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Event Related Potentials in a Two Stimuli Auditory Oddball Task in Concussed College Athletes: A Linguistic Component Replication Study

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EVENT RELATED POTENTIAL CHANGES IN A TWO STIMULI AUDITORY
ODDBALL TASK IN CONCUSSED COLLEGE ATHLETES: A LINGUISTIC
COMPONENT REPLICATION STUDY

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Dedication

Dr. Patricia Lara

My deepest gratitude goes to Dr. Patricia Lara, who has unselfishly dedicated herself to the success of her students. Without your endless support and encouragement, this thesis would have not reached its completion. Your strength and character is a continuous inspiration to strive for the very best. The wisdom and knowledge that you have instilled in me will always be a significant contribution to my future success and I will forever be grateful. I want to thank you from the bottom of my heart and express my deepest gratitude for believing in me.

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by

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THESIS

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Abstract

Concussions affect an estimated 1.6 to 3.8 million individuals annually and can result in persistent symptoms and cognitive impairments in attention and memory. Concussions are a rising health concern especially in concussion management. Event Related Potentials (ERP) may more accurately assess cognitive recovery making better return to play decisions. In 2013, Sanchez found no significant difference between concussed athletes and non-concussed individuals in the in amplitude of the P300 ERP component using an auditory oddball task consisting of 2 different consonant, vowel (CV) syllables. Because participants were instructed to maintain a mental and verbal count of the target stimuli, a significant difference between the two groups was found in the latency of the P300a at electrode site FCz. Sanchez (2013) attributed these findings to the complexity of the linguistic component explaining that an increase in complexity increases the cognitive demands required for task completion. The purpose of the current study was to replicate Sanchez' (2013) study by removing the variable of keeping a mental or verbal count of the target stimuli. Results from the present study revealed no statistically significant difference between the two groups in the P300a or b suggesting that the linguistic complexity did not affect the amplitude and latency of the P300 in concussed athletes.

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Chapter 1: Introduction

Head injuries are no longer just an issue for professional athletes as they are now a major concern for athletes of all ages at all levels of play. There is an estimated of 4 to 5 million concussions that occur annually, with increases emerging among middle school athletes (ImPACT, Applications, Inc., 2015). A concussion or mTBI, is described as an injury that is caused by a bump, or jolt to the head (Salvatore & Fjordbak, 2011). Individuals that suffer concussions may experience signs and symptoms for a period of 7-10 days (Salvatore & Fjordbak, 2011). Concussions are difficult to diagnose because not all concussion symptoms are easily visible or appear immediately in the individual. The Centers for Disease Control and Prevention describes mild traumatic brain injuries as a “silent epidemic” because of its severely underestimated impact on a person’s health. Despite the term of “mild,” the deficits seen in concussed individuals are anything but “mild” and have major implications in an individual’s cognition (CDC, 2015). A symptomatic individual may experience confusion, disorientation, unsteadiness, dizziness, headache, and visual disturbances (Giza & Hovda, 2001).

What is even more concerning is that athletes are often unenthusiastic about reporting concussions or concussion-like symptoms. One of the possible reasons that athletes fail to report concussion like symptoms is the fear they may be taken out of the game at that point in time and possibly be withheld from play in future games. For example, when NFL athletes were asked in face-to-face interviews about their concussion history, only 15% of them reported a history of concussion. However, when this same group of individuals was asked to report the incidence anonymously, 75% of them reported a history of concussion (Guskiewicz et al., 2005). Taking into consideration today’s sports culture, in the minds of many young athletes striving to become professional athletes, time spent away from their sport due to a concussion may decrease their chances of reaching the collegiate or professional level. A study conducted by the National Collegiate Athletic Association and the American Institute for Research found that athletes have

significantly high expectations (84%) for reaching professional athletic careers (Beamon & Bell, 2002).

Another reason that a concussion may go unreported is that a concussion may be unrecognized by coaches and trainers due to the lack of training and education on the subject. Thus coaches and trainers are unable to identify that a concussion has occurred. Often, people associate a concussion with a loss of consciousness, but 90% of diagnosed concussions do not involve a loss of consciousness (ImPACT, Applications, Inc., 2015). Rather concussion may present as difficulty with attention, concentration, memory, emotional instability, and depression. (Potter & Barrett, 1999).

Researchers continue to study the epidemiology and impact of TBI because TBI's remain one of the greatest health problems not just in the United States but internationally (McCrea, 2008). One of the reasons concussions are on the rise may be attributed to players becoming bigger, stronger, and faster; therefore, the impacts athletes are sustaining in contact sports are greater, harder, and rougher (Gessel, Fields, Collins, Dick, & Comstock, 2007). As more personal stories from athletes that sustain concussions come to light regarding their experience with concussions and the long-term effects that they deal with, it is crucial that research continues to increase our knowledge in this area. "The occurrence of concussions in contact sports is a problem of such magnitude that improvements in diagnosis and management are desirable" (Gosselin, Theriault, Leclerc, Montplaisir, & Lassonde, 2006). Increased knowledge about concussions may lead to improved return to play and/or return to academics decision making process.

The increase in the incidence of concussion and the call for improvements in the diagnosis and management of concussion requires the implementation of more sophisticated instruments to examine neural function following a concussion. Event Related Potentials (ERP) is one measure that has been used to examine functional brain activity in concussed individuals. To the investigators knowledge, only a limited number of studies use ERP to examine the

recovery process in concussed individuals (Broglia, Pontifex, O'Connor, & Hillman, 2009). As a result, a gap exists in the literature. The current study attempts to decrease the gap and increase the knowledge base on recovery of concussion using Event Related Potentials (ERP). The current study uses ERP to examine functional brain activity at the level of the cortex in response to a linguistic oddball paradigm task in two groups of individuals, non-concussed and individuals with concussion. ERP is time-locked to a specific stimulus providing information about the electrophysiologic behavior in the millisecond time range. Due to its excellent temporal resolution, ERP is a significant addition to the management of concussion.

The studies that examine electrophysiologic behaviors in concussed individuals use a simple task called the “oddball” task. The oddball task consists of presentations of a high probability non-target stimuli mixed with low probability target stimuli. In the task, the participant is required to discriminate between the non-targets from the target stimuli. In the studies that use ERP to examine cognitive processes in concussed individuals the measure of interest is the P300 component. The P300 component is associated with attention. Previous studies that use the oddball task and ERP to examine electrophysiological behavior demonstrate differences in the amplitude and latency of the P300 ERP component. These results suggest that individuals with concussion have difficulty with attention.

1.1 Concussion

The CDC (2015) defines concussions as “a type of traumatic brain injury- or TBI - caused by a bump, blow, or jolt to the head or by a hit to the body that causes the head and brain to move rapidly back and forth. This sudden movement causes the brain to bounce around or twist in the skull, stretching and damaging brain cells resulting in chemical changes in the brain.” Other sources like the First International Symposium on Concussion in Sports, further expanded the definition to include the following five criteria: 1: a concussion may be caused by either a direct blow to the head or to another portion of the body that results in an impulsive force that is therefore transmitted to the head; 2: there are immediate and short lived deterioration of

neurological functions attributable from a concussion; 3: there are neuropathological changes from the concussion, though in the acute stage the clinical symptoms imitate a functional disorder rather than actual structural damages; 4: the concussion may have various clinical symptoms and range in severities, which may or may not indicate that there was a loss of consciousness; and 5: the concussion is generally associated with normal structural neuroimaging results (Gosselin, Theriault, Leclerc, Montplaisir, & Lassonde, 2006). While different definitions of concussions are used, all agree a concussion causes severe neurological, emotional, and physical changes that impact an individual's well-being.

1.1.1 Incidence

At the global level the incidence of concussions continue to increase. Annual rates from the United States, Australia, and the United Kingdom suggest that approximately 100-160 per 100,000 individuals are admitted to the hospital following concussion and/or concussion related symptoms. Not surprisingly, concussions are now seen across all age groups. Carroll et al., (2004) reported on the WHO Collaborating Centre Task Force on Mild Traumatic Brain Injury reports that 25% of mild TBIs are seen in children 5-14 years of age.

At the national level, the CDC (2015) reports an incidence of 1.6 to 3.2 million recreational/sports related traumatic brain injuries a year. However, the suspicion is that the incidence is significantly higher. One of the reasons that the incidence of concussion may be dramatically under estimated is that at the present time, there is no biologic marker or diagnostic tests with perfect sensitivity to detect a concussion (McCrea, Hammeke, Olsen, Leo, Guskiewicz, 2004). An additional factor that leads to the underreporting of concussions is the fact that athletes may not recognize that they have sustained a concussion (Gosselin, Theriault, Leclerc, Montplaisir, & Lassonde, 2006). At the local level, Puga, (2011) reported that the incidence of sports related concussions admitted to the emergency departments in the El Paso area hospitals was statistically smaller than the incidence reported by athletic trainers in the El Paso high schools. Furthermore, a cursory inspection of the incidence of concussion reported by

El Paso high school athletes during baseline testing suggests an incidence of approximately 25%. These rates suggest that at the local level concussions are also underreported.

Guskiewicz, et al., (2000) reported nationally that approximately 5% of high school and collegiate athletes experience a concussion each season. However, similar to local, national and global findings, the incidence of concussion may be underreported. Reasons that concussions are underreported include whether the number of concussions is determined by athlete self-report, sideline diagnosis, or admission to a hospital emergency room. In addition, the athlete's lack of knowledge regarding concussion and concussion-like symptoms may influence whether the athlete will report a concussion or history of concussions.

A possible explanation for an athlete's lack of knowledge regarding concussion is that the symptoms of concussions are not as obvious as a broken bone or an open wound. Since concussions are not visible to the eye, someone with a concussion may "look normal." However, a concussion is a very serious injury that is identified primarily by symptoms that the individual cannot simply "walk off." Furthermore, team physicians and athletic trainers are under scrutiny not only for failure to accurately diagnose a concussion, but also because of difficulty determining a recovery timeline. As a result, researchers continue to examine and study the long-term effects of concussions and how to effectively manage sports related concussions (Lau, 2011).

1.1.2 Neurological Dysfunction

Biomechanical forces such as shearing, stretching, and twisting that occur during a concussion result in neurological dysfunction (Giza & Hovda, 2001). The physical damage to the brain following a concussion results in a series of pathophysiological events. These events are: (i) immediate neural depolarization; (ii) discharge of excitatory neurotransmitters, (iii) ionic changes; (iv) glucose metabolism fluctuations; (v) altered cerebral blood flow; and (vi) diminished axonal function (Giza & Hovda, 2011). This neurological dysfunction occurs because the brain sustains a traumatic injury and in turn, the results of those events manifest into the signs

and symptoms of cognitive deficits including difficulty with attention and concentration, impaired coordination, deficits in memory, and emotional changes.

Furthermore, Giza and Hoyda (2001) suggest that pairing the clinical sign or symptom with the specific physiologic disruption is difficult because in a concussion the brain lesion is not localized. The trauma that occurs in the brain as a result of a concussion may lead to long lasting changes in cognitive potential despite the lack of initial evidence pointing to a deficit.

Additionally, Giza and Hoyda (2001) report that individuals that suffer from concussion may present with normal Glasgow Coma Scale scores in spite of having tremendous amount of change in the cerebral metabolism. This suggests that in-depth clinical assessment is important in uncovering the cognitive deficits related to “altered cerebral physiology.”

1.1.3 Structural Damage

The physiology of concussions in the past decade has seen scientific developments from previous theories of the pathophysiology of neuronal injury (McCrea, 2008). It was previously assumed that the clinical signs and symptoms of a concussion were due to the destruction or sheering of the neuronal axons. However, the extensive research demonstrates that the pathophysiology of an mTBI does not indicate that the neurons have been destroyed, rather it indicates the neurons are dysfunctional (McCrea, 2008). Cell death following an mTBI is very rare and is associated to the severity of the injury. McCrea (2008) states that mild concussions likely produce no permanent damage to the cells. Meaning that, if there was permanent cell damage, it would lead to long-term symptoms and deficits. Whereas in severe traumatic brain injuries containing significant forces, produces cellular death and dysfunction with marked functional consequences. At the cellular level, injuries in the mil mTBI range from total and rapid reversible cellular dysfunction which results in slow but also complete recovery (Iverson, 2005). Moderate mTBI, at the cellular level, show slow but incomplete recovery, and severe mTBI demonstrates cell death (Iverson, 2005). Furthermore, the clinical manifestation of an mTBI results from successive neuronal dysfunction that is due to the shifts in ions, alterations in

metabolism, an impaired connectivity, and the changes in neurotransmission (McCrea, 2008).

1.1.4 Syndromes

The cerebral pathophysiology in a human is affected for a number of days following a concussion. As a result, many of the symptoms will resolve between 7 to 10 days with most disappearing within 3 months following the concussion. However, there are individuals that continue to experience symptoms on a long-term basis (Potter et. al., 2001). This long term and persistent symptomology that results in chronic cognitive and neurobehavioral disturbances is known as Post-Concussion Syndrome (ImPACT, App., Inc., 2015). Another syndrome associated with concussion is Second Impact Syndrome. (SIS). SIS occurs when an athlete receives a second injury to the head before the athlete has fully recovered from the original concussion. According to McCrea (2008) the second impact causes the brain to immediately begin swelling before the symptoms from the first injury have subsided resulting in devastating consequences and possibly death. Concussions can lead to syndromes that leave long term effects in cognitive functioning. Therefore, it is critical to find additional measures that will examine cognitive function, such as attention, since attention is a fundamental prerequisite for higher order cognitive processes. One measure that may be of significant value in concussion management in measuring attention is Event Related Potential (ERP).

1.2 Event Related Potential (ERP)

According to Bressler (2006) and Handy (2005) ERP examines the underlying processes of cognition. ERP measures electrical activity produced in the brain in response to the stimuli presented. ERP are generated by changes in the polarization of cell membranes in the nervous system (Hillyard & Picton, 2011). ERP's provide specific information regarding an event at a precise time because they are time locked to a specific event. Therefore, ERP provide real-time information in the millisecond time range (Handy, 2005). While spatial resolution is not one of ERP strengths, it does provide information about a location of where the process is occurring relative to electrode placement. The electrical activity is measured using a skullcap with

electrodes attached so it is minimally invasive. Those reasons make ERP an ideal choice for the management of concussion. Although ERP is primarily used in aphasia research, there is a gradual increase in the number of studies that use ERP in concussion research.

ERP is seen as a series of patterned voltage changes in the ongoing EEG that are time locked to sensory, motor, and cognitive events (Hillyard & Picton, 2011). These patterned voltage changes are seen in an ERP waveform as a series of positive and negative peaks that are identified by their time of occurrence and polarity (Bressler, 2006). Similarly Handy (2005) explains that an ERP waveform consists of a series of peaks and troughs due to voltage deflections. These voltage deflections reflect the sum of several relatively independent latent components. Table 1.2 shows the major cognitive and language ERP components.

Table 1.1 Major Cognitive ERP Components

TASK RELATED ERP COMPONENT	COGNITIVE EVENT
N100	Recognition of Auditory Stimuli
P200	Recognition of Visual Stimuli
N200	Recognition of change in repetitive Auditory Stimuli
P300	Attention; Memory Updating
N400	Semantic Processing
P600	Syntactic Processing

ERP components are measured by the peak amplitudes and latencies. The degree of engagement that a cognitive process is associated with is the amplitude of a component. Variations in amplitudes are measured in microvolts and are dependent on the demands of the

task that the participant is exposed to at that particular point in time. Latency is measured in milliseconds using onset, rise time, peak latency, and/or duration.

To identify specific ERP components on a waveform a letter and a number are associated together. The two letters that are used to identify amplitude polarity are “P” and “N.” A positive upward deflection is indicated by the letter “P” and a negative downward deflection is indicated by the letter “N”. The number following the letter indicates the latency and is measured in milliseconds. There are several ERP components associated with language processes. Both the N400 and the P600 are language related components. The N400 is a negative-going peak that is typically elicited in response to a violation of a semantic expectation and occurs at approximately 400 ms following the onset of the stimulus. The P600 is a positive-going wave that is elicited by syntactic violations and occurs at approximately 600 ms following the onset of the stimulus (Luck, 2005).

Some ERP components are associated with cognition. One of the ERP components associated with cognition is the P300. The P300 is a positive going wave associated with attention and is elicited by unexpected stimuli and occurs at 300 ms following onset of the stimulus. The P300 is the component of interest for this study. The P300 component was first reported at the New York Psychiatric Institute by Sam Sutton and colleagues (Polich, 1993). They observed that the P300, or P3, was a component that reflected a large positive directed peak that occurred when the patient was instructed to discriminate between two tones, non-target tones and target tones. The results showed that the P300 occurred upon the presentation of the target tone (Polich, 1993).

The P300 ERP component is traditionally observed in studies using an oddball paradigm that presents a sequence of events representing two categories, with one of those categories occurring less frequently (Gray, Ambady, Lowenthal, & Deldin, 2003). ERP studies show that the P300 ERP component is primarily seen at electrode sites FCz, Cz, CPz, and Pz. For example, in a study conducted on participants with mild head injuries the P300a was displayed at electrode

sites FCz and Cz, whereas the P300b was displayed at electrode sites CPz and Pz (Segalowitz, Bernstein, & Lawson, 2001).

1.3 P300a and P300b

In ERP studies that examine attention, there are two subcomponents of the P300 that are observed. These subcomponents are the P300a (P3a) and P300b (P3b). According to Bressler (2006) the P3a and P3b are distinguished by their temporal amplitudes. A P300a is described as a frontal component whereas a P300b occurs later and is observed in the parietal region. Further, the P300a is elicited by the unexpected novel stimuli. On the other hand, the amplitude of the P3b is dependent on the probability of the stimuli occurring and the latency reflects the degree of difficulty in categorizing the stimuli.

Other research found that the P300a is seen as the “novelty detection” and the P300b is referred to as the “target detection” (Fusar-Poli, 2010). The P300a deviations are visible at the frontocentral area of the brain and typically occur around 280-350ms (Luck, 2005). The P300a is elicited by task irrelevant stimuli and is considered to be a marker of involuntary orienting of attention and novelty (Squires et. al., 1975). Handy (2005) describes the P300b wave as a positive going wave that peaks at about 300-600ms after the detection of infrequent targets embedded in a series of background stimuli.

Furthermore, the P300 component is elicited with higher-order cognitive operations such as selective attention and resource allocation (Donchin & Coles, 1988). Others confirm that the P300 component is a measure of attention that arises independently of behavioral responding (Gray, Ambady, Lowenthal, & Deldin, 2003). The P300 ERP component is examined in cognitive research because attention is a prerequisite for successful accomplishment of many other higher order cognitive processes.

1.4 Auditory Oddball Paradigm

The oddball paradigm is one of the most widely used experimental tasks used in attentional research. Attentional studies that use ERP and visual oddball tasks have found

significant differences in amplitude of the P300 ERP component. For example, Brogolio, Pontifex, O'Connor, and Hillman (2009) used a visual oddball paradigm and found persistent decreases in the amplitude of the P300 component three years post-concussion. While the visual oddball paradigm is traditionally used with ERP to examine attention, the auditory oddball paradigm offers some of the same possibilities when investigating interactions between the P300 ERP component, attention and processing capacity (Polich & Kok, 1995). For example, De Beaumont et. al., 2009, used an auditory oddball paradigm to examine the effects of concussion on cognitive and motor functions 30 years post-concussion.

The results showed a P300 amplitude attenuation and latency delay even 30 years after a concussion was sustained. An auditory oddball paradigm uses target and non-target tones that the participant is required to distinguish. The present study uses a variation of the auditory oddball task. This variation consists of using a linguistic component instead of tones. This variation was done because some ERP studies on attention in healthy individuals have shown left lateralization in the temporoparietal electrode sites of the N200 component. This suggests that a linguistic element will not interfere with the auditory oddball paradigm. In addition, the addition of the linguistic element may increase the demands of the task resulting in increased amplitudes of the attentional ERP components.

1.4.1 Linguistic Component

While a traditional auditory oddball task is routinely used with tones, this study contained a linguistic component in which target and non-target speech sounds were utilized in replacement of the tones. Minimal research has been published examining the effects on the use of a tonal task rather than the use of a linguistic task in an oddball paradigm. In the research that has been published in this area, it states that there has been no statistically significant differences amongst participants in the use of tones versus speech sounds. Sanchez (2013) also discussed that adding a linguistic component does not interfere with the oddball task paradigm. Due to these findings, a premise consisting of a variation of the traditional oddball task (tonal task) will

be used with the added linguistic component.

In order to incorporate the detection between the target and non-target speech component, the target sound of /kʌ/ (pronounced as [kuh]) was selected, whereas the non-target sound as /tɑ/ (pronounced as [tah]) was chosen. The target and non-target speech components were designated as such due to the fact that they are acquired early in auditory development. Seebach (1994) indicated research has shown that the prenatal auditory environment exposure accounts for the acquisition of basic speech contrasts. The following target and non-target components follow the subsequent criteria: both linguistic components have similar phonetic features; both components are voiceless stop-plosive consonants; and both differ by only their place of articulation, alveolar and velar placements.

1.5 Immediate Post-Concussion Assessment and Cognitive Testing

Currently, behavioral methodology such as the ImPact (ImPACT, Applications, Inc., 2015) is used to assess the recovery of cognitive function post-concussion. The ImPACT is a behavioral assessment instrument used by more than 10,000 trained medical professionals, a majority of teams in the National Football League (NFL), the Major League Baseball (MLB), the National Hockey League (NHL), more than 1,000 universities and colleges, over 7,400 high schools, and 900 clinical centers (ImPACT, Applications, Inc., 2015).

The ImPACT is a computerized evaluation system that assesses neurocognitive function and is scientifically validated. According to the literature, the ImPACT is a computerized neuropsychological screening battery that is designed for the assessment of sport-related concussions (Iverson, Lovell, & Collins, 2006). The ImPACT has comprehensive normative data that includes 75,000 assessment results and is continually being updated. The ImPACT has the largest database of clinical research including 190 peer reviews and over 125 independent studies on concussion management (ImPACT, Applications, Inc., 2015). This behavioral assessment tool measures several aspects of neurocognitive functioning including working memory,

attention span, reaction time, response variability, nonverbal problem-solving, and sustained and selective attention.

The ImPACT assessment tool is considered an important piece in the evaluation and management of concussion. In addition to assessing cognitive function post-concussion, the ImPACT assists trained health care professionals monitor the recovery of an individual's cognitive processes after a concussion. Furthermore, the ImPACT is an invaluable tool in educating athletes, coaches, and parents on the post-concussion status and is used in the return to play or return to academics decision making process. Due to its extensive validity and reliability measures, the results of the ImPACT are accepted by the medical community and considered an up-to-date best practice.

1.5.1 Interpreting ImPACT

The ImPACT consists of six modules that evaluate attention, working memory, and processing speed that yield composite scores in the areas of verbal memory, visual memory, processing speed, reaction time, and impulse motor control (Moser, Glatts, Schatz, 2012). The ImPACT composite scores were assembled in order to provide a summary of information regarding the different cognitive domains. According to the ImPACT, “thus far ImPACT's studies have indicated the verbal memory, visual memory, processing speed, reaction time and symptom scores assist in making a determination between concussed and non-injured individuals” (ImPACT, Applications, Inc., 2015). In addition the self-reporting from the individual yields a total symptom score.

Based on the results obtained from the ImPACT, a clinician can identify any impairments due to the concussion. Results from the ImPACT are used to monitor recovery as results can be compared to baseline or data from non-concussed individuals. Baseline assessment using the ImPACT prior to the start of the season is recommended for athletes. Baseline assessment results are utilized for comparison purposes should a concussion occur. Table 1.1 displays the six modules included in the ImPACT behavioral assessment instrument. Due to the increase in

number of athletes sustaining sports-related concussions, the complete recovery and safe return to participate in sports is determinant on the examination of the results from the ImPACT along with the Total Symptom Score (Salvatore & Fjordbak, 2011).

Table 1.2 ImPACT Assessment Modules

Module	Task	Description
Module 1	Word Discrimination	Evaluates attentional processes and verbal recognition memory
Module 2	Design Memory	Evaluates attentional processes and visual recognition memory
Module 3	X's and O's	Measures visual working memory as well as visual processing speed
Module 4	Symbol Matching	Evaluates visual processing speed, learning and memory
Module 5	Color Matching	Represents a choice reaction time task and also measures impulse control and response inhibition
Module 6	Three Letter Memory	Measures working memory and visual-motor response speed

ImPACT Assessment modules by module number, the task, and a description of the task (ImPACT, Applications, Inc., 2015).

1.5.2 Concussion Management Model

The ImPACT employs a Concussion Management Model (Figure 1.1). The Concussion Management Model is a five step protocol that is used in making safe and appropriate return-to-play decisions for athletes. The appropriate use of the protocol helps prevent the likelihood of any long-term injuries.

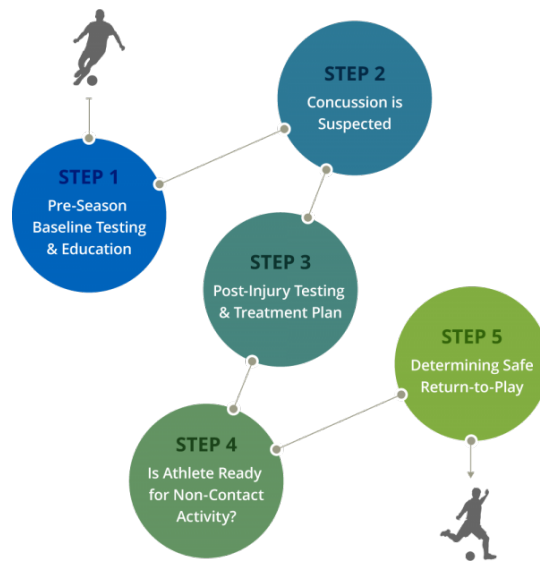


Figure 1.1 Concussion Management Five-Step Protocol

The Concussion Management Model is a five step protocol currently used to make safe and appropriate return-to-play decisions for athletes (ImPACT, Applications, Inc., 2015).

At the present time the ImPACT is used by health care professionals to make academic and return-to-play decisions, however it should never be the only assessment instrument used to make this decision. Therefore, this study examines attention in a group of concussed individuals to investigate the utility of ERP in the management of concussion.

1.5.3 ERP, Oddball, and Concussion

Research conducted using the auditory oddball paradigm has consistently revealed amplitude attenuation along with a delay in latency of the P300 component. The studies reviewed below utilized an auditory oddball paradigm along with ERP to analyze attention.

In a study by Pratap-Chand, Sinniah, & Salem (1988) the researchers compared 20 participants with minor head injuries to 20 individuals with no previous history of head injuries to examine differences in electrophysiologic performance. The results from the study show significant abnormalities of the P300 ERP component in amplitude and latency in participants with a concussion 4 days after the injury occurred. The study also reports a recovery was seen

as evidenced by increased amplitude in the P300 component when repeated testing was completed 30 days after the original test. This suggests that auditory oddball paradigm and ERP are additional measures that can be used to assess cognitive recovery in participants with mild head injuries.

In another study conducted by Bierbrauer and Weissenborn (1998), the recovery of 15 patients within 24 hours of a mild head injury as well as at weeks 1, 3, and 8 after the head injury was examined. The 15 participants in the experimental group presented with mild to severe head injuries. The participants were compared to a group of age matched healthy participants. The results show that the P300 component remained affected up to two months post injury. Furthermore, the results also show that in participants with mild head injuries, the P300 component was not as severely attenuated as individuals with severe head injuries.

Similarly, the study conducted by Rugg, Pickles, Potter, Doyle, Pentland, & Roberts (1992) found consistent latency delays in the P300 ERP component of individuals sustaining closed head injuries 6 months post injury. Even more significant are the findings of De Beaumont et al. (2009) who found attenuation in amplitude of the P300 ERP component in individuals that were 30 years post-concussion. The 56 participants, between 50 and 65 years of age, were former university level athletes. Fifty of these participants were hockey players and the remaining were football players. In addition to the ERP recordings conducted, the participants were also administered a concussion history questionnaire, the Mini-Mental Status Examination, and a general health questionnaire. Results from the study show that cognitive slowness is present in individuals even 30 years post-concussion. The P300 component remains affected over such a long period of time due to factors such as the severity of the concussion or whether an individual has a history of concussions.

Sanchez (2013) reports that there does not appear to be a full recovery as evidenced by decrease in amplitude and increased latency of the P300 ERP component. Others have reported similar results for example Gosselin, Theriault, Leclerc, Montplaisir, and Lassonde (2006) found

a reduction in amplitude and latency of the P300 component are present in athletes that were symptomatic and asymptomatic post-concussion when compared to the healthy individuals. Despite that these patients no longer displayed concussion like symptoms, ERP results still indicated their brain potentials remain affected. The results from these studies suggest that ERP can detect abnormalities in neural activity related to processes such as attention in concussed individuals.

The research using ERP and the auditory oddball paradigm are limited. In attempt to decrease the gap in the literature, Sanchez (2013) used ERP to examine attention in individuals with a concussion. To investigate attention and processing, Sanchez (2013) used a variation of the auditory oddball paradigm by adding a linguistic component because Shucard et al. (2004) found that the P300 ERP component elicited using CV syllable sounds. The authors found increased amplitudes of the P300 on target sounds than on non-target sounds. This suggests that a P300 can still be elicited when a linguistic component is added to the auditory oddball paradigm.

Chapter 2: Methods

2.1 Purpose of the Study

Concussions that result from participation in sports are on the rise and are now a major public health issue that is affecting the lives of 3.8 million people annually (Broglia, Pontifex, O'Connor, & Hillman, 2009). Concussion injuries are seen as temporary and void of any long-term consequences because they are being misdiagnosed and not properly managed. While there are behavioral assessments instruments such as the ImPACT, these behavioral measures should not be the only instruments used to diagnose and manage concussions. Mild head injuries are generally given a prognosis ranging from 'good' to 'excellent,' because a majority of patient complaints are difficulty with attention and concentration, and will often alleviate as time passes. However, the literature suggests although concussion like symptoms may resolve within 7-10 days, in some individuals concussions may affect cognitive functioning for months and even years after the injury. The long term effects of mild head injuries on cognitive performance have not been well examined (Segalowitz, Bernstein, Lawson, 2001).

Implementing sensitive instrumentation such as ERP as an additional measure in concussion assessment may assist in development of more precise diagnosis and prognosis. ERP has the ability to detect small and timely changes in cognitive functioning that will clarify discrepancies between the athlete's self-report and the neurocognitive assessments (Broglia, Pontifex, O'Connor, & Hillman, 2009). As a result, ERP is the logical choice to study attention in concussed individuals. Therefore, the purpose of the present study is to replicate Sanchez (2013) and compare the results found between the two studies. A secondary purpose is to compare the electrophysiologic performance between a group of concussed individuals with a group of non-concussed participants. Similar results in a replication of Sanchez (2013) would further demonstrate the need for ERP as an additional measure in the management of concussions.

2.2 Research Question

Is there a statistically significant difference in peak latency and amplitude measurements of the P300a and P300b ERP components between athletes with concussions and non-concussed individuals across central electrode sites using an auditory oddball task with a linguistic component?

2.3 Experimental Design

The current study is a replication study of Sanchez (2013). Sanchez (2013) is a between subject study design that consists of two groups of participants.

2.4 Variables

The independent variables in this study are the participants with no prior history of concussions (control group; NC01 – NC10) and the participants with concussions (experimental group; CA01 – CA05). The dependent variables are the peak amplitude and latency of the P300a and P300b components at electrode sites FCz, Cz, CPz, and Pz. The P300a is defined as the highest positive going peak occurring between 280-350ms. The P300b is defined as the highest positive going peak occurring between 350-600ms. These operational definitions are the same as the ones used in Sanchez (2013).

2.5 Participants

Fifteen college age males participated in this study. One group of participants included ten college aged males with no history of concussion, “non-concussed.” The non-concussed individuals were assigned to the control group and identified with the letters NC. The second group consisted of five college aged male athletes with a history of concussion, “concussed.” The concussed individuals were assigned to the experimental group and were identified with the letters CA. Participants ranged in age from 18 years to 25 years of age. See table 2.1 for the participant characteristics of the control group. See table 2.2 for participant characteristics of the experimental group.

Table 2.1: Participant Characteristics (Control Group)

Non-Concussed Participants	Age	Gender
NC01	21	M
NC02	24	M
NC03	22	M
NC04	25	M
NC05	25	M
NC06	24	M
NC07	25	M
NC08	20	M
NC09	25	M
NC10	24	M
Mean	23.5	

Table 2.2: Participant Characteristics (Experimental Group)

Participant	Age	Sex	Time Since Injury	Nature of Injury	Loss of Consciousness	Time Unconscious	Persistent Symptoms
CA01	19	M	10 days	Ice Hockey Occipital Impact Hit from behind	Yes	30 Seconds	Yes
CA02	25	M	35 months	Ice Hockey Frontal Impact Pushed into wall	No	None	No
CA03	18	M	5 days	Ice Hockey Right Temporal Impact Fight	Yes	2 Minutes	Yes
CA04	22	M	58 months	Ice Hockey Temporal impact Hit head on ice	No	None	No
CA05	25	M	24 months	Tennis Right frontal Impact Ball to head	Yes	1 Minute	No

Table 2.2 provides a detailed perspective of the participants with a history of concussion. The following sports were represented: ice hockey (n=4) and tennis (n=1). Nature of Injury section details the sport, location of impact, and cause of injury.

The inclusion criteria for the control group included college age between 18-25 years of age, male, no history of traumatic head injuries, and normal or corrected to normal hearing. Inclusion criteria for the experimental group included college age between 18-25 years of age, male, and a diagnosis of a concussion by a medical doctor or physician. All participants assigned to the experimental group were referred to the Concussion Management Clinic at the University of Texas at El Paso by their athletic trainer and/or physician. The control group and experimental groups were similar in age, gender, and education level. All participants met the inclusion criteria.

Prior to testing, all procedures, benefits and risks related to the research project were comprehensively explained to each participant as per provided by the University of Texas at El Paso IRB guidelines. The participant's rights not to participate or withdraw from the study at any time during the study were explained to the participant. Participant was informed that their participation was voluntary in this study. Once all questions were answered to the satisfaction of the participant, the participants signed a written informed consent.

2.6 Procedures

A concussion history questionnaire was administered to participants in the experimental group. The purpose of the concussion history questionnaire was to obtain detailed information regarding: the number of previous concussions, dates of concussions, a description of the accident and any symptoms that the participant may have sensed after the injury. Each participant's hearing was tested in a soundproof hearing screening booth. The hearing screening occurred in both the left and right ears at 25 decibels at 1000 Hz, 2000Hz, and 4000Hz. Following the hearing screening, participants in the experimental group completed neurocognitive testing using the ImPACT test.

2.6.1 Electrophysiologic Procedures

Following neurocognitive testing, the electrophysiologic task was completed. The ERP was recorded from 64 active Ag/AgCl electrodes (Biosemi Active Two system) using a linguistic auditory “oddball” procedure. Participants were fitted with an elastic electrode cap with 64 electrodes attached. The electrodes are systematically distributed across the frontal, parietal, temporal, and occipital areas of the head according to the International 10-20 System. To determine the best fitting cap, the participant’s head was measured. The cap is centered at the intersection of the Cz electrode, specifically from the midpoint of the anterior and posterior (nasion to inion) measurement to the midpoint of the side to side (inter-tragus to inter-tragus) measurement. The electrodes were filled with Signa electrode gel to decrease impedance. The ocular references were placed above and below the left eye. The temporal references were placed on the left and right temples. The mastoid references were placed on the left and right mastoid. All electrodes were references to the mastoids. Figure 2.2 illustrates a schematic representation of the electrode placement on the cap.

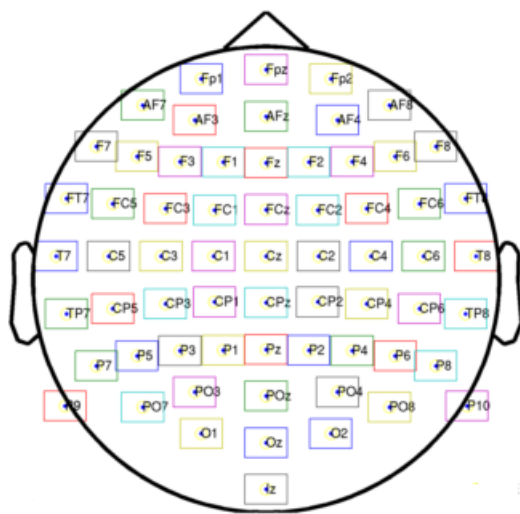


Figure 2.1 Skull Cap Electrode Layout

This illustration is a schematic representation specifically for the 64 electrode layout and represents the location of each electrode using this specific placement.

2.6.2 Experimental Task Procedures

The participant was seated comfortably in a 6 X 6 ft. soundproof booth in front of the Entuitive Touchmonitor. The participant was asked to place his hands in their lap at the start of the procedure. The participant was then asked to visually fixate on the white square in the middle of the black screen (Figure 2.1) and to listen to the auditory stimuli that was presented. No motor response was required from the participant.

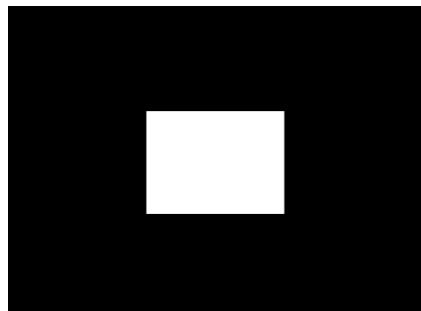


Figure 2.2 Observational White Sample

Participants instructed to visually fixate on the white square in the middle of the black screen during task.

A linguistic auditory oddball task using two consonant-vowel syllables, /ta/ and /ku/ were used to assess the stimuli-locked electrophysiological changes. Administration of the oddball paradigm using ERP lasted approximately 24 minutes.

2.7 Stimuli

The experimental task is the same one used in Sanchez (2013). The experimental task is an auditory oddball paradigm that involves the auditory presentation of two English consonant-vowel syllables. These two syllables are spoken in a male voice and are binaurally presented one at a time through the speakers at 80 dB HL placed two feet away from the participant. The two speech sounds used for this experimental task included /tʌ/ (pronounced as [tuh]) and /kʌ/

(pronounced as [kuh]). These sounds were selected for the following reasons: their phonetic features are similar; both sounds are voiceless, stop-plosive consonants; and both sounds differ only by their place of articulation; alveolar and velar, respectively. Superlab (Superlab Pro, Cedrus Corp.) software was used to create the oddball task and to present the linguistic auditory stimuli to the participant.

Two blocks of 200 stimuli were presented to the participant; 160 of those being non-target tones (/tʌ/), and 40 of those being target tones (/kʌ/) in random sequence. The second block was inverted to control for any electrophysiological differences associated with detection of different phonetic components of the CV sounds (Sanchez, 2013). The paradigm of 80-20 was used in order to control for the frequency of stimuli presented. The auditory CV sounds are presented at 80dB. Each stimulus has a duration of 50 milliseconds and a rise and fall time of 10 milliseconds along with an interstimulus interval (ISI) of 1000 milliseconds. A schematic representation of the experimental task is presented below.

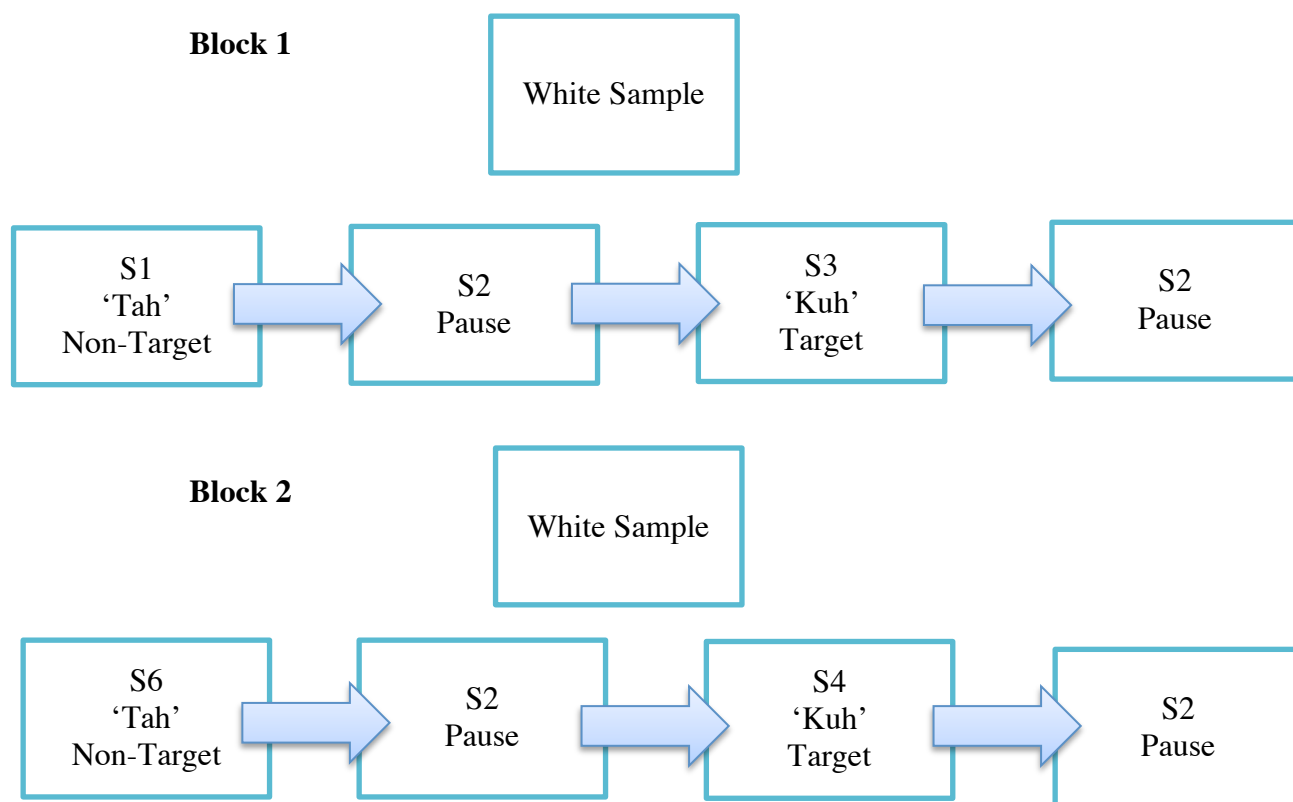


Figure 2.3 Schematic Representation of Experimental Task

2.8 Triggers

Triggers, or event markers, are used to mark, measure and analyze distinct time segments within an EEG waveform. They mark the events within a trial. For clarification, triggers (known as event markers) will be used in the remainder of this study. See Table 2.9 for placement of the triggers in the current study.

Table 2.3 Triggers per Trial

Triggers (Event Markers)	S1	S2	S3	S4	S6
Stimuli	‘Ta’	Pause	‘Ku’	‘Ku’	‘Ta’
Quantity Presented	160	400	40	40	160

In the above table of the schematic representation, S refers to the trigger that was used for the purpose of recording. The white sample was continuous throughout the entire task. In block one, following the 80-20 paradigm, S1 marks the onset of the auditory stimulus and is the non-target sound, followed by S2 which is the onset of an ISI (interstimulus interval) that lasts for 1000ms, followed by S3 which is the auditory stimulus for the target sound, and ends with S2 which is the auditory stimulus for the non-target sound.

Block 1: White Sample □ (S1□S2) □ (S3□S2)

In block two, also following the 80-20 paradigm, S6 marks the onset of the auditory stimulus and is the non-target sound, followed by S2 which is the onset of an ISI (interstimulus interval) that lasts for 1000ms, followed by S4 which is the auditory stimulus for the target sound, and ends with S2 which is the auditory stimulus for the non-target sound.

Block 2: White Sample □ (S6□S2) □ (S4□S2)

The triggers were not shown to the participant during the experimental task, but were marked during the ERP recordings. The events in the task were randomized but followed an 80-20 paradigm in that 80 percent of the sounds were non-target sounds and 20 percent of the sounds were the target. Once the first block was completed the second block began without any distinctive pausing so the participant would not know that the new block had begun. At the onset of block two, the block was inverted from the previous block to ensure that the participants would not detect or suspect a pattern to the non-target and target sounds in the oddball paradigm.

2.9 Data Collection

Electrical activity was recorded from the 64 electrodes that were placed on the skull cap according to the International 10-20 System. All electrodes were referenced to the left and right mastoids. All electrodes were referenced to the mastoids. The four electrodes placed on the lower outer canthi and the orbital ridge of the right eye and the right and left temple were used to correct and tract eye blinking artifacts (Handy, 2005; Jasper, 1958; Rugg & Coles, 1997; & Luck, 2005). Active Two from Biosemi was used to record the electrical signals. Electrical signals were transmitted from the electrodes at a rate of 2,048 Hz. The low cut off for the bandpass was set at 0.1Hz with a 12dB slope and a high cutoff was set at 30 Hz. A notch filter filtering out noise coming from any surrounding electrical power lines and electrical illumination was used and set at 60 Hz.

2.9.1 Data Analysis

Segmentation is the process that divides the electrophysiologic data into temporal blocks or time windows. These time windows are called epochs. Epochs are created so that the individual trials can be analyzed and averaged. Segmentation of ERP data is completed from one trigger to another trigger. Cognitive response latencies were determined by the occurrence of the P300a and the P300b waveform. Amplitude was measured by the voltage variations that occurred at the point of the P300a and P300b peak latencies. Analysis of the ERP data was completed using Brain Vision Analyzer (Cortech Solutions, 2008) with a sampling rate set at 512

Hz. Unwanted noise or artifacts were eliminated and filtered at 0.1 Hz for the low cut off and 30 Hz for the high cutoff. Segmentation of S3 and S6 was performed to create 1000 ms epochs. Grand averages were calculated. Generation of cortical activation maps was completed using spatial analysis. This was in the form of topographic maps. Topographic mapping was completed utilizing electrode Cz, because of its central location. Therefore it is the best electrode to visualize overall cortical activation. Cortical Activation maps were generated at the P300a and P300b positive peaks.

2.9.2 Statistical Analysis

A 2 x 4 mixed factorial ANOVA was used to compare the differences between and within the control group and experimental group. Similar to Sanchez (2013), independent samples t-tests were completed to compare individual peak amplitude and latency at the CPz, Cz, Pz, and FCz electrode sites. The Mann-Whitney U test was completed as the nonparametric investigation of the null hypothesis in that two groups are from the same population against the alternative hypothesis.

Chapter 3: Results

3.1 ImPACT Results

The Cognitive Efficiency Index (CEI) provides an overall score that takes into account both the speed (reaction time) and accuracy (percent of correct responses) of the individual's performance. In order to be considered valid, the score would have to be above a 0.20. The following modules from the ImPACT test (ImPACT, Applications, Inc., 2015) were selected for analysis: X's and O's, which measures visual working memory and processing speed; Symbol Match, which measures visual processing speed; and Color Match, which measures reaction time and impulse control. The total of incorrect responses in the Color Match and the X's and O's modules are combined to obtain the Impulse Composite Control (ICC) score. The Reaction Time Composite (RTC) score is calculated by obtaining the average reaction time for correct responses in X's and O's, Symbol Match, and Color Match. Total Symptom Scores (TSS) provides a total for all 22 symptoms that are self-reported by the individual. The symptoms are rated from not present (0) to severe (6). A higher score reflects a higher symptom total. Table 3.1 presents the results obtained from the ImPACT test for the CEI, ICC, RTC, and TSS.

3.1.1 Concussion: Acute Stage

Participants CA01 and CA03 were in the acute stage of concussion (10 and 5 days, respectively), had overall scores that differed from those of the other three concussed participants that were approximately 2 or more years post-concussion. ImPACT results for CA01 showed that the participant's responses were compromised by incorrect responses and a decrease in speed. This is demonstrated by a RTC percentile score of <1% that contributed to a negative CEI score (-0.46). Participant CA03 had a CEI score that indicated that there was a compromise between both speed (RTC = 1%) and accuracy, resulting in a score of 0.1 that rendered the CEI score invalid. Both participants CA01 and CA03 had ICC scores of 12 and 14, respectively, which suggest they were impulsive and inaccurate. Individuals with a concussion will report a higher number of symptoms depending on the severity of the concussion. This is seen in

participants CA01 and CA03 whose TSS scores of 13 and 73, respectively, are higher than the post-acute participants.

3.1.2 Concussion: Post-Acute Phase

Participants CA02, CA04, and CA05 had valid CEI scores. The RTC scores for participants CA02 (RTC = 69%), CA04 (RTC = 86%), and CA05 (RTC = 52%) contributed to their valid CEI scores. These participants had low ICC composite scores suggesting a low level of impulsivity.

Additionally, the three participants in the post-acute phase of concussion reported no symptoms.

Table 3.1 ImPACT Results

Participant	Cognitive Efficiency Index	Impulse Control Composite	Reaction Time Composite (percentile scores)	Classification Ranges	Total Symptom Score
CA01*	-0.46	12	<1%	Mildly Impaired	13
CA02	0.51	3	69%	Average	0
CA03*	0.1	14	1%	Mildly Impaired	73
CA04	0.56	1	86%	High Average	0
CA05	0.28	4	52%	Average	0

* Acute stage participants

3.2 Grand Average Waveforms

Figures 3.1 to 3.4 show the grand average waveforms at the electrode sites FCz, Cz, CPz, and Pz, at both the P300a and P300b components. A peak amplitude measure was utilized to analyze the waveforms with an operational definition of 280-350ms for the P300a, and 300-600ms for

the P300b component (Sanchez, 2013). To provide consistency in determining specific amplitude and latency data points for each site and condition, two individual raters examined the grand average waveforms and collected grand average data points. This was completed to ensure that data points were representative of and met the operational definition of both P300a and P300b. Therefore, this would demonstrate that the data collected had inter-rater reliability.

3.2.1 Electrode sites FCz and Cz

The ERP waveforms show differences between the non-concussed group and the concussed group. A decrease in amplitude and an earlier latency for P300a in the concussed group was seen at FCz electrode site. The concussed group's waveform show a decrease in amplitude and a delay in latency of the P300b at electrode site FCz. Similarly a decrease in amplitude and delay in latency for the P300b was seen at electrode site Cz for the P300a for the non-concussed group. However a decrease in amplitude with an earlier latency of the P300b was seen in the concussed group.

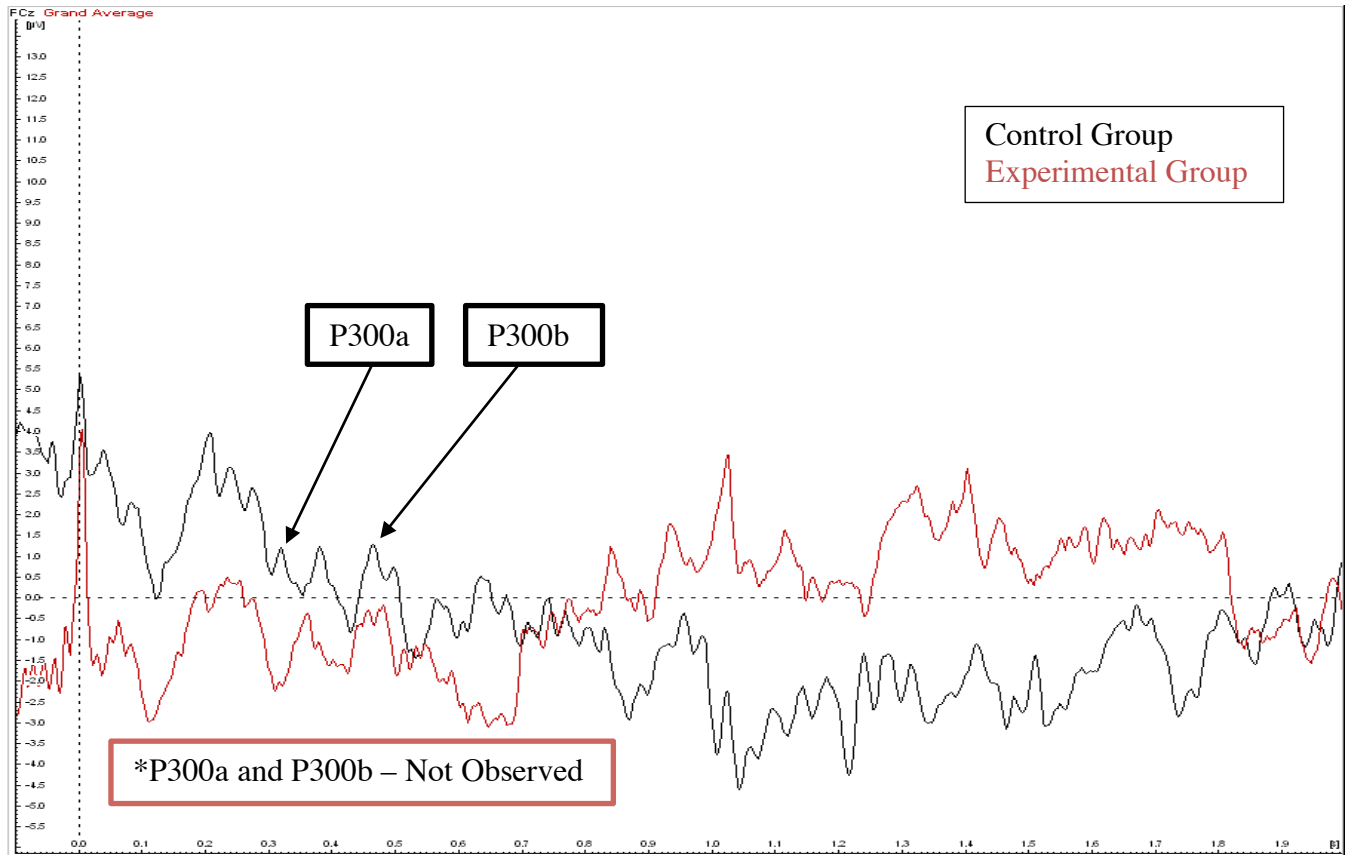
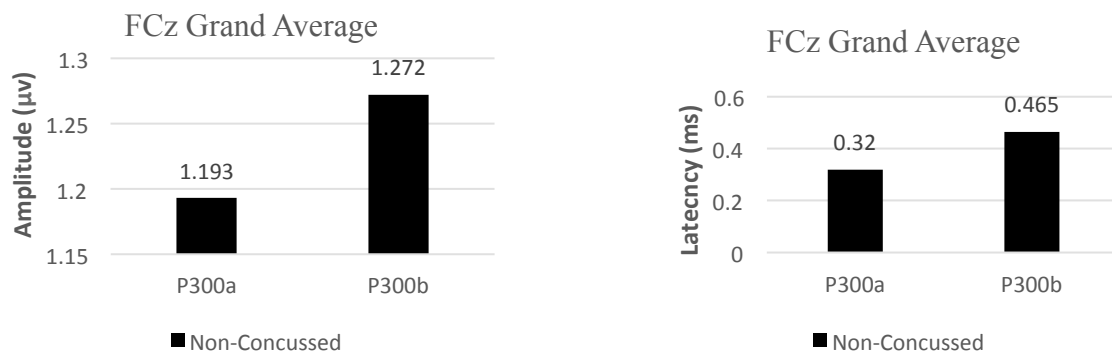


Figure 3.1 FCz Grand Average Waveform

Grand Averaged ERP Waveforms at electrode site FCz for P300a and P300b ERP components.
 *The P300a or P300b components were not observed within the operational definition.

Table 3.2 FCz Grand Averages: Amplitude and Latency



Corresponding Graphs to the FCz Grand Average Waveform at the P300a & P300b components. Experimental Group did not display a P300a or P300b within the operational definition.

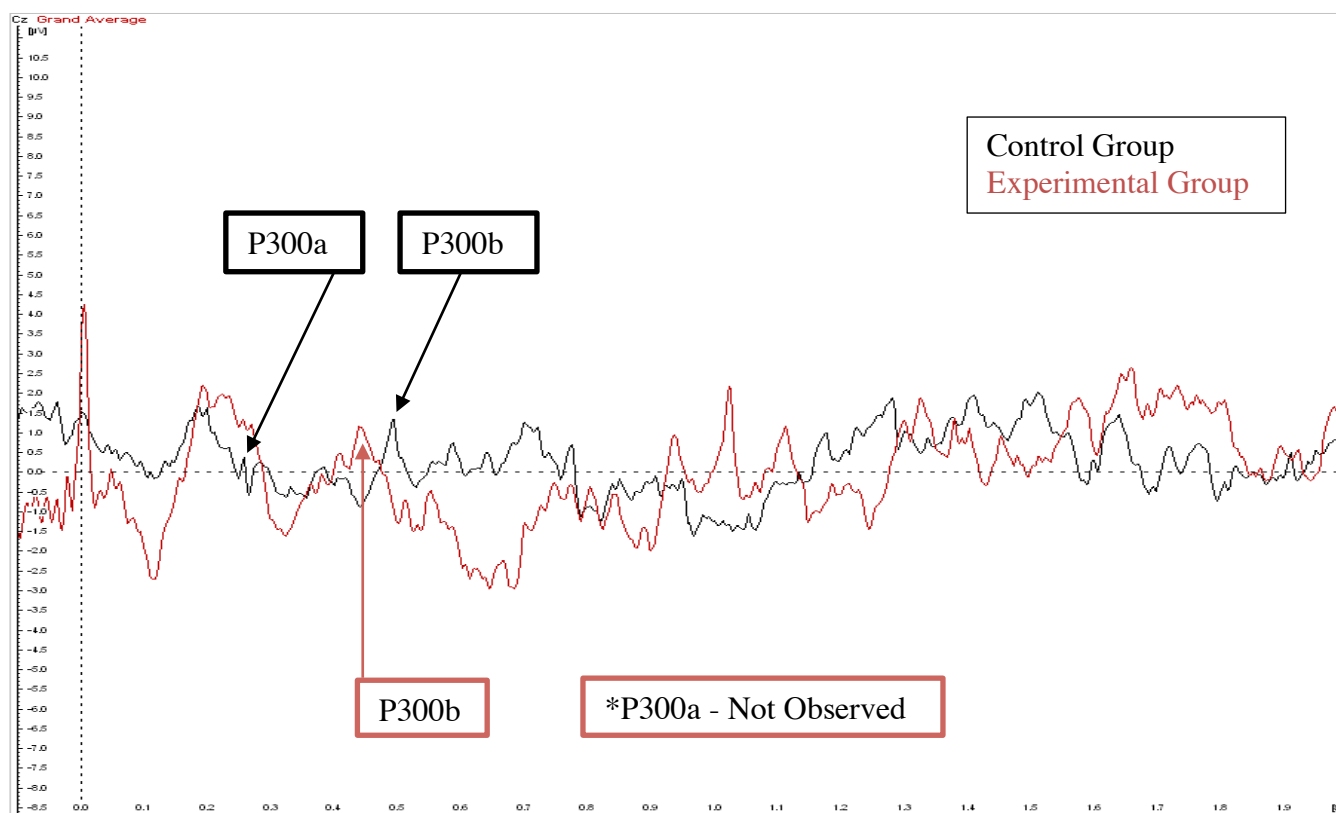
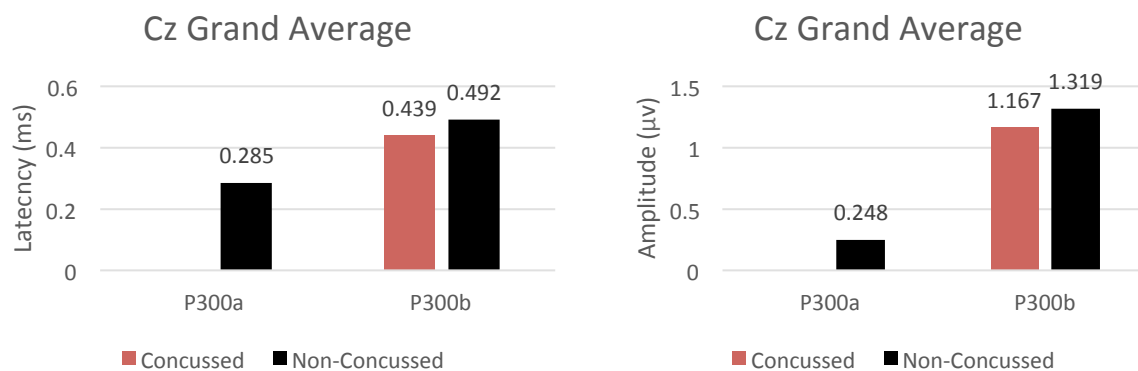


Figure 3.2 Cz Grand Average Waveform

Grand Averaged ERP Waveforms at electrode site Cz for P300a and P300b ERP components.

** The P300a component was not observed within the operational definition.*

Table 3.3 Cz Grand Averages: Amplitude and Latency



Corresponding Graphs to the Cz Grand Average Waveform at the P300a & P300b components. Experimental Group did not display a P300a within the operational definition.

3.2.2 Electrode Sites CPz and Pz

At the CPz electrode site, the concussed group displayed a lower amplitude but a latency equal to that of the non-concussed group for P300a. On the other hand, there was a decrease in amplitude and earlier latency for P300b in the concussed group. At the last electrode site, Pz, the concussed group displayed a decrease in amplitude and a delay in latency in both P300a and P300b. Across all four sites there was a decreased amplitude for both P300a and P300b components for the concussed group.

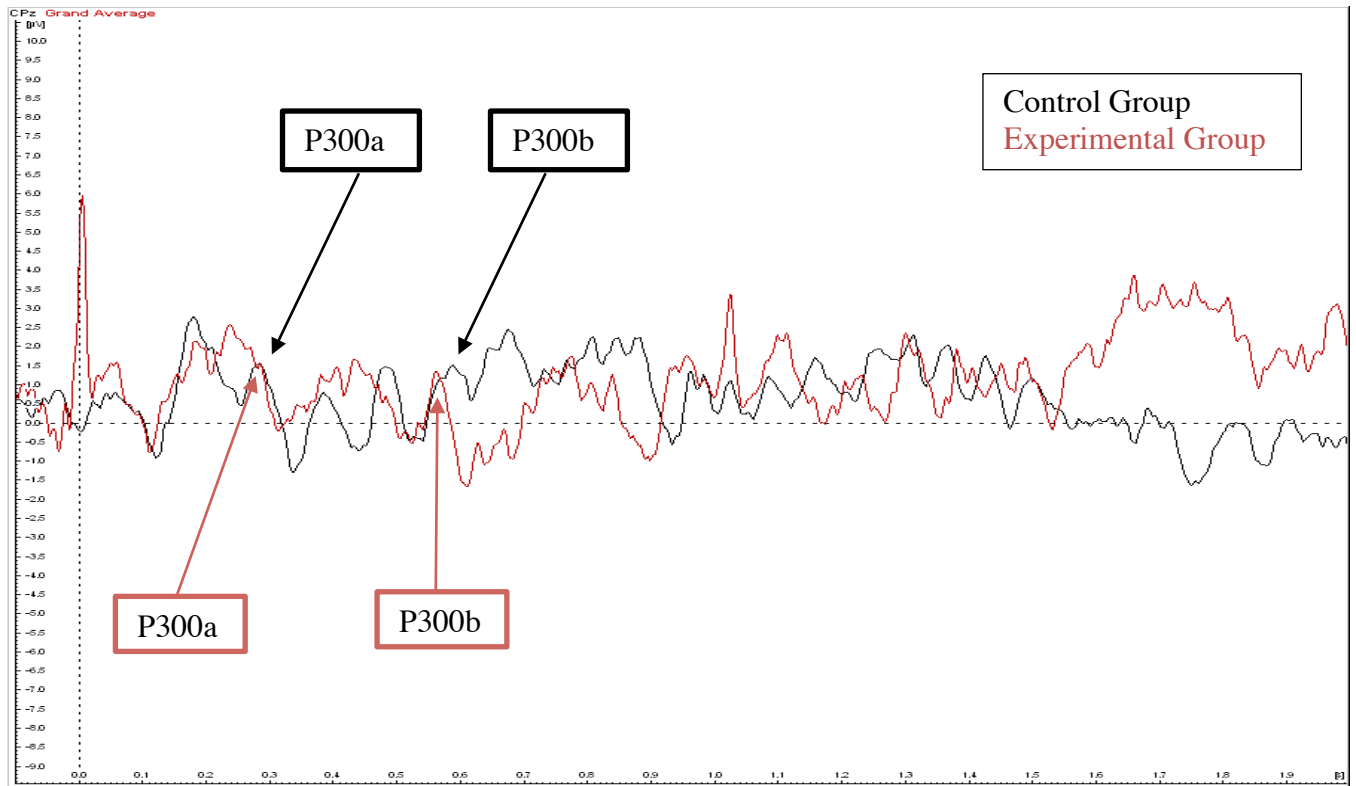
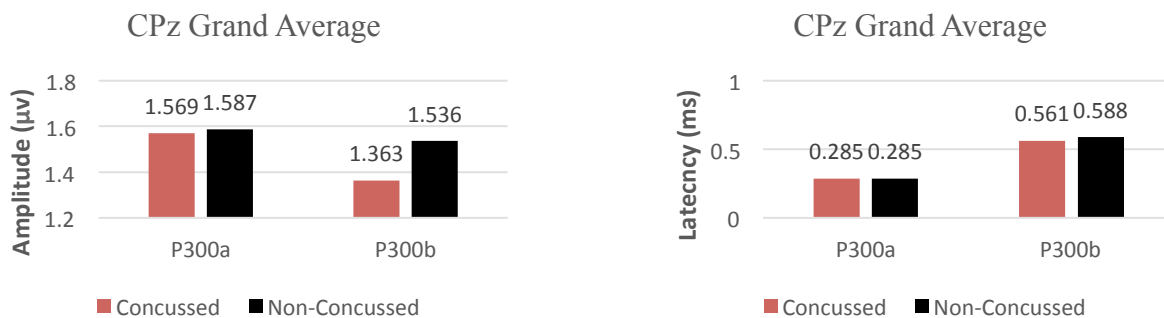


Figure 3.3 CPz Grand Average Waveform

Grand Averaged ERP Waveforms at electrode site CPz for P300a and P300b ERP components.

Table 3.4 CPz Grand Averages: Amplitude and Latency



Corresponding Graphs to the CPz Grand Average Waveform at the P300a & P300b components.

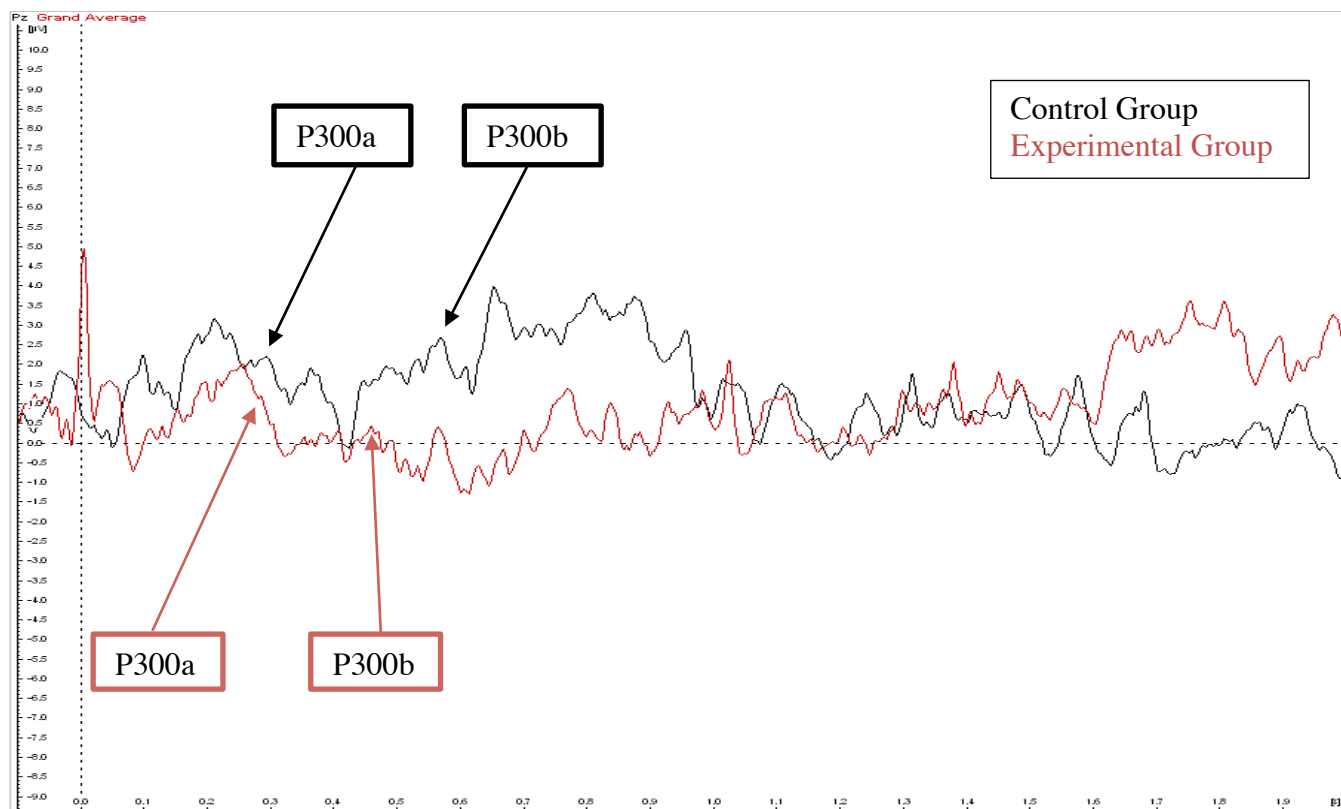
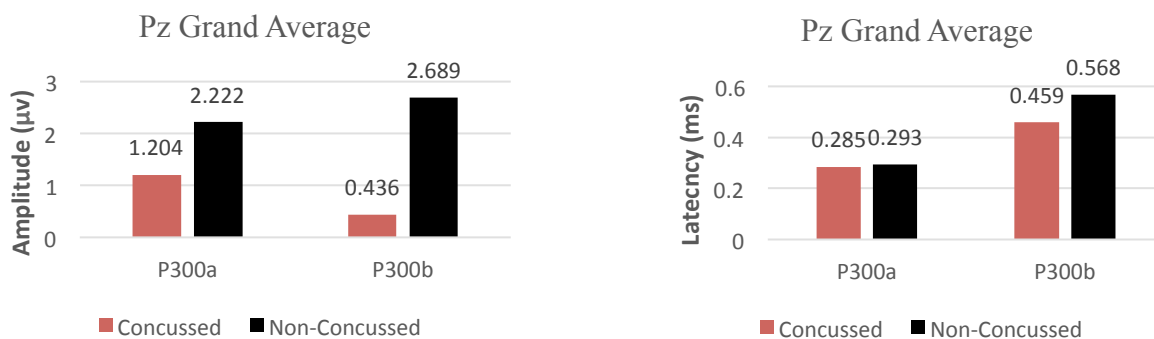


Figure 3.4 Pz Grand Average Waveform

Grand Averaged ERP Waveforms at electrode site Pz for P300a and P300b ERP components.

Table 3.5 Pz Grand Averages: Amplitude and Latency



Corresponding Graphs to the Pz Grand Average Waveform at the P300a & P300b components.

3.3 Statistical Analyses

3.3.1 ANOVA's

The data analysis conducted was a series of 2 x 8 Analysis of Variance with group (non-concussed and concussed) as independent variables. P300 amplitude and latency were the dependent variables used to examine the joint and interactive effects of group and electrode site. The design is thus a 2 x 4 factorial design where the electrode sites are a within subjects factor and the conditions are a between subjects factor. The level of significance was set at 5% (two-tailed). The ANOVA did not identify any statistically significant latency effects for P300a for group ($F(1,12) = 3.57, p = .08$); site ($F(3,36) = .25, p = .86$); or group by site ($F(3,36) = .80, p = .49$), or for P300b for group ($F(1,12) = .46, p = .50$); site ($F(3,36) = 1.41, p = .25$); or group by site ($F(3,36) = .42, p = .61$). The ANOVA also did not identify any significant amplitude effects for group ($F(1,12) = 3.57, p = .08$); site ($F(3,36) = .25, p = .86$); or group by site ($F(3,36) = .80, p = .49$) of the P300a component, or group ($F(1,12) = .76, p = .39$); site ($F(3,36) = .71, p = .54$); or group by site ($F(3,36) = .55, p = .64$) of the P300b component.

3.3.2 T-Tests

Independent samples t-tests were conducted to compare the differences of amplitude and latency at each electrode site. The independent sample t-test results for amplitude and latency of the P300a and P300b components at electrode sites FCz, Cz, CPz, and Pz are presented in Table 3.5 and Table 3.6. Amplitude and latency of the P300a and P300b components were taken for electrode site FCz. Despite the absence of the P300a amplitude in the concussed group, there was not a statistically significant difference between the P300a amplitude ($t(11) = 1.10, p = .29$) in the concussed ($m = 2.32, SD = 3.51$) from the non-concussed ($m = -.33, SD = 2.65$). The P300b component also did not have a statistically significant difference ($t(12) = 1.14, p = .27$) in the concussed ($m = 3.02, SD = 2.11$) from the non-concussed group ($m = 1.25, SD = 1.32$). Latency of the P300a component did not show a statistically significant difference ($t(13) = -.71, p = .48$) in either group (concussed: $m = .31, SD = .02$; non-concussed: $m = .32, SD = .03$). The latency of

the P300b component did not have a statistically significant difference ($t(13) = -1.02, p = .32$) for either group (concussed: $m = .43, SD = .08$; non-concussed: $m = .48, SD = .09$).

The Cz electrode site did not have any statistically significant differences in amplitude or latency in the P300a or P300b ERP components. The amplitude at electrode site Cz in the concussed group was not statistically significant for the P300a component ($t(8) = -.07, p = .94$) in either group (concussed: $m = 1.01, SD = 1.18$; non-concussed: $m = -.54, SD = 5$). For the amplitude of the P300b component at electrode site Cz, there was no statistically significant difference ($t(11) = -.13, p = .99$) in either group (concussed: $m = 2.71, SD = 2.57$; non-concussed: $m = 2.13, SD = 1.38$). Latency at electrode site Cz did not show statistically significant differences for the P300a component ($t(12) = -1.35, p = .2$) in either group (concussed: $m = .3, SD = .02$; non-concussed: $m = .32, SD = .02$), nor did the P300b component ($t(12) = -.24, p = .08$) in either group (concussed: $m = .47, SD = .09$; non-concussed: $m = .48, SD = .09$).

The CPz electrode site had no statistically significant differences in amplitude or latency of the P300a or P300b components in either group although amplitudes were lower in both components of the concussed group, and an equal latency was observed for P300a in both groups. Amplitude of CPz for the P300a component was not statistically significant ($t(9) = .12, p = .9$) for either the concussed group ($m = 1.68, SD = 2$) nor the non-concussed group ($m = 1.79, SD = 1.81$). The P300b component's amplitude was not statistically significant ($t(13) = .27, p = .79$) for either group (concussed: $m = 3.05, SD = 3.19$; non-concussed: $m = 2.64, SD = 1.31$). The latency of P300a did not show a statistically significant difference ($t(13) = -2.2, p = .48$) for either group (concussed: $m = .3, SD = .02$; non-concussed: $m = .32, SD = .03$), nor did P300b ($t(13) = -.77, p = .45$) in either group (concussed: $m = .47, SD = .09$; non-concussed: $m = .51, SD = .09$).

A lower amplitude and earlier latency in the concussed group of both P300 components was noted in grand average waveforms. There was no significant differences in amplitude of either P300a ($t(9) = .42, p = .68$) for either group (concussed: $m = 2.96, SD = 2.84$; non-concussed: $m = .55, SD = 2.04$), nor P300b ($t(10) = 1.13, p = .283$) for either group (concussed: $m = 3.96, SD = 4.64$; non-concussed: $m = 1.74, SD = 1.98$) at electrode site Pz. Latency differences were not statistically significant for P300a ($t(13) = -1.97, p = .07$) in either group (concussed: $m = .3, SD = .02$; non-concussed: $m = .33, SD = .03$) nor for P300b ($t(13) = -.5, p = .62$) in either group (concussed: $m = .46, SD = .08$; non-concussed: $m = .49, SD = .09$).

Table 3.6 Mean Measures for Amplitude by Group and Site

<i>Site</i>	<i>Concussed</i>		<i>Non-Concussed</i>		<i>t</i>	<i>df</i>	<i>p</i>	<i>Mann-Whitney U</i>
	<i>m</i>	<i>SD</i>	<i>m</i>	<i>SD</i>				
FCz P3a	2.33	3.51	-0.33	2.65	1.11	11	0.29	0.20
FCz P3b	3.02	2.11	1.26	1.33	1.15	12	0.27	0.12
Cz P3a	1.01	1.18	-0.54	5	-0.07	8	0.94	0.89
Cz P3b	2.71	2.57	2.13	1.38	-0.01	11	0.99	0.60
CPz P3a	1.68	2	1.79	1.81	0.13	9	0.90	1.00
CPz P3b	3.05	3.19	2.64	1.31	0.27	13	0.79	0.85
Pz P3a	2.96	2.84	0.55	2.04	0.42	9	0.68	0.09
Pz P3b	3.96	4.64	1.74	1.98	1.13	10	0.28	0.37

Table 3.7 Mean Measures for Latency by Group and Site

<i>Site</i>	<i>Concussed</i>		<i>Non-Concussed</i>		<i>t</i>	<i>df</i>	<i>p</i>	<i>Mann-Whitney U</i>
	<i>m</i>	<i>SD</i>	<i>m</i>	<i>SD</i>				
FCz P3a	.31	.02	.32	.03	-0.71	13	0.48	0.44
FCz P3b	.43	.08	.48	.09	-1.02	13	0.32	0.37
Cz P3a	.3	.02	.32	.02	-1.35	12	0.20	0.19
Cz P3b	.47	.09	.48	.09	-0.24	12	0.80	1.00
CPz P3a	.3	.02	.32	.03	-2.2	13	0.48	0.47
CPz P3b	.47	.09	.51	.09	-0.77	13	0.45	0.59
Pz P3a	.3	.02	.33	.03	-1.97	13	0.07	0.07
Pz P3b	.46	.08	.49	.09	-0.5	13	0.62	0.85

3.4 Cortical Activation Maps

Cortical activation maps are images that capture the cortical activation taking place in the brain in response to stimuli and are represented by a variety of colors varying between blue, green, yellow, and red. Each color is associated with a level of activity and is organized on a spectrum as follows: blue indicates no cortical activation; green is reduced cortical activation; yellow displays moderate cortical activation; and red corresponds with adequate or increased activation. The following figures illustrate the cortical activation maps derived at the P300a and P300b components at trigger 3. Cortical activation maps were captured for the electrode sites FCz, Cz, CPz, and Pz at trigger 3 for the P300a and P300b components of the grand averages for both groups. Trigger 3 represents the onset of the target stimulus presented to the participant (Figures 3.5, 3.6, 3.7, and 3.8 illustrate the cortical activation maps taken at the time-locked trial of trigger 3).

3.4.1 FCz & Cz Cortical Activation Maps

The P300a component for FCz displayed moderate cortical activity distributed across the scalp with primary activity in the right frontal, right temporal, and right parietal lobes for the concussed group. The non-concussed group showed moderate cortical activation in the left frontal lobe. At the P300b component for FCz, there was reduced cortical activation, with no cortical activation localized in the frontal lobe and a small area of moderate cortical activation in the left frontal lobe of the concussed group. The non-concussed group, however, continued to show moderate cortical activation in the left frontal lobe. Cortical activation maps of Cz displayed similar activation in the concussed group's P300a component as that of P300a at FCz, with moderate activation spread throughout the cortices and some concentration in the right frontal, right temporal, and right parietal lobes. The P300b component at the same site for the concussed group displayed reduced cortical activation throughout, with very similar activation seen in the P300b component at FC

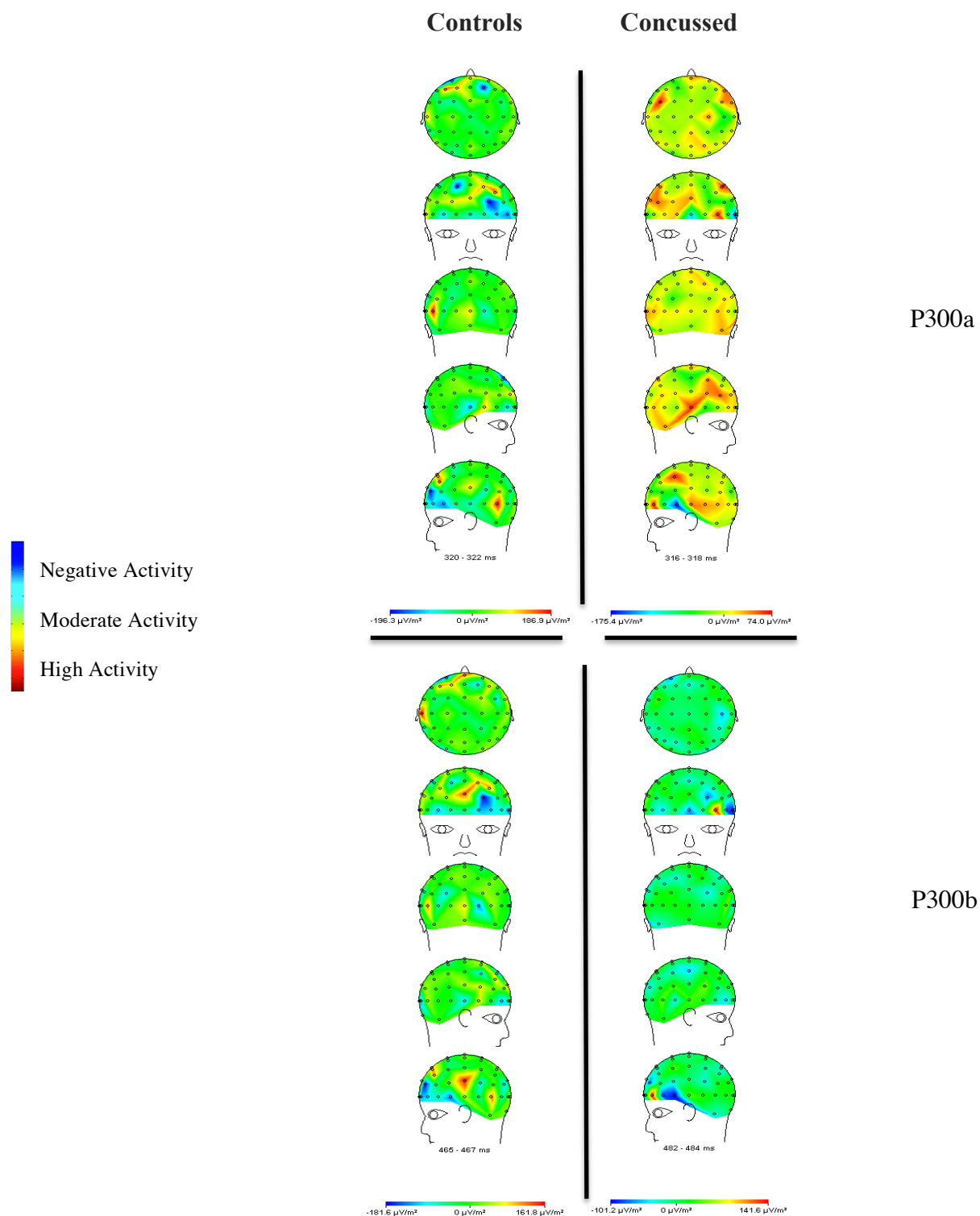
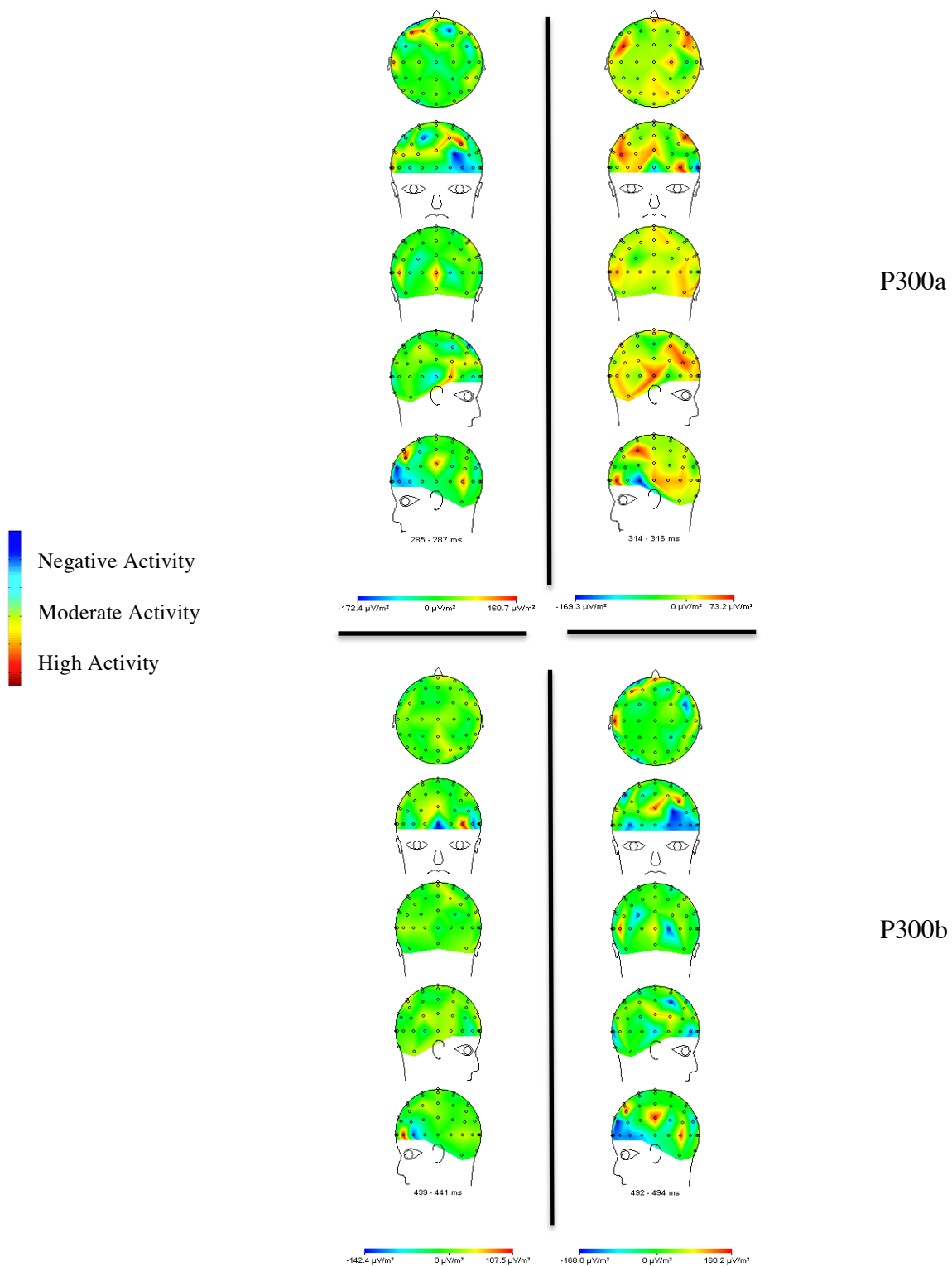


Figure 3.5 FCz Cortical Activation Map

Cortical activation map at electrode site FCz at Trigger 3.

Controls

Concussed



3.4.2 CPz & Pz Cortical Maps

Although not as greatly dispersed, moderate cortical activation was spread throughout the cortices for the concussed group at the P300a component for CPz, while the P300b component showed a small area of moderate to increased cortical activation in the left frontal lobe. At Pz, for the P300a component, the concussed group displayed reduced cortical activation and some moderate activation in the frontal lobe with a more slight increase of activation on the left side. The P300b component of the concussed group showed no cortical activation in some areas of the frontal lobe with a very small area in the left temporal lobe where there was increased cortical activation. This final site and component (P300b at Pz), unlike the others, had cortical activation that was very similar between the non-concussed and concussed group. The non-concussed group showed very similar cortical activation at the P300 and P300b components throughout the four electrode sites.

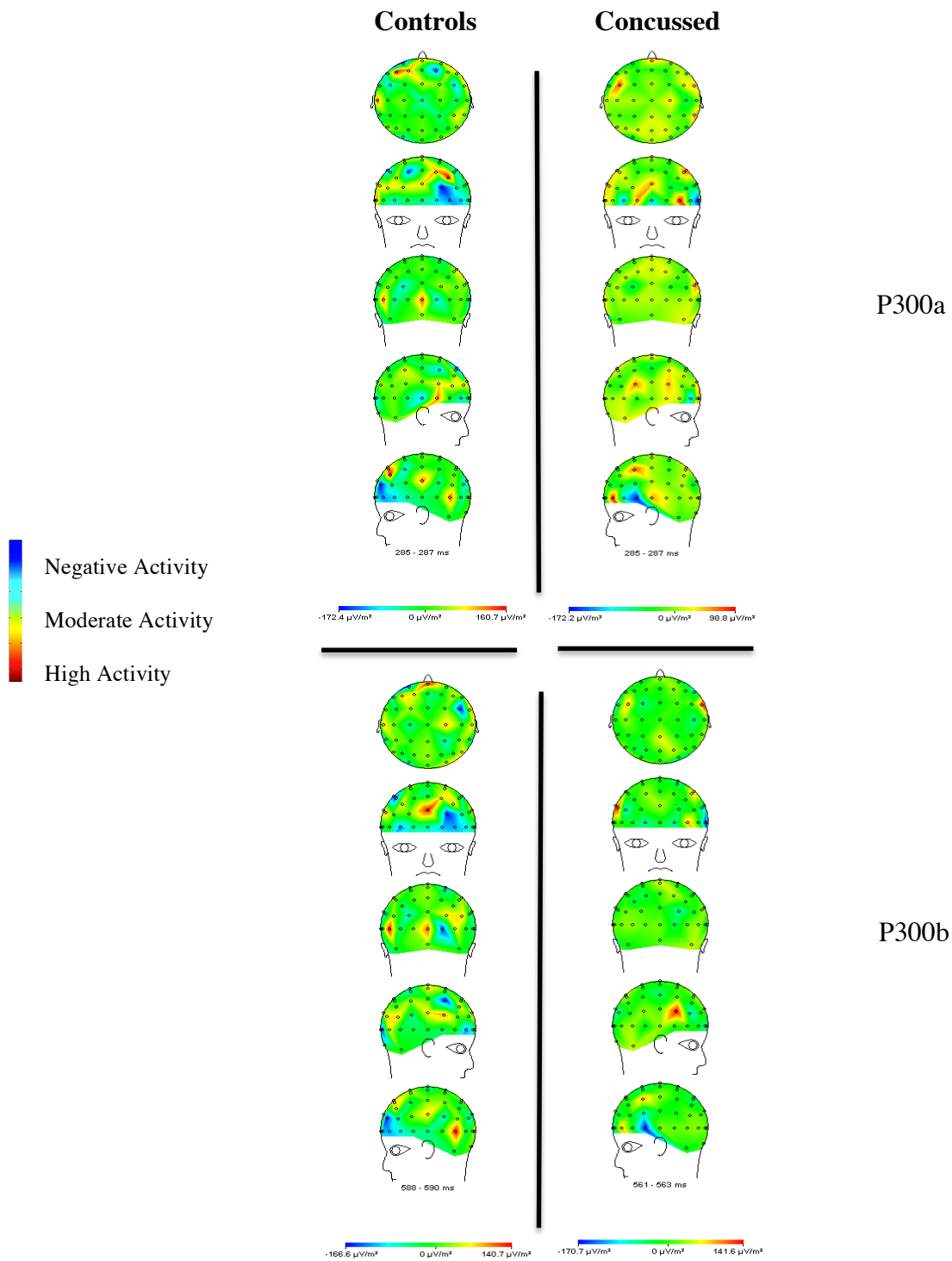


Figure 3.7 CPz Cortical Map

Cortical activation map at electrode site CPz at Trigger 3

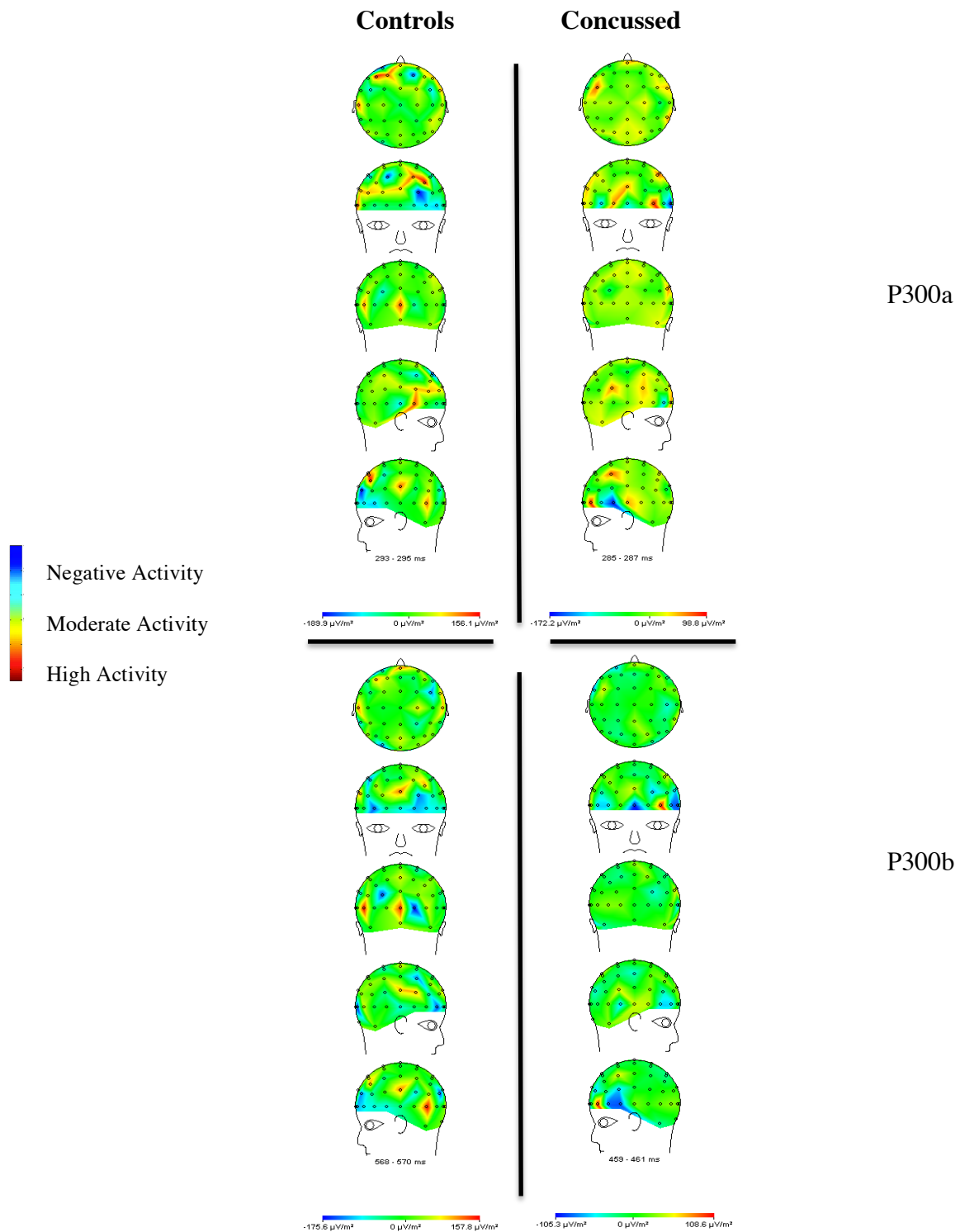


Figure 3.8 Pz Cortical Map

Cortical activation map at electrode site Pz at Trigger 3.

Chapter 4: Discussion

4.1 Findings

The statistical analysis show that there is no statistically significant difference in temporal and amplitude measurements in the P300a and P300b components between concussed and non-concussed athletes across the four central electrode sites. These results contradict the results found by Sanchez (2013). The present study hypothesized that there would be a statistically significant difference in ERP performance measures between the experimental group when compared to the control group since Sanchez (2013) found that there was a statistically significant difference in amplitude and latency of the P300a and P300b components. The results of this study found that there was no statistically significant difference between the two groups, therefore the hypothesis is not supported.

This study utilizes the traditional auditory oddball paradigm with the variation of a linguistic component. The traditional auditory oddball paradigm incorporates single sounds of different frequencies, whereas the variation of the linguistic component that was created by Sanchez (2013) incorporated CV syllables. Despite the variation of the linguistic component, the task successfully serves the purpose of eliciting the P300 components. The results from this study confirm the reliability of the P300 component in the use of the auditory oddball paradigm with a linguistic component, as did the original study in Sanchez (2013). The confirmation of the P300 component from the added linguistic factor serves as an additional control in this study, being that it compares differences within participants.

Grand averaged waveforms and grand averaged cortical maps measured at the P300a and P300b components demonstrate electrophysiological differences between the two groups. Although not statistically significant, through visual inspection the results reveal differences between the two groups when analyzing the P300 attentional components. These differences are seen in the electrophysiological reaction (amplitude and latency) from the non-target and target stimuli in all four electrode sites.

Sanchez (2013) indicated that the results found in her study may have been associated with the athlete's motivation to return to play, resulting in the athletes trying to perform their best on the task. However, the athletes that participated in the current study were informed that the results derived from this assessment would have no bearing on when they were able to begin the return-to-play protocol. This step was completed so that the athletes would not have any inherent motivation to perform well and so that results could be taken from a naturalistic environment without any intrinsic factors playing a role in the results.

4.2 Supporting and Contradicting Literature

Gray et al. (2003) describes the P300 component as serving as the covert measure of attention that arises independently of behavioral response. Studies from De Beaumont et al. (2007), Shucard et al. (2004), Potter et al. (2001) and Rugg et al. (1988), reveal consistent findings under the oddball paradigm in which the paradigm demonstrates that a P300 component was elicited during the presentation of the target stimuli. In this study, visual inspection and statistical analysis confirms the results from the previous literature, therefore indicating that this study also captures adequate P300 components during the presentation of target stimuli during an auditory oddball paradigm. This is observed in the control group, at both the P300a and P300b components, at all four electrode sites in the measurement for amplitude.

As seen in the results of Theriault et al. (2009), even when neurocognitive test results demonstrate an individual has recovered from a concussion, the P300 ERP components show a reduction in amplitude. In this study, ImPACT testing conducted on concussed athletes in the post-acute stage show valid scores, as would be expected for individuals not in the post-acute stage, however amplitude continues to appear decreased in comparison to the non-concussed group. The present study confirms the findings of Theriault et al. (2009) where the results show a reduction in amplitude of the P300 ERP component in concussed patients. In this study there is a reduction in amplitude at the P300a and P300b components at all four electrode sites in the concussed group when comparing to the control group. These findings may be attributed to the

consequences of concussions. Sanchez (2013) suggest that although the concussed participants detected the presentation of the target stimuli, their electrophysiological reaction has become affected. This is validated in the cortical activation maps, in which the differences of amplitudes between groups are observed. This demonstrates the value of ERP in observing attentional differences in individuals with a concussion, as long term effects on cognitive performance have not been well examined. After reviewing these findings, it may be presumed that the attentional components in the concussed group are in fact affected.

When comparing the results of this study with previous research by De Beaumont et al. (2009), Gosselin et al. (2006), and Rugg et al. (1992), results from previous research indicate a latency delay between the two groups, and the results from this study also indicate a latency delay from the non-concussed group. There was only one site, FCz, at the P300b component in which the concussed group has a longer latency delay. The results from this study support the findings from the studies conducted by Potter et al. (2001) and Sivak et al. (2008), in which the results indicated no significant differences between the groups regarding latencies. However, this study hypothesized that the concussed group would demonstrate a delay in latency.

In the study conducted by De Beaumont et al. (2007), the results shows that individuals with more than one concussion have stronger P300 ERP component differences when compared to individuals with only one concussion. Individuals with multiple concussions may show greater irregularities in electrophysiological data. In other words, the ERP differences in waveforms and cortical activation maps will be more pronounced. In addition De Beaumont et al. (2007), suggests that ERP may be more suited for assessing cognitive processes in individuals with multiple concussions.

4.3 Replication Study Comparison

When comparing the results of Sanchez (2013) to the current study, differences in cortical activation maps in the concussed group were found. The concussed group displayed moderate dispersed cortical activation, more than the concussed group of Sanchez (2013).

Sanchez (2013) found that concussed individuals displayed generalized scalp voltage activity that was decreased throughout the cerebral cortex during the experimental task.

The only electrode site that displayed similar results to Sanchez (2013) was site Pz for the P300b component. Both studies showed results of lower amplitude and earlier latency in the concussed group. In the current study, at electrode sites FCz and Cz results show that the concussed group did not display a P300a component. The P300a operational definition is a positive deflecting peak occurring between 280-350 milliseconds. An absence of the P300a at electrode sites FCz and Cz was because the highest peak amplitude only reached negative values and did not pass into the positive microvolts axis. For the current study the concussed group exhibited lower amplitudes of the P300a and P300b at all electrode sites compared to the control group. This is consistent with the literature.

Conversely, in Sanchez (2013), the concussed group demonstrated higher amplitudes of the P300 ERP component in more than half of the electrode sites when compared to the control group. Finally in the current study, no statistically difference was found between the experimental and control groups for the P300a and P300b at any of the electrode sites. This contradicts the results found in Sanchez (2013). Sanchez (2013) suggests that the statistically significant difference found in the study was attributed to the added linguistic component which would increase the demands of the task. However, the results of the present study suggest that the added linguistic component had no effect on electrophysiologic performance during an attentional task.

4.4 Limitations

One of the limitations of this study, as in the original study, is that this study did not control for the amount of concussions an individual was diagnosed with prior to taking part in the study. As a result participants in the experimental group ranged had experienced one to multiple concussions. This was done because the experimental group was recruited from the Concussion Management Clinic at the University of Texas at El Paso and as such only

participants that were referred to the clinic for concussion management were included in the sample. This may have influenced the results. For example, in a study by De Beaumont et al. (2007), the number of concussions were shown to result in differences of the P300 ERP components.

Another limitation of the current study is the small sample size for the experimental group. In addition, the sample of individuals in the acute stage of concussion was even smaller. Future research should target a larger sample size and pursue a minimum of twenty concussed athletes. The small sample size for the experimental group may have contributed to the statistical results that found no statistically significant difference. There was also a lack of homogeneity in the experimental group. In regards to the control group, there was no randomization when selecting participants to participate in this study. A majority of the studies previously mentioned in the literature have larger sample sizes in the experimental group. In addition, a larger sample size will also increase the signal to noise ratio. In order to try to account for the small sample size, a large number of trials was used in the experimental task.

4.5 Conclusions

The results obtained from the present study contradict the results from Sanchez (2013). While no statistically significant difference was found, visual inspection of the ERP waveform show a decrease in amplitude and increase in latency of the P300a and P300b in the group of concussed athletes. This suggests that the addition of the linguistic component does not increase the demands of the task as Sanchez (2013) suggests. There are electrophysiological differences, though not statistically significant, present between the control group and the experimental group. This is evident through visual inspection of the grand average waveforms and grand average cortical maps. Furthermore, the present study eliminated one of the variables used in Sanchez (2013), keeping mental track of all target CV sounds. The difference in study results could be attributed to this change in variable manipulation. Finally, the results of this study

suggest that ERP is a valuable addition to the management of concussion in individuals as it can detect neural changes years after the onset of a concussion.

4.6 Clinical Implications

Participants may benefit from the study by understanding their performance results in addition to being informed of the lasting effects a concussion may have on an individual. Despite athletes reporting they feel “better” within a couple of days after sustaining a concussion, athletes must understand the magnitude and effects that concussions present. Athletes that are asymptomatic may continue to have secondary effects due to concussion years after the initial injury. The implementation and use of ERP will reveal that concussion symptoms are still internally present. ERP measures may be useful during the evaluation process before higher-order cognitive processes are tested using cognitive communication tests (Sanchez, 2013).

ERP may lead to the establishment of a time frame during which electrophysiological recovery occurs after the onset of a concussion. However, further research and data is recommended to track the changes and recovery of the P300 component after the onset of a concussion occurs. It is strongly recommended that this study be replicated. In addition, future considerations may be able to utilize ERP as a measurement for post-concussion recovery in conjunction with neurocognitive testing. ERP results may provide a greater representation of the recovery of the patient in order to provide a more accurate “return to play” decision.

4.7 Future Research

Future research that examines ERP in the assessment of concussions is necessary to assist in the comprehension of P300 changes post-concussion. The variability in results between Sanchez (2013) and the current study shows that there is a need for further research in order to clarify electrophysiological data. Additionally, future research should focus on establishing a recovery pattern in electrophysiological data in individuals with a concussion. The recovery pattern should include ERP assessments at time points of 3-10 days, 2 weeks, 1 month, and 3 months post-concussion. Once a large population sample is collected this data will assist in

establishing a timeline of recovery in ERP components. Furthermore, research must also include the assessment of female individuals. The literature on concussed and non-concussed female athletes is limited. On the literature review conducted no ERP studies on female athletes were found. This is an area that should be targeted because more and more females are engaging in sports that demand physical contact.

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Appendix

A

INFORMED CONSENT

University of Texas at El Paso (UTEP) Institutional Review Board
Informed Consent Form for Research Involving Human Subjects (Ages 18-Adult)

Protocol Title: Event related potential changes in a two-stimulus auditory oddball task in concussed college athletes: A linguistic component replication study

Principal Investigator: Christopher Roosmalen M.Ed., Graduate Student Clinician

Advisor: Patricia Lara PhD., C.C.C.-SLP, Speech Language Pathology

Thesis Committee Members:

UTEP College of Health Sciences: Department of Rehabilitation Sciences; Speech Language Pathology Program

In this consent form "you" always means the study subject. If you are a legally authorized representative (such as a parent or guardian), please remember that "you" refers to the study subject.

1. Introduction

You are being asked to take part voluntarily in the research project described below. Please take your time making a decision and feel free to discuss it with your friends and family. Before agreeing to take part in this research study, it is important that you read the consent form that describes the study. Please ask the study researcher or the study staff to explain any words or information that you do not clearly understand.

2. Purpose of the Study

You have been asked to take part in a research study that uses event related potentials (EEG) to compare brain activity in non-concussed and concussed participants when listening to spoken consonant-vowel syllable sounds. College level athletes and college level non-athletes from the University of Texas at El Paso will be participating in this study.

The rationale: This study will provide a post-concussion management program to athletes who have suffered a concussion in order to assist in their recovery process. A concussion may result in deficits of cognitive functioning in areas such as: problems with memory and concentration; sleeping pattern disturbances; and/or drastic emotional changes. In most concussion cases, the symptoms will generally resolve naturally within 7 to 10 days from the onset of concussion. A majority of concussed individuals will have a complete and total recovery within 3 months, however there is a minority of concussed individuals that will continue to experience symptoms on a long-term basis. "Return to play" decisions are based on behavioral test results and clinical observations. However, additional instruments used to assess changes in brain activity are necessary. For that reason, it is imperative to have a greater understanding in the functional processes that are involved in the recovery of a concussion. Research will focus on finding an effective means of assessing a concussion.

Approximately, 20 subjects (10 individuals who sustained a concussion and 10 non-concussed individuals) will be enrolling in this study at UTEP.

You are being asked to be in the study because you (1) suffered a single concussion, (2) multiple concussions, or (3) a non-concussed subjects for the purpose of comparison. If you decide to enroll in this study, your involvement will be required for approximately four 1-hour sessions on four separate days. (1st visit: 3-7 days post-concussion. 2nd visit: 2 weeks post-concussion. 3rd visit: 1 month post-concussion. 4th visit: 3 months post-concussion.)

3. Procedure

If you agree to take part in this study, you will be provided with an explanation regarding the use of event related potentials. Also during your first visit, you will be asked to fill out the self-report medical and concussion history questionnaires. In addition, your hearing will be tested with a hearing screening. You will begin by taking a 15-20 minute ImPACT test, which will assess your memory, reaction time, speed, and concentration. This is not an IQ test.



To complete the ImPACT test, you will only need to sit in front of a computer monitor. There is a separate information sheet regarding this test that you will read and sign following this form. After the ImPACT assessment is completed, the principal investigator will take head measurements and apply the non-invasive electrode cap according to the Biosemi procedure using conduction gel and electrodes. You will then be comfortably seated in a 6 x 6 soundproof room in front of a touchscreen computer monitor to complete the task. The experimental task requires that the participant listen with attention to the auditory stimuli that is being presented. No motor response will be required from you.

4. Risks, Discomforts and Benefits

There are no known risks associated with this research. However, you may experience slight fatigue during the testing conditions. If you feel fatigued, you will be given the opportunity to rest.

5. What will happen if I am injured in this study?

The University of Texas at El Paso and its affiliates do not offer to pay for or cover the cost of medical treatment for research related illness or injury. No funds have been set aside to pay or reimburse you in the event of such injury or illness. You will not give up any of your legal rights by signing this consent form. You should report any such injury to Christopher Roosmalen at (915) 401-9229 and to the UTEP Institutional Review Board (IRB) at (915-747-8841) or rb.orsp@utep.edu.

6. Benefits

There will be no direct benefits to you for taking part in this study. However, you may benefit from this study by knowing the outcome of your performance using event related potentials. This research may lead to a better understanding of what is involved in the recovery of a concussion and this in turn may assist in the provision of a more accurate diagnosis, prognosis, and "return to play" decisions.

7. Options

You have the option not to take part in this study. There will be no penalties involved if you choose not to take part in this study.

8. Funding

Internal Funding:

Funding for this study is provided by UTEP Department of Speech Language Pathology.

9. Costs

There are no direct costs to you. However, you will be responsible for travel to and from the research site and any other incidental expenses.

10. Compensation

There is no monetary compensation for taking part in this study.

11. Refusal or Withdrawal

Taking part in this study is voluntary. You have the right to choose not to take part in this study. If you do not take part in the study, there will be no penalty towards you. If you choose to take part, you have the right to stop at any time. However, we encourage you to talk to a member of the research group so that they know why you are leaving the study. If there are any new findings during the study that may affect whether you want to continue to take part, you will be told about them. The researcher may decide to stop your participation without your permission, if he or she thinks that being in the study may cause you harm, and/or there is not sufficient effort on your part to complete the testing.

12. Contact Information

You may ask any questions you have now. If you have questions later, please call Christopher Roosmalen at (915) 401-9229 or caroosmalen@miners.utep.edu. You may also contact the principal investigator's advisor, Dr. Patricia Lara at (915) 747-7250 or at plara2@utep.edu. If you have questions or concerns about your participation as a research subject, please contact the UTEP Institutional Review Board (IRB) at (915-747-8841) or irb.orsp@utep.edu.



13. Confidentiality

Your part in this study is confidential therefore, all information collected in this study will remain confidential. Only the principal investigator (Christopher Roosmalen) and his research advisor (Dr. Patricia Lara) will have access to this information. In addition, none of the information will identify you by name. Instead, identification numbers will be used. All records will be stored in a locked cabinet in the Brain, Voice and Language Lab at the UTEP Speech Clinic (1101 N. Campbell, El Paso, Tx. 79902). For further protection, only the principal investigator and her advisor will have access to the locked cabinet. Computer information will be stored in the lab computers and password secured. Only the principal investigator and his advisor will have access to the password. The results of this research study may be presented at meetings or in publications; however, your identity will not be disclosed in those presentations.

14. Mandatory Reporting

If information is revealed about abuse or neglect to the elderly or disabled, the law requires that this information be reported to the proper authorities.

15. Authorization Statement

I have read each page of this paper about the study (or it was read to me). I know that being in this study is voluntary and I choose to be in this study. I know I can stop being in this study without penalty. I will get a copy of this consent form now and can get information on results of the study later if I wish.

Participant Name: _____ Date: _____

Participant Signature: _____ Time: _____

Consent form explained/witnessed by: _____
Signature

Printed Name

Date: _____ Time: _____



Vita

Christopher Roosmalen was born in Madison, Wisconsin and raised between Madison, Wisconsin and El Paso, Texas. Under full scholarship, he completed his undergraduate education in Columbus, Ohio where he received his Bachelor of Arts in 2007. He continued his graduate studies and received a Master of Education in Administration from the University of Texas at El Paso in 2010. In 2013, Mr. Roosmalen pursued his second master degree in Speech-Language Pathology at the University of Texas at El Paso with an expected graduation date of May 2015.

Mr. Roosmalen worked as a research assistant from 2013-2015 in the ERP and Aphasia lab at the University of Texas at El Paso. He conducted research focusing on investigating the changes in event-related potentials (ERP) in individuals with Aphasia as well as individuals diagnosed with a concussion. His research interest and experience led him to complete a thesis on the electrophysiological changes in individuals with concussions using an auditory oddball task with an added linguistic component. The focus of the research was on attention differences in individuals with no prior head injury as opposed to individuals who had been diagnosed with a concussion.

Education:

Bachelor of Arts, Integrated Social Sciences, The Ohio State University, June 2007

Master of Education, Administration, University of Texas at El Paso, May 2010

Master of Science, Speech Language Pathology, University of Texas at El Paso, May 2015

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This thesis was typed by Christopher Anthony Roosmalen.