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Changes in cerebral activation in individuals with and without visual vertigo during optic flow: A functional near-infrared spectroscopy study

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ARTICLE INFO	A B S T R A C T
Keywords: Brain imaging Brain function Neuroimaging Balance Near-infrared spectroscopy	Background and purpose: Individuals with visual vertigo (VV) describe symptoms of dizziness, disorientation, and/or impaired balance in environments with conflicting visual and vestibular information or complex visual stimuli. Physical therapists often prescribe habituation exercises using optic flow to treat these symptoms, but it is not known how individuals with VV process the visual stimuli. The primary purpose of this study was to use functional near-infrared spectroscopy (fNIRS) to determine if individuals with VV have different cerebral activation during optic flow compared with control subjects.
	Methods: Fifteen individuals (5 males and 10 females in each group) with VV seeking care for dizziness and 15 healthy controls (CON) stood in a virtual reality environment and viewed anterior-posterior optic flow. The support surface was either fixed or sway-referenced. Changes in cerebral activation were recorded using fNIRS during periods of optic flow relative to a stationary visual environment. Postural sway of the head and center of mass was recorded using an electromagnetic tracker.
	<i>Results</i> : Compared with CON, the VV group displayed decreased activation in the bilateral middle frontal regions when viewing optic flow while standing on a fixed platform. Despite both groups having significantly increased activation in most regions while viewing optic flow on a sway-referenced surface, the VV group did not have as much of an increase in the right middle frontal region when viewing unpredictable optic flow in comparison with the CON group.
	Discussion and conclusions: Individuals with VV produced a pattern of reduced middle frontal cerebral activation when viewing optic flow compared with CON. Decreased activation in the middle frontal regions of the cerebral cortex may represent an alteration in control over the normal reciprocal inhibitory visual-vestibular interaction in visually dependent individuals. Although preliminary, these findings add to a growing body of literature using functional brain imaging to explore changes in cerebral activation in individuals with complaints of dizziness, disorientation, and unsteadiness. Future studies in larger samples should explore if this decreased activation is
	modified following a rehabilitation regimen consisting of visual habituation exercises.

1. Introduction

Visual vertigo (VV) describes symptoms of dizziness, disorientation, and/or impaired balance induced by environments with conflicting visual and vestibular information or complex visual stimuli (Bronstein, 1995). Individuals with vestibular disorders often report exacerbation of their symptoms in such environments, which can lead to avoidance behaviors resulting in activity limitations and participation restrictions (Staab, 2012). Individuals with VV are highly visually dependent (Bronstein, 1995), giving greater weight to visual information for the maintenance of balance. These visually dependent individuals may display increased postural sway with full-field visual motion stimuli (Bronstein, 1995; Rábago and Wilken, 2011).

The pathophysiology underlying VV is not well understood. During resting state functional magnetic resonance imaging (fMRI), individuals with visually induced dizziness had decreased functional connectivity in the right superior temporal gyrus, likely indicative of decreased weighting and sensory integration (cortical-level processing) of vestibular information at rest (Van Ombergen et al., 2017). Individuals with dizziness and VV also have more nonspecific hemispheric white

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matter abnormalities (hyperintensities) than individuals with dizziness without VV (Pollak et al., 2015).

Two fMRI studies have noted differences in brain activation between patients with unilateral vestibular neurectomy or chronic subjective dizziness and healthy controls (Indovina et al., 2015; Deutschländer et al., 2008). Individuals with chronic subjective dizziness and healthy controls both responded strongly in the superior temporal gyrus to sound-evoked vestibular stimuli (loud short tone bursts), while patients with chronic subjective dizziness had less cerebral activation in several areas, including the right posterior insula and superior temporal gyrus, left anterior insula, inferior frontal gyrus and anterior cingulate cortex, and bilateral hippocampus (Indovina et al., 2015). A similar pattern of reduced activation was seen in patients with unilateral vestibular neurectomy in comparison to healthy controls in response to narrow field-of-view optokinetic visual motion stimuli, with reduced activity in the posterior insula, superior temporal gyrus, and hippocampus (Deutschländer et al., 2008). Although visually-evoked symptoms are elicited in individuals with VV, it has not been investigated if they also generate abnormal patterns of cerebral activation in response to full-field visual motion stimuli. Because fMRI requires that the participant lie supine and motionless during imaging, it precludes assessment of how vestibular and visual stimuli affect upright balance tasks.

Optic flow is the continual change of images on the retina that occurs from movement of the visual environment, and provides important afferent information for control of posture and gait speed (Lappe, 2009). Optic flow, in the form of visual habituation exercises, is often prescribed to patients with VV. These habituation exercises have been shown to decrease VV symptoms when incorporated into rehabilitation regimens (Pavlou et al., 2013; Pavlou et al., 2004). While optic flow stimuli are often utilized by clinicians, evidence-based stimulus parameters are not yet known and its mechanisms are poorly understood. Therefore, understanding the cerebral responses to optic flow stimuli may help to elucidate these mechanisms and help us to better define the stimulus parameters needed to optimize rehabilitation. The primary purpose of this study was to determine if individuals with VV have different cerebral activation during optic flow compared with control subjects.

2. Material and methods

2.1. Participants

Thirty participants between the ages of 18 and 65 years old were included in the study. All participants were right-handed, as determined by the Edinburgh Handedness Inventory-Short Form (Veale, 2014). Individuals with VV were included after being evaluated by a board-certified neurologist, who made a determination based on the findings of the qualitative and quantitative examination. In addition, the individuals with VV had to rate at least two of the nine items on the Visual Vertigo Analogue Scale (VVAS) above zero (VVAS positive) (Dannenbaum et al., 2011), and report a score of 31 or greater on the Dizziness Handicap Inventory (DHI), indicating a moderate handicap (Whitney et al., 2004). Scores on the VVAS range from 0 (no VV) to 100 (severe VV) (Dannenbaum et al., 2011). Healthy men and women served as near age- (within three years of the patient's age) and gendermatched controls (CON).

Subjects were ineligible to participate in the study if they had: corrected binocular visual acuity worse than 20/40, macular degeneration, or glaucoma; unwillingness to abstain from alcohol for 48 h prior to testing; known pregnancy; and/or body weight > 118 kg. Additionally, CON were ineligible to participate in the study if they had a: history of otologic or neurologic disease; history of migraine; or abnormal vestibular function tests. Individuals with VV using medications that may have affected balance or cerebral blood flow were tested at least 48 h after taking the last dose. Written informed consent was obtained from all participants and the study was approved by the University of Pittsburgh Institutional Review Board. The study was carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for experiments involving humans.

2.2. Experimental design

A cross-sectional experimental study consisting of four combinations of two anterior-posterior (AP) optic flow stimulation frequencies (single sine and sum of sines) and two platform conditions (fixed and sway-referenced) was performed. Each of the four combinations were performed twice for a total of eight trials during a single visit. During each trial, a blocked design (e.g., A-B-A-B-A) was employed, where A was comprised of a stationary visual field and B was comprised of one of the two types of AP optic flow stimulation frequencies. As part of the A-B-A-B-A design, each block was presented for 36 s for a total of 3 min for each trial. While viewing the visual stimuli, participants stood on a fixed or sway-referenced platform during the entire trial. During swayreferenced trials the platform rotated about an axis collinear with the ankles, such that body sway and platform motion were directly proportional. Optic flow moved independently of the sway-referenced platform. The order of the first four trials was randomly assigned, and this order was repeated a second time.

2.3. Visual stimuli

The visual stimulus was back-projected onto a three-screen wide field-of-view (180° horizontal and 70° vertical display). Participants faced the front screen that was 1.5 m away (Fig. 1). An AP optic flow stimulus was selected to simulate the "moving room" paradigm used in previous research (Haibach et al., 2008; Stoffregen and Smart, 1998; Haibach et al., 2009; Schmuckler, 1997). The structure of the optic flow was designed to evoke a strong postural response (Stoffregen, 1985). The visual stimulus parameters replicated those used in a previous study investigating the effects of optic flow on postural control (Sparto et al., 2006). It consisted of a checkerboard with alternating black and white rectangles on the side screens to provide lamellar optic flow in the peripheral field of view and a bullseye pattern of alternating black and white rings on the front screen to provide radial optic flow in the central field of view. For AP optic flow, there were two motion stimuli: single sine (frequency = 0.25 Hz; peak amplitude = 8 cm) and sum of sines (sum of three sines: frequency = $\pi/10$, $\pi/13$, $\pi/17$ Hz, peak amplitude: 3.76 cm, 4.88 cm, 6.39 cm, respectively). Both stimuli had an RMS velocity of 8.88 cm/s. The sum of three sines was used to produce changes in the scene velocity that would be difficult to anticipate (Andersen and Dyre, 1989). The baseline (control) condition was a stationary bullseye and checkerboard.

2.4. Measurements

2.4.1. Cerebral activation: near-infrared spectroscopy

fNIRS is a non-invasive functional neuroimaging method that measures changes in the volume and oxygenation of blood. fNIRS allows for imaging during functional tasks such as standing balance and gait. During imaging, flexible fiber optic cables deliver low levels of light ($< 0.4 \text{ W/cm}^2$) to sources on the scalp. This light diffuses through the tissues to a depth of approximately 5–8 mm in the outer cerebral cortex (Boas and Dale, 2005). Light that is not absorbed is detected and flexible fiber optic cables carry the light back to photon detectors within the fNIRS instrument. The change in intensity of visible red to near-infrared light between sources and detectors that are placed on the scalp is measured. During task performance, regional changes in oxyhemoglobin (HbO₂) and deoxyhemoglobin (Hb) concentration change the absorption of light in the brain.

A 32-channel continuous wave fNIRS instrument (CW6 Real-time

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