

# **HHS Public Access**

Author manuscript *J Neurol Phys Ther.* Author manuscript; available in PMC 2021 April 01.

Published in final edited form as:

J Neurol Phys Ther. 2020 April; 44(2): 156–163. doi:10.1097/NPT.00000000000310.

## Changes in Cortical Activation during Dual-Task Walking in Individuals with and without Visual Vertigo

Carrie W. Hoppes, PT, PhD<sup>a,1</sup>, Theodore J. Huppert, PhD<sup>b</sup>, Susan L. Whitney, PT, PhD<sup>b</sup>, Pamela M. Dunlap, PT<sup>b</sup>, Nikki L. DiSalvio, PT<sup>c</sup>, Kefah M. Alshebber, PT, PhD<sup>d</sup>, Joseph M. Furman, MD, PhD<sup>b</sup>, Yong H. Kwon, PT, PhD<sup>e</sup>, Andrea L. Rosso, PhD, MPH<sup>b</sup>

<sup>a</sup>Army-Baylor University Doctoral Program in Physical Therapy, Fort Sam Houston, TX, USA

<sup>b</sup>University of Pittsburgh, Pittsburgh, PA, USA

<sup>c</sup>University of Southern California/Rancho Los Amigos National Rehabilitation Center, Los Angeles, CA, USA

<sup>d</sup>University of St. Augustine for Health Sciences, Austin, TX, USA

<sup>e</sup>Yeungnam University College, Nam-gu, Daegu, South Korea

## Abstract

**Background and Purpose:** Persons with vestibular disorders are known to have slower gait speed with greater imbalance and veering during dual-task walking than healthy individuals, but the cerebral mechanisms are unknown. The purpose of this study was to determine if individuals with visual vertigo (VV) have different cerebral activation during dual-task walking compared with control subjects.

**Methods:** Fourteen individuals with VV and fourteen healthy controls (CON) were included (mean 39 years old, 85% women). A cross-sectional experimental study consisting of four combinations of two surfaces (even and uneven) and two task conditions (single and dual-task) was performed. Participants walked over an even (level flooring) or uneven (wood prisms underneath carpeting) surface, either quietly or while reciting every other letter of the alphabet. Changes in cerebral activation over the bilateral prefrontal cortices was recorded using functional near-infrared spectroscopy (fNIRS) during four task conditions relative to quiet standing. Gait speed and cognitive performance was recorded.

**Results:** There were no between-group differences in cognitive performance. Both groups slowed when walking on an uneven surface or performing a dual-task, and participants in the VV group walked more slowly than those in the CON group in all conditions. Participants with VV had decreased cerebral activation in the bilateral prefrontal regions in comparison to CON participants in all conditions.

Corresponding Author: Carrie W. Hoppes, PT, PhD, Phone: 571-212-4660, Fax: n/a, carrie.w.hoppes.mil@mail.mil. <sup>1</sup>Present Address: Army-Baylor University Doctoral Program in Physical Therapy, ATTN: MAJ Carrie Hoppes (MCCS-WBB-GT), 3630 Stanley Road, Building 2841, Suite 1301, JBSA-Fort Sam Houston, TX 78234

This work was previously presented as a platform presentation at the 30th Bárány Society Meeting, Uppsala, Sweden in June 2018. **Video Abstract** available for more insights from the authors (see Video, Supplemental Digital Content 1, available at: Hoppes\_SDC1.mp4)

## due to shifted attention away from the cognitive task to prioritize maintenance of dynamic balance.

#### Keywords

brain imaging; brain function; neuroimaging; gait; near-infrared spectroscopy

## 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.<sup>1</sup> 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.<sup>2</sup>

Persons with vestibular disorders are known to have slower gait speed<sup>3,4</sup>, greater ataxia<sup>3</sup>, and increased veering during dual-task walking in comparison to healthy controls.<sup>3</sup> They also display a cautious gait during dual-task walking, with increased foot contact, double support, stride time, and variation in stride time, as well as decreased percentage of time spent in the swing phase of gait.<sup>5</sup> The underlying mechanisms for these decrements in dual-task performance in individuals with vestibular disorders is not well understood. Therefore, exploring the cerebral responses during dual-task walking may help to elucidate these mechanisms.

The middle frontal region of the brain has been documented as an active region during vestibular stimulation in many studies,<sup>6</sup> including caloric stimulation,<sup>7</sup> auditory-evoked vestibular stimulation,<sup>8,9</sup> and galvanic vestibular stimulation.<sup>10–13</sup> The activation of this region has been attributed to its role in performing oculomotor and fixation tasks,<sup>11,14</sup> and its connections to both visual association areas,<sup>8</sup> spatial navigation and memory areas.<sup>15</sup> There are several reports of middle frontal gyrus abnormalities in vestibular disorders. Functional changes have been observed in individuals with persistent mal de debarquement, <sup>15</sup> individuals with bilateral vestibular hypofunction,<sup>16</sup> and individuals with chronic subjective dizziness.<sup>17</sup>

The prefrontal cortex has often been studied for its importance in walking.<sup>18</sup> A systematic review noted that when walking was compared to quiet standing and when dual-task walking was compared to walking, the included studies variably concluded that there was increased, decreased, and unchanged prefrontal cortex activation in older adults.<sup>19</sup> As individuals with vestibular disorders can have impaired gait during dual-task walking and abnormal middle frontal gyrus cortical activation, we hypothesized that individuals with VV may similarly have impaired gait and changes in prefrontal cortex activity during dual-task walking. The purpose of this exploratory study was to determine if individuals with VV have different cerebral activation during dual-task walking compared with control subjects.

## Methods

#### **Participants**

Twenty-eight 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.<sup>20</sup> Individuals with VV were included after being evaluated by a board-certified neurologist. Visual vertigo was differentiated from other functional vestibular disorders (phobic postural vertigo, space-motion discomfort, chronic subjective dizziness) based on impairments related to visual motion stimuli (see review in <sup>21</sup>). The individuals with VV had to rate at least two of the nine items on the Visual Vertigo Analogue Scale (VVAS) above zero,<sup>22</sup> and report a score of 31 or greater on the Dizziness Handicap Inventory (DHI), indicating a moderate handicap.<sup>23</sup> The VVAS is valid and responsive to change, making it a useful tool for identifying and evaluating the progression of symptoms of visual vertigo.<sup>24</sup> Healthy men and women served as near age- (within three years of the participant with VV's age) and gender-matched controls (CON). Participants were additionally matched based on their primary language; one VV subject was a non-native English speaker.

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 hours prior to testing; known pregnancy; and/or body weight greater than 118 kilograms. Additionally, participants in the CON group 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 hours 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.

### **Experimental Design**

Participants were challenged not only with a cognitive task, but also by adding an uneven walking surface<sup>25</sup> to simulate real life situations (i.e., walking over grassy or rocky terrain). A cross-sectional experimental study consisting of four combinations of two surfaces (even and uneven) and two task conditions (single and dual-task) was performed. The full track was a 55 m oval, with the 15 m straightaways used for data collection. The even surface consisted of level flooring, while the uneven surface consisted of 1.5 cm high wood prisms arranged randomly at a density of 26 pieces/m<sup>2</sup> underneath carpeting to hide them from view (Figure 1).<sup>25</sup> The single task consisted of walking quietly, while the dual-task consisted of walking and reciting every other letter of the alphabet aloud, always starting with 'B'.<sup>26</sup> This cognitive dual-task paradigm was selected based on its extensive use in other studies of fNIRS assessment of prefrontal cortical activation during walking and to allow comparison with other populations.<sup>27–31</sup> A total of four trials of the four combinations were performed during a single visit. The order of the trials was randomly assigned. An example of a single trial of the single and dual-task conditions used to explore differences in cerebral activation in individuals with visual vertigo and healthy controls is provided Table 1.

Performance during the dual-task was recorded for the cognitive task as the number of alphabet sets completed, the number of alphabet errors, and gait speed. Gait speed was measured as the time it took the subject to walk the 15 m straightaway at their self-selected pace.

#### Measurements

**Cerebral Activation: Near-Infrared Spectroscopy**—Changes in cortical activity over the right and left prefrontal cortices were measured using functional near-infrared spectroscopy (fNIRS) and compared to quiet standing. 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 gait.<sup>32–34</sup> During imaging, flexible fiber optic cables deliver low levels of light (<0.4 W/cm<sup>2</sup>) to sources on the scalp. This light diffuses through the tissues to a depth of approximately 5-8 mm in the outer cerebral cortex. <sup>35</sup> 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 nearinfrared light between sources and detectors that are placed on the scalp is measured. During task performance, regional changes in oxyhemoglobin (HbO<sub>2</sub>) and deoxyhemoglobin (Hb) concentration change the absorption of light in the brain.

An 8-channel continuous wave fNIRS instrument (OctaMon; Artinis Medical Systems; Netherlands) was used to record changes in HbO<sub>2</sub> and Hb concentration at 850 nm and 760 nm, respectively. A fNIRS headband consisting of 2 sources and 8 detectors was used (Figure 2) to assess two regions of interest: right and left prefrontal cortical regions. Each of the prefrontal regions of interest had four channels, comprised of one source and four detectors. The probe covered approximately bilateral Brodmann areas BA9, BA44, BA45, and BA46, which were studied because of their relevance to executive function and dual-task activation.<sup>36</sup> Optical data were collected at 10 Hz and stored using OxySoft (Artinis Medical Systems; Netherlands).

**fNIRS data processing**—A custom-built MATLAB-based software program was used to analyze all optical data.<sup>37</sup> Light intensity signals were first converted to changes in optical density over time and then converted to HbO<sub>2</sub> and Hb estimates, as a measure of cerebral activity, via the modified Beer-Lambert law with a partial pathlength correction of 0.1 for both wavelengths (note: partial pathlength corrects for the differential pathlength factor [DPF] and the partial volume correction [PVC]; 0.1 = ([DPF]=6)/([PVC]=60).<sup>38</sup> The timecourse of hemoglobin changes for each source-detector pair was analyzed using a general linear model (GLM) [*Hbx*] =  $X * \beta + \epsilon$  where [*Hbx*] is the change in concentration of HbO<sub>2</sub> or Hb, X is the design matrix encoding the timing of stimulus events, and  $\beta$  is the coefficient (weight) of that stimulus condition for that source-detector channel. The design matrix was constructed from the convolution of the stimulus timing and duration with a canonical hemodynamic response function (see details in <sup>37</sup>).

In this analysis, no motion correction or physiological filtering preprocessing was applied. Instead, physiological noise and motion artifacts were dealt with statistically within the GLM.<sup>39</sup> To reduce effects of motion artifacts and systemic physiology, an iteratively auto-

regressively whitened, weighted least-squares model was used to solve the general linear equation.<sup>37</sup> This regression model uses an n<sup>th</sup> order auto-regressive filter determined by an Akaike model-order selection to whiten both sides of the GLM expression. The regression coefficients ( $\beta$ ) and their error-covariance are estimated, and used to define statistical tests between task conditions (single and dual-task) or baseline (quiet standing). The subject-level analysis to investigate if the task conditions elicited a significant brain activation compared with quiet standing was performed using a GLM with a canonical function of the timing of the single and dual-task stimuli as a regressor.<sup>37</sup> The timing of the four conditions was specified in the design matrix. The regression model was solved sequentially for each data file for each participant. All source-detector pairs within a file were solved concurrently yielding a full covariance model of the noise, which was used in group-level analysis. T-tests were used to determine if the regression coefficients were statistically non-zero.

**Statistical Analyses**—Demographic and performance data were analyzed using commercial statistical software (IBM SPSS Statistics 22, IBM Corporation, Armonk, NY) and optical data were analyzed using our open-source MATLAB (Mathworks, Natick, MA) toolbox for NIRS<sup>40</sup>. Descriptive statistics were calculated for demographic variables. Demographic data and cognitive performance data were checked for normality using Shapiro-Wilk tests, and between-group comparisons were made using dependent *t*-tests or Wilcoxon Signed Ranks tests where appropriate. Differences in gait speed between groups (VV and CON) across condition (single task on even and uneven surface, dual-task on even and uneven surface) and trial (first, second, third, fourth) was tested using a mixed analysis of variance (ANOVA) and assessed for interaction and main effects. Simple comparisons were then made using a repeated measures ANOVA in each group with a Bonferroni correction.

For each of the four task and surface combinations, group-level analysis of the fNIRS data was performed using a linear mixed effects model, using the task-related regression weights ( $\beta$ ) from the first-level GLM as the dependent variable and subject as a random effect. A modified version of the MATLAB function fitLME (linear mixed effects model estimator) was used to solve the weighted maximum likelihood estimate of the parameters (see Santosa et al<sup>40</sup>). The model was whitened using the error-covariance of the first level GLM model. A three-way ANOVA was used to look at main and interaction effects of group (VV and CON), surface (even and uneven), and task (single and dual-task) to determine whether HbO<sub>2</sub> levels differed by any of these factors. The rational for comparing the cortical activation across each trial within a condition was to determine if there was a practice effect. To control for multiple comparisons, a false discovery rate (FDR)-correction was used with the significance level set at 0.05 (q 0.05).<sup>41</sup>

#### Results

The individuals with VV were diagnosed with a variety of central and/or peripheral vestibular disorders. The VV group mean score on the VVAS and DHI was 60 (SD 21) and 51 (SD 16), respectively. There was no difference in age (VV and CON mean 39 years [SD 11]), height (VV mean 168 cm [SD 7], CON mean 172 cm [SD 9]), and weight (VV mean

68 kg [SD 9], CON mean 77 kg [SD 17]), or education levels (Z = -0.207; p = 0.836) between the two groups.

Gait speed met the assumption of normality for the mixed ANOVA. Results revealed a main effect of trial ( $F_{(3,75)} = 54.795$ , p < 0.001,  $n_p^2 = .687$ ), condition ( $F_{(2.3,56.5)} = 131.235$ , p < 0.001,  $n_p^2 = 0.840$ ), and group ( $F_{(1,25)} = 12.021$ , p = 0.002,  $n_p^2 = 0.325$ ), and an interaction effect between trial and condition ( $F_{(4.1,103)} = 2.792$ , p = 0.029,  $n_p^2 = 0.100$ ). CON subjects were faster on all conditions compared with subjects with VV. In the VV group, average gait speed was significantly different among conditions (dual-task on uneven surface = 0.66 m/s, dual-task on even surface = 0.74 m/s, single task on uneven surface = 0.76 m/s, single task on even surface = 0.84 m/s, p < .001), except there was no significant difference between dual-task walking on even surface and single-task walking on uneven surface. Also, the VV group had a significantly faster average gait speed in the second through fourth trials (second = 0.75 m/s; third = 0.78 m/s; fourth = 0.79 m/s) than for the first trial (0.68 m/s), p = 0.003.

Similarly, the CON group had a significantly different average gait speed with each condition (dual-task on uneven surface = 0.87 m/s, dual-task on even surface = 0.97 m/s, single task on uneven surface = 0.98 m/s, single task on even surface = 1.08 m/s, p < 0.001), except there was no significant difference between dual-task walking on even surface and single-task walking on uneven surface. Control subjects had significantly different average gait speeds among all trials (first = 0.9 m/s, second = 0.97 m/s, third = 1.01 m/s, fourth = 1.01 m/s, p = 0.016) except between the third and fourth trials.

Regarding cognitive performance, there were no between-group differences in the number of alphabet sets completed (even surface Z = -1.291; p = 0.197; uneven surface Z = -1.795; p = 0.073) or in the number of errors (even surface Z = -0.842; p = 0.400; uneven surface Z = -0.630; p = 0.529) during the dual-task walking conditions (Table 2). There was no performance effect of the cognitive task (individuals did not perform better across the trials),  $F_{(1,109)} = 1.925$ , p = 0.168,  $n_p^2 = 0.017$ .

During single and dual-task walking on an even surface, VV subjects had no significant differences in cerebral activation between the walking tasks and quiet standing, but there were non-significant reductions in activation in the bilateral prefrontal regions (Table 3). In contrast, the CON group had non-significant increases in activation in the bilateral prefrontal regions. Because of the relative reduction in HbO<sub>2</sub> in the prefrontal regions of the VV group and relative increase in HbO<sub>2</sub> in the same regions of the CON group, there was a significantly lower activation of the bilateral prefrontal regions in the VV participants compared with CON participants.

During single task walking on an uneven surface, VV subjects had non-significant increases in activation in the bilateral prefrontal regions (Table 3). The CON subjects displayed a significant increase in HbO<sub>2</sub> in the bilateral prefrontal regions (right prefrontal: t = 4.39, p < 0.001, false discovery rate [FDR]-corrected; left prefrontal: t = 4.42, p < 0.001, FDRcorrected). The relatively small increase in HbO<sub>2</sub> in the prefrontal regions of the VV participants compared with the robust increase in the same regions of the CON participants

resulted in significantly lower prefrontal activation in the VV group compared with the CON group.

During dual-task walking on an uneven surface, VV subjects had a robust reduction in activation in the left prefrontal region (t = -8.62, p < 0.001, FDR-corrected) and a non-significant reduction in activation in the right prefrontal region (Table 3). In CON, there was a significant increase in activation in the left prefrontal region (t = 3.02, p = 0.02, FDR-corrected) and a non-significant increase in activation in the right prefrontal region. As in the other task conditions, the relative decrease in HbO2 in the prefrontal regions of the participants with VV combined with the increase in the same regions of the CON participants resulted in significantly lower prefrontal activation in VV group compared with the CON group.

A main effect was found for group for oxyhemoglobin. Individuals with VV had decreased concentrations of oxyhemoglobin in both the right ( $F_{(1,96)} = 6.24$ , p = 0.01) and left ( $F_{(1,96)} = 17.12$ , p < 0.001) prefrontal regions of interest in comparison to CON (Figure 3). There was no main effect for surface and no main effect for task. There were no interaction effects for group\*surface, group\*task, surface\*task, or group\*surface\*task.

A main effect was found for group for deoxyhemoglobin. Individuals with VV had decreased concentrations of deoxyhemoglobin in both the right ( $F_{(1,96)} = 18.58$ , p < 0.001) and left ( $F_{(1,96)} = 5.34$ , p = 0.02) prefrontal regions of interest in comparison to CON. A main effect was found for surface for deoxyhemoglobin in the right prefrontal region of interest but not in the left prefrontal region of interest. Individuals with VV had decreased concentrations of deoxyhemoglobin in the right ( $F_{(1,96)} = 4.54$ , p = 0.04) prefrontal region of interest in comparison to CON. A main effect was found for task for deoxyhemoglobin in the left prefrontal region of interest in comparison to CON. A main effect was found for task for deoxyhemoglobin in the left prefrontal region of interest. Individuals with VV had decreased concentrations of deoxyhemoglobin in the right prefrontal region of interest. Individuals with VV had decreased concentrations of deoxyhemoglobin in the right prefrontal region of interest. Individuals with VV had decreased concentrations of deoxyhemoglobin in the right prefrontal region of interest. Individuals with VV had decreased concentrations of deoxyhemoglobin in the left ( $F_{(1,96)} = 5.05$ , p = 0.03) prefrontal region of interest in comparison to CON. There were no interaction effects for group\*surface, group\*task, surface\*task, or group\*surface\*task.

## Discussion

This study utilized fNIRS to explore the patterns of cortical activation in individuals with and without VV during dual-task walking. Individuals with VV had less activity in the prefrontal cortex than CON. This reduced pattern of activation is similar to the decreased glucose metabolism and decreased resting state connectivity observed in the middle frontal gyrus in individuals with persistent mal de debarquement.<sup>15</sup> In individuals with bilateral vestibular hypofunction, weaker resting state connectivity was found between the posterior insula and middle frontal gyrus.<sup>16</sup> Individuals with chronic subjective dizziness showed lesser activation in the bordering inferior frontal gyrus and superior temporal gyrus and reduced connectivity between the left inferior frontal gyrus and right superior temporal gyrus than healthy controls.<sup>17</sup>

Regardless of condition, individuals with VV had less activity in the prefrontal cortex than CON. This functional change in prefrontal cortex activity may be a result of VV and not a

response to the single and dual-task walking conditions. In a similar population, individuals with VV produced a pattern of reduced middle frontal cerebral activation when viewing optic flow compared with CON.<sup>42</sup> Decreased activation in the middle frontal regions may represent an alteration in control over the normal reciprocal inhibitory visual-vestibular interaction in these visually dependent individuals.<sup>42</sup> Persons with VV are known to have more white matter changes than persons with dizziness but without VV.<sup>43</sup> In 3 of 9 persons with VV and white matter abnormalities, the white matter abnormalities were due to a vascular cause.<sup>43</sup> Structural vascular anomalies cannot be excluded as a source for functional changes in blood flow observed in these individuals with VV.

Both the VV and CON groups tended to increase their gait speed with each trial, indicative of a practice effect. This has also been observed in older adults during this dual-task, though an uneven surface was not tested by Holtzer et al.<sup>44</sup> This is the first study of prefrontal cortex recruitment during walking on an uneven surface. We found that an uneven surface has similar effects to a cognitive dual-task performed on an even surface concerning prefrontal cortex activation as measured by fNIRS. Both the VV and CON groups slowed down when they encountered an uneven surface or performed a dual-task. The VV group walked significantly more slowly overall than the CON group. One possible interpretation of our findings is that the individuals with VV may have shifted attention away from the cognitive task and prioritized dynamic balance. Persons with unilateral vestibular impairment and healthy controls both adopt a more conservative gait pattern during dualtask walking.<sup>5</sup> Persons with bilateral vestibular loss have slower gait speed than healthy controls during dual-task walking, but similar cognitive performance.<sup>4</sup> The VV and CON groups performed similarly on the cognitive task in our study. Bessot et al<sup>4</sup> suggest that reducing gait speed during dual-task walking is a strategy to avoid imbalance and falls, indicating prioritization of the walking task over the cognitive task. Lesser prefrontal cortex activation in individuals with VV may indicate a shift of cognitive resources to other cortical areas for maintenance of dynamic balance. Future research should explore changes in cortical activation in conjunction with gait analysis to determine if individuals with VV also adopt a more cautious, slower gait during dual-task walking.

Individuals with VV report symptoms of dizziness, disorientation, and/or impaired balance induced by environments with conflicting visual and vestibular information or complex visual stimuli.<sup>1</sup> It is possible that cognitive resources in these individuals may be overwhelmed by a surplus of visual input. In comparison to healthy controls, persons with prefrontal stroke showed a trend toward loss of tonic inhibition over early somatosensory cortical processing.<sup>45</sup> The prefrontal areas have an important role in regulating transmission of somatosensory information, and damage to these areas manifests as a decreased ability to suppress task-irrelevant sensory information.<sup>45</sup> Lesser prefrontal cortex activation in individuals with VV may indicate an inability to suppress irrelevant or facilitate relevant visual information, leading to complaints of dizziness and imbalance.

An alternative explanation is that lesser prefrontal cortex activation in individuals with VV may suggest that they are performing at or near their maximal ability to activate the prefrontal regions. Chatterjee et al<sup>46</sup> used fNIRS to explore prefrontal cortical activity in 33 adults with chronic post-stroke during single and dual-task walking. They found that those

individuals with lower cognitive function ( 27 on the Mini-Mental State Examination) were unable to recruit (activate) the prefrontal regions possibly due to lesser availability of cognitive reserves, which they termed a 'recruitment ceiling.'<sup>46</sup> In contrast to our study, those with lower cognitive function also had decreased cognitive performance and walking speed than those with higher cognitive function. Individuals with multiple sclerosis also had smaller increases in prefrontal cortical activation than healthy controls during dual-task walking.<sup>47</sup> The authors concluded that the individuals with multiple sclerosis were unable to allocate additional attentional resources during complex walking tasks.<sup>47</sup> Individuals with VV may not be able to effectively recruit the prefrontal regions for optimal performance, as indicated by their slower gait speed.

The differential brain responses observed in individuals with VV occurred despite similar performance on the cognitive task as CON. The literature on cognitive performance in persons with vestibular disorders during a dual-task is mixed. In some studies, decreased performance was found,<sup>5,48–50</sup> whereas in other studies there was no difference in performance.<sup>4,51</sup> The dual-task paradigm utilized in this study was a language task, while walking requires central processing of visual, vestibular, and somatosensory information. It is possible that less interference, evidenced by the similar cognitive performance of both groups, was observed between language pathways and postural control pathways. In younger and older adults with and without a history of falls, the greatest interference was observed during a visually-presented sentence completion task while standing on a compliant surface. <sup>51</sup> The visual task may have placed competing demands on visual pathways, resulting in decreased performance both on the cognitive task and on postural stability.<sup>51</sup> Future research should explore changes in cortical activation during visually-presented cognitive tasks during dual-task walking.

#### Limitations

Limited areas of the brain were imaged with fNIRS due to the headband design and depth of penetration. Also, the study was limited to a small sample of individuals with and without VV. Despite these limitations, we demonstrate the feasibility of applying fNIRS to explore cortical activation during dual-task walking in real time.

## Conclusions

The results of this study suggest that individuals with VV have lower prefrontal cortex activation than CON during the performance of dual-task walking. These findings are similar to other reports of functional abnormalities of the middle frontal gyrus in clinical vestibular syndromes but are unique because we were able to perform our imaging while subjects were upright and ambulating. The decreased cortical activity in individuals with VV may be due to shifted attention away from the cognitive task to prioritize maintenance of dynamic balance. It is not known if lesser activity in the prefrontal regions during dual-task walking in individuals with VV is a physiological impairment or a coping mechanism. These differences in cerebral activation may be a biomarker for a treatment-based classification approach to examination and intervention of vestibular disorders. Perhaps, this information may inform prognosis or be useful in tracking or determining recovery. Future studies

should explore if this decreased activation in the prefrontal cortex is modified following rehabilitation.

## Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

## Acknowledgments:

The authors give special thanks to Emily Wasson, Colleen Danaher, and Dr. Brooke Klatt for their help on this project. We also wish to thank Dr. Hendrik Santosa for his assistance with analysis of the optical data and Dr. Patrick Sparto for his assistance with analysis of gait speed.

Funding: Partial support for this project was funded by a grant (P30 AG024827) from the Pittsburgh Claude D. Pepper Older Americans Independence Center, the Eye and Ear Foundation, and training grants from the National Center for Advancing Translational Sciences (KL2 TR000146) and the National Institute on Aging (1 K01 AG053431-01). Participant recruitment was facilitated by the Clinical and Translational Science Institute, supported by the National Institutes of Health through Grant Number UL1TR001857.

The authors wish to thank the U.S. Army Medical Center of Excellence Visual Information Division (Television) for producing the video abstract.

## References

- Bronstein A Visual vertigo syndrome: clinical and posturography findings. Journal of Neurology, Neurosurgery & Psychiatry. 1995;59(5):472–476.
- Staab JP. Chronic Subjective Dizziness. CONTINUUM: Lifelong Learning in Neurology. 2012;18(5):1118–1141. [PubMed: 23042063]
- Roberts JC, Cohen HS, Sangi-Haghpeykar H. Vestibular disorders and dual task performance: impairment when walking a straight path. Journal of Vestibular Research. 2011;21(3):167–174. [PubMed: 21558642]
- Bessot N, Denise P, Toupet M, Van Nechel C, Chavoix C. Interference between walking and a cognitive task is increased in patients with bilateral vestibular loss. Gait & Posture. 2012;36(2):319– 321. [PubMed: 22465706]
- Nascimbeni A, Gaffuri A, Penno A, Tavoni M. Dual task interference during gait in patients with unilateral vestibular disorders. Journal of Neuroengineering and Rehabilitation. 2010;7(1):47. [PubMed: 20854671]
- 6. Lopez C, Blanke O. The thalamocortical vestibular system in animals and humans. Brain Research Reviews. 2011;67(1):119–146. [PubMed: 21223979]
- 7. Dieterich M, Bense S, Lutz S, et al. Dominance for vestibular cortical function in the non-dominant hemisphere. Cerebral cortex (New York, NY: 1991). 2003;13(9):994–1007.
- 8. Van Ombergen A, Heine L, Jillings S, et al. Altered functional brain connectivity in patients with visually induced dizziness. NeuroImage: Clinical. 2017;14:538–545. [PubMed: 28331800]
- Miyamoto T, Fukushima K, Takada T, de Waele C, Vidal P- P. Saccular stimulation of the human cortex: A functional magnetic resonance imaging study. Neuroscience Letters. 2007;423(1):68–72. [PubMed: 17662530]
- Lobel E, Kleine JF, Bihan DL, Leroy-Willig A, Berthoz A. Functional MRI of Galvanic Vestibular Stimulation. Journal of Neurophysiology. 1998;80(5):2699–2709. [PubMed: 9819274]
- Bense S, Stephan T, Yousry TA, Brandt T, Dieterich M. Multisensory Cortical Signal Increases and Decreases During Vestibular Galvanic Stimulation (fMRI). Journal of Neurophysiology. 2001;85(2):886–899. [PubMed: 11160520]
- Stephan T, Deutschländer A, Nolte A, et al. Functional MRI of galvanic vestibular stimulation with alternating currents at different frequencies. NeuroImage. 2005;26(3):721–732. [PubMed: 15955481]

- Della-Justina HM, Gamba HR, Lukasova K, Nucci-da-Silva MP, Winkler AM, Amaro E. Interaction of brain areas of visual and vestibular simultaneous activity with fMRI. Experimental Brain Research. 2015;233(1):237–252. [PubMed: 25300959]
- Sweeney J, Mintun M, Kwee S, et al. Positron emission tomography study of voluntary saccadic eye movements and spatial working memory. Journal of neurophysiology. 1996;75(1):454–468. [PubMed: 8822570]
- 15. Cha Y- H, Chakrapani S, Craig A, Baloh RW. Metabolic and functional connectivity changes in mal de debarquement syndrome. PLoS One. 2012;7(11):e49560. [PubMed: 23209584]
- Göttlich M, Jandl NM, Wojak JF, et al. Altered resting-state functional connectivity in patients with chronic bilateral vestibular failure. NeuroImage: Clinical. 2014;4:488–499. [PubMed: 24818075]
- 17. Indovina I, Riccelli R, Chiarella G, et al. Role of the insula and vestibular system in patients with chronic subjective dizziness: An fMRI study using sound-evoked vestibular stimulation. Frontiers in Behavioral Neuroscience. 2015;9:1–12. [PubMed: 25653603]
- Leff DR, Orihuela-Espina F, Elwell CE, et al. Assessment of the cerebral cortex during motor task behaviours in adults: a systematic review of functional near infrared spectroscopy (fNIRS) studies. Neuroimage. 2011;54(4):2922–2936. [PubMed: 21029781]
- Pelicioni PH, Tijsma M, Lord SR, Menant J. Prefrontal cortical activation measured by fNIRS during walking: effects of age, disease and secondary task. PeerJ. 2019;7:e6833. [PubMed: 31110922]
- 20. Veale JF. Edinburgh Handedness Inventory–Short Form: a revised version based on confirmatory factor analysis. Laterality: Asymmetries of Body, Brain and Cognition. 2014;19(2):164–177.
- 21. Staab JP, Eckhardt-Henn A, Horii A, et al. Diagnostic criteria for persistent postural-perceptual dizziness (PPPD): Consensus document of the committee for the classification of Vestibular Disorders of the Bárány Society. Journal of Vestibular Research. 2017;27(4):191–208. [PubMed: 29036855]
- 22. Dannenbaum E, Chilingaryan G, Fung J. Visual vertigo analogue scale: an assessment questionnaire for visual vertigo. Journal of vestibular research : equilibrium & orientation. 2011;21(3):153. [PubMed: 21558640]
- Whitney SL, Wrisley DM, Brown KE, Furman JM. Is perception of handicap related to functional performance in persons with vestibular dysfunction? Otology & Neurotology. 2004;25(2):139– 143. [PubMed: 15021773]
- Dannenbaum E, Chilingarian G, Fung J. Validity and Responsiveness of the Visual Vertigo Analogue Scale. Journal of Neurologic Physical Therapy. 2019;43(2):117–121. [PubMed: 30883499]
- 25. Thies SB, Richardson JK, DeMott T, Ashton-Miller JA. Influence of an irregular surface and low light on the step variability of patients with peripheral neuropathy during level gait. Gait & posture. 2005;22(1):40–45. [PubMed: 15996590]
- Brandler TC, Oh-Park M, Wang C, Holtzer R, Verghese J. Walking while talking: investigation of alternate forms. Gait & Posture. 2012;35(1):164–166. [PubMed: 21944476]
- Holtzer R, Mahoney JR, Izzetoglu M, Wang C, England S, Verghese J. Online fronto-cortical control of simple and attention-demanding locomotion in humans. Neuroimage. 2015;112:152– 159. [PubMed: 25765257]
- Holtzer R, Schoen C, Demetriou E, et al. Stress and gender effects on prefrontal cortex oxygenation levels assessed during single and dual-task walking conditions. European Journal of Neuroscience. 2017;45(5):660–670. [PubMed: 28028863]
- Holtzer R, Verghese J, Allali G, Izzetoglu M, Wang C, Mahoney JR. Neurological gait abnormalities moderate the functional brain signature of the posture first hypothesis. Brain topography. 2016;29(2):334–343. [PubMed: 26613725]
- Holtzer R, Yuan J, Verghese J, Mahoney JR, Izzetoglu M, Wang C. Interactions of subjective and objective measures of fatigue defined in the context of brain control of locomotion. The Journals of Gerontology: Series A. 2017;72(3):417–423.
- Holtzer R, Mahoney JR, Izzetoglu M, Izzetoglu K, Onaral B, Verghese J. fNIRS Study of Walking and Walking While Talking in Young and Old Individuals. The Journals of Gerontology: Series A. 2011;66A(8):879–887.

- Miyai I, Tanabe HC, Sase I, et al. Cortical Mapping of Gait in Humans: A Near-Infrared Spectroscopic Topography Study. NeuroImage. 2001;14(5):1186–1192. [PubMed: 11697950]
- Suzuki M, Miyai I, Ono T, Kubota K. Activities in the frontal cortex and gait performance are modulated by preparation. An fNIRS study. NeuroImage. 2008;39(2):600–607. [PubMed: 17950626]
- 34. Perrey S Possibilities for examining the neural control of gait in humans with fNIRS. Frontiers in Physiology. 2014;5(204).
- Boas DA, Dale AM. Simulation study of magnetic resonance imaging–guided cortically constrained diffuse optical tomography of human brain function. Applied Optics. 2005;44(10):1957–1968. [PubMed: 15813532]
- Fuster J The Prefrontal Cortex Anatomy, Physiology and Neuropsychology of the Frontal Lobe. 1997.
- Barker JW, Aarabi A, Huppert TJ. Autoregressive model based algorithm for correcting motion and serially correlated errors in fNIRS. Biomedical optics express. 2013;4(8):1366–1379. [PubMed: 24009999]
- Strangman G, Franceschini MA, Boas DA. Factors affecting the accuracy of near-infrared spectroscopy concentration calculations for focal changes in oxygenation parameters. Neuroimage. 2003;18(4):865–879. [PubMed: 12725763]
- 39. Huppert T Commentary on the statistical properties of noise and its implication on general linear models in functional near-infrared spectroscopy. Neurophotonics. 2016;3(1).
- 40. Santosa H, Zhai X, Fishburn F, Huppert T. The NIRS Brain AnalyzIR Toolbox. Algorithms. 2018;11(5):73.
- Benjamini Y, Hochberg Y. Controlling the false discovery rate: a practical and powerful approach to multiple testing. Journal of the Royal Statistical Society Series B (Methodological). 1995:289– 300.
- 42. Hoppes CW, Sparto PJ, Whitney SL, Furman JM, Huppert TJ. Changes in cerebral activation in individuals with and without visual vertigo during optic flow: A functional near-infrared spectroscopy study. NeuroImage : Clinical. 2018;20:655–663. [PubMed: 30211002]
- 43. Pollak L, Osherov M, Berkovitz N, Beckerman I, Stryjer R, Tal S. Magnetic resonance brain imaging in patients with visual vertigo. Brain and Behavior. 2015;5(11):>e00402-n/a.
- 44. Holtzer R, Izzetoglu M, Chen M, Wang C. Distinct fNIRS-Derived HbO2 Trajectories During the Course and Over Repeated Walking Trials Under Single-and Dual-Task Conditions: Implications for Within Session Learning and Prefrontal Cortex Efficiency in Older Adults. The Journals of Gerontology: Series A. 2018;74(7):1076–1083.
- 45. Bolton DA, Staines WR. Attention-based modulation of tactile stimuli: a comparison between prefrontal lesion patients and healthy age-matched controls. Neuropsychologia. 2014;57:101–111. [PubMed: 24650526]
- 46. Chatterjee SA, Fox EJ, Daly JJ, et al. Interpreting Prefrontal Recruitment During Walking After Stroke: Influence of Individual Differences in Mobility and Cognitive Function. Frontiers in Human Neuroscience. 2019;13(194).
- 47. Hernandez ME, O'Donnell E, Chaparro G, et al. Brain Activation Changes During Balance- and Attention-Demanding Tasks in Middle- and Older-Aged Adults With Multiple Sclerosis. 2019:1.
- Andersson G, Yardley L, Luxon L. A dual-task study of interference between mental activity and control of balance. The American Journal of Otology. 1998;19(5):632–637. [PubMed: 9752972]
- 49. Yardley L, Gardner M, Bronstein A, Davies R, Buckwell D, Luxon L. Interference between postural control and mental task performance in patients with vestibular disorder and healthy controls. Journal of Neurology, Neurosurgery & Psychiatry. 2001;71(1):48–52.
- Yardley L, Papo D, Bronstein A, et al. Attentional demands of continuously monitoring orientation using vestibular information. Neuropsychologia. 2002;40(4):373–383. [PubMed: 11684171]
- Shumway-Cook A, Woollacott M, Kerns KA, Baldwin M. The effects of two types of cognitive tasks on postural stability in older adults with and without a history of falls. Journals of Gerontology. 1997;52(4):M232–M240. [PubMed: 9224435]



### Figure 1.

The uneven surface consisted of wood prisms attached to plywood via wood screws (A) underneath carpeting (B).



## Figure 2.

Each participant wore a functional near-infrared spectroscopy headband that consisted of 2 sources (white with letter "S") and 8 detectors (grey) on the forehead, distributed between the left and right prefrontal regions.

Hoppes et al.



#### Figure 3.

Change in cerebral activation (oxyhemoglobin concentration) in the right and left prefrontal regions of interest during four task conditions in individuals with visual vertigo (dark grey) and healthy controls (light grey). Error bars represent the standard error.

#### Table 1.

An example of a single trial of the single and dual-task conditions used to explore differences in cerebral activation in individuals with visual vertigo and healthy controls. Task order was pseudo-randomized with the constraint that even and uneven surface walking always alternated.

Tasks and Instructions to Participants							
20 seconds quiet stance: "Stop and Rest"							
20 seconds standing and reciting every other letter of the alphabet: "Stand and alphabet. Start with B"							
20 seconds quiet stance: "Stop and Rest"							
15 meters of even surface walking: "Walk"							
(walking around semi-circular end of track)							
20 seconds quiet stance: "Stop and Rest"							
15 meters of uneven surface walking: "Walk"							
(walking around semi-circular end of track)							
20 seconds quiet stance: "Stop and Rest"							
20 seconds standing and reciting every other letter of the alphabet: "Stand and alphabet. Start with B"							
20 seconds quiet stance: "Stop and Rest"							
15 meters of even surface walking and reciting every other letter of the alphabet: "Walk and alphabet. Start with B"							
(walking around semi-circular end of track)							
20 seconds quiet stance: "Stop and Rest"							
15 meters of uneven surface walking and reciting every other letter of the alphabet: "Walk and alphabet. Start with B"							
(walking around semi-circular end of track)							
20 seconds quiet stance: "Stop and Rest"							

#### Table 2.

Cognitive performance during dual-task conditions in individuals with visual vertigo and healthy controls.

Group	Task Condition	Mean Number of Alphabet Sets Completed	SD Number of Alphabet Sets Completed	Mean Number of Errors	SD Number of Errors
Visual Vertigo	Dual task, even surface	0.93	0.26	1.55	2.78
	Dual task, uneven surface	0.86	0.40	1.75	2.66
Healthy Controls	Dual task, even surface	1.02	0.45	0.98	1.50
	Dual task, uneven surface	1.00	0.38	1.20	1.58

SD = standard deviation

#### Table 3.

Change in cerebral activation (oxyhemoglobin concentration) compared to quiet standing during four task conditions in individuals with visual vertigo and healthy controls.

Group	Task Condition	Prefrontal Region	Beta	SE	t	р	q
Visual Vertigo	No task, even surface	Right	-1.81	1.52	-1.19	0.24	0.43
	No task, even surface	Left	-1.10	1.49	-0.74	0.46	0.71
	Dual task, even surface	Right	-1.60	1.52	-1.05	0.29	0.50
	Dual task, even surface	Left	-0.97	1.47	-0.66	0.51	0.76
	No task, uneven surface	Right	0.71	1.50	0.47	0.64	0.79
	No task, uneven surface	Left	0.54	1.46	0.37	0.71	0.79
	Dual task, uneven surface	Right	-1.48	1.50	-0.99	0.32	0.52
	Dual task, uneven surface	Left	-12.56	1.46	-8.62	< 0.001	< 0.001 *
Healthy Controls	No task, even surface	Right	4.01	1.66	2.42	0.02	0.07
	No task, even surface	Left	4.06	1.71	2.38	0.02	0.07
	Dual task, even surface	Right	2.18	1.63	1.33	0.18	0.37
	Dual task, even surface	Left	3.61	1.68	2.15	0.03	0.10
	No task, uneven surface	Right	7.23	1.65	4.39	< 0.001	< 0.001 *
	No task, uneven surface	Left	7.49	1.69	4.42	< 0.001	< 0.001 *
	Dual task, uneven surface	Right	4.18	1.62	2.57	0.01	0.06
	Dual task, uneven surface	Left	5.02	1.66	3.02	< 0.01	0.02*

Beta = regression coefficients; SE = standard error; t = t-statistic; p = p-value; q = q-value;

\* indicates p 0.05, false discovery rate-corrected.