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Characterizing high-velocity angular vestibulo-ocular reflex function in service members post-blast exposure

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Abstract

Blasts (explosions) are the most common mechanism of injury in modern warfare. Traumatic brain injury (TBI) and dizziness are common sequelae associated with blasts, and many service members (SMs) report symptoms worsen with activity. The purpose of this study was to measure angular vestibulo-ocular reflex gain (aVOR) of blast-exposed SMs with TBI during head impulse testing. We also assessed their symptoms during exertion. Twenty-four SMs recovering from TBI were prospectively assigned to one of two groups based on the presence or absence of dizziness. Wireless monocular scleral search coil and rate sensor were used to characterize active and passive yaw and pitch head and eye rotations. Visual analog scale (VAS) was used to monitor symptoms during fast walking/running. For active yaw head impulses, aVOR gains were significantly lower in the symptomatic group (0.79 ± 0.15) versus asymptomatic (0.87 ± 0.18), but not for passive head rotation. For pitch head rotation, the symptomatic group had both active (0.915 ± 0.24) and passive (0.878 ± 0.22) aVOR gains lower than the asymptomatic group (active 1.03 ± 0.27 , passive 0.97 ± 0.23). Some SMs had elevated aVOR gain. VAS scores for all symptoms were highest during exertion. Our data suggest symptomatic SMs with TBI as a result of blast have varied aVOR gain during high-velocity head impulses and provide compelling evidence of pathology affecting the vestibular system. Potential loci of injury in this population include the following: disruption of pathways relaying vestibular efference signals, differential destruction of type I vestibular hair cells, or selective damage to irregular afferent pathways—any of which may explain the common discrepancy between reports of vestibular-like symptoms and laboratory testing results. significantly reduced pitch aVOR in symptomatic SMs and peak symptom severity during exertional testing support earlier findings in the chronic blast-exposed active duty SMs.

Keywords

Blast; Traumatic brain injury; Angular vestibulo-ocular reflex; Scleral search coil

Introduction

Mild traumatic brain injury (mTBI) due to blast exposure has emerged in recent years as the “signature injury” of modern military conflicts in southwest Asia (Warden 2006). Service members (SMs) exposed to blast with resultant TBI commonly report a constellation of symptoms including headache, dizziness, and imbalance (Terrio et al. 2009), a presentation that may reflect pathology within the vestibular pathways (Hoffer et al. 2009, 2010). Despite the growing prevalence of TBI following blast exposure among deployed and returning SMs, there is a paucity of evidence characterizing TBI with its associated sensorimotor and vestibular sequelae (Scherer and Schubert 2009).

Intact vestibular function is essential for gaze stability during rapid head movements and contributes to automatic postural responses during external perturbations. The angular vestibulo-ocular reflex (aVOR) generates compensatory eye movements that are opposite in direction, but equal in magnitude to head movement. Patients with attenuated vestibular responses due to peripheral vestibular loss commonly complain of oscillopsia (blurred vision with head movement), vertigo (the illusion of movement), dysequilibrium (sensation of being off balance), and motion intolerance (Schubert and Minor 2004). These symptoms can severely limit a SMs ability to perform his or her military duties in or out of an operational environment (Scherer and Schubert 2009).

The true incidence of vestibular pathology in SMs exposed to blast is not yet known. Hoffer et al. recently reported a “clinically significant dizziness pattern” in an overwhelming majority (98%) of blast-exposed SMs with TBI within the first 72 h after injury. The authors noted those complaining of ‘vestibular’ symptoms decreased to 76% during the sub-acute injury phase (4–30 days post-injury; Hoffer et al. 2010). These findings are consistent with a model of peripheral vestibular recovery in which acute symptoms partially resolve following early static vestibular compensation (Strupp et al. 1998; Black et al. 1996; Abeln et al. 1981).

Hoffer et al. have also expanded the characterization of blast sequelae noting that a subset of SMs exhibits post-traumatic exercise-induced dizziness (PTEID). In PTEID, the patient complains of headaches and dizziness that begin *during* exercise as opposed to *afterward* (Hoffer et al. 2008). Gottshall has reported that SMs previously endorsing complaints of dizziness while running noted a resolution of symptoms after 12–16 weeks of vestibular physical therapy that included pitch plane gaze stabilization exercises. The study found that resolution of a patients' symptoms coincided with normalization of their pitch plane gaze stabilization test (GST) scores (Gottshall 2009; Gottshall and Hoffer 2010). These findings suggest that symptoms of dizziness associated with exertion following blast exposure may be related to abnormal compensatory eye movement responses during moderate (1.8 Hz)- to high (3.2 Hz)-frequency pitch head movements experienced during fast walking or jogging (Grossman et al. 1988).

Objective clinical and functional laboratory findings in blast-exposed SMs are highly variable with deficits reported in dynamic visual acuity, postural stability, and rotational chair outcomes (aVOR gain, phase, and symmetry; Hoffer et al. 2010). Given the multiple effects associated with blast injuries, such variability is not surprising. We have theorized that existing, comprehensive vestibular function tests may not be sufficiently sensitive to

identify pathology in this patient population, given the predominately low- to mid-frequency and velocity testing range of conventional ENG and rotational chair assessments (Scherer et al. 2007; Scherer and Schubert 2009). Given the frequency- and velocity-dependent nature of the vestibular system (Paige 1989), we hypothesize that many blast-exposed personnel may undergo variable degrees of peripheral vestibular recovery within the low- to mid-frequency functional range without corresponding recovery to high-frequency, velocity and acceleration stimuli.

Partial to complete resolution of aVOR gain deficits within weeks of onset of vestibular neuritis (VN) to *low-velocity* assessments is well established (Brandtberg and Magnusson 1990; Nadol 1995). Persistent deficits (years) have been documented when subjects are assessed with high-velocity head movement testing and oculomotor recording methods (Aw et al. 2001). Such findings may partially explain the significant degree of variability on objective testing measures reported in symptomatic blast-exposed personnel.

The scleral search coil has been widely used to quantify the “pathophysiological signature” of oculomotor disorders in the brainstem and cerebellum (Leigh and Zee 2006). It is considered the most reliable method of measuring high-velocity eye movements in human subjects (Leigh and Zee 2006; Roy and Tomlinson 2004; Eggert 2007). Examples include the search coil method successfully describing aVOR function, saccade dynamics, and dynamic visual acuity in healthy control and patients with unilateral and bilateral vestibular hypofunction (Schubert et al. 2008); characterizing aVOR function in subjects with cerebellar disease (Walker and Zee 1999); and identifying reduced aVOR latencies, increased aVOR gain (eye velocity/head velocity), and improved 3-D eye alignment during active head rotation compared with passive rotation in both healthy control and subjects with peripheral vestibular deficits (Della Santina et al. 2002).

To date, no study has investigated high-velocity active and passive aVOR function in patients with TBI or blast exposure. The use of the scleral search coil technique to assess aVOR responses to rapid active and passive head movement stimuli provides the ability to assess the vestibular system under frequency, velocity, and head rotation metrics that are more representative of activities of daily living (Grossman et al. 1988). The purpose of this study was to characterize high-velocity aVOR function in SMs with head injury following blast exposure. We hypothesized that the sub-group of patients endorsing symptoms of imbalance, dizziness, vertigo, oscillopsia, motion intolerance, and dysequilibrium would have significantly different aVOR function than subjects in an asymptomatic patient control group. We also hypothesized that there would be a negative correlation between a subject's report of vestibular-like symptoms during exertional treadmill testing and that individual's pitch aVOR gain.

Methods

Twenty-four patient subjects (mean 28.8 ± 9 years; range 20–57; 23 men) convalescing or undergoing rehabilitation at Walter Reed Army Medical Center (WRAMC) participated in the study. Informed consent was obtained as approved by the WRAMC Division of Clinical Investigation, Johns Hopkins School of Medicine IRB, and the University of Maryland IRB. Participation in this prospective, non-blinded, nonrandomized descriptive study was voluntary. Upon entry into the study, all subjects were assigned a unique alphanumeric code to ensure patient confidentiality and were assigned to one of two groups based upon patient presentation during the initial clinical history. Subjects endorsing symptoms of vertigo, oscillopsia, dysequilibrium, motion intolerance, dizziness, or imbalance (established via interview or questionnaire) were assigned to the “symptomatic” (i.e., “dizzy”) group. Subjects not reporting the above symptoms were assigned to the “asymptomatic” (i.e.,

“control”) group. All participants were active duty SMs diagnosed with a mild or moderate TBI due to blast exposure within 1 year of evaluation.

Inclusion criteria necessitated a definitive diagnosis of TBI within 1 year of injury. All TBI diagnoses were made by a credentialed Department of Defense (DOD) provider based on the mechanism of injury (i.e., blast); loss or alteration of consciousness and duration; presence and duration of post-traumatic amnesia. Each SM did have CT or MRI imaging studies to investigate damage (VA/DOD Clinical Practice Guidelines 2009). All study participants sustained no less than one blast exposure confirmed by review of medical records and a detailed clinical history. In addition to explicit blast-related trauma (e.g., perforated tympanic membranes, fractures, limb loss, burns), subjects commonly reported seeing a blast/blinding light; feeling the heat of a blast; or post-blast symptoms of tinnitus and sudden hearing loss. Cognitive ability sufficient to provide informed consent and follow simple commands was also a prerequisite to study participation.

Exclusion criteria included trauma to, or retained shrapnel in, the face, skull, cervical spine, or eyes as well as conditions that would preclude wireless search coil testing (i.e., corneal damage). Pre-morbid histories of vestibular or central nervous system pathology or visual deficits limiting one's ability to foveate a target during head movement were similarly exclusionary. Subjects with lower extremity weight bearing precautions due to orthopedic trauma were unable to participate in exertional treadmill testing though such injury was not deemed an exclusion criterion (search coil still possible).

Wireless scleral search coil technique

Head velocity data was collected with a rate sensor attached to a specially modified set of safety goggles referred to as the “head-mounted assembly”. Eye velocity data were collected using a monocular 2D *wireless* scleral search coil (WSC) system consisting of a wireless scleral search coil (Fig. 1), head-mounted assembly, receiver box, and laptop computer (Roberts et al. 2008). The wireless scleral search coil is an annular contact lens that contains a small coil of fine wire and a capacitor embedded in a biocompatible polymer. Like the conventional “wired” search coil, the lens is placed on the eye over the sclera near the corneal junction where it adheres by natural mild suction. While similar in many respects to a conventional wired scleral search coil system (Robinson 1963), the WSC system uses a resonant scleral coil with no connecting wire. Instead, a transmitter sends a stream of pulses to the eye coil, and a receiver then detects the resonant oscillations re-radiated from the eye coil. The relative intensity of the signal, as received by sets of orthogonal receiver coils, determines the orientation of the eye coil (Roberts et al. 2008). This approach retains the accuracy, precision, and high sampling rate of the traditional wired coil system, with added advantages of increased comfort to the subject and system portability. These features enabled the acquisition of eye movement data of laboratory quality in the clinical setting of WRAMC. Eye movements were sampled at 1,000 Hz.

Wireless search coil validation

The WSC technique was validated against the traditional wired magnetic search coil in two independent experiments (Fig. 2). Monocular recordings were obtained in subjects with no history of vestibular pathology. Both wired and wireless search coil experiments were conducted in each subject, separated by no more than 30 min. Methods in the validation study were identical to those approved for assessing patient subjects at WRAMC. These included a behavioral calibration sequence, then yaw and pitch active and passive head impulses. All active and passive head movements were supervised or performed by the same investigator to minimize inter-examiner variability associated with the head impulse technique. The same search coils (sterilized between subjects) were used for the respective

wired and wireless coils experiments and limited to the left eye only. Intraclass correlation coefficient (ICC) analyses were performed for each head movement condition to characterize reliability of the wireless search coil method in this unique patient population. We found a mean 11.5% difference between aVOR gain measurements recorded in the wired versus the wireless condition, for each subject. In wired scleral search coil experiments, ~10% variability of aVOR gain across separate testing sessions has been established (Schubert 2009), thus we determined this 11.5% variability (between wired and wireless measures) to be acceptable.

Repeatability for the wireless scleral search coil technique was measured for active and passive yaw plane impulses in blast-exposed patients with TBI. Successive head impulses in this population were measured for four distinct conditions to determine consistency of the response. Intraclass correlation coefficient (ICC) analysis for yaw plane impulses yielded reliability measures of $r = 0.57$ (active) and $r = 0.65$ (passive). ICC analyses for pitch plane impulses demonstrated reliability of the measure for both active ($r = 0.75$) and passive ($r = 0.51$) conditions.

Head impulses

Each subject was screened for available active, pain free range of motion, and vertebrobasilar insufficiency (Husni et al. 1966; Mitchell et al. 2004). Next, the examiner administered two to three drops of a topical ophthalmic anesthetic and inserted the wireless search coil. After verifying patient comfort and appropriate coil placement on the eye, the examiner fit the subject with the head-mounted assembly. We used adjustable bands to secure the assembly to the subject, tightened both above and below the subject's occiput to further stabilize the assembly and limit slip during head movement. Subjects were seated 1.5 m from a 2 cm red dot (target) and calibration grid in room lit conditions. A behavioral calibration using eye rotations ± 5 degrees to 30 degrees was performed.

Eye-head movement trials consisted of a series of head impulses including both subject generated (i.e., "active") and examiner administered (i.e., "passive") rotations. Four distinct head impulse rotation conditions were recorded: (1) passive yaw, (2) active yaw, (3) passive pitch, and (4) active pitch. Approximately 40 impulses of each type (20 in each direction) were generated per trial with peak amplitudes of $\sim 25^\circ$. When the eye-head movement testing was completed, the contact lens was removed. Each subject was screened for corneal abrasion using fluorescein staining and a Woods lamp. Subjects were monitored for 30 min after coil removal, to allow the topical eye anesthetic to wear off and to ensure subject comfort.

Eye movement analysis

aVOR gain (eye velocity/head velocity) was analyzed using custom software written in the MATLAB™ (Math-Works, Natick MA) and LabVIEW™ (National Instruments Inc., Austin TX) programming environments. aVOR gain was determined for peak eye and head velocities, calculated separately for each head impulse (Scherer et al. 2008). Slow component eye velocity measurement excluded any component of the response that may have been attributed to a non-vestibular eye rotation, such as a saccade. Non-vestibular eye rotations were identified based on the presence of (1) a biphasic velocity waveform; (2) an eye movement occurring in the same direction as the head (anti-compensatory) for yaw, upward, or downward directed pitch impulses; or (3) an identified step of position in the raw data trace. *Compensatory saccades* (CSs) were identified in the eye velocity trace as occurring in the opposite direction of the head rotation. CS during pitch head impulses were distinguished from blinks by examination of the vertical eye rotation trace. Those trials for which a slow component eye movement response could not be identified were excluded.

Exertional protocol

Following eye-head movement testing, the subject performed 10 min of self-selected fast walking or jogging (sufficient to induce pitch plane head movement) on an Alter-G™ anti-gravity treadmill (Fremont, CA). The Alter-G treadmill allows a subject's load-bearing body weight to be decreased while walking/running, thereby increasing a deconditioned subject's tolerance for functional activity while limiting risks associated with high-impact ground reaction forces. Unweighting was accomplished by fitting each subject with a neoprene skirt, then zipping them into a pneumatic chamber that enclosed the lower extremities and the treadmill. With an airtight seal, the "Alter-G" uses differential air pressure to unweight the subject. Based on our clinical experience in the patient population, we reduced weight bearing by 50% to standardize the treadmill task at a level that would allow maximum subject participation, despite the high-frequency of orthopedic, neurologic, and cardiorespiratory impairments.

Before, during, and 2 min after the exertional test, subjects were asked to record their sensation of vertigo, oscillopsia, motion intolerance, and dysequilibrium using a visual analog scale (VAS; Herdman et al. 2003). All VAS included word anchors describing the related symptoms at the bottom and top of a 10-cm line. Subjects marked their perception of symptoms with a pen on each of the four lines in each of the three phases of the test. Subjects were presented with a new sheet to mark during each phase to ensure independent reporting from the prior response.

Statistical analysis

Effect size calculations from prior scleral search coil experiments established that twelve subjects per group were required to obtain a statistical power of 0.80 for impulse testing (Schubert et al. 2006). Statistical analysis was performed using SAS 9.2 software (Cary, NC). Analysis of variance (ANOVA) was used to assess group differences between symptomatic and asymptomatic SMs for pitch and yaw plane aVOR responses to active and passive head movements. ANOVA was also used to analyze group differences across three levels of time (pre-, per-, and post-testing) for independently collected VAS reports of vertigo, oscillopsia, motion intolerance, and dysequilibrium. Post hoc Tukey–Kramer adjustment was used to control for multiple comparison of group means. A subject factor was included in the model to control for inter-subject variability over repeated measures. Spearman's correlation coefficient was used to determine associations between pitch plane aVOR gain (active and passive) and the individual's complaints of vertigo, oscillopsia, motion intolerance, and dysequilibrium during the exertional protocol. Only pitch plane head movements were considered in this analysis given the primary displacement of head rotation in a vertical plane during running (Grossman et al. 1988). Spearman's correlation coefficient was used to control for non-normally distributed data. Alpha was set at 0.05.

Results

Demographics

The symptomatic group consisted of 12 subjects (all men) ranging in age from 20 to 57 years (mean 30 ± 10 years). The mean duration of symptoms was 121 days with an average of four blast exposures. Ten subjects in this group sustained mixed (blunt/blast trauma) as a result of improvised explosive device (IED) detonation with subsequent closed head trauma. Two symptomatic subjects relayed a history consistent with a single blast exposure (no blunt trauma). Nine subjects in the symptomatic group presented with co-morbid injuries in two or more body systems (e.g., orthopedic, gastrointestinal) in addition to their clinical diagnosis of TBI. Eleven subjects in the symptomatic group reported regular headaches of varying frequency and severity. Orthopedic trauma included lower extremity limb loss, complex

fractures limiting weight bearing, and spinal burst fractures. Those without multi-system involvement were diagnosed solely with TBI.

The asymptomatic group consisted of 12 subjects (11 men) ranging in age from 20 to 41 years (mean 28 ± 7 years). Their mean duration of symptoms was 141 days with an average of two exposures to blast. Like the symptomatic group, ten subjects recounted a history suggestive of mixed blast and blunt trauma, while the remaining two described a mechanism of injury consistent with an isolated, blast only event. Only three subjects in this group reported regular headaches.

Two subjects were consented into the study and not subsequently tested. These individuals (subjects 7 and 11) were symptomatic and blast-exposed, but unable to participate due to scheduling conflicts with their established plan of care. A third SM (subject 6, asymptomatic group) was neither blast-exposed nor diagnosed with TBI, and his data is not included in this report.

aVOR gain

aVOR gain data from active and passive trials in subjects #12 (asymptomatic) and #24 (symptomatic) were excluded from yaw plane impulses due to excessive noise/inability to identify consistent slow component eye velocity (SCEV) responses to successive head impulses. Similarly, aVOR gain for active and passive pitch plane impulses from subjects #12 (asymptomatic) and #13 (symptomatic) was excluded from analysis due to excessive noise/inability to identify consistent SCEV responses to successive head impulses.

The aVOR gain responses to active and passive head impulses are reported in Table 1. As indicated, only 22 data sets were analyzed for the yaw and pitch plane conditions, respectively. Mean head velocities ranged between $\sim 110^\circ\text{--}150^\circ/\text{s}$ for active pitch and yaw head movements and $82\text{--}113^\circ/\text{s}$ for passive pitch and yaw head movements. Consideration of “normal” versus “abnormal” aVOR gains for yaw plane head impulses was based on a normative value of 1.00 (± 0.15) for yaw and pitch plane impulses (Schubert et al. 2006).

Yaw plane impulses—We found a significant interaction effect between head movement and group factors for yaw plane impulses. These results revealed aVOR gain differences between the two groups during active head movements only ($F = 3.79$, 1 DF) ($P = 0.0005$). The symptomatic group had a mean active yaw aVOR gains (0.79 ± 0.15) lower than the asymptomatic group (0.87 ± 0.18 ; Fig. 3). As a group, passive yaw impulses were similar (symptomatic 0.78 ± 0.14 vs. asymptomatic 0.75 ± 0.18), Fig. 3. Six SMs ($n = 2$ symptomatic and $n = 4$ asymptomatic) were found to have aVOR gains above 1.0 for yaw head impulses (Table 1).

Pitch plane impulses—For pitch head rotation, both active and passive aVOR gains were significantly lower in the symptomatic group (active 0.92 ± 0.24 , passive 0.88 ± 0.22) relative to the asymptomatic group (active 1.03 ± 0.27 , passive 0.97 ± 0.23 ; $F = 9.18$, DF 1, $P = 0.004$). However, fourteen SMs ($n = 6$ symptomatic and $n = 8$ asymptomatic) were found to have aVOR gains above 1.0 for active pitch up head rotations, Table 1. In particular, one symptomatic SM with TBI had slow component (aVOR) gains as high as 1.58, Fig. 4.

Symptom report characterization with exertion

VAS data were collected in $n = 16$ subjects during exertional treadmill testing. Eight subjects were unable to participate in this portion of the study due to lower extremity weight bearing restrictions from fractures, joint pathology, or limb loss. Exertional testing included

VAS symptom severity reports for vertigo, oscillopsia, motion intolerance, and dysequilibrium from $n = 10$ symptomatic and $n = 6$ asymptomatic subjects. Two SMs (#10 and #13) reported a history consistent with exposure to isolated barotrauma (i.e., “blast only”); both were in the symptomatic group. All others reported histories consistent with exposure to combined blast and blunt head trauma. A way to distinguish between the relative symptoms severities of these two groups was to calculate the sum of each group’s mean severity scores for the four subscales. This number was reported as a raw number with a maximum value of 40 (10 points per sub-scale possible).

Pre-exertional testing of VAS symptoms at baseline revealed a mean combined symptom severity of score of 2.54 in the subjects reporting blast only exposure and 2.68 in the group reporting mixed trauma. This difference was not significant ($P = 0.16$). Per-exertional symptom severity for blast only subjects was calculated at 20.5, while subjects reporting mixed trauma etiology had a mean combined symptom severity of 6.86. Despite the large apparent disparity between these scores, the difference was not found to be statistically significant ($P = 0.13$).

Vertigo—Analysis of the mean group effect for reports of vertigo as measured by VAS showed symptomatic SMs (1.99/10 cm) were significantly higher ($P < 0.0001$) than the asymptomatic SMs (0.3 cm). Analysis of the time effect showed these SMs also had a significantly elevated ($P < 0.0001$) report of vertigo during (1.89 cm) and after (1.44 cm) exertion compared to baseline (0.11 cm).

Oscillopsia—Analysis of the mean group effect for reports of oscillopsia as measured by VAS showed symptomatic SMs (2.37/10 cm) were significantly higher ($P < 0.0001$) than the asymptomatic SMs (0.14 cm). Analysis across three levels of time revealed a significantly elevated ($P < 0.0001$) oscillopsia score during (1.98 cm) exertion and after (1.38 cm) exertion relative to baseline (0.41 cm).

Motion intolerance—Analysis of mean group effect for report of motion intolerance (via VAS) was significantly elevated ($P < 0.0001$) in symptomatic SMs (3.42/10 cm) relative to the asymptomatic SMs (0.25 cm). Analysis of the time effect showed a significantly elevated ($P < 0.0001$) VAS motion intolerance score during exertion (2.73 cm) and post-exertion (2.46 cm) relative to baseline (0.33 cm).

Dysequilibrium—Analysis of the mean group effect for report of dysequilibrium (VAS) was significantly greater ($P < 0.0001$) in the symptomatic SMs (1.11/10 cm) relative to the asymptomatic SMs (0.22 cm). Analysis of the time effect revealed significantly elevated ($P < 0.004$) VAS dysequilibrium score during exertion (0.97 cm) and post-exertion (0.79 cm) relative to baseline (mean 0.24 cm).

Pitch plane aVOR correlation with per-exertional symptom report

Of the $n = 16$ subjects who participated in the exertional treadmill testing protocol, correlations were performed with data from $n = 15$ subjects (Table 2). Pitch plane aVOR data from subject #13 were excluded due to noise. When we considered the *variant* aVOR gain (i.e., that aVOR gain with the greatest variance from 1.00 be it abnormally elevated or depressed), we found a significant negative correlation between passive pitch aVOR gain and dysequilibrium.

Discussion

Preliminary evidence in symptomatic SMs with TBI suggests that blast exposure can significantly impair aVOR function. Our data reveal a degree of variability in eye movement responses to rapid head impulses that may be distinctly characteristic of this population. This variability is likely related to multifaceted and complex injuries resulting from singular or concomitant blast effects from one or multiple blast exposures. While the body of literature describing sensorimotor sequelae associated with blast is growing, our data represents the first characterization of aVOR responses in individuals who have sustained both pure blast-induced (17%) and mixed (blast—blunt) head trauma. This injury profile has been characterized as “blast plus” (Hoffer et al. 2009).

aVOR responses to yaw plane impulses

We found yaw aVOR gain differences between groups only for *active* impulses and not during *passive* head impulses. One explanation for this finding may be that the asymptomatic subjects are able to more effectively generate active eye movements augmented by efference copy (EC) signals from cortical pre-motor areas during active head movements (Della Santina et al. 2002; Roy and Cullen 2004). Classically defined by Von Holst and Mittelstaedt, an EC is a copy of a motor command (i.e., motor efference) that relays the expected sensory results of one's own actions to central processing areas for the purpose of maintaining perceptual stability and accurately guiding behavior (Von Holst and Mittelstaedt 1950; Cullen 2004). This explanation for observed differences in the high-velocity active aVOR response could in part explain why symptomatic blast-exposed SMs have not been diagnosed with vestibular pathology in greater numbers, despite the overwhelming prevalence of ‘vestibular-like’ sequelae associated with this injury pattern (Terrio et al. 2009; Hoffer et al. 2010). It is conceivable that the underlying pathophysiology in blast-induced dizziness may be related to the shearing of cortical neuronal pathways, which carry EC signals to the brainstem vestibular nuclei (rostral MVN) where differential encoding of cervical proprioceptive signals, peripheral vestibular afference, vestibulo-cerebellar, and cortical inputs have been shown to occur (Roy and Cullen 2001). Cortical shearing could also affect neurons in the limbic system (Wiener et al. 2002) or in the ventral interparietal areas (Klam and Graf 2003), which have been shown to generate dramatically different neural responses during active versus passive head movements in primates (Cullen 2004).

Furman and Whitney have highlighted the challenges associated with vestibular rehabilitation in other patient populations with central dizziness to include: less favorable global outcomes, slower progression, and longer treatment times (Furman and Whitney 2000). The increasing likelihood that the central nervous system may be implicated in chronic blast-related dizziness may have significant implications for the natural course of recovery and/or compensation, which should be considered in managing the SMs duration of rehabilitation and return to duty.

aVOR responses to pitch plane impulses

Our data also revealed a significantly lower mean active and passive aVOR gain to pitch head impulses in the symptomatic group relative to the asymptomatic group. Previous studies suggest that aVOR gains should measure near 1.0 in normal subjects (Roy and Tomlinson 2004), less than 0.85 in persons with vestibular hypofunction (Schubert et al. 2006), and in excess of unity (~1.15) in subjects with cerebellar pathology (Walker and Zee 1999). Even though the mean aVOR gain value in the symptomatic group was above 0.85 (suggesting an adequately compensatory eye movement response in aggregate), sub-analysis of the groups revealed that 6/12 symptomatic subjects demonstrated mean aVOR gains

below 0.85 in contradistinction with only 1/12 subjects in the asymptomatic group. The mean group aVOR response in the symptomatic group was bolstered markedly by abnormally elevated gains in two of the twelve symptomatic subjects (#10 and #18), which also increased variability, characteristic of TBI.

The explanation for the elevated pitch plane gains in select subjects (e.g., #10, #14, #18, #19, and #21) is not readily apparent. In addition to the possibility of disinhibition of the aVOR in response to an insult of the flocculus or nodulus (Walker and Zee 1999), some of the elevated gain measurements seen in pitch plane impulses (e.g., #10) may be partially explained by an overall increase in the subject's compensatory eye movement velocity given frequent and early (i.e., reduced latency) occurrence of compensatory saccades during the pitch impulse trials (Fig. 4). Conversely, there were also several symptomatic subjects who generated insufficiently compensatory eye movement responses to pitch plane impulses (e.g., #1, #9, #17, #23), a pattern commonly associated with vestibular hypofunction. In aggregate, the degree of variability of aVOR gain responses in this population suggests that a symptomatic patient's perception of dizziness or other vestibular symptoms may manifest with either pathologically elevated or decremented aVOR responses.

Our findings of diminished aVOR gain responses to high-velocity head movements in many of the symptomatic SMs could also be a function of the selective disruption of type I hair cells or irregular afferent pathways in blast-exposed individuals. Single unit recordings in primates have identified afferent fibers that fire with both regular and irregular patterns characterized by coefficients of variation <0.075 and >0.15 , respectively (Goldberg and Fernandez 1976). Irregular afferents are believed to encode high-frequency, high-velocity, and high-acceleration head movements of the nature generated in this study (Goldberg et al. 1985; Huller et al. 2005). In contrast, regular afferents are thought to encode less dynamic, low-frequency movements of endolymph (such as would occur in caloric or sinusoidal rotary chair testing) (Park et al. 2005). Irregular afferents innervate either type I or a mixture of type I and type II hair cells. Regular afferents innervate primarily type II hair cells (Goldberg et al. 1985). Given this degree of specificity in the anatomical structure and physiologic function of the vestibular end organ, one might expect that selective loss of type I hair cells due to blast exposure could cause a degradation of high-velocity aVOR eye movement responses even in the presence of normal vestibular responses to low-moderate velocity and frequency testing measures. Park et al. have hypothesized a similar pathophysiological model to explain observed differences in the low-frequency sensitivity of the canals in patients with Ménière's disease (Park et al. 2005). The authors theorized that a differential loss of type II hair cells with corresponding degradation in regular afferent pathways could explain the presence of observed asymmetries seen in vestibular functioning at low frequencies (caloric irrigation) not seen during rapid head impulses. It is similarly conceivable that blast overpressure transmitted through the skull could differentially effect the crista ampularis and the type I hair cells located in the most responsive, central region of the cupula with the same types of tensile, and shear strains that occur in blunt head trauma (Kocsis and Tessler 2009). Cernak and colleagues have exposed rats and rabbits to primary blast via a "shock tube" to investigate effects on lung and brain histology, yet we are unaware of similar methods used as a platform to investigate function of the vestibular system (Cernak et al. 1996, 2001a, b). In this case, single unit recording of regular and irregular afferents would be useful to confirm or disprove differential effects of blast exposure on the aVOR pathways.

Compensatory saccades

Compensatory saccades were used by subjects in both groups in response to both yaw and pitch plane head movements—though in many cases, they were neither accurate (consistent overshoots) nor appropriate (not necessary to bring the eye to target). The presence of

compensatory saccades was unusual given the mean age of these subjects. Previous work in our laboratory has demonstrated that significant increases in CS frequency are not commonly noted in normal subjects before the 5th decade of life (Schubert et al. 2008). The prevalence of increased saccade recruitment across both groups may be a gaze stabilization strategy in this population.

Symptom responses to exertional treadmill testing

While the presence of significant group differences in VAS symptom severity during treadmill testing was not unexpected given the study design (i.e., prospective assignment of subjects to symptomatic or asymptomatic groups based on clinical presentation), the significant differences in symptom severity during each of the three levels of time assessed (i.e., pre-, per-, and post-exertion) support prior reports. Blast-exposed SMs have been reported to have earlier onset “vestibular-like” symptoms than do non-blast-exposed individuals (Hoffer et al. 2008, 2010). While subjects in our study were not segregated based on mechanism of injury (blast only vs. mixed blast-blunt), our findings suggest the blast-exposed SMs experience peak symptom severity during exertion rather than afterward.

The association of “vestibular-like” symptoms measured during fast walking or jogging on a treadmill was more strongly correlated with *passive* pitch plane aVOR gain. The moderately negative correlations suggest greater symptom severity in persons with weaker pitch plane aVOR gains—though only dysequilibrium was found to be significantly correlated. In contrast, aVOR gain during *active* head impulses trended to have a much lower correlation. Though we were not statistically powered to specifically address this difference, this preliminary finding may suggest a diminished capacity to recruit active compensatory eye movement strategies during exertional activities such as running or fast walking in the blast-exposed population with TBI. This finding also demonstrates the importance of assessing the aVOR in SMs with PTEID using *unpredictable* pitch head impulses as a measure of fitness to return to duty.

Conclusion

Our finding of depressed active aVOR gain in symptomatic SMs with TBI relative to a non-dizzy control group provides preliminary evidence implicating central processing of second-order vestibular afference and efference copy signals. This observation may explain the apparent discrepancy between high rates of dizziness reported by blast-exposed SMs and the relatively sparse evidence available to support a diagnosis of vestibulopathy. These findings may also suggest a differential destruction of type I hair cells or disruption of irregular afferent VOR pathways, explaining the common pattern of normal laboratory vestibular function testing in patients with mTBI. In addition, reduced pitch aVOR and significantly elevated symptom severity during exertional testing appear to be a unique symptom in blast-exposed SMs.

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References

- Abeln W, Bienhold H, Flohr H. Influence of cholinomimetics and cholinolytics on vestibular compensation. *Brain Res* 1981;222:458–462. [PubMed: 6116524]

- Aw S, Fetter M, Cremer P, Karlburg M, Halmagyi G. Individual semicircular canal function in superior and inferior vestibular neuritis. *Neurology* 2001;57:768–774. [PubMed: 11552001]
- Black FO, Wade SW, Nashner LM. What is the minimal vestibular function required for compensation? *Am J Otolaryngol* 1996;17:401–409. [PubMed: 8817017]
- Brandtberg K, Magnusson M. The dynamics of the vestibulo-ocular reflex in patients with vestibular neuritis. *Am J Otolaryngol* 1990;11:345–351. [PubMed: 2264587]
- Cernak I, Savic J, Malicevic Z, Zunic G, Radosevic P, Ivanovic I, Davidovic L. Involvement of the central nervous system in the general response to pulmonary blast injury. *J Trauma* 1996;40(3 Suppl):S100–S104. [PubMed: 8606388]
- Cernak I, Wang Z, Jiang J, Bian X, Savic J. Ultrastructural and functional characteristics of blast injury-induced neurotrauma. *J Trauma* 2001a;50(4):695–706. [PubMed: 11303167]
- Cernak I, Wang Z, Jiang J, Bian X, Savic J. Cognitive deficits following blast injury-induced neurotrauma: possible involvement of nitric oxide. *Brain Inj* 2001b;15(7):593–612. [PubMed: 11429089]
- Cullen KE. Sensory signals during active versus passive movement. *Curr Opin Neurobiol* 2004;14:698–706. [PubMed: 15582371]
- Della Santina CC, Cremer PD, Carey JP, Minor LB. Comparison of head thrust test with head autorotation test reveals that the vestibulo-ocular reflex is enhanced during voluntary head movements. *Arch Otolaryngol Head Neck Surg* 2002;128(9):1044–1054. [PubMed: 12220209]
- Eggert T. Eye movement recordings: methods. *Dev Ophthalmol* 2007;40:15–34. [PubMed: 17314477]
- Furman JM, Whitney SL. Central causes of dizziness. *Phys Ther* 2000;80:179–187. [PubMed: 10654064]
- Goldberg JM, Fernandez C. Physiology of peripheral neurons innervating otolith organs of the squirrel monkey I. Response to static tilts and to long-duration centrifugal force. *J Neurophysiol* 1976;39(5):970–984. [PubMed: 824412]
- Goldberg JM, Baird RA, Fernandez C. Morphological studies of the mammalian vestibular labyrinth. *Prog Clin Biol Res* 1985;176:231–245. [PubMed: 2987974]
- Gottshall, K. Vestibular-visual-cognitive interaction tests in patients with blast trauma. Abstract #180; Association for research in otolaryngology midwinter meeting; Baltimore, Md.. 14–19 Feb; 2009.
- Gottshall KR, Hoffer ME. Tracking recovery of vestibular function in individuals with blast-induced head trauma using vestibular-visual-cognitive interaction tests. *J Neurol Phys Ther* 2010;34(2):94–97. [PubMed: 20588095]
- Grossman GE, Leigh RJ, Abel LA, Lanska DJ, Thurston SE. Frequency and velocity of rotational head perturbations during locomotion. *Exp Brain Res* 1988;70:470–476. [PubMed: 3384048]
- Herdman S, Hall C, Schubert M, Das V, Tusa R. Recovery of dynamic visual acuity in unilateral vestibular hypofunction. *Arch Otolaryngol Head Neck Surg* 2003;129:819–824. [PubMed: 12925338]
- Hoffer, M.; Gottshall, K.; Balough, B.; Balaban, C. Vestibular difference between blast and blunt head trauma. 2008; Association for research in otolaryngology abstract number 964; Phoenix Az.. 14–18 Feb; 2008.
- Hoffer ME, Donaldson C, Gottshall KR, Balaban C, Balough B. Blunt and blast head trauma: different entities. *Int Tinnitus J* 2009;15(2):115–118. [PubMed: 20420334]
- Hoffer ME, Balaban C, Gottshall K, Balough B, Maddox M, Penta J. Blast exposure: vestibular consequences and associated characteristics. *Otol Neurotol* 2010;31:232–236. [PubMed: 20009782]
- Hullar TE, Della Santina CC, Hirvonen TP, Lasker DM, Carey JP, Minor LB. Responses of irregularly discharging chinchilla semicircular canal vestibular-nerve afferents during high-frequency head rotations. *J Neurophysiol* 2005;93(5):2777–2786. [PubMed: 15601735]
- Husni EA, Bell HS, Storer J. Mechanical occlusion of the vertebral artery. *JAMA* 1966;196(6):101–104. [PubMed: 4956119]
- Klam F, Graf W. Vestibular signals of posterior parietal cortex neurons during active and passive head movements in macaque monkeys. *Ann NY Acad Sci* 2003;1004:271–282. [PubMed: 14662466]
- Kocsis J, Tessler A. Pathology of blast-related brain injury. *JRRD* 2009;46(6):667–672.

- Leigh, J.; Zee, D. The neurology of eye movements, fourth edition. Oxford University Press; Oxford: 2006.
- Mitchell J, Keene D, Dyson C, Harvey L, Prueve C, Phillips R. Is cervical spine rotation is cervical spine rotation, as used in the standard vertebrobasilar insufficiency test, associated with a measurable change in intracranial vertebral artery blood flow? *Man Ther* 2004;9:220–227. [PubMed: 15522647]
- Nadol J. Vestibular neuritis. *Arch Otolaryngol Head Neck Surg* 1995;112:162–172.
- Paige GD. Nonlinearity and asymmetry in the human vestibulo-ocular reflex. *Acta Otolaryngol* 1989;108:1–8. [PubMed: 2788346]
- Park HJ, Migliaccio AA, Della Santina CC, Minor LB, Carey JP. Search-coil head-thrust and caloric tests in Meniere's disease. *Acta Otolaryngol* 2005;125:852–857. [PubMed: 16158532]
- Roberts, D.; Shelhamer, M.; Wong, M. A new “wireless” search-coil system; Proceedings of the eye tracking research & applications symposium; Savannah, Georgia. 26–28 March; 2008. p. 197–204.
- Robinson DA. A method of measuring eye movement using a scleral search coil in a magnetic field. *IEEE Trans Biomed Electron BME* 1963;10:137–145.
- Roy JE, Cullen KE. Selective processing of vestibular reafference during self-generated head motion. *J Neurosci* 2001;21:2131–2142. [PubMed: 11245697]
- Roy JE, Cullen KE. Signal processing in the vestibular system during active versus passive head movements. *J Neurophysiol* 2004;91:1919–1933. [PubMed: 15069088]
- Roy FD, Tomlinson RD. Characterization of the vestibulo-ocular reflex evoked by high-velocity movements. *Laryngoscope* 2004;114(7):1190–1193. [PubMed: 15235346]
- Scherer M, Schubert M. TBI and vestibular pathology as co-morbidity following blast exposure. *Phys Ther* 2009;89(9):980–992. [PubMed: 19628578]
- Scherer M, Burrows H, Pinto H, Somrack E. Characterizing self reported dizziness and otovestibular impairment among blast injured traumatic amputees, a pilot study. *Mil Med* 2007;172:731–738. [PubMed: 17691686]
- Scherer MR, Migliaccio A, Schubert MC. Effect of vestibular rehabilitation on passive dynamic visual acuity. *J Vestib Res* 2008;18(2–3):147–157. [PubMed: 19126985]
- Schubert, M. Variability in the aVOR to head impulse testing; Association for Research in Otolaryngology Midwinter Meeting; Baltimore, Md.. 14–19 Feb; 2009.
- Schubert MC, Minor LB. Vestibulo-ocular physiology underlying vestibular hypofunction. *Phys Ther* 2004;84:373–385. [PubMed: 15049730]
- Schubert M, Migliaccio A, Della Santina C. Dynamic visual acuity during passive head thrusts in canal planes. *J Assoc Res Otolaryngol* 2006;7(4):329–338. [PubMed: 16810569]
- Schubert M, Migliaccio A, Clendaniel R, Allak A, Carey J. Mechanism of dynamic visual acuity recovery with vestibular rehabilitation. *Arch Phys Med Rehabil* 2008;89:500–507. [PubMed: 18295629]
- Strupp M, Arbusow V, Maag KP, Gall C, Brandt T. Vestibular exercises improve central vestibulospinal compensation after vestibular neuritis. *Neurology* 1998;51(3):838–845. [PubMed: 9748036]
- Terrio H, Brenner L, Ivins B, et al. Traumatic brain injury screening: preliminary findings in a US army brigade combat team. *J Head Trauma Rehabil* 2009;24(1):14–23. [PubMed: 19158592]
- VA/DoD Clinical Practice Guideline for Management of Concussion/mTBI. 2009. Accessed at <http://www.dcoe.health.mil/ForHealthPros/TBIInformation.aspx> on 26 July 2010
- Von Holst E, Mittelstaedt H. Das reafferenzprinzip. *Naturwissenschaften* 1950;37:464–476.
- Walker MF, Zee DS. Directional abnormalities of vestibular and optokinetic responses in cerebellar disease. *Ann NY Acad Sci* 1999;871:205–220. [PubMed: 10372073]
- Warden D. Military TBI during the Iraq and Afghanistan wars. *J Head Trauma Rehabil* 2006;21:398–402. [PubMed: 16983225]
- Wiener SI, Berthoz A, Zugaro MB. Multisensory processing in the elaboration of place and head direction responses by limbic system neurons. *Brain Res Cogn Brain Res* 2002;14:75–90. [PubMed: 12063131]

Fig. 1.
Wireless search coil with capacitor located medially on the eye

Fig. 2.

Raw eye (*black*) and head (*gray*) velocity traces during active rightward yaw head impulses in the same subject wearing the wireless and then wired search coil. Compensatory eye velocities are inverted for ease of comparison. Difference in plotted aVOR gain between the wireless ($n = 16$, 0.99 ± 0.05) and wired ($n = 22$, 1.02 ± 0.03) experiments was 2%

Fig. 3.

Order of aVOR gains are active left, active right, passive left, and passive right.

Symptomatic Patients: Active yaw impulses are not presented for subject #24 due to excessive noise. Mean active yaw aVOR gain 0.79 ± 0.15 ; mean passive yaw aVOR gain 0.78 ± 0.14 . Asymptomatic Patients: Mean active yaw aVOR gain 0.87 ± 0.18 ; mean passive yaw aVOR gain 0.75 ± 0.18

Fig. 4.

Subject generates more compensatory saccades (CS) in response to active and passive upward impulses, compared with downward impulses. Note the high slow component eye velocities for the up rotations, which may reflect influence from the CS. *Bottom middle panel* illustrates active upward impulses and a still elevated aVOR after removal of any CS that occurred before the peak eye velocity

Table 1
aVOR gain and one standard deviation for active and passive head impulses in yaw and pitch

Subject	Yaw active left	Yaw active right	Yaw passive left	Yaw passive right	Pitch active up	Pitch active down	Pitch passive up	Pitch passive down
1 ^a	0.86 (0.03)	0.85 (0.10)	0.73 (0.06)	0.84 (0.05)	0.80 (0.09)	0.91 (0.08)	0.78 (0.08)	0.59 (0.20)
2 ^a	0.81 (0.05)	0.91 (0.05)	0.77 (0.04)	0.81 (0.11)	0.97 (0.07)	0.96 (0.21)	1.00 (0.08)	1.06 (0.27)
3	0.81 (0.06)	1.07 (0.09)	0.82 (0.04)	0.90 (0.09)	1.04 (0.08)	1.00 (0.17)	1.00 (0.10)	1.19 (0.13)
4	0.34 (0.05)	0.68 (0.11)	0.38 (0.10)	0.56 (0.04)	1.18 (0.30)	1.70 (0.18)	0.84 (0.07)	1.59 (0.26)
5	0.84 (0.04)	0.85 (0.02)	0.80 (0.02)	0.81 (0.02)	1.00 (0.12)	0.93 (0.11)	0.89 (0.08)	0.75 (0.12)
8	0.73 (0.06)	0.85 (0.14)	0.73 (0.25)	0.68 (0.07)	1.00 (0.07)	1.00 (0.25)	1.03 (0.16)	1.10 (0.36)
9 ^a	0.85 (0.07)	0.73 (0.07)	0.79 (0.02)	0.75 (0.06)	0.70 (0.04)	0.65 (0.09)	0.70 (0.14)	0.80 (0.14)
10 ^a	0.85 (0.17)	1.07 (0.30)	0.79 (0.19)	1.00 (0.20)	1.58 (0.46)	1.05 (0.23)	1.48 (0.50)	1.08 (0.08)
12	0.90 (0.61)	0.87 (0.31)	0.87 (0.01)	0.79 (0.10)	*	*	*	*
13 ^a	0.88 (0.05)	0.78 (0.05)	0.80 (0.08)	0.82 (0.12)	*	*	*	*
14	0.74 (0.07)	0.96 (0.05)	0.70 (0.06)	0.70 (0.06)	**	0.99 (0.79)	**	1.28 (0.64)
15 ^a	0.50 (0.16)	0.68 (0.05)	0.50 (0.07)	0.76 (0.13)	1.07 (0.09)	0.52	0.74 (0.18)	0.67 (0.30)
16	0.79 (0.04)	0.80 (0.04)	0.44 (0.12)	0.74 (0.21)	0.60 (0.13)	0.66 (0.05)	0.67 (0.23)	0.60 (0.03)
17 ^a	0.78 (0.11)	1.00 (0.16)	0.84 (0.21)	1.05 (0.37)	0.53 (0.27)	0.67 (0.34)	0.75 (0.33)	0.84 (0.36)
18 ^a	0.61 (0.04)	0.82 (0.03)	0.60 (0.06)	0.71 (0.04)	**	1.26 (0.16)	1.22 (0.08)	1.19 (0.40)
19	0.91 (0.14)	1.18 (0.28)	0.79 (0.19)	1.19 (0.21)	1.66 (0.78)	0.66 (0.36)	**	**
20	0.73 (0.20)	0.88 (0.07)	0.51 (0.12)	0.70 (0.21)	0.97 (0.17)	0.97 (0.17)	1.05 (0.12)	0.90 (0.26)
21	0.89 (0.04)	1.12 (0.15)	0.82 (0.14)	0.99 (0.06)	1.26 (0.17)	1.10 (0.49)	1.20 (0.17)	0.94 (0.37)
22 ^a	0.81 (0.18)	0.96 (0.16)	0.93 (0.23)	0.98 (0.17)	1.08 (0.44)	1.02 (0.17)	0.98 (0.26)	0.77 (0.21)
23 ^a	0.78 (0.07)	0.89 (0.06)	0.67 (0.07)	0.84 (0.08)	0.83 (0.07)	0.83 (0.11)	0.83 (0.05)	0.77 (0.08)
24 ^a	*	*	0.46 (0.23)	0.56 (0.16)	0.97 (0.32)	0.97 (0.57)	0.79 (0.23)	0.53 (0.23)
25	0.95 (0.17)	0.97 (0.16)	0.68 (0.07)	0.80 (0.11)	0.85 (0.10)	0.86 (0.10)	0.85 (0.04)	0.90 (0.03)
26	0.97 (0.04)	1.02 (0.05)	0.84 (0.10)	0.82 (0.10)	0.88 (0.12)	1.02 (0.11)	0.83 (0.16)	1.00 (0.17)
27 ^a	0.47 (0.12)	0.58 (0.05)	0.62 (0.07)	0.58 (0.16)	1.06 (0.04)	0.94 (0.16)	0.99 (0.05)	0.88 (0.26)

* Excess baseline noise

** Indeterminable slow eye velocity

S_p Symptomatic group

Table 2

Mean Spearman's correlation coefficient comparing visual analog scale (VAS) symptoms with pitch aVOR gain in $n = 15$ subjects that participated in the exertional treadmill protocol. Individual VAS and aVOR gains were first determined. Mean active and passive aVOR included both upward and downward head impulses. Variant active and variant passive aVOR included that aVOR gain value with the greater variance from normal (gain of 1.0, hypo or hyper). The variant aVOR gain presumed a more abnormal response would have a greater impact on the subject's symptom report

Symptom	Mean active aVOR	Variant active aVOR	Mean passive aVOR	Variant passive aVOR
Vertigo	$r = -0.17$	$r = -0.13$	$r = -0.33$	$r = -0.29$
Oscillopsia	$r = -0.22$	$r = -0.14$	$r = -0.33$	$r = -0.27$
Motion Intolerance	$r = -0.36$	$r = -0.34$	$r = -0.51$	$r = -0.49$
Dysequilibrium	$r = -0.25$	$r = -0.15$	$r = -0.42$	$r = -0.60^*$

*
 $p < 0.05$