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Functional brain imaging of multi-sensory vestibular processing during computerized dynamic posturography using near-infrared spectroscopy

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ABSTRACT

Functional near-infrared spectroscopy (fNIRS) is a non-invasive brain imaging method that uses light to record regional changes in cerebral blood flow in the cortex during activation. fNIRS uses portable wearable sensors to allow measurements of brain activation during tasking. In this study, fNIRS was used to investigate how the brain processes information from multiple sensory modalities during dynamic posturography. Fifteen healthy volunteers (9M/6F; ages 28 +/− 9 yrs) participated in the posturography study while undergoing fNIRS brain imaging. Four standard conditions from the sensory organization test (SOT) were performed and a bilateral fNIRS probe was used to examine the cortical brain responses from the frontal, temporal, and parietal brain regions. We found that there was bilateral activation in the temporal–parietal areas (superior temporal gyrus, STG, and supramarginal gyrus, SMG) when both vision and proprioceptive information were degraded; forcing reliance on primarily vestibular information in the control of balance. This is consistent with previous reports of the role of these regions in vestibular control and demonstrates the potential utility of fNIRS in the study of cortical control of vestibular function during standing balance tasks.

Introduction

Maintenance of upright stance relies on the integration of sensory information about a person's spatial orientation obtained from vestibular organs, cutaneous and proprioception receptors, and vision (Lee and Lishman, 1975; Magnusson et al., 1990; Nashner et al., 1982). Current theories suggest that during everyday experiences, the relative information available from these channels must be continuously reweighted (Mahboobin et al., 2005; Mergner and Becker, 2003; Peterka and Loughlin, 2004). For example, when entering a dimly lit room, the postural control system must adjust to the loss of accurate visual input. Although models of sensory reweighting typically assign this integrative role to the central nervous system, direct evidence of the cortical structures involved with this is sparse.

In particular, because of technological restrictions, the role of brain activity in this multi-sensory integration process as it relates to standing postural control has not been directly studied. In general, neuroimaging techniques such as magnetic resonance imaging (MRI) or positron emission tomography (PET) require the patient's head to remain motionless and to lie in the supine position. While FDG (^{18}F-florodeoxy-glucose) based PET is unique in that the compound can be injected outside the PET scanner (e.g. during walking or balance (la Fougere et al., 2010; Shimada, 2012)) and later imaged, the long half-life of the PET compound (108-min) precludes good temporal resolution and prevents the sequential repeated measurements needed to quantify brain activity during the different phases of the SOT paradigm. Research with individuals who have peripheral and central vestibular disorders has implicated regions of the temporal and parietal cortex in multi-sensory integration including the inferior parietal lobe, superior temporal gyrus and supramarginal gyrus (Dieterich and Brandt, 2008). In addition, functional neuroimaging of caloric stimulation (Dieterich et al., 2003; Fasold et al., 2002), vestibular evoked myogenic potential (VEMP) stimulation (Schlindwein et al., 2008), and galvanic vestibular stimulation (Stephan et al., 2005) in healthy persons produces similar findings.

Computerized posturography assessment involves a set of clinical tests used to assess posture and balance control. The sensory organization test (SOT, NeuroCom, Inc) is a component of computerized dynamic posturography that assesses how people use different combinations of sensory feedback to maintain upright stance (Nashner and Peters, 1990). The SOT is based on a series of sensory combinations involving the loss, or degradation, of accurate visual and/or proprioceptive feedbacks about the person's orientation. Proprioceptive information about the angular position of the ankle joint is degraded by sway-referencing the standing support surface in the sagittal plane. In the clinical test, eye closure or sway-referencing of the visual

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enclosure compromises accurate visual feedback. By manipulating the sensory information through these sway referencing and light/dark conditions, the SOT protocol is used to systematically test the person's ability (or inability) to compensate for the loss of sensory information and to maintain postural control. While in some cases balance problems may be due to uncompensated vestibular deficits, dynamic posturography specifically evaluates overall balance ability and provides information on potential fall risk (Furman and Whitney, 2000). In particular, multi-sensory integration dysfunction is often the cause of secondary balance problems associated with brain disorders including multiple sclerosis (Jackson et al., 1995), stroke (Bonan et al., 2004a,b; Ikai et al., 2003), Parkinson's (Nocera et al., 2010; Toole et al., 1996) and Alzheimer's (Suttanon et al., 2012). The SOT paradigm consists of a standard set of six conditions as described by Nashner and Peters (1990) where visual and proprioceptive information are altered or removed. Four of these conditions (SOTs I, II, IV, and V) are designed to probe the interaction of vestibular and proprioceptive information in the presence or absence of visual information (e.g. eyes open/closed). The other two conditions (SOTs III and VI) use a moving visual scene (visual sway-referencing) to examine the effect of conflicting visual information. In clinical practice, SOTs I, II, IV, and V are used to evaluate vestibular disorders while the remaining two conditions have been suggested to be less reliable as clinical tools (Barin, 1992). In this study, only these four vestibular SOT conditions were examined due to both technical limitations and to limit subject fatigue associated with the length of the experiment needed to test all six conditions in pairwise combinations.

In this study, we used a novel brain imaging technique called functional near-infrared spectroscopy (fNIRS). fNIRS uses low levels of light to measure blood flow and blood oxygenation changes in the brain. Thus, fNIRS measures the hemodynamic response in the brain and provides similar information to functional magnetic resonance imaging (fMRI). Several previous studies (reviewed in Steinbrink et al., 2006) have shown close correspondence between fNIRS and fMRI signals with temporal and spatial (linear) correlations of up to $R = 0.98$ (Huppert et al., 2006b) and $R = 0.86$ (Huppert et al., 2006a), respectively. Unlike fMRI, fNIRS is a portable technique that uses fiber optic cables mounted in a wearable head cap. This lightweight head cap allows imaging of the brain even during ambulatory movement and has previously been used to record brain activity during cued stepping (Huppert et al., in press), walking (Miyai et al., 2001; Suzuki et al., 2008), and balance (Karim et al., 2011) studies. The purpose of this study was to record changes in brain activity in healthy volunteer participants, using fNIRS during the four vestibular SOT conditions.

Methods

Experimental subjects

Fifteen healthy, right-handed volunteers (9M/6F, aged 28 +/− 9 yrs) participated in this study. After providing informed consent, all subjects were screened for self-reported histories of vestibular, balance, or mobility impairments. This study was approved by the University of Pittsburgh Institutional Review Board protocol.

Dynamic posturography

All posturography was performed using a NeuroCom (Clackamas OR, USA) Equitest™ posturography platform (see Fig. 1A) while fNIRS data was recorded. fNIRS signals were recorded during testing of four postural conditions corresponding to SOT I (fixed floor — eyes open in light), SOT II (fixed floor — eyes open in dark), SOT IV (sway-referenced floor — eyes open in light), and SOT V (sway-referenced floor — eyes open in dark). Comparisons among these four conditions allow examination of subject balance and brain responses to the loss of accurate visual and proprioceptive feedbacks.

During clinical posturography, each condition is tested separately. However for this fNIRS brain study, this paradigm was modified such that a pair of SOT conditions was tested sequentially in a blocked design. This design is therefore more consistent with standard functional testing in fMRI or fNIRS, which both provide relative measurements of changes in brain activity and require a statistical comparison between conditions acquired within the same scan. In this study, the postural conditions were paired into four comparisons as shown in Table 1. Each fNIRS scan consisted of an initial baseline condition (45 s), a test condition (45 s), and a repeat of the baseline condition (60 s). For each condition-pair, test conditions had less sensory information than the corresponding baseline conditions. The effect of the transition from baseline to test condition was reversed during the final baseline condition.

The comparison presentation order was randomized across subjects. For each subject the four scan series were presented twice making eight total scans. After every two scans, the participant was given a seated rest period for a minimum of 2-min. The total participation time for this study was approximately 60 min including: subject consenting (5–10 min), instrumenting the subject with the fNIRS head cap (20–30 min), and posturography with breaks (26–30 min). For pairs 1 and 2, the Equitest™ posture data was recorded as three separate files due to a limitation of the Equitest™ system that did not allow for smooth transition from fixed to sway-referenced platform as this is not normally done in a clinical setting.

fNIRS instrumentation

During fNIRS recordings, flexible fiber optic cables deliver low levels of light (<0.4 W/cm^2) to an arrangement of source positions on the scalp (see Fig. 1B). Each position contains two wavelengths of light (690 nm and 830 nm), which are used to separate absorption changes differentially due to oxy- and deoxy-hemoglobin. Based on data from previous modeling studies (Wang et al., 1995), the light emitting from a source position in the fNIRS head cap diffuses through the tissue and penetrates the outer 5–8 mm of the cerebral cortex. Light is then detected as it exits the head using a discrete set of fiber optics that carry light back to photon detectors on the fNIRS instrument. Thus, the amount of light traveling between light source locations to detector positions is directly related to the absorption of the underlying tissue between measurement source-detector pair. During evoked brain activity, regional changes in blood flow to the active cortical region alter concentrations of oxy- and deoxy-hemoglobin, differentially changing the light absorption characteristics at different wavelengths due to the optical absorption profile differences in the two hemoglobin states. Changes in hemoglobin can be recovered from fNIRS measurements at multiple wavelengths using the modified Beer–Lambert law. By spatially arranging the optical sensors on the head, the location of the brain signal can be approximated as reviewed in Boas et al. (2004).

In this study, fNIRS data was recorded using a 32-channel continuous wave fNIRS instrument (CW6 real-time system; TechEn Inc; Milford, MA). The instrument uses two different wavelengths of light at 690 nm and 830 nm within the optical window, which allows changes of both oxy- and deoxy-hemoglobin to be recorded. The fNIRS bilateral head cap is made from plastic materials and Velcro and contained 8 sources and 16 detectors. The source-detector pairs were arranged in a nearest neighbor geometry with 3.2 cm source-detector spacing, creating 30 source-detector combinations. fNIRS data were sampled at 4 Hz. Custom acquisition software described in Abdelnour and Huppert (2009) allowed for real-time visualization of brain activity. The acquisition software allows for events to be manually marked by the operator throughout the task to indicate the transitions between SOT conditions. Although manual synchronization is somewhat suboptimal, the Equitest system that was used in this study was a clinical device that could not be modified for research