A Proposed Mechanism for Visual Vertigo: Post-Concussion Patients Have Higher Gain From Visual Input Into Subcortical Gaze Stabilization

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Purpose. Post-concussion syndrome (PCS) is commonly associated with dizziness and visual motion sensitivity. This case–control study set out to explore altered motion processing in PCS by measuring gaze stabilization as a reflection of the capacity of the brain to integrate motion, and it aimed to uncover mechanisms of injury where invasive subcortical recordings are not feasible.

Methods. A total of 554 eye movements were analyzed in 10 PCS patients and nine healthy controls across 171 trials. Optokinetic and vestibulo-ocular reflexes were recorded using a head-mounted eye tracker while participants were exposed to visual, vestibular, and visuo-vestibular motion stimulations in the roll plane. Torsional and vergence eye movements were analyzed in terms of slow-phase velocities, gain, nystagmus frequency, and sensory-specific contributions toward gaze stabilization.

Results. Participants expressed eye-movement responses consistent with expected gaze stabilization; slow phases were fastest for visuo-vestibular trials and slowest for visual stimulations ($P < 0.001$) and increased with stimulus acceleration ($P < 0.001$). Concussed patients demonstrated increased gain from visual input to gaze stabilization ($P = 0.005$), faster slow phases ($P = 0.013$), earlier nystagmus beats ($P = 0.003$), and higher relative visual influence over the gaze-stabilizing response ($P = 0.001$), presenting robust effect sizes despite the limited population size.

Conclusions. The enhanced neural responsiveness to visual motion in PCS, combined with semi-intact visuo-vestibular integration, presented a subcortical hierarchy for altered gaze stabilization. Drawing on comparable animal trials, findings suggest that concussed patients may suffer from diffuse injuries to inhibiting pathways for optokinetic information, likely early in the visuo-vestibular hierarchy of sensorimotor integration. These findings offer context for common but elusive symptoms, presenting a neurological explanation for motion sensitivity and visual vertigo in PCS.

Keywords: concussion, gaze stabilization, visual motion, vestibular system, motion processing

Concussion constitutes a serious public health concern worldwide.[1] Classified as mild traumatic brain injuries (mTBIs), it amounts to 70% to 90% of all hospitalized brain injuries.[2] Beyond the immediate costs for health care, concussion has a profound effect on people's quality of life. It is estimated that 15% to 45% of concussed patients develop long-lasting sequalae in the form of post-concussion syndrome (PCS),[3] affecting millions of people around the world. Common symptoms involve fatigue, cognitive impairment, visual symptoms, and dizziness[4,5] brought on by injuries to the central nervous system.[6] Several studies have shown that this non-vestibular form of dizziness is predominantly triggered by visual motion,[7–12] with investigations showing that 80% of concussed individuals may experience visual motion hypersensitivity, often referred to as visual vertigo.[13] It has long been estimated that diffuse axonal injuries serve as a key mechanism of injury in PCS,[14] but due to the complex nature of these injuries the symptom-specific mechanisms are often difficult to isolate.[15]

Motion processing and postural control rely on a finely tuned neural integration of visual, vestibular, and proprioceptive information.[16] Concussion has been shown to alter the visual information pathways across the brain, ranging from the basal ganglia to several cortical areas.[17,18] It is also known that concussion can lead to maladaptive gaze control, influencing both voluntary gaze shifts[19] and optokinetic gaze stabilization,[9,20] indicating a mechanism of injury that can influence both fundamental subcortical motion integration as well as higher level sensory processing. It has been proposed that this increased responsiveness to visual cues leads to sensory reweighing, where visual motion gains in relevance compared to the mismatched vestibular input.[9] Recent years have shown an increased interest in ocular motor biomarkers for concussion.[19] Although it has

been shown that neural structures important for oculomotor control, such as the corpus callosum and superior colliculus, are susceptible to injuries following mTBI,[19] the significance of these mechanisms remains poorly understood.

We have recently been able to outline the basic neural pathways integrating visual and vestibular information toward gaze-stabilizing eye movements.[21] As visuo-vestibular misprocessing likely underlies symptoms of non-vestibular dizziness,[16,18,22] it appears likely that this pathway may be affected in PCS. Gaze stabilization is comprised of the optokinetic reflex (OKR), which serves to minimize retinal slip by moving the eyes in the same direction as the stimulus, and the vestibulo-ocular reflex (VOR), which compensates for a head movement by reflexively moving the eyes in the opposite direction.[23] These eye movements were embedded in our neural template at the dawn of vertebrate life[21] and represent clear indicators of our spatial and postural processing through their interconnectivity at a neuronal level.[24–28] Damage to their integration will lead to distinct changes in the gaze-stabilizing motor output, meaning that a systematic investigation of the OKR, the VOR, and their joint integration may allow us to deduce the mechanism of injury underlying visually induced dizziness in PCS. Having recently established a method for using gaze stabilization to evaluate sensory motion processing in humans[29,30] and correlating this response to activity in the subcortical neural network,[21] we aimed to implement and contextualize these findings in a clinical population.

The present study aimed to evaluate the gaze-stabilizing responses to passive visual, vestibular, and visuo-vestibular motion in PCS and healthy controls. The OKR and VOR were analyzed and discussed within the context of visuo-vestibular sensorimotor processing. Drawing comparisons to relevant findings from animal trials, we explored possible central mechanisms for visually induced dizziness in PCS, as well as the subcortical basis for visuo-vestibular sensory reweighing. Finally, we explored gaze-stabilizing eye movements as biomarkers for PCS and how they may guide rehabilitation efforts.

Methods

Participants

Patients ($n = 10$) were recruited from a local neurorehabilitation clinic, and the control group consisted of age-matched healthy adults ($n = 9$). (See Supplementary A1 for an overview of the participants.) Inclusion criteria for the PCS group required being clinically diagnosed mTBI at least 3 months prior, an absence of other neurological disorders or sensory system disorders, no recent medication changes, and describing post-concussive symptoms of discomfort to visual motion. The mean time since injury was 28.6 ± 29.1 months, and the duration of symptoms was 28.3 ± 29.2 months. All patients underwent prior clinical assessment and met PCS classification guidelines.[31] Written consent was obtained from all participants, and the study was conducted in accordance with the tenets of the Declaration of Helsinki (ethics review board approval: 2018/1768-31/1). The study adhered to STROBE guidelines.

Prior to inclusion, all participants underwent a comprehensive clinical testing battery conducted by a medical doctor and a neuropsychologist. Exclusion criteria included impaired ocular motor control or gaze function assessed through a clinical ocular motility examination, or any self-reported vestibular or somatosensory deficits. Participants were not allowed to have started any new medication affecting the central nervous system within the last 3 months, nor could they suffer from any diagnosed neurological or sensory condition beyond PCS. Eye examinations were performed to ensure normal eye motility and stereoscopic vision (TNO test ≤ 60 arcsec), and all subjects were able to fuse the visual image when exposed to the experimental setup. Intact peripheral vestibular function was assessed through head impulse tests in all three planes of the semicircular canals. Central vestibular ocular motor function was further evaluated by testing for the absence of skew deviation. Somatosensory contributions to balance were assessed through an enforced Romberg's test on a padded foam surface with eyes closed. One patient was excluded due to poor binocular vision, and one control was excluded due to the presence of latent nystagmus in darkness.

Symptom Assessment

All participants were required to complete two questionnaires: the Dizziness Handicap Inventory (DHI)[32,33] and the Visual Vertigo Analogue Scale (VVAS).[34,35] PCS was diagnosed according to the *International Classification of Diseases*, 10th Revision (ICD-10) criteria, relying on the patient's clinical history and subjective symptomatology.[36] Non-directive interviews were conducted to gather information about patient injury mechanisms. This assessment aimed to exclude confounding factors, including pre-existing neurological and psychiatric complaints, that could influence PCS symptoms or visual processing, as well as discrepancies in therapies. Subjects routinely expressed similar trajectories involving having suffered a subjectively minor concussion and developing symptoms over the following week that were aggravated after they went back to work, which generally happened within the first days or weeks. All participants had received a neurological assessment, reported considerable personal suffering due to PCS, and requested a leave of absence from work or school. All patients were actively undertaking visual rehabilitation therapy[37] that had started within the previous year, and they described no other concurrent treatment. The interviews also provided information on the patients' educational and professional backgrounds for matching purposes with the control group. Two patients were excluded, one due to pre-existing neurological symptoms of light sensitivity and the other due to a history of stroke.

Eye-Movement Tracking

Gaze-stabilizing eye movements were recorded using the Chronos Eye Tracking Device (C-ETD) from Chronos Vision GmbH (Berlin, Germany). Video eye tracking at 100 Hz was used to record each eye individually, ensuring high spatial resolution (<0.05° for vertical and horizontal, <0.1° for torsional eye movements). The C-ETD, worn on the head, also featured two accelerometers for six-dimensional head tracking (translation and rotation). This allowed calculation of ocular motor gain based on the participant's head position relative to their eye movements. The C-ETD was individually calibrated by having each participant perform a series of eye movements between fixed fixation points with a known angle of separation. Real-time eye-movement record-

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ings were monitored using the C-ETD software, and any instances of signal quality loss or non–gaze-stabilizing movements were identified by a researcher and resulted in the repetition of the specific trial.

Testing Procedure

Participants were exposed to a triad of visual, vestibular, and visuo-vestibular motion stimulations in the roll plane; the role plane was selected due to the corresponding gaze-stabilizing response lacking voluntarily influences that may confound the results, and it exhibits a more dynamic range of responses.[38–40] These simulations were carried out through optokinetic rotations on a projected screen, whole-body rotations in a mechanized sled in darkness, and whole-body rotations while viewing the optokinetic pattern. Participants were seated in the mechanized sled at all times during the protocols. These began with 20 seconds of baseline recordings at visual and vestibular rest following by the respective stimulation. These were carried out at a fixed amplitude of 28° at three different accelerations of 7°/s^2, 14°/s^2, and 28°/s^2, resulting in stimulation durations of 1.4 seconds, 2.0 seconds, and 2.8 seconds, respectively; acceleration was chosen as the independent variable to reflect natural motion patterns, and amplitude was fixed to ensure comparable retinal motion for all trials. After its motion, the stimulus was kept at the end angle for 20 seconds before the recording was terminated. The direction of stimulation was always in the counter-clockwise direction, resulting in the visually induced gaze response being in the opposite direction to those observed during visual and visuo-vestibular trials. This directional effect was negated in the analyses as data was collected as scalar values, and previous studies have shown no effect of directionality on ocular motor response patterns.[29]

Both visual and vestibular stimuli were carried out at comparable intensities and produced joint motor outputs of ocular torsion and vertical vergence. By comparing these gaze-stabilizing responses, it was possible to ascertain the neural integration of visual and vestibular motion processing both jointly and independently. This allowed us to investigate the impact of visual and vestibular motion on the physiological eye-movement response and how this may have been altered in concussed patients.

Optokinetic Stimulation. The optokinetic stimulation utilized in this study involved the presentation of a matrix of white dots displayed on a black background (Fig. 1A). All visual elements were presented on a projector screen (resolution, 1024 × 768; contrast, 2000:1; update frequency, 60 Hz). The dots moved uniformly at constant angular accelerations. Each dot had a visual angle of 1.15°, and the optokinetic stimulation covered a visual angle of 50.35° horizontally and 32.08° vertically. The room was kept dark with the only light source being the projected screen, which was maintained at fixed luminosity during all trials. Subjects were seated in the motorized sled for subsequent vestibular and visuo-vestibular trials, ascertaining a fixed eye-screen distance of 195 cm.

Vestibular Stimulation. A custom-built motorized sled was used to provide the vestibular signal through whole-body rotations. The sled operates on two distinct belts connected to separate AC Brushless Servo Motors (Baldor BSM90C, 400 V; ABB Motors and Mechanical, Fort Smith, AK, USA) (Fig. 1B). This setup enabled precise and controlled movements around an adjustable center of rotation. This center was set between subjects' eyes, on the glabella to account for interindividual variations in height. The room was kept in complete darkness for the duration of the vestibular stimulation. Participants were given instructions to maintain a straight-ahead gaze at an imagined reference point in front of them. Subjects were required to continue fixating on the imagined target directly ahead to achieve a stable position for accurate eye recording during the entirety of the trial. This was assessed in real time to ensure that the trial could be repeated should the gaze not remain centered and during the analysis phase to remove any confounding movements. The head of each subject was fastened to the chair using hook-and-loop straps to minimize unwanted head movements; all head movements were evaluated using the accelerometer data embedded in the C-ETD. Any confounding head movements were identified at the very termination of the trial, caused by the stop of the sled, and therefore had no impact on the eye-movement analyses.

Visuo-Vestibular Stimulation. The joint visuo-vestibular stimulation was carried out by rotating participants according to the same principles as outlined for vestibular trials while they were exposed to the static visual image outlined for the optokinetic trials (Fig. 1C). This allowed for an equivalent relative rotation of the visual field on the retina in the opposite direction of the head tilt during body rotation. The integration of visual and vestibular inputs provided a comprehensive examination of their interplay and their impact on sensory processing during the experiment.

Data Analysis

Gaze Evaluation. Ocular torsion and vertical vergence are joint motor outputs to visual and vestibular stimulations in the roll plane, the former being more sensitive to visual input than the latter.[41] Torsion, quantified through iris feature tracking, was used to measure the effects of both visual and vestibular rotations. The C-ETD software indexed the torsion signal quality between 0 and 1, with a higher value indicating a better match. All values below 0.5 were excluded from the analysis. To ensure accurate torsion measurements and minimize confounding factors, two tracking lines on each side of the pupil were selected for both eyes. The best quality eye was chosen, as indicated by having the highest number of frames with a signal quality above 0.5, and the torsional data were obtained by averaging the best quality lines on each side of the pupil. Vertical vergence was calculated by subtracting the position of the left pupil from the right pupil. The resulting signals for both torsion and vertical vergence were plotted and analyzed using OriginPro 2017 software (OriginLab, Northampton, MA, USA). Visual inspection was performed to identify nystagmus responses or confounding eye movements. Any slow phase coinciding with unexpected eye movements was excluded to ensure data integrity and maintained visual fixation during statistical analysis. All analyses were performed on the raw ocular motor data. Subjects were verbally instructed to keep their eyes open 1 second in advance of the active stimulation in order to avoid confounding blinks in the recording. Input data from the C-ETD were digitized together with the chair information prior to being imported into the computer, allowing the synchronization of each individual eye, head position, and position of the chair.

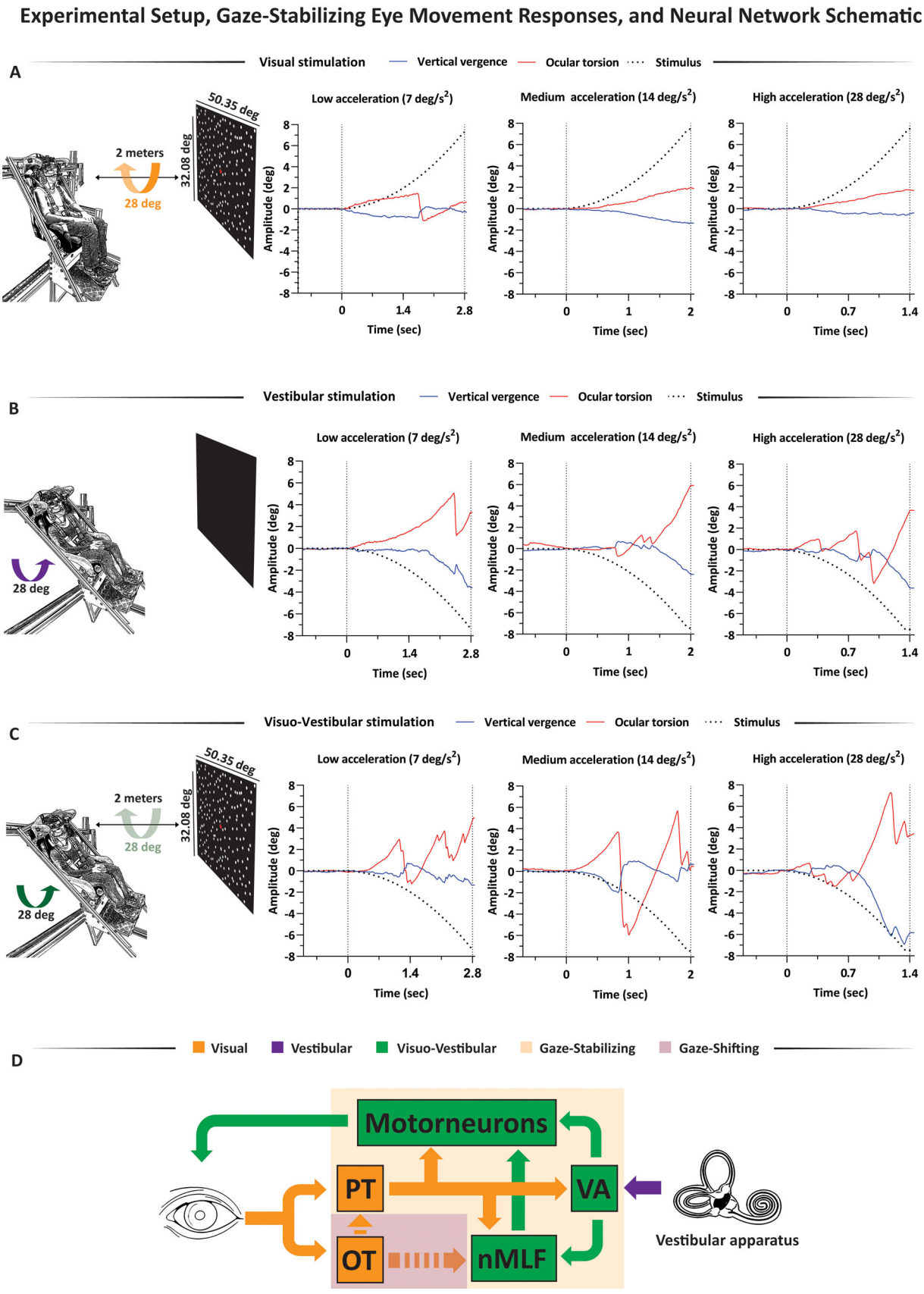

Figure 1. (**A**–**C**) Experimental setup and eye-movement responses to visual (**A**), vestibular (**B**), and visuo-vestibular (**C**) stimulations. The figure outlines the experimental setup (*left*), with the direction of visual (*orange*), vestibular (*purple*), and visuo-vestibular (*green*) stimulations carried out at three different accelerations at an amplitude of 28°; *opaque green* indicates chair movement and *translucent green* the relative optokinetic motion. The projector screen was presented at a visual angle of 50.35° horizontally and 32.08° vertically, with each *dot* being presented at an angle of 1.15°. Representative traces of gaze-stabilizing eye-movement responses are shown for each stimulation (*right*),

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conducted at low, medium, and high accelerations. For graphical reasons, optokinetic responses plotted in the visual stimulation have inverted polarity, whereas the stimulus amplitude has been divided by a factor of 4. Traces terminate at 2.8 seconds, 2 seconds, and 1.4 seconds for low, medium, and high accelerations, respectively. (**D**) A schematic of the basic subcortical neural network underlying gaze stabilization (adapted from Wibble et al.[21]). Key structures involved in gaze-stabilizing eye movements are shown in *yellow*, and those responsible for gaze shifts are shown in *red*. The flow of information is highlighted by *intact arrows* for gaze stabilization and *dashed arrows* for gaze shifts. nMLF, nucleus of the medial longitudinal fasciculus; OT, optic tectum (superior colliculus in mammals); PT, pretectum; VA, vestibular area.

Slow-phase velocities for both torsion and vertical vergence were obtained for all trials. Each such slow phase was manually traced to retrieve its velocity by dividing its amplitude in degrees with its duration in seconds. Additionally, time stamps of all nystagmus beats, as indicated by the start of each quick phase, were evaluated to examine their temporal distribution. The proportional influence of each sensory modality was determined for each trial and patient group using the slow-phase velocities. Eye-stimulus gain was calculated by comparing the acceleration of slow-phase velocities with the corresponding stimulus acceleration. Head position was also monitored to confirm that the head remained at rest during optokinetic stimulation and rotated as expected during whole-body rotations. To ensure data fidelity, the analysis included all slow-phase data points collected from all participants and trials.

Statistical Analysis. Statistical analysis was performed using SPSS Statistics 28 (IBM, Chicago, IL, USA). The eye-movement parameters analyzed included mean torsional and vergence slow-phase velocities, torsional gain relative to stimulation acceleration, and nystagmus beat frequency as mean values for each trial, as well as mean nystagmus beat time distribution adjusted for stimulation length. The Shapiro–Wilk test and P–P plots were used to assess normal distribution, and the Levene test was used to assess homoscedasticity for each grouping factor.

Mean torsional velocities, nystagmus frequency, and nystagmus mean time distribution met the requirements of normal distribution and homoscedasticity. A square root transformation was applied to achieve normality for mean vergence velocity and torsional gain variables. A two-way repeated measures analysis of variance (RMANOVA) with a full factorial design was conducted for each dependent variable using the grouping factor group (patient or control) as the between-subject factor and treating stimulation and acceleration levels as repeated factors. Post hoc pairwise comparisons with Bonferroni correction were performed to describe the results of simple and triple interaction effects in each RMANOVA model. For the nystagmus mean time distribution variable, a linear mixed model with a full factorial design was used, with group as the between-subject factor and stimulation and acceleration levels as repeated measures. Post hoc pairwise comparisons with Bonferroni correction were performed to investigate the results of simple and triple interaction effects.

To assess sensory-specific contributions to the visuo-vestibular gaze-stabilizing response, the mean slow-phase velocities during visual and vestibular trials were divided by those recorded during visuo-vestibular stimulations. This calculation provided an indexed value reflecting the contributions of visual and vestibular input. The validity of this calculation was confirmed by comparing visuo-vestibular slow-phase velocities with the sum of visual and vestibular slow-phase velocities. An RMANOVA was conducted for both torsion and vergence contributions, with accelerations and sensory modality as within-subject factors and group as a between-subject factor. Post hoc pairwise comparisons with Bonferroni correction were performed to investigate the results of simple and triple interaction effects.

Data Availability and Sharing

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Results

A total of 171 trials were performed, exposing all participants to visual, vestibular, and combined visuo-vestibular stimulations at three different accelerations. Eye-tracking analysis was performed on all resulting nystagmus slow phases ($n = 223$ for nine controls; $n = 331$ for 10 patients). Statistical analyses were performed on the mean values collected for each participant ($N = 19$), averaged for each trial.

Measuring Visual and Vestibular Motion Sensitivity Through Eye Tracking

Ascertaining the Physiological Response. The first ambition of this study was to determine that the experimental setup allowed for measuring subcortical motion integration (Fig. 1D). Statistical analysis was carried out on all participants to compare modalities and accelerations to investigate whether or not the outcome corresponded to previously outlined response patterns for subcortical gaze stabilization.

The gaze-stabilizing responses were significantly affected by both stimulation modality (visual, vestibular, or visuo-vestibular stimulation) and acceleration. This was observed across all participants, where the slowest slow-phase velocities were retrieved for visual trials and the highest velocities for visuo-vestibular trials at all accelerations (Fig. 2). Similarly, the slowest responses were observed during the lowest stimulus acceleration, whereas the highest acceleration produced the fastest slow phases for all modalities. This was however observed in a triple interaction effect and therefore carried lower statistical power (Supplementary A2). This effect was most evident in the torsional response but was also highly significant for vertical vergence.

This means that the responses behaved in the expected manner, reflecting basic neural functions where the VOR was increasingly favored over the OKR at increasing accelerations. Although it has been shown that vertical vergence is sensitive to accelerations of the visual field, this study also showed that the same holds true for ocular torsion.

Increased Optokinetic Sensitivity in PCS. Having established that the methodological framework corresponded with the expected responses, we were able to investigate how multisensory motion processing may be affected in concussed individuals. Representative traces comparing the gaze-stabilizing responses between a patient and a

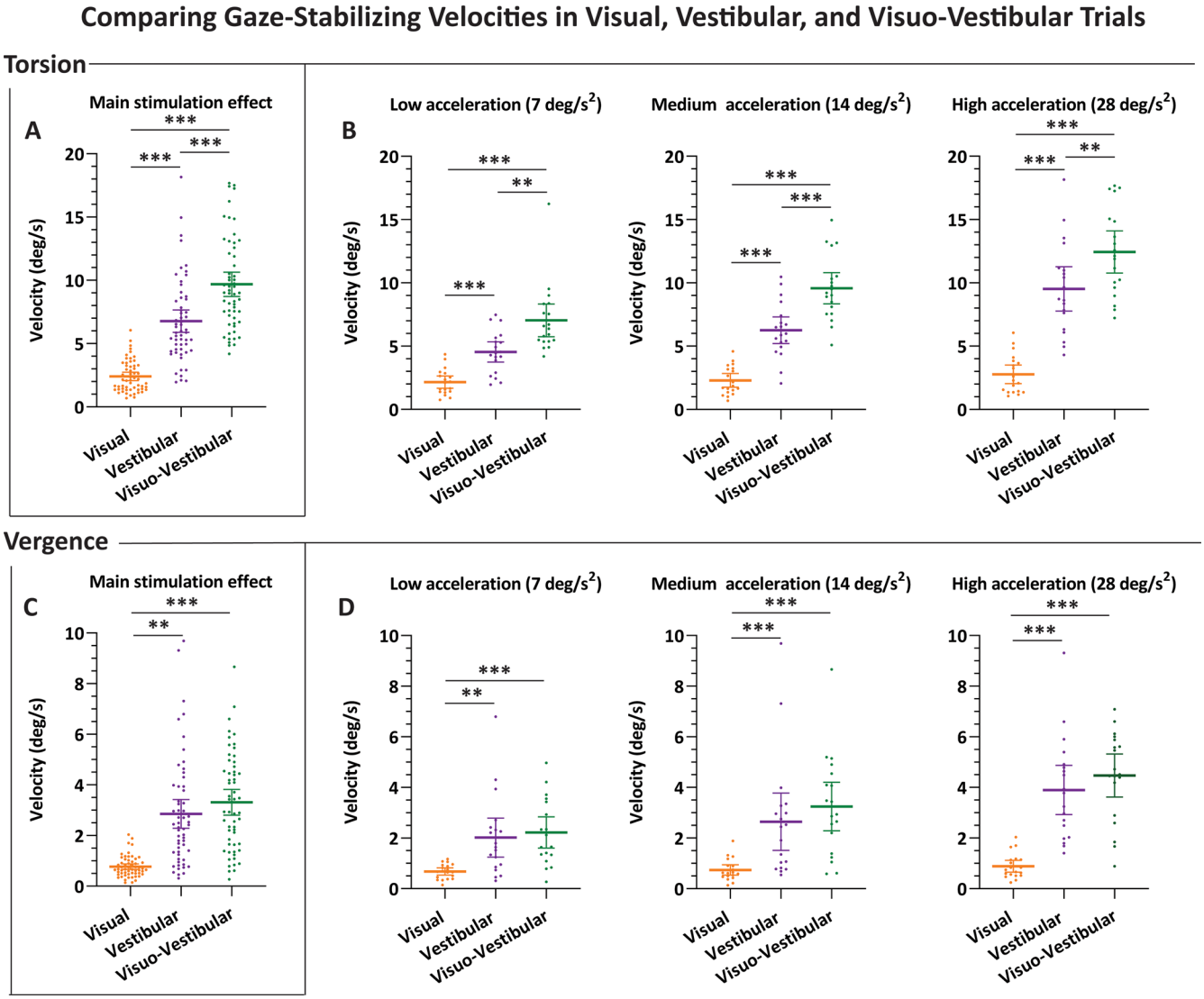

Figure 2. (**A–D**) Categorical scatterplots illustrating the main effect of sensory modality on mean torsional velocity ($F_{2,34} = 117.151$; $P < 0.001$; $\eta_p^2 = 0.873$) (**A**) and vergence velocity ($F_{2,34} = 52.060$; $P < 0.001$; $\eta_p^2 = 0.754$) (**C**). Significant interaction effects of sensory modality and acceleration intensity were observed for torsional velocity ($F_{4,14} = 28.625$; $P < 0.001$; $\eta_p^2 = 0.891$) (**B**) and vergence velocity ($F_{4,14} = 7.932$; $P = 0.001$; $\eta_p^2 = 0.694$) (**D**). Data are presented as absolute values (degrees per second), with means (*lines*) and 95% CIs (*error bars*). *$P < 0.05$, **$P < 0.01$, ***$P < 0.001$. These findings show that slow-phase velocities were lowest for visual stimulations and highest for visuo-vestibular simulations at all accelerations.

healthy control can be seen in Figures 3A, 3E, and 3I. Results show that patients expressed faster slow phases compared to healthy controls in an interaction effect with stimulation modality, indicating that this response was affected only in visual and visuo-vestibular trials (Figs. 3B, 3C, 3F, 3G, 3J, 3K). This means that controls and patients integrated vestibular motion in a comparable fashion, but concussed individuals' gaze stabilization was more sensitive to visual motion and was maintained when vestibular motion references were introduced.

Optokinetic Influences Over Eye-Movement Gain

As the gaze-stabilizing responses aim to secure an image on the retina they may be evaluated through their eye-stimulus gain. This signifies how much the eyes move in relation to the stimulus and consequently the sensitivity of the brain to the specific type of motion. By quantifying the acceleration between the slow phases from the start of each stimulation and its peak, we were able to quantify this gain. As ocular torsion has a more dynamic range of motion, this response was chosen for this analysis.

Ocular motor gains were significantly different among visual, vestibular, and visuo-vestibular trials ($F_{1.47,34} = 154.821$; $P < 0.001$; $\eta_p^2 = 0.901$). The highest gain was observed in visuo-vestibular stimulations (mean = 0.65; 95% confidence interval [CI], 0.59–0.70) followed by those observed during vestibular trials (mean = 0.39; 95% CI, 0.34–0.45; $P < 0.001$). The lowest gain was observed in visual stimulations (mean = 0.16; 95% CI, 0.12–0.21), which significantly differ compared to both vestibular ($P < 0.001$) and visuo-vestibular stimulations ($P < 0.001$).

This means that additional sensory information allowed a higher gaze-stabilizing gain, reducing the effects of reti-

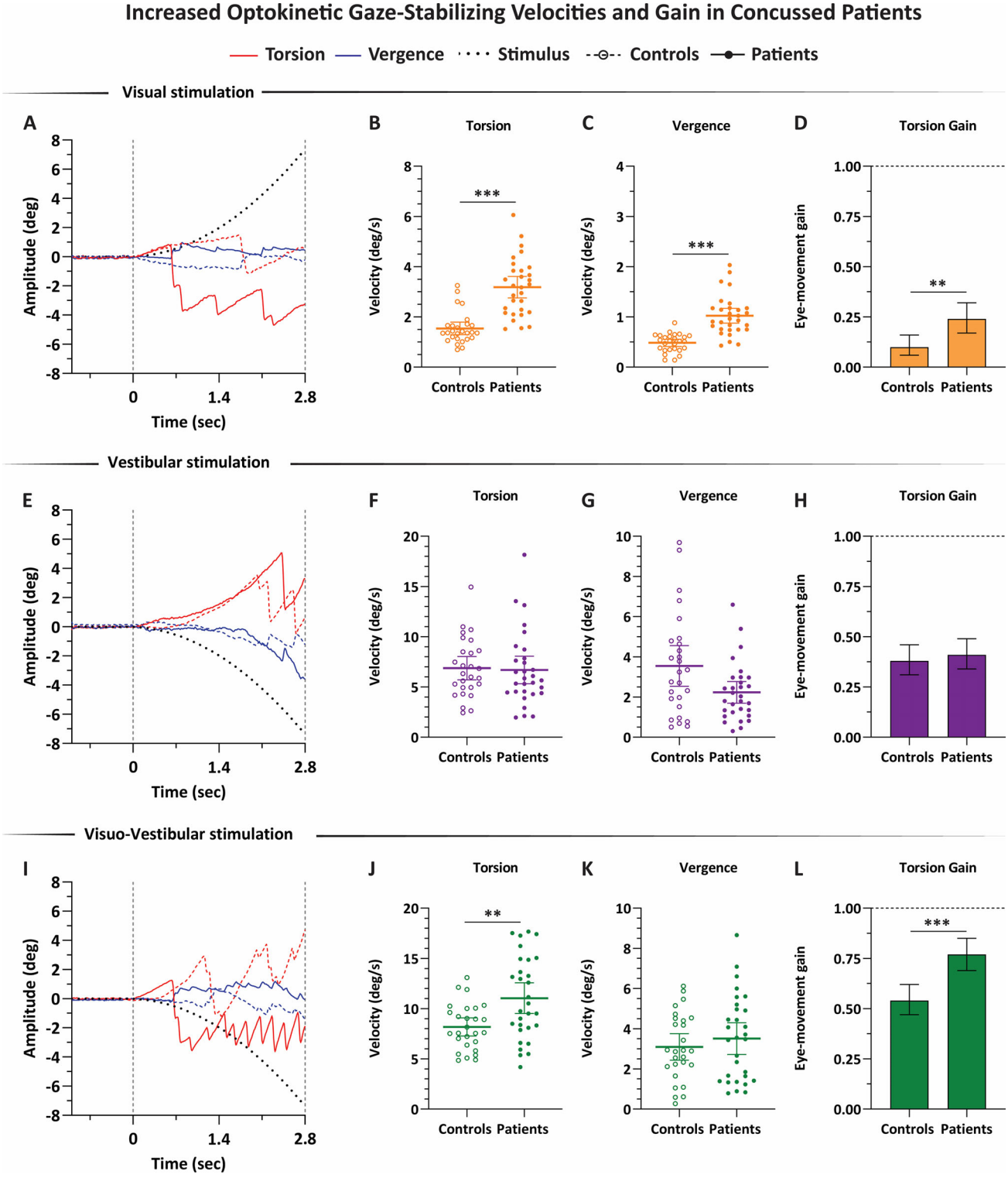

Figure 3. Representative traces comparing torsional (*red*) and vertical vergence (*blue*) responses between a healthy individual (*dashed lines*) and a patient with PCS (*intact line*) are presented during visual (**A**), vestibular (**E**), and visuo-vestibular (**I**) stimulations at 7°/s^2. For graphical reasons, optokinetic responses plotted in the visual stimulation have inverted polarity, whereas the stimulus amplitude has been divided by a factor of 4. Traces terminate at 2.8 seconds. Categorical scatterplots show the interaction effect between groups and sensory modalities on visual (**B**, **C**), vestibular (**F**, **G**), and visuo-vestibular (**J**, **K**) mean torsional velocity ($F_{2,16} = 5.811$; $P = 0.013$; $\eta_p^2 = 0.421$) (**B**, **F**, **J**) and vergence velocity ($F_{2,16} = 5.221$; $P = 0.018$; $\eta_p^2 = 0.395$,) (**C**, **G**, **K**). Data are presented as absolute values (degrees per second) with means (*lines*) and 95% CIs (*error bars*). The significant effect of sensory modality on torsion gain between groups is presented through histogram plots for visual (**D**), vestibular (**H**), and visuo-vestibular (**L**) trials ($F_{2,16} = 7.503$; $P = 0.005$; $\eta_p^2 = 0.484$). The gain was calculated as the ratio between the torsional acceleration (calculated as the velocity difference from the initial to the fastest slow phase over time) and the stimulation acceleration, where a gain of 1 indicates a perfect match. *$P < 0.05$, **$P < 0.01$, ***$P < 0.001$. These findings show that patients expressed faster slow-phase velocities and gain during visual and visuo-vestibular stimulations compared to controls.

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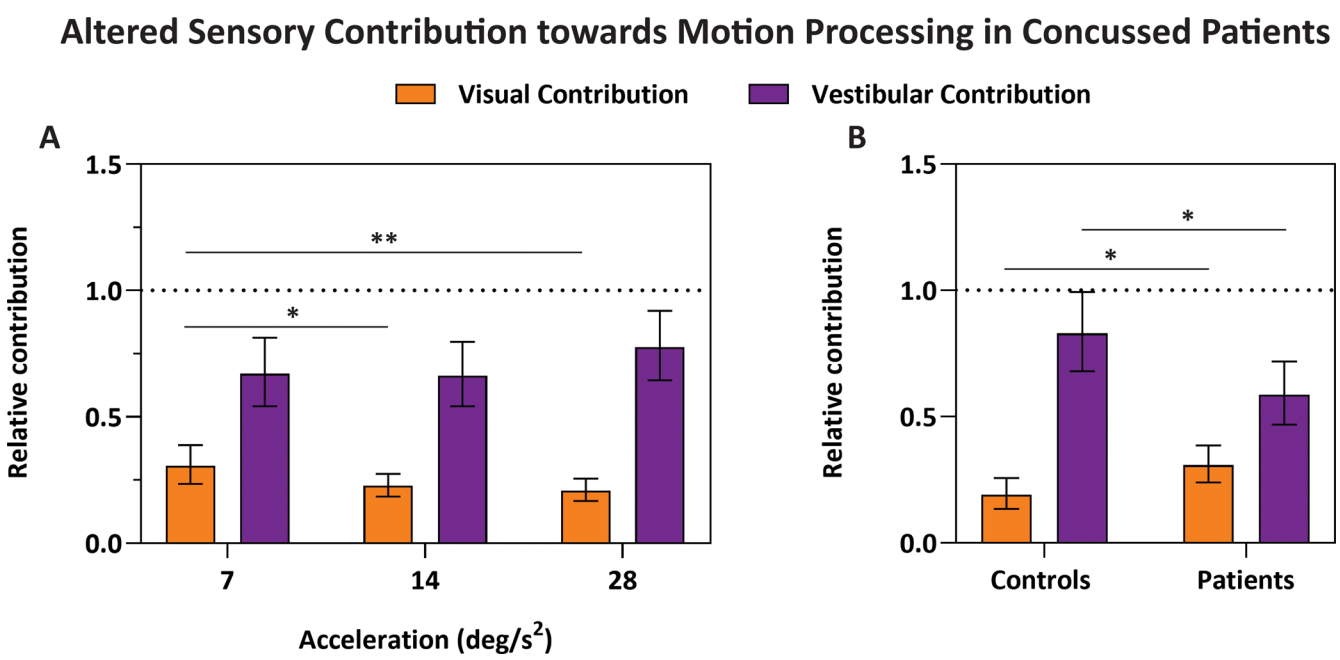

Figure 4. (**A**) Histogram plots of slow-phase velocities illustrating the effect of acceleration on the mean visual and vestibular contributions as a proportion of the visuo-vestibular response with 95% CIs as *error bars* ($F_{2,16} = 8.684$; $P = 0.003$; $\eta_p^2 = 0.521$). These findings show that the visual contribution decreased at higher accelerations for torsional gaze stabilization. (**B**) Histogram plots illustrating the interaction effect of groups and sensory modality contribution toward the integrated visuo-vestibular torsional response, presented as the relative contribution of visual and vestibular input toward the joint response ($F_{1,17} = 21.863$; $P < 0.001$; $\eta_p^2 = 0.563$). These findings show that the relative contribution toward gaze-stabilizing responses in patients was more dependent on visual motion and less reliant on vestibular input compared to controls.

nal slipping. Concussed patients expressed a significantly altered ability to adjust this gain for optokinetic input, as revealed in their increased gains during visual and visuo-vestibular trials (Figs. 3D, 3H, 3L). This means that concussed patients were more readily affected by increased visual motion, both in isolation as well as combined with vestibular self-motion during visuo-vestibular trials.

Measuring the Sensory Contributions in Visual and Vestibular Motion Integration

Robust Multisensory Integration Toward Gaze Stabilization. Given the robust summative nature of visual and vestibular torsional slow-phase velocities towards the visuo-vestibular response, we were able to calculate the percentual contribution of each sensory system to the combined response. Initially, we aimed to ascertain that visual and vestibular responses remained firmly integrated on both controls and patients by comparing the summed values for visual and vestibular slow-phase velocities to the isolated visuo-vestibular results. This revealed no significant difference, meaning that sensory input was integrated in a comparable and robustly summative manner between visual and vestibular motion ($F_{1,17} = 0.806$; $P = 0.382$). This remained true for each acceleration intensity ($F_{2,16} = 1.066$; $P = 0.368$), which is similar to what has been previously outlined according to both neuronal and clinical investigations.[21,29,30] Both torsional ($F_{1,17} = 148.105$; $P < 0.001$; $\eta_p 2 = 0.897$) and vergence ($F_{1,17} = 47.506$; $P < 0.001$; $\eta_p^2 = 0.736$) responses indicated that the vestibular influence was generally higher than the visual contribution across all participants and trials. This means that the relative contribution of the visual and vestibular systems disfavored the visual input with increased accelerations in all participants (Fig. 4A).

A Neural Basis for Visual Dependency in PCS. The statistical model made it evident that concussed patients expressed increased visual influences in their sensorimotor processing of motion as indicated by the torsional response (Fig. 4B). As the robust visuo-vestibular integration was retained, this means that the neural integration favored visual information in concussed patients. Altogether, this finding highlights the neuronal basis for the visual dependency and hypersensitivity frequently described in concussion.

Analysis of Nystagmus Frequency and Distribution Over Time

Nystagmus beats (i.e., quick phases) were recorded and their distributions plotted over time (Figs. 5A–5C). Twenty-six trials produced no such beats, leaving 145 trials to be included for a total of 191 nystagmus beats for controls and 270 for patients; note that the number of included beats was lower than the included slow phases due to blinks. There was no significant difference between modalities and groups in terms of nystagmus frequency, meaning that visual, vestibular, and visuo-vestibular input did not register as different motion intensities on this neuronal level.

There was, however, a clear temporal shift in how the optokinetic response was distributed between groups ($F_{1,33.56} = 6.334$; $P = 0.017$). Results show that nystagmus beats to visual trials were seen earlier in the patient group compared to controls (Fig. 5D). This difference became increasingly evident at higher accelerations. This means that

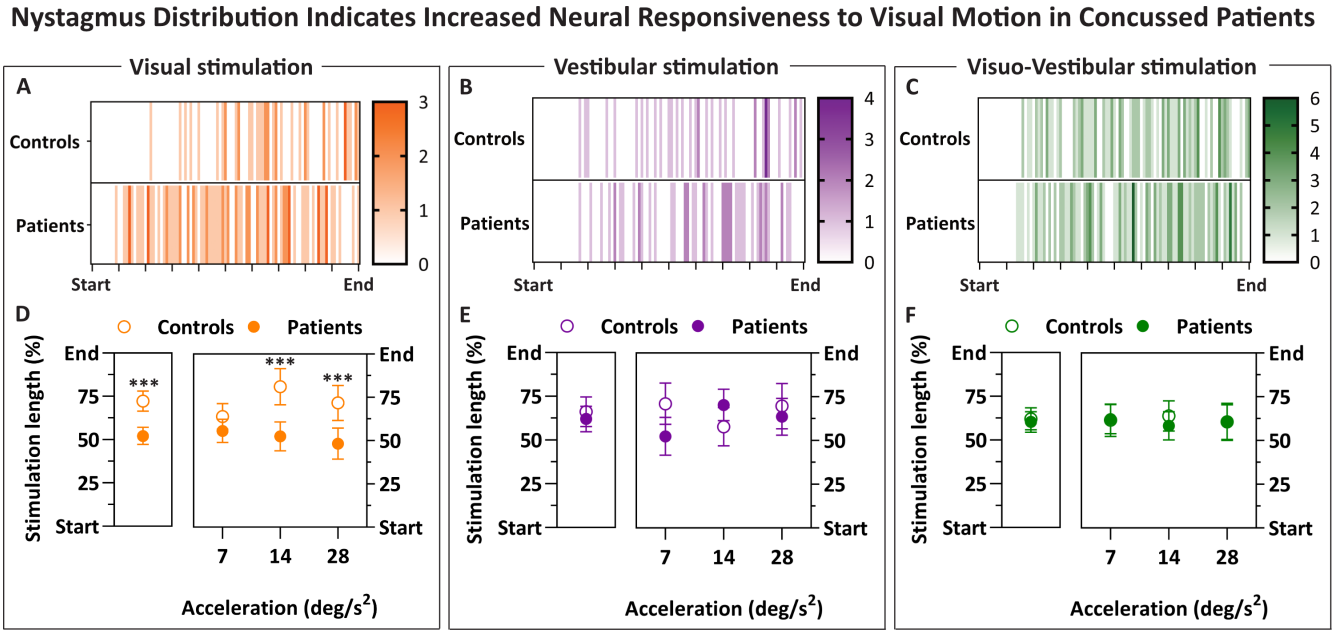

Figure 5. (**A–C**) Heatmap illustrating the onset of all nystagmus beats recorded for patients and controls from the start to the end of the stimulation length across all acceleration intensities during visual (**A**), vestibular (**B**), and visuo-vestibular (**C**) trials. To adjust for different durations across accelerations the temporal distribution is presented between normalized start and end times, where each tick represents an increase of 10% of the total trial duration. (**D–F**) Interval plots were created to depict the sensory effect ($F_{2,46.48} = 8.219$; $P < 0.001$) on the mean nystagmus time distribution for patients and controls for visual (**D**), vestibular (**E**), and visuo-vestibular (**F**) trials (main effects are presented in the *left rectangle* of the respective stimulation and the interaction effect in the *right rectangle*). Patients saw earlier onsets of nystagmus beats during visual trials in a significant interaction effect with acceleration and group (patient or control) compared to vestibular and visuo-vestibular stimulations ($F_{4,52.14} = 4.482$; $P = 0.003$). *Error bars* signify 95% CIs. *$P < 0.05$, **$P < 0.01$, ***$P < 0.001$. These findings show that patients expressed an expedited nystagmus beat distribution during visual stimulations compared to controls.

the process of integrating optokinetic information toward gaze stabilization was faster in patients but its scalar magnitudes were retained, as there was no difference in nystagmus beat frequencies between groups.

Discussion

The present study aimed to investigate the visuo-vestibular mechanisms of gaze stabilization in PCS. Results revealed consistent changes in concussed gaze stabilization, signifying enhanced optokinetic sensitivity as the OKR acted as the driving factor toward amplified gaze stabilization in the patient group, through both faster slow-phase velocities during visual and visuo-vestibular trials and an earlier distribution of optokinetic nystagmus. The distribution of these optokinetic responses, compared with the intact vestibular gaze-stabilizing responses, offers new insights into possible mechanisms underlying visual vertigo following traumatic brain injuries.

Altered Gaze Stabilization in Concussion

The integrative nature of visual and vestibular information toward the conjoint gaze-stabilizing response allows for quantifying the relative importance of each system. We have previously implemented this methodology to measure how sensory contributions are shifted based on visual content[29] and motion acceleration.[30] These studies showed that altered visual information density did not alter the visual contribution, but increased acceleration caused a shift in favor of vestibular contribution. It is known that sensory misprocessing may lead to a reweighing of sensory information.[9] For example, vestibular dysfunction may lead to individuals being more reliant on visual cues.[22,42,43] This study shows that concussion may lead to significant sensory reweighing and increase the relative influence of visual input over vestibular information. This altered ratio indicates how the brain integrates and prioritizes motion information in a numerical and objective fashion and may offer important clinical perspectives for serious but elusive complaints that remain difficult to diagnose.[44,45] Although the current setup requires dedicated equipment not widely available, this study exemplifies how the methodology can be used to objectively evaluate sensory weighing in a population.

This study found that concussed individuals expressed significantly increased torsional gain to visual and visuo-vestibular motion. When discussing the potential neural mechanisms underlying these findings, it may be helpful to consider the function and evolutionary benefits of the resulting motor outputs. The aim of gaze-stabilizing eye movements is to maintain a visual scene on the retina, either by mitigating retinal slip through the OKR or by preventing visual motion through the VOR.[46] A gain of one means that there is no relative motion on the retina, as it perfectly compensates for the motion of either the visual scene or the head. The dynamic torsional gain decreases with increased visual motion velocities and amplitudes, indicating a decreased optokinetic sensitivity in its neural integration.[47] It is consequently telling that the optokinetic gain was potently increased in the concussed group. This study

separated velocity and acceleration, with gain being quantified as the acceleration of the eye movement in relation to the acceleration of the stimulus. This allowed us to investigate ocular motor responsiveness over time in addition to the mean increase in slow-phase velocities. The increased gain found in this study suggests an increased sensorimotor responsiveness to optokinetic stimuli in concussed patients. This signifies that the optokinetic processing system in PCS exhibits increased responsiveness to visual motion. It is difficult to hypothesize if this enhanced activity may generate symptoms of motion hypersensitivity or if subjective symptoms and ocular motor findings are separate entities of a joint mechanism of injury.

A Suggested Mechanism for Visual Vertigo

Vertigo stems primarily from a mismatched integration of visual and vestibular input,[16] which jointly drive the gaze-stabilizing response through fundamental brainstem circuitry.[21] We therefore propose that the present findings indicate that the mechanism underlying visual vertigo can be found in the subcortical hierarchy of visuo-vestibular integration toward gaze stabilization. The vestibular system detects inertia through the vestibular apparatus.[48] As the head moves at a fixed velocity, the lack of inertial changes means that the vestibular system stops its signaling despite its moving.[48] This adaptation is mitigated through the vestibular storage mechanism (VSM), which serves to extend the capacity of the brain to integrate motion.[48] An increased nystagmus frequency indicates greater activity in this system.[48,49] This study showed that the VSM, as triggered by vestibular motion, was not significantly affected in PCS. In contrast, the accelerated onset of the OKN to optokinetic stimulation indicates that the relay of visual motion information was expedited. This finding fits well within a framework of amplified subcortical signaling of visual information, as such a mechanism would explain why the distribution of OKN was moved forward in time while the overall frequency was retained through an intact integration of motion information in the VSM; the mechanism of injury must be earlier in the subcortical hierarchy (i.e., before optokinetic input is integrated with vestibular data) (Fig. 1D). The specific cause for this altered integration may stem from complex injuries which are difficult to pinpoint but likely involves diffuse axonal injuries frequently seen in concussed patients, and which may involve injured pathways across the central nervous system leading to disinhibited optokinetic pathways. Visual vertigo, or visually induced dizziness, is categorized by traditionally vestibular symptoms caused by visual motion.[22] This has long been theorized to depend on a visual dependency following sensory reweighing, traditionally caused by a loss of vestibular function.[22,50] It has also been shown that concussed patients with visual vertigo may express increased optokinetic afternystagmus, reflecting a visual hypersensitivity in the VSM,[51] and visual motion hypersensitivity can occur in a range of clinical conditions, including concussion, vestibular injuries, Parkinson's disorder, and migraine.[5] The increased relative contribution of visual input toward the gaze-stabilizing response in the patient group summarily fits well within the theoretical framework and wider literature of visual vertigo, offering an objective description of visual dependency in concussed patients.

The limited number of participants in the present study and the diverging clinical histories of the patients make it difficult to come to any precise conclusions regarding the specific level of injury underlying these findings. As concussion causes diffuse whole-brain injury, it appears likely that several widely spread injuries may contribute to the decreased optokinetic inhibition previously discussed. One may, however, consider that gaze stabilization relies on a few key nodes in the brainstem that may be modified by cortical or cerebellar input.[21,52–54] It is noteworthy that the findings in this study are nearly identical to those observed during comparable stimulation protocols in animal trials where the tectum, superior colliculus in mammals, was damaged.[21] One may therefore speculate that the findings in the present study stem from a reduction in the suppression of pretectum by the superior colliculus. It is also known that the superior colliculus is susceptible to diffuse axonal injury[19] and that voluntary eye movements originating in the superior colliculus, such as saccades, pursuits, and convergence, are frequently affected in concussion.[55]

Concerning further limitations in the interpretation of the findings, the effect size in the present study allowed sufficient statistical power for main effects and interaction effects between two variables, whereas triple effects were underpowered, meaning that the effects of acceleration between groups and sensory modalities as presented in Supplementary A2 should be considered as general trends rather than robust statistical findings, which can also be seen in their overlapping confidence intervals. Some overlap of confidence intervals can also be seen in Figure 4, where the dynamic gaze-stabilizing gain has been used to calculate the relative influence of vision and vestibular input toward the joint eye-movement response. The statistical analyses account for these overlaps with sufficient statistical power. The post hoc analyses that compare single modalities (e.g., the visual response at an acceleration of 14°/s^2 compared to the response at 28°/s^2) should, however, be viewed as general trends that merit further investigation in future studies. A more physiological limitation could be that attention and alertness were not controlled for in the present study; these factors may influence the OKR in such a way that focused attention may explain the increased slow-phase velocities during optokinetic viewing.[56] Cortical processes can therefore be expected to influence the eye-movement responses despite their basic and reflexive nature. Concussed individuals are, however, expected to express decreased visual attention and alertness, which would produce inverse eye-movement responses compared with those presently identified.[57,58]

Conclusions

Patients with PCS and visual vertigo retained their vestibular processing but exhibited magnified visual contributions toward the gaze-stabilizing response. Drawing from comparable findings in animal trials, these findings indicate decreased inhibition of neural pathways relaying optokinetic information, causing a relative hypersensitivity to visual motion that may contribute to both altered gaze-stability and symptoms of dizziness as presented in visual vertigo. This likely occurs early in the subcortical hierarchy of visuo-vestibular integration, as vestibular function was unaffected. Although the study recruited a limited population size, these findings may have clinical implications in guiding rehabilitation protocols and showcase gaze stabilization as a promising biomarker for concussion and motion processing disorders. The limited number of participants nevertheless makes

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it difficult to generalize the findings to the rather broad patient group suffering from visually induced dizziness, and future studies may benefit from a more cohesive study population.

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