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Research report

Frontal activation and connectivity using near-infrared spectroscopy: Verbal fluency language study

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ABSTRACT

Near infrared spectroscopy (NIRS) is an optical technique with high temporal resolution and reasonably good spatial resolution, which allows non invasive measurement of the blood oxygenation of tissue. The current work is focused in assessing and correlating brain activation, connectivity and cortical lateralization of the frontal cortex in response to language-based stimuli, using NIRS. Experimental studies were performed on 15 normal right-handed adults, wherein the participants were presented with a verbal fluency task. The hemodynamic responses in the pre- and anterior frontal cortex were assessed in response to a Word generation task in comparison to the baseline random Jaw movement and Rest conditions. The functional connectivity analysis was performed using zero-order correlations and the cortical lateralization was evaluated as well. An increase in oxy- and a decrease in deoxy-hemoglobin were observed during verbal fluency task in the frontal cortex. Unlike in the pre-frontal cortex, the hemodynamic response in the anterior frontal during verbal fluency task was not significantly different from that during random Jaw movement. Bilateral activation and symmetrical connectivity were observed in the pre-frontal cortex, independent of the stimuli presented. A left cortical dominance and asymmetry connectivity was observed in the anterior frontal during the verbal fluency task. The work is focused to target the pediatric epileptic populations in the future, where understanding the brain functionality (activation, connectivity, and dominance) in response to language is essential as a part of the pre-surgical evaluation in a clinical environment.

1. Introduction

Over the past few decades, a new technology for monitoring functional brain activity based on the absorption and scattering properties of near-infrared light (NIR) is developing. The technology uses diffuse NIR light (termed as diffuse optical imaging or near-infrared spectroscopy) in order to obtain useful information from thick tissue samples that are highly scattering in nature, including the brain monitoring through the scalp [56].

Near-infrared spectroscopy (NIRS) employs launching of NIR light (between the wavelengths of 650–900 nm, which corresponds to ∼2 eV photons) on to the tissue surface and detecting the scattered and attenuated NIR signal. The blood components of oxy- (HbO) and deoxy-hemoglobin (HbR) exhibit low absorption and enhanced scattering, thus allowing deeper tissue penetration of the NIR light [7] and quantification of oxy- and deoxy-Hb concentrations in the tissue. NIRS can also detect 'fast' signals in the order of 50–200 ms [4], which is a more direct measure of the neuronal activity than the hemodynamic signals. In other words, NIRS is the only neuroimaging modality that can measure the hemodynamic and metabolic responses associated with neuronal activity, as well as measure neuronal activity directly. Additionally, in comparison to the existing and widely used noninvasive neuroimaging modalities such as EEG, MRI, PET, or SPECT, NIRS can provide excellent temporal sensitivity as well as reasonable spatial sensitivity [56].

To date, NIRS technology has been applied for various functional brain mapping studies. Some of the many applications (sample references listed) of NIRS to neuroimaging include: (i) cerebral response to visual [21,37,46], auditory [50] and somatosensory stimuli [16,40]; (ii) cerebral response to motor system [8,24,53] and language [52]; and (iii) prevention and treatment of

Abbreviations: EEG, electroencephalogram; *f*MRI, functional magnetic resonance imaging; HbO, oxy-hemoglobin; HbR, deoxy-hemoglobin; HbT, total hemoglobin; HomER, hemodynamic evoked response; HRF, hemodynamic response function; MRI, magnetic resonance imaging; NIR, near infrared; NIRS, near infrared spectroscopy; PET, positron emission tomography; PMT, photon multiplier tube; SPECT, single photon emission computed tomography.

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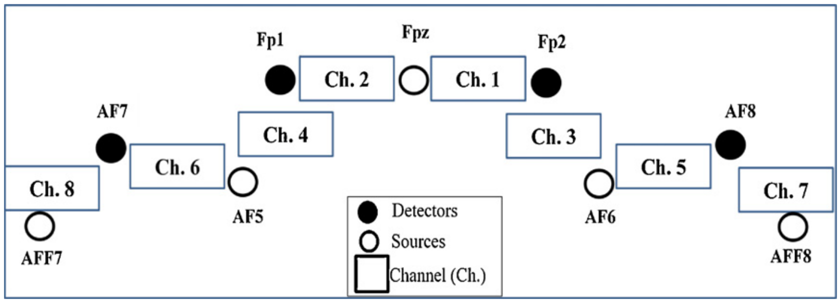

Fig. 1. Source–detector layout corresponding to the prefrontal and the anterior frontal region of standard 10-10 [30] electrode placement system. The solid circles and hollow circles used in the figure represent detectors and sources respectively. The hollow squares represent the path between the sources and detectors (i.e. channels). All the even number channels correspond to the left frontal cortex, and the odd number channels correspond to the right frontal cortex.

seizures [1,54,55,59] and psychiatric concerns such as depression [11,36,41], Alzheimer disease [13,20,25] and schizophrenia [15,42], as well as stroke rehabilitation [6,38,48,57]; (iv) detection of brain ischemia [34,43], necrosis, and hemorrhage [61].

In the area of language development and brain activation/functionality using NIRS, researchers have performed studies using various experimental paradigms in normal adults and pediatric populations [5,22,23,35,49]. The studies were focused primarily in understanding the differences in the hemodynamic responses in different (typically frontal and temporal) regions of the brain in response to language-based stimuli [22,23,29,33,35,45,49]. In addition, a few researchers have analyzed the cortical lateralization and dominance features of the brain in different populations, based on their application focus (e.g. schizophrenia, epilepsy) [18,31,33,39,58,60].

All the language studies carried out so far using NIRS [18,22,29,31,33,35,39,45,49,58,60] have focused on the brain activity differences and/or cortical dominance. However, the fundamental aspect of the brain connectivity across spatial regions of the frontal cortex during a language task has not been performed to date.

In the current study, NIRS is used to understand the brain activation, functional connectivity, as well as the cortical lateralization in response to verbal fluency task. The study was performed using a multi-channel NIRS instrument to non-invasively map the frontal cortex of 15 normal adults in response to three stimuli – a verbal fluency Word generation task, random Jaw movement task, and Rest conditions. The hemodynamic responses in terms of HbO, HbR, and HbT were used to statistically evaluate the differences in the brain activation amongst the three stimuli. Additionally, the functional connectivity of the left and right cortex was evaluated along with the cortical lateralization for left or right dominance. The brain activation, connectivity, and lateralization results were compared for any correlations amongst each other. The future goal of our research team is in non-invasive pre-surgical evaluation of epileptic children (in comparison to normal controls) using NIRS approach to map the activation and connectivity of the critical regions of the brain controlling language and motor functions.

2. Materials and methods

2.1. Instrumentation

A frequency-domain based optical imaging system, Imagent (ISS, Inc., Champaign, IL) was used to perform the studies. This near-infrared optical spectrometer (Imagent) is a multi-channel system with 32 intensity-modulated laser diodes (16 emit 690 nm laser light, and the remaining 16 at 830 nm wavelength), and four gain-modulated photomultiplier tube (PMT) detectors that collect the optical signals at both the wavelengths separately. The light sources are electronically multiplexed at a frequency of 100 Hz (10 ms on-time per laser diode) to time-share the four optical detectors. The modulation frequency, which can be adjusted from (100 to 300 MHz) was set at 110 MHz. This frequency was chosen due to the fact that it allows for maximum depth penetration of optical signals into the tissue [19]. The entire instrument is computer controlled and the frequency-domain measurements (DC, AC, and phase shift) are obtained from different source–detector locations using a Fast-Fourier-Transform data acquisition card.

In the current study, the frontal cortex of the brain was imaged using 5 laser diodes sources (at each wavelength, 690 and 830 nm) and 4 detectors. The source–detector layout (based on the 10–20 electrode placement) on the pre- and anterior frontal cortex is schematically shown in Fig. 1. A custom-built "brain cap" was used to hold the source and detector fibers in place during the imaging studies. Optical signals were acquired in real-time (at ~1.3 Hz) from each source–detector pair or channel (Ch.), in response to the stimuli presented (described in Section 2.3) using the software package (BOXY) of the instrument.

2.2. Participants

Fifteen normal and right handed adults were enrolled for the current study that was performed at The Brain Institute of Miami Children's Hospital (Miami, FL). This study was approved by the Florida International University's (FIU) Institutional Review Board (IRB) and written consent(s) were obtained from the participants.

2.3. Stimulus and procedure

The current NIRS study is focused on understanding how the brain responds to language cognitive tasks in the pre-frontal and anterior frontal cortex of the brain. Participants were seated in a comfortable chair (upright) in a quiet room and the custom-built optical cap was placed on their head (with minimal hair interference). The participants were asked to respond to the language-based verbal fluency task(s) presented to them. Prior to the block-designed tasks, there was an initial 30-s Rest period. This was followed by the block-designed task that consisted of a 30-s of Word generation (W), 30-s of random Jaw movement (J) and 30-s of Rest (R). During the Rest period, the participants were asked to minimize their thoughts and look at the sky (through the window). During the Word generation task the participants were asked to say as many possible words (without repeating) beginning with a randomly presented alphabet. During the Jaw movement task, the participants were asked to randomly move their jaw without actually speaking. The physiology behind the used block design is that the, W task consists both of cognitive thinking and Jaw movement due to the requirement of task, as explained above, which necessitate both thinking and speaking. The process of speaking cannot be separated from Jaw movement and hence J task (which entails pure Jaw movement) was used without any cognitive thinking, thus providing the contrast between the two tightly coupled W and J tasks. The hypothesis of the study is that the hemodynamic response during a language-based cognitive task will be different from baseline Rest condition or under random Jaw movement, with no cognitive (verbal) response to presented stimuli. The W–J–R block was repeated 5 times on each participant. The entire study on each participant was repeated a second time after a 30 min span between repetitions. During these NIRS studies, the participants were asked to keep their head still with minimal movement.

2.4. Optical data analysis

Optical measurements (in terms of AC, phase shift, and averaged AC (i.e. DC)) were obtained in real-time in response to the activation stimuli presented for each block (5), repetition (2), and participant (15). The acquired optical data contains information of the attenuated diffuse NIR light emerging from the frontal cortex of the brain. In the current studies, only the average of the modulated light signal (i.e. DC signal) was employed in post-processing real-time one-dimensional (1D) hemodynamic responses across each source–detector pair (or channel). As stated previously, the raw optical data was acquired and saved using the BOXY software. The data was further post-processed using a HomER [28] (Hemodynamic Evoked Response) software, developed in the Photon Migration Lab (PMI) at Massachusetts General Hospital (MGH, Harvard, http://www.nmr.mgh.harvard.edu/PMI), HomER provides an easy way to process and visualize the data in terms of hemody-