Abstracts

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Podium Abstract 1

Overview of funding opportunities and research supported by the National Institute on Aging

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The National Institute on Aging (NIA) leads a broad scientific effort to understand the nature of aging and to extend the healthy, active years of life. NIA is also the primary federal agency supporting and conducting Alzheimer's disease (AD) research. Over the last several years the institute has seen an unprecedented increase in federal appropriations for AD and AD-related dementias (ADRD) which has translated into generous funding pay lines. The NIA has had a long-standing interest in funding research to investigate the mechanisms underlying age-related changes in sensory and motor function both in the context of healthy aging and neurodegenerative disease. The presentation will provide an overview of NIA's interests in vestibular research and balance, current funding pay lines, notices of funding opportunities of relevance to vestibular researchers and training opportunities for junior investigators.

Podium Abstract 2

Overview of funding opportunities and research supported by the National Institute on Deafness and other Communication Disorders

Amy Poremba, Ph.D.
Program Director, NIDCD

Dr. Amy Poremba will present an overview of current research funding opportunities for students, postdoctoral fellows, early-stage investigators, and established investigators. Past and current funding levels will be presented for an overview of the priorities of each institute and current priorities for funding will be addressed.

Keynote Abstract 1

Screening for Vestibular Disorders

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When patients enter the health care system with complaints that might be consistent with vestibular disorders, or when they mention such complaints in the course of visits focused on other health problems, they are not immediately referred for objective tests of vestibular system (VNG). Instead, the health care provider may take a history, or give the patient a history questionnaire. The clinician might then use some screening tests that can be easily performed in the exam room. Only then, if the clinician is a medical provider who is knowledgeable about the vestibular system and if that provider has access to a facility where VNG's are performed, the patient might be referred for a VNG. Alternatively, the patient might just be referred for a basic hearing test battery, or no further tests might be ordered, depending on the background of the clinician and the resources available. Therefore, having valid and reliable screening tests is important. Despite the large number of screening tests and history questionnaires in the literature, the value of these mechanisms for accurate screening of vestibular disorders remains unclear. Screening is notoriously unreliable, more art than science. This talk will review the literature on screening for vestibular disorders, including history questionnaires, quality-of-life self-ratings, head impulse testing, Fukuda stepping test, Romberg testing, tandem walking, blood pressure screening, and use of the basic hearing test battery to predict VNG outcome. These tests are relevant to medical providers, rehabilitation clinicians, and also epidemiologists who perform local and population-based studies of vestibular disorders.

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Podium Abstract 3

Executive functions in patients with bilateral and unilateral peripheral vestibular dysfunction

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Patients with peripheral vestibular dysfunction (PVD) suffer from cognitive difficulties in several visuo-spatial as well as non-visuo-spatial domains. Associations of PVD and executive problems have been made, but no study investigated a range of different executive domains in patients with PVD. We administered a broad neuropsychological test battery of basic and complex executive functions to 84 patients with different kinds of PVD (34 chronic bilateral, 29 chronic unilateral, 21 acute unilateral) and 49 healthy controls matched for age, education, and sex. Descriptive data analysis showed that patients with PVD scored lower in specific executive domains than healthy controls. Results indicate that patients with PVD should be screened for specific executive impairments and could benefit from a cognitive training targeting executive functions.

Podium Abstract 4

Otolith-ocular Function and Compensatory Effect of Neck Following Vestibular Loss

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Vestibular inputs converge broadly with other sensory information across various brain functions. These multimodal contributions range from control of gaze and posture to higher-level mechanisms that mediate spatial orientation and motion perception. At the level of vestibulo-ocular reflex (VOR), there is a close interaction between vestibular signals and proprioceptive inputs that encode the position of the neck. Neck proprioceptors provide information about the position of the head relative to the trunk and they can be used by the brain to optimize gaze control with respect to the head and body positions. The neural pathways that mediate these responses are not well understood, but physiological observations suggest that the brain can adapt to perturbations in vestibular function by using inputs from the neck. Here we studied the contribution of neck inputs to otolith-ocular function at different stages of recovery from vestibular loss. We used video-oculography (VOG)-based measurement of static ocular counter-roll (vOCR) determined 30 seconds after the dynamic tilt to assess otolith function. To elucidate a compensatory effect of neck proprioception, vOCR was measured with 30° static whole-body tilt (WBT) and head-on-body tilt (HBT). The vOCR with WBT is primarily driven by the otolith inputs, whereas with HBT there is also a neck contribution. Fifty-six subjects were recruited including patients with acute (9 days [mean]), subacute (61 days), and chronic (985 days) unilateral loss of vestibular function, as well as a group of healthy controls. The gain of vOCR on the lesion side was lower with WBT than with HBT in the acute and subacute groups but not in the chronic group or controls (HBT: acute: 0.11±0.01, subacute: 0.14±0.01, chronic: 0.13±0.02, healthy control: 0.17±0.01/ WBT: acute: 0.08±0.01, subacute: 0.11±0.01, chronic: 0.13±0.02, healthy control: 0.18±0.01). The time course of vOCR response was affected as well with a reduced amplitude and slower response in the acute stage of vestibular loss. The vOCR with WBT, as opposed to HBT, could distinguish among the patient groups at various stages of vestibular loss. These findings show a compensatory effect of neck proprioception that can enhance otolith-ocular function following vestibular loss and vOCR as a potential valuable clinical marker to track recovery following vestibular loss.

Podium Abstract 5

Bone Conducted Vibration for the Symptomatic Relief of Vertigo - Clinical Trial Phase 2 Results

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Vertigo—the false perception of motion or rotation—is often the result of damage and dysfunction of vestibular end organs. Despite the high incidence of vestibular vertigo in the adult population (~7.4%, Agrawal et al 2013), available treatments require pharmaceuticals, surgical intervention, and/or extensive physical therapy.

The OtoBand, a lightweight, battery powered, externally worn device developed by Otolith Labs, is a novel device that can rapidly reduce or relieve vestibular vertigo by sending a low frequency vibration to vestibular end organs through bone conduction.

We report results from an ongoing phase 2 double-blind counter-balanced sham-controlled study designed to quantify changes in vertigo severity associated with use of the OtoBand in participants during recurring episodes of vertigo. This study was carried out in a telehealth setting to accommodate COVID restrictions and to test the device in a real-world setting. Inclusion criteria included a Dizziness Handicap Inventory score > 35, chronic vertigo (condition for at least 90 days) with at least one episode of vertigo per week, and provided a self-reported diagnosis of their vestibular pathology (benign paroxysmal positional vertigo, Meniere's disease, vertiginous migraine, or vestibular neuritis/labyrinthitis).

In this study, the OtoBand device produced a single frequency between 50 and 65 Hz at a patient-controlled force level between 0.4 N_{RMS} to 0.8 N_{RMS}. A sham device operating at a different frequency and a different range of patient-controlled force levels was also supplied with an identical form factor to the OtoBand, with vibrations from both devices easily perceived by participants. Participants were provided with an OtoBand and a sham device in a random, counterbalanced order for two weeks each. Participants were instructed to wear their device whenever experiencing an episode of vertigo and to report on the severity of vertigo episode at several time points, and an overall rating of efficacy after each use.

With "responder" defined as a participant who rated the device as helping on at least half of uses, a significant main effect of OtoBand over sham device was found using a generalized linear mixed-effects logistic model (odds ratio = 3.13, 95%, CI = [1.75–5.61], $p < 0.001$). This indicates that the OtoBand was found to be significantly more helpful to participants during vertigo episodes than the sham.

A continuing pilot study with a larger sample size and medically confirmed medical diagnoses is currently underway, with a large-scale pivotal study planned for mid-2023.

Keynote Abstract 2

CRISPR-Cas9 Mediated Targeting of a DFNA9 Pathogenic Variant for Gene Therapy in an Auditory and Balance Disorder

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Impressive advances in gene discovery in the auditory system have occurred in the last decades, making specific targeted approaches for therapeutics realistic goals of great interest. Hearing loss (HL) is an increasingly significant health problem in populations worldwide, with a substantial proportion due to genetic causes. Some auditory disorders are also accompanied by abnormalities in the vestibular system. Given the health burden and ongoing rapid discoveries, it is now essential to pursue new strategies for specific early interventions that could prevent or mitigate severity and progression of hearing and vestibular disease. One such disorder is DFNA9, an adult-onset sensorineural HL with balance dysfunction, reported with 41 missense variants and two in-frame deletions in *COCH,* encoding cochlin, the most abundantly detected protein in the inner ear. This disease model is representative of the majority of dominant genetic HL disorders due to a deleterious gain-of-function of the mutant cochlin. *COCH* mutations result in a distinct aggregative histopathology in inner ear structures, pathognomonic for DFNA9, and multimerization of mutant cochlin *in vitro*. Dominant negative properties of mutant cochlin are consistent with evidence that *COCH* haploinsufficiency in DFNA9 does not lead to the pathology in humans, and heterozygous mice in the *Coch* null mouse model have normal hearing function similar to wild-type littermates. Cochlin contains a 5' motif known as LCCL (***Limulus*** clotting factor **C**, **C**ochlin and mammalian **L**ate gestation lung protein [Lgl1]) in which 20/41 *COCH* variants are located; 17 of 41 variants are clustered in a 3' vWFA2 domain. The LCCL domain has a novel fold and is proposed to protect *Limulus* from bacterial infection and could serve a similar defensive function in the inner ear. Phenotypically, the onset of HL and vestibular symptoms in humans with *COCH* variants in the 5' region of the gene is in the 5th-6th decade whereas the onset of HL is in the 2nd-3rd decade and is not characterized generally by a vestibular disorder. A genomic medicine approach resulting in gene silencing of the mutant *COCH* allele (p.A449T) in a humanized mouse model is underway, with disruption of the p.A449T dominant mutation using CRISPR-Cas9 maintaining the normal allele and rescuing hearing and balance.

We first generated a fibroblast cell line using a skin biopsy from an individual with the *COCH* p.A449T variant to assess whether we could rescue hearing *in vivo*. Using *Easi*CRISPR, we created a humanized mouse model in CBA/J with the *COCH* p.A449T mutation and flanking human sequence to match the gRNAs targeting the human mutation. We transfected cells with a plasmid carrying SaCas9-KKH and a guide RNA targeting A449T, and assessed editing with next-gen sequencing. The Cas9 successfully created indel disruption only in the variant allele, with an editing efficiency of 43% and with no disruption of the normal allele. Auditory brainstem response (ABR) as well as distortion product otoacoustic emission (DPOAE) analyses of 3-4 month-old mice showed significantly elevated thresholds for both $Coch^{A449T/+}$ (heterozygous) and $Coch^{A449T/A449T}$ (homozygous) mice, as compared to their $Coch^{+/+}$ (wild-type) littermates, at all tested frequencies. There was no significant difference between the heterozygotes and homozygotes, reflecting the dominant nature of the mutation. Vestibular sensory evoked potentials (VsEP) were measured also at 3-4 months of age and thresholds were significantly elevated for heterozygous and homozygous mice compared to the wild-type littermate controls. *Coch* p.A449T mice showed severe swimming abnormalities: both heterozygous and homozygous mutants exhibited underwater tumbling, with homozygous mutants performing much worse than heterozygous animals. Round window micro-injection of an AAV encoding CRISPR-Cas9 and guide RNA has been performed and phenotype rescue is being assessed.

We have shown successful targeting of a *COCH* pathogenic variant using a CRISPR-Cas9 mediated approach *in vitro* and are testing rescue in a novel mouse model *in vivo*. If successful, this strategy is expected to inform gene therapy in other autosomal dominant HL disorders, the majority of which are due to missense pathogenic variants rather than truncation or loss of gene function. Notably, these AD disorders are often characterized by late-onset presentation, providing a window of opportunity for therapeutic intervention.

Podium Abstract 6

Manipulating gene expression in adult vestibular type II hair cells promotes transdifferentiation toward the type I hair cell phenotype

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The vestibular epithelia of mammals have two markedly distinct hair cell types, I and II. Type I and II hair cells have different hair bundles, calcium-binding proteins, synaptic connections with both afferent and efferent nerve fibers, and expression of ion channels. Type I cells emerged in evolution as tetrapods moved onto land, possibly in response to novel challenges of locomotion and balance out of water. Adult type II hair cells retain some features of immature hair cells, such as expression of the transcription factors Atoh1 and Sox2, whereas type I hair cells are more differentiated. This difference may explain why new type II cells, but not type I cells, can form in adult epithelia after damage (Golub et al. 2012; González-Garrido et al. 2021). The regenerated type II cells alone do not restore vestibular function, suggesting that type I hair cells are essential. To explore the differentiation of type I and II hair cells from each other, and as a stepping stone to functional regeneration of the inner ear, we have investigated whether adult type II cells can be transformed to type I cells by deleting expression of Sox2.

Our results show that deleting Sox2 causes a significant number of type II cells to acquire anatomical (Stone et al. 2021) and physiological traits that are type I markers. Of note, primary afferent neurons alter their synaptic contacts with the hair cells from bouton synapses to the extraordinary calyceal terminals typical of type I synapses. Whole-cell recordings from the newly generated calyces showed the unusual non-quantal transmission that is a key functional distinction of type I-calyceal synapses. This transmission is thought to be mediated by a large and negatively activated potassium conductance described only in type I hair cells. Indeed, our whole-cell recordings from Sox2-deleted type II hair cells show transformation of the type II potassium conductance toward type I-like size and voltage dependence. These results suggest that a relatively small number of manipulations can produce functional differentiation of newly generated hair cells in adult vestibular inner ear.

References

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Podium Abstract 7

Sox2 is required to maintain the morphology and afferent innervation of type II hair cells and to regulate motor behaviors of adult mice

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Amniotes have two types of vestibular hair cell, type I and type II, that have very different morphology, synapses, molecular properties, and physiology. In adult mice, deletion of Sox2 from type II hair cells causes them to transdifferentiate toward the type I fate - i.e., to lose type II-specific anatomic and molecular features and to acquire features unique to type I hair cells (Stone et al. 2021). In addition, the bouton afferent terminals that typically contact type II hair cells are replaced by a partial or full calyx-type terminal as the hair cell transdifferentiates.

We asked whether this type II-to-I shift affects motor behavior and vestibular reflexes. We found that, instead of undergoing the typical reduction in locomotor activity as they age, experimental mice (those with type II-to-I transdifferentiation) had elevated locomotor activity, as reflected by increased velocity and distance traveled during brief (5-minute) periods in a bright cage. Experimental mice also had more exploratory behavior, as measured in the elevated plus maze or in 72-hour open field. Some experimental mice had better performance (lasted longer) on the rotarod than control mice. Mice had a small decrease in gains for the angular vestibulo-ocular reflex in the horizontal plane at 4 months but not at 8 months after the fate switch was initiated. However, mice with type II-to-I transdifferentiation exhibited no circling or head-bobbing behaviors, which often occur after substantial loss of either hair cells or hair cell function.

Because we found no evidence for off-target Sox2 deletion from vestibular pathway neurons, we surmise that the observed changes were due to type II-to-I hair cell transdifferentiation. In future studies, we hope to determine if changes in behavior reflect the gain of type I hair cells, the loss of type II hair cells, and/or destabilization of the vestibular periphery and how these changes affect central neurophysiology.

References

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Podium Abstract 8

Characterizing Hair Cell and Afferent Neuron Properties in Human Vestibular Organs

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The vast majority of what is known about human vestibular function has been inferred from rodent models due to the inaccessibility of human inner ear organs. There are a few reports of electrophysiological recordings from cells isolated from human inner ear (Oghalai et al. 1998, Lim et al. 2014, Quinn et al. 2021), but detailed investigations of freshly harvested adult vestibular cells are still lacking. Here, we obtained vestibular neuroepithelia from adult translabyrinthine surgical patients and performed electrophysiological and immunohistochemical studies.

Colorado Multiple Institution Review Board approval was obtained (COMIRB# 19-1340). The surgical team obtained ampullae and utricles from consenting patients undergoing translabyrinthine surgical approaches. Neuroepithelia were transferred in-ice cold sterile saline to the laboratory within one hour of harvest. For electrophysiological recordings, the tissue was transferred to L-15 solution following incubation in L-15/bovine serum albumin and cells were mechanically dissociated as previously described (Rennie & Streeter 2006). Whole cell patch clamp recordings were performed on isolated hair cells and afferent terminals to characterize voltage-dependent currents. Pharmacological agents were applied via extracellular perfusion. For immunohistochemistry, end organs were fixed and stained with a combination of antibodies targeting Myosin7a, CtBP2 and Tubulin3. Imaging was performed with a Zeiss LSM 780 confocal microscope.

Six patients (ages 29-77 years, 4M, 2F) with vestibular schwannomas and non-serviceable ipsilateral hearing loss prior to surgery were studied. None reported vertigo. Recordings were obtained from type I and type II hair cells and afferent terminals up to 5 hours following dissociation. Hair cells had a mean capacitance of 8.9±5.4pF (n = 7, SD). Type I hair cells exhibited low voltage-activated currents and large outward currents in response to standard voltage protocols. Mean resting potential was -60.4±7.2 mV (n=14) and peak outward was 3.37±1.30 nA at +20 mV (n=15). Putative type II HCs exhibited higher input resistance and outward current above -50mV. A hyperpolarization-activated current (I_h) was observed in 4 hair cells. Afferents exhibited rapid transient inward Na^+ current, outward current (I_K) and I_h. Peak I_K was 3. 77±2.51 nA (n=4) and I_h was 331±191 pA (n=3). Single action potentials occurred with depolarizing steps in current clamp. Perfusion with the K^+ channel blocker 4-aminopyridine (1 mM) blocked low voltage-activated currents in type I cells and inactivating I_K in calyx afferents.

Immunohistochemical labeling of cristae and utricles allowed identification of hair cells, afferent terminals, and ribbon synapses.

We performed electrophysiological recordings and immunostaining on vestibular cells extracted during human surgical inner ear procedures. Whole cell recordings from hair cells and afferent terminals revealed ionic currents that qualitatively resemble currents in cells from rodent vestibular epithelia. Rapid access to adult human vestibular epithelia allows translational studies crucial for better understanding human peripheral vestibular function.

Podium Abstract 9

Quantitative Aspects of Vestibular Mitochondria

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In this study, we quantified multiple aspects of mitochondrial structure in the vestibular periphery. Our main hypothesis in this research is that mitochondria are structurally heterogeneous, depending on which hair cell type is under consideration and the specific locations of mitochondria in relation to other hair cell organelles. One such structural relationship that we have reported on previously is the polarization of mitochondrial crista junctions (CJs), openings of the internal mitochondrial membrane into the intermembrane space that is likely responsible for transport of molecules from the mitochondrial matrix out to the cytoplasm.

Inner ear vestibular tissue obtained from Long-Evans rats under an approved UIC IACUC procedure was used for electron microscope tomography. Data were processed with the IMOD (v. 3.13.6) software package (Kremer et al., 1996) and serial tomograms were joined using the etomo subroutine (IMOD). Manual segmentation was done with the 3dmod subroutine (IMOD) to obtain final models. Reconstructions were visualized using 3dmod (IMOD), including its SLICER option, to track relevant features in three dimensions. Several IMOD drawing tools (Sculpt, Join, Warp, Interpolator) and a proximity analysis subroutine (Mtk) with its randomization feature, were also used.

Quantitative analyses were performed to test our hypothesis, including counts of total mitochondria within both types of hair cells (with a comparison to cochlear hair cells), efferent boutons, and afferent calyces, counts of CJs on either side of a mitochondrion in relation to other cellular organelles, analyzing polarization ratios (side toward vs side away) vs distances, bioenergetic calculations of ATP production, and an Mtk proximity analysis test was performed using CJ randomization as a control. Results support our hypothesis of structural heterogeneity of mitochondria, as CJs are polarized toward specific organelles within the cell and appear to be non-randomly distributed. Finally, vestibular hair cells have less than half the number of mitochondria compared to cochlear hair cells, although certain of these are quite a bit larger than cochlear mitochondria.

These results have functional implications for the various structural differences. CJ polarization toward organelles that use energy can transport ATP more efficiently. For example, the cuticular plate is an organelle that functions to return stereocilia rootlets back to their original position. Our results show a non-random orientation of mitochondrial crista junctions toward the cuticular plate. These structural differences may provide key information to better understand their function and to address mitochondrial deafness and dizziness disorders.

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Keywords: Mitochondria, vestibular hair cells, vestibular afferents, vestibular efferents.

Podium Abstract 10

Novel methodology and experimental ratings for real-time computational detection of pilot spatial disorientation

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Pilot spatial disorientation (SD) continues to be a leading cause of Class A mishaps and fatalities in aviation even after the broad introduction of SD training. Active countermeasures, such as adaptive displays or auditory cueing, have potential to further assist pilots with maintaining appropriate orientation of the aircraft. A necessary component of such a system, however, is a method by which to estimate possible SD being experienced and detect when intervention is warranted in real-time. Computational models of human orientation perception provide an unobtrusive means by which to estimate the impact of misperceptions, over time, on overall SD state. To overcome limitations of previously proposed SD models, we developed an experimental methodology to collect quantitative ratings of SD in response to inertial motion stimuli. This enabled identification and characterization of computational tools best suited for capturing SD as rated empirically. The state-of-the-art 'Observer' model of human orientation perception was leveraged in series with candidate algorithms to capture the temporal dynamics of SD. Importantly, these algorithms combine multiple, multidimensional, disparate aspects of orientation perception to compute a single, unidimensional metric of SD that can be readily used as a trigger for an active countermeasure system. To establish appropriate configurations for the computational tool, we collected experimental ratings of SD in a ground-based motion simulator. The Tilt Translation Sled was configured to provide inertial motion stimuli in the coronal plane (lateral drift and roll-tilts) in coupled relationships to represent a helicopter in hover, in a degraded visual environment, in the presence of wind. Nine subjects provided SD ratings in response to 50 experimental motion trials ranging from 15-30 seconds. At some point in each trial, the subject display switched from a mission-related visual search task, to instrument displays, representing a pilot making a cross check of instruments. At this moment they were tasked to compare their perception at the moment of the transition to the veridical information depicted on the instrument displays. Subjects rated their SD on a visual analog scale which they calibrated to during training trials. From a multidimensional trade space of algorithm types and parameter values, a subset of candidate computational tools was identified that reasonably predicted mean empirical SD estimates. An important finding from this investigation was that there was no single optimal computational tool, and model-based detection of SD likely should be tuned to specific use-cases. Our characterization methodology was designed to be generalizable such that the computational framework can be readily applied to different environments, vehicles, situational contexts, etc. Signal detection performance has been shown to impact operator usability of assistive systems, and as such, use of the system may also warrant personalization by the individual pilot. A follow-on methodology involving human-in-the-loop control of the simulated helicopter is proposed in order to characterize potential performance and safety benefits of integrating a real-time SD detection and pilot aiding system into flight decks.

Podium Abstract 11

Perception-Model Analysis of the Somatogravic Illusion in an Airplane Accident

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Background: It is difficult for accident investigators to objectively determine whether spatial disorientation may have contributed to a fatal airplane accident. In this presentation, we evaluate three methods to reconstruct the possible occurrence of the somatogravic illusion based on flight data recordings from an airplane accident.

Methods: The outputs of two vestibular models were compared with the "standard" method, which uses the unprocessed gravito-inertial acceleration (GIA).

Results: All three methods predicted that the changing orientation of the GIA would lead to a somatogravic illusion when no visual references were available. However, the methods were not able to explain the first pitch-down control input by the pilot flying, which may have been triggered by the inadvertent activation of the go-around mode and a corresponding pitch-up moment. Both vestibular models predicted a few seconds delay in the illusory tilt from GIA due to central processing and sensory integration.

Conclusions: While it is difficult to determine which method best predicted the somatogravic illusion perceived during the accident without data on the pilot's pitch perception, both vestibular models

go beyond the GIA analysis in taking into account validated vestibular dynamics, and they also account for other vestibular illusions. In that respect, accident investigators would benefit from a unified and validated vestibular model to better explain pilot actions in accidents related to spatial disorientation.

Reference

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Podium Abstract 12

A review of sensorimotor readaptation following spaceflight

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The need to move and maintain awareness of spatial orientation in altered gravity environment drives sensorimotor adaptation and learning to acquire a new set of synergies optimized for the novel environment. The perceptual and motor coordination problems experienced postflight reflect the recalibration of predicted versus actual movement feedback that is required for readaptation back to the natural gravitational state. The duration of microgravity exposure has a significant effect on both the magnitude of the sensorimotor decrements and the time course of recovery to preflight performance levels. This effect of spaceflight duration is illustrated by comparing results from Shuttle and the International Space Station (ISS) astronauts for reentry motion sickness, neurological exams, computerized dynamic posturography, and functional field tasks (prone-to-stand and tandem walk). Exponential time constants of recovery also vary by task complexity and visual conditions, e.g., 21 vs 87 hr for tandem walk eyes open versus eyes closed following 6-month ISS missions. Neither reentry motion sickness nor postflight functional performance appear altered with prior flight experience. While anecdotal reports suggest prior flight experience may result in some carry over of fine motor strategies needed to control motion in the novel "microgravity" state, this postflight recalibration to "normal gravity" appears necessary with each subsequent mission. The early sensorimotor decrements have implications for the completion of critical mission tasks during and following g-transitions. Interventions are necessary to optimize crew performance for success on upcoming exploration missions.

Keynote Abstract 3

Vestibular dysfunction in patients with sporadic and NF2-related vestibular schwannomas.

Richard Lewis

Vestibular schwannomas (VS), benign tumors that develop from Schwann cells of the vestibular nerve, are usually sporadic (sVS) but are also highly characteristic of neurofibromatosis type 2 (NF2), where they typically are bilateral (NF2/VS). VS tumors present with progressive vestibular symptoms, but the pathophysiology underlying vestibular dysfunction in VS patients remains uncertain, and the relationship between pre-intervention (e.g., surgery, chemotherapy, radiation therapy) vestibular metrics with post-intervention outcomes is not understood. Here I present preliminary data from an observational study that examines vestibular pathophysiology in sVS and NF2/VS patients and the vestibular implications of standard interventions by analyzing vestibular function within a conceptual framework based on understanding the changes in afferent vestibular signal and noise. *Signal* (afferent firing encoding vestibular parameters) is reflected behaviorally by response *accuracy* (response amplitude relative to the ideal amplitude), while *noise* (random afferent firing), quantified as the signal-to-noise ratio, is reflected by response *precision* (inverse of response variability). In addition to quantifying vestibular abnormalities in the two VS populations, we also examined the relationship between vestibular dysfunction, clinical vestibular disability, and non-vestibular (MRI imaging, molecular biologic) parameters. Our results suggest different patterns of dysfunction of vestibular-mediated behaviors in sVS and NF2/VS, in which response accuracy and precision were degraded in sVS but only response precision will be degraded in NF2/VS. Relating vestibular dysfunction to clinical vestibular disability (e.g., dizziness, ataxia, quality of life) suggests that in both sVS and NF2/VS, vestibular imprecision is the main correlate of clinical disability.

Furthermore, our preliminary results suggest that relationship between MRI and vestibular function shows both common and disease-specific patterns in sVS and NF2/VS, and that molecular biologic measures relate to vestibular function in both VS groups in a manner that recapitulates auditory-molecular biologic relationships. Lastly, we examined the relationship between pre-intervention vestibular (and other) metrics and *post-intervention* outcomes, including surgical outcomes is sVS and NF2/VS, where our results suggest that poor precision (e.g., high afferent noise) and/or poor accuracy (e.g., low afferent signal) pre-operatively will associated with the best surgical outcomes; chemotherapy (bevacizumab) outcomes in NF2/VS which suggest that poor vestibular precision is associated with better vestibular outcomes after chemotherapy than better precision; and radiation therapy (RT) outcomes, where hypothesize that good pre-RT precision (low noise) and accuracy (high signal) will be associated with worse chronic post-RT vestibular outcomes.

Podium Abstract 13

Diagnostic Differentiation of Meniere's Disease and Vestibular Migraine with Vestibular Perceptual Thresholds and Inner Ear Imaging Characteristics

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Background: Patients presenting with recurrent episodic vertigo and dizziness such as Meniere's disease (MD) and vestibular migraine (VM) can present a diagnostic challenge as they can both produce similar symptoms of recurrent vertigo, tinnitus, motion intolerance, and hearing loss. Current diagnostic criteria are based on patient history with little contribution from objective measures. Vestibular perceptual thresholds, which refer to the smallest appreciable stimulus detected by the participant in various translations and rotations of body movement, have been shown to have the potential to differentiate different types of vestibular dysfunction. In addition, recent evidence suggests that delayed gadolinium (Gd)-enhanced high-resolution magnetic resonance imaging (MRI) of the inner ear may enable visualization of vestibular and cochlear endolymphatic hydrops. Herein, we compare vestibular perceptual thresholds and imaging of the inner ear in patients with definite MD, patients with definite VM, and normal control (NC) subjects.

Methods: MD patients (n=16), VM patients (n=26), and healthy normal control subjects (n=34) underwent perceptual threshold testing. Five perceptual thresholds were compared among subjects: three linear motion translation at 1.0 Hz (inter-aural (y-translation), naso-occipital (x-translation), and earth-vertical (z-translation)), one rotatory motion at 1.0 Hz (yaw rotation about an earth-vertical axis), and roll-tilt at 0.2 Hz. MD subjects underwent clinical vestibular testing (cervical vestibular evoked myogenic potential [cVEMP] and video head impulse test [vHIT]) and 4-hr delayed intravenous Gd-enhanced MRI of the inner ear. All subjects completed a dizziness handicap inventory (DHI).

Results: MD subjects had significantly elevated z-translation thresholds compared to VM and NC subjects ($t=2.134$, $p=0.02$ and $t=2.134$, $p=0.002$, respectively). MD subjects had significantly elevated x-translation thresholds compared to VM subjects ($t=2.094$, $p=0.046$). MD subjects also demonstrated significantly elevated roll-tilt thresholds compared to VM subjects ($t=2.078$, $p=0.024$). Perceptual thresholds from all other motions were not significantly different among the groups ($p>0.05$). Z-thresholds in MD patients positively correlated with endolymphatic volume ($r2=0.65$, $p=0.009$). Clinical vestibular tests (cVEMP, vHIT)) and subjective DHI scores did not correlate with perceptual thresholds in any motion or imaging findings ($p>0.05$).

Conclusions: Perceptual threshold testing may provide insight into the underlying pathophysiology of the disease process (e.g. elevated z-translation thresholds in MD patients may support saccular dysfunction while elevated roll-tilt thresholds may suggest permanent peripheral damage of the inner ear) and may improve diagnostic precision of episodic

vestibular disorders. Further, threshold measurements may provide a physiologic marker for endolymphatic hydrops. Future avenues for research include whether determining threshold measurements and inner ear imaging can be used to differentiate comorbid MD and VM.

Podium Abstract 14

Electrodermal and Postural Responses in Dizzy Adults: Diagnostic Indicators of Vestibular Migraine

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Introduction: No reliable biometric measurement of vestibular involvement with migraine is currently available.

Objective: Measures of autonomic nervous system and postural responses could serve as quantifiable indicators of vestibular involvement with migraine.

Methods: A convenience sample of 22 young healthy adults (34±9 years old) and 23 young adults (34±8 years old) diagnosed with vestibular migraine (VM) participated. A rod and frame test and clinical outcome measures of dizziness and mobility were administered. Participants stood on foam while viewing two dynamic virtual environments. Trunk acceleration in three planes and electrodermal activity (EDA) were assessed with wearable sensors. Linear mixed models were used to examine magnitude and smoothness of trunk acceleration and tonic and phasic EDA. A Welch's t-test and associations between measures were assessed with a Pearson Correlation Coefficient. Effect sizes of group mean differences were calculated using Cohen's d.

Results: Visual dependence was present in 83% of the VM population. Individuals with VM exhibited lower baseline EDA ($t(4.17)= -7.2$, $p = 0.001$) and greater normalized trunk accelerations in the vertical ($t(42.5)= 2.861$, $p = 0.006$) and medial ($t(46.6)= 2.65$, $p = 0.01$) planes than healthy participants. Tonic EDA activity increased significantly across the period of the trial ($F (1,417) = 23.31$, $p = 0.001$) in the VM group. Significant associations appeared between vertical trunk acceleration and EDA, Dizziness Handicap Inventory, and Activities of Balance Confidence tools.

Conclusions: Higher tonic EDA activity in healthy adults results in more accurate postural reactions. Results support the supposition that EDA activity and postural acceleration are significantly different between VM and healthy individuals when accommodating for postural instability and visual-vestibular conflict.

Podium Abstract 15

Vestibular Function and Balance in People with Diabetes Mellitus

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Over 400 million people worldwide suffer from diabetes mellitus (DM) and related medical problems.[1] Sensory system dysfunction driving balance impairment, such as retinopathy and peripheral neuropathy of the feet, are common consequences of DM, elevate fall risk, and serve as a barrier to obtaining the amount of physical activity needed for disease management and health. Unfortunately, the same biochemistry propagating retinopathy and peripheral neuropathy may also adversely affect vestibular function[2,3]; potentially further exacerbating balance impairments. Therefore, the purpose of this ongoing descriptive study is to characterize vestibular func-

tion and determine its relationship to balance in people with DM and peripheral neuropathy (DMPN). Twenty people with DMPN (19 male, 70.8 ± 8.4 years old, 32.4 ± 4.9 kg/m^2, DM duration 19.1 ± 10.5 years, HbA1c 7.1 ± 0.9 %), 14 people with DM (13 male, 69.6 ± 8.7 years, 30.5 ± 5.2 kg/m^2, DM duration 18.4 ± 8.0 years, HbA1c 7.6 ± 2.0 %), and 16 healthy controls (15 male, 72.2 ± 8.1 years old, 31.1 ± 4.9 kg/m^2) matched for biological sex, age, and body mass index, have been enrolled thus far. Cervical and ocular vestibular evoked myogenic potential (VEMP) tests were used to measure otolith function as total response (sum of left and right inter-amplitudes) and categorized as normal versus abnormal function (absent response or > 33% asymmetry). Sinusoidal harmonic acceleration and step velocity rotational chair testing protocols were used to measure horizontal semicircular canal function as vestibulo-ocular reflex (VOR) gain, phase, and GainTC (VOR gain at .64 Hz x the average of four time constants).[4] Balance and physical activity were quantified with the Functional Gait Assessment (FGA) and one-week of activity watch data (average daily steps), respectively. One-way ANOVA, Kruskal-Wallis, or multiple linear models were used to assess group differences in outcomes. Group differences were not detected in VEMP outcomes or GainTC (all $p > .17$). An effect of frequency was observed for VOR gain and phase (both $p < .01$), and a group by frequency interaction ($p = .03$), attributable to greater phase lag at .64 Hz in DMPN (mean = -14.0°) versus DM (-4.2°) and control groups (-7.6°), was also observed. The DMPN group registered the worst balance (FGA = 18.1; $p < .01$) and the lowest amount of physical activity (daily steps = 5175.1). Presently, study findings suggest otolith function of people with DMPN is similar to people with DM without PN of similar disease duration and glycemic control, and similar to age and body mass index matched controls. However, a unique and abnormal finding of an excessive phase lag at .64 Hz during sinusoidal harmonic acceleration, along with expected deficiencies in balance and physical activity were observed in the DMPN group. With continued study, we intend to assess within and between group associations of vestibular function, balance, and physical activity. As such, final study findings are anticipated to inform and refine balance rehabilitation efforts in the promotion of physical activity and health in people with DMPN.

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Podium Abstract 16

Impaired stationarity perception is associated with increased VR sickness

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Stationarity perception refers to the ability to perceive the surrounding visual environment as world-fixed during self-motion. Perception of stationarity depends on mechanisms that evaluate the congruence between retinal/oculomotor signals and vestibular head movement signals. In a series of psychophysical experiments, we systematically varied the congruence between retinal/oculomotor and vestibular head movement signals to find the range of visual gains that is compatible with perception of a stationary environment. On each trial, human subjects wearing a head-mounted display executed a trained yaw head movement (~15 deg over 1 sec) and reported whether the visual gain was perceived to be too slow or fast. A psychometric fit to the data across trials yields the visual gain most compatible with stationarity (point of subjective equality, PSE) and the sensitivity to visual gain manipulation (just-noticeable difference, JND). Across conditions, we varied 1) the spatial frequency of the visual stimulus, 2) the retinal stimulus location (central versus pe-

ripheral), and 3) the scene-fixed versus head-fixed nature of the oculomotor signal. At the end of each condition, participants completed the Simulator Sickness Questionnaire (SSQ) to assess symptoms and severity of induced virtual reality (VR) sickness. Results demonstrate that stationarity perception is most precise (lowest JND) and accurate (PSE»1) with scene-fixed fixation, central retinal stimulus location, and low spatial frequency visual patterns. Other circumstances lead to a reduced gain perceived as stationary (PSE<1) and impaired sensitivity (increased JND). A linear mixed-effects (LME) model was fit to investigate how psychophysical performance (PSEs, JNDs) related to sickness. Results indicate a significant association between PSEs and the Nausea subscore of the SSQ, as well as between the JNDs and the oculomotor and disorientation subscores of the SSQ. To our knowledge, these are the first results to demonstrate an association between these psychophysical measures and VR sickness.

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Podium Abstract 17

Vestibular Adaptation Mitigates Vertigo and Nystagmus Associated with High Strength MRI

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Vestibular symptoms of vertigo, dizziness, imbalance and sometimes nausea are often reported by people in high-field strength magnets (>4 Tesla) used for MRI. Magnetic vestibular stimulation (MVS) explains these symptoms as arising from utricular currents interacting with the magnetic field to create a Lorentz force that deflects the semicircular canal cupulae to a constant position, simulating a constant-acceleration of the head which produces a constant-velocity slow-phase nystagmus response. Because of adaptation there is a decrease in the nystagmus response the longer the patient stays within the magnet, and a corresponding secondary response with an oppositely directed nystagmus after the subject exits the MRI bore. We sought a simple technique to mitigate these powerful, uncomfortable sensations as experienced during entry and exit from the MRI bore.

First, we used a 3D linear control systems model of the vestibulo-ocular reflex (VOR), which incorporated adaptation, central velocity storage, and rotational feedback elements. We simulated three entry and exit durations (20, 120, 300 seconds) into and out of the magnetic field of an MRI machine and found that the horizontal VOR nystagmus peak slow-phase response (SPV) was lower the longer the duration to enter or exit the magnet. Second, we experimentally recorded the nystagmus response from 4 healthy human subjects as they underwent the same protocol with a 7-Tesla magnet. After entry all subjects were kept in the magnet for 5-minutes. Objectively, we confirmed that the horizontal nystagmus peak SPV was less with longer durations, even though the nystagmus SPV just prior to exiting was not changed by the entry duration. Subjectively, longer durations also mitigated vestibular symptoms, and no vestibular symptoms were reported during the 300 second entrance and exit protocol.

We conclude that longer duration (>120 seconds) entry and exit of the MRI bore allows vestibular adaptation to mitigate objective and subjective symptoms of MVS, but not the eventual velocity of the constant nystagmus while within the magnet. A 120 second duration could be an effective and practical trade-off suitable for clinical application.

Podium Abstract 18

Moving MRI: Imaging a Moving Body with a Moving MRI magnet

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Moving MRI (mMRI) is a novel method we are developing to study how the brain processes signals from the vestibular system and other sources during bodily motion such as tilts and rotations. Moving a subject's head relative to the magnetic field of an MRI scanner creates image artifacts and confounding physiological stimuli, obscuring neuronal activation arising from motion. In mMRI, the scanner magnet and subject move in synchrony such that the subject's head remains stationary in the magnet, suppressing motion artifacts and extraneous magnetic field-induced stimuli. We expect this to enable for the first time high quality functional MRI (fMRI) scans revealing the brain networks that process vestibular and other inputs reflecting bodily motion. Additionally, mMRI may prove useful for mapping brain tissue deformation and fluid flow when the body undergoes large scale motions, with implications for traumatic brain injury and flight physiology research.

In this report we detail our progress in creating the first mMRI scanner. The major engineering challenge in reaching this goal is developing a means to safely and controllably move an MRI magnet. All components of the motion platform near the magnet must be completely nonmagnetic and not harmed by the magnet's field. We use a conduction cooled liquid cryogen-free 1.5T compact superconducting extremity (arm and leg) magnet. Our motion platform comprises a pair of pneumatic cylinders that can tilt the magnet up to 15 degrees from horizontal. The tilt angle is controllable by the host computer of the MRI scanner.

We expect that tilting a magnet should result in field shifts and distortion due to mechanical strain of the magnet structure. Additionally, residual relative motion between the magnet assembly (main magnet, gradient coils, RF coil) and the subject will result in image artifacts. We are making progress in reducing these artifacts to produce MR images of adequate quality. For example, we found a simple linear relationship between the static tilt angle and field shift. By recording the angle during scanning, degraded images obtained with the magnet in motion may be postprocessed to reduce the field shift and relative motion artifacts.

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Keynote Abstract 4

Natural statistics and multisensory processing in spatial orientation: Behavioral modeling and clinical implications

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Perception of spatial orientation involves a weighted fusion of visual, vestibular, proprioceptive and somatosensory signals, as well as cognitive signals about statistical regularities within the natural environment. When one of these signals deteriorates or breaks down, such as the vestibular signal in bilateral vestibulopathy, compensation can occur by relying more on the remaining cues. How sensory signals are weighted and reweighted in spatial orientation has remained difficult to quantify since the quality of these signals can typically not be measured in isolation. I will present our recent work combining experimental psychophysics with a reverse engineering approach based on Bayesian inference principles to characterize sensory reweighting across the life span and in individual bilateral vestibular patients. This personalized quantification approach could aid in the diagnostics and prognostics of multisensory integration deficits in vestibular disorders, and contribute to the evaluation of the effect of rehabilitation therapies, including balance training exercises.

Podium Abstract 19

Computational Models of Active Human Motion Control

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Active control of motion is one of the most critical tasks for humans, with broad impacts on quality of life. It includes both control of the body (e.g., maintaining balance and gait) and of vehicles such as automobiles, airplanes, and spacecraft. While the quality of the active control is highly variable among individuals, it is not completely known why these discrepancies exist. Hence, to study the effects of vestibular processing on motion control, we developed computational models of humans controlling a machine using a joystick while onboard the machine. In our closed-loop models, machine motion results in inputs to peripheral and central vestibular processing, which provides an estimate of motion that is compared to desired motion. Finally, the brain determines a compensatory motor command, which causes the machine to move via a joystick. An innovation in modeling was the inclusion of a minimum sensory threshold before determining a motor command, under the assumption that selecting a joystick input requires a command input larger than corresponding neural noise [1]. We aimed to A) develop a closed-loop human-machine model that includes state-of-the-art spatial orientation and motor-control components [2, 3], and B) validate and refine this model using human experiments.

Modeling (Matlab/Simulink) and experimental validation were performed for an Earth-vertical yaw rotation task to limit vestibular organ stimulation to the semicircular canals. Healthy subjects (18-40 years) were seated in a standard clinical motorized rotary chair (Neurokinetics) in complete darkness while listening to white noise. Subjects were instructed to use a joystick to minimize chair velocity while experiencing a pseudo-random unpredictable sum-of-sines “disturbance” ranging between 0.004-1.7 Hz.

The closed-loop model predicted drastic frequency dependence in the quality of nullification of disturbances while the overall performance was mediocre. The most effective nullification was predicted to occur in a small band of medium-range frequencies (0.01-0.1 Hz) due to combined interactions of the high-pass filter vestibular dynamics, low-pass filter motor control dynamics, and low-pass filter machine dynamics. Human experimental data mostly followed the overall frequency response predicted by the model. Model parameters of the central nervous system delay and motor control effort were tuned to enhance the prediction accuracy.

Our novel computational model utilizes up-to-date spatial orientation and motor control blocks and accurately predicts the experimental human motion control quality. Such models are valuable as they help understand, predict, and potentially mitigate adverse performance episodes in humans.

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Podium Abstract 20

The otolith vermis: a systems neuroscience theory of the Nodulus and Uvula

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The Nodulus and Uvula (NU), which are lobules X and IX of the cerebellar vermis, play a central role in vestibular information processing. Decades of research have involved the NU in a multitude of functions, including the resolution of sensory ambiguity in the inner ear’s otolith organs, the use of gravity signals to detect head rotations, the control of the velocity storage, and the differential processing of head motion that is self-generated or externally imposed.

Here I examine these findings through the lens of the internal model hypothesis, a theoretical framework for information processing. I propose that the NU implement a forward internal model to anticipate the activation of the otoliths and generate sensory prediction errors to refine internal estimates of self-motion or facilitate learning.

I show that a Kalman filter based on this framework can explain the various functions of the NU, as well as neurophysiological observations and the consequences of NU lesions. This underscores the NU's central role in processing information from the otoliths, and supports their designation as the "otolith vermis."

Keynote Abstract 5

Are Head Direction Cell Responses Commutative in 3D – and Why it Matters

Jeffrey S. Taube, Dartmouth College
Abstract for Keynote Address to Vestibular Conference

Our research interests encompass understanding the neurobiological mechanisms that underlie our abilities to navigate and our sense of spatial orientation. In particular, my research program has focused on understanding our 'sense of direction' and its underlying neurobiological mechanisms. To this end and using rodents as a model, we have studied a population of so-called 'head direction cells', which discharge as a function of the animal's directional heading. My talk will briefly discuss our current understanding of where and how the head direction signal is generated in the brain. I will then focus on how head direction cells respond in 3-D, particularly when the animal is moving in planes other than Earth horizontal, and why understanding this issue is important.

Podium Abstract 21

Integration of Self-Motion and Visual Cues for Navigation in Younger and Healthy-Aging Older Adults

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Our brains must combine information from our self-motion cues (proprioception and vestibular) as well as our vision to help us navigate and update our cognitive spatial map. It is unclear whether individuals across the lifespan combine these senses optimally for navigation (Bates & Wolbers, 2014). To quantify sensory combination and weighting strategies, well-aging older and younger adults completed a homing task (Chen et al., 2017). The Varjo VR3 head-mounted display was used to display visual cues in immersive VR. Participants physically walked towards a target via multiple waypoints with visual landmarks to help them encode their spatial location. Participants then walked back to the target with either visual-cues only, self-motion cues only, or congruent cues (both vision and self-motion). They also completed a condition where visual cues were covertly shifted relative to self-motion cues to quantify sensory weighting. In other words, when participants were forced to make a trade-off regarding two "correct" locations, how they split the difference allowed us to determine sensory cue reliance. Both younger and older adults demonstrated improved accuracy in the combined cue condition relative to the single cue conditions. Younger adults visual-only performance was similar to their combined cue performance. Younger adults visual-only error was about 20 cm while their combined cue accuracy was about 18 cm. Older adults had higher error in all conditions (visual error was about 50 cm, self-motion was about 90 cm, and combined cue error was about 22 cm) but received greater relative multisensory benefit. Regardless of age, participants weighted vision higher than self-motion cues (observed visual weight = 60%, self-motion = 40%). This closely aligns with the sensory weights predicted from participants' single-cue variability (predicted visual weight = 55%, self-motion = 35%). Both older adults and younger adults show evidence of optimal integra-

tion, suggesting that sensory cue-combination strategy may not explain age-related declines in navigational abilities related to spatial updating. High inter-individual variability was found across groups, suggesting that sensory weighting strategies may be inconsistent during the experiment. Our study demonstrates that older adults may have decreased navigation ability due to sensory cue combination deficits, though additional work is needed to determine why some continue to optimally integrate their senses in older age while others do not. Our study shows that simple behavioral interventions, such as training vestibular and proprioception cue use for spatial updating, may improve navigational deficits caused by impairments in sensory integration for some older individuals.

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Podium Abstract 22

Navigation deficits are associated with vestibular and cognitive dysfunction in chronic mild traumatic brain injury

Linda J. D'Silva, Lucas Meitler, Jacob Sosnoff, Jeffrey M. Hausdorff, Prabhakar Chalise, Hannes Devos.

Purpose/Hypothesis: 1) To compare navigation ability in the community setting between people with persistent symptoms after mild traumatic brain injury (mTBI) and age-matched controls, 2) to examine the vestibular and cognitive contributions to navigation ability in chronic mTBI.

Fourteen people between 40-64 years of age (mean age: 53.75 ± 7.3 years) who were between 3 months to 2 years post-injury [mean: 46 weeks (range: 18-88)] and fourteen age and sex-matched controls (mean age 53.79 ± 7.4).

Navigation ability was tested by time in seconds to walk a predetermined path in the hospital setting using a map. Measures of vestibular function included dynamic balance measured by the Functional Gait Assessment (FGA), and path integration measured by end-point error on the Triangle Completion Test (TCT). Global executive function was assessed using the MoCA, simple search ability was tested by normalizing the Trail-making test (subtracting TMT-A from TMT-B), visuospatial cognition was measured using the symbol digit modalities test (SDMT), and symptoms were measured by the post-concussion symptom scale (PCSS). Based on normality of data, either independent sample t-tests or Mann Whitney U tests were used to compare between group outcomes. Linear regression was used to examine the relationship between navigation ability and the independent variables of vestibular and cognitive function.

Results: Participants with mTBI took longer to navigate to their destination (363.36 ± 91.29 versus 269.85 ± 20.28 seconds, $p=0.001$) compared to controls. They had lower FGA scores (20.5 (IQR: 9) versus 28.5 (IQR: 2), $p<0.001$), greater endpoint error on the TCT (67.63 ± 34.5 versus 44.86 ± 14.3 cm, $p=0.03$), longer time to complete the TMT (61.81 (IQR: 46.51) versus 40.46 (IQR: 12.8), $p=0.01$), lower scores on the SDMT (65.43 ± 13.2 versus 83.43 ± 15.46, $p=0.003$), and higher symptom severity on the PCSS ($p<0.001$). Independent variables that explained 77% of the variance in navigation ability were FGA ($R^2=0.60$, $p<0.001$), and MoCA score ($R^2=0.77$, $p<0.001$).

Conclusions: Navigation in an ecologically valid condition in the hospital took significantly longer for people with persistent symptoms after a mTBI compared to controls. People with mTBI and persistent symptoms have poorer dynamic balance, impaired path integration, poorer executive function, and visuospatial deficits compared to age-matched controls. Dynamic balance and global cognitive function were most predictive of navigation deficits. Vestibular and cognitive deficits that persist months after a mTBI and can lead to reduced community activities.

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Keynote Abstract 6

From Balance to Velocity Storage: Two Research Pearls from a Clinician's Point of View

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Clinic research often involves investigations that attempt to find relationships between disease characteristics and fundamental physiologic or genetic characteristics associated with a particular disease. Such phenotype-genotype investigations for rare diseases and syndromes are common to the NIH. And while such investigations are extremely important to the understanding of disease and function, such descriptive studies are often limited with respect to the generalization of findings beyond the disorder and population the research is intended to serve. However, such investigations can also be extremely instrumental in facilitating research towards a better understanding of normal physiology through understanding how an individual adapt in the face of abnormal function. However, our understanding of patient outcomes is fundamentally linked to how our clinical assessments evaluate our patients and the stimuli we use to elicit patient outcomes.

Patient's outcome measures are fundamentally influenced by the stimuli used to evaluate them. Are we always using the correct stimuli to measure what we intended to evaluate? How many assumptions are we making with respect to the relationship between the stimulus, the physiology, and function? This presentation will focus on two research studies that highlight generalizable vestibular and balance principles that may serve to better our understanding of how we both select the stimuli we use to evaluate our patient's physiology as well as how we interpret our patient's outcome measures.

The first study focused on the influence of an individual's personal limits of stability (LOS) on their reported outcomes sway measure. Limits of stability were determined from 60 healthy volunteers recruited into three age groups of young, middle-aged, and elderly. Individual measures of LOS were significantly lower than theoretical estimates of the LOS in healthy adults. Implications of an individual's personal LOS for determining postural stability and risk for falls during the sensory organization test will be discussed.

The second study investigated the implications of stimulus frequency when assessing velocity storage (VS) for patients with peripheral and central vestibular pathology. Rotational data from approximately 300 patients and healthy controls from 535 visits were analyzed to explore the optimal sinusoidal acceleration and velocity step stimuli to best recruit and reflect VS function and dysfunction. Correlations and multiple regression analyses were performed to highlight the relationships and contributions of various sinusoidal and step stimuli to provide evidence confirming a known low-frequency dependency of the VS and investigate unique clinical phenotypes sparing the common sacrificing of VS as a consequence of vestibulopathies.

Both studies will attempt to further elucidate the relationship between stimuli and clinical response to improve our clinical practice and our understanding of patient outcomes.

Podium Abstract 23

Rapid gaze-shift adaptation during self-generated vestibular prosthetic stimulation

Kantapon Pum Wiboonsaksakul, Charles C Della Santina, Kathleen E Cullen

The brain must differentiate between externally-generated and self-generated sensory inputs to build stable perception and generate appropriate behavior. Specifically for vestibular prosthesis users, the brain must learn to utilize prosthetic vestibular input to maintain visual and postural stability while also suppress/cancel these reflexes when they are counter-productive to behavioral goals. Here, we leveraged a gaze-shift task—a naturalistic behavior that requires the gating/canceling of vestibular input—to directly investigate how self-generated prosthetic stimulation affects reorientation behaviors. In a monkey with bilateral vestibular deficits, we implanted a vestibular prosthesis that senses head rotation and transforms this movement into vestibular nerve stimulation, substituting for the damaged periphery. The monkey was trained to make eye-head coordinated gaze shifts between horizontal targets while the head, eye, and gaze positions were recorded. Each session comprised a three-block learning paradigm: baseline gaze-shifts, gaze-shifts with prosthetic stimulation, and washout without stimulation. We hypothesized that 1) prosthetic stimulation would first engage vestibular reflex pathways, resulting in impeded head movements and truncated gaze-shifts but also that 2) the brain would then adapt to this new sensory input and no longer engage the reflex when it is counterproductive. Consistent with our predictions, gaze position error initially increased after stimulation onset and then exponentially decayed within ~80 trials. Prosthesis-evoked vestibulo-ocular reflex (VOR) gain and change in head position impeded by the prosthesis-evoked vestibulo-collic reflex (VCR) showed a similar decay though both at a slower rate (~200 trials), suggesting that the suppression/canceling of VOR and VCR both contributed to the observed improvement in gaze accuracy. In addition, early washout trials and catch trials during learning showed oppositely-directed gaze position error, indicating a central adaptation in addition to the observed reflex suppression/cancellation. This central adaptation could be due to the updating of the gaze controller or the updating of a forward internal model to predict and cancel self-generated prosthetic sensory input. Together, these results show that the brain can quickly adapt to self-generated prosthetic stimulation to improve behavioral performance. Importantly, these findings provide new insights on how prosthetic inputs interact with different vestibular pathways in a context-specific way.

Podium Abstract 24

Discharge properties of neurons in the 8th nerve, vestibular nucleus and abducens nucleus may explain suboptimal VOR characteristics in response to unilateral and bilateral neuroprosthetic stimulation.

James Phillips, Leo Ling, Christopher Phillips, Amy Nowack, Yoshiko Kojima, Jay Rubinstein, Shawn Newlands

Introduction: Vestibular neuroprostheses aim to restore vestibular function after the loss of vestibular hair cells. These devices were designed to restore primarily the angular vestibulo-ocular reflex (aVOR) by selectively stimulating afferent fibers of each ampullar nerve. These devices have been successful in providing controlled vestibular activation in patients, and clinically relevant recovery of function. However, aVOR restoration has been suboptimal in human subjects; e.g., low or pulsatile eye velocity, incorrect timing, and fluctuating direction errors. To understand the mechanisms underlying the suboptimal aVOR response to neuroprosthetic stimulation (eVOR), we recorded eye movement behavior and neural activity during such stimulation.

Methods: Rhesus monkeys were implanted with unilateral or bilateral vestibular neuroprostheses designed for human use. Each device generated biphasic pulse stimulation (BPS) modulated either in current amplitude or pulse frequency. Eye movements were recorded in the dark with scleral coils in awake behaving animals. Unit activity was recorded from 8th nerve afferents, identified vestibular nuclear neurons, and abducens neurons.

Results: Neuroprosthetic BPS produced electrically elicited VOR (eVOR) in the plane of the targeted (implanted) canal(s) above threshold current levels. As current was increased, eye movements were elicited out of plane. High eVOR eye velocities could

only be achieved at current levels eliciting significant out of plane eye movements. eVOR directions suggested canal-canal or canal-otolith summation. Low pulse rate stimulation elicited brief velocity pulses, while higher pulse rates elicited sustained eVOR velocity. Velocity saturated with high pulse rate, and then decreased at higher rates.

Afferent fibers displayed time locked discharge in response to BPS with different thresholds. The probability of eliciting a spike increased with increasing current level. Individual afferent fibers often responded to BPS of sites in multiple canals. Differences were observed between afferents types.

Secondary vestibular neurons displayed time locked discharge in response to BPS above current thresholds corresponding to behavioral thresholds. The probability of a spike increased with increasing current amplitude and decreased with increasing pulse frequency, typically saturating below P=1.0. Changes in current level often changed the timing but not the number of elicited spikes. Most neurons responded to stimulation from multiple canal electrodes at higher current levels. Differences were observed between behaviorally identified neuron types.

Abducens neurons displayed complex response characteristics comparable to vestibular neurons, but at longer latency.

Conclusion: These results suggest that neural activation with eVOR is qualitatively different than that underlying natural aVOR. These differences limit the ability of neuroprosthetic stimulation to reproduce natural VOR responses.

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Podium Abstract 25

Pitch and roll perturbations under conditions of controlled acceleration and vestibular prosthesis

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Several therapies and implantable prosthetics have emerged to treat bilateral vestibular loss (BVL). These prosthetics translate signals from a gyroscope into vestibular afferent stimulation. While prosthetics have found significant success in humans (Chow et al., 2021), there are a number of open questions regarding how to best optimize prosthetic stimulation paradigms under various conditions. Notably, the vestibular system relies on input from two different peripheral channels, regular and irregular afferents, which encode head motion with substantially different temporal dynamics (Sadeghi 2007). Thus, this difference is an important consideration in the context of optimizing biomimetic stimulation protocols. Our goal was to first assess and compare postural responses in normal Rhesus Macaque monkeys versus monkeys with bilateral vestibular labyrinthectomy. We then investigated which prosthetic stimulation protocols (static, regular, irregular, or super-irregular) best restored function following bilateral vestibular labyrinthectomy.

To assess postural responses, we applied sinusoidal and transient perturbations in the pitch and roll axes. In experiments, unrestrained macaque sat in their natural stance within a chamber secured to a hexapod motion platform. Postural response for pitch and roll were assessed using sinusoidal perturbations at five different frequencies (0.25, 0.5, 1, 2, and 5Hz) at both a 5degrees/sec and 10degrees/sec peak angular velocity. We further assessed responses to un-cued, transient tilt perturbations (with accelerations of 200, 500, and 1000 deg/s^2 and peak velocities of 20, 40, and 60 deg/s.) Measurements included IMU head and platform movement tracking, markerless pose estimation with DeepLabCut, and weight distribution tracking via force plate.

Overall, comparison of postural responses in normal Rhesus Macaque monkeys and those with BVL revealed disparities in both axes. Notably, for both normal and BVL animals, postural responses were symmetrical between leftward and rightward roll perturbations but were asymmetrical between anterior and posterior pitch. In the roll axis, transient tilts of the BVL animal showed an earlier, hypermetric, and reversed head motion response compared to normal animal. The BVL animal demonstrated better compensation for anteriorly-directed pitch when compared to posteriorly-directed pitch perturbations. These results pair well with the previously suggested vision- and proprioceptive-dependent BVL condition (Cullen and Brooks 2015). For sinusoidal perturbations in both axes, the BVL animal demonstrated greater postural sway (i.e. greater head-in-space movement) than normal, given the motion was predictable, the BVL animal showed better recovery for sinusoid motion than for the transients.

In addition, we found that unilateral anterior canal prosthetic stimulation protocols, which mimicked patterns of the native vestibular afferents, restored some function following bilateral vestibular labyrinthectomy. Further, we found the greatest restoration of function by matching the dynamics of irregular afferents, the primary contributors to vestibulospinal pathways.

These studies begin to elucidate the contribution of vestibular signals to postural control and how these vary with the predictability, direction, and intensity of the perturbation, while also testing future stimulation paradigms and their optimized conditions for performance. As vestibular implants become more widespread, understanding how they interact with the brain and how we can optimize them for various daily circumstances will aid in improving life for those suffering vestibular loss.

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Keynote Abstract 7

Vertigo and motion perception: More than meets the eye?

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The vestibular system includes both the otoliths and semicircular canals. The semicircular canals have been extensively studied as the vestibulo-ocular reflex (VOR) that is responsible nystagmus. However, many patients have dizziness symptoms that go beyond this and may be attributed to the linear acceleration sensing organs including the utricle and saccule. Central integration with vision also plays an important part in self motion perception. After unilateral loss of vestibular function, it is well described that humans as well as animals have changes in vertical perception which can also manifest as ocular counter-rotation and head tilt. However, study of the function of the otolith organs in human heading perception has been relatively limited.

Normal human heading perception has some unusual and unexpected properties. The perception of the lateral aspect of headings is overestimated with both visual and inertial stimuli. The differences in the coordinate system used by inertial (body based) and visual headings (retina based) and the problem this presents for multisensory integration. Although it has been hypothesized that these are converted to a common coordinate system prior to multisensory integration this appears not to be the case. The underlying neurophysiology compensates for this by having people look in the direction they want to go, rather than undergo a coordinate system reconciliation.

Visual inertial heading integration will be considered in terms of the factors required. These include the relative reliability of these stimuli, timing, direction differences, visual field size, the perception of common causation, and motion profile. Relative reliability determines the weight given to each stimulus when they are integrated but doesn't seem to influence if they are integrated or not. Visual-vestibular integration occurs over a surprisingly large difference in direction and even when individuals do not consciously perceive the stimuli to have common causation. Visual field size had surprisingly little effect. Timing differences of up to 250 ms are well tolerated. The visual motion profile does not need to match the inertial motion for multisensory integration to occur.

Individuals with unilateral vestibular hypofunction were found to reliably have inertial heading perception deviated towards the side of their vestibular lesion. This deviation was reliably present even decades after the lesion suggesting it does not recover spontaneously. It is hypothesized that this deviation may be the cause of chronic dizziness and fatigue symptoms in this population.

Adaptation of inertial heading perception could be induced by exposing people to rotating environments or shifting situations in which the visual heading was consistently offset in one direction. The potential to use this for vestibular rehabilitation is being explored.

Podium Abstract 26

Assessing noisy Galvanic Vestibular Stimulation capabilities for inducing stochastic resonance in lateral translation vestibular perceptual thresholds

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We are studying the use of noisy Galvanic Vestibular Stimulation (nGVS) as a means of inducing a phenomenon known as stochastic resonance (SR), where a particular non-zero level of added sensory noise might enhance the response to a weak periodic input signal (A. P. Mulavara et al., 2011). Several studies have noted improved vestibular roll tilt perceptual thresholds (Galvan-Garza et al., 2018), as well as balance (Goel et al., 2015; A. P. Mulavara et al., 2011) and locomotor performance (A. Mulavara et al., 2015; Temple et al., 2018) while utilizing nGVS, that was attributed to possible SR induced enhancements of vestibular afferents. However, other studies have noted little evidence of SR occurring with nGVS in young healthy individuals (Assländer et al., 2021). We aim to systematically test various nGVS waveforms' impact on 1 Hz lateral translation vestibular perceptual thresholds in healthy individuals, to investigate which may best enhance vestibular performance. Vestibular perceptual thresholds will be computed from 100 trials of left/right translations adjusted by a three-down-one-up (3D1U) algorithm, using three different nGVS profiles, tested at five different noise amplitudes (including zero-noise sham) each. A machine learning algorithm previously developed (Voros et al., 2022) will be utilized to objectively classify presence of SR-like phenomena for each subject and nGVS profile. Furthermore, to investigate a potential means of reducing the number of trials needed to compute vestibular thresholds, subjects will report confidence (50-100%) for each of their translation reports. If vestibular thresholds computed with confidence reports and fewer trials are found to display similar values and SR-like phenomena seen when utilizing 100 trials, then these methods could be utilized to reduce the time needed to measure vestibular thresholds in individuals, potentially avoiding fatigue and improving threshold testing methods. Such benefits could be valuable in assessing future SR-induced vestibular performance improvements, as well as measuring vestibular perceptual thresholds in general. Overall, this study could be instrumental in determining if nGVS can serve as a viable countermeasure to improve vestibular performance in those with potential deficits, such as astronauts returning to gravitational environments after long-duration exposure to microgravity.

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Podium Abstract 27

The Impact of Hypoxia on Vestibular Thresholds

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Pilots, mountaineers, and even airline passengers are exposed to a variety of factors that may impact their ability to sense where they are relative to the environment including hypoxia. Past studies have demonstrated that severe hypoxia adversely impacts vestibular function in animals. Despite the potential for hypoxia to impact our ability to sense where we are within space no prior studies have examined the impact of hypoxia on vestibular function in humans. Given this state of knowledge, we performed a study to begin to investigate how mild hypoxia impacts human vestibular thresholds. In order to address this question,15 participants completed multiple sessions of a z-translation threshold test on a MOOG movement platform while breathing gases with an oxygen content consistent with 0 feet (21% O_2) and 8,000 feet (15% O_2) above sea level. Thresholds were determined based upon participants' responses on a 2 alternate forced choice recognition task using a staircase to adaptively select the next stimulus. We found that 86.67% of the participants' median z translation thresholds were higher when breathing gases with an oxygen content comparable to 8,000 feet than when breathing gases with an oxygen content comparable to 0 feet. The median z translation threshold was 24.11% higher in the hypoxia condition. In other words, larger movements up/down were needed for participants to reliably sense z-translation motion. The results of the present study suggest that mild hypoxia (i.e., roughly equivalent to that experienced at 8,000 feet; the altitude limit to which commercial air lines must pressurize) can impact our ability to reliably sense whether we moved up or down. Specifically, when hypoxic it takes larger movements for humans to sense the motion. Additional research is needed to determine the exact mechanism(s) of this effect, if this impacts other elements of human spatial orientation, and if this generalizes to other types of motions (e.g., roll-tilts).

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Podium Abstract 28

Influence of Visual Afference on Self-Motion Perceptual Training

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Aging, as well as vestibular pathology, are each characterized by changes in vestibular self-motion perception. Specifically, the perception of a passive whole-body roll tilt motion stimulus has been found to (1) degrade with age [1] and (2) correlate strongly with balance [2,3], suggesting that changes in vestibular perception may contribute to subclinical changes in postural control. Recent evidence showing that roll tilt perception can be improved with training [4,5] supports that self-motion perception may represent a potentially modifiable risk factor for balance dysfunction. However, efforts to determine the impact of vestibular perceptual training on balance control are constrained by a lack of knowledge into the training parameters best suited to drive improvements in self-motion perception. We recently showed that a 5-day training protocol, consisting of thirteen EPOCHs of 100 trials each, led to a 17.68 to 23.77% improvement in roll tilt perceptual thresholds [5]. Our protocol used a simple feedback schema whereby participants were (a) tilted in the dark, (b) asked to judge the direction of tilt, and (c) provided distinct binaural auditory tones for correct and incorrect answers. Despite a significant effect at the group level, we observed two disparate cohorts within the training group (N = 20). Approximately half of the training group (11/20, 55%) improved at the post test assessment by more than 2-standard deviations (i.e., 33.2%), and were labeled as "responders" [4]; by extension, 45% of the cohort showed little change between the baseline and posttest assessments and were label "non-responders". To determine if the heterogenous response to the training protocol was related to the chosen feedback schema we designed the present study to determine if learning could be enhanced with the provision of a visual feedback cue. In a new cohort of 10 healthy adult

volunteers (Age 25.3±3.3), we replicated the prior study, but added visual feedback after each response during the return to an upright position. At posttest we found a nominal and insignificant ($p>0.05$) increase in roll tilt thresholds of 1.7±56%, and consistent with our prior study, the response to the training protocol varied widely within the group. However, unlike the previous study where only a simple auditory tone was used [4], three out of the 10 participants who received visual feedback showed a large increase in thresholds, averaging a 69.7±52.35% increase in thresholds at posttest. Interestingly, in the remaining 7 participants we found a robust decrease in thresholds of 32.36±16.29%. These data support that a visual feedback cue may enhance learning in a subset of individuals, while in others it may provide potentially conflicting feedback resulting in a worsening of self-motion perception. Additional studies are required to determine the source of the variability in perceptual training, including the potential influence of baseline visual motion perception.

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Podium Abstract 29

Modeling the impact of galvanic vestibular stimulation on human self-orientation perception in the presence of physical stimuli

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Galvanic vestibular stimulation (GVS) has a myriad of promising applications ranging from rectifying vestibular hypofunction and improving self-motion thresholds to enhancing simulator immersion and countering motion sickness. However, the utility of GVS is contingent on our ability to predict resultant human perception, particularly in the presence of physical motion. To this end, we developed a computational model of human perception due to both physical and GVS-induced virtual motion, based on the “observer model” for spatial orientation perception during passive motions (Clark et al., 2019; Merfeld et al., 1993; Merfeld & Zupan, 2002). Foundational to this effort, recent works have quantified the frequency dynamics of bipolar GVS applied to the mastoid processes of macaque monkeys (Forbes et al., 2023; Kwan et al., 2019). Incorporating these findings, we present an observer model, for passive motions in the dark, augmented to account for the influence of GVS on vestibular sensory afferents in humans. To account for anatomical differences between humans and primate models, and to model the individual afferent contributions of both physical and electrical stimuli, we collected perception of roll tilt data in human participants (N=13) during static roll tilts across a range of GVS intensities. Perception of tilt was measured via a subjective haptic orientation task, and direct current GVS was supplied to participants in the bipolar configuration, both concordant and discordant with physical tilt. Perceptions of tilt were found to be affected by GVS (with the sign of the current corresponding to the right mastoid’s polarity) averaging about -0.49 deg/mA, with consistent effects observed across individuals. To further inform and validate this model, we have designed a secondary experiment to dynamically assess perceptions of roll tilt in subjects during dynamic roll tilt in the presence of a dynamic GVS waveform, both with low (<0.5Hz) frequency content across a range of peak stimulus intensities. The realization of this model offers the potential to computationally assess and design GVS waveforms to achieve specific perceptual responses in humans.

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Podium Abstract 30

Model of Motion Perception Following Sudden Transitions of Visual Cue Availability

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Existing models of motion perception do not capture motion perception during all common flight scenarios. For example, we are not aware of any existing model that aptly predicts the dynamics of motion perception following sudden transitions in the availability of visual cues (e.g. as an aircraft pilot experiences flying into or out of a cloud). It is important that we understand spatial orientation and motion perception in commonly occurring flight scenarios because spatial disorientation is associated with adverse failure modes (aircraft crashes). By developing computational models of orientation perception that are robust to sudden changes in visual cues, we can better understand the potential spatial disorientation that occurs around such transitions.

For the present study, we first collected empirical human subject data on motion perception during extended periods of Earth vertical yaw motion. The specific Earth vertical yaw rotations that our human subjects experienced were designed to elicit different perceptions of orientation with and without visual cues. Therefore, when a sudden change in the availability of visual cues occurred during a period of misperception of angular velocity in the no visual cues case, we were able to characterize the ensuing pattern of orientation perception. Data collection was performed on 28 unique subjects. The subjects were tasked with pressing a button every 90 degrees in order to record their perception of motion. Visual scenarios included two control conditions: no visual cues (i.e., in the dark) and visual cues (i.e., rotating dots providing angular vection) the entire time. The two test conditions were: suddenly losing visual cues and suddenly gaining visual cues.

We hypothesized that the existing pathway for sensory conflict associated with visual angular vection is effectively low pass filtered before being integrated with vestibular pathways. Therefore, we modified an existing model of orientation perception [1] and were able to have the modified form [with low pass filtering] match out results. While speculative, this low pass filter mechanism may be associated with the ambiguity in visual motion cues being caused by self-motion or scene-motion.

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Podium Abstract 31

Why velocity storage changes in response to peripheral vestibular damage

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Peripheral vestibular cues are processed by a central mechanism known as velocity storage. This mechanism plays an important role in directing the dynamic response to yaw rotation. For example, during constant angular velocity rotation, horizontal eye movements and perceived angular velocity exponentially decay with a velocity storage time constant of ~15-30 s in normal individuals. Notably, the vestibular periphery input decays much faster, around 6 s. Peripheral vestibular damage leads to a substantial reduction in the velocity storage time constant. For example, the diagnostic range for complete unilateral loss is 6-12 s. However, the underlying mechanism linking vestibular damage and changes in the time constant is not fully understood. In this study, we aimed to address this gap. We built on a theory that the brain uses Bayesian optimal processing to compute the ideal velocity storage time constant and does so based on the statistics of vestibular noise and experienced motion. More specifically, although a longer time constant would improve the accuracy of the central estimate of angular head velocity, it may also amplify neural noise, which degrades precision. Thus, in determining the optimal time constant. the brain may be striving to strike a balance between accuracy and precision. In this study, we applied a Bayesian Kalman filter model to investigate the optimal velocity storage time constant for unilateral damage. To account for the unknown effect of unilateral damage on vestibular noise, we developed five scenarios based on literature. As detailed in our paper (Madhani et al. 2023), for all scenarios, predictions were significantly reduced compared to those of normal individuals and consistent with clinical observations. Furthermore, interactions between age-related hair cell loss and peripheral vestibular damage were also modeled. Together, results suggest that the brain optimizes the velocity storage time constant based on the vestibular signal-to-noise ratio and emphasize the highly consequential role of noise in neurocomputations performed by the brain.

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Podium Abstract 32

The role of sensory noise in closed-loop sensorimotor control

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Sensory, perceptual, and motor processes are affected by noise, which is defined as random disturbances in neural processes [1]. In closed-loop tasks like postural control, it is thought that performance is degraded due to neural noise in sensory and motor systems. However, it is complicated to study the role of noise in closed-loop tasks because noise result in variability in the motor output, which is fed back into the sensory inputs, potentially causing more variability in the motor output. Thus, the problem has been studied using both computational models and experiments. Examples of computational approaches include posture models that posit that postural sway arises from neural noise [2]. Conversely, postural sway and performance in manual control are correlated across subjects with perceptual thresholds, which assay sensory noise according to signal detection theory; notably, these correlations do not consider closed-loop behaviors. We brought together these approaches to test the hypothesis that sensory noise degrades performance in closed-loop orientation control, using: 1) closed-loop computational models; 2) experimental closed-loop task performance; and 3) vestibular perceptual threshold as an assay of sensory noise. We modeled tasks in which subjects sat on a motorized chair that could be controlled using a joystick. In one study we performed experiments and modeling for yaw-axis control, in which subjects experienced a random motion and were instructed to use the joystick to keep themselves at rest. We also modeled results from a published study showing a correlation between performance in a roll-tilt self-orientation control task and vestibular thresholds [4]. Performance in different gravity environments was also studied using a centrifuge. In the closed-loop model, we assumed based on decision-making theory that subjects would make joystick inputs only when they had reliable vestibular cues - i.e., the sensory input exceeded sensory noise. Model predictions closely matched experimental [4] results, including frequency responses. Subjects with lower vestibular thresholds (i.e., less neural noise) had less variable manual control performance, with a similar slope between manual control performance and thresholds for model and experimental results. Thus, the results strengthen support for the hypothesis that vestibular noise worsens closed-loop control performance. Model variations had little impact on results, showing robustness. Manual control performance was better (i.e., less variable) in higher G levels in both model and experimental [4] results, supporting the hypothesis that better performance results from increased vestibular signal-to-noise ratio in higher G level.

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Podium Abstract 33

Links between vestibular perception and cognition in healthy aging

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A growing body of evidence suggests relationships between age-related changes in vestibular function and cognition. However, literature to date has focused on vestibular reflexive pathways and potential links between vestibular perception and cognition have not been thoroughly examined. Thus, we assessed a comprehensive vestibular threshold test battery and standard assessments of cognitive function previously seen to be linked to vestibular dysfunction across a broad age-range (21-86 years of age; n=52). Overall, both vestibular perceptual thresholds and cognitive function demonstrated significant age-related changes. Regression analyses controlling for age and demographic variables identified a relationship between vestibular perceptual thresholds and cognitive assessments for only low frequency roll tilt (i.e., medio-lateral earth horizontal rotation) thresholds, reflecting canal-otolith integration, and earth-vertical superior-inferior translation thresholds, probing saccular function. No other significant relationships to cognitive measures were seen for other measures probing perception predominantly mediated by the semi-circular canals or utricle. Thus, our evidence suggests a link between cognition and modality specific vestibular perception in healthy aging.

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Podium Abstract 34

Sensory contributions to frontal plane balance control during stance and stepping-in-place gait in younger and older healthy adults

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Control of body orientation during stance and metronome paced stepping-in-place (SiP) gait was measured in 20 younger (25-43 years) and 20 older (65-82 years) healthy adults. Balance was perturbed by continuously applied pseudorandom rotational stimuli (six 36.6-s cycles) at 3 amplitudes (1°, 3°, 6° peak-to-peak) that evoked frontal plane sway in 3 test conditions: surface-tilt with eyes open (SS/EO) and closed (SS/EC), and visual scene tilt (VS/EO). Lateral body displacement measures at hip and shoulder levels were used to estimate center-of-mass (CoM) tilt angle with respect to an axis at ankle height centered between the feet. For each test, the frequency-dependent relationship between the stimulus tilt and the evoked CoM sway angle was represented by a frequency response function (FRF) that characterized response sensitivity (gain) and timing (phase). Parameters of a relatively simple feedback model of balance control were estimated from fits to average FRFs. Parameters included 1) sensory weights that represent the relative contribution of different sensory systems to balance control with a proprioceptive weight (W_{prop}) estimated from SS/EO and SS/EC tests, and a visual weight (W_{vis}) estimated from VS/EO tests, 2) neural controller parameters that translate integrated sensory information to corrective torque, 3) torque feedback parameters, and 4) time delay. This report focuses on the sensory contributions. For each of the 3 test conditions, for both stance and SiP, and for both younger and older subjects, W_{prop} and W_{vis} decreased with increasing stimulus amplitude demonstrating amplitude-dependent sensory reweighting. For each of the 3 test conditions, for both stance and SiP, and at each stimulus amplitude W_{prop} and W_{vis} were larger for older than

for younger subjects indicating age-related differences in sensory utilization for balance. For both younger and older subjects on surface-tilt tests, W_{prop} on SiP tests was about 40% smaller than on stance tests indicating a reduced ability to use proprioception for balance control during SiP. On SS/EC tests smaller W_{prop} implies increased vestibular reliance (larger W_{vest}) during SiP compared to stance. Additionally, comparing younger and older subjects, the higher reliance on proprioception on the SS/EC test in older subjects indicates their reduced ability to use vestibular cues for balance. For both younger and older subjects on VS/EO tests, W_{vis} was remarkably larger (~10 times) on SiP than on stance tests indicating a greatly enhanced reliance on vision for balance during SiP gait. Additionally, older subjects were less able to reduce W_{vis} with increasing stimulus amplitude on SiP than younger subjects. At the 1° stimulus amplitude, W_{vis} in older subjects was only 5% larger than in younger subjects, but at the 6° amplitude, W_{vis} was 2 times larger in older than in younger subjects.

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Poster Abstracts

Poster Abstract 1

Age-Related Changes in the Gerbil Peripheral Vestibular System

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The vestibular system plays a crucial role in maintaining balance and head orientation. As we age, vestibular function declines, leading to balance disorders and impaired quality of life. This can also result in falls, which can cause injury or death. However, the underlying causes of vestibular dysfunction with age are not well understood.

In this study, we aimed to investigate vestibular function in young adult and aging gerbils using electrophysiological and behavioral approaches. Whole-cell patch clamp methods were used to record from type-I and type-II hair cells prepared from semicircular canal crista of gerbils at different ages. In young adults (postnatal day (P)30-60), we found that type-I cells exhibited typical low and high voltage-activated K^+ currents that did not inactivate in response to standard voltage protocols. Type-II hair cells demonstrated outward K^+ currents that inactivated at depolarized membrane potentials and slowly activating hyperpolarization-activated currents (I_h) at potentials negative to the resting potential. Peak outward K^+ currents at +20 mV were 3,885 ± 449 pA (mean ± SEM, n = 16) in type-I hair cells and 2,104 ± 342 pA (n = 11) in type-II hair cells. Similar K^+ currents were seen in both hair cell types at advanced ages (P265-308). Extracellular application of the K^+ channel blocker 4-aminopyridine (4-AP, 1 mM) blocked more than 50% of the outward current in both hair cell types at P30-60. 4-AP also blocked ~65% of the outward K^+ current in 2 type I hair cells at P265.

Balance function was tested using an accelerating rotarod and balance beam. Initial results suggest that advanced age gerbils performed significantly worse suggesting a decline in vestibular function. Ongoing experiments will further evaluate how age-related changes in hair cell and afferent properties may impact vestibular function.

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Poster Abstract 2

Electrodermal and Postural Responses in Dizzy Adults: Diagnostic Indicators of Vestibular Migraine

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Introduction: No reliable biometric measurement of vestibular involvement with migraine is currently available.

Objective: Measures of autonomic nervous system and postural responses could serve as quantifiable indicators of vestibular involvement with migraine.

Methods: A convenience sample of 22 young healthy adults (34±9 years old) and 23 young adults (34±8 years old) diagnosed with vestibular migraine (VM) participated. A rod and frame test and clinical outcome measures of dizziness and mobility were administered. Participants stood on foam while viewing two dynamic virtual environments. Trunk acceleration in three planes and electrodermal activity (EDA) were assessed with wearable sensors. Linear mixed models were used to examine magnitude and smoothness of trunk acceleration and tonic and phasic EDA. A Welch's t-test and associations between measures were assessed with a Pearson Correlation Coefficient. Effect sizes of group mean differences were calculated using Cohen's d.

Results: Visual dependence was present in 83% of the VM population. Individuals with VM exhibited lower baseline EDA ($t(4.17) = -7.2$, $p = 0.001$) and greater normalized trunk accelerations in the vertical ($t(42.5) = 2.861$, $p = 0.006$) and medial ($t(46.6) = 2.65$, $p = 0.01$) planes than healthy participants. Tonic EDA activity increased significantly across the period of the trial ($F(1,417) = 23.31$, $p = 0.001$) in the VM group. Significant associations appeared between vertical trunk acceleration and EDA, Dizziness Handicap Inventory, and Activities of Balance Confidence tools.

Conclusions: Higher tonic EDA activity in healthy adults results in more accurate postural reactions. Results support the supposition that EDA activity and postural acceleration are significantly different between VM and healthy individuals when accommodating for postural instability and visual-vestibular conflict.

Poster Abstract 3

2023 Vestibular-oriented research meeting, June 25, 2023

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Amniotes have two types of vestibular hair cell, type I and type II, that have very different morphology, synapses, molecular properties, and physiology. In adult mice, deletion of Sox2 from type II hair cells causes them to transdifferentiate toward the type I fate - i.e., to lose type II-specific anatomic and molecular features and to acquire features unique to type I hair cells (Stone et al. 2021). In addition, the bouton afferent terminals that typically contact type II hair cells are replaced by a partial or full calyx-type terminal as the hair cell transdifferentiates.

We asked whether this type II-to-I shift affects motor behavior and vestibular reflexes. We found that, instead of undergoing the typical reduction in locomotor activity as they age, experimental mice (those with type II-to-I transdifferentiation) had elevated locomotor activity, as reflected by increased velocity and distance traveled during brief (5-minute) periods in a bright cage. Experimental mice also had more exploratory behavior, as measured in the elevated plus maze or in 72-hour open field. Some experimental mice had better performance (lasted longer) on the rotarod than control mice. Mice had a small decrease in gains for the angular vestibulo-ocular reflex in the horizontal plane at 4 months but not at 8 months after the fate switch was initiated. However, mice with type II-to-I transdifferentiation exhibited no circling or head-bobbing behaviors, which often occur after substantial loss of either hair cells or hair cell function.

Because we found no evidence for off-target Sox2 deletion from vestibular pathway neurons, we surmise that the observed changes were due to type II-to-I hair cell transdifferentiation. In future studies, we hope to determine if changes in behavior reflect the gain of type I hair cells, the loss of type II hair cells, and/or destabilization of the vestibular periphery and how these changes affect central neurophysiology.

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Poster Abstract 4

Auditory and Otolithic but Not Semicircular Canal Function are Associated with Decreased Cognition in Adults.

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Background: Auditory loss is well-known to be associated with cognition in adults. Emerging research demonstrates that cognitive impairment is greater among people with vestibular dysfunction, but the specific vestibular deficits driving these associations are unclear. This study leveraged a large cohort with comprehensive physiologic testing to examine associations between cognition and vestibular function. We hypothesized that otolithic function would have more associations with cognition than semicircular canal function.

Methods: Records from the University of Washington Dizziness and Balance Center Data Repository were retrospectively reviewed for people undergoing comprehensive vestibular and auditory testing between 2018-2022. Cognition was measured using the Montreal Cognitive Assessment (MoCA). Pure tone audiometry and word recognition scores were obtained. Each vestibular test was scored on an ordinal scale from 0 (normal) to a maximum score of 1-4. Three composite scores were calculated as the sum of ordinal scores divided by the number of tests included in that composite score. Canal loss scores were calculated from video nystagmography (during head shake, positioning/al, and caloric testing); video head impulse test; rotational chair testing, and dynamic visual acuity. Otolithic loss scores were calculated from cervical and ocular vestibular evoked myogenic potentials and subjective visual vertical. A total vestibulopathy score was calculated from all tests completed. Maximum possible scores were 1.78 for canal loss, 1.80 for otolitic loss, and 1.76 for total vestibulopathy, with higher scores indicating greater vestibular impairment. Spearman correlations were used to examine associations between vestibular composite scores and cognition (MoCA sub-scores and total score).

Results: A total of 243 records were included, with 153 (63.0%) female participants. Mean age (standard deviation) was 55.6 (15.5) years, and total MoCA score was 25.5 (3.4). Mean air pure tone average was 19.33 (16.72) dB for the right and 21.61 (19.82) dB for the left. Word recognition means were 93.27% (16.68%) for the right and 92.56% (19.20%) for the left. Mean scores were 0.28 (0.18) for total vestibulopathy, 0.21 (0.21) for canal loss, and 0.23 (0.25) for otolithic loss. Pure tone audiometry was not associated with any cognitive function. Word recognition was associated with visuospatial/executive function in the right (r=0.59, p=0.022) and left (r=0.138, p=0.047) ears. Higher vestibulopathy scores were correlated with worse visuospatial/executive function (r=-0.17, p=0.007). Canal loss scores were not associated with MoCA total or subscores. Greater otolithic loss scores were associated with worse visuospatial/executive function (r=-0.21, p=0.001), attention/vigilance (r=-0.14, p=0.004), language/repetition (r=-0.14, p=0.028), and total MoCA scores (r=-0.18, p=0.006).

Conclusions: This study used composite scores to summarize vestibular function across various physiologic tests. Word recognition was associated with cognition. Otolithic involvement was associated with worse global cognition and worse function across multiple cognitive domains. Higher levels of vestibulopathy scores were correlated more specifically with visuospatial/executive function, consistent with prior research and potentially reflecting shared pathways in hippocampal and basal ganglia areas. These findings suggest the importance of screening cognition in people referred for dizziness and balance concerns. Associations between cognition and vestibular function also indicate potential shared neurologic pathways that could be targeted in novel therapeutic interventions.

Poster Abstract 5

Molecular characterization of type I and II vestibular hair cells in adult mice using RNAseq

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The five sensory organs in the mammalian vestibular system contain specialized mechanosensory hair cells (HCs) that respond to head motions and regulate activity of the vestibular nerve. Mammalian HCs are categorized as either type I or type II. Despite limited studies into each specific cell type function, it is likely that type I and II HCs have distinct roles because they differ in their morphology, physiology, and innervation. Although both HC types are distributed throughout each mature sensory epithelium, several studies have identified regional differences with respect to HC density, bundle morphology, afferent innervation, and other features. Currently, we understand very little about the genes controlling the mature phenotypes of type I and II HCs and their synapses with vestibular afferent neurons, and there are only a few reliable markers for each HC type.

In this study, we explore the transcriptomes of vestibular HCs in utricles of adult C57Bl6/J wild-type mice. We dissociated utricular epithelia and sequenced mRNA from single HCs and supporting cells using the 10X Genomics platform on two different sets of samples, using either single cell or single nucleus RNA sequencing (sc/sn RNAseq). Once sequenced, we used the R-studio/Seurat Library to analyze both datasets separately. After QC filtering, we found ~3,000 cells in each run had high-quality transcriptomes. We generated cell clusters for each run based on transcriptional similarities. After running a combined Seurat analysis, we verified HC and supporting cell clusters based on expression of known marker genes (e.g., *Pou4f3* for HCs and *Gjb2* for supporting cells). We further analyzed HC data to identify four sub-clusters (HC subtypes) based on expression of known HC marker genes. The four subtypes were: type ll (e.g. *Calb2*-positive), type l (e.g. *Spp1-positive),* striolar type l (e.g. *Ocm*-positive), and an unknown HC cluster.

To validate expression of *novel* genes, we identified genes with an average read count >2 that were highly enriched (>2X) in one subtype versus another. This yielded 70 genes across the four clusters. To select genes of interest, we used the gEAR (Gene Expression Analysis Resource) portal to reference other RNAseq datasets on HCs, and we used DAVID to perform GO analysis. We are now validating expression of several genes that were enriched in one cluster versus the others using hybridization chain reaction/fluorescent *in situ* hybridization or immunolabeling, in order to 1) determine if they are useful markers for adult murine vestibular HCs and 2) assess if comparable subtypes of vestibular HCs are present in other vestibular organs. We are assessing HC type-specific and zone-specific expression of the selected genes. This study is identifying and characterizing new subtypes of type I and II HCs in adult utricles and new markers for type I and II HCs in adult mice.

Poster Abstract 6

Bone Conducted Vibration for the Symptomatic Relief of Vertigo - Clinical Trial Phase 2 Results

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Vertigo—the false perception of motion or rotation—is often the result of damage and dysfunction of vestibular end organs. Despite the high incidence of vestibular vertigo in the adult population (~7.4%, Agrawal et al 2013), available treatments require pharmaceuticals, surgical intervention, and/or extensive physical therapy.

The OtoBand, a lightweight, battery powered, externally worn device developed by Otolith Labs, is a novel device that can rapidly reduce or relieve vestibular vertigo by sending a low frequency vibration to vestibular end organs through bone conduction.

We report results from an ongoing phase 2 double-blind counter-balanced sham-controlled study designed to quantify changes in vertigo severity associated with use of the OtoBand in participants during recurring episodes of vertigo. This study was carried out in a telehealth setting to accommodate COVID restrictions and to test the device in a real-world setting. Inclusion criteria included a Dizziness Handicap Inventory score > 35, chronic vertigo (condition for at least 90 days) with at least one episode of vertigo per week, and provided a self-reported diagnosis of their vestibular pathology (benign paroxysmal positional vertigo, Meniere's disease, vertiginous migraine, or vestibular neuritis/labyrinthitis).

In this study, the OtoBand device produced a single frequency between 50 and 65 Hz at a patient-controlled force level between 0.4 N_{RMS} to 0.8 N_{RMS}. A sham device operating at a different frequency and a different range of patient-controlled force levels was also supplied with an identical form factor to the OtoBand, with vibrations from both devices easily perceived by participants. Participants were provided with an OtoBand and a sham device in a random, counterbalanced order for two weeks each. Participants were instructed to wear their device whenever experiencing an episode of vertigo and to report on the severity of vertigo episode at several time points, and an overall rating of efficacy after each use.

With "responder" defined as a participant who rated the device as helping on at least half of uses, a significant main effect of OtoBand over sham device was found using a generalized linear mixed-effects logistic model (odds ratio = 3.13, 95%, CI = [1.75–5.61], $p < 0.001$). This indicates that the OtoBand was found to be significantly more helpful to participants during vertigo episodes than the sham.

A continuing pilot study with a larger sample size and medically confirmed medical diagnoses is currently underway, with a large-scale pivotal study planned for mid-2023.

Poster Abstract 7

A Simple Model for Mechanical Activation and Compound Action Potential Generation by the Utricle in Response to Sound and Vibration

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Air-conducted sound (ACS) and bone-conducted vibration (BCV) are routinely used to excite and test the otolith organs by evoking compensatory vestibular compound action potentials (vCAPs) and vestibular evoked myogenic potentials (VEMPs) tests. The onset of the phasic ACS and BCV stimuli results in short-latency compound action potentials in the otolith afferents with calyx-shaped synapses in type I hair cells, and high-frequency sinusoidal stimuli lead to the generation of the precisely timed phase-locked action potentials in these afferents. Despite previous studies on neural responses, the mechanism behind how sound and vibration result in short-latency action potentials is poorly understood. Our study aims to present and validate a relatively simple mathematical model for the mechanical displacement of sensory hair bundles and synchronized action potential generation in the utricle in response to auditory-frequency ACS and BCV.

Utricular mechanics was modeled by developing a 2-degree-of-freedom mechanical model to determine the vibration of the epithelium relative to the temporal bone and the vibration of the otoconial layer relative to the epithelium in response to ACS and BCV. The relative motion between epithelium and the otoconial layer was used to determine hair bundle shear and the mechano-transduction current. The calculated current drove a simple integrate-and-fire (IAF) model, predicting the mean action potential time of the population of sensitive neurons. A saturating nonlinearity was used to describe the number of units recruited, and a Gaussian distribution defined the population variance in timing. vCAPs were simulated by convolving the distribution of action potentials with an extracellular voltage kernel. We validated our model by comparing our predicted data to the experimentally measured vibration of the epithelium using laser doppler vibrometry and vCAP measurements for ACS and BCV. The validated model was then driven by experimentally measured stapes velocity in a human cadaver to predict the potential damage to the utricle during loud ACS blast waves.

Our results show the magnitude and latency of the short-latency vCAPs due to transient ACS and BCV scale with the hair bundle shear rate. The magnitude of vCAPs scales with linear acceleration for pulse BCV shorter than 0.8 ms and switches to responding to linear jerk for stimuli lasting longer than 0.9 ms. Immediately after blast exposure, hair bundle angular deflection reaches ± 1 radian, which is a deflection two orders of magnitude larger than physiological stimulation. Such deflection suggests severe damage to hair bundles due to acoustics blast waves.

Our model can be utilized to predict utricular hair bundle shear, short latency action potential generation in calyx-bearing afferents, and vCAPs in response to transient ACS and BCV. Our results have potential use in designing ACS and BCV and interpreting the subsequent evoked responses in clinical and research settings.

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Poster Abstract 8

Whole Organ Imaging of the Mammalian Vestibular System

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Aging is associated with an increased risk of falling, which is contributed to by diminished balance. However, the precise anatomical changes occurring within the vestibular system as it ages are debated 1,2. In this study, we used immunofluorescence, tissue clearing, and 2-photon microscopy to visualize the anatomical changes that occur as the vestibular system ages. The entire temporal bone was dissected and decalcified, instead of dissecting individual vestibular organs, to minimize tissue damage and distortions during dissection. We compared two clearing methods, an aqueous-based modified ScaleS method and a solvent-based ethyl cinnamate method (which have both been successful in clearing cochleae in previous studies)3,4, to find which works best for the vestibular organs. These methods allow imaging of the entire vestibular system sensory cells in their native orientations. Our goal is to quantify hair cells and synapses within the entire vestibular epithelia in mature (1-2 months) and aged (36-40 months) gerbils using automated analyses involving machine-learning algorithms. We provide some preliminary progress of imaging and analysis. Our study will aid in a deeper understanding of the anatomical changes in the mammalian vestibular system with age.

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Poster Abstract 9

Impaired stationarity perception is associated with increased VR sickness

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Stationarity perception refers to the ability to perceive the surrounding visual environment as world-fixed during self-motion. Perception of stationarity depends on mechanisms that evaluate the congruence between retinal/oculomotor signals and vestibular head movement signals. In a series of psychophysical experiments, we systematically varied the congruence between retinal/oculomotor and vestibular head movement signals to find the range of visual gains that is compatible with perception of a stationary environment. On each trial, human subjects wearing a head-mounted display executed a trained yaw head movement (~15 deg over 1 sec) and reported whether the visual gain was perceived to be too slow or fast. A psychometric fit to the data across trials yields the visual gain most compatible with stationarity (point of subjective equality, PSE) and the sensitivity to visual gain manipulation (just-noticeable difference, JND). Across conditions, we varied 1) the spatial frequency of the visual stimulus, 2) the retinal stimulus location (central versus peripheral), and 3) the scene-fixed versus head-fixed nature of the oculomotor signal. At the end of each condition, participants completed the Simulator Sickness Questionnaire (SSQ) to assess symptoms and severity of induced virtual reality (VR) sickness. Results demonstrate that stationarity perception is most precise (lowest JND) and accurate (PSE»1) with scene-fixed fixation, central retinal stimulus location, and low spatial frequency visual patterns. Other circumstances lead to a reduced gain perceived as stationary (PSE<1) and impaired sensitivity (increased JND). A linear mixed-effects (LME) model was fit to investigate how psychophysical performance (PSEs, JNDs) related to sickness. Results indicate a significant association between PSEs and

the Nausea subscore of the SSQ, as well as between the JNDs and the oculomotor and disorientation subscores of the SSQ. To our knowledge, these are the first results to demonstrate an association between these psychophysical measures and VR sickness.
Acknowledgements: Research was supported by NIGMS of NIH under grant number P20 GM103650 and by NSF under grant number IIS-1911041

Poster Abstract 10

Temporal Integration of Multisensory Stimuli in Migraine

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Multisensory cues generated by a single event arrive at the brain asynchronously due to variable delays in transmission, encoding, and processing. The brain must accommodate for these asynchronies in order to form a maximally useful impression of the surrounding world. The time offset over which multiple sensory inputs are interpreted as "synchronous" is known as the temporal binding window (TBW). Patients with migraine tend to have difficulty processing multisensory stimuli. For these reasons, we hypothesized that patients with migraine might have abnormal (widened) TBWs, leading to sensory confusion and potentially offering an explanation for their particular sensitivity to multimodal sensory stimuli.

We compared the TBWs of patients with migraine to normal controls using visual + vestibular stimuli (10 ms light flash and 1 Hz raised cosine yaw rotation about the earth vertical axis) and visual + auditory stimuli (10 ms light flash and 10 ms 1000 Hz tone burst). We also compared the vestibular sensitivity of our subjects to their TBW involving vestibular stimuli, a relationship that previously has proven robust among patients with vestibular hypofunction.

Data were collected from 9 people, among whom three met criteria for classic migraine. None of these patients met criteria for vestibular migraine or persistent postural-perceptual dizziness. We found a strong correlation between the TBWs involving visual + vestibular stimuli and visual + auditory stimuli ($r=0.98$, $pp<0.001$). Subjects with migraine had higher TBW than normal subjects (mean (SD); 287 ms (187) and 147 ms (132), respectively, for the visual + vestibular TBW). As opposed to previous work demonstrating that vestibular thresholds to roll+pitch motion were improved in migraine patients, we found that their thresholds to our yaw rotations were higher than average. Unlike in patients with more dramatic vestibular loss, we did not find convincing evidence that our patients' sensitivity to rotations was related to their TBW ($r=0.65$, $p=0.08$).

We conclude that the individual TBW "set points" are wider in patients with migraine than in those without, offering a possible explanation for their difficulty managing multisensory input and manifesting high levels of motion sickness. The TBW can be reduced with training, offering a possibly remedy for motion sickness and other migraine-related symptoms.
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Poster Abstract 11

Accelerating Visual Self-Motion is not Misperceived as Gravity when Judging Body Orientation on Earth or in Space

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When judging body orientation, the vestibular system provides us with information about the direction of gravity, while visual cues usually give cues about the relation between the body and the environment, both of which are integrated to provide a unified percept of upright and the direction of gravity. Physical acceleration can sometimes be confused with gravity (the somatogravic illusion). Can humans also reinterpret visual acceleration cues (vection) as gravity? If so, experiencing accelerating visually-induced self-motion (but not constant velocity self-motion) should impact subsequent estimates of body orientation – especially in the microgravity of space. To test this hypothesis, we immersed a cohort of 12 astronauts and a cohort of 20 control participants in a virtual hallway environment in which they experienced lateral self-motion, either at constant speed or at constant acceleration (0.8m/s/s) for 20s. They then set the orientation of the virtual floor to match where it was before the motion to indicate their orientation relative to that floor. The astronauts performed this task before, during and after their space flights, while the control participants were tested at similar intervals. Unexpectedly, we found that self-motion at a constant speed (but not at constant acceleration) had a small but significant impact on their perceived orientation when tested in space but not during any test sessions (by astronauts or controls) on Earth. We conclude that visually perceived self-acceleration is not misinterpreted as gravity – contrary to our hypothesis. Some of the potential mechanisms by which self-motion at constant speed might impact perceived body orientation will be discussed.

Poster Abstract 12

Characterizing the effect of noise exposure on sound evoked head movements in rats

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Previous studies by our lab showed noise exposure at 110 and 120 dB results in attenuation of the vestibular short latency-evoked potential (VsEP) in rats (Stewart 2021). Furthermore, there is a reduction in calretinin-stained terminals associated with striolar calyx-only afferents in the sacculus and utricle. These afferents are activated by sound and bone-conducted vibration (BCV) (Chen et al. 2021, Zhu et al. 2011, Vulovic and Curthoys 2011), and play a major role in vestibular-evoked myogenic potentials (VEMP) that are dependent on the vestibulocollic reflex (VCR) pathways (Colebatch and Halmagyi 1994, Murofushi et al 1995). We hypothesize that noise-induced damage to otolith irregular afferents that reduces VsEP responses should also reduce sound-induced head movements via VCR pathways in noise-exposed animals.

A head-mounted IMU and headphones attached via a surgically-implanted headpost were used to characterize the response. Headphones were aligned with the individual rat's ears. Animals were comfortably restrained with their heads able to move freely. A Cambridge Electronic Design (Cambridge, UK) system was used to collect IMU data and deliver the sound stimulus to the speakers. Stimuli were air-conducted clicks (duration 0.5 ms, 70 dB, 0.3-0.5 mm from ear canal).

Trials were defined as the 80ms interval after delivery of a click. We observed characteristic head-movement responses in the roll axis away from the side of the stimulus with a latency of 10-20ms. Downward head movements in the pitch axis also occurred regardless of stimulus side. Movement patterns and latencies were consistent across individual animals, and matched similar findings in guinea pigs obtained previously in our lab (unpublished data).

In the lateral eyed rat, the click-induced head roll is expected to cause a compensatory downward rotation of the ipsilateral eye concomitant with an upward rotation of the contralateral eye via the VOR pathways. This would be consistent with the ocular VEMP observed in frontal eyed humans (Kanter, Gurkov 2012), and matches BCV-induced oVEMP in guinea pigs (Vulovic and Curthoys, 2011).

These sound-induced head movements imply a behavioral role for sound sensitive saccular and utricular afferents in the VCR pathways. Future studies will investigate noise-induced changes in this behavior in parallel with changes in the VsEP.

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Poster Abstract 13

Galvanic Vestibular Stimulation as an Alternative Display Modality: Directional Sensitivity and Visual Dual Tasking

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Prior research has demonstrated that humans are capable of processing data from dual sensory pathways simultaneously (Wickens 1981), suggesting the usefulness of alternative sensory display modalities to prevent visual and auditory sensory overload. The vestibular system has potential as an alternative sensory display modality, as it can be perceivably stimulated through Galvanic Vestibular Stimulation (GVS). This has been initially demonstrated in our previous study (Smith et al., 2022). GVS applies low-level electrical currents to the mastoid processes, stimulating the vestibular system and providing varying vestibular sensations, depending upon the type of current applied. These signals can be in the form of sine-wave currents of varying amplitudes, polarity (direction), and frequencies. We therefore designed a research study exploring the effects that a visually distracting search task would have on users' ability to distinguish between GVS stimuli of varying frequencies and direction of unipolar currents. This IRB-Approved study evaluated 10 subjects in baseline GVS threshold conditions as well as GVS thresholds while completing a visual-search task. The baseline threshold was determined using a three-down-one-up staircase algorithm to determine the users' just noticeable difference in their ability to distinguish between different signals. For frequency thresholds, a signal A (bipolar sine wave at 50Hz, ±0.6mA amplitudes, 1 second in duration) was compared to a signal B (varying the frequency of signal A ±40Hz). The threshold of perceivable difference was defined as the difference in frequency required of signal B for subjects to just distinguish it as being higher or lower frequency than the 50 Hz of signal A. This same concept was then applied to a polarity thresholding task. Polarity thresholds involved delivering unipolar, 50Hz stimuli (starting at ±1mA) in either the left (+) or right (-) direction from the electrodes on the mastoids, and decreasing amplitude as subjects correctly identified the direction of current. These two thresholding tasks were then repeated, in a counterbalanced order, while subjects were distracted by performing a visual search task. By comparing subject performance between these two conditions, this study provides valuable insight into the impact of visual distractions on the efficacy of utilizing GVS as an alternative display modality.

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Poster Abstract 14

Cognitive biases in vestibular psychophysics: vestibular thresholds may be lower than you think

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There has been tremendous interest in the use of vestibular perceptual thresholds to both understand the physiology and pathophysiology of the vestibular system, and also as a potential clinical tool. For example, these thresholds vary with pathology and age, and are highly correlated with postural performance. Vestibular perceptual thresholds are typically assayed by having subjects repeatedly experience motions provided by a motorized platform, and then making perceptual judgements about the direction of motion. Small motions are used, meaning that subjects are often uncertain, and it is known that humans use past information to make decisions when uncertain.

Thus, we tested three hypotheses: 1) perceptual responses are affected by their preceding trial; 2) perceptual responses tend to be biased opposite of the *preceding response* because of cognitive biases, but are not biased by the *preceding stimulus*; 3) when fits do not account for these cognitive biases, thresholds are overestimated. We are not aware of reports studying these hypotheses for vestibular and direction-recognition tasks.

We studied normal subjects and found evidence supporting each hypothesis. First, subjects tended to make perceptual responses that were opposite of the preceding trial. Second, responses were dependent on the preceding response, not stimulus, suggesting a cognitive bias. Third, this cognitive bias caused thresholds to be overestimated. We developed an enhanced psychometric curve fit that accounts for these effects, and found that thresholds were lower that if a traditional psychometric curve fit is used ($p<0.005$, average 5.5% for yaw, 7.1% for interaural, maximum 28%).

Since the results indicate the magnitude of cognitive bias varies across subjects, this enhanced model can reduce measurement variability and potentially improve the efficiency of data collection.

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Poster Abstract 15

Head movement kinematics during gait tasks distinguish individuals with vestibular loss

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Background: Head kinematics are altered in individuals with vestibular schwannoma (VS) during short duration gait tasks (i.e., Functional Gait Assessment (FGA), both before and after surgery, yet whether these differences extend to longer duration gait tasks is unknown.

Objective: This study aimed to compare head kinematics in individuals with VS relative to controls during gait tasks of relatively short versus extended duration, and to identify correlations between traditional clinical and quantitative head kinematic measures.

Methods: 18 subjects participated; 9 VS subjects were assessed pre and 6 weeks postoperatively. Functional, physiological, and subjective clinical assessments were performed, including head kinematic measures of both the FGA as well as 30 second gait exercises. Correlations between clinical and head kinematic measures, among 17 gait tasks, were computed.

Results: Analysis of kinematic measures revealed that differences in range of motion and its internal variability primarily distinguish VS from control subjects, for both pre and postoperative time points. Variability measures were more informative among the FGA tasks performed over a relatively short duration, whereas range of motion measures were more informative for the gait tasks performed over an extended duration. Additionally, pre and postoperative head kinematics during FGA and gait exercises correlated with DVA and VHIT measures.

Conclusions: Vestibular schwannoma subjects experienced more changes in the variability and range of their head motion during short and extended-duration gait tasks, respectively, in contrast to healthy controls. Variability and range of motion kinematic measures provide information regarding the different strategies VS individuals deploy to maintain functional locomotion.

Keywords: Head kinematics, vestibular rehabilitation, gait stability, vestibular schwannoma, unilateral vestibular deafferentation.

Poster Abstract 16

Report of oscillopsia in ataxia patients correlates with activity, not vestibular ocular reflex gain.

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Background: Patients with cerebellar ataxia report oscillopsia, "bouncy vision" during activity, yet little is known how this impacts daily function. The purpose of this study was to quantify the magnitude of oscillopsia and investigate its relation to vestibulo-ocular reflex (VOR) function and daily activity in cerebellar ataxia.

Methods: 19 patients diagnosed with cerebellar ataxia and reports of oscillopsia with activity were examined using the video head impulse test (vHIT), Oscillopsia Functional Index (OFI), and clinical gait measures. Video head impulse data was compared against 40 healthy controls.

Results: OFI scores in ataxia patients were severe and inversely correlated with gait velocity ($r = -0.55$, $p < 0.05$), but did not correlate with VOR gains. The mean VOR gain in the ataxic patients was significantly reduced and more varied compared with healthy controls. All patients had abnormal VOR gains and eye/head movement patterns in at least one semicircular canal during VHIT with passive head rotation.

Conclusions: Patients with cerebellar ataxia and oscillopsia have impaired VOR gains, yet severity of oscillopsia and VOR gains are not correlated. Patients with cerebellar ataxia have abnormal oculomotor behavior during passive head rotation that is correlated with gait velocity, but not magnitude of oscillopsia.

Keywords: Oscillopsia, cerebellar ataxia, vestibular ocular reflex, gaze stability, gait.

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Poster Abstract 17

The loss of the α9/10 Nicotinic Acetylcholine Receptor Subunit Impairs Postural Stability in Mutant Mice

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The vestibular system plays a crucial role in ensuring gaze and postural stability in daily life. The signals transmitted from the vestibular sensory organs to the brain have been well characterized via neurophysiological recording experiments focused on single afferents within the VIII nerve. However, the VIII nerve also comprises efferent fibers that project from the brain back out to the vestibular sensory organs. To date our understanding of the role and function of these efferent vestibular projections remains limited in mammals. One proposal is that the mammalian efferent vestibular system plays a role in the long-term calibration of central vestibular pathways, for example during development (1).

To test this possibility, we studied vestibular function in mice lacking the functional α9 and α10 subunits of the nicotinic acetylcholine receptor (nAChR) gene family and compared their performance to control mice. Prior in-vitro studies have shown that these nAChR receptor subunits mediate efferent activation of the vestibular periphery and are also largely isolated to the inner ear (2). Vestibular function was assessed using i) standard tests of vestibular function, ii) quantification of the vestibular-ocular reflex, and iii) quantification of balance during challenging self-motions tasks. First, vestibular function was characterized using standard vestibular tests including contact righting and air righting, in which the mouse is rotated and allowed to right itself either on a surface or during falling. The ability of the mouse to correct its position is indicative of potential vestibular dysfunction. Second, the vestibular-ocular reflex was tested by placing head-fixed mice within a bodytube on a motion platform. The degree of gaze stability provided by the canal-driven angular VOR was measured via video recording eye movements during sinusoidal rotation (0.2-2 Hz, 16 deg/s), in both light and dark conditions. The visual surround was then similarly rotated separately to assess corresponding optokinetic responses. Finally, to quantify balance, we performed balance beam and swim testing. In the balance beam test, the mouse was placed at one end of a 6mm wide balance beam and traversed to a goal box at the other end, while head dynamics were recorded with a head-mounted inertial measurement unit (IMU). The swim test was similarly conducted, with IMU instrumented mice being lowered into a pool of water and allowed to swim for 1 minute to eliminate proprioceptive input. Overall, our initial results indicate that α9/10 knockout mice mainly display impaired postural stability rather than deficits in gaze stability.

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Poster Abstract 18

Assessing relationships between postural stability in quiet stance and vestibular perceptual thresholds

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Vestibular function has been linked to balance deficits. While traditional measures of vestibular reflexes do not well correlate to quiet stance balance, a growing body of evidence suggests that measures of vestibular perception are associated with quiet stance balance performance. However, past studies across the age-span have focused on categorical balance performance (i.e., ability to complete balance test conditions) or a small number of young, healthy participants. As such, this study quantified quiet stance balance performance alongside a broad battery of vestibular perceptual thresholds in 100 participants (18-89 years) in order to elucidate changes in vestibular function with age, which correlate to changes in quiet stance balance performance. Vestibular perceptual thresholds were determined in all participants with standard methods using a battery of tests designed to ascertain perception predominantly mediated by each vestibular end-organ in isolation in addition to a measure of central vestibular function (canal-otolith integration). Participants also completed a standard quiet narrow stance balance test (i.e., modified Romberg Test of Standing Balance) to assess postural stability. Center of pressure (CoP) measurements were collected from a triaxial force plate at a sampling rate of 100 Hz. The main quantitative metric of postural stability outcome metric was the mediolateral root mean square distance (ML RMSD) of the CoP as our previous research found that ML RMSD showed the strongest correlation with perceptual thresholds. Overall, our data once again showed that all vestibular thresholds increased with age; the largest age-related changes were seen for z-axis superior-inferior translations (z-translations) while the smallest age-related changes were seen for roll-tilt (i.e., earth-horizontal rotation about a naso-occipital axis) and yaw rotations. As well, ML RMSD also increased with age for all 8 balance test conditions. We further analyzed the relationships between vestibular perception and postural stability during eyes-closed standing on foam using regression analyses. Overall, a significant association was seen between the ML RMSD and both roll-tilt and z-translation thresholds in regression analyses that controlled for the effects of age, as well as other demographic variables. However, no other significant relationships were noted between vestibular thresholds and quiet stance balance performance. These findings add to the accumulating evidence suggesting that the vestibular encoding of canal-otolith integration and otolith function — assayed by 0.5 Hz roll tilt and 1 Hz Z-translation vestibular thresholds respectively — contribute to balance control, supporting the direct impact of vestibular dysfunction on imbalance and fall risk.

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Poster Abstract 19

Vestibular Adaptation Mitigates Vertigo and Nystagmus Associated with High Strength MRI

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Vestibular symptoms of vertigo, dizziness, imbalance and sometimes nausea are often reported by people in high-field strength magnets (>4 Tesla) used for MRI. Magnetic vestibular stimulation (MVS) explains these symptoms as arising from utricular currents interacting with the magnetic field to create a Lorentz force that deflects the semicircular canal cupulae to a constant position, simulating a constant-acceleration of the head which produces a constant-velocity slow-phase nystagmus response. Because of adaptation there is a decrease in the nystagmus response the longer the patient stays within the magnet, and a corresponding secondary response with an oppositely directed nystagmus after the subject exits the MRI bore. We sought a simple technique to mitigate these powerful, uncomfortable sensations as experienced during entry and exit from the MRI bore.

First, we used a 3D linear control systems model of the vestibulo-ocular reflex (VOR), which incorporated adaptation, central velocity storage, and rotational feedback elements. We simulated three entry and exit durations (20, 120, 300 seconds) into and out of the magnetic field of an MRI machine and found that the horizontal VOR nystagmus peak slow-phase response (SPV) was lower the longer the duration to enter or exit the magnet. Second, we experimentally recorded the nystagmus response from 4 healthy human subjects as they underwent the same protocol with a 7-Tesla magnet. After entry all subjects were kept in the magnet for 5-minutes. Objectively, we confirmed that the horizontal nystagmus peak SPV was less with longer durations, even though the nystagmus SPV just prior to exiting was not changed by the entry duration. Subjectively, longer durations also mitigated vestibular symptoms, and no vestibular symptoms were reported during the 300 second entrance and exit protocol.

We conclude that longer duration (>120 seconds) entry and exit of the MRI bore allows vestibular adaptation to mitigate objective and subjective symptoms of MVS, but not the eventual velocity of the constant nystagmus while within the magnet. A 120 second duration could be an effective and practical trade-off suitable for clinical application.

Poster Abstract 20

Calcitonin-Gene Related Peptide Levels in Vestibular Migraine, Biomarker Potential

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Calcitonin gene-related peptide (CGRP) is a neuropeptide that has been shown to be a key element of the trigeminovascular pathway of migraine, acting as a trigger for vasodilation and neurogenic inflammation. It has previously been shown to be elevated in tear fluid of ictal chronic and episodic migraine headache patients (Kamm et al 2019). CGRP shows potential as a biomarker for vestibular migraine.

Participants were grouped according to migraine headache status into migraine headache patients, vestibular migraine patients and controls. Tear fluid was collected from each eye. CGRP levels were quantified by ELISA (Phoenix Pharmaceuticals Inc.) following the manufacturer's instructions. The volume of each sample was measured before running the assay. The assays were performed using a 96well plate in duplicate, and the results were presented as nanograms per milliliter. The samples were normalized to the time required to collect the sample, this serves as a proxy for tear fluid flow rate.

Mean CGRP concentration in tear fluid was higher in migraine patients (headache and vestibular migraine) compared to controls (83 +/-75 vs 23ng/mL +/-9, p=0.058, ANOVA). Preliminary comparisons show that the tear CGRP concentrations in vestibular migraine patients are elevated relative to controls (91 +/-75 vs 23ng/mL +/-9, p=0.037, ANOVA). Although not significantly elevated, CGRP concentrations in migraine headache patients appear to show a similar trend when compared to controls (81 +/-78 vs 23ng/mL +/-9, p=0.082, ANOVA). No significant difference in tear CGRP concentration was found between migraine headache patients and vestibular migraine patients (81 +/-78 vs 91ng/mL +/-75, p=0.72, ANOVA).

We have identified an ELISA assay that can detect CGRP concentrations in tear fluid. Preliminary results suggest increased tear concentrations of CGRP in all migraine patients (headache and vestibular migraine) compared to controls, and in vestibular migraine patients compared to controls. Given our low number of samples, we believe these results are encouraging and merit further investigation of CGRP as a potential biomarker for vestibular migraines.

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Poster Abstract 21

Non-Quantal Transmission from Type I Hair Cell Can Drive Vestibular Nerve Afferent Responses and Maintain Normal Vestibulo-ocular Reflex

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The majority of vestibular nerve afferents receive inputs from both Type I hair cells (HC-I) and Type II hair cells (HC-II) in the vestibular end organ. In addition to the quantal vesicular glutamate transmission from both types of hair cells, HC-I provides a unique non-quantal transmission to calyx nerve terminals driven largely by potassium ions. We investigated whether the non-quantal component alone was sufficient to maintain a functional transmission of head movement related signals by the vestibular nerve. We used two strains of mice (male and female, P30-P60): (1) vesicular glutamate transporter-3 (Vglut3) KO mice were used as a model lacking quantal transmission in the inner ear, and (2) intratympanic (IT) injection of the AMPA receptor antagonist NBQX was used in wild type C57BL/6 (WT) mice to acutely suppress the quantal transmission. Function of the phasic afferents was evaluated by quantifying the vestibular sensory evoked potentials (VsEP) and the vestibulo-ocular reflex (VOR) was used as a behavioral measure. Surprisingly, we found that Vglut3 KO mice (that lack quantal release of glutamate, have no ABR response and are deaf) have a normal VOR response gain and phase. In WT mice, bilateral IT injections of NBQX abolished the first peak of the ABR (20 - 180 minutes post injection), suggesting adequate delivery and sustained activity of NBQX throughout testing. In contrast, the VsEP response remained robust during the same time period after IT injection of NBQX. Our findings show that the non-quantal transmission from HC-I is sufficient for driving the activity of at least the most phasic vestibular nerve afferent fibers and can produce a normal VOR response.

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Poster Abstract 22

Frequency dependence of human vestibulo-ocular reflex (VOR) thresholds

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While human perceptual thresholds have been widely investigated, the relationship between vestibulo-ocular reflex (VOR) and perceptual thresholds with humans in yaw rotation as a function of frequency remains unclear. We are aware of only one study (Haburcakova et al, 2012) that compared forced-choice human perceptual thresholds with monkey vestibulo-ocular reflex (VOR) thresholds in upright

- showing a clear divergence of the VOR and perceptual thresholds at frequencies below 0.5Hz. Our goals were to measure the frequency dependence of human VOR thresholds for yaw rotation both in upright and supine positions, compare these with same human perceptual thresholds, and investigate the impact of gravity on yaw rotation responses. First, perceptual thresholds were measured at 4 frequencies (0.2, 0.5, 1 and 2Hz) using a forced choice task with motion provided by a Moog 6DOF motion platform for 8 subjects. For subsequent eye movement recordings, the subjects wore a video-oculography EyeSeeCam Sci system (EyeSeeTech GmbH, Munich, Germany) that had a sampling rate of 500 Hz. To quantify VOR thresholds, we utilized the method of constant stimuli with the individual stimuli scaled to be 25%, 50%, 100%, 200%, 400% and 800% of each subject's perceptual threshold. The comparison between psychometric (perceptual) and oculometric (VOR) width parameter (i.e. threshold) was performed to detect the relationship as a function of frequency. We report that: (a) VOR thresholds when upright and supine were almost identical and were relatively constant at each of the 4 frequencies, (b) perceptual thresholds increased significantly at the lowest frequency of 0.2Hz when upright only (i.e., not when supine), (c) VOR thresholds at all 4 frequencies were slightly lower than perceptual thresholds for both upright and supine positions. We conclude that the integration of otolith and horizontal canal signals could contribute constant perceptual thresholds at lower frequencies when supine position, and that some neural noise accumulated after the VOR and perceptual pathways diverge could affect vestibular perception. This study provides further insight into how canal-otolith integration contributes to perceptual thresholds and differences between human VOR and perceptual thresholds.

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Poster Abstract 23

Model of vestibular implant stimulation in rhesus labyrinth estimates current spread to facial and cochlear nerves

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To understand the spread of current in a vestibular implant intended to restore the sense of balance following loss of inner ear hair cell function, we developed a detailed model of the geometry of the inner ear. Previous work in our lab modelled the spread of current from spherical electrodes to the divisions of the vestibular nerve innervating the five vestibular end organs (Hedjoudje et al., 2019), but current spread to the facial and cochlear nerves was not considered and it used outdated software. Here we present an updated model that includes activation of the facial nerve and all six branches of the vestibulocochlear nerve. The model was also optimized to work with more easily available software and implement parallel computing to speed up computational time.

To simulate the complex anatomy of the inner ear and adjacent structures, a normal rhesus macaque temporal bone was scanned using micro-MRI and reconstructed to generate model geometry with physiological tissue conductivities, including anisotropic nerve conductance (Hayden et al., 2011; Hedjoudje et al., 2019). Solidworks was used to refine the geometry and place spherical electrodes in the semicircular canals. COMSOL Multiphysics was used for meshing and finite element modelling (FEM) of electrical currents, assuming quasistatic conditions. Two stimulating electrodes near the ampulla in each model canal, using a reference in the common crus, were individually simulated. Custom MATLAB scripts using the COMSOL-MATLAB Livelink package were used to automate simulation of electrode pairs and extract FEM data. The extracellular potential field at model neuron nodes of Ranvier was calculated and convolved in time with a single biphasic cathodic pulse. These were input to stochastic, nonlinear dynamic spiking models with randomized parameters of 2,415 vestibular afferent axons, 1,000 cochlear afferent axons, and 500 facial afferent axons, each with randomized initial conditions to determine action potential initiation. The pulse amplitude threshold above which prosthetic stimulation elicited an action potential at the medial end of the model axon within 2 ms of pulse delivery was determined for each axon. Each axon was given a unique location on the neuroepithelium and trajectory through its nerve. We implemented parallel computing of the neuromorphic model in MATLAB to speed computational time on multiprocessor computers.

Relative axon recruitment was calculated for each nerve branch for a given electrode pair and stimulus pulse amplitude. Simulation of spike generation and propagation of 3,915 neurons for one electrode combination took ~11 minutes to compute on a 3.5-GHz 16-core 64-bit PC running Windows 10. This is significant improvement from our previous model, which took 400 minutes per electrode to simulate 2,415 axons. Extension of this model with different electrode designs and to human anatomy should facilitate development of electrode designs, surgical techniques, and stimulus paradigms for the use of vestibular implants in the treatment of human patients with severe vestibular hypofunction. The updates of the model to work with Solidworks and implement parallel computing should also make it more easily accessible for other researchers to use.

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Poster Abstract 24

Model of Motion Perception Following Sudden Transitions of Visual Cue Availability

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Existing models of motion perception do not capture motion perception during all common flight scenarios. For example, we are not aware of any existing model that aptly predicts the dynamics of motion perception following sudden transitions in the availability of visual cues (e.g. as an aircraft pilot experiences flying into or out of a cloud). It is important that we understand spatial orientation and motion perception in commonly occurring flight scenarios because spatial disorientation is associated with adverse failure modes (aircraft crashes). By developing computational models of orientation perception that are robust to sudden changes in visual cues, we can better understand the potential spatial disorientation that occurs around such transitions.

For the present study, we first collected empirical human subject data on motion perception during extended periods of Earth vertical yaw motion. The specific Earth vertical yaw rotations that our human subjects experienced were designed to elicit different perceptions of orientation with and without visual cues. Therefore, when a sudden change in the availability of visual cues occurred during a period of misperception of angular velocity in the no visual cues case, we were able to characterize the ensuing pattern of orientation perception. Data collection was performed on 28 unique subjects. The subjects were tasked with pressing a button every 90 degrees in order to record their perception of motion. Visual scenarios included two control conditions: no visual cues (i.e., in the dark) and visual cues (i.e., rotating dots providing angular vection) the entire time. The two test conditions were: suddenly losing visual cues and suddenly gaining visual cues.

We hypothesized that the existing pathway for sensory conflict associated with visual angular vection is effectively low pass filtered before being integrated with vestibular pathways. Therefore, we modified an existing model of orientation perception [1] and were able to have the modified form [with low pass filtering] match out results. While speculative, this low pass filter mechanism may be associated with the ambiguity in visual motion cues being caused by self-motion or scene-motion.

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Poster Abstract 25

A Modified Two-Dimensional Sensory Organization Test that Assesses both Anteroposterior and Mediolateral Postural Control

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The Sensory Organization Test (SOT) was designed to measure changes in postural control in response to unreliable visual and/or kinesthetic feedback [1]. However, secondary to the manipulation of sensory cues in only a single direction, the SOT is capably of only describing postural control in the sagittal plane. We aimed to characterize postural responses to a modified version of the SOT designed to simultaneously challenge both anteroposterior and mediolateral postural control. Twenty-one healthy adult volunteers (Mean age: 30.6±10.2) completed the standard anteroposterior one-dimensional (1D) SOT, in addition to a modified SOT with the support surface sway referenced to both anteroposterior and mediolateral postural sway (two-dimensional, 2D). Our primary analysis compared mediolateral, as well as anteroposterior postural sway (i.e., root mean square distance of the center of pressure) measured during the standard one-dimensional (i.e., pitch tilt) and the novel two-dimensional (i.e., roll and pitch tilt) sway referenced paradigms. We found that the 2D sway referenced conditions yielded a selective increase in mediolateral postural sway relative to the standard 1D conditions for both wide ($h^2 = 0.66$) and narrow ($h^2 = 0.78$) stance conditions, with anteroposterior postural sway being largely unaffected ($h^2 = 0.001$ to 0.103, respectively). In addition, the ratios between mediolateral postural sway in the sway referenced conditions and postural sway in the corresponding stable support surface conditions were greater for the 2D (2.99 to 6.26 times greater) compared to 1D trials (1.25 to 1.84 times greater), consistent with a greater degradation of viable proprioceptive cues in the 2D paradigm. Given these positive findings, future studies should investigate the clinical utility of this modified SOT as a means by which to better characterize sensory contributions to postural control in the presence of various sensorimotor pathologies, including vestibular hypofunction.

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Poster Abstract 26

Quantifying the influence of magnetic vestibular stimulation on spatial tasks

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Strong magnetic fields induce dizziness, vertigo, and nystagmus due to Lorentz forces acting on the cupula in the semi-circular canals [1]. Studies using passive motion, galvanic or caloric vestibular stimulation have shown that vestibular information can interfere with cognitive tasks with spatial components [3]. In this study, we were interested in the influence of magnetic vestibular stimulation (MVS) on spatial cognition.

30 participants solved a mental rotation task in a 7 Tesla MRI scanner with an egocentric and an allocentric strategy. The findings of previous studies suggest that only the egocentric strategy should be affected by altered vestibular information. The allocentric strategy served as a control condition. The strength of MVS was manipulated within participants by letting them solve the task inside the bore with two different head positions, resulting in a stronger and a weaker stimulation condition [3].

Response time analysis showed that overall participants responded slower under stronger stimulation than under weaker stimulation. This effect of magnetic vestibular stimulation on response times was only present in the egocentric mental rotation task but not when participants used the allocentric strategy. However, participants showed inter-individual differences, and the strength of the individual effect could not be linked to the individual stimulation strength quantified by nystagmus.

The findings of our study suggest that MVS could influence cognitive tasks with spatial components in MRI scanners. The effect of magnetic vestibular stimulation should therefore be considered in fMRI studies using spatial tasks, as it could be a possible confounder. In the future magnetic vestibular stimulation could serve as a tool to investigate the interrelation of vestibular information and spatial cognition.

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