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THE RELATIONSHIP BETWEEN P300 EVOKED POTENTIALS AND PREFRONTAL CORTEX OXYGEN USE: A COMBINED EEG AND NIRS STUDY

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ABSTRACT

THE RELATIONSHIP BETWEEN P300 EVOKED POTENTIALS AND PREFRONTAL CORTEX OXYGEN USE: A COMBINED EEG AND NIRS STUDY

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The P300 subcomponent, P3b, is an event related potential detected at the scalp surface when a working memory comparison results in differences between the contents of working memory and incoming stimulus information. Previous research has indicated that as infrequent targets become more difficult to detect (morphologically similar to a frequent non-target stimulus) the P300 becomes attenuated. fMRI research has also indicated increased prefrontal cortex (PFC) activity during P300 generation. To examine the relationship between P3b amplitude and PFC activity participants performed an easy and difficult target detection task in both EEG and NIRS called the oddball. The EEG and behavioral results confirmed prior reports that difficult to detect targets result in attenuated P3b amplitude, as well as increased misses and reaction time, in comparison to easy to detect targets. NIRS results indicated that detection of targets generally lead to greater increases in oxygenated hemoglobin and decreases in deoxygenated hemoglobin in lateral compared to medial optodes. Additionally, oxygenated hemoglobin increased in the right medial PFC in easy compared to difficult conditions. Taken together, the results of this study and theories behind P3b attenuation suggest that the right medial PFC is involved in attention to salient stimulus features (bottom-up attention) and the lateral PFC is involved in sustained attention to the task (top-down attention). Thus, P3b attenuation is reflective of delimiting attention to salient features and allowing task driven attention to initiate the working memory comparison.

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LIST OF SYMBOLS AND ABBREVIATIONS

ACC: Anterior Cingulate Cortex

ATP: Adenosine Triphosphate

BOLD: Blood Oxygen Level Dependent

CBF: Cerebral Blood Flow

CPT: Continuous Performance Test

CG: Cingulate Gyrus

dB: Decibels

ΔOD: Change in Optical Density

EEG: Electroencephalogram

ERP: Event Related Potential

fMRI: Function Magnetic Resonance Imaging

HbO: Oxygenated Hemoglobin

HbR: Deoxygenated Hemoglobin

HbT: Total Hemoglobin (HbR + HbO)

HRF: Hemodynamic Response Function

ICA: Independent Component Analysis

INS: Inferior Insula

IPL: Inferior Parietal Lobe

IT: Inferior Temporal Cortex

kΩ: Kiloohm

μV: Microvolt

NIRS: Near Infrared Spectroscopy

NMR: Nuclear Magnetic Resonance

OD: Optical Density

P300: ERP component with positive peak around 300ms

P3a: P300 subcomponent with anterior scalp location

P3b: P300 subcomponent with central-posterior location

PCA: Principal Component Analysis

PET: Positron Emission Tomography

PFC: Prefrontal Cortex

PPC: Posterior Parietal Cortex

PrCS: Precentral Sulcus

STS: Superior Temporal Sulcus

INTRODUCTION

The selection of appropriate objects in the environment is an important aspect of survival. If an organism is unable to remember what foods are safe to eat or how to direct attention to potentially dangerous foods or other objects, this would have a negative impact on the organism's survival. Humans and other animals have brain systems that support the functions of memory and orientation of attention. Research by Sutton et al. showed an event related potential (ERP) component detected in central electroencephalograph (EEG) electrodes, which they called the P300 and hypothesized to be related to target detection and stimulus uncertainty (Sutton, Braren, Zubin, & John, 1965). More recent hypotheses, however, have emerged in support of the P300 as an index of attentional and memory functions (Polich, 2007; Polich, 2012).

P300 event related potential components detected by EEG are usually produced by an oddball paradigm. Different variants of the oddball task exist. The single stimulus oddball task presents subjects with an infrequent stimulus dictated as the target, in which the participant must respond to by counting or a button press. The two stimulus oddball repeatedly presents the subject with a frequent standard stimulus not requiring a response and an infrequent, low probability, target stimulus requiring a response. The three stimulus oddball involves the presentation of a standard, an infrequent low probability target requiring response, and a novel or distractor of low frequency and probability which doesn't require a response (Polich, 2007). The P300 is a signal produced from averaging preprocessed EEG signals and is defined by its positive amplitude from baseline to peak and latency occurring around 300ms post target presentation. The amplitude and latency

can vary depending on task conditions, stimulus modality, subject age, and many other factors (Polich, 1986; 1987; 2007; 2012). Regardless, the need for attention and a response to the target during the oddball task will produce a P300 (Polich, 2012). For the sake of consistency the term P300 will be used here to refer to the canonical event whereas the P3a and P3b subcomponents, related to frontal attention areas and temporal-parietal memory areas respectively, will be elaborated on later and used when referring to their specific roles in the P300 event.

Newer neuroimaging modalities have become available since the discovery of the P300 and have been used to inform our knowledge about the brain structures that are responsible for producing the signal. fMRI can detect changes in paramagnetic effects of deoxygenated hemoglobin related to brain function. This signal is called the blood oxygen level dependent (BOLD) signal (Ogawa, Lee, Nayak, & Glynn, 1990). Using BOLD and ERP measures as well as decompositions of ERPs known as independent component analysis (ICA), a hypothesis to explain the P300 has emerged which relates frontal attention areas to the P3a subcomponent, and temporal-parietal memory areas to the P3b (Bledowski et al., 2004; Polich, 2007; Potts, Liotti, Tucker, & Posner, 1996; McCarthy, Luby, Gore, & Goldman-Rakic, 1997; Mulert et al., 2004).

Using fMRI is costly and physically restricting, but other measures, such as near infrared spectroscopy (NIRS), are cheaper and more mobile. Similar to fMRI, NIRS measures changes in oxygenation of hemoglobin as a function of the brains metabolic needs (Boas & Franceschini, 2009). Almost no published research exists in which the oddball task has been used during a NIRS recording, although a couple of reports exist (Akgül, Sankur, & Akin 2005; Kennan et al., 2002). In response to this gap in research, the

current study will examine the prefrontal cortex (PFC) using NIRS and the posterior P300 using EEG while subjects perform oddball tasks of varying difficulty to assess attentional resource allocation as a function of task difficulty.

EEG and ERPs

Before the research and theory behind the P300 ERP component can be reviewed it is important to understand where EEG and ERP signals originate. Electrical activity in the brain is the result of ionic currents in axons of neurons being initiated by biochemical messengers attaching to the appropriate neurotransmitter receptor (da Silva, 2009). These ionic currents can be detected at the surface of the scalp using recording electrodes that transmit the signal to an amplifier. EEG data is represented as a series of positive and negative amplitude changes over time. These changes in amplitude, called oscillations, are reflective of the activity of specific populations of neurons, called neuronal masses. Thus, EEG records brain activity as it relates to behavior, attention, memory, emotion, sensation, perception, and consciousness.

As the EEG signal travels from the neurons to the detecting electrode it must travel through other brain masses, cerebral spinal fluid, bone, and skin. The result is a signal that cannot be localized to the brain region beneath the electrode (called the inverse problem) and thus EEG has poor spatial resolution. However, EEG has extremely high temporal resolution as it measures electrical potentials that occur within milliseconds of stimulation or action. Despite the lack of spatial resolution, EEG electrodes are typically placed according to a standard system called the 10-20 system, in which letters denote the region beneath the electrode, even numbers are over the right hemisphere, and odds over the left (e.g., F2 = right frontal, O7 = left occipital, Cz = central midline).

While EEG can typically be thought of as the electrical activity of neurons detected at the scalp, this is an over-simplification. Various factors play into whether the activity of

neurons will be detected at the scalp in the first place. Furthermore there are severe limitations regarding the ability to localize the source of an EEG signal. EEG is measured at the scalp, some distance from the neurons generating the signal, and detection of the signal only occurs if the neurons are arranged regularly and activated synchronously. Typically, this means that the neurons are in a specific morphological arrangement, called palisade, where the main axes of the dendritic trees are parallel to each other, but perpendicular to the cortical surface. In the palisade pattern the neurons can be activated causing the flow of a current that has components which travel parallel to the axon and are synchronized. Components which are perpendicular to the axons cancel out, thus creating a detectable dipole field. The EEG does not detect the action potential, but rather synchronized excitatory and inhibitory postsynaptic potentials of neuronal masses. These changes in membrane potential are slower and cover a larger area of the axon allowing for synchronization of neuronal firing and a detectable field potential at the scalp surface (da Silva & Van Rotterdam, 2004).

Groups of neurons in a palisade pattern and their supporting cells can be thought of as a neuronal mass which fire in rhythmic patterns called oscillations. Thus, EEG can be defined as the scalp-based recording of the oscillatory electrical events of neuronal masses in a palisade pattern. This oscillatory nature has been observed on the course of minutes for one cycle or as fast as 600 Hz. The observed frequencies have been categorized into different frequency bands: delta (.05-4 Hz), theta (4-8 Hz), alpha (8-12 Hz), beta (12-30 Hz), and gamma (>30 Hz). Frequency bands are not functionally defined and neuronal masses can oscillate at more than one frequency, while neighboring frequency bands can compete in the same mass. Since different frequencies can be generated by one neuronal

mass, the role a particular frequency band plays in brain process is difficult to determine without knowing the generating source as well as events eliciting the activation (Buzsáki & Draguhn, 2004).

The inverse problem of EEG, as well as the ambiguity of the function of electrical oscillations recorded from the scalp, make it difficult to distinguish the meaning of transient events, such as ERP components. In an effort to understand the meaning of changes in scalp recorded EEG data, researchers commonly use an averaging procedure centered on a particular stimulus event that is marked (flagged) in the data. This methodology is called evoked potential or ERP. To generate an ERP, the raw EEG data is flagged every time some experimental manipulation takes place, data segments of equal length are extracted based on the stimulus flag (e.g., 100 ms before flag to 1000 ms after flag),. Segments of data from the same experimental condition are then averaged together. The idea behind this procedure is to reduce the signal-to-noise ratio, by assuming that common transient events will synchronize when combined and random events will average to zero. The remaining waveform is similar in appearance to the raw EEG record in that there is a series of positive and negative deflections over time. With the ERP, however, what remains is assumed to be components of data that are solely related to the experimental manipulation or task. The deflections in the ERP are labeled according to their directional polarity, the order in which it occurred (e.g., N2 for second negative), or latency (e.g., N200 for negative at 200 ms). For example, the first positive going component that also occurs at 100 milliseconds can be labeled both as P1 (order) or P100 (latency; Key, Dove, & Maguire, 2005)

The difficulty of localizing a signal detected using EEG makes it difficult to comment on the generators of the signals detected at the scalp. This handicap extends to ERPs. Further, the components detected at the scalp may be the result of latent components being mixed before detection (Kappanmen & Luck, 2012). Despite these challenges, EEG and ERP contain useful information regarding cognitive and behavioral events. One commonly studied ERP component is called the P300 as it is a component with a positive peak that begins to appear around 300ms post stimulation. P300s occur in any task that requires the detection of a target stimulus, thus is frequently researched (Polich, 2007). The P300 is thought to be related to the detection of a target and represent different processes related to the detection of a target such as memory and attention (Polich, 2007; Polich, 2012).

Context Updating Theory of P300

The context updating theory of P300 suggests that the P300 is an index of activities related to revision of the mental representation of a stimulus (Donchin, 1981). Evidence that the model may be valid comes from the initial stimulus train and oddball experiments. When Sutton and colleagues (1965) developed a method to readily produce a P300, they had presented subjects with a cue that informed the participant of the stimulus modality (visual or auditory) of the next stimulus. When the cue was followed by the incorrect modality it was found that the P300 appeared, thus these researchers related the P300 to stimulus uncertainty (Sutton et al., 1965).

Subsequent research using a series of stimuli with unpredictable target deviants also found P300 like waves, but a P300 like wave was also reported by researchers who did not require a response to the deviant stimuli (Ritter, Simon, & Vaughan Jr., 1972; Roth, 1973). In what is considered the first oddball study, Squires et al. (1975) were able to show that there are indeed two different P300-type waves. While using a traditional two-stimulus oddball paradigm participants were required to either attend or ignore (by reading a book) auditory stimuli. Both conditions revealed a P300-type wave, but the P300 detected during the attention condition was larger and had a central-posterior electrode location while the P300 produced in the ignore condition had an anterior electrode distribution. They named the anterior component P3a and the posterior component P3b. Furthermore an analysis technique called principal component analysis (PCA) revealed that these components were likely produced by different neuronal masses and not a reiteration of the P300 as was previously understood. These authors concluded that task relevant target detection leads to

P3b generation, while P3a is generated by deviant stimuli without task relevance (Squires, Squires, & Hillyard, 1975).

To test the findings of Squires et al., the three stimulus oddball was introduced. In this version of the oddball task, attention is paid to all stimuli, but there is an additional infrequent and task irrelevant stimulus. Results from initial studies using this paradigm confirmed that the P3a is generated in response to deviant low probability stimuli that are task irrelevant while P3b is generated in response to low probability task relevant stimuli (Courchesne, Hillyard, & Galambos, 1975). These studies were taken by proponents of the context updating theory as evidence that stimuli entering the processing stream undergo a working memory comparison. When stimulus signals enter the processing stream they are compared to the contents of working memory, if the contents do not match then a P300 is produced as the contents of working memory are updated, if they do match only the sensory evoked components (N100, P100, N200) are produced (Polich, 2007). Thus, in this model, the P300 events are an index of the change in working memory contents.

For a change in working memory storage to occur, an organism must first orient its attention towards the new stimulus. Orientation is a function of attention, and thus P300 may also index functions of attention. Indeed, when subjects participate in two and three stimulus oddball tasks in which the discrimination between standard and target is made more difficult, thus needing more focused attention, the amplitude decreases and latency increases for the P300 (Polich, 1987; Comerchero & Polich, 1999). These results suggest that P300 events may index attentional resources being used for the detection of a stimulus so that increased focused attention results in lower amplitude P300s and decreased use of focused attentional resources results in higher amplitude P300s.

Research attempting to determine the meaning of the P300 signal has turned to other imaging techniques that may advance this field of study and detect the generators of this component. The context updating theory provides an informative perspective behind the meaning of the P300. However, new hypotheses using fMRI data are emerging to more specifically define the meaning of the P300.

fMRI and Oddball

A confound associated with EEG and ERP data is that scalp topography does not precisely indicate the location of the underlying neural generator. To address this weakness researchers have begun to use other imaging modalities, like fMRI, to better inform the understanding of P300 generators (Bledowski et al., 2004; McCarthy et al., 1997; Mullert et al., 2003). fMRI is not without limitations, one issue is that the signal detected is delayed depending on the oscillation frequency of the neuronal mass. Specifically, the timing of BOLD signal changes (.5-5s following neuronal activation) is reflected by the relationship between gamma and beta bands (Magri, Schridde, Murayama, Panzeri, & Logothetis, 2012). This means that localizing the source of an electrical event that is detected within milliseconds using EEG can be difficult and it may only be possible to determine structures involved in the overall task (McCarthy et al., 1997). Below, the basis of the fMRI BOLD signal is briefly reviewed along with a comprehensive review of fMRI research utilizing the oddball task.

When a neuron is active, its membrane potential depolarizes and afterwards returns to its resting potential. This requires energy in the form of adenosine triphosphate (ATP) which is largely produced in the neuron's cell body by the oxidation of glucose. The oxygen for this process is delivered by hemoglobin via capillaries which cover the whole brain. There are only a few hundred microns between capillaries which gives fMRI high spatial resolution. When atomic nuclei with the nuclear magnetic resonance (NMR) property are placed in a strong and static magnetic field they will begin to precess (rotate on an axis) parallel (low energy) or anti-parallel (high energy) in relation to the magnetic field. Most

atomic nuclei take on the low energy state and thus can be excited into the high energy state using a resonant frequency. Once exciting energy is removed, the atomic nuclei return to the low energy state. The energy released during the return to the parallel state can be recorded and is the basis of the MR signal. fMRI uses a series of magnets to align the precession of hydrogen nuclei that are ubiquitous in water. (Heutell, Song, & McCarthy, 2009). Deoxygenated hemoglobin (HbR) is paramagnetic and affects the precession of hydrogen atoms, which affects the MR signal detected (Thulborn, Waterton, Matthews, & Radda, 1982). The MR signal increased in brightness as a function of brain activity not due to an increase in oxygenated hemoglobin (HbO), but a decrease in suppression of the MR signal induced by HbR (Heutell, Song, & McCarthy, 2009). This signal is referred to as the BOLD signal and has been used in many experiments to localize brain activity, including activity related to oddball tasks.

The utilization of fMRI in conjunction with oddball tasks has led to the localization of brain regions that are active during the oddball task and differently active depending on task conditions. This means that fMRI could be used to localize brain regions related to the orienting to and detecting of task relevant stimuli. Based on fMRI and positron emission tomography (PET) findings that a network involving prefrontal, temporal, and parietal regions is active during working memory, one group employed the oddball task during fMRI to see if similar regions were active, thereby lending indirect support to the role of the P300 indexing working memory (McCarthy et al., 1994; McCarthy et al, 1996; Smith, et al., 1995). Participants went through 8 experimental runs, in each run they were shown the character sting ‘OOOOO’ as the standard and ‘XXXXX’ as the target at a ratio of 1024 standards to 55-63 targets across all runs. The response to targets was to silently count

them; there was no response for standards. Standards and targets were presented for .5s per 1.5s (1sec between trials) with at least twelve standards between targets. The data was analyzed by taking the first six MR images before and eight after target presentation. Results showed that transient MR signal increases occurred as soon as 1.5s following target onset in the middle frontal gyri and inferior parietal lobe-areas that had previously been identified as being involved with working memory. The authors were careful to point of that the activation detected was likely not in response to the synaptic activity related to generating the P300, but the more sustained activation of a neuronal system active during target detection (McCarthy et al., 1997).

The next logical path for fMRI-oddball research was to examine the brain activations in response to a three stimulus oddball. Researchers approaching this problem also used fMRI compatible high density EEG to record both EEG and fMRI simultaneously and then used the fMRI results to constrain EEG localization analysis. Participants were presented with two conditions in a three stimulus oddball task. The circle condition consisted of a circle as the standard, a larger circle as the target, and the distractor as a square. In the square condition the standard was a square, the target a larger square, and the distractor a circle. Stimuli were colored blue and presented once every 2s for 75ms (2s between trials) in two runs consisting of 350 stimuli each. Probabilities of target, distractor, and standard were .05, .05, and .9 respectively. The ERP results confirmed previous results finding the P3a component in anterior electrodes in response to distractor stimuli and P3b in central-posterior electrodes in response to target stimuli. fMRI restricted source analysis revealed six bilateral regional sources of electrical activity: PFC, precentral sulcus (PrCS), inferior parietal lobe (IPL), posterior parietal cortex (PPC), inferior temporal cortex (IT),

and anterior insula (INS). Two lateralized sources were detected, one in the right superior temporal sulcus (STS) the other in the right cingulate gyrus (CG). Sources found to be responsible for P3b generation included IPL, PPC, and IT. Sources related to P3a generation included PrCS and INS. The remaining sources may be related to other components for instance bilateral PFC sources activated roughly 500ms post stimulus (in line with latencies reported for P3a and P3b) were found in both target and distractor conditions. The authors concluded that parietal and temporal areas were responsible for the generation of P3b while precentral areas and insula were related to P3a (Bledowski et al., 2004).

The fMRI findings presented here support the context updating theory in that brain areas associated with working memory and attention orientation are activated. The studies reviewed in this section found PFC activation that was anticipated given previous research using attentional tasks as well as parietal and temporal activation (Bledowski et al., 2004; McCarthy et al., 1997). Given evidence provided by fMRI, however, new theories now exist to better elucidate the meaning of the P300. While context updating theory is still referred to for its perspective on the larger truth behind the meaning of the P300, the new theories focus more on the attention and working memory neural networks involved in target detection that might produce the P300 signals.

P300 Meaning

EEG and ERP data contain useful information, but do not directly reflect all the activity of neurons involved in a neural network. The P300 signal results from EEG data that reflects the activity of certain neurons. Therefore, the P300 does not provide a complete picture of the neural activity related to target detection, rather it is a starting point for understanding how behavioral and cognitive processes work. While the P300 certainly seems to be well correlated with the detection of task relevant targets, considering fMRI data and neuropsychological theories in addition to EEG findings has helped provide a way to understand complex neural events and their relationship to behavior and cognition. The context updating theory hypothesized that a working memory comparison produced the P300 when new stimulus information did not match contents of working memory. Additionally, research on attentional networks and subsequent fMRI-oddball studies found that attention related areas were certainly involved in a target detection network. With all this new information new theories have emerged from the context updating theory.

The results from fMRI and ERP studies have led to a hypothesis that the P300 may be an index of neuronal inhibition related to limiting extraneous neural activity to facilitate the transfer of stimulus information from frontal to temporal and parietal areas (Polich, 2007). Points in support of this view include the findings of oddball studies showing that rare stimuli illicit larger P300s than common stimuli and rare stimuli also elicit PFC activity (Polich, 1986; McCarthy et al., 1997). In this view the P3a is produced by attention driven working memory changes and the P3b results from temporal and parietal activation during memory updating. Studies in both monkeys and humans have found evidence of a

pathway communicating information from attentional and working memory frontal areas to temporal and parietal regions (Simons & Spiers, 2003). As infrequent and rare stimuli may be biologically important, it would be beneficial to have a system dedicated to detecting such stimuli and delimiting unnecessary neural activity while promoting resources be dedicated to attention and memory.

The P300 may reflect activity of an inhibitory system acting on attention and memory, as such, every P300 can be thought to consist of P3a and P3b subcomponents. However, the topography and timing of both components are modulated by affects such as attentional arousal, task demands, and modality, such that when only attentional processes are engaged the P300 has an anterior distribution (P3a) and when subsequent memory processes are engaged the P300 has a central-posterior distribution (P3b; Polich, 2007). Indeed, the study by Bledowski et al. discussed in the previous section found prefrontal activity in both target and distractor conditions, but detected prefrontal, parietal, and temporal activity in target conditions (Bledowski et al., 2004). Furthermore, structural MRI research has found prefrontal grey matter (brain tissue consisting of main cell body and dendrites) volumes are positively correlated with P3a amplitude and parietal lobe grey matter volume is positively correlated with P3b amplitude (Ford et al., 1994). Neuroelectrical arguments supporting the view that rare and task relevant stimuli attract focal attention comes from research suggesting that P300 waves are the result of theta and delta oscillation synchronizations, and the P3b is in part due to alpha desynchronization (Başar-Eroglu, Başar, Demiralp, & Schurmann, 1992; Yordanova, Kolev, & Polich, 2001). Human studies have shown midline theta activity is generated by the PFC and may modulate communication between PFC and medial temporal lobe during memory tasks

(Anderson, Rajagovindan, Ghacibeh, Meador, & Ding, 2009; Ishii et al., 1999). Additionally, monkey studies have shown coupled theta activity between area V4 of occipital cortex and the PFC are related to visual task short-term memory performance (Liebe, Hoezer, Logothetis, & Rainer, 2012). The evidence from neuroimaging studies has supported the idea that the P300 components are related to attention and working memory as proposed by the context updating theory.

Taken together the evidence reviewed suggests that a network exists between prefrontal, temporal, and parietal lobe structures for attention and memory processes meant for the detection of relevant, but infrequent, stimuli. The P300 waves may also index the delimiting of other neuronal functions as the P300 waves are typically larger than other ERP components and P300 amplitudes decrease in studies in which subjects perform an oddball task in addition to another task that engages attention and memory processes (Isreal, Chesney, Wickens, & Donchin, 1980; Polich, 2007). Furthermore, some studies have shown that words correlated with a larger P300 during encoding are subsequently recalled more accurately, lending support to the idea that the P300 may be the result of neural inhibition related to focused attention and memory consolidation (Fabiani, Karis, & Donchin, 1986). All of the imaging evidence gathered so far and resulting theories agree the P300 waves index attention and memory processes associated with the detection of novel and task relevant stimuli.

New Perspectives Using NIRS

fMRI and EEG recordings have helped to detect brain activity related to attention and memory function particularly as it pertains to the detection of rare, alerting, and/ or task relevant stimuli. While EEG may be relatively affordable, fMRI is not and access to scanners may be limited. Fortunately, other means of measuring cerebral blood flow (CBF) and the related behavioral and cognitive functions exist. One such method is near infrared spectroscopy (NIRS). As the current study utilized NIRS, I briefly discuss the NIRS measurement and review NIRS studies related to target detection, attention, and memory.

NIRS, in studies of the brain, utilizes near infrared light from 650-950 nanometers emitted by lasers placed on the scalp to detect changes in the concentration and oxygenation of hemoglobin in the brain tissue (Boas & Franceschini, 2009). The light is sent through the scalp and disperses in a multitude of directions through the brain and surrounding tissues and is then recorded by a detector elsewhere on the scalp. Some of the light is sensed by the detector(s), but some of the light is also absorbed by the tissue and some of the light exits the head without detection (Orbig et al., 2000). NIRS is capable of discerning between HbO and HbR concentrations. However, determining concentrations of HbO and HbR is not the measurement of NIRS so some changes must be made to the detected signal (Huppert, Diamond, Franceschini, & Boas, 2009).

NIRS is a measure of light intensity (how bright a light is) measured in units of power (dB). Since the goal of NIRS is to determine changes in HbO and HbR, the light intensity must be converted to hemoglobin concentrations. To do this, computer software is used that performs transformations on the signal converting the measure from light

intensity to optical density, that is, how much light was absorbed by the tissue. Lastly, as it is known that HbO and HbR are the strongest absorbers of visible and near infrared light, optical density can be converted into hemoglobin concentrations. Research using NIRS has limitations regarding spatial resolution as NIRS is only capable of detecting changes in hemoglobin concentration within the first centimeter of cortex (Boas & Franceschini, 2009). In that first centimeter the changes in HbO and HbR can be detected, especially large transient events related to cognitive and behavioral function. Research on the cat brain has shown that when oxygen is supplied to a brain region it is not as localized as one might think. Rather, there is an initial increase in HbR within 1-2s that is thought to be highly localized as the brain is using oxygen that is already available near the active region. This is followed by over-compensatory oxygen delivery to areas 3-5 cm around the active area peaking around 6 seconds after a neural event (Malonek & Grinvald, 1996). fMRI has received more research attention and can image the whole brain, however, NIRS offers the benefits of mobility for the subject and is more cost effective.

Although not used to the same extent as in EEG or fMRI, the oddball paradigm has been used with NIRS. Using an auditory oddball paradigm one group performed a simultaneous EEG and NIRS study to detect changes in hemoglobin concentrations related to the oddball task. EEG data was collected from a single electrode at position Pz and NIRS data was collected with a 9x9 cm optical array with 24 recording optodes over the left temporal cortex. Standard stimuli were 1000Hz tones while target stimuli were 1500Hz, stimuli were presented for 100ms with 1.5s between stimuli. Tones were presented with 19s between targets so hemodynamic activity could return to baseline. The article did not make clear what the response to targets was to be. Analysis of the EEG data showed the

typical P300 (P3b) event following the appearance of the target stimulus at electrode Pz. The analysis of NIRS recordings taken from the left temporal region showed significant changes in the hemodynamic response function (HRF) for HbO (Kennan et al., 2002). The results of this study are in line with fMRI and PET studies that found temporal activation during working memory or oddball tasks (Bledowski et al., 2004, Kirino, Belger, Goldman-Rakic, & McCarthy, 2000; McCarthy et al., 1997; Smith et al., 1995; Warbrick, Reske, & Shah, 2013). In a different study, using the exact same visual oddball task from McCarthy et al. (1997) described earlier, participants performed the task while undergoing NIRS recordings targeting the prefrontal region. The aim of this particular study was to determine if NIRS signals could be broken into different frequency bands, but the authors were able to determine that there were hemoglobin changes related to the task in PFC regions (Akgül, et al., 2005). The oddball paradigm has not received much attention in NIRS studies, but a similar paradigm called the continuous performance test (CPT) has been used finding similar results (Rosvold, Mirsky, Sarason, Bransome, & Beck, 1956).

Although there does not seem to be any literature linking the oddball and CPT one article describes the CPT as being characterized by rapid presentation, response to a target, and low target probability (Cornblatt & Kellp, 1994). Toichi et al. examined the difference in PFC activation during tasks of higher cognitive function and attention tasks (2004). They used four different experiments, but of particular interest is an experiment using CPT. While performing the CPT participants were shown a series of single letters over the course of 30s at a rate of either .5 or 1s per trial and had to respond by clicking a mouse whenever an X or O was on screen. The different task conditions made the task more difficult as stimuli were presented more rapidly. Analysis of the NIRS data revealed an increase in

HbO, HbR, and total hemoglobin (HbT) during attention tasks, particularly during the CPT, compared to resting baseline. Furthermore, the more difficult CPT increased in HbR even more than the easier CPT. While comparing CPT results to verbal and non-verbal cognitive tasks the authors concluded that as more attention is needed to perform the task, resources in the frontal cortex are recruited (Toichi et al., 2004). The results of this study were in line with an earlier NIRS finding using the CPT that found an increase in HbR and HbO in the right hemisphere PFC during task compared to baseline (Fallgater & Strik, 1997).

In summary, NIRS is used to monitor the oxygenation of hemoglobin in the first centimeter of the cerebral cortex by emitting light through the skull that can be detected at the scalp surface. The use of NIRS for studying cognitive and behavioral functions has not seen the fanfare of fMRI, but offers a more cost effective way to look at similar measures. While the oddball in particular has not been used in NIRS as much as it has in fMRI and EEG, the CPT, which is similar to the oddball, has seen some use. The findings in NIRS using both the oddball and CPT corroborate fMRI and PET findings that the PFC is involved in tasks which require attention to a rare target stimulus (Akgül et al., 2005; Fallgater & Strik, 1997; Kirino et al., 2000; McCarthy et al., 1994; McCarthy et al., 1996; McCarthy et al., 1997; Warbrick et al., 2013).

Research Questions and Hypotheses

The detection of a rare target stimulus may prove to be beneficial for an organism so the neuronal activity related to such behaviors has received much research. Target detection paradigms such as the oddball task or CPT are typically used to test and assess this behavior in the laboratory. Research using these paradigms has found that the PFC, temporal lobe, and parietal lobe are involved in the detection of a rare target (Akgül et al., 2005; Bledowski et al., 2004; Fallgater & Strik, 1997; Kennan et al., 2002; Kirino et al., 2000; McCarthy et al., 1997; Mullert et al., 2004; Smith et al., 1995; Toichi et al, 2004; Warbrick et al., 2013). Particular electrical events related to the detection of a target, P300 waves, have been the main focus of much of the EEG research looking at target detection. Current theories believe that the anterior P3a subcomponent is related to frontal attention driven working memory comparisons while the central-posterior P3b is the result of temporal-parietal memory storage processes (Polich, 2007). NIRS studies have very rarely used the oddball paradigm, but the few that have or used the CPT, have indicated results similar to those of fMRI in finding increased activation of the PFC (Akgül et al., 2005; Fallgater & Strik, 1997; Kirino et al., 2000; McCarthy et al., 1997; Toichi et al., 2004; Warbrick et al., 2013) .

One study has already determined that the role of the PFC is not related to the movement needed to make a response, since both covert (counting) and overt (button presses) result in PFC activation (Kirino et al., 2000). Previous studies also indicate that the PFC's role during target detection tasks is to modulate attention (Polich, 2007; Polich, 2012). Thus far, very few studies have used the oddball paradigm in NIRS, one aim of this

study was to address this research gap. As the oddball task is commonly used to assess neural correlates of target detection, introducing NIRS to this area of research allowed for more robust data sets and cost effective imaging measures. It is currently unknown how the PFC may be using oxygen differently as a function of the difficulty of the oddball task, and therefore how the PFC participates in attention and working memory. To address this a two difficulty condition odd ball study (easy and difficult as defined by target size relative to standard) was performed. Lastly, it is generally unknown how changes in hemoglobin oxygenation are related to the electrical events taking place in a neuronal mass outside of knowing oxygen is necessary. This knowledge gap was addressed by comparing changes in P300 waves to changes in hemoglobin oxygenation.

The current study examined the activity of the PFC using NIRS and detected the posterior P300 (P3b) using EEG (separately) while subjects performed a two-stimulus oddball task with two levels of difficulty. One level was a difficult discrimination between blue circles of different size (target diameter = 3.6cm, standard d = 4cm) and the other level was an easy discrimination between blue circles of different size (target d = 2.8cm, standard d = 4cm). A difficult discrimination has been used in previous research to examine the use of attentional resources compared to easier discriminations, as the more difficult task requires more attention (Polich, 1987; Comerchero & Polich, 1999).

The hypotheses were: 1) EEG data will reflect previous findings, there will be decreased amplitude in the P300 detected at location Pz for difficult compared to easy tasks, 2) NIRS data will show differential prefrontal activation in the form of different levels of HbO and HbR between easy and difficult conditions, and 3) there will be a correlation in easy-difficult difference scores between NIRS signals and EEG signals.

METHODS

Participants

Forty volunteers participated in this study. The number of participants was chosen based on a sample size estimate performed using the G*Power application to determine how many subjects would be needed for a powerful regression (Faul, Erdfelder, Lang, & Buchner, 2007). The sample size estimate using power = 0.8, alpha = 0.05, and Cohen's f^2= 0.35 (a large effect) for the planned difference score regression revealed the need for 25 participants. As EEG and NIRS data are easily contaminated by physiological and environmental signals, a more conservative number of participants was chosen. Of the forty participants 28 identified as female and twelve identified as male. Two participants were left handed. Participants had an age range of 18-33, *M* = 21.33, *SD* = 3.61. Participants were randomly assigned to the NIRS session or EEG session before arriving. This experimental protocol was approved by the Northern Michigan University Institutional Review Board (Project #HS16-737).

Stimuli

Stimuli were blue circles created using pixlr.com. The shade of blue was HTML code #0000ff. A transparent square background was made with dimensions 160 x 160 pixels (4.23 x 4.23 cm). A circle brush tool was used to make three circles of different sizes (in diameter): 4cm, 3.6cm, and 2.8cm. The circle brush was centered at pixel coordinates X: 80 and Y: 80 so the circle was centered on the square background. The standard stimulus was the 4cm circle in all conditions, the 3.6cm circle was the target stimulus in hard conditions, and the 2.8cm circle was the target stimulus in easy conditions. All stimuli were presented on a black background. These sizes were based on a previous visual oddball experiment (Comerchero & Polich, 1999).

Task

The task was designed in E-Prime2 software and presented on a 23in HP Compaq LA2306x monitor at a resolution of 1920 x 1080 pixels. The screen brightness was set to "10" (out of 100) to avoid apparent-motion after effects and reduce participant fatigue. Participants were seated 70cm from the monitor. Each trial started with the presentation of either a standard or target stimulus for 75ms. The stimulus was followed by a black screen for 2000ms making each trial 2075ms long. Participants were asked to respond only to the designated target once it appears on screen using the center key on a 5 key Chronos response pad (Figure 1).

Figure 1: Chronos Response Pad. Subjects responded to target stimuli by pressing the center button on the Chronos.

There was one practice session of two blocks without the imaging equipment. The practice session consisted of one block for the easy condition and one block for the hard condition. There were two targets and 18 standards in each block. The practice session was completely randomized.

The experiment was broken into eight blocks. Four blocks, two each of the easy and difficult condition, were performed in both EEG and NIRS. Each block consisted of 15 targets to 185 standards with at least 9 standards between targets (at least 18.675s between targets) to allow for cerebral blood flow in brain areas activated only to the target to return to baseline (Kennan et al., 2002). The order of NIRS and EEG sessions were randomly determined and counterbalanced. Presentation of the easy or difficult task blocks was randomized as well.

Imaging Equipment

This thesis project used both NIRS and EEG measures. NIRS is used to measure the oxygenation of hemoglobin in the first centimeter of the cerebral cortex. EEG is used to measure the electrical activity of certain populations of neurons.

EEG

An EGI Net Amps 300 EEG amplifier was used in conjunction with 64 channel Geodesic Hydrocel nets. Different net sizes were used to fit each participants head appropriately. The Hydrocel nets are partially aligned with the 10-20 system, but also records from unstandardized locations (Figure 2). The data was recorded to a Mac Pro 5.1 computer using NetStation 4.5.4 software. Following data collection preprocessing was performed in NetStation 4.5.4. EEG was used in this project to determine if the paradigm used in the project produces the same results as previous studies. Therefore, data was extracted from electrode Pz. Data was recorded to a reference at electrode Cz, however, was re-referenced to the mastoid electrodes (Squires et al., 1975).

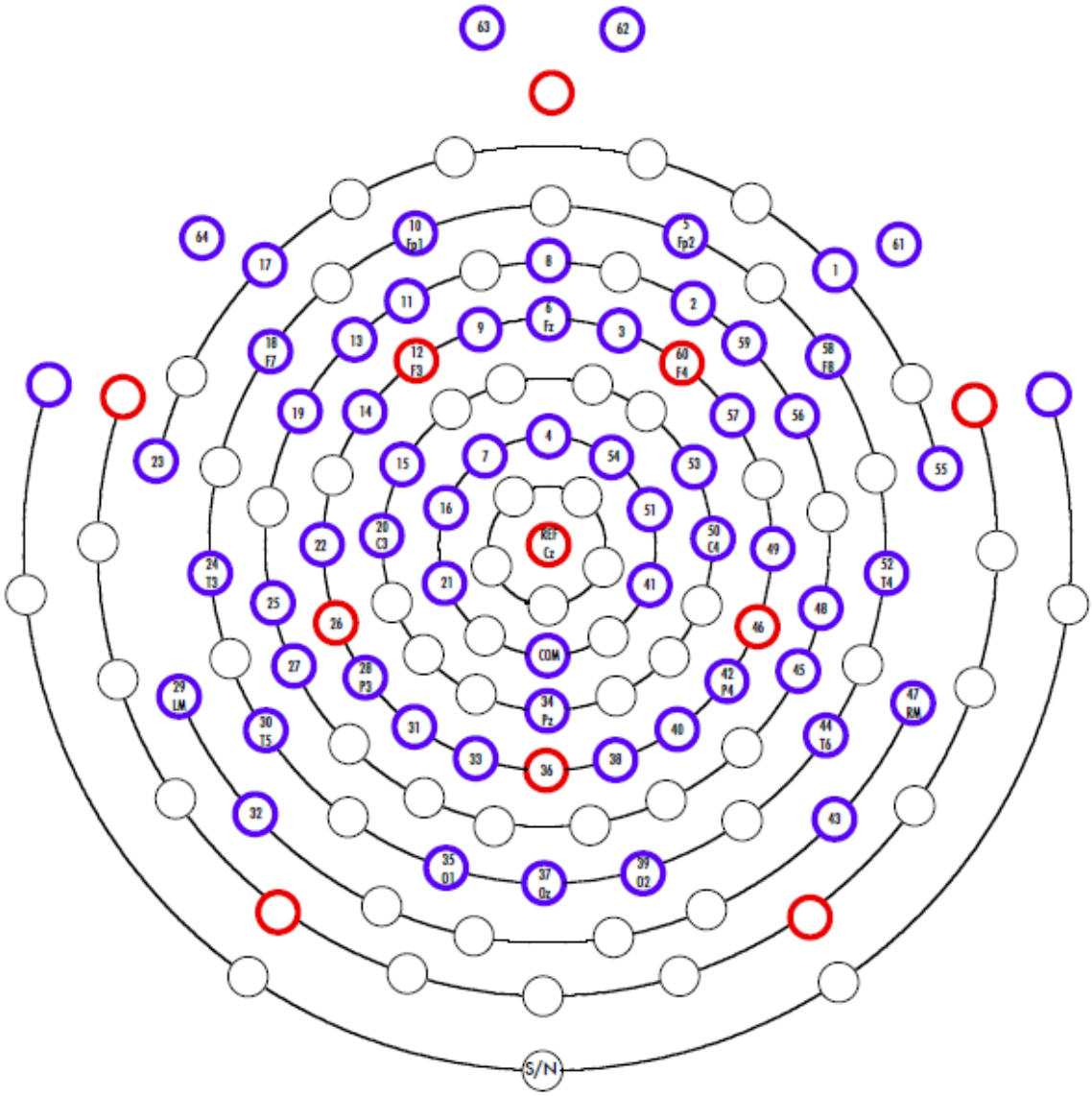

Figure 2: Hydrocel Net Layout. Layout of the 64 channel hydrocel EEG net used in the experiment. Retrieved from: ftp://ftp.egi.com/pub/support/Documents/net_layouts/hcgsn_64.pdf

NIRS

A TechEN Continuous Wave 6 (CW6) system was used for collecting NIRS data. The data was collected using the CW6 executable software and stored to an HP ProDesk 600. Preprocessing of data took place in Homer2 software. The CW6 system uses two wavelengths of light, 690nm and 830nm, to determine hemoglobin oxygenation levels. A custom head probe was used to examine the PFC. The head probe consisted of two separate

arrays that are attached at the center by Velcro to allow for independent placement over the hemispheres. Each array consisted of two lasers and three detectors with a 3cm separation between laser and detector. Each array was placed according to the 10-20 system. The left hemisphere array was placed so the mark for Fp1 was below the left-most medial detector and the right hemisphere array was placed so the mark for Fp2 was below the right-most medial detector (Figure 3).

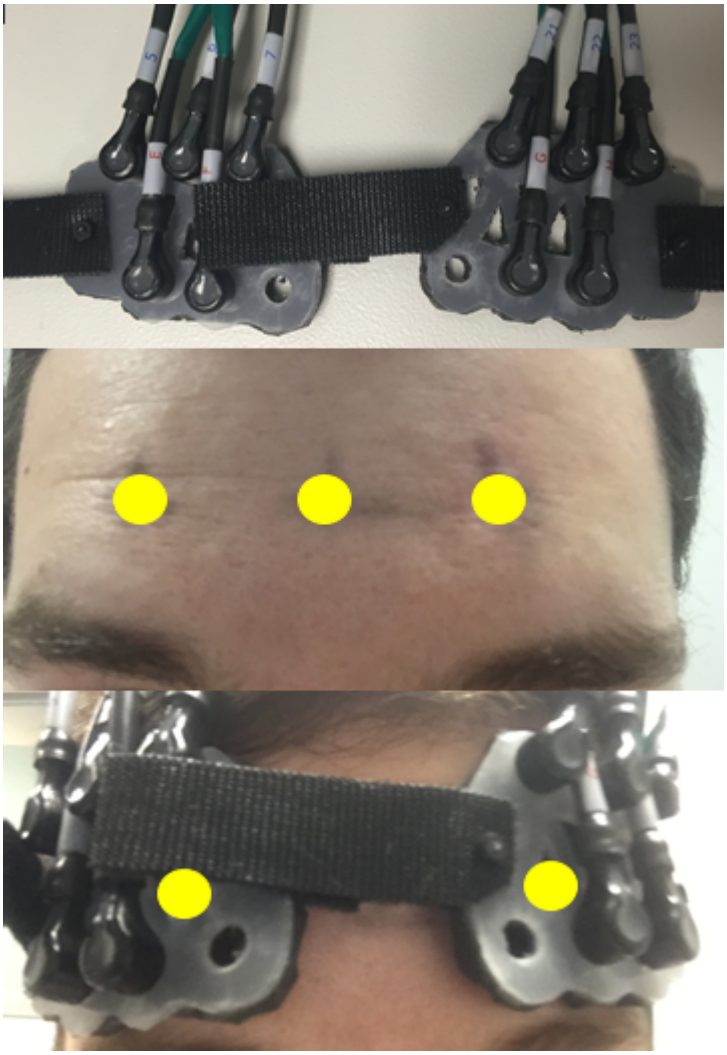

Figure 3: NIRS Array. Top: NIRS array consisting of 6 detectors and 4 lasers. Middle: Markings for proper NIRS placement; Subject left = Fp1, center = FpZ, subject right = Fp2. Bottom: NIRS array on head, yellow dots indicate locations of Fp1 and Fp2.

Procedure

EEG setup

Participants had their heads measured and marked with a reference point at the vertex, electrode Cz's location in the 10-20 system. The Geodesic HydroCel nets were soaked in an electrolyte solution for five minutes before use to amplify the signal from scalp to electrode. The net was placed so that the vertex reference electrode was on top of the reference point drawn on the subject's head. The net was then plugged into the amplifier and the net impedance (resistance in the wires) measured. Electrodes were adjusted by moving electrodes or adding electrolyte solution to electrodes until all electrodes were below 75 kΩ impedance. EGI recommends recording below 100 kΩ, the current experiment used a more conservative cutoff based on previous research, although some electrodes were kept below 100 kΩ if reducing impedance to 75 kΩ was too time consuming (Carlson & Reinke, 2010). Once signal quality was confirmed the experimental task was initiated.

NIRS setup

Participants' heads were measured and marked according to the 10-20 system coordinates Fp1 and Fp2. The left optode array was placed over Fp1 so that the mark was below the medial detector; the right optode array was be placed over Fp2 so that the mark was below the medial detector. The array was secured to the head using Velcro, an ace bandage, and cloth headband. The CW6 software for recording NIRS data was then initiated. The system lasers were turned on and quality of signal inspected so that the light intensity at the detectors is between 80dB and 120dB. The gains (sensitivity) of the

detectors were automatically adjusted to detect signals within the 80-120dB range using the CW6 automatic gains function set to 100dB. Once a quality signal was confirmed and gains set the experiment was initiated.

Experiment

Both EEG and NIRS sessions utilized the same experiment: four blocks of task, two each of easy and difficult condition with at least nine standards between targets. The use of EEG or NIRS first was randomly counter balanced, and block order was randomized. Participants were seated 70 cm from the screen. Before performing the experimental blocks participants performed a practice block for each condition without any imaging equipment. The practice blocks consisted of 18 standards to two targets with no limit on time between targets. Following the practice blocks, participants performed the NIRS and EEG experiment blocks. The NIRS and EEG experiment contained two easy and two difficult conditions per imaging modality. Each experimental block consisted of 15 targets to 185 standards with at least nine standards between targets. The participant's task was to press the center button on a Chronos response pad in response to the easy target in easy target conditions and the difficult target in difficult condition as quickly as possible while making no response to standard stimuli (see Appendix 1 for instructions; Figure 4). Participants were offered a brief rest period after each block and an extended rest period with the chance to use the rest room between EEG and NIRS recordings.

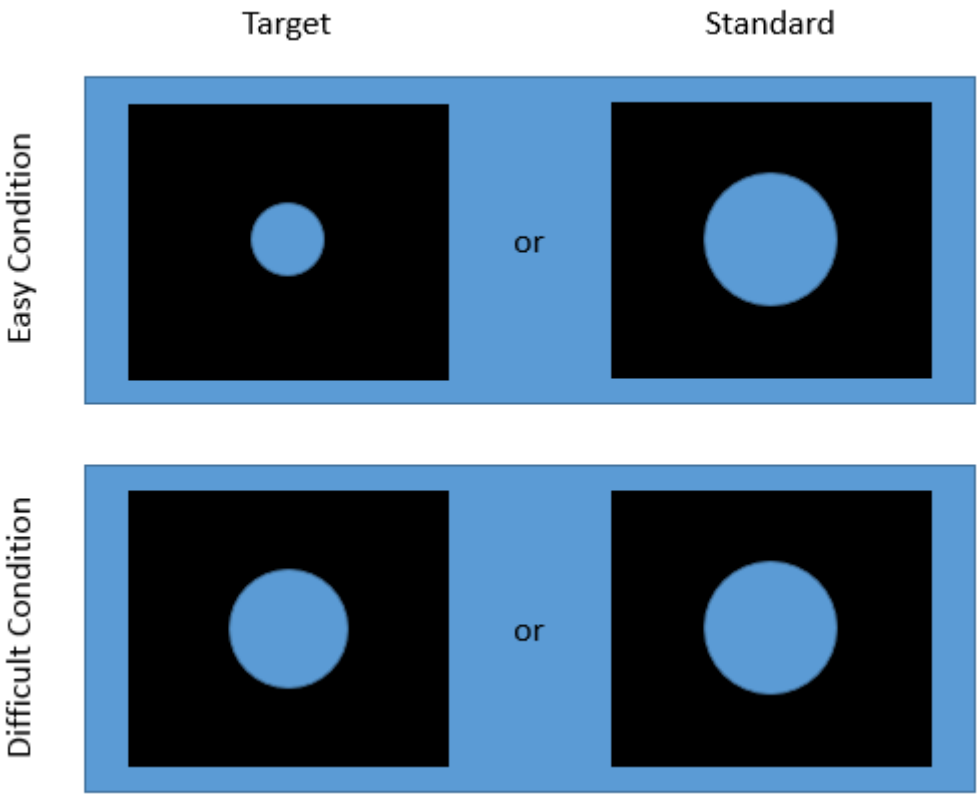

Figure 4: Experimental Task Example. Participants were shown either a target or a standard, called the regular circle at the center of the screen. Responses were made when the target was seen, no response was made when the standard was seen.

Data Preprocessing

EEG

EEG data was preprocessed using NetStation software. Data was high pass filtered at .1hz, low pass filtered at 40hz, and notch filtered at 60hz to remove electrical activity recorded from the environment or otherwise not produced by the brain. Following filtering the data was segmented to -100ms pre-stimulus and 750ms post stimulus. The segments went through artifact detection. The artifact detection tool in NetStation detected artifacts by defining thresholds for the following operations: bad channels, eye blinks, and eye movements. Bad channels were defined by any channel exceeding 100μV; eye blinks were defined by any eye blink channel exceeding 70μV; eye movements were defined by any ocular movement channel exceeding 30μV. Bad channels were marked when recording in that channel was bad for more than 20% of data. Segments were marked as bad if more than ten channels were marked as bad, or if eye blinks or eye movements were detected. After artifact detection the good segments were averaged across conditions, only segments containing detected targets were used. The averaged segments were then re-referenced to the average of the mastoid electrodes in accordance with previous oddball studies (Squires et al., 1975). Following preprocessing of individual data the segments from all participants were grand averaged across conditions. The grand averaged data and individual data were then baseline corrected (as separate data sets), a process for establishing a zero point, according to data 100ms prestimulus. Based on previous research and inspection of the grand averaged ERP, data from 350-600ms post stimulus was extracted for analysis

(Comerchero & Polich, 1999). Data was extracted from individual ERPs not the grand averaged ERP.

NIRS

NIRS data was preprocessed using Homer2 software. NIRS measures light intensity so the first step was to convert intensity to optical density (OD). Motion artifact correction was performed using a principal component analysis (PCA) method available in Homer2; a value of 0.8 was used to conservatively remove variance related to motion artifacts from the data (Brigadoi et al., 2014). The HmrMotionArtifact algorithm was also used to detect artifacts related to movement. The algorithm determined whether data was a motion artifact based on the following inputs: data which exceeded a certain change in amplitude threshold (AMPThresh), data that had an amplitude change greater than a certain number of standard deviation (SDThresh), the time period over which the change was measured (tMotion), and extends time frame marked for bad data by 'n' seconds (tMask). In this study the values were: AMPThresh = 0.1 ΔOD, SDThresh = 50 SD, tMotion = 0.5s, and tMask = 1s. Data was rejected from analysis if marked for a motion artifact 1s before and 6s after stimulus presentation. A lowpass filter of 0.5 was used to remove contaminate physiological artifacts such as heart beat. The processed OD data was then converted into hemoglobin concentrations using a modified Beer-Lambert law (Huppert et al., 2009). Next, the HRFs for HbO and HbR were calculated by selecting data 1s before the stimulus and 20s following the stimulus and averaging across conditions. The E-prime2 experiment software recorded the accuracy of target detection and only segments of data containing a detected target were used. Once segments were removed from individuals the segments were averaged across the group according to condition to make the group average HRF.

Individual data averaged across conditions was extracted for statistical analysis. Initially analysis of 5-10s in both measures was planned based on preliminary results. Based on inspection of the HbO and HbR HRFs, data from 2-12s post stimulus was extracted for HbO and data from 5-15s post stimulus was extracted for HbR. The final time frames were selected since they included the planned time frames and more of the recorded activity.

Data Analysis

Reaction Time and Accuracy Data

Reaction time from presentation of target to button press was examined as a function of task difficulty and imaging modality using a 2 × 2 repeated measures ANOVA (2 conditions, 2 imaging modalities). A series of t-tests was initially planned for analysis of behavioral results, in which combined EEG and NIRS reaction times and accuracy would be examined as a function of task difficulty. However, after data collection it was apparent that there may have been differences in reaction time and accuracy as a function of imaging modality and it was important to examine these differences objectively.

Imaging Data

Amplitude data for the P3b subcomponent was extracted from electrode Pz. Only the data from accurately detected targets was used. A two tailed, matched pairs, t-test was used in SPSS to compare difference in Pz P300 amplitude between the two conditions. The aim of this particular test was to confirm that the current experiment could replicate previous findings and therefore validly apply the task to another imaging modality.

NIRS HbO and HbR HRF data was analyzed using a 2 × 4 × 2 repeated measures ANOVA (2 hemispheres, 4 optodes, 2 conditions) in SPSS. The goal of this analysis was to determine if there were specific effects for hemisphere, optode, and/ or condition. Of particular interest was the potential interaction effect between hemisphere, optodes, and conditions. This interaction would support the hypothesis that specific regions of the PFC are differentially activated as a function of task difficulty. Furthermore, this interaction was

to be used to guide the selection of data to be used for regression analysis in conjunction with the EEG data. More will be said on the regression analysis below.

Regression analysis between the changes in HbO and HbR HRFs and P300 amplitude was performed. Initially it was planned to do a stepwise multiple linear regression with P300 amplitude as the dependent variable and HbO and HbR amplitude as independent variables. The data to be used for this regression between difference scores was to come from an optode revealed to have detected significant activity in the hemisphere × optode × condition interaction. The HbO data did have the significant interaction, however, the HbR data did not. As a result I chose to use the optode which detected significant differences between conditions in HbO as the opotde to use for both HbO and HbR data. Difference scores were calculated by subtracting individual participants' easy data from difficult data in EEG, HbO, and HbR. These difference scores were used to determine the relationship between changes in P300 amplitudes, mean HbO, and mean HbR activity. Although unplanned a priori, bivariate correlation analysis was also performed and will be discussed.

RESULTS

Behavioral Results

Data was collected from 40 participants (female = 28, left handed = 2, age range = 18-33, M = 21.33, SD = 3.61). Reaction time and accuracy data came from participants who provided useable EEG and NIRS data (n = 35), one participant was excluded due experimenter error, one due to noise in EEG data, and three due to hardware errors (e.g., EEG net didn't fit properly, NIRS array moved too much).

The results of the 2 × 2 repeated measures ANOVA on reaction time and accuracy are reported here (n = 35, female = 24, left handed = 1, age range = 18-33, M = 21.29, SD = 3.18; Figure 5). Results of analysis of reaction time data indicated main effects for condition where easy task reaction times (M = 499.19ms, SE = 10.83ms) were faster than difficult task reaction times (M = 584.35ms, SE = 15.71ms), M diff = -85.16ms, SE diff = 8.34ms, $F(1,34) = 104.302$, $p < 0.001$, $\text{eta}^2 = 0.754$, power > 0.999 . There were also main effects for modality such that reaction times were faster in NIRS (M = 532.33ms, SE = 12.54ms) compared to EEG (M = 551.21ms, SE = 14.66ms), M diff = -18.88ms, SE diff = 9.27, $F(1,34) = 4.151$, $p = 0.049$, $\text{eta}^2 = 0.109$, power = 0.508. The interaction between condition and modality was not significant for reaction times $F(1,34) = 0.184$, $p = 0.67$, $\text{eta}^2 = 0.005$, power = 0.07.

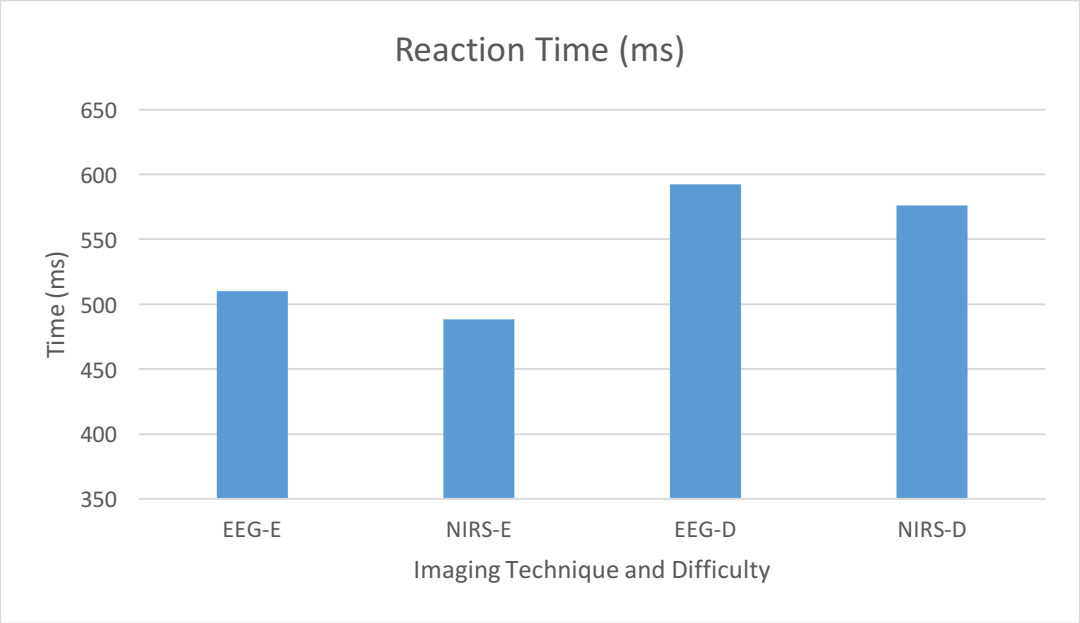

Figure 5: Reaction Time Bar Graph. Reaction times were faster for easy compared to difficult tasks. Additionally, regardless of condition, participants were faster in the NIRS sessions than the EEG sessions.

Results of the analysis of accuracy data indicated main effects for condition in which participants were more accurate during the easy task (M = 1.5 misses, SE = 0.332 misses) compared to the difficult task (M = 7.41 misses, SE = 0.68 misses), M diff = -5.91 misses, SE diff = 0.569 misses, $F(1,34) = 108.048$, $p < 0.001$, $\text{eta}^2 = 0.761$, power > 0.999 (Figure 6). The main effect of modality was non-significant, $F(1,34) = 2.077$, $p = 0.159$, $\text{eta}^2 = 0.058$, power = 0.288. The interaction between condition and modality was non-significant as well, $F(1,34) = 1.583$, $p = 0.217$, $\text{eta}^2 = 0.044$, power = 0.231.

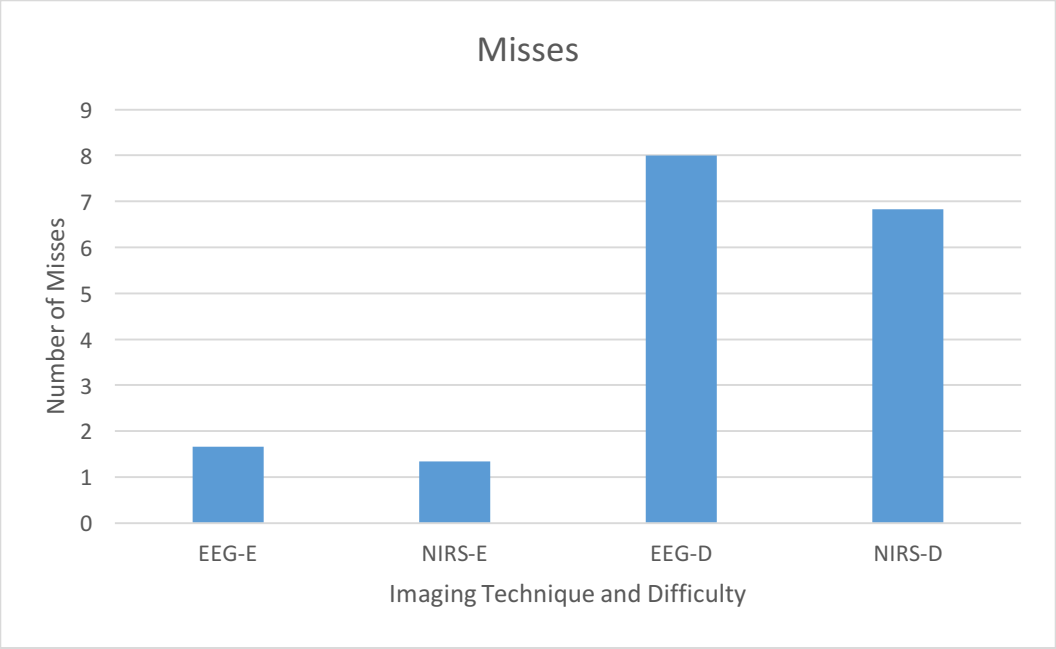

Figure 6: Accuracy Bar Graph. Participants were more accurate in the easy compared to difficult conditions. Although there are differences in accuracy between the imaging modalities, the difference in accuracy between EEG and NIRS tasks was not significant.

EEG Results

EEG data was collected from 40 participants, four subjects were excluded due to experimenter error, noise in the recording, or lack of data. Results of the matched pairs t-test performed on the P3b are presented here (n = 36, female = 25, left handed = 1, age range = 18-33, M = 21.19, SD = 3.18). The difference between P300 amplitudes in electrode Pz produced by easy (M = 9.66 µV, SD = 6.67) and difficult conditions (M = 7.28 µV, SD = 5.16) was significant, M diff = 2.38 µV, SD diff = 5.78, $t(35) = 2.468$, $p = 0.019$, $d_z = 0.41$, power = 0.66 (Figure 7).

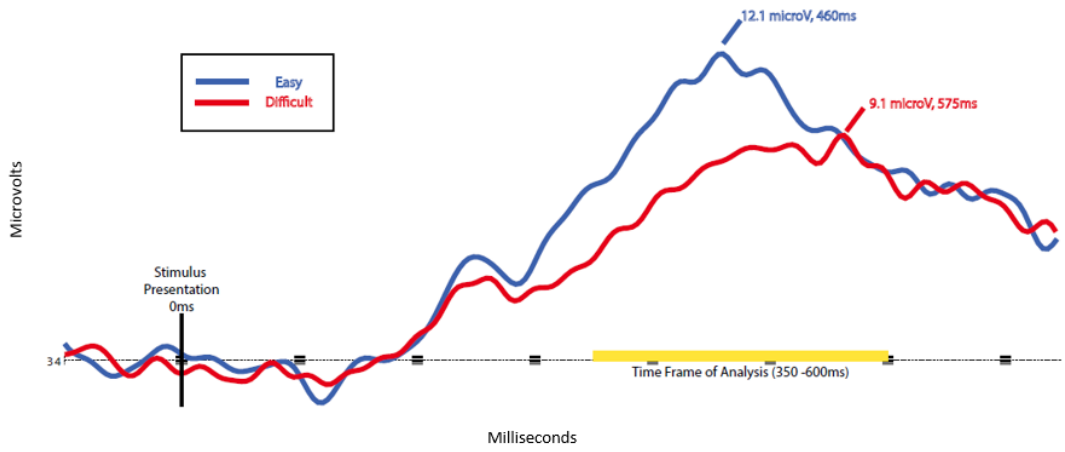

Figure 7: Easy vs Difficult ERPs. Blue: ERP response to easy targets in electrode Pz (34). Red: ERP response to difficult targets in electrode Pz (34). The results of the current study provided further evidence that the P300 subcomponent, P3b, attenuates as a function of task difficulty.

NIRS Results

NIRS data was collected from 40 participants, four subjects were excluded from analysis due to hardware difficulties (e.g., array moving) or lack of data. Results of the 2 × 4 × 2 repeated measures ANOVA on HbO and HbR data are presented here (n = 36, female = 25, left handed = 1, age range = 18-33, M = 21.19, SD = 3.18).

HbO

The HbO measurement's main effect for condition was not significant, $F(1,35)$ = 0.805, p = 0.376, eta^2 = 0.022, power = 0.141, nor was the main effect for hemisphere, $F(1,35)$ = 0.919, p = .344, eta^2 = 0.026, power = 0.154. The main effect for optode was significant, $F(3,35)$ = 10.032, $p < 0.001$, eta^2 = .223, power = 0.998. Post hoc pairwise comparison for optode revealed that lateral optodes generally recorded greater increases in HbO compared to medial optodes (Table 1). The condition × hemisphere, $F(1,35)$ = 0.553, p = 0.462, eta^2 = 0.016, power = 0.112, the condition × optode, $F(3,105)$ = 2.283, p = 0.083, eta^2 = 0.061, power = 0.562, and the hemisphere × optode, $F(3,105)$ = 0.282, p = 0.838, eta^2 = 0.008, power = 0.103 interactions were all non-significant. Lastly, the hemisphere × optode × condition interaction was significant, $F(3,105)$ = 4.984, p = 0.003, eta^2 = 0.125, power = 0.905. Post hoc pairwise comparisons of the hemisphere x optode x condition interaction revealed that the medial most optode over the right hemisphere detected significantly greater levels of oxygenated hemoglobin in easy conditions (M = 0.031, SE = 0.016) compared to difficult conditions (M = -0.023, SE = 0.019), M diff = 0.055, SE diff = 0.024, p = 0.03 (Figure 8). Another pairwise comparison on the same interaction also revealed that in easy conditions the medial most optode over the right hemisphere (M =

0.031, *SE* = 0.016) and its neighbor (*M* = 0.044, *SE* = 0.016) recorded higher levels of HbO compared to left hemisphere medial optode (*M* = -0.008, *SE* = 0.015) and its neighbor (*M* = 0.015, *SE* = 0.016), *M* diff = 0.039, *SE* diff = 0.014, *p* = 0.008 and *M* diff = 0.029, *SE* diff = 0.014, *p* = 0.046, respectively (Figure 9).

(I) Optode	(J) Optode	Mean Difference (I-J)	Std. Error	Sig.[b]
1 = medial	2	-.019*	.004	.000
	3	-.027*	.007	.001
	4	-.036*	.009	.000
2	1	.019*	.004	.000
	3	-.008	.005	.151
	4	-.017*	.008	.038
3	1	.027*	.007	.001
	2	.008	.005	.151
	4	-.009	.005	.100
4 = lateral	1	.036*	.009	.000
	2	.017*	.008	.038
	3	.009	.005	.100
(I) Optode	(J) Optode	Mean Difference (I-J)	Std. Error	Sig.[b]
1 = medial	2	.001	.003	.639
	3	.009*	.003	.010
	4	.019*	.005	.000
2	1	-.001	.003	.639
	3	.007*	.003	.006
	4	.018*	.005	.001
3	1	-.009*	.003	.010
	2	-.007*	.003	.006
	4	.011*	.004	.005
4 = lateral	1	-.019*	.005	.000
	2	-.018*	.005	.001
	3	-.011*	.004	.005

Table 1: Medial to Lateral Optode Changes. Top: Changes in HbO. Bottom: Changes in HbR. Demonstrates that lateral optodes usually recorded significantly larger increases in HbO and decreases in HbR in lateral optode pairs regardless of condition

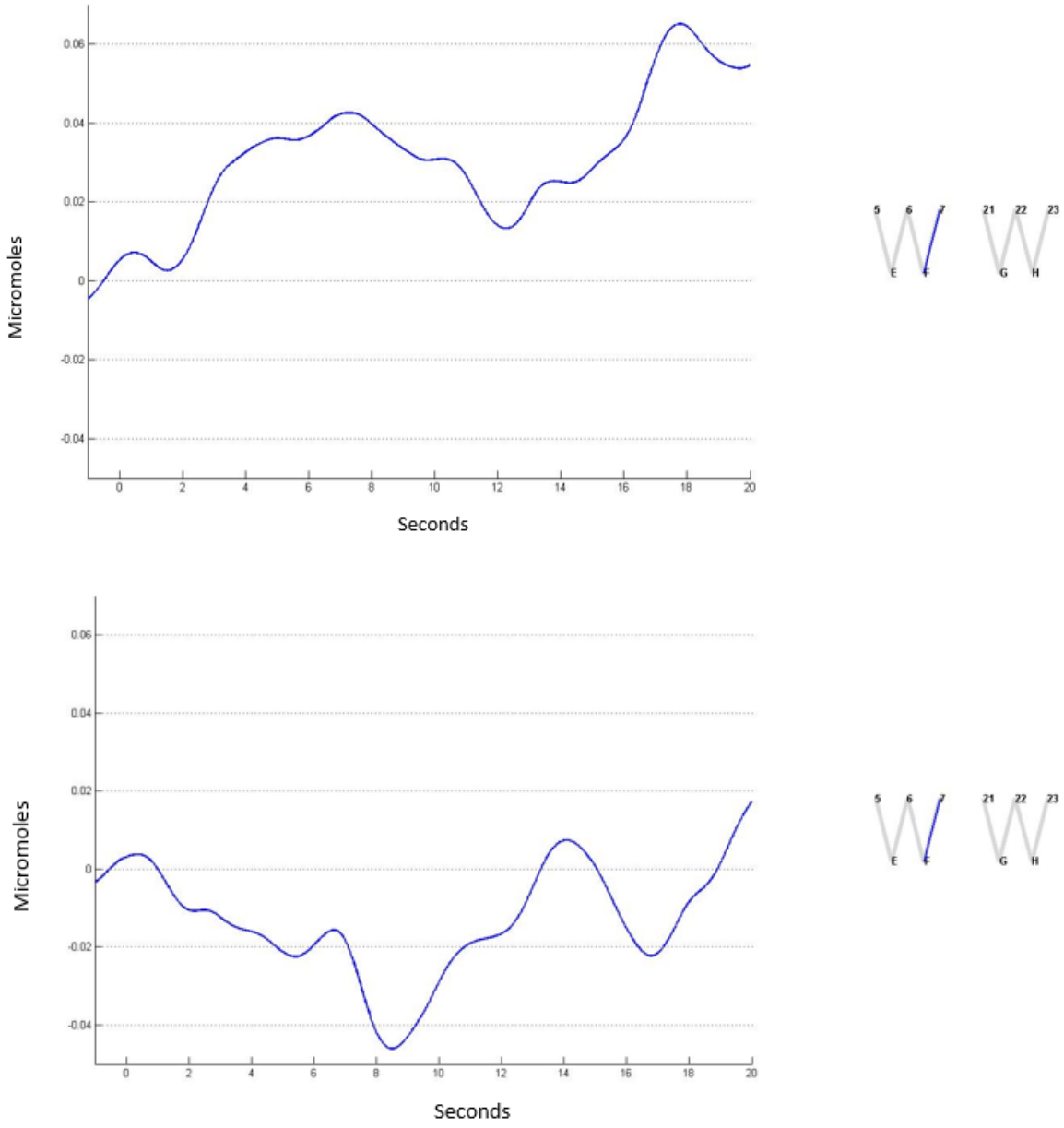

Figure 8: HbO Hemisphere × Optode × Condition, Condition Comparison. Top: Easy. Bottom: Difficult. Significant differences between the medial most right hemisphere optode easy and difficult recording were found when analyzing data extracted from 2-12s post stimulus presentation.

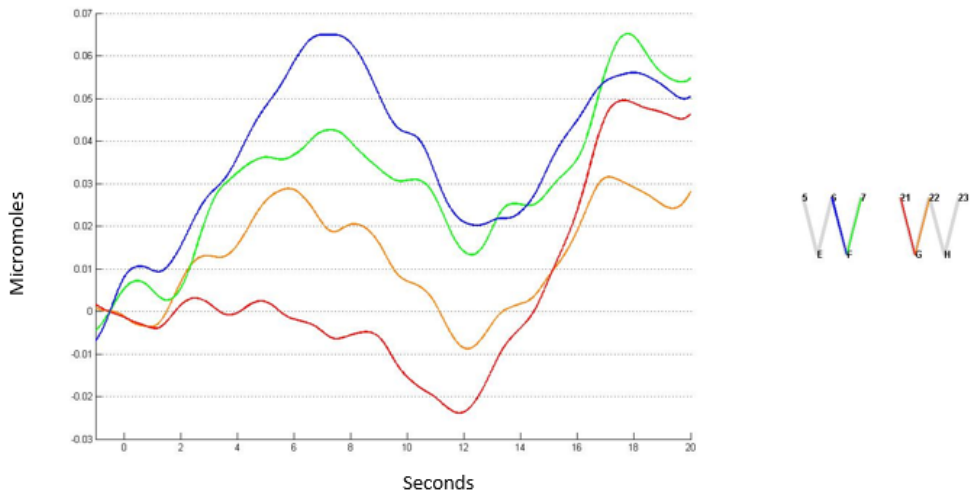

Figure 9: HbO Hemisphere × Optode × Condition, Hemisphere Comparison. Analysis revealed that in the easy condition the right hemisphere medial optodes (F-6, F-7) recorded higher levels of HbO relative to the left hemisphere (G-22, G-21).

HbR

The HbR measurement's main effect for condition was not significant, $F(1,35) = 0.067$, $p = 0.797$, $\text{eta}^2 = 0.002$, power = 0.057. There were significant main effects for hemisphere in which the right hemisphere ($M = -0.02$, $SE = 0.005$) had greater decreases in HbR than the left ($M = -0.009$, $SE = 0.004$), M diff = -0.011, SE diff = 0.005, $F(1,35) = 4.508$, $p = 0.041$, $\text{eta}^2 = 0.114$, power = 0.542. There was also a main effect for optode, $F(3,35) = 11.325$, $p < 0.001$, $\text{eta}^2 = 0.244$, power > 0.99. Post hoc pairwise comparisons for optode revealed lateral optodes generally recorded larger decreases in HbR than medial optodes (see Table 1). The interaction effects for condition × hemisphere, $F(1,35) = 1.458$, $p = 0.235$, $\text{eta}^2 = 0.04$, power = 0.217, hemisphere × optode, $F(3,105) = 1.281$, $p = 0.285$, $\text{eta}^2 = 0.035$, power = 0.334, and hemisphere × optode × condition, $F(3,105) = 1.711$, $p = 0.169$, $\text{eta}^2 = 0.047$, power = 0.436, were not significant. A significant interaction did exist in the optode × condition comparison, $F(3,105) = 2.737$, $p = 0.047$, $\text{eta}^2 = 0.073$, power = 0.649. Post hoc pairwise comparisons of the optode × condition interaction revealed that

in the easy conditions the lateral most optodes recorded statistically significant decreases in HbR compared to all other optodes and in the difficult conditions all optodes significantly differed from each other (Table 2; Figure 10).

Condition	(I) Optode	(J) Optode	Mean Difference (I-J)	Std. Error	Sig.[b]
1 = easy	1 = medial	2	-.002	.005	.588
		3	.002	.005	.740
		4	.014*	.005	.004
	2	1	.002	.005	.588
		3	.004	.003	.174
		4	.017*	.006	.009
	3	1	-.002	.005	.740
		2	-.004	.003	.174
		4	.013*	.004	.007
	4 = lateral	1	-.014*	.005	.004
		2	-.017*	.006	.009
		3	-.013*	.004	.007
2 = difficult	1 = medial	2	.005*	.002	.040
		3	.016*	.004	.001
		4	.025*	.006	.000
	2	1	-.005*	.002	.040
		3	.011*	.003	.004
		4	.020*	.006	.001
	3	1	-.016*	.004	.001
		2	-.011*	.003	.004
		4	.009*	.003	.012
	4 = lateral	1	-.025*	.006	.000
		2	-.020*	.006	.001
		3	-.009*	.003	.012

Table 2: HbR Condition × Optode. In easy conditions the lateral most optode recorded significantly lower levels of HbR than all other optodes. In difficult conditions all optodes recorded significantly different levels of HbR relative to each other.

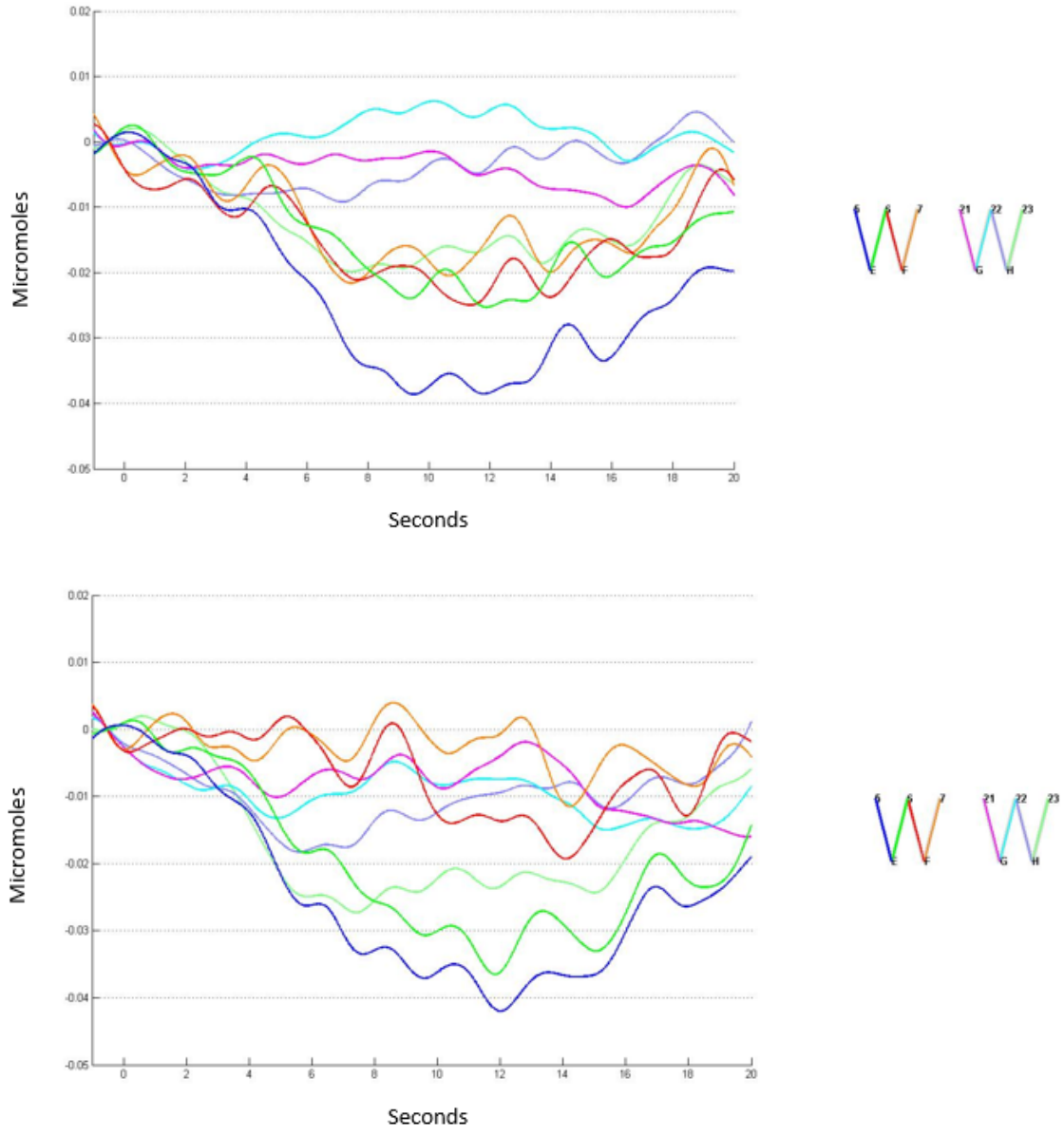

Figure 10: HbR Condition × Optode. Top: Easy, lateral optode pairs (E-5 and H-23) recorded greater decreases in HbR than medial optode pairs (F-7 and G-21). Bottom: Difficult, all optode pairings recorded significantly different changes in HbR relative to each other.

Regression results

EEG and NIRS data were collected from 40 participants, five subjects were excluded from analysis. One was excluded due to experimenter error, one due to lack of EEG-ERP segments, and three due to hardware complications. Planned regression analysis results are discussed first, followed by a secondary correlation analysis that was unplanned prior to data collection.

A stepwise multiple linear regression was performed with P300 amplitude difference scores as the dependent variable and HbO and HbR HRF difference scores as the predictor variables. The results were non-significant and due to the way SPSS handles insignificant stepwise regressions no regression equation was given as no variables qualified as significant predictors. To examine the relationship between the variables further a bivariate correlation between the three difference scores was performed. The results indicated no relationship between EEG and HbO, $r = -0.003$, $p = 0.985$ nor EEG and HbR, $r = -0.181$, $p = 0.299$. There was a moderate inverse relationship between HbO and HbR, $r = -0.553$, $p = 0.001$.

DISCUSSION

Behavioral Discussion

The results of statistical tests on reaction times and accuracy in the easy and difficult oddball tasks were in line with previous findings. Other studies had previously shown greater accuracy and reduced response times to easy targets compared to difficult targets (Comerchero & Polich, 1999; Polich, 1987; Polich, 2007; Polich, 2012). The current study also found faster reaction times and greater accuracy to easy targets compared to difficult targets.

The current study used stimuli that were similar to those used by Comerchero & Polich (1999). As such, it is most appropriate to compare the behavioral results of the current study to Comerchero & Polich's findings. In general the current study found similar results, in that easy targets were detected faster and more accurately. Interestingly, participants in the current study were slower and less accurate than those in the Comerchero & Polich study (Table 3). Likely contributors to differences between the current study and the Comerchero & Polich study were that the current study did not use an additional non-target distractor (e.g., a square) and the current study used a lower percentage of targets to standards. Another plausible explanation for this difference is the area of visual angle taken up by the targets between the two studies. The current study used the same dimensions (in cm) for the stimuli as Comerchero & Polich, but the current study placed the participants around half the distance from the screen (70cm vs 1.5m; differences due to response pad

and EEG cable restraints). As a result the retinal representation was larger in the current study. This may have led to a difference in reaction time and accuracy as the stimuli had different retinal representations between the studies. Another reason for the discrepancies may be due to the amount of time and intensiveness of the EEG and NIRS setup. That is, Comerchero & Polich used an EEG system that only recorded from three electrodes, whereas the current study used an EEG net that covers the whole head and face. Therefore the physical setup may have hindered the participants' performance.

Reaction Times (ms)	**Easy**	**Difficult**	**Easy - Difficult**
C&P 1999	474	557	-83
EEG	510	593	-83
NIRS	489	576	-87
Combined	499	584	-85
Accuracy (% hit)	**Easy**	**Difficult**	**Easy - Difficult**
C&P 1999	99.3	82.9	16.4
EEG	94.5	73.4	21.1
NIRS	95.6	77.3	18.3
Combined	95.0	75.3	19.7

Table 3: Reaction Time and Accuracy Differences. Comparison of Comerchero & Polich 1999 behavioral results (C&P 1999) to behavioral results of the current study broken down by session and then combined. Although the raw numbers are not the same between the studies the reaction time and accuracy differences between conditions are comparable between the two studies.

Overall, the behavioral results reflected those of previous studies: greater accuracy and faster reaction times to easier targets. While the behavioral results of the current study did not exactly match those of previous studies, the relative difference between reaction times and accuracy as a function of task difficulty were very similar (see Table 3). Possible explanations for discrepancies between the current study and previous studies may include differences between ratios of targets to standards, use of non-target distractors, the difference between size of retinal representation, lack of exclusion criteria based on behavioral responses, and more physical distraction in the current EEG system relative to

those used in previous studies. Although there were differences between the current study and previous studies, the important finding is that the current study's results were comparable to previous studies' results based on the relative differences between easy and difficult reaction times and accuracy. Once again showing that targets which were distinct from standards results in faster accuracy and reaction time.

One reason for the "capture" of attention by easy targets may be due to the salience of the features of easy targets initiating bottom-up processing (stimulus driven) whereas the difficult targets were not as distinct and therefore less salient and only top-down (task driven) processes were used as difficult targets require more effort to identify. That is, in easy tasks, top-down processing drives bottom-up processing as a successful method of task completion, where-as in difficult conditions the lack of salience makes bottom-up processing unsuccessful. The discussion on top-down vs bottom-up processing will be continued in the imaging discussion and conclusion sections where it will also be related to P3b attenuation and context updating theory.

Imaging Discussion

Similar to the behavioral results, the results of the imaging data from the current study are comparable to those found in previous studies. The differences between the current study and previous studies are only in the exact numerical outcomes of the data, not the relative difference between conditions. It was hypothesized that the EEG data would reflect previous findings in that P3b amplitude in difficult conditions would be attenuated. Furthermore, it was hypothesized that there would be a difference between NIRS measures based on task difficulty. Lastly, it was hypothesized that there would be some sort of relationship between EEG and NIRS measures as a function of task difficulty.

Hypothesis 1: P3b Attenuation

The results of the EEG analysis were in line with previous findings that targets which were easier to detect produced larger P300s than those produced by difficult targets (difficulty as defined by target size relative to a non-target standard; see Figure 4). As mentioned previously, the stimuli used in the current study were based on those used by Comerchero & Polich (1999) and thus, the imaging results of the current study may be comparable. Comerchero & Polich found peak amplitudes of roughly 19 μV and 15 μV for easy and difficult P300s respectively; the current study found peak amplitudes of 12.1 μV and 9.1 μV for easy and difficult P300s respectively (see Figure 7). While the exact measures are not the same, as with the behavioral data, the relative difference between task P300s in the current study were statistically significant and similar to previous findings (Comerchero & Polich, 1999; Polich, 1987). Differences between the current findings results and previous studies' results may be the result of differences in recording systems

such as the use of 64 electrodes in the current study compared to three in Comerchero & Polich (1999). Additionally, the particular EEG system that was used for the current study records with roughly ten times the amount resistance (75-100 kΩ vs 7-12 kΩ) within the recording electrodes compared to those used in other studies, which may be the reason for overall EEG attenuation in the current study compared to previous studies. While there were slight differences in EEG recording outcomes in comparison to previous studies, the relative differences as a function of task difficulty were maintained.

The EEG findings presented here have confirmed the findings of previous studies; P3b amplitude was found to attenuate in the difficult task relative to the easy task. According to current theories of P300 meaning, attenuation as a function of difficulty was due to the lack of delimiting extraneous corticoelecitrcal activity related to salience detection, so that other methods of task completion could be performed (Polich, 2008). This could be interpreted as meaning the P3b attenuates due to a limiting of bottom-up attention as difficult targets are not salient and therefore limiting salience detection would help in allowing top-down attention to direct more successful means of task completion. If the result of the comparison is that the incoming stimulus information does not match and is a target, this causes a change in working memory and consolidation of memory for the new stimulus within working memory that is reflected in the movement of the P300 from an anterior (P3a) to central-posterior location (P3b). The results of the EEG data analysis from the current study supports previous findings that the P300 attenuation is due to a lack of limiting extraneous brain activity which also indirectly indexes the relative difference between incoming target stimulus signals and the contents of working memory. Furthermore, given that the task was modified slightly to work more appropriately in NIRS

it has also been demonstrated that NIRS can be used in conjunction with EEG paradigms without sacrificing EEG validity.

Hypothesis 2: Differential PFC Activation

Few studies had utilized the oddball task outside of EEG so an important goal of the current study was to examine how the oddball effected NIRS measures of HbO and HbR within the PFC (Akgül et al., 2005; Kennan et al., 2002). Additionally, NIRS data was collected and analyzed with the goal of examining the relationship between changes in EEG and NIRS signals as a function of task difficulty. It was hypothesized that there would be significant differences in HbO and HbR concentrations as a function of task difficulty. The results did not indicate main effects for condition in either NIRS measure, however, significant interactions between main effects, including condition, support the hypothesis that different oddball task conditions would result in differential activation of the PFC. In particular it was observed that the medial most optode over the right hemisphere recorded higher concentration of HbO in easy compared to difficult conditions. Additionally, the condition × optode interaction for HbR was significant such that in easy conditions the lateral most optode recorded significantly different concentrations of HbR relative to all other optodes and in difficult conditions all optodes recorded different concentrations of HbR (see Table 2). Another interesting finding was that different parts of the PFC showed different concentrations of HbO and HbR during the task. The results of this study provided evidence that different parts of the PFC play a role in the task regardless of condition and some areas are more active depending on condition. These findings were also interpreted as corroborating previous research showing lateral PFC activation due to attention to the task (top-down) where-as medial PFC activation is

associated with attention to salient stimulus features (bottom-up); this is discussed in more detail below.

Previous research that used the oddball paradigm in imaging modalities outside of EEG is very limited, but has pointed to activation in the prefrontal, temporal, and parietal cortices as the main contributors to generation of both P3a and P3b (Bledowski et al., 2004; Clark, Fannon, Lai, Benson, & Bauer, 2000; Kirino et al., 2000; McCarthy et al., 1998; Mullert et al., 2004; Stevens, Laurens, Liddle, & Kiehl, 2006). Studies that had utilized the oddball paradigm outside of EEG had typically used fMRI. Since fMRI measures are similar to that of NIRS, and there were only a couple of NIRS studies that used the odd ball, the results of the current study were compared to findings from fMRI as well as NIRS (Akgül et al., 2005; Kennan et al., 2002). As described in the introduction, fMRI BOLD signal increases due to a reduction in the paramagnetic effects of HbR. Although this may have implicated HbR as being better correlated with changes in BOLD signal, researchers have observed that HbO changes detected with NIRS were better correlated with BOLD changes (Cui, Bray, Bryant, Glover, & Reiss, 2011; Strangman, Culver, Thomson, & Boas, 2001).

Previous fMRI studies found that the PFC played a role in generation of P3a and P3b subcomponents, but it played a more extensive role in P3a generation. Overall, it has been determined that some prefrontal activation during the odd ball task is due to obtaining stimulus information that is rare or potentially rewarding rather than obtaining stimulus information dictating the stimulus as a target (Bledowski et al., 2004; Rodgers et al., 2004). Thus, the detection of potentially rare or rewarding stimuli, is driven by the stimulus features, and can be thought of as a bottom-up process. The current findings support a role

for the medial PFC in bottom-up processing driven by top-down processing. While this may seem contradictory, bottom-up and top-down processing do not represent dichotic concepts which do not interact, rather strategies for successful task completion probably utilize both in tandem (Sarter et al., 2001). The current study found significant differences in HbO in an optode placed over the 10-20 coordinate Fp2 (roughly right medial/ superior PFC, see Okamoto et al., 2004) such that greater amounts of HbO were detected in easy relative to difficult conditions, additionally a significant difference in HbO concentration was observed in the easy condition between the right medial most optode and its neighbor compared to the left medial most optode and its neighbor. This may support the theory that prefrontal activation during the oddball task is due to salience (morphological and frequency differences relative to standard) since the missed targets are presumed to be missed due to a lack of perceptual difference between the contents of working memory and incoming signals (i.e., the current stimulus was morphologically too similar to the contents of working memory and not perceived as a target). If it is true that right medial PFC activation in odd ball tasks is due to detecting salient stimulus features, then one would expect novel and infrequent targets to elicit greater activity (i.e., increases in HbO) relative to targets that are perceptually similar to the standard stimuli. This study aimed at examining a neural system in which the task condition would guide where attention was directed (top-down), and it was believed that the difficult condition would require more focused attention. While participants may have focused more during the difficult task, the results in HbO suggested that bottom-up control was initiated during the easy conditions. The behavioral results showing better accuracy and faster reaction time to easy targets corroborated this conclusion as well.

Examination of the HbR data did not reveal a significant three-way interaction between the main effects which suggested that changes in HbR were not as sensitive at indexing changes related to target detection as HbO. This may in part be explained by previous research suggesting that HbR data was more variable than HbO and therefore less sensitive to task-elicited signals (Strangman et al., 2002). Although the three-way interaction was not detected in HbR other effects were significant in HbR and HbO that may be in line with fMRI research and theories of P300 meaning. Both HbO and HbR showed main effects for optode regardless of condition or hemisphere (recall optodes are paired based on laterality). Further inspection of the data revealed that the greatest changes in HbO and HbR concentration are seen laterally and descend in a linear fashion through the more medial optodes (see Table 1). Along with this finding in HbR, main effects were observed for hemisphere such that the right hemisphere recorded the greatest decreases in HbR. Furthermore, an interaction was observed between condition and optode for HbR within the easy condition such that the lateral optode pairs recorded significantly lower levels of HbR than all other optode pairs and in the difficult condition all optodes recorded differently from each other (see Table 2).

The finding that the right hemisphere had greater decreases in HbR supports findings in fMRI studies that the right PFC was involved in attention (Aron et al., 2004; d'Alfonso et al., 2000; Davidson & Irwin, 1999; Etkin et al., 2011; Peterson & Posner, 2012; Small et al., 2003). Although this finding was the opposite of the CPT studies (CPT found increased HbR), it may be the case that the use of multiple targets and non-targets in CPT causes HbR to index responses differently in CPT versus oddball (Fallgatter & Strik, 1999; Toichi et al., 2004). Additionally, the way easy and difficult were defined by the

CPT and the current study were different in that the CPT made the task more difficult by increasing the speed of presentation and the current study made targets morphologically similar to standard stimuli. These explanations mean that increases in HbR in the PFC could be the effect of non-target novel stimuli effecting the overall task outcomes.

The role of the right medial PFC in attention is further supported by the current study's finding that the medial most optode over the right hemisphere recorded significantly higher levels of HbO in easy compared to difficult conditions and within the easy condition this effect was lateralized to the right hemisphere. The results indicated that the saliency of the easy target resulted in increased activity as a result of processing driven by stimulus features (bottom-up). Current theories of P300 meaning suggest that the P3b component appears as the result of attention driven comparisons of incoming stimulus information to the contents of working memory (Polich, 2008). The current study provided evidence that supports this interpretation of P300 subcomponents as the more distinct targets (easy targets) better captured attention as shown by faster reaction times and increased accuracy.

Research on the roles of the PFC and parietal cortex on top-down and bottom-up processing has shown that the parietal cortex is active during bottom-up attention and the lateral PFC is involved in top-down processing (Buschman & Miller, 2007). This supports the idea that the P300 is the result of frontal attention areas driving a working memory comparison, that is, frontal attention areas involved in top-down task related processing help drive the bottom-up attention towards stimulus features. Furthermore, studies of emotion have found that the right PFC may be involved in directing attention towards emotionally significant features of stimuli (d'Alfonso et al., 2000; Davidson & Irwin, 1999;

Etkin et al., 2011; Small et al., 2003). As stimuli that elicit emotional feelings and behaviors are meant to communicate information that is important for survival, it may be the case that the same prefrontal region involved in directing attention to emotionally salient stimuli also direct attention to other motivationally salient stimuli such as targets (Cardinal, Parkinson, Hall, & Everitt, 2002).

Along with the right PFC, the amygdala is also known to be involved in the assessment of abstract dimensions of stimuli such as motivational importance and novelty (Cunningham & Brosch, 2012; Cunningham et al., 2008; Hamann et al., 2002; Portas et al., 2000; Sander et al., 2003; Wicker et al., 2003). The medial PFC has been implicated as part of a network with the amygdala in which the medial PFC mediates responses to stimuli which had previously been used in fear conditioning (Milad & Quirk, 2002; Quirk et al., 2003). Another portion of the PFC, the anterior cingulate cortex (ACC), also has connections to the amygdala that have been implicated in attentional bias to fearful faces as increased ACC gray matter is correlated with nonconscious attention bias to threats (Carlson et al., 2012; Carlson, Cha, & Mujica-Parodi, 2013). Additionally, the medial PFC has been linked to reward processing, as rewards can be viewed as stimuli humans and other animals are motivated to obtain, the medial PFC may be involved in directing attention to motivationally important stimuli (Rodgers et al., 2004). Altogether this may mean that the detected right medial PFC activity is associated with a network including the amygdala which directs attention to salient and motivationally relevant stimulus features. Given the significant decreases in HbR regardless of condition and the significant increases in HbO in the medial most optode over the right hemisphere during easy compared to

difficult conditions, the findings support a role for the right medial PFC in directing attention to salient stimuli and lateral PFC in sustained task driven attention.

Hypothesis 3: EEG and NIRS Relationship

One of the goals of the current study was to determine if there is a relationship between changes in HbO, HbR, and P300 amplitude. It was hypothesized that changes in HbO and HbR concentrations as a function of task difficulty would predict changes in P300 amplitude as a function of task difficulty. It was predicted that a relationship would be found between NIRS and EEG measures as previous research had implicated the PFC in generation of P300 waves. The regression analysis was not significant. Although it was known ahead of time that the PFC was more involved in the generation of P3a as opposed to P3b, there was also research which indicated the PFC was involved in general task attention (i.e., executive control). As this study used difference scores to examine the relationship in changes, it was predicted that changes in NIRS and EEG as a function of task difficulty would be related. The lack of a relationship may be indicative that the role of the PFC in P3b attenuation is limited, thus the observed attenuation may have been the result of processes occurring elsewhere such as the parietal or temporal lobes. As the parietal lobe plays an important role in processing stimulus features and generation of the P3b component, activity from the parietal lobe measured with NIRS would probably be better correlated with EEG measures as the parietal lobe's contribution to attenuation is greater (Bledowski et al., 2004; Polich, 2007; Polich, 2012; Potts et al., 1996; McCarthy et al., 1994; McCarthy et al., 1996; McCarthy et al., 1997; Mulert et al., 2004; Smith et al., 1995). While the current study did not succeed in finding a relationship between EEG and NIRS measures, this does not mean that NIRS should not be used for studying the

relationship between CBF and scalp detected corticoelectrical signals. Rather, future studies may need to first consider how many generators contribute to the formation of a particular signal (electrical or optical) and examine the relationship between the generation of the two signals within a single region.

A bivariate correlation was also used to determine if there was any relationship at all between measures, and a moderate inverse correlation was found between HbO and HbR. This relationship is generally well known in the NIRS research community (Prakash et al., 2007). What is interesting is that the time frames used to analyze HbO and HbR data covered different, but overlapping, epochs. It is known that increases in BOLD signal peak around 5s post stimulus presentation as HbR's paramagnetic effects on precessing hydrogen atoms decrease. This decrease in paramagnetic effects is related to the decrease in concentration in HbR as a result of large amounts of HbO being delivered to active brain regions (Heutell et al., 2009). Thus, the findings of the current study support previous findings that increases in HbO are typically accompanied by decreases in HbR (Prakash et al., 2007). This also means that even though HbR measures are more variable, the fact that HbO and HbR generally have an inverse relationship provides evidence that the current study's findings of decreased HbR and increased HbO in lateral compared to medial optodes is valid.

Limitations

The current study was developed as a within subjects design, although it could also have been devised as between subjects study. Had a between subjects design been used the effects of just the easy task or just the difficult task compared to baseline or standard stimulus could have been examined. A between groups may have been useful in determining how reaction times, accuracy, EEG signals, and NIRS signals change over time without the influence of multiple conditions. However, the use of within subjects design did not greatly affect the outcomes of the current study as the aim of the current study was to see how the average brain handles an easy task relative to a difficult task. Comparing groups that performed just the easy or just the difficult task or comparing these groups to a group that had done both, does not directly address the hypothesis that when a person does both tasks the PFC will be activated differently. Specific to this experiment it would also have been beneficial to analyze target activity to standards, but there is no easy and valid way to extract data from the standard stimulus presentation due to the way the experiment was programmed in E-Prime and how flags were pruned from the data.

Another limitation of the current study was the lack of cut-off criteria in which participants would be excluded on the basis of false positives, abnormally low or high reaction times, or abnormally low or high accuracy. Cut-off criteria for false positives was not included due to how the experiment was programmed in the software environment. Although it would have been possible to include cut-off criteria based on accuracy and

reaction time the choice was made to not include this cut-off as a previous study had designed the stimuli used in the current study based on accuracy in a pilot study (Comerchero & Polich, 1999).

Lastly, had full head coverage of NIRS been possible the current study may have been able to examine the relationship between NIRS signals from other brain regions and the EEG activity.

CONCLUSIONS

The current study aimed to address three hypotheses: 1) P3b amplitude would attenuate during the difficult compared to easy tasks, 2) HbO and HbR data would show differential activity in the PFC as a function of task difficulty and, 3) there would be a relationship between P3b, HbO, and HbR difference scores (easy-difficult) where changes in HbO and HbR difference concentrations predict P3b amplitude differences as a function of task difficulty. The first two hypotheses were supported by the results of the data analysis. P3b amplitude was found to attenuate as a function task difficulty where P3b amplitude associated with accurately detected difficult targets was attenuated. In the NIRS data it was observed the HbO concentration in the right medial PFC attenuated in response to difficult targets (or increased in response to easy targets) and increases in HbO along with decreases in HbR were observed in lateral compared to medial optodes. Although there was attenuation in both the P3b and HbO HRF amplitude due to difficult targets, there was not a significant relationship between EEG and NIRS measures, thus the third hypothesis was not supported.

Taken together the results of the current study show that the PFC does not contribute to the attenuation of the P3b, thus the attenuation is due to activity of another neural mass presumably in the parietal lobe (Bledowski et al., 2004; Polich, 2007; Polich, 2012; Potts et al., 1996; McCarthy et al., 1994; McCarthy et al., 1996; McCarthy et al., 1997; Mulert et al., 2004; Smith et al., 1995). The NIRS results corroborate previous research that the right medial PFC is associated with attention generally as well as attention to rare, salient, or potentially rewarding stimuli (Aron et al., 2004; d'Alfonso et al., 2000;

Davidson & Irwin, 1999; Etkin et al., 2011; Peterson & Posner, 2012; Rodgers et al., 2004; Sarter et al., 2001; Small et al., 2003; Wood & Grafman, 2003). Additionally, research examining the amygdala and its role in the analysis of salient stimulus figures has shown functional connections between the amygdala and right medial PFC (Carlson et al., 2012; Carlson et al., 2013; Cunningham & Brosch, 2012; Cunningham et al., 2008; Hamann et al., 2002; Portas et al., 2000; Sander et al., 2003; Wicker et al., 2003). This further supports that the right medial PFC is involved in attention to salience and reward and thus bottom-up processing, as salient and rewarding stimulus features grab attention. The finding that HbO increases and HbR decreases in lateral compared to medial optodes regardless of condition although, to a greater extent in the difficult condition (see Table 1), provided evidence supporting previous findings that lateral PFC is involved in sustained task related attention, or top-down attention (Sarter et al., 2001; Wood & Grafman 2003). Thus, easy targets were salient enough that bottom-up processing was initiated as a means of successful task completion.

In regards to the context updating which states that P3b generation is the result of an attention driven working memory comparison, this means that lateral PFC areas associated with top-down attention during the overall task drove the right medial PFC to direct attention to salient stimulus features in the easy condition and shunt these signals to the parietal lobe for the working memory comparison. However, in the difficult condition, as the target was not as salient as in easy conditions, right medial PFC activity was attenuated. As such, the right medial PFC HbO concentration attenuated due to lack of salience in the difficult conditions and P3b attenuation was due to the similarities between the target and standard in difficult conditions. Thus, delimitation of extraneous neural

activity reflected in P3b amplitude in easy conditions may reflect attentional bias to salience and a lack of limiting in difficult condition reflects an increase in activity related to other methods of task completion. Although it may seem that attenuation in HbO and P3b are due to the same reason, right medial PFC HbO attenuation is likely related to a reduction in general bias to salience not salience relative to the standard as is the case for P3b since the P3b is produced by a working memory comparison. Previous findings have also shown that the right medial PFC was involved in making fear associations in a network with the amygdala (Milad & Quirk, 2002; Quirk et al., 2003). Given what is known about the amygdala and salience appraisal it can be said that the right medial PFC activation in the current study is due to learning that the small circle is important regardless of the working memory comparison. This study has provided evidence that the lateral PFC was associated with sustained task related (top-down) processing whereas the right medial PFC was associated with stimulus feature driven (bottom-up) processing. This fits with the context updating theory of P300 generation in that the lateral PFC drives the right medial PFC to direct salient stimulus information to the parietal lobe for working memory comparison, where attenuated P3b amplitude in response to difficult targets reflects inhibition of attentional bias and the perceptual differences between incoming signals and the contents of working memory.

While the current study found support for two of three hypotheses, the current study would need to be replicated to corroborate the findings. Replication in this instance would be a logical step as the second hypothesis was “two-tailed” in that it was unknown how task conditions would affect NIRS measures. Thus, a future study should aim to replicate the general pattern of increased HbO and decreased HbR in lateral PFC relative to medial

PFC in the task regardless of condition and increased HbO in right medial PFC for easy compared to difficult conditions. Lastly, by using a task other than the oddball, future studies should aim to test the conclusion of the current study that lateral PFC is associated with top-down processing and that the right medial PFC is associated with bottom-up processing.

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APPENDIX A

Instruction Script

Protocol for "Neuroimaging Target Responses"

Greet & welcome participant, have them fill out the informed consent, get handedness information and transfer to spread sheet. Ask participant to turn off phone. Seat participant 70cm from screen. Read practice instructions before practice, EEG instructions before EEG, and NIRS instructions before NIRS.

Read the following instructions:

Welcome to the practice/ EEG/ NIRS session. In this experiment you will be shown a series of circles in random order on the computer screen. There are three kinds of circles: the regular circle, the target 1 circle, and the target 2 circle. The experiment has two conditions: one condition in which you will be shown the regular circle and the Target 1 circle in random order and one condition in which you will be shown the regular circle and the target 2 circle in random order. Each trial will consist of either a regular or target circle followed by a blank screen. Your task in these experiments is to press the center blue button on the response box in front of you as soon as you see the target 1 circle in target 1 trials and target 2 circle in target 2 trials. You will not make any responses to the regular circle. Each circle will only be on screen briefly so stay attentive. (Skip to EEG/ NIRS or continue for practice) Do you have any questions or concerns?

Please place your left/ right arm on the left/ right arm rest and place your left/ right hand so you can comfortably press the center blue button with your pointer finger.

EEG/ NIRS: Please avoid excessive blinking, the best time to blink is one second after a circle has disappeared. If possible do not blink during the blank screen following a target circle. Also avoid unnecessary movements wrinkling your face, clenching your jaw, wiggling your legs, or touching the NIRS array/ EEG net. Of course you may blink, sneeze, cough, yawn, scratch, etc. as needed. Overall just try to remain still, relaxed, and focused on the task. Do you have any questions or concerns? Please place your left/ right arm on the left/ right arm rest and place your left/ right hand so you can comfortably press the center blue button with your pointer finger.