. Thus, VSR have a lower gain than other responses elicited by vestibular inputs. Nonetheless, they have a shorter latency than baroreceptor responses, and thus are important in stabilizing blood pressure at the onset of large changes in body position in space. We have shown that the sensitivity of neurons in the brainstem region that plays a primary role in cardiovascular regulation, the rostral ventrolateral medulla (RVLM), is lower in conscious than in decerebrate cats, showing that higher centers of the brain can suppress the gain of VSR. Such suppression of VSR is necessary to assure that the responses only occur during changes in body position of sufficient magnitude to cause peripheral blood pooling and lability in blood pressure. Our current work is exploring the feedforward neural mechanisms through which expectation of movement alters the gain of VSR and baroreceptor reflexes.

SP21-3

Vestibular Disorder and Autonomic Interaction

RECENT ADVANCES IN ORTHOSTATIC HYPOTENSION PRESENTING ORTHOSTATIC DIZZINESS OR VERTIGO

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Orthostatic hypotension (OH), a proxy for sympathetic adrenergic failure, is the most incapacitating sign of autonomic failure. Orthostatic dizziness (OD) is known to be the most common symptom of OH. However, recent studies have demonstrated that 30–39% of patients with OH experienced rotatory vertigo during upright posture (i.e., orthostatic vertigo, OV), which challenges the dogma that OH induces dizziness and not vertigo. A population-based study on spontaneously occurring OD across a wide age range showed that the one-year and lifetime prevalence of OD was 10.9 and 12.5%, respectively. Approximately 83% of patients with OD had at least one abnormal autonomic function test result. So far, 11 subtypes of OD have been proposed according to the pattern of autonomic dysfunction, and generalized autonomic failure of sympathetic adrenergic and parasympathetic cardiovagal functions was the most common type. Four different patterns of OH, such as classic, delayed, early, and transient type have been found in patients with OD. The head-up tilt test and Valsalva maneuver should be performed for a comprehensive evaluation of sympathetic adrenergic failure in patients with OD/OV.

SP22-1

BPPV-Pathogenesis

BIOMECHANICAL ORIGINS OF BENIGN PAROXYSMAL POSITIONAL VERTIGO**Richard D RABBITT***Department of Bioengineering, Otolaryngology, University of Utah, USA*

Benign paroxysmal positional vertigo (BPPV) is the most common cause of vertigo and has origins in pathological responses of one or more semicircular canals to gravity or acceleration of the head. The goal of this presentation is to foster an intuitive understanding of semicircular canal biomechanics and how it underlies neural responses to gravito-inertial acceleration in health and disease. Cupula displacements, afferent neural discharge, and eye movements will be discussed in the context of diagnostic maneuvers and repositioning treatments for both canalithiasis and cupulolithiasis forms of BPPV.

SP22-2

BPPV-Pathogenesis

DOES MEDICAL ILLNESS SUCH AS OSTEOPOROSIS AND VIT D DEFICIENCY MATTER FOR PATIENTS WITH BPPV?**Seong-Hae JEONG***Department of Neurology, Chungnam National University Hospital, Daejeon, Korea*

Although the mechanism of positional vertigo is well recognized in benign paroxysmal positional vertigo (BPPV), the underlying cause of otoconial degeneration and detachment from the otoconial beds remains to be elucidated. Until now, advanced age, head or ear trauma, other inner ear disorders, and female sex are known predisposing factors for BPPV. Recently, there has been reported on deranged calcium metabolism in idiopathic BPPV. In this talk, it will mention that the current research and its clinical impact on medical illness such as decreased bone density and vitamin D deficiency in BPPV.

SP23-1

Cochlear Implant and Vestibular Function

VESTIBULAR AND BALANCE DYSFUNCTION IN CHILDREN WITH SENSORINEURAL HEARING LOSS AND COCHLEAR IMPLANTS**Sharon L CUSHING**^{1,2,3}, Karen A GORDON^{2,3}, Blake C PAPSIN^{1,2,3}¹*Department of Otolaryngology, Hospital For Sick Children, Canada*²*Department of Otolaryngology, Head And Neck Surgery, University of Toronto, Canada*³*Department of Archie's Cochlear Implant Laboratory, Hospital For Sick Children, University of Toronto, Canada*

Vestibular dysfunction is the most common associated feature in children with sensorineural hearing loss. Up to 70% of children with profound sensorineural hearing loss will display some element of vestibular impairment with nearly 40% displaying profound bilateral areflexia. In these children vestibular dysfunction translates into poor balance, a risk factor for injury in addition to implant failure. While cochlear implantation itself poses a risk to vestibular end-organ function, the biggest predictor and risk factor for vestibular impairment in a child with sensorineural hearing loss is the underlying etiology of their deafness. There are several congenital and acquired causes of hearing loss that display a high likelihood of concurrent vestibular impairment.

The current talk will focus on the prevalence, characteristics, consequences and diagnosis of combined cochleoves-tibular loss in children. It will also review the functional impact of this multisensory deficit and explore current and future treatment options in these children.

SP23-2

Cochlear Implant and Vestibular Function

VESTIBULAR FUNCTION AND IMBALANCE FOLLOWING COCHLEAR IMPLANTATION**Stephen John O'LEARY**^{1,2}, William SHUTE¹, Matthew PAYNE¹, Daniel WONG¹, Michelle MORAN^{1,2}, David SZMULEWICZ^{1,2}¹*Department of Otolaryngology, University of Melbourne, Australia*²*Department of Ent, Royal Victorian Eye And Ear Hospital, Australia*

Here we present several new studies on dizziness with our cochlear implant patients. First, a retrospective clinical review of the incidence of imbalance following cochlear implantation was undertaken looked at 150 patients aged 75 years and over. We found that dysquilibrium was reported in 20% of all patients early after cochlear implantation and this did not vary with age. The incidence was similar to that seen younger recipients. This suggests that the underlying pathology is similar across age, even though the risks of imbalance are greater in the elderly because of a fear of falling.

To further understand the nature of dizziness shortly after CI surgery, we have recently undertaken a prospective study exploring whether the vestibular ocular reflex (VOR) differs in the first month following implantation. Video Head Impulse Testing was undertaken pre-operatively and then 1, 7 and 28 days after surgery. This study found that the VOR gain did not vary with time after CI surgery, which suggests that peri-operative dizziness does not arise from pathology of the lateral semicircular canal, and most likely has a different aetiology.

Finally, we present some interesting case studies of patients who have become dizzy in the months after CI surgery. We note that this is often associated with a reduction in their residual hearing, which suggests that delayed dysquilibrium in these cases may be associated with endolymphatic hydrops.

SP23-3

Cochlear Implant and Vestibular Function

VESTIBULAR PROBLEMS AFTER COCHLEAR IMPLANTATION**Yoon Chan RAH**^{1,2}, **Ja-Won KOO**¹¹*Department of Otorhinolaryngology – Head & Neck Surgery, Seoul National University College of Medicine, Seoul National University Bundang Hospital, Korea*²*Korea University College of Medicine, Korea University Ansan Hospital, Korea*

Purpose: To explore vestibular problems after cochlear implantation (CI) by categorizing them according to clinical course and changes in objective vestibular function.

Method: Vestibular symptoms were divided into three categories by their time course and nature on 62 patients (66 ears). Etiologies were determined by analyzing the symptoms in combination with changes in objective vestibular function, measured using the caloric and/or video head impulse test.

Results: Preoperatively, vestibular function was normal in 31 cases (47.0%), unilaterally hypofunctional in 14 (21.2%), and bilaterally hypofunctional in 21 (31.8%). Eight cases (12.1%) reported dizziness before surgery. A total of 18 cases (27.3%) experienced postoperative dizziness. Ten patients experienced immediate transient dizziness (including 2 cases of benign positional paroxysmal vertigo); four experienced immediate prolonged dizziness (including 3 cases of bilateral vestibular hypofunction); and four experienced recurrent episodic dizziness (including 3 cases of suspicious endolymphatic hydrops). The sums of the maximal slow-phase velocities (SPVs) of the implanted ears were changed from $23.12 \pm 16.22^\circ/\text{sec}$ to $11.53 \pm 12.35^\circ/\text{sec}$ after implantation ($p = 0.004$) with very little changes in the other side ($32.04 \pm 17.22^\circ/\text{sec}$ to $31.06 \pm 22.05^\circ/\text{sec}$).

Conclusion: Careful preoperative evaluation of vestibular status is important, especially when deciding implantation in the only vestibular functioning ear or simultaneous bilateral implantation.

SP23-4

Cochlear Implant and Vestibular Function

COMPENSATION OF VESTIBULAR FUNCTION AND PLASTICITY OF VESTIBULAR NUCLEUS AFTER UNILATERAL COCHLEOSTOMYMyung-Whan SUH¹, Jaihwon HYUN², Ah-Ra LYU³, Dong Woon KIM^{4,5}, Sung Jae PARK³, Jin Woong CHOI³, Gang Min HUR⁶, **Yong-Ho PARK**^{3,5}¹*Department of Otorhinolaryngology, Seoul National University Hospital, Korea*²*Department of Otolaryngology-head And Neck Surgery, Dankook University Hospital, Korea*³*Department of Otolaryngology-head And Neck Surgery, College of Medicine, Chungnam National University, Korea*⁴*Department of Anatomy, College of Medicine, Chungnam National University, Korea*⁵*Department of Brain Research Institute, College of Medicine, Chungnam National University, Korea*⁶*Department of Pharmacology, College of Medicine, Chungnam National University, Korea*

Dizziness and vertigo frequently occur after cochlear implantation (CI) surgery, particularly during the early stages. It could recover over time but some of the patients suffered from delayed or sustained vestibular symptoms after CI. This study used rat animal models to investigate the effect of unilateral cochleostomy on the vestibular organs over time. Twenty-seven Sprague Dawley rats underwent cochleostomy to evaluate the postoperative changes in hearing threshold, gain and symmetry of the vestibular ocular response, overall balance function, number of hair cells in the crista, and the c-Fos activity in the brainstem vestibular nucleus. Loss of vestibular function was observed during the early stages, but function recovered partially over time. Histopathological findings demonstrated a mild decrease in vestibular hair cells numbers. Increased c-Fos immunoreactivity in the vestibular nucleus, observed in the early stages after cochleostomy, decreased over time. Cochleostomy is a risk factor for peripheral vestibular organ damage that can cause functional impairment in the peripheral vestibular organs. Altered vestibular nucleus activity may be associated with vestibular compensation and plasticity after unilateral cochleostomy.

SP24-1

Pathophysiologic Mechanism of Functional and Psychiatric Vestibular Disorders

INTRODUCTION AND OVERVIEW: IT'S NOT THE 20TH CENTURY ANY LONGER**Jeffrey P STAAB***Department of Psychiatry And Psychology, Mayo Clinic, USA*

Much of what scientists and clinicians believe about functional and psychiatric disorders arose in the 19th and 20th centuries, a time of great advances in structural anatomy and cellular physiology. In neuro-otology, as in other specialties, many diseases and disorders were linked to structural and cellular underpinnings, but certain disease forms defied easy explanation by these mechanisms. Some were defined as functional problems (i.e., arising from aberrant organ functioning of uncertain cause). Others were attributed to psychological processes. Flawed ideas dominated disease concepts and diagnostic strategies. Depending on country and culture, disease forms that could not be explained by structural or cellular biology were either ignored or automatically attributed to psychological causes. The term functional became synonymous with psychogenic, psychosomatic, and aphysiologic, used for conditions considered outside the realm of "real" diseases. Various theories linked these problems to personal and familial adversity.

Fortunately, 21st century research is shedding new light on these problems. In this symposium, three investigators will present evidence that challenges existing ideas about links between biological and psychosocial processes in vestibular disorders. Professor Mark Carpenter (Canada) will describe physiologic responses to postural threat. Dr. Iole Indovina (Italy) will show functional neuroimaging data elucidating links between vestibular, visual, and anxiety-related regions in the brain. Dr. Claas Lahmann (Germany) will show that lifetime adversity affects symptom severity similarly in patients with structural and functional vestibular disorders. These findings provide building blocks for more sophisticated models of postural control and spatial orientation in health and disease.

SP24-2

Pathophysiologic Mechanism of Functional and Psychiatric Vestibular Disorders

ADVERSE LIFE EVENTS AND PSYCHOLOGICAL MORBIDITY IN STRUCTURAL AND FUNCTIONAL VESTIBULAR DISORDERS

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Increased rates of lifetime trauma were found in patients with medically unexplained symptoms with an association between trauma and symptom severity and patients suffering from posttraumatic stress disorder report more somatic symptoms.

Although somatoform symptoms often appear to be unspecific and involve multiple organ systems, pseudoneurological symptoms including dizziness are more strongly associated with exposure to natural disasters than cardiorespiratory, gastrointestinal, and musculoskeletal symptoms.

In a recent study – the first to examine the association between trauma-related factors comparing functional and organic vestibular disorders no differences were found between the two patient groups with regard to number or impact of traumatic life events after controlling for gender and age. Also, there were no differences in scores on a history of adverse childhood events and indicators of current posttraumatic stress symptoms of intrusion and avoidance. However, both groups showed elevated rates of clinically relevant posttraumatic stress symptoms, 15% in structural and 18% in functional vestibular disorders. This is in line with previous reports of partial or full posttraumatic symptoms also among patients with structural vestibular disorders. Regardless of whether vestibular symptoms were structural or functional, previous trauma and posttraumatic stress symptoms of avoidance and intrusion predicted to some extent the variance of balance symptoms and handicap, mainly those associated with psychological and autonomic symptoms of anxiety.

SP24-3

Pathophysiologic Mechanism of Functional and Psychiatric Vestibular Disorders

EMOTIONS, COGNITIONS, AND REFLEXIVE RESPONSES TO POSTURAL THREAT

Mark G CARPENTER

Department of Kinesiology, The University of British Columbia, Canada

Associations between anxiety and symptoms of vestibular dysfunction have been established, and supported by evidence in animals of neuro-anatomical connections between neural regions that process threat-related responses (fear, anxiety, arousal and vigilance) and the vestibular system. This presentation will review recent evidence from studies examining the effect of postural threat on human vestibulo-spinal reflexes (VSR) and vestibulo-ocular reflexes (VOR). Postural threat was manipulated in healthy individuals, by having subjects stand at the edge of an elevated platform, or under the threat of a balance perturbation, in order to examine within-subject changes in vestibular reflex responses and correlate these changes with state changes in fear, anxiety and arousal. Threat effects on VSR gain were demonstrated by increases in the coherence, gain and cumulant density peaks of ground-reaction forces and postural leg muscle responses to stochastic vestibular stimulation, and increases in the amplitude of vestibular-evoked myogenic potentials (VEMPs), elicited in both neck, and lower-leg muscles during stance. VOR pathways were also influenced by threat, based on observed increases in ocular-VEMP amplitudes, and increases in video-Head Impulse Test gains when standing under threatening conditions. Observed increases in gains of eye smooth pursuit, saccade and opto-kinetic nystagmus with threat, suggest that threat-related changes in VOR gain under threatening conditions is likely attributed to the modulation of vestibular nuclei, as well as nuclei controlling eye muscles. Significant correlations between changes in VSR and VOR gain and state changes in fear, anxiety and arousal support the association between human emotion and vestibular reflex response to threat.

SP24-4

Pathophysiologic Mechanism of Functional and Psychiatric Vestibular Disorders

FUNCTIONAL BRAIN IMAGING OF VESTIBULAR-VISUAL-ANXIETY SYSTEM INTERACTIONS IN HEALTH AND ILLNESS

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Background: Previous work suggested that anxiety-related personality traits of neuroticism and introversion (N&I) may influence activity of brain regions that process visual, vestibular and anxiety information in response to vestibular stimulation in normal individuals. These traits also may be risk factors for persistent postural perceptual dizziness (PPPD), a neurotologic syndrome of chronic non-vertiginous dizziness and hypersensitivity to complex visual stimuli. Brain mechanisms underlying these effects are unknown.

Methods: Using functional magnetic resonance imaging, we studied the effects of N&I in healthy controls (HCs, $n = 26$) and patients with PPPD ($n = 18$) during (1) sound-evoked vestibular stimulation and (2) visual motion stimulation from immersive videos of rollercoaster rides.

Results: Brain responses to vestibular stimulation correlated positively with N&I in visual areas V1 to V4 in HCs but not PPPD patients. Comparing vertical to horizontal rollercoaster movement during visual stimulation, higher activity in V1 and V2 correlated with N&I in HCs and PPPD patients, though more strongly in V1 in PPPD patients than HCs. Independently of N&I, PPPD patients relative to HCs, had reduced activity during vestibular stimulation in parieto-insular vestibular cortex, anterior insula, hippocampus and anterior cingulate cortex.

Conclusions: N&I modulated activity in visual cortex during vestibular and visual stimulation in HCs. This effect was absent for vestibular stimulation and amplified for visual stimulation in PPPD patients. Independently of N&I, PPPD patients had decreased activity in several brain regions that process vestibular and anxiety-related information. These changes may underlie core symptoms of PPPD and explain the risk that N&I conveys for this disorder.

SP25-1

VEMP (Basic) – The Neural Basis of Vestibular Evoked Myogenic Potentials

CERVICAL AND OCULAR VESTIBULAR EVOKED MYOGENIC POTENTIALS TO HIGH FREQUENCIES SHOW SEMICIRCULAR CANAL DEHISCENCE

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In patients with CT-verified SSCD to investigate the effect of frequency on the n10 component of the ocular vestibular-evoked myogenic potential (oVEMP n10) and on the p13-n23 component of the cervical vestibular-evoked myogenic potential (cVEMP p13-n23) evoked by air conducted sound (ACS) and bone conducted vibration (BCV) at the midline forehead at the hairline (Fz).

Methods: A hand-held vibrator provided BCV stimulation was used, using surface EMG electrodes beneath both eyes, to record oVEMP n10 and over SCM, to record cVEMP p13-n23. The stimulus ACS and BCV at either Fz or at the vertex of the skull (Cz) were tone bursts ranging from 125 Hz to 8000 Hz. Healthy subjects were tested in the same paradigm.

Results: In response to ACS and Fz BCV from 125 Hz until 8000 Hz in SSCD patients the oVEMP n10 amplitude beneath the contraSSCD is present.

In response to ACS and Fz BCV from 125 Hz until 8000 Hz in SSCD patients the cVEMP p13 – n23 amplitude over the ipsi SSCD sternocleidomastoid muscle is present. In healthy subjects ACS and BCV oVEMPs n10 is present and reproducible until 1000 Hz while in SSCD ACS oVEMPs n10 is present up to far higher frequencies (8000 Hz). **Conclusion:** Testing cVEMP and oVEMP with ACS and BCV allows very simple, very fast identification of a probable unilateral SSCD just using one single frequency. We recommend to test patients at 4000 Hz.

SP25-2

VEMP (Basic) – The Neural Basis of Vestibular Evoked Myogenic Potentials

CHARACTERISTICS OF OVEMPS IN RESPONSE TO AIR-CONDUCTED SOUND AND BONE-CONDUCTED VIBRATION

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Vestibular evoked myogenic potentials (VEMPs) recorded by surface electrodes have been used clinically to assess vestibular function. The ocular vestibular evoked myogenic potentials (oVEMPs), which were first reported by Rosengren et al. in 2005, are short-latency, initially negative surface EMG potentials recorded from beneath the eyes in response to air-conducted sound (ACS) and bone-conducted vibration (BCV). The oVEMP is considered to represent vestibular function mediated by crossed otolith-ocular pathways, since it is present in patients without hearing, but absent on the contralateral side in those with unilateral vestibular loss. The oVEMPs originate from extraocular muscles since exenteration of intraorbital contents resulted in absence of oVEMPs but exenteration of the eyeball with preservation of extraocular muscles did not affect oVEMPs. A recent study by Weber et al. (2012) have shown that the oVEMPs originate from the inferior oblique muscles by recording single unit activity of human extraocular muscles. Clinical studies using patients with vestibular neuritis and vestibular schwannoma have shown that oVEMPs to BCV as well as ACS mainly reflect the function of the utricle and the superior vestibular nerve systems, although there remains some controversies in the origin of oVEMPs to ACS. The origin of the oVEMPs to ACS and BCV in the inner ear does not seem to be completely identical because the effects of head tilt on the oVEMPs are different between oVEMPs to ACS and oVEMPs to ACS. Furthermore, best frequencies to evoke oVEMPs are different between ACS and BCV.

SP25-3

VEMP (Basic) – The Neural Basis of Vestibular Evoked Myogenic Potentials

NEURAL PATHWAYS OF VEMP: INSIGHTS FROM CLINICAL FINDINGS

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Nowadays, vestibular evoked myogenic potential (VEMP) has been widely used as a clinical test of the otolith organs. cVEMP has been regarded as a test of the uncrossed sacculo-colic reflex, while oVEMP has been regarded as a test of the crossed utriculo-ocular reflex. On this occasion, I reviewed clinical findings to confirm neural pathways of VEMP.

– 1. cVEMP

cVEMP can be predominantly evoked on the ipsilateral SCM to the stimulated ear. cVEMP can be normal or abnormal in vestibular neuritis. cVEMP disappeared by selective nerve section of the inferior vestibular nerve with preservation of caloric responses. In a patient with unilateral brainstem lesions due to multiple sclerosis, only cVEMP to the contralateral ear stimulation was normal. Patients with tilting or translation sensation in the pitch plane tend to have abnormal cVEMP without abnormal findings in other vestibular tests. These evidences strongly support that cVEMP reflects the uncrossed sacculo-colic reflex.

– 2. oVEMP

oVEMP can be predominantly evoked on the area below the lower eyelid contralateral to the stimulated ear. oVEMP results had association with caloric tests in patients with vestibular neuritis. In a patient with unilateral brainstem lesions due to multiple sclerosis, oVEMPs were abnormal on both sides. Patients with tilting or translation sensation in the roll plane tend to have abnormal oVEMP without abnormal findings in other vestibular tests. These evidences strongly support that oVEMP reflects the crossed utriculo-ocular reflex.

SP25-4

VEMP (Basic) – The Neural Basis of Vestibular Evoked Myogenic Potentials

CONTROLLING THE BASELINE MUSCLE CONTRACTION POWER AND ITS SIGNIFICANCE**Myung-Whan SUH¹**, Ja-Won KOO¹¹*Department of Otorhinolaryngology, Seoul National University Hospital, Seoul, Korea*

Objectives: The objective of this study was to evaluate several different methods that can control the baseline muscle contraction power during vestibular evoked myogenic potentials (VEMP). Blood pressure (BP) manometry feedback method, rectified VEMP (rVEMP), and binaural simultaneous (bSIM) cVEMP recordings were performed.

Methods: Sixty ears of 30 normal volunteers were prospectively investigated. The vestibular evoked myogenic potentials were recorded under 3 different conditions: in the feedback-negative (FB-) condition, in the feedback-positive (FB+) condition, and in a supine condition. Thirty VEMP measurements were performed among 20 normal subjects with the conventional non-rectified VEMP (nVEMP) and rVEMP. Two different methods of cVEMP measurement were performed in 22 subjects. The two methods were (1) monaural sequential (mSEQ) measurement and (2) binaural simultaneous (bSIM) measurement.

Results: The mean IAD ratio was smaller in the FB+ condition than in the FB- and supine conditions, but the difference was without statistical significance. The nVEMP IAD increased significantly according to increasing neck rotation. The IAD in rVEMP was almost similar from 0° to 30°. The IAD ratio of bSIM cVEMP response demonstrated a statistically significant test-retest reliability (ICC = 0.691, $p = 0.015$). However, the IAD ratio of mSEQ cVEMP response did not demonstrate a statistically significant test-retest correlation.

Conclusions: Feedback using a BP manometer may have limited clinical significance. More stable IAD ratio may be obtained with a narrower normal range and a smaller variation but it was not significant. Rectified VEMP is capable of correcting asymmetrical muscle contraction power. In contrast, it cannot correct the asymmetry if muscle contraction power asymmetry is 44.8% or larger. Results implicate that bSIM cVEMP not only saves time, but it also has an advantage of a more reliable test-retest outcome.