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Sleep Deprivation And Recovery: The Effects Of P300 Three And Six Hours Post Recovery

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SLEEP DEPRIVATION AND RECOVERY: THE EFFECTS OF P300 THREE AND SIX HOURS POST RECOVERY

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In Partial Fulfillment

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Doctor of Audiology

By

Kimberly Ann Brauer

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ABSTRACT

The P300 waveform is an auditory evoked potential (AEP) elicited through a decision making process. Due to the endogenous nature of the P300 response, which requires participants to actively respond to an auditory stimuli, it has been used as on objective measure to evaluate the cognitive processes of attention and memory. Previous studies have looked at the P300 before and after sleep deprivation as well as after brief rest periods. Evidence shows that a decline in P300 amplitudes and increase in latency are seen after 24 hours of sleep deprivation and improvements in the P300 are seen after a recovery period. Limited research has been conducted on the effects on P300 amplitude and latency during post recovery periods of three or more hours. The present study was designed to determine the effects of P300 three and six hours post recovery using an oddball paradigm (standard = 1000 Hz; target = 2000 Hz). AEPs were recorded for five conditions: baseline, sleep deprived, 110 minute recovery, three hours post recovery and six hours post recovery. Measures of P300 amplitude and latency were taken from Fz, Cz and Pz electrode sites. Peak to base amplitude and peak to peak amplitude of the P300 were also measured. Fourteen college and university students ages 18-25 were included in this study. Results indicated a significant decrease in P300 amplitude from the six hour post recovery condition compared to the baseline ($p < .05$) as well as the six hour post recovery condition and sleep deprived condition ($p < .05$). There were no significant changes in P300 latency across conditions. The results suggest that three to six hours after a brief recovery period of 110 minutes, cognitive decline is exacerbated.

KEYWORDS: P300, sleep deprivation, recovery, auditory late response, evoked potential

This abstract is approved as to form and content

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INTRODUCTION

When the human body is forced to stay in a state of wakefulness for a long period of time, it becomes sleep deprived. Multiple studies have shown that individuals such as car and truck drivers, night nurses, medical students, physicians, pilots and other night time workers are subject to conditions that will cause sleep deprivation and thus a decrease in cognition, alertness, psychological and physiological performance, effective decision making and reaction time (Harrison and Horne, 2000; Costa, 1997; Philip, Taillard, Sagaspe, Vltat, Sanchez-Ortuno, Moore, … Bioulac 2004, Kingshott, Cosway, Deary, & Douglas, 2000; Lee, Kim & Suh, 2003; Jain, Mahajan, Jain & Babbar 2010; Moore, 2013; Beaumont, Batejat, Coste, Doireau, Beers, Chassard, … Lagarde, 2001). A brief glimpse of the types of sleep deprived individuals will aid in the understanding of the importance of sleep deprivation studies.

Drivers who lack an adequate nights rest are of interest in sleep deprivation studies because of the potential hazards they pose on society. Elke De Valck and Raymond Cluydts revealed that drivers who have only had 4.5 hours of sleep compared to those with 7.5 hours of sleep have a statistically significant increase in lane drifting (De Valck & Cluydts, 2001). Reaction time, age, duration of the drive and break times predict level of performance while driving. Interestingly young drivers were on the road for longer durations and had a higher amounts of "sleep debt" (Philip, Taillard, Quera-Salva, Bioulac, & Akerstedt 1999; Panjwani, Ray, Catterjee Bhaumik & Kumar 2010).

Physicians, nurses, and medical students must maintain a high level of performance to maintain the quality of care needed for their patients. It would be assumed that if medical personnel were sleep deprived, they would pose a greater risk to

their patients due to unforeseen errors. According to Caruso & Hitchcock, an increased prevalence for medical errors has been seen in sleep deprived nurses (Caruso & Hitchcock, 2010). It is well known that physicians and medical students will work 24 and 48 hour shifts with little to no sleep thus increasing the probability of mistakes.

Trans-meridian pilots encounter sleep deprivation of varying magnitudes (Costa, 1997). With the increased exposure of flight time and obligation to their passengers, proper strategies for "sustained and optimum mental performance" should be revolutionized (Panjwani et al. 2010). This would not only provide safety to the passengers but it would also increase awareness of safety and proper sleep/rest protocols for the pilots.

For more than a century, sleep deprivation studies have been conducted to discover negative effects associated with a lack of sleep (Zukerman, Goldstein & Babkoff, 2007). Some of these studies have been used to determine the effects of caffeine on cognitive performance during a sleep deprived state (Valck & Cluydts 2001; Liberman, Tharion, Shukitt-Hale, Speckman and Tully, 2002; Beaumont et al. 2001) while other studies have aimed to determine how affect, socially interactive decisions, cognitive deterioration, reaction time and odor identification accuracy are affected while sleep deprived (Anderson & Dickerson, 2009; Killgore & McBride, 2006; Franzen, Siegle & Buysse, 2008). Though these studies are informative, there are variations in the results. Behavioral, physiological and electrophysiological measures have all been used to determine the effects of sleep deprivation. However, it is important to get an objective and quantifiable measurement of cognitive performance.

Computerized neurocognitive tests are used to accurately and objectively measure the reactions of research participants. Specifically, the P300 which is an endogenous event-related potential (ERP), is said to be related to cognitive processes, discrimination and working memory (Lee et al. 2003). In addition, it was concluded that the decrease in amplitude and increase in latency of P300 after sleep deprivation was due to cognitive decline (Lee et al., 2003) and not to the difference in an alert and drowsy state (Kosino, Nishio, Murata et al. 1993).

Previous studies have measured the effects of P300 amplitude and latency following various durations of sleep deprivation after a nap (Morris, So, Lee, Lash & Becker 1992; Lee et al. 2004). Amplitude and latency measurements have also improved after brief recovery periods of 10 and 110 minutes (Matthyssen, 2013). However, there is a lack of conclusive evidence on the effects of sleep deprivation for longer durations post recovery.

The objective of the study is to measure the amplitude and latency of the P300 at intervals of three and six hours post recovery following sleep deprivation of approximately 24 hours and a brief nap of 110 minutes. A delay in P300 latency has been linked to abnormal cognitive processing and is thought to represent a delay in information processing (Picton, 1992). It is hypothesized that the P300 amplitude will decrease and latency will increase three and six hours post recovery. Specifically, this study aims to determine when the decline in P300 amplitude and increase in latency will reoccur, thus showing the duration of cognitive improvement gained from a brief 110 minute nap following 24 hours of sleep deprivation.

LITERATURE REVIEW

Auditory Evoke Potentials

Evoked potentials are pulses of electrical activity in the brain that occur when a sensory nerve pathway is stimulated. Three primary types of sensory evoked potentials exist, auditory evoked potentials (AEPs), visual evoked potentials (VEPs) and somatosensory evoked potentials (SSEPs) (McPherson, 1996). When sound is presented to elicit an electrical response, it activates the auditory system (the ear, the auditory nerve or auditory regions of the brain) and is referred to as an auditory evoked reponse (AER) (Hall, 2007). Once evoked, electrical activity can be recorded and displayed on a screen for analysis.

Recorded auditory evoked potentials are obtained with the use of electrodes, strategically placed on the scalp. When an acoustic signal is presented, it causes a minute electrical impulse to travel between neurons from the inner ear to the auditory nerve and then on to the brainstem, the midbrain, thalamus and up through the auditory cortex (Hall, 2007; Matthyssen 2013; Riley 2008). Specific areas along the auditory cortex are called generator sites. Waveforms represent the activity at each of these generator sites and are shown in a graph with amplitude on the Y axis and latency on the X axis. Amplitude (measured in microvolts (μV)) represents threshold estimation and latency is used to identify the generator sites and sites of lesion. Waves of electrical impulses take less than one second to travel through the auditory pathway. Thus, latencies are described in milliseconds (Hall, 2007). Each generator site is represented at approximate

latencies which makes it possible to analyze the morphology, latency and amplitude of specific areas of the auditory pathway.

There are three primary response classifications of AEPs that are based on latency of the response. These are early, middle and late latency responses. These responses can be further categorized into two main types: endogenous and exogenous potentials. Exogenous responses, which are synonymous to early and middle latency potentials, are requisite responses to sound. Endogenous potentials or late latency potentials are either manipulated by a slight change in stimulus or they require the participant to perform a task (Kraus & Nicol, 2005). The versatility of AEPs has made a significant impact both clinically and experimentally.

Clinically, auditory evoked potentials are valuable in the detection of cochlear hearing loss, retrocochlear lesions and central auditory processing disorders. They are also used to manage central auditory processing disorders, monitor intraoperative procedures and measure auditory implant function. Audiologist and clinicians also benefit from the use of AEPs when testing infants, cognitively impaired or difficult to test patients and those individuals who need assessment for medicolegal compensation (Cebulla, Sturzebecher, & Wernecke, 2000; Matas, Matas, Oliveira, & Goncalves, 2010; Neumann, & Kotchoubey, 2004; Robier, Lamaire, Garreau, Ployet, Martineau, Delver & Reynaud, 1993; Tsui, Wong, & Wong, 2002).

Auditory evoked potentials are also demeaned as a valuable tool in research. Since the inception of AEPs, experiments have been conducted to determine how AEPs work, what types and categorizations there are, which parameters are the best to use, what the most effective electrode placements are, when to use AEPs clinically and what

diagnostic procedures are best. AEPs have also been used to study disorders, diseases and cognitive abilities to name a few. Though there are many fascinating research publications to review, this study will be incorporating the expertise of the past experimental endeavors of sleep deprivation researchers. Specifically, the AEPs that will be focused on in this study will place emphasis on P300 waveforms which will aid in the determination of cognitive function while sleep deprived. An explanation of the various types of AEPs will further contribute to the understanding of the late latency potentials used in this study.

Differentiation and Categorization of Auditory Evoked Potentials. As mentioned previously, there are two main types of AEPs. Subject recordings can be either endogenous or exogenous in nature. In addition there are three primary categories of AEPs: early, middle and late latency responses. Early and middle latency responses are exogenous and late latency responses are endogenous. For the purpose of understanding early, middle and late latency AEPs, the exogenous and endogenous nature of these responses will be discussed first.

Endogenous and Exogenous Potentials. In 1965, the work of Sutton, Braren, Zubin and John brought to light the difference between exogenous and endogenous AEP responses. Exogenous responses are evoked by a stimulus that does not have to be attended to by the participant. On the other hand, endogenous potentials are evoked by the cognitive acknowledgement of the differences in the stimuli presentation. Which means that the participant must attend to the incoming stimuli and consciously respond with a deliberate action.

Categorization of AEPs can also be done by determining the latency of the response in relation to the stimulus (Riley, 2008). Exogenous responses are early and middle latency responses which include: Electrocochleography (ECochG), Auditory Brainstem Response (ABR), Auditory Middle Latency Response (AMLR), N1, and P2. While endogenous potentials are classified as N2, P3, N4 and P5 (see Figure 1 for a tracing of the AEPs and ERPs). Each classification is representative of neural generators that travel along the auditory pathway starting with the cochlea and Auditory (VIIIth) nerve, moving centrally towards the primary auditory cortex and ending in the association areas (Hall, 2007; McPherson, 1996; Goldstein and Adrich, 1999).

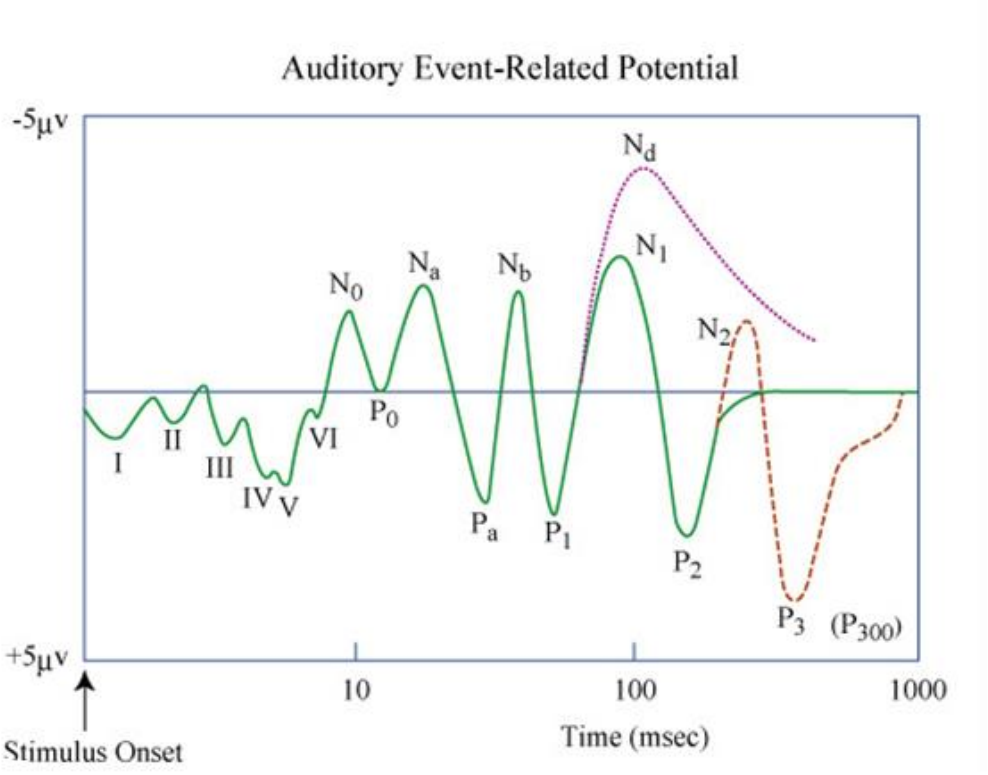

Figure 1: Auditory Evoked/Event Related Potential Waveform Morphology. From: MIT Open Course Ware. Origin: HST.722J/9.044J Brain Mechanisms for Hearing and Speech, Fall 2005.

Early-Latency Auditory Evoked Potentials. Waves produced within 10 ms after stimulus presentation represent both cochlear and retrocochlear responses along the auditory nerve and low midbrain structures (Kraus & Nicol, 2009). Electrocochleography (EcochG) and Auditory Brainstem Response (ABR) are the most commonly used early evoked potentials.

Electrocholeography. ECochG is considered the earliest of all AEPs with its origin from the cochlea and the eighth cranial nerve. The response is elicited by an abrupt stimulus and can be seen within the first 2-3 ms after stimulus presentation. To record the response it is best to use a near-field recording with a tiny electrode placed on the eardrum or by method of a transtympanic placement on the round window of the cochlea (Hall, 2007)

ECochG consists of cochlear microphonics (CM) and two receptor potentials, the summating potential (SM) and the action potential (AP). The first observed component is the CM which is an alternating electrical potential that occurs at the basal turn of the cochlea and is measured at the level of the hair cells. The movement of the hair cells imitates the phase and amplitude of the incoming stimulus and can be seen as a waveform with positive peaks and negative troughs (Kraus & Nicol, 2009; Hall, 2007). These waves continue the entire length of the stimulus and can mask the underlying summating and action potentials. Use of an alternating current can lessen the effects of the CM so the summating and action potential can be seen (Hall, 2007). The summating potential is a direct current potential that most likely is a reflection of the distortion products of hair cell activity which arises from the cochlea. SM is a direct current potential that can be seen as a separate peak that precedes the action potential or as a bump that rests at the

slope of the action potential. The action potential (or compound action potential) is an alternating current response that consists of the summed responses of thousands of distal auditory nerve fibers firing in synchrony (Kraus & Nicol 2009; Hall, 2007)

Clinically, ECochG evoked potential recordings play a significant role in the identification of audiologic, otologic, and neurologic abnormalities. Specifically, the most common use of ECochG testing is in the diagnosis, assessment and monitoring of Meniere's disease (also known as Endolymphatic Hydrops). Other uses of ECochG include: enhancement of wave I of the ABR during neurodiagnostic assessments and interoperative monitoring when the auditory system is at risk (Odabasi, Hodges, & Balkany, 2000). Unfortunately, one of the limitations of ECochG is that analysis of the summating and action potentials are variable and can lead to misdiagnosis of a Meniere's patient. Only about 60% of Meniere's patients are found to have an elevated SP/AP amplitude ratio which is a relatively low value. Improvement in diagnostic sensitivity of ECochG may be seen in the future with consideration of both amplitude and duration of the ECochG components. Other limitations of ECochG include: the responses provide information up to but not beyond the auditory nerve and the ECochG is not a good test for hearing sensitivity (Hall, 2007; Dauman, 1991; Gibson, 1991; Ferraro & Tibbils, 1999).

Auditory Brainstem Response. The ABR is an evoked potential that was first discovered 1967 by Sohmer and Feinmesser while investigating electrococheography. However, it was not until 1970 that Jewett, Romano & Williston examined the ABR in more detail. Later, in 1979 Hallowell Davis introduced the term ABR (Hall, 2007).

The ABR response is elicited during the first 10 ms after the onset of the stimulus presentation. Two primary types of stimuli, tone-bursts and click stimuli, are used to elicit the response. Tone-bursts are used when it is necessary to obtain frequency specific information regarding hearing sensitivity, while click stimuli provides a broadband of high-frequency information regarding hearing sensitivity. Not only do these neural impulses provide a measure of hearing sensitivity, but they also provide information about lesions of auditory pathway. In other words, it is the integrity of the auditory (VIIIth) nerve and brainstem that is being tested (Hood & Berlin 1986; Moller, 1994; Goldstein & Aldrich 1999; Hall, 2007).

In order to analyze the ABR recording, it is important to note that the ABR response produces a waveform that consists of seven peaks and troughs that represent portions of the auditory brainstem. These peaks are labeled with Roman Numerals I -VII. However, waves I through V are consistently used for analysis and interpretation. Wave I typically occurs approximately 1.5-2 ms after the onset of the stimulus. Each remaining wave follows in succession in approximately 1 ms intervals. Wave I-III originates from the auditory pathway that is stimulated with an ipsilateral presentation of sound. However, wave V is representative of activity in the midbrain auditory structures that are recorded with a contralateral stimulus presentation (Hall, 2007). Specifically, Wave I is generated by the distal portion of the auditory nerve while wave II arises from the proximal portion of the auditory nerve. Wave III arises from the cochlear nucleus, wave IV arises from the superior olivary complex, while wave V arises from the Lateral Lemniscus as it terminates in the Inferior Colliculus. Wave VI and VII are generated primarily in the Inferior Colliculus. In adults, wave V generally has the largest amplitude

making it more discernible than waves I-IV (Moller & Jannetta, 1985). Wave identification along with the latency of the ABR waveform is important in the discovery of auditory brainstem abnormalities. Latencies are also essential in the detection and probable causes of hearing loss. There are three main latencies used in the analysis of ABRs: absolute latency of wave V, inter-peak latencies (IPL) between waves I and II, waves I and V and waves III and V (Katz, 1994).

The clinical significance of the ABR is seen when conducting audiologic evaluations on infants and difficult-to-test patients. ABRs can also be used in the identification of a retrocochlear pathology such as an acoustic neuroma and cerebello-pontine angle tumors, the diagnosis of multiple sclerosis, neurological evaluation of patients in a coma and intraoperative monitoring (Hashimoto et al., 1981). Limitations of ABRs include: the ABR is not a hearing test, it can only estimate hearing sensitivity and the ABR is not a test of auditory function above the brainstem. (Kusakari et al. 1981, Goldstein & Aldrich, 1999; Hall, 2007)

Middle-Latency Auditory Evoked Potentials. Middle latency responses typically occur between 10 and 50 ms after the onset of a stimulus presentation. Middle latency auditory evoked potential (MLAEP) recordings are represented by a series of positive and negative waves that originate from multiple generators which are primarily represented by the thalamus-cortical pathways and to some degree from the inferior colliculus and the reticular formation (Katz, 2007). Three primary MLAEPs will be discussed: the auditory middle latency response (AMLR); the P 50 and the 40-Hz response of the auditory steady state response (ASSR).

Auditory Middle Latency Response. Interestingly, auditory middle latency responses (AMLRs) were the first auditory evoked potential to be recorded with the use of computer-averaging techniques (Geisler, Frishkopf, & Rosen, 1958). AMLRs have a latency of approximately 12 to 50 ms after the onset of a stimulus presentation. The AMLR waveform consists of positive (P) and negative (N) peaks that are labeled as follows: Po, Na, Pa, Nb, and Pb (Hall, 2007). Pa is considered a constant and frequently used component of the AMLR with latencies occurring around 25 ms post-stimulus. However, Pb is a variable and evasive component that is not always seen in normal adult subjects. Latencies of Pb occur at approximately 50 ms post-stimulus when discernible.

Clinically, the AMLR is used for electrophysiological assessment of low frequency hearing thresholds, determination of cochlear implant function, detection of lesions in the auditory pathway, and overall assessment of the integrity of the central auditory pathway. One of the limitations of the AMLR is that the electrophysiological response of the Pa is not easily seen in children. They must be asleep to elicit the response, however, the use of sedatives has the capability of disrupting the response. As a child matures, the detectability of the Pa increases from 20% to 90% by age 12 (Hall, 2007; Moller 1994; Goldstein & Aldrich 1999; McPherson & Ballachanda, 2000). Another limitation of the AMLR is the limited diagnostic capability due to the variability of responses in normal adults.

The P50. The P50 (P1) is a middle latency event-related response that occurs approximately 50 ms after the onset of an auditory stimulus. This test is used to measure auditory sensory gating (the brain's ability to inhibit or filter irrelevant information) by comparing the amplitudes of responses. Responses are evoked using a paired-click

paradigm that uses two auditory stimuli (clicks). Each click is presented 500 ms apart. Once both of the P50 responses are present, the brain's response to each stimulus is measured and compared as a ratio (test/condition ratio or T/C ratio). When the ratio of the brain's response to the second stimulus is significantly less than the brain's response to the first click, it is claimed that sensory gating is intact. However, individuals with psychiatric and neurological disorders such as schizophrenia, post-traumatic stress disorder and Parkinson's disease have a tendency to show a weak suppression of the second response (T/C ratio < 0.40) (Hunter, Nereida, Ponicsan, & Randal, 2007; Freedman et al., 2002; Rasco, Skinner & Garcia, 2000; Teo, Rasco, Mefte, Skinner, Boop & Garcia-Rill, 1997).

40 Hz Auditory Steady State Response. The 40-Hz auditory steady state response (40-Hz ASSR) is recorded in a similar fashion to the AMLR previously discussed. The 40-Hz response was named because of the rate of signal presentation which is approximately 40 per second or 40 Hz. The 40-Hz response is considered a steady-state rather than a transient response because the waveforms mimic the stimulus, repeating itself time and time again. The generator sites of the 40-Hz ASSR are not well defined but it is thought that the thalamic areas are involved (Ross, Herdman, & Pantev, 2005). In adults the AMLR components Pa and Pb are recorded with latency intervals occurring approximately every 25 ms or 40 times per second. When the rate of stimulation is in synchrony with the response, the overlap that occurs at 40 Hz causes an augmentation of the AMLR components at the rate of 40/sec. Thus, the enhanced amplitude of the 40 Hz response makes detection easier at low intensity levels. The ASSR is said to provide a more accurate prediction of hearing sensitivity the ABR with predicted thresholds within

10 to 15 dB of behavioral thresholds. (Luts, Desloovere, & Wouters, 2006). However, the test has not been used clinically because of its susceptibility to the influence of age, state of arousal, and drug interactions (Hall, 2007; Goldstein & Aldrich, 1999).

Late-Latency Auditory Evoked Potentials. Late-latency auditory evoked potentials or auditory late responses (ALRs) occur between 60 and 250 ms after the onset of a stimulus. ALR waveforms are typically much larger in amplitude with gently sloping peaks as compared to early and middle latency responses that have sharp narrow peaks. ALR waveform morphology is better defined and easier to decipher when the participant is alert and paying attention to the stimuli presented. When it comes to describing ALRs, terminology can be ambiguous and inconsistent. To alleviate some of the confusion, there are two common approaches used to describe late-latency potentials. One approach categorizes responses based on latency and temporal sequences of the ALR components. The other approach categorizes AERs based on whether they are exogenous or endogenous (Hall, 2007). The later of these two approaches will be the one used for the purpose of this discussion.

Exogenous Auditory Evoked Potentials. Auditory late-potentials are exogenous in nature which means that the amplitude and latency of the response is determined by characteristics of the stimulus such as intensity and frequency. The participant has no conscious awareness of the responses that are elicited from the stimulus, nor do they have any control over how they respond. ALR latencies are usually recorded between 100 and 200 ms following the onset of the stimulus with the primary potentials labeled P1, N1 and P2 (Hall, 2007).

The P1 response is represented by a positive peak falling in the vicinity of 60 to 80 ms after the onset of the stimulus which is generated by late thalamic activity in the early auditory cortex. The P1 is the last waveform of the middle latency response, is part of the specific sensory system and can be manipulated with various test parameters (McPherson & Ballachanda, 2000).

The N1 response, once generated, is depicted by a negative peak between 90 and 100 ms and is representative of activity from a non-specific polysensory system that falls within the contralateral supratemporal auditory cortex (McPherson & Ballachanda, 2000). Other researchers have suggested the N1 response is representative of synchronous neural activity and is believed to have multiple generator sites found in the primary and secondary auditory cortex (Martin, Tremblay & Korczak, 2008; Näätänen, 1992; Näätänen & Picton, 1987). The N1 component is thought to represent the onset of the response (Alain & Tremblay, 2007).

The P2 response is represented by a positive peak at approximately 175 ms and is said to be generated from the non-specific polysensory system with activity abounding from the lateral-frontal subratemporal auditory cortex (McPherson & Ballachanda, 2000). Others suggest that P2 activity encompasses multiple generators such as the Mesencephalic reticular activating system (Knight, Hillyard, Woods, & Neville, 1980) the Sylvian fissure at the level of the somatosensory area S2 (Hari, Hämäläinen, Hämäläinen, Kekoni, Sams, & Tiihonen, 1990) and the reticular formation in the brainstem responsible for transmitting sensory input (Beine, 2007).

Though P1, N1 and P2 are believed to come from separate cortical sources, the complex (P1-N1-P2) is investigated together and considered one unit (Crowley &

Colrain, 2004). It is suggested that the P1-N1-P2 components are representative of activity in the central auditory system (Martin, Sigal, Krutzberg, & Stapells, 1997; Ostroff, Martin, & Boothroyd, 1998; Sharma & Dorman, 1999, 2000; Whiting, Martin, & Stapells, 1998) thus making the P1-N1-P2 electrophysiological responses an effective means of evaluating central auditory processing (Ponton, Vasama, Tremblay, Kwong, & Don, 2001; Tremblay, Kraus, McGee, Ponton, & Otis, 2001).

Endogenous Event-Related Potentials. Endogenous potentials are similar to exogenous potentials in that both potentials need stimulus presentation for elicitation of the response. The difference in endogenous potentials is that they are event-related, meaning the participant must be actively conscience and cognitively aware of the change in stimulus being presented. Endogenous potentials occur approximately 200-600 ms after the onset of the stimulus and include the N2, P300 and N400 event-related responses. For the purpose of this discussion the N2 and N400 will be discussed briefly followed by a more in depth explanation of the P300.

The N2 is considered the first of the ALR endogenous responses. It occurs at approximately 180-325 ms after the onset of the stimulus and is seen as a negative peak. The N2 response is elicited from an oddball paradigm in which a deviant stimulus is presented in succession with multiple standard stimuli presentations. When the deviant stimulus is presented, the participant is cognitively aware of this difference and responds accordingly (Patel & Azzam, 2005).

The N400 is represented by a negative peak occurring approximately 400 ms after the onset of a stimulus presentation. The elicitation of this potential occurs endogenously when a participant is presented with a series of sentences with a multitude of semantic

differences. The greater the semantic difference the more robust the N400 response (Kutas & Hillyard, 1980). In 1984, Kutas and Hillyard discovered that priming (words that trigger and expected ending in a sentence) does affect the expected outcome of a sentence. The N400 response is said to be greatly dependent upon higher-level processing tasks and related to the process involved in decision making. Researchers believe that multiple endogenous sources are responsible for N400 activity but the exact generator sites are not clearly defined (Kutas & Hillyard, 1980; Hagoort & Kutas, 1995; McPherson, 1996).

P300. During the early to mid 1960's, extensive research on what is now known as the P3 (P300) was being conducted. Two published articles came from this research, one by Davis (1964) that highlighted studies conducted by asking the participants to discriminate between different auditory stimuli, the other by Sutten, Braren, Zubin and John (1965), highlighting studies conducted to validate the existence of the P3 response. Both of these studies confirmed that the P3 was an endogenous response elicited by a cognitive awareness and discrimination of the stimulus presented.

The P300 is a robust response which can be seen as a waveform with a positive peak at approximately 250-500 ms. Criteria for identification of the P300 response varies slightly among researchers. Matthyssen, 2013 compiled a summary of criteria used to identify the P300 response (refer to Table 1). The P300 is elicited not by the stimulus itself, but by the event-related action of the participant deciphering between two stimuli which is a reflection of short-term memory (Lindin, Zurron, & Diaz, 2004).

Table 1. Summary of criteria used to identify the P300 response.

Author(s)	Criteria to Identify P300 Peak
Croft, Gonsalvez, Gabrial, & Barry (2003)	Most positive peak between 250 and 600 ms.
Comerchero & Polich (1998)	Largest positive peak between 250 and 450 ms.
Gonsalvez & Polich (2002)	Most positive peak within the window of 250 and 600 ms.
Jocoy et al. (1998)	Most positive peak between 220 and 450 ms.
Krishnamurti (2001)	Largest positive peak following N200 component, between 250 and 700 ms.
Lee et al. (2004)	Any positive peak within the window of 260 and 500 ms. Used the second peak if there were two.
Lee, Kim & Suh (2003)	Any positive peak within the window of 260 and 500 ms. Used the second peak if there were two.
Lindin, Zurron & Diaz (2007)	Largest positive peak between 250 ms that follows a negative trough with latency of 180 and 350 ms (N100).
Polich, Ellerson & Cohen (1996)	Largest positive going peak after the N100-P200-N200 complex, between 250 and 400 ms.
Spongberg & Decker (1990)	Largest peak occurring after the N100-P200-N200 complex between 200 and 400 ms.
Zuckerman, Goldsteine & Babkoff (2007)	Largest positive-going peak between 250 and 450 ms.

(Matthyssen, 2013)

Though the P300 is typically thought of as only one waveform, it is actually made up of two waveforms, the P3a and P3b. The P3a is elicited independently from the listener's attention when there is a large difference in the target and deviate stimuli. It has a shorter latency than the P3b and is characterized by frontal topography (Knight, Scabini, Woods, & Clayworth, 1989; Patel & Azzam, 2005). The P3b has the largest amplitude over the parietal region with waveforms produced by the listener's ability to discriminate the changes in auditory stimuli. Thus, the P3b is affected by attention (Morgan, Cranford & Burk, 1997). Of the two waveforms, the P3b is the component that is typically known as the "P3" or "P300" and is elicited when someone presses a button in response to a deviant stimuli presentation in an oddball paradigm (Knight et al., 1989; Polich, 2004).

Commonly, auditory, visual and somatosensory stimuli are used to conduct P300 testing (Gaeta, Friedman, & Hunt, 2003). The stimulus is commonly presented using an oddball paradigm where frequent stimuli are presented continuously until interrupted by a deviant stimuli. The subject is typically asked to count the infrequent stimuli or press a button to show active discrimination between the two stimuli presented. As the complexity of the task increases, the latency of the P3 response also increases (Davis, 1964).

The cognitive process of attention, discrimination and working memory are thought to be a reflection of higher order neurophysiologic activity at the coritcal (Lee et al., 2003) and sub-cortical levels (Wood; Allison; Goff; Williamson & Spencer, 1980; Halgren; Squires; Wilson; Rohrbaugh; Babb & Crandell, 1980). Possible cortical generator sites reported include frontal regions (Wood & McCarthy, 1986), centro-

parietal regions (Goff, Allison, & Vaughan, 1978), the temporal parietal junction (Knight et al., 1989) and auditory cortical regions (Rogers, Baumann, Papanicolaou, Bourbon, Alagarsamy, & Eisenberg, 1991). Suggested sub-cortical generator sites consists of the hippocampal region (Halgren et al. 1980) and dorsal thalamic regions (Yingling & Hosobuchi, 1984). Other generator sites such as the mesencephalic reticular formation, medial thalamus, and prefrontal cortex are considered possible contributers to the P300 response because attention is imperative for the participant to actively respond to the stimuli (Yingling & Hosobuchi, 1984).

For nearly half a century, P300 testing has been conducted to investigate neurologic and psychiatric disorders and determine the generator sites associated with each. Picton and Hillyard (1988) suggested that any disorder should be tested with the P300 response to determine "global cognitive dysfunction" (Swink, 2010). Other researchers have suggested using the P300 response to monitor the effectiveness of therapy, in that, P300 latencies reflect a demand on cognitive processing and intra-subject variability of the P300 response is low (Goodin, Squires, & Starr, 1983; Polich & Starr, 1983). For example, if a patient is undergoing therapy and the P300 latency decreases, the examiner can conclude that the therapy is contributing to the improvement of the patient's processing ability. If however, the latency increases then the opposite is true (Swink, 2010).

There are many factors that play into the inter- and intra-subject variables associated with P300 latencies and amplitudes. Normal intra-subject variability in latency of the P300 waveform is between 17 and 57 ms when identical stimulus parameters are used (i.e. intensity, frequency, and duration). The 40 ms gap is due to long

time effects such as the time of day as well as short time effects such as changes in stimulus sequence, evaluation of the stimulus and the selection of the response (Holm, Ranta-aho, Sallinen, Karjalainen & Muller, 2005). Amplitude and latency of the recorded P300 can also be affected by the number of frequent stimuli directly preceding the target stimuli. When the number of preceding stimuli is increased the P300 amplitudes are also increased but the latency is decreased (Holm et al., 2005). Arousal state is another inter-subject variable that can affect the P300 response. Circumstances that can affect arousal include: circadian rhythms, food intake, morning/evening activities, ultradian rhythms, seasonal variation, menstrual cycle and personal preferences (Polich & Kok, 1995). Interestingly, variation in P3 were seen depending on circadian rhythms (Geisler & Polich, 1990), lack of food consumption was found to reduce P3 amplitude (Geisler & Polich, 1992) and fluctuations in neural electrophysiology activity, which changes arousal state, can affect the P3 (Lin and Polich, 1999). However, menstrual cycle and seasonal changes did not have a significant effect on P3 responses (Polich & Kok, 1995).

In addition to inter- and intra-subject variables, environmental factors can also play an important role in P3 response recordings. Exercise, mental fatigue, drugs, caffeine and sleep deprivation are among the environmental factors used to manipulate P3 responses. When the body is aroused through exercise, food intake, high body temperature, and normal sleep the P3 amplitude increases and latency decreases. However, if the subject is denied food, consumes alcohol, or becomes sleep deprived, the P3 amplitude decreases and latency increases due to a reduction in the state of arousal (Polich & Kok, 1995). For research purposes, P300 recordings were used to study the

effects of sleep deprivation at three and six hours after a brief 110 min nap, following 24 hours of sleep deprivation.

Sleep

Sleep is a natural biological function encompassed by all. Eloquently defined in the Merriam-Webster Dictionary (2014), it is "the natural periodic suspension of consciousness during which the powers of the body are restored". Such restorative functions include but are not limited to mental restoration and body temperature regulation as well as endocrine and immune system function (Penzel & Kesper, 2006; Saper, Scammel & Lu, 2005). Prior to the 1950's, researchers believed in a passive sleep theory in which the brain, from shear lack of stimulation, passed into a sleep state (Kelly, 1981). Since that time, researchers have theorized that sleep is an active process with complex cyclical changes following a temporal pattern which initiates changes in the brain's electrical activity (Markov & Goldman, 2006; Penzel & Kesper, 2006).

As sleep sets in, the body passes through four non-rapid-eye-movement (NREM) phases followed by one rapid-eye-movement (REM) phase. Each of these five phases follow in succession from one to five creating a sleep cycle. Each NREM-REM cycle lasts approximately 90 to 120 minutes (Markov & Goldman, 2006; Rauchs, Desgranges, Foret, & Eustache, 2005). The cycle then repeats approximately 4 to 6 times per night (Penzel & Kesper, 2006).

Stage 1 of NREM sleep is characterized by a light sleep where an individual can drift in and out of sleep and is easily startled awake. The eyes begin to move slowly and muscle activity is limited. There is also a decrease in heart rate, deeper breaths are taken,

and the body is more relaxed (Bennett, 1977; NIH, 2014). This stage provides the transition needed from being awake to falling asleep as well as from the end on one full sleep cycle (REM) to the beginning of another (NREM). This stage is from 1 to 7 minutes long taking up approximately 2 - 5 % of total sleep time. If a person is disturbed while trying to fall asleep, there is an extension of stage 1 sleep duration (Markov & Goldman, 2006; Rauchs, Desgranges, Foret & Eustache, 2005).

Stage 2 is entered when quick bursts of rapid EEG waves called *sleep spindles* occur. At this time eye movement stops and brain waves are slow (Bennett, 1977; NIH, 2014). In addition to sleep spindles there is also an appearance of K-complex waves (large negative wave following a positive peak) (Rechtschaffen & Kales, 1968). Individuals in this stage of sleep are said to be sleeping soundly but can be easily awakened. Stage 2 constitutes 45 to 55 % of total sleep time given an average night of sleep (Markov & Goldman, 2006; Rauchs et al., 2005)

Once a person is sleeping soundly, stage 3 of NREM sleep follows. This stage lasts only a few minutes, approximately 5 to 8 % of an individual's sleep time (Markov & Goldman, 2006). During this stage there is an appearance of low-amplitude delta waves present in 20 to 50% of the EEG waveforms. During this stage it is much harder to arouse an individual. Their heart rate, blood pressure, muscle tone and body temperature decrease and their breathing deepens (Bennett, 1977).

During stage 4 of NREM sleep, it is extremely difficult to awaken someone and muscle tone is even more relaxed than the previous stage. It is during this stage that the aforementioned restorative functions occur. Stage 4 sleep lasts approximately 40 minutes and constitutes 10 to 15 % of sleep time. The electrophysiological characteristics of this

sleep stage includes slow-wave activity with delta waves seen in more than 50 % of EEG recordings (Bennett, 1977; Markov & Goldman, 2006; Rauchs et al., 2005). Together, stages 3 and 4 are considered deep sleep (NIH, 2014).

Once NREM stages 1 through 4 are complete (approximately 90 minutes, total) the first REM sleep stage begins (Markov & Goldman, 2006). REM sleep phases are short in the beginning and gradually get longer with each sleep cycle. The longest REM sleep period occurs in the last third of an 8 hour sleep session. This stage is characterized by rapid, continuous eye movements throughout the entire REM period (Penzel & Kesper, 2006), breathing becomes rapid, irregular and shallow while muscles become paralyzed (only temporarily) (NIH, 2014). REM sleep constitutes 20 to 25 % of total sleep time and has EEG waves that are similar to recordings taken from someone who is awake (Markov & Goldman, 2006). Much like NREM sleep, REM sleep can be categorized into two different stages: phasic and tonic sleep (Markov & Goldman, 2006). The phasic stage ensues myoclonic twitches (body jerks) with EEG recordings that are seen as spikes from the ponto-geniculo-occipital (PGO) area. The tonic stage is where the body has a significant declination in muscle tone with theta waves traveling through the hippocampus (Bennett, 1977).

Typically, the first REM sleep period occurs approximately 70 to 90 minutes after stage 1 NREM sleep begins. With each new night of sleep, the initial REM period is relatively short during the first sleep cycle with long periods of deep sleep. Each following sleep cycle then has periods of REM sleep that increase as deep sleep decreases. When the 8 hour sleep session is nearing the end, most individuals are spending their sleep time in stages 1 and 2 as well as REM sleep (NIH, 2014).

The optimal amount of sleep is needed to reap the benefits of feeling fresh and alert. It is recommended that the average person get 7 to 8 hours of sleep per night to incorporate 4 to 6 sleep cycles. When each of these 4 to 6 sleep cycles is complete, an individual has encountered about 20 to 25 % of REM sleep. REM sleep is of great importance because it has been correlated with intellectual functioning. Each individual requires varied amounts of sleep depending on age, genetics, prior sleep history and the use of stimulants and depressants such as drugs or caffeine (Markov & Goldman, 2006).

Sleep Deprivation

Many environmental factors such as noise induced disruptions as well as physiological factors such as insomnia or sleep apnea can cause disruptions in nightly sleep sessions. When sleep is disturbed, it causes varying levels of sleep loss: sleep reduction, sleep fragmentation, and sleep deprivation (total sleep loss) (Boonstra, Stins, Daffertsofer, & Beck, 2007). When an individual stays up much later and/or wakes up much earlier than they are accustomed to, sleep reduction occurs. If someone wakes up repeatedly through the night (i.e. coughing throughout the night), they experience sleep fragmentation. However, if someone endures prolonged hours of no sleep, sleep deprivation sets in. Whether these disruptions are brief, such as coughing in the middle of the night or being awakened by a startling sound, or long such as periods of insomnia, long work hours or all night study sessions, they can have adverse effects on intellectual and physical performance.

When the body is deprived of sleep at any level, it leaves a person feeling drowsy and makes it difficult for them to concentrate. (NIH, 2014). Other daily functions that

often suffer due to sleep disruption include thermoregulation, learning and memory (Markov & Goldman, 2006). In addition, behavioral changes can occur when sleep is disrupted and sleep deprivation occurs, such changes are increased anxiety, hostility, tension, confusion, decrease or loss of short-term and long-term memory, reaction time, and depression. Lastly, physical changes can be seen through hand tremors, visual hallucinations and changes in the red cell adenosine triphosphate (ATP) levels (Jeong, Kim, Kim, Chae, Go & Kim, 2001).

Sleep deprivation can also hinder the restoration of neurons and protein building blocks. Lack of sleep can cause neurons to become depleted causing pollution and byproducts from normal cellular activity to build up and cause malfunction. Neuronal connections suffer because the brain does not get the chance to exercise these connections which can lead to deterioration in neuronal activity. Children and young adults who suffer from sleep deprivation have a reduction in the amount of growth hormone that is released during deep sleep. Lack of deep sleep can also hinder the body's cell production and breakdown of proteins which delays restoration from stress and exposure to ultraviolet rays. As the body falls into deep sleep, the activity in areas of the brain that control emotions, decision-making processes and social interactions slows down drastically. This suggests that without prolonged periods of deep sleep, emotional and social functioning can be affected while awake (NIH, 2014).

Circadian Rhythm. Another factor that can greatly affect sleep patterns is the circadian rhythm which is essentially a biological clock that works on a 24 hour basis. These rhythms control mental and physical changes that occur throughout both day and night. The technical term for this biological clock is suprachiasmatic nucleus or SCN.

The SCN is located in the hypothalamus; it can be described as a pair of brain structures that are the size of a pinhead and contain approximately 20,000 neurons. Due to the location of the SCN which lies slightly above the points at which the optic nerve crosses in the hypothalamus, light reaches the retina through photoreceptors and sends a signal through the optic nerve to the SCN. This signal then travels to other regions of the brain, namely the pineal gland. The pineal gland then responds to this light signal and turns off the production of melatonin (the hormone that induces sleep). Melatonin increases after night fall and serves as the body's natural sleep signal which causes drowsiness. Without the SCN, other functions that are governed by the sleep/wake cycle would be affected. These functions include: body temperature, hormone secretion, urine productions and changes in blood pressure (NIH, 2014).

Over the years, studies have been conducted to investigate possible interactions between sleep deprivation and the influence of circadian rhythm on cognitive performance (Zukerman, Goldstein, & Babkoff, 2007). Williamson and Friswell (2011) found that participants who were sleep deprived had significantly slower responses and were at a low point in the circadian rhythm. However, participants that were not sleep deprived were found to be at a high point in the circadian rhythm and had faster responses. Thus, they concluded that circadian rhythm and a person's sleep/wake cycle interact causing poorer performance when sleep deprived. Let et al. (2003) studied the effects of sleep deprivation on simple repetitive tasks in conjunction with changes in body temperature. They found that performance on simple repetitive tasks varied as body temperature changed, with performance better in the morning and poorer in the evening. They also discovered that cognitive function during high complexity tasks did not worsen

through the day. Thus, cognitive function seems to be linked with circadian rhythms with performance increased in the morning when body temperatures are low and declining in the evening when body temperatures are higher (Lee et al., 2003; Williamson & Friswell, 2011).

Importance of Sleep Deprivation Studies. For more than a century studies have been conducted to determine the significance of sleep and sleep deprivation on cognitive performance (Babkoff et al, 2008; Ikegami, Ogyu, Arakomo, Suzuki, Mafune…Nagata, 2009; Zukerman et al., 2007). As mentioned previously, the importance of these studies greatly affect the health and well-being of not only the person suffering from sleep deprivation but also the individuals whose health, safety and even lives are at the mercy of professionals who are subject to long work hours. Though the previous statement seems drastic, many patients, airline passengers, motorists, and military personnel would disagree. When professionals are subject to many nights of little or no sleep their cognition, reaction time and decision making abilities become impaired, performance suffers and lives are endangered.

Medical Students and Residents. According to the American Medical Association, the average workweek for a resident physician is around 74.2 hours/weeks. Interns average 85 hours/week for all specialties and surgical specialties often require up to 100 hours/week (Jacques, Lynch, & Samkoff, 1990). It was a work load like this that caused the death of a woman at a teaching hospital in New York. After investigation in 1984, the grand jury declared the cause of death to be fatigue. At that time, controversy was raised regarding the effects of sleep deprivation in the medical field (Jacques et al., 1990). Friedman, Bigger & Kornfeld (1971) found that sleep deprivation adversely

affected an intern's ability to perform routine activities, it affected their mood, decreased their vigor, lowered their ego, made impacts on their social affection and decreased their self-perceived abilities. A study by Jain et al. (2010) was conducted to determine the effects of partial sleep deprivation on cognition and alertness of medical students. They used auditory event related potentials (P300) to look at cognitive performance and a sleep questionnaire (Stanford Sleepiness Scale (SSS)) to evaluate alertness. The results of the study revealed a significant decrease in P300 amplitude and latency along with a decline in reaction time (RT), indicating that cognitive performance and reaction time suffered with partial sleep deprivation.

Pilots and Drivers. Pilots are subjected to night-time departures, early morning arrivals, flying in and out of time zones and long hours of flight, all of which have an adverse effect on attention, vigilance and disruption of circadian rhythms. Fatigue has been noted as the cause of plane crashes throughout the history of flying. In 2008, a pilot from a Honolulu based Go! Airlines fell asleep during a 50 minute flight and overshot their destination by more than thirty miles. In 2009, fifty people were killed during a Continental Connection flight that landed on a house. Pilots apparently failed to respond to a stall warning properly and lost control of the flight. Countless numbers of other incidences have occurred due to pilot fatigue (Caldwell, 2012). John Caldwell (2012) conducted a study examining the interaction between inadequate sleep of pilots and circadian rhythms. In his research, he points out that:

> "fatigue-related performance problems in aviation have been consistently underestimated and underappreciated, despite the fact that decades of research on pilots and other operational personnel has clearly established that fatigue from insufficient sleep significantly degrades basic cognitive performance, psychological mood and fundamental piloting skills."
> (Caldwell, p. 85, 2012)

Additionally, Caldwell, Caldwell, Brown & Smith (2004) investigated the impact that sleep deprivation had on cognition, alertness, self-reported alertness, and flight performance of F-117 pilots. They found a pilot's basic skills were degraded by over 40 % which affected their ability to maintain headings with precision, make altitude adjustments correctly, and maintain air speeds. Basically, the results provide a list of relevant effects that sleep deprivation has on pilots and suggests that aviators and commanders should consider these effects when conducting training, making schedules and maintaining operations.

Unfortunately, drowsiness among car and truck drivers is becoming a generally accepted risk factor for traffic safety (De Valck & Cluydts, 2001). Mitler, Miller, Lipsitz, Walsh and Wylie (1997) proclaimed that in the United States, commercial truck accidents injure more than 110,000 people and kill over 500 more every year. Furthermore, driver fatigue has been stated as the cause of these accidents between 1 and 56% of the time. Self-reported studies show that sleepiness related car accidents range from 4 to 16.1 % and truck driving accidents fall into the 24.8 % range (Arnold, Hartley, Corry, Hochstadt, Penna & Feyer, 1997; Fell, 1995; Lyznicki, Deoge, Davis & Williams, 1998; Rizzo, 1999). Mitler et al. (1997) investigated sleep and drowsiness patterns of 80 truck drivers. They reported that these truck drivers obtained less sleep than was required to be alert while driving. They also discovered that drivers on the road late at night or early in the morning were more susceptible to falling asleep or being in a sleep-like state.

Military Personnel. According to Caldwell & Caldwell (2005), military personnel must occasionally work 24 hours a day 7 days a week to complete a successful mission. In addition to sleep deprivation, this type of mission can cause a multitude of stressors

thus affecting cognitive performance (Lieberman et al., 2002). Drowsiness among soldiers can also lead to accidents. For example, the Air Force reported Class A mishaps caused by "insufficient operator attention", due to drowsiness, to be at 8 % between 1972 and 2000 and at 4 % between 1990 and 1999 (Caldwell & Caldwell, 2005). That means about half of all insufficient sleep related accidents occurred in the last 9 years of the stated 28 year time span. Additionally, Navy Seals must endure a ritual called "hell week" where trainees are subjected to continuous 24 hour activity that includes: surf immersion, and boat push-ups, as well as other psychological and physiological stress factors. Most of the training for Navy Seals is conducted in wet, cold and unpredictable conditions (Smoak, Singh, Day, Norton, Kyle, Pepper & Deuster, 1998). These conditions lead to extreme fatigue and increase the probability of accidents due to "insufficient operator attention" (Caldwell & Caldwell, 2005).

In summary, it is of great interest to medical residents, pilots, truck drivers and military personnel for authoritative figures to take sleep deprivation studies seriously. These professions are among many that can lead to undue exposure of potentially detrimental practices for patients, passengers, motorists and soldiers. However, this poses the timeless question of which studies are the most accurate and give conclusive evidence to cognitive function and performance.

Study Protocols. Though many studies have been conducted over the past century, results vary depending on the test protocol used. Moderator variables, methodological problems, time variations and subjective sleep habits have been suggested as potential variables in protocol.

According to Philibert (2005), moderator variables include tests that measure: cognitive abilities, motor performance, mood and the extent of sleep loss, task duration and task complexity. Other factors such as various controls used can also contribute to differences across studies. For example, when conducting sleep deprivation studies, researchers can choose to have participants that are sleep deprived for 24 hours while other researchers can choose 36 or 48 hours of sleep deprivation. Other controls include number of hours rested before and after sleep deprivation and specific tasks used when testing motor and cognitive function.

Lee et al. (2003) demonstrated that methodological issues can affect cognitive performance between studies. Factors such as the environment, personal characteristics and test characteristics can be the culprit of these differences. Lee and his colleagues demonstrated that the task used to test cognitive performance while sleep deprived could lead to varying results.

Another variable was demonstrated by Hsieh, Li & Tsai (2010) when they reported that performance deteriorated as the time to complete the task was lengthened. Interestingly, they also demonstrated that incentives such as monetary rewards, increased participant response accuracy when given long, tedious tasks. Lastly, subject variables such as how a person sleeps prior to sleep deprivation and how the subject is affected by sleep deprivation can give significantly different results when conducting sleep deprivation studies which can lead to difficulty when comparing outcomes (Philibert, 2005). For this reason, it is important to use conclusive results such as late-latency auditory evoked potential P300 measures to obtain accurate and consistent results of cognitive function during sleep deprivation testing.

P300 and Sleep Deprivation. For more than a decade, changes in P300 amplitude and latency have been used as an objective measure of cognitive performance while sleep deprived. As mentioned earlier the P300 is elicited not by the stimulus itself, but by the event-related action of the participant deciphering between two stimuli which is a reflection of short-term memory (Lindin, Zurron, & Diaz, 2004). Multiple tasks can be used to perform P300 testing, however the most commonly used task is the oddball paradigm where two noticeably different pure tone frequencies are used.

Panjwani et al. (2010) and Zukerman et al. (2007) used an oddball paradigm and found no significant change in P300 amplitude but found a significant increase in latency of sleep deprived participants compared to their baseline measures. Panjwani et al. (2010) utilized a frequent stimuli of 750 Hz and an infrequent or oddball stimuli of 2000 Hz when testing 9 males between the ages of 25 and 30. Zukerman et al. (2007) used a frequent stimuli of 200 Hz and an infrequent stimuli of 650 Hz when testing 18 undergraduate and graduate students. Each researcher recorded responses following 24 to 40 hours of sleep deprivation.

Jain et al. (2010), Qi et al. (2010), Lee et al., (2004) and Lee et al. (2003) found significantly increased latency and significantly decreased amplitudes of P300 responses when using an oddball paradigm. Lee et al. (2004) and Lee et al. (2003) both used subjects that were sleep deprived for 37 to 38 hours and implemented a frequent stimuli of 1000 Hz and an infrequent stimuli of 2000 Hz.

Just recently, Matthyssen (2013) found significant increases in latency and decreases in amplitude of the P300 response as a function of sleep deprivation across 24 participants. Matthyssen (2013) used an oddball paradigm with 1000 Hz pure tone

serving as the standard and a 2000 Hz pure tone serving as the deviant stimuli. In addition to sleep deprivation, Matthyssen (2013) studied the effects of a 10 minute and 110 minute nap. There were no significant differences in baseline measures compared to the 10 minute recovery period nor were there any significant differences in the 10 min recovery period and the sleep deprived state. Though there was no significant difference in the sleep deprived state and the 110 minute recovery period, a paired sample T-test revealed a significant increase in amplitude and decrease in latency compared to the 10 minute recovery period. In other words, a 110 minute recovery period appears to be more effective than a 10 minute recovery period.

Recovery Period and Sleep Deprivation. Utilizing a recovery period (nap) in sleep deprivation studies allows researchers to assess how effective a recovery period will be in the improvement of P300 latency and amplitude and thus the improvement of cognitive function. A multitude of studies utilized rest periods ranging from 10 to 120 minutes. Tietzel and Lack (2002) determined that a 10 minute nap, which only included the first NREM sleep cycle, increased alertness, vigor and performance as well as decreased fatigue in participants. While Milner & Cote (2009) reported that naps utilizing the first and second sleep NREM sleep cycle improved performance but not alertness or fatigue. Brooks and Lack (2006) found that a 5 minute nap gave no benefit, a 10 minute nap produced immediate, lasting benefits, and a 20 to 30 minute nap showed no benefits until later in the day. The lack of benefit from 20 and 30 minute naps is said to be caused by sleep inertia which is when a person loses their ability to think and perform when first waking up (Milner & Cote, 2009). Arousal during REM sleep causes a feeling of confusion and grogginess thus delaying the ability to process information. Therefore, it

takes longer for the benefit of the 20 or 30 minute nap to take effect. Panjwani et al. (2010) investigated longer naps lasting 120 minutes as compared to 15 minutes. They found that 120 minute naps were more beneficial than 15 minute naps. Similarly, Matthyssen (2013) found that a 110 minute nap was more effective than a 10 minute nap.

There are many factors that can cause a variance in results. For example, the length of time between the nap and testing, the time of day the naps were taken and the length of sleep deprivation prior to the nap. Milner and Cote (2009) discovered that naps taken after shorter durations of sleep deprivation are more effective than naps taken after 30 or more hours of sleep deprivation. Naitoh (1981) found that evening naps ranging from 7:00 pm to 9:00 pm increased sleep inertia (as cited in Milner & Cote, 2009). Lavie and Weler (1989) found naps to be more productive when taken between 3:00 pm and 5:00 pm. According to Milner & Cote (2009), other factors such as individual sleep needs, regular sleep/wake patterns, quality of sleep and amount of sleep obtained prior to waking can also have an impact on the effectiveness of naps.

Though the previously listed factors play an important role in sleep deprivation studies, it is necessary to take into consideration the length of a full sleep cycle. In order to avoid sleep inertia, a nap should fall before REM sleep commences (10 min) or after it is over. A full sleep cycle lasts anywhere from 80 to 110 minutes. When someone has napped for 110 minutes, they will have undergone a full NREM-REM sleep cycle and should be at higher EEG arousal state (Polich & Kok, 1995) and not in the midst of an REM sleep stage which causes sleep inertia (Tietzel & Lack, 2002). These factors, combined with a significant improvement in P300 amplitude and decrease in latency found by Matthyssen (2013), is the basis for the use of 110 minute nap in this study.

Purpose

Previous studies have assessed the effects of P300 amplitude and latency on sleep deprivation. Specifically, previous unpublished studies conducted by Matthyssen and Franklin (2013), Riley and Franklin (2008), Tourtillott and Franklin (2002) and Staples and Franklin, (2001) assessed P300 responses after a brief recovery period. However, further investigation of P300 declination post recovery has not been investigated. Thus, the purpose of this study is to not only confirm previous results measuring behavioral and neurophysiological changes in the P300 but to also investigate post recovery periods of three and six hours to determine when there is a significant decrease in P300 amplitude and increase in latency as a result of continued sleep deprivation post 110 minute recovery period. In other words, investigators what to know how long it takes for the recovery effects to wear off and the effects of sleep deprivation to be seen again.

Research Questions

The current study was developed to address the following questions.

1. Is there a statistically significant difference in the latencies of the auditory evoked P300 response:
    a. Between baseline and sleep deprivation conditions?
    b. Between the sleep deprivation condition and 110 minute recovery period?
    c. Between the recovery period condition and three hours post recovery?
    d. Between the recovery period condition and six hours post recovery?

2. Is there a statistically significant difference in the amplitude of the auditory evoked P300 response:
    a. Between baseline and sleep deprivation conditions?
    b. Between the sleep deprivation condition and 110 minute recovery period?
    c. Between the recovery period condition and three hours post recovery?
    d. Between the recovery period condition and six hours post recovery?

METHODS

Participants

Prior to testing, approval was obtained from the Missouri State University IRB (October 20, 2014; approval # 15-0153). Seventeen graduate and undergraduate students from Missouri State University and Ozark Community College volunteered to participate in this study. The participant pool consisted of seven males and ten females between the ages of 18 and 25. Each individual was required to have an initial screening that included: otoscopy (to rule out any outer or middle ear anomalies that could affect testing), tympanometry to determine normal middle ear function (using a 226 Hz probe tone frequency, typanometric pressure should be between -100 and 50 daPa, ear canal volume between .8 and 1.6 cm^3 and peak compliance between .3 and 1.4 mmho), and a basic audiologic evaluation to determine that behavioral hearing thresholds were within normal limits (25 dB HL or better at 500, 1000, 2000 and 4000 Hz).

In addition to the basic screening a thorough case history was conducted to rule out any psychiatric or neurological disorders (see Appendix A) and a sleep log was completed for three consecutive days prior to testing to determine if participants had any sleep related disorders or sleep disturbance (see Appendix B). Participants were required to have at least 6 hour of sleep each night for 3 consecutive nights prior to inducing sleep deprivation.

Consent forms were signed by each participant prior to testing (see Appendix C). This form explained experimental procedures and asked for consent to uphold all of the requirements of the study which includes not napping until otherwise indicated. Prior to

each test run participants were required to fill out a Stanford Sleepiness Scale (SSS) to rate their level of alertness (see Appendix D). After the experiment, each participant was given a form for debriefing (see Appendix E).

Instrumentation

Two primary forms of instrumentation was used during this experiment. The initial screening instrumentation and that used to evoke an auditory P300 which is a late electrophysiological potential. Each will be introduced separately.

Screening Equipment. In the following order: otoscopic examination was performed with a Welch-Allyn otoscope; tympantometric measures were conducted with a Grason-Stradler Inc. (GSI) Tympstar impedance bride; basic audiometric testing was done with an Interacoustics AC 40 audiometer using ER-3A insert earphones in a double walled IAC, Inc. Controlled Acoustical Environment testing suite.

Electrophysiological Evoked Potential Equipment and Settings. A Compumedics NeuroScan with a SynAmp II amplifier was used to generate and record all late auditory evoked P300s. Stimuli was created with the Sound module of the Gentask software which was then routed bilaterally from the amplifier to ER-3A earphones. Electroencephalographic (EEG) recordings was obtained via QuickCaps, which is an elastic cap that has 21 and 32 silver-silver chloride sintered electrodes embedded and spaced to fit the participants scalp using the International 10-20 system (see Figure 2). Three non-inverting electrodes were placed at Cz, Fz, and Pz and referenced to two inverting electrodes placed at M1 and M2 (on the mastoids). An additional electrode was placed on the forehead to be used as a ground. To monitor

vertical electrooculographic activity (VEOG), and electrode was placed above and below the right eye. Electrooculography (EOG) refers to a technique used to monitor muscle activity around the eye, such as eye blinks (Simon, Schultz & Rassmann, 1977). This activity was then filtered out of the recordings to ensure accuracy of the P300 readings.

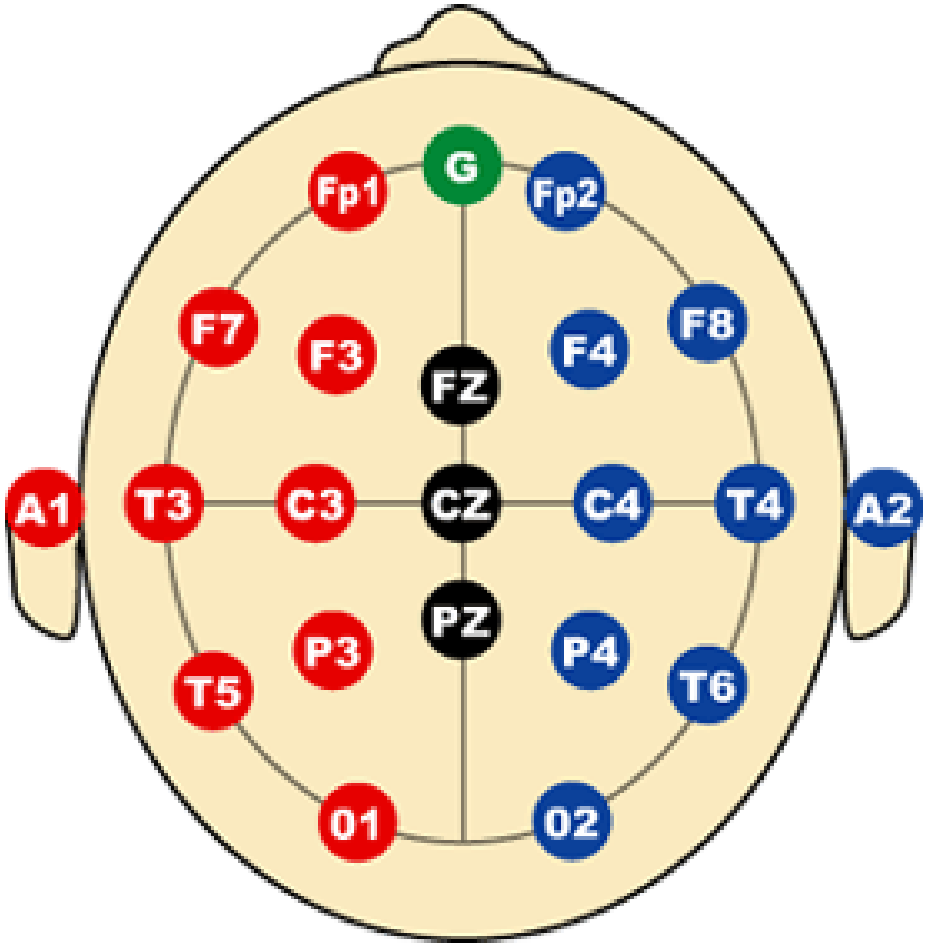

Figure 2. International 10-20 system (Wang, Lee & McKeown, 2009).

To prepare the subjects for electrode placement on each mastoid, above and below the right eye and on the forehead, the skin was scrubbed using NuPrep abrasive skin gel (McPherson 1996). Additionally, the scalp was prepared using a blunt tipped syringe to lightly abrade the skin and a conductive EEG gel (QuikGel) was injected through the QuickCap and applied to the scalp directly to secure placement at each electrode site.

Recording of the auditory P300 was obtained after the cap and electrodes were secure and impedance readings were at or below 5000 ohms with no more than 3000 ohms between each electrode. (Jocoy et al., 1998). Time-locked EEG activity was extended from -50 to 700 ms for each sweep (Lindin et al., 2004; Qi et al., 2010). To establish a baseline that will correct for the DC level of background EEG activity, sweeps started 50 ms prior to the onset of stimulus-activated waveforms which were determined by a trigger that is time-locked to the onset of the stimulus (Martin, Sigal, Kurtzberg, Stapells, 1997). EEG activity was amplified 500 times, was analog filtered from 1 to 40 Hz using a slope of 24 dB/octave and then digitized with the Compumedics PC based NeuroScan system and SynAmp II amplifier (Matthyssen, 2013; Riley, 2008). These digitized epochs will then be sent to an offline microcomputer to be averaged and digitally filtered. During this process, ocular movement artifacts were removed (Semlitsch, Anderer, Schuster, & Presslich, 1986) and artifacts exceeding ± 50 μV were rejected (McPherson, 1996; Picton, 1990).

Calibration. Auditory stimuli that was generated with the NeuroScan system, was calibrated at all stimulus levels by using a Larson Davis 800B sound level meter with a Quest 2 cc coupler. The signal was routed in series from the SynAmp II amplifier to

the ER-3A insert earphones to a 2 cc coupler that will then be coupled with the sound level meter for measurement. All sounds were detected by a microphone by using a linear setting. The following settings were used on the sound level meter to calibrate the signal: attenuator was set from 30 to 90 dB; sound was set for fast continuous detection to assess the variability of the sound.

Stimuli. This research is continuation of a previous study conducted by Matthyssen (2013). Therefore, identical stimulus parameters were used for the current study. A Blackman windowed pure tone stimuli and an "oddball" paradigm were used to elicit the P300 waveform. The "oddball" paradigm consisted of a standard (1000 Hz pure tone) and a target (2000 Hz pure tone) stimuli. Each condition had a sequence that consisted of 500 tones with a target/non-target ratio of 0.15. The intertrial interval (ITI) was set at 916.67ms. The intensity of each tone was set at 75 dB sound pressure level and lasted 50 ms. Target tones was presented pseudorandomly and had a minimum of three standard tones between them. Upon completion, the averaged responses of both the 2000 Hz target tone and the 1000 Hz standard tone was be compared.

Recovery Period. A 110 minute recovery period was used to allow each participant to undergo one full NREM-REM sleep cycle which typically ranges from 90 to 110 min (NIH, 2014). One full sleep cycle should leave a participant at higher levels of EEG arousal (Polich & Kok, 1995). For example, in a study conducted by Matthyssen in 2013, a significant difference in amplitude as a function of sleep deprivation was found for the P300 after a 110 min recovery period. This shows the positive effects of a 110 minute recovery period.

Procedures

Data Collection. Each participant was tested following five separate conditions: baseline, after 24 hours of sleep deprivation, 30 minutes after a 110 min recovery period as well as three and six hours post recovery. To ensure accuracy, comparable recordings were be obtained for both the baseline and sleep deprivation conditions during a three hour time window from 7:00am to 12:00pm. Baseline date was collected between one and three weeks prior to sleep deprivation. In addition the data collected for the sleep deprived state was done in a 24 hour period, over the weekend so that participants had a full day of recovery before returning to work and/or school.

Participants previously agreed through signed consent to wake up at their normal time in the morning, refrain from naps throughout the day and arrive in the lab by 9:00pm prior to undergoing sleep deprivation. They each reported the time of arousal as to ensure 24 hours of sleep deprivation. Participants were then strictly monitored in a controlled environment (the home simulation lab) to ensure the induction of sleep deprivation. Throughout the night, participants were restricted from excessive exercise, tobacco, the use of caffeine and alcohol consumption. Otherwise, they were encouraged to spend the night doing as they please (study, read, watch movies, play games, talk, etc). They consumed food and non-caffeinated beverages that were provided for them. Testing commenced in the morning after 24 hours of sleep deprivation. Each participant was tested in accordance with their reported wake time the previous day to ensure that a 24 hour period has passed. After testing the sleep deprived participants they were each taken to a dark, quiet room to rest for a period of 110 minutes. When the rest period

commenced, a third P300 test was administered. Participants stayed awake and were tested two more times. Once, three hours post recovery, then six hours post recovery.

At each testing interval, participants were brought into the testing booth where a recliner was provided for them. They were asked to relax and refrain from any excessive movements and/or eye blinks. Each participant endured two runs at each of the five conditions. This helped to familiarize the participant with the task, aid in their understanding of what was expected and served to insure reliability of the responses. During stimulus presentation, participants were asked to differentiate the target stimuli and respond to it as quickly and accurately as possible by pushing a button and keeping a mental count of each target stimuli. The subjective responses were then compared to the P300 electrophysiologic readings to assess reliability of the response waveforms. Participants were monitored closely throughout the evoked potential recordings in every condition (baseline, sleep deprived, recovery and three and six hours post recovery). When the experiment was complete, each participant was taken home to ensure their safety.

Data Analysis. Evoked potential recordings from each participant was evaluated offline at the experimenter's discretion. Each event-related/evoked potential sample was replicated twice while each response was considered an individual account. The responses were then be overlaid and compared to ensure reliability. Two experienced audiologist observed the waveforms and verified that they were replicable. Then peaks were picked from each participants averaged waveforms (Walker, 2005; Matthyssen 2013). The P300 was the only waveform evaluated for the purpose of this study. Further explanation of peak picking can be found in the results section.

RESULTS

This study investigated the effects of sleep deprivation and recovery as well as three and six hours post recovery on the P300 auditory late response (ALR) waveforms. Of the seventeen subjects tested, the data of fourteen subjects was utilized to compile the results. Three subjects were excluded due to inability to record consistent P300 evoked potentials across several runs.

P300 evoked potentials were measured during five time periods; baseline (BL), sleep deprived (SD), 30 minutes post recovery (PR), three hours post recovery (PR3) and six hours post recovery (PR6). P300 amplitudes and latency were recorded at three different sites; Fz (frontal lobe), Cz (vertex) and Pz (parietal lobe). The amplitude of the P300 evoked potential was measured in microvolts with the P300 latency determined by measuring from the onset of stimulus presentation to the midpoint of the most prominent peak between 220 and 400 ms. A summary of the criteria used to identify the P300 response can be found in Table 1. Peak to base amplitudes as well as peak to peak amplitudes were measured and analyzed for the purpose of this study. Previous research conducted by Soskins, Rosenfeld and Niendam (2001), indicated that the peak to peak measurement of the P300 correctly diagnosed oddball versus frequent stimuli in 26 out of 26 (100%) of cases. The researchers also mention a double blind field experiment where the peak to peak index performed better than the peak to base index once again. Lastly, they found that the peak to peak index is highly correlated with the duration of recovery of the P300 to the pre-stimulus baseline EEG.

Amplitudes and latencies of the P300 waveforms were measured and labeled by the experimenter and agreed upon by an experienced audiologist. Two trials were recorded for each variable run and were labeled run (a) and run (b). These trials showed 90% replicability, therefore, it was deemed allowable to average the results of run (a) and (b) together. For example, grand averaged P300 waveforms recorded for participant 14 at Cz in all conditions can be seen in Figure 3. A list of the individual mean averages for amplitude peak to base, amplitude peak to peak of run (a) and run (b) for each condition can be seen in Tables 2-11. For ease of comparison, the means and standard deviations for P300 peak to base amplitude, peak to peak amplitude and latency measured at each site and in each condition can be seen in Table 12 - 20 and in Figures 4-6.

Greenhouse-Geisser analysis of Variance (ANOVA) for repeatable measures were performed at each site, Fz, Cz and Pz and included five conditions: baseline, sleep deprived, post 110 minute recovery (rest/sleep), three hours post recovery and six hours post recovery. Additional post hoc analysis were performed for pair wise comparison using the Bonferroni method.

Mean Amplitude of the P300 across Conditions

As previously mentioned two measures of amplitude were conducted and analyzed. One measure was taken from the peak of the P300 wave form to the base (amp). The other measure was taken from the peak of the P300 to the negative peak of the following trough (ampx). For both the peak to base and peak to peak measures of amplitude, there is a steady decline in mean amplitudes from BL to the PR6 condition.

For measures taken from Fz the mean amp of the P300 for baseline is 5.51 µV with a standard deviation of 2.93. The mean amplitude drops to 3.66 µV with a standard deviation of 2.00 six hours after the recovery period. Similar results for Cz amplitudes show that the mean baseline amplitude starts at 6.29 µV with a standard deviation of 8.062 and then declines to 4.05 µV with a standard deviation of 2.60 six hours after the recovery period. This pattern continues with mean amplitudes taken from Pz; the baseline mean amplitude is 5.32 µV with a standard deviation of 3.26 which declines to a mean amplitude of 3.73 with a standard deviation of 2.27 at the six hour post recovery mark. The only exception is the difference seen in the mean amplitude of Fz from BL to the SD state where the mean average rises slightly from 5.51 µV to 6.03 µV before continuing to decline through the six hour post recovery period.

Similarly, for measures taken from Fz the mean ampx of the P300 for baseline is 11.58 µV with a standard deviation of 6.596. The mean amplitude drops to 7.56 µV with a standard deviation of 3.22 six hours after the recovery period. Similar results for Cz amplitudes show that the mean baseline amplitude starts at 14.61 µV with a standard deviation of 8.062 and then declines to 9.01 µV with a standard deviation of 5.722 six hours after the recovery period. This pattern continues with mean amplitudes taken from Pz; the baseline mean amplitude is 13.23 µV with a standard deviation of 7.149 which declines to a mean amplitude of 8.65 at the six hour post recovery. The only exception as with the peak to base amplitude, is the difference seen in the mean amplitude of Fz from BL to the SD state where the mean average rises slightly from 11.58 µv 11.86 µv before continuing to decline through the six hour post recovery period. Two graphs depicting

the mean amp and ampx of Fz, Cz, and Pz in all conditions can be seen in Figure 4 and Figure 5.

Three separate ANOVAs were run for peak to base amplitudes measured at each site, Fz, Cz and Pz and included each of the following conditions: BL, SD, PR, PR3 and PR6. There were no significant differences between conditions when measured at Fz, Cz or Pz. Additionally, three separate ANOVAs were run for peak to peak amplitude measured at each site, Fz, Cz and Pz and included the five conditions listed above. Results for Fz showed no significant differences between conditions. Results for Cz pairwise comparisons showed a significant difference between peak to peak amplitudes measured at the baseline condition and the six hour post recovery condition (md = 5.59; p = .042) as well as a significant difference from the sleep deprived condition to the six hour post recovery condition for (md = 3.38, p = .013). Results for Pz showed a significant difference between the sleep deprived condition and the six hour post recovery condition (md = 3.202; p = .012).

Latency of the P300

In Tables 12 - 20 the means and standard deviations of each condition (BL, SD, PR, PR3 and PR6) are recorded for Fz, Cz and Pz electrode sites. Notice that the latencies vary between 257.9 ms and 309.46 ms with no pattern of longer latencies correlated with sleep deprivation. In Tables 21-25 the individual average latency of run a and b for all conditions can be seen.

Three separate ANOVAs were run for latency of the P300 waveform measured at each site, Fz, Cz and Pz and included each of the following conditions: BL, SD, PR, PR3

and PR6. There were no significant differences found in the latency of the P300 waveform between conditions at Fz, Cz or Pz.

Grand averaged P300 waveforms recorded at Cz for BL, SD, PR, PR3 PR6

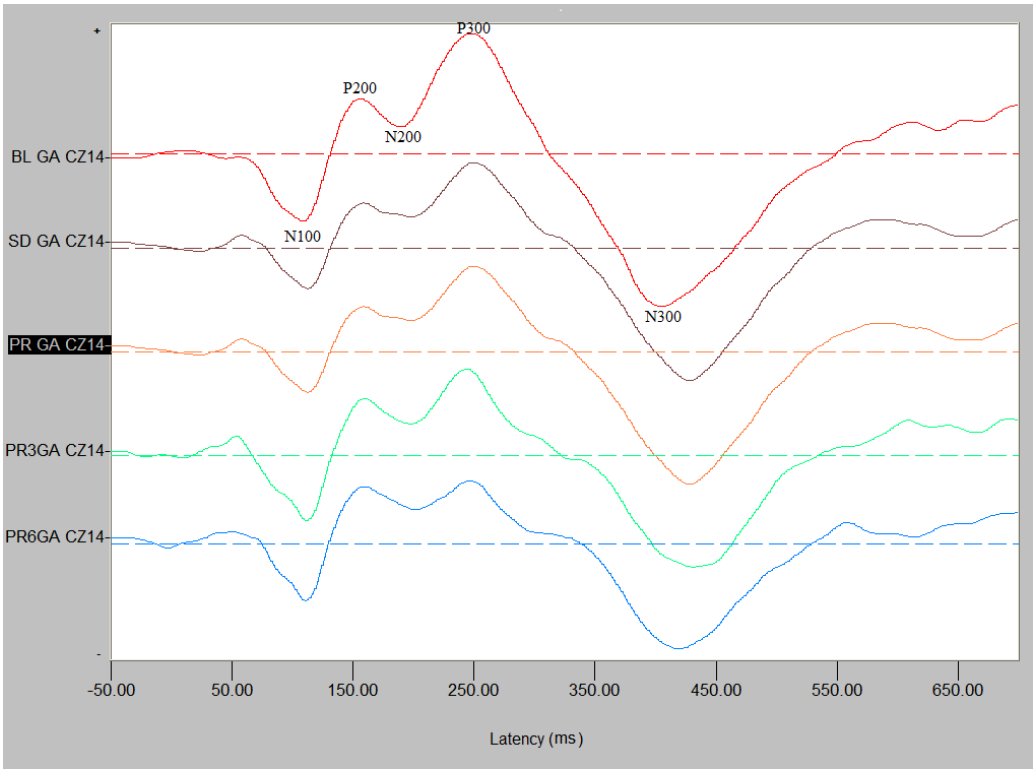

Figure 3. Grand averaged P300 waveforms recorded at Cz for each of the following conditions: Baseline (BL), sleep deprived (SD), 30 minutes post recovery (PR), three hours post recovery (PR3) and six hours post recovery (PR6). Baseline was measured after at least 6 to 8 hours of sleep for three consecutive nights prior to recording. Sleep deprivation measures were taken after approximately 24 hours of sleep deprivation. Post recovery measures were taken after 110 minute recovery period (rest/sleep). Three hour and six hour post recovery periods were obtained three and six hours after the 110 minute recovery period with no additional rest. Notice the gradual decline in amplitude measured from the peak of P300 to the peak of the negative trough following the P300.

Table 2. Average Peak to Peak Amplitude of Run (a) and (b) Baseline

Participant	**Fz ampx (µV)**	**Cz ampx (µV)**	**Pz ampx (µV)**
1	13.10	14.04	12.76
2	15.55	19.49	18.33
3	6.61	7.54	4.40
4	27.15	33.41	30.63
6	7.07	10.67	9.51
7	17.63	26.91	22.27
8	10.20	14.26	14.50
10	15.78	20.65	17.40
11	4.98	7.42	9.04
12	9.97	7.77	6.38
13	7.48	6.38	6.32
14	7.30	11.48	8.70
15	2.08	8.58	14.73
16	17.28	15.89	10.32
M	11.58	14.61	13.23
SD	6.60	8.06	7.15

Table 3. Average Peak to Peak Amplitude of Run a and b Sleep Deprived

Participant	**Fz ampx (µV)**	**Cz ampx (µV)**	**Pz ampx (µV)**
1	12.87	6.26	10.55
2	9.74	13.22	14.03
3	8.81	7.65	4.52
4	19.03	17.40	12.53
6	11.14	18.56	16.94
7	12.30	19.26	19.95
8	11.02	12.29	14.50
10	15.55	17.87	13.23
11	6.26	10.09	7.77
12	17.87	13.46	12.30
13	11.71	6.14	6.61
14	2.20	2.90	6.38
15	2.32	3.48	6.72
16	25.29	25.06	19.95
M	11.86	12.40	11.85
SD	6.28	6.67	5.02

Table 4. Average Peak to Peak Amplitude of Run a and b 30 Min. Post Recovery

Participant	Fz ampx (µV)	Cz ampx (µV)	Pz ampx (µV)
1	14.85	12.76	12.30
2	12.76	13.80	10.55
3	5.56	4.40	2.66
4	13.92	16.94	13.92
6	11.02	16.70	14.61
7	14.85	21.69	20.65
8	4.17	6.64	9.16
10	12.29	16.35	12.64
11	5.56	9.86	8.12
12	5.10	4.62	4.94
13	4.93	5.10	5.22
14	5.66	6.77	5.42
15	5.66	7.17	10.52
16	19.78	19.62	15.31
M	9.72	11.60	10.43
SD	5.05	5.97	4.93

Table 5. Average Peak to Peak Amplitude of Run a and b 3 Hrs. Post Recovery

Participant	Fz ampx (µV)	Cz ampx (µV)	Pz ampx (µV)
1	3.66	8.45	11.40
2	8.45	11.40	9.96
3	5.50	5.50	5.02
4	13.87	20.57	17.94
6	9.56	13.55	11.80
7	14.99	19.62	21.21
8	6.06	7.17	7.73
10	10.20	19.05	14.43
11	7.09	9.49	7.73
12	6.67	5.56	5.27
13	6.30	3.98	4.30
14	4.58	6.34	5.70
15	2.55	4.70	6.69
16	18.02	16.50	12.44
M	8.39	10.84	10.11
SD	4.51	5.96	5.10

Table 6. Average Peak to Peak Amplitude of Run a and b 6 Hrs. Post Recovery

Participant	Fz ampx	Cz ampx	Pz ampx
1	10.28	A	4.78
2	8.53	10.84	10.44
3	8.85	5.90	6.38
4	6.93	13.15	9.80
6	8.69	14.19	10.76
7	11.64	18.34	18.02
8	9.01	9.01	13.95
10	8.29	16.66	13.23
11	5.34	7.25	5.42
12	8.37	6.06	5.10
13	2.31	2.83	2.63
14	4.22	4.86	5.26
15	1.27	2.47	3.98
16	12.12	14.67	11.40
M	7.56	9.01	8.65
SD	3.23	5.72	4.52

Table 7. Average Peak to Base Amplitude of Run (a) and (b) Baseline

Participant	Fz amp (μV)	Cz amp (μV)	Pz amp (μV)
1	7.47	4.23	4.26
2	7.83	8.84	7.25
3	3.44	3.00	1.38
4	13.42	17.54	13.75
6	3.77	5.35	3.90
7	5.45	11.45	8.42
8	4.90	6.82	8.10
10	4.91	7.32	6.29
11	3.39	3.24	3.90
12	4.63	2.58	1.69
13	3.51	3.08	2.89
14	3.64	6.05	5.12
15	7.29	2.36	4.26
16	8.48	6.14	3.29
M	5.51	6.29	5.32
SD	2.93	4.17	3.26

Table 8. Average Peak to Base Amplitude of Run (a) and (b) Sleep Deprived

Participant	Fz amp (μV)	Cz amp (μV)	Pz amp (μV)
1	8.28	1.08	5.80
2	4.54	5.64	5.50
3	3.09	2.78	1.79
4	9.34	7.86	4.08
6	7.03	10.46	8.70
7	2.23	6.73	6.32
8	6.79	5.43	8.29
10	7.76	6.96	4.55
11	3.94	5.56	4.05
12	7.37	4.60	3.60
13	7.68	4.58	3.82
14	2.33	2.05	3.11
15	2.78	1.56	.56
16	11.35	11.64	7.97
M	6.03	5.50	4.86
SD	2.87	3.13	2.39

Table 9. Average Peak to Base Amplitude of Run (a) and (b) 30 Min. Post Recovery

Participant	Fz amp (μV)	Cz amp (μV)	Pz amp (μV)
1	8.74	6.39	7.99
2	5.52	6.02	3.89
3	3.02	1.85	1.28
4	5.07	7.08	4.98
6	4.91	8.77	7.43
7	5.11	8.74	7.26
8	2.15	3.69	5.31
10	3.51	6.38	6.01
11	3.74	5.13	4.05
12	1.89	1.11	1.45
13	2.41	2.32	2.52
14	2.25	3.04	2.88
15	2.71	2.97	3.48
16	9.40	8.43	4.98
M	4.31	5.14	4.54
SD	2.35	2.64	2.14

Table 10. Average Peak to Base Amplitude of Run (a) and (b) 3 Hrs. Post Recovery

Participant	Fz amp (μV)	Cz amp (μV)	Pz amp (μV)
1	1.96	2.15	4.11
2	3.46	4.21	3.25
3	2.41	2.67	2.67
4	5.14	11.00	7.91
6	5.42	7.19	5.29
7	6.15	8.34	8.27
8	4.20	4.62	5.25
10	3.82	7.95	6.26
11	4.20	5.60	4.11
12	3.19	.97	.10
13	3.48	2.82	2.51
14	3.41	4.48	4.50
15	2.63	1.80	2.17
16	8.82	8.18	5.49
M	4.16	5.14	4.42
SD	1.78	2.99	2.24

Table 11. Average Peak to Base Amplitude of Run (a) and (b) 6 Hrs. Post Recovery

Participant	Fz amp (µV)	Cz amp (µV)	Pz amp (µV)
1	7.12	A	3.39
2	4.92	4.85	3.90
3	3.10	.70	2.79
4	.61	6.15	3.34
6	4.05	6.28	5.00
7	4.23	7.44	5.76
8	6.52	6.78	9.93
10	2.70	6.69	5.36
11	3.22	3.98	2.48
12	3.94	1.80	1.32
13	.68	1.28	1.48
14	1.22	2.54	2.93
15	3.29	1.97	1.29
16	5.60	6.27	3.36
M	3.66	4.05	3.73
SD	2.00	2.60	2.27

Table 12. Mean and Standard Deviation of Fz Peak to Base Amplitude

Fz Amp Average (μV)	Mean	Std. Deviation
BL	5.51	2.93
SD	6.03	2.87
PR	4.31	2.35
PR3	4.16	1.78
PR6	3.66	2.00

Note. Baseline (BL), Sleep Deprived (SD), 30 Min Post Recovery (PR), Three Hours Post Recovery (PR3), Six Hours Post Recovery (PR6), Peak to Base Amplitude (Amp), Standard (Std).

Table 13. Mean and Standard Deviation of Fz Peak to Peak Amplitudes

Fz Ampx Average (μV)	Mean	Std. Deviation
BL	11.58	6.596
SD	11.86	6.284
PR	9.72	5.051
PR3	8.39	4.512
PR6	7.56	3.229

Note. Baseline (BL), Sleep Deprived (SD), 30 Min Post Recovery (PR), Three Hours Post Recovery (PR3), Six Hours Post Recovery (PR6), Peak to Peak Amplitude (Ampx), Standard (Std).

Table 14. Mean and Standard Deviation of Fz Latencies

Fz Ampx Average (μV)	Mean	Std. Deviation
BL	295.22	49.497
SD	309.04	42.386
PR	307.04	53.080
PR3	307.75	52.141
PR6	309.46	40.969

Note. Baseline (BL), Sleep Deprived (SD), 30 Min Post Recovery (PR), Three Hours Post Recovery (PR3), Six Hours Post Recovery (PR6), Latencies (Lat), Standard (Std).

Table 15. Mean and Standard Deviation of Cz Peak to Base Amplitude

Fz Amp Average (μV)	Mean	Std. Deviation
BL	6.29	4.17
SD	5.50	3.13
PR	5.14	2.64
PR3	5.14	2.99
PR6	4.05	2.60

Note. Baseline (BL), Sleep Deprived (SD), 30 Min Post Recovery (PR), Three Hours Post Recovery (PR3), Six Hours Post Recovery (PR6), Peak to Base Amplitude (Amp), Standard (Std).

Table 16. Mean and Standard Deviation of Cz Peak to Peak Amplitudes

Fz Ampx Average (μV)	Mean	Std. Deviation
BL	14.61	8.062
SD	12.40	6.659
PR	11.60	5.966
PR3	10.84	5.956
PR6	9.01	5.722

Note. Baseline (BL), Sleep Deprived (SD), 30 Min Post Recovery (PR), Three Hours Post Recovery (PR3), Six Hours Post Recovery (PR6), Peak to Peak Amplitude (Ampx), Standard (Std).

Table 17. Mean and Standard Deviation of Cz Latencies

Fz Ampx Average (μV)	Mean	Std. Deviation
BL	267.72	42.365
SD	285.81	51.693
PR	284.82	56.514
PR3	286.24	56.253
PR6	257.90	87.981

Note. Baseline (BL), Sleep Deprived (SD), 30 Min Post Recovery (PR), Three Hours Post Recovery (PR3), Six Hours Post Recovery (PR6), Latencies (Lat), Standard (Std).

Table 18. Mean and Standard Deviation of Pz Peak to Base Amplitude

Fz Amp Average (μV)	Mean	Std. Deviation
BL	5.32	3.26
SD	4.86	2.39
PR	4.54	2.14
PR3	4.42	2.24
PR6	3.73	2.27

Note. Baseline (BL), Sleep Deprived (SD), 30 Min Post Recovery (PR), Three Hours Post Recovery (PR3), Six Hours Post Recovery (PR6), Peak to Base Amplitude (Amp), Standard (Std).

Table 19. Mean and Standard Deviation of Pz Peak to Peak Amplitudes

Fz Ampx Average (μV)	Mean	Std. Deviation
BL	13.23	7.149
SD	11.85	5.017
PR	10.43	4.930
PR3	10.11	5.104
PR6	8.65	4.524

Note. Baseline (BL), Sleep Deprived (SD), 30 Min Post Recovery (PR), Three Hours Post Recovery (PR3), Six Hours Post Recovery (PR6), Peak to Peak Amplitude (Ampx), Standard (Std).

Table 20. Mean and Standard Deviation of Pz Latencies

Fz Ampx Average (μV)	Mean	Std. Deviation
BL	267.75	40.947
SD	281.54	40.251
PR	285.39	54.877
PR3	287.24	51.281
PR6	267.58	34.498

Note. Baseline (BL), Sleep Deprived (SD), 30 Min Post Recovery (PR), Three Hours Post Recovery (PR3), Six Hours Post Recovery (PR6), Latencies (Lat), Standard (Std).

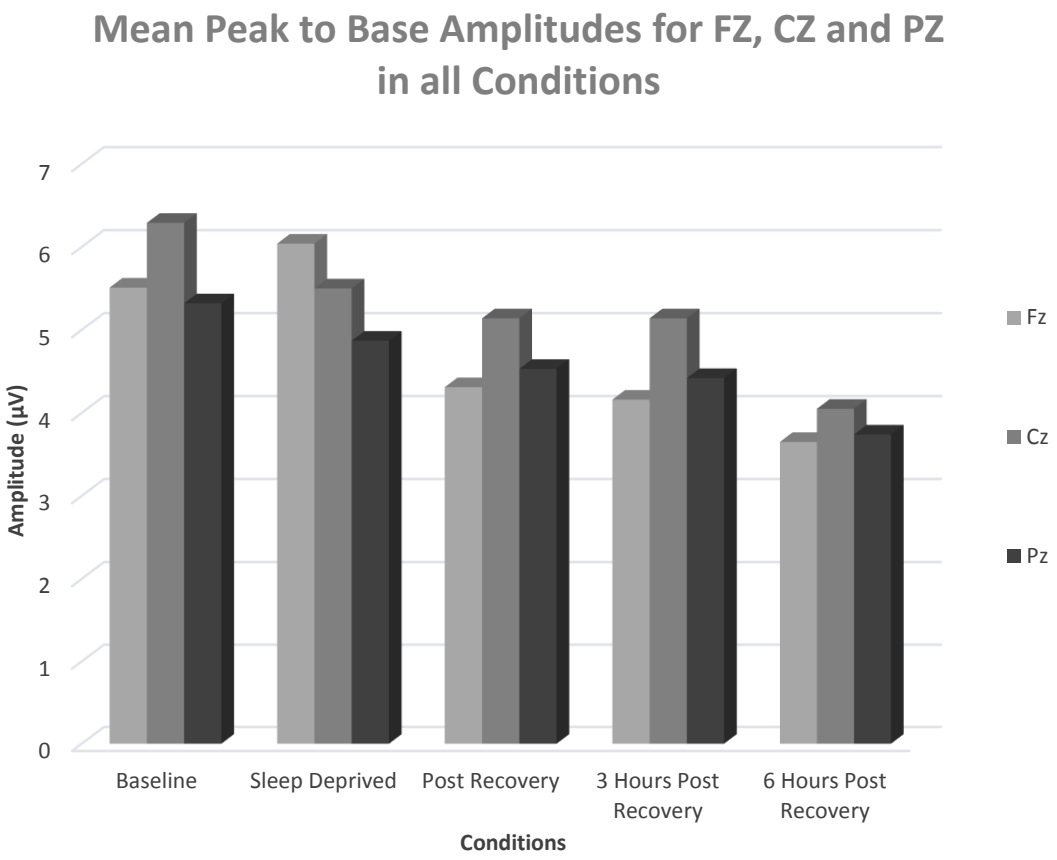

Figure 4. Mean Peak to Base Amplitudes for Fz, Cz and Pz in all Conditions.

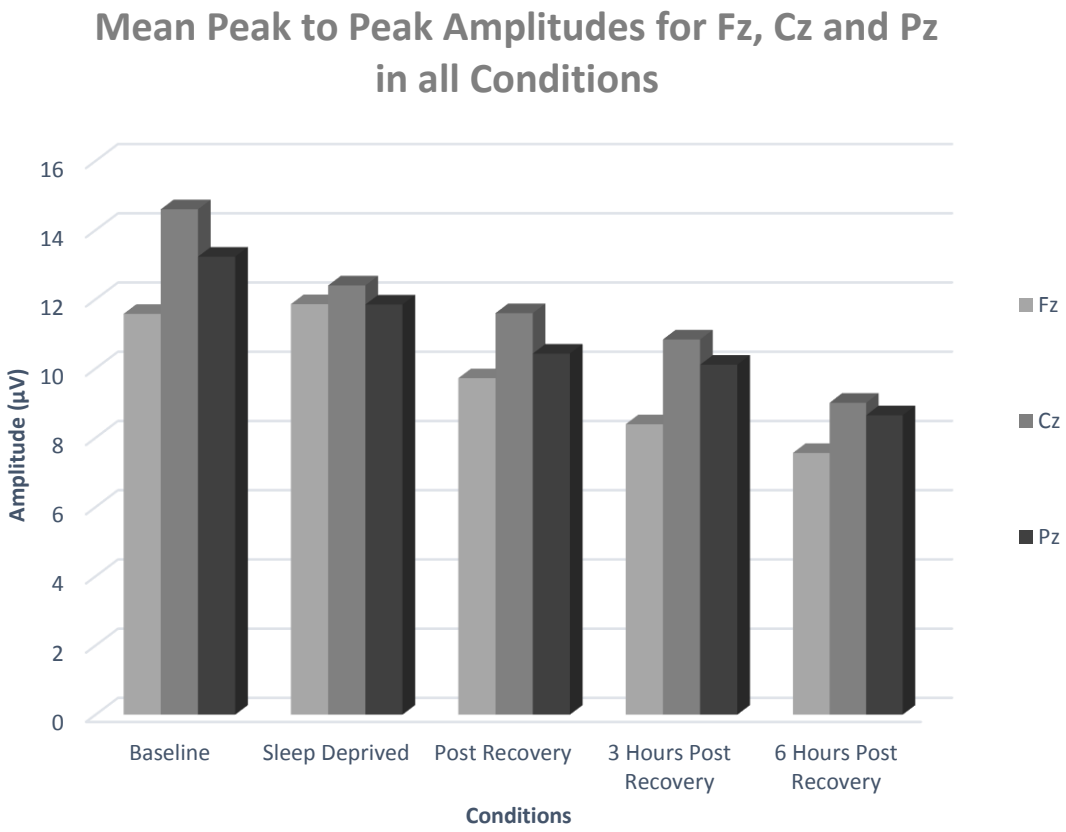

Figure 5. Mean Peak to Peak Amplitudes for Fz, Cz and Pz in all conditions.

Table 21. Average Latency of Run a and b Baseline

Participant	Fz lat (ms)	Cz lat (ms)	Pz lat (ms)
1	297.07	253.19	255.19
2	303.06	299.07	269.15
3	380.85	372.87	370.88
4	257.18	251.20	261.17
6	223.27	245.21	251.20
7	303.06	225.27	225.27
8	275.13	275.13	279.12
10	269.15	267.15	223.64
11	342.95	261.17	261.17
12	243.22	243.22	247.21
13	338.96	249.20	255.19
14	219.28	231.25	235.24
15	336.97	235.25	275.13
16	342.95	338.96	338.96
M	295.22	267.72	267.75
SD	49.50	42.37	40.95

Table 22. Average Latency of Run a and b Sleep Deprived

Participant	Fz lat (ms)	Cz lat (ms)	Pz lat (ms)
1	301.06	233.24	259.18
2	328.99	293.09	287.10
3	366.89	366.89	346.94
4	245.21	245.21	251.20
6	319.02	241.22	243.22
7	305.05	225.27	229.26
8	261.17	267.15	281.12
10	269.15	259.18	291.09
11	251.20	253.19	259.18
12	293.09	245.21	251.20
13	334.97	334.97	243.22
14	386.84	372.87	338.96
15	338.96	328.99	321.01
16	325.00	334.97	338.96
M	309.04	285.81	281.54
SD	42.39	51.69	40.25

Table 23. Average Latency of Run a and b 30 Min. Post Recovery

Participant	Fz lat (ms)	Cz lat (ms)	Pz lat (ms)
1	317.02	249.20	251.20
2	317.02	279.12	283.11
3	398.80	402.79	394.81
4	255.19	261.17	267.15
6	245.21	251.20	253.19
7	305.05	227.26	227.26
8	366.89	378.86	380.85
10	257.18	261.17	267.15
11	328.99	267.15	269.15
12	350.93	328.99	319.02
13	334.97	243.22	241.22
14	235.24	247.21	249.20
15	235.24	237.23	237.23
16	350.93	350.93	354.92
M	307.04	284.82	285.39
SD	53.08	56.51	54.88

Table 24. Average Latency of Run a and b 3 Hrs. Post Recovery

Participant	Fz lat (ms)	Cz lat (ms)	Pz lat (ms)
1	334.97	221.28	251.20
2	313.03	305.05	287.10
3	392.82	392.82	392.82
4	251.20	249.20	257.18
6	241.22	249.20	261.17
7	311.04	227.26	229.26
8	356.91	366.89	376.86
10	311.04	261.17	269.15
11	334.97	255.19	255.19
12	346.94	350.93	317.02
13	235.24	237.23	239.23
14	215.29	249.20	249.20
15	328.99	305.05	297.07
16	334.97	336.97	338.96
M	307.75	286.24	287.24
SD	52.14	56.25	51.28

Table 25. Average Latency of Run a and b 6 Hrs. Post Recovery

Participant	Fz lat (ms)	Cz lat (ms)	Pz lat (ms)
1	311.04	0	239.23
2	326.99	287.10	285.11
3	366.89	364.89	249.20
4	325.00	239.23	271.14
6	326.99	235.24	289.10
7	317.02	233.24	233.24
8	263.16	279.12	277.13
10	285.11	247.21	251.20
11	340.96	257.18	259.18
12	321.01	319.02	259.18
13	227.26	223.27	225.27
14	239.23	239.23	237.23
15	346.94	346.94	340.96
16	334.97	338.96	328.99
M	309.46	257.90	267.58
SD	40.97	87.98	34.50

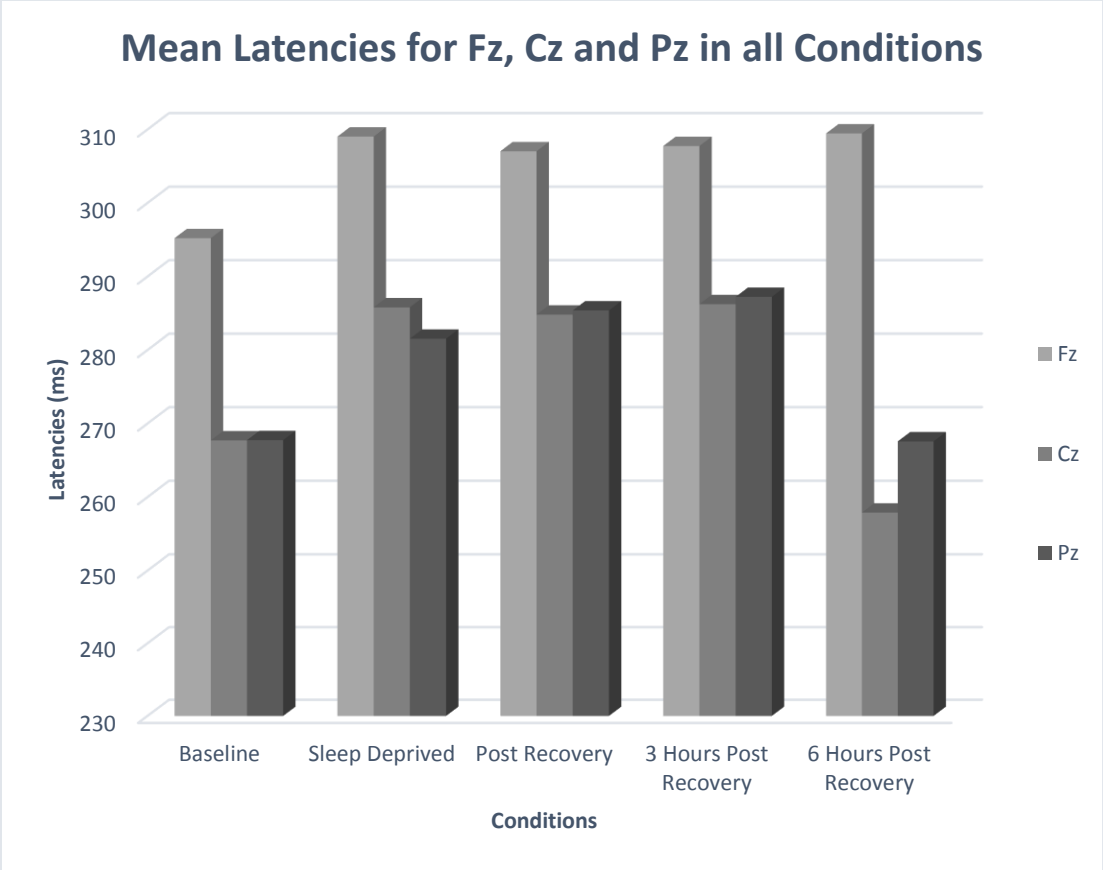

Figure 6. Mean Latencies for Fz, Cz and Pz in all conditions.

DISCUSSION

Sleep deprivation has been studied for centuries. It is well known that under these conditions, neuronal activity is compromised. When neuronal activity is compromised, an individual's ability to think and act quickly is also at stake. In order to determine the extent of the effects of sleep deprivation, researchers use objective measures such as the P300 auditory late response (ALR). As previously discussed the P300 is an endogenous response that is elicited when a subject is paying attention to an auditory stimuli. This response produces a P300 waveform that can be measured and analyzed objectively.

The purpose of this study was to analyze the effects of sleep deprivation, recovery and post recovery on the P300 waveform. The results indicated a significant difference in peak to trough amplitude of the P300 waveform from baseline conditions to the 3 and 6 hour post recovery conditions. These findings are in alignment with previous research that reveal statistically significant differences in the P300 wave forms following sleep deprivation (Jain, et al., 2010, Lee et al., 2004 & Qi et al., 2010). This research was designed to answer the following questions: (1) is there a statistical difference in the P300 ALR waveforms between baseline and sleep deprived conditions; (2) is there a statistical difference in the P300 ALR waveforms between the sleep deprived and recovery conditions; (3) is there a statistical difference in the P300 ALR waveforms between the 110 minute recovery period and the 3 and 6 hour post recovery periods. Though these were the questions that needed to be answered in accordance with the design of the study, it was interesting to see the manifestation of answers provided during the analysis of the P300 waveforms.

Implications of the Sleep Deprived P300

The amplitude of the P300 wave form represents the objective measurement of cognitive resources available to evaluate the stimuli (McPherson, 1996). Latency is known to reflect the amount of time that is required for a participant to categorize and evaluate a stimuli (Hall, 2007). Three major factors that can contribute to the change in P300 amplitude and latency are: the abundance of cognitive resources available to evaluate the stimulus being presented (McPherson, 1996), habituation and circadian variation (Morris et al., 1992).

When a participant is sleep deprived a decrease in the P300 amplitude is caused by a decrease in the innate resources of cognition available to evaluate the stimulus (McPherson, 1996). According to Lee et al. (2004) and Lee, Kim, & Suh (2003), after 38 hours of sleep deprivation using the oddball paradigm (frequent pure tone = 1000 Hz; infrequent pure tone = 2000 Hz), their subjects show a significant decrease in amplitude and increase in latency of the P300 waveform. Similarly, Jain et al. (2010) and Qi et al. (2010) also reported a significant difference in P300 amplitude and latency. Additionally, Matthyssen (2013) reported a significant decrease in amplitude and increase in latency after a 23 to 26 hours of sleep deprivation.

Interestingly, this study did not show a significant difference between the baseline condition and the sleep deprived conditions for amplitude or latency even when amplitude was measured from peak to base and from peak to trough. So, why the difference in this study and others that have gone before it? Circadian rhythm could have had an effect on the outcome. According to Geisler & Polich (1992) Circadian rhythm can have an effect on the P300 amplitude in that smaller amplitudes are obtained in the

afternoon and larger amplitudes obtained in the morning. All of the sleep deprived measures were obtained between 7:00 am and 9:00 am. Baseline measures and sleep deprived measures were obtained within one to two hours of each other, to control for Circadian rhythm variations. Therefore, it is not likely that this had an impact on the outcome of the P300 amplitude and latency measures.

Habituation can also impact the P300 waveforms (Geisler & Polich, 1992). When a participant becomes familiar with the rarity of a novel stimuli habituation can occur. This can cause a decrease in amplitude and increase in latency. To control for this, the participants were each given more than an hour between each test condition. Due to the fact that there was no significant difference between amplitude and latency of the P300 waveform between baseline and sleep deprived measures, habituation likely did not occur.

According to a study done by Panjwani et al. (2010), researchers found a significant difference in latency of the P300 after 24 hours of sleep deprivation but no significant difference in amplitude of the P300. Similarly, no significant difference in amplitude of the P300 between baseline and sleep deprived state was found in this study.

When recording the P300 amplitude and latency, several studies incorporate the use of an oddball paradigm. As previously mentioned, Lee, Kim, and Suh (2003) and Lee et al. (2004) used an oddball paradigm with a frequent pure tone presented at 1000 Hz and an infrequent or target pure tone at 2000 Hz. Similarly, an oddball paradigm with a 1000 Hz frequent and 2000 Hz target stimuli was utilized for this study. Though discriminating between each pure tone and responding to the target stimuli is considered a relatively easy task for those with normal cognitive function, someone that is sleep

deprived can experience delays in mental processing which can have critical effects in performance. For example, reaction time, psychomotor skills, cognitive performance, logical reasoning, short-term and long term memory and even basic language skills have shown declination in performance when sleep deprived for 24 hours or more (Caldwell & Caldwell, 2005; Hsieh, Li, & Tsai, 2010; Jain et al., 2010; Panjwani et al., 2010). These are important implications when considering individuals with careers in which sleep deprivation occurs more often than not.

One of the differences noticed in the current study and the one done by Matthyssen (2013) was that the participants in her study had to count the target stimuli. The participants in this study did not count the target stimuli but pressed a button when they heard the target stimuli instead. Some studies have indicated that P300 amplitude depends on selective attention with P300 amplitude being higher with stimuli that is attended to versus a lesser amplitude for target stimuli that is unattended to (Talsma & Kok, 2002). Thus, counting the target stimuli may have resulted in larger amplitudes across conditions making it easier to determine whether or not a significant difference has occurred. However, according to McPherson, there are three main methods used to measure late auditory evoked potentials. The first method is by a passive means where the participant listens but does not acknowledge the difference in stimuli. The second is an active method where the participant actively presses a button or counts the target stimuli. The third method is when the participant ignores the stimuli and reads a book while listening to the stimuli. Thus it can be concluded that attending to the target stimuli by pressing the button instead of counting still resulted in P300 waveforms with a higher

amplitude and did not affect the outcome of the measures between this study and the study done by Matthyssen.

In this study participants were asked to respond to the target stimuli by pressing a button each time the 2000 Hz pure tone was presented. If responses were not recorded, the participants were alerted by knocking on the door or window of the test booth. Once alerted, participants were back on track and responding to stimuli once again. In the event that a participant started to fall asleep or did not respond during several presentations, the presentation run was stopped and restarted. In retrospect, having participants count the target stimuli would allow them to serve as their own control for alertness and accuracy during the test runs.

Implications of 110 Minute Recovery Period

Though research on sleep deprivation has been conducted for generations, it has not been until more recently that the counter measures of sleep deprivation have been studied. One of the more popular counter measures looked at is a rest period or nap. Brief duration naps from 9.1 minutes to 30 mins have been shown to improve performance after periods of sleep deprivation (Brooks & Lack, 2006: Hayashi, Motoyoshi & Hori, 2005; Hayashi, Ito & Hori, 1999; Tietzel & Lack, 2001). In an unpublished study done Matthyssen (2013), a brief 10 minute nap following 24 hours of sleep deprivation was not a sufficient period of time to overcome the adverse cognitive effects of sleep deprivation. However, the 110 minute recovery period used, followed a trend of shortened P300 latency and increased P300 amplitude which, though not

significant, indicated that 110 minute recovery period was sufficient enough time to overcome some of the effects of sleep deprivation.

During this study the 110 minute recovery period was used. Participants were sleep deprived for a period of approximately 24 hours, tested and then allowed to lay down for the allocated rest period of 110 minutes. During observation of the recovery period, it was noted that each of the initial 17 subjects fell asleep quickly and slept until they were awakened one hour and 50 minutes later. It is important to note that there were no significant differences in amplitude or latency of the P300 waveform following the recovery period. However, when measuring peak to base and peak to trough amplitudes of the P300, there was a trend for recovery of the P300 amplitude seen at the Fz (frontal lobe) generator site only. P300 amplitude measured at Cz and Pz generator sites did not mimic this trend.

In order to understand the potential impact of the 110 minute recovery period, there are two additional topics that need to be addressed. One is called the REM rebound phenomenon. Basically, when someone falls asleep, the body goes through what is called a sleep cycle. As mentioned previously, each sleep cycle consists of a series of stages with a rest period at the end of each of these cycles. When a person finally as the opportunity to sleep after being sleep deprived, the amount of time spent in each sleep cycle decreases which allows the body to fall into a "deeper sleep" at a faster rate (Bonnet & Arand, 1996). This causes a decrease in metabolic rate and thus an expedited improvement in performance than that seen from a normal sleep cycle. Given this information, one would believe then that an improvement in P300 amplitude and latency would be seen after a 110 minute recovery period. Yet, there was not a significant

improvement in the P300 amplitude and latency following the 110 minute recovery period. This can be explained by the possible effects of sleep inertia the second topic up for discussion.

Sleep inertia refers to an individual's experience of disorientation, confusion and sleepiness that occur after awakening (Tassi, Muzet, 2000). Studies have shown that during a sleep episode, the longer someone is in slow-wave sleep the greater sleep inertia will be (Dinges, Orne & Orne, 1985; Muzet, Nicolas, Tassi, Dewasmes & Bonneau, 1995; Rosekind, Smith & Miller et al., 1995). Thus, it stands to reason that participants may have experienced sleep inertia after their 110 minute recovery period. To aid in overcoming sleep inertia, testing was conducted 30 minutes after the recovery period. Without more research on the effects of sleep inertia measured during sleep deprivation studies which incorporate a recovery period, the above conclusions are only speculation.

Implications of 3 and 6 Hour Post Recovery

The main purpose of this study was to determine the effects of a 3 and 6 hour post recovery period on P300 amplitude and latency. Previous studies have yet to include testing after post recovery periods of more than 3 hours. Originally, it was thought that an increase in amplitude would be noted after the recovery period. Once amplitude and latency improved, the goal of this research was to determine how long it would take after the recovery period to see a significant decline in the P300 amplitude and increase in latency once again. Interestingly, this was not the case. As previously mentioned there was not a significant difference found in P300 amplitude and latency from baseline to sleep deprived measures, nor was there a significant difference found in P300 from the

sleep deprived to the recovery measures. What was found however, was a significant difference in the baseline and the 6 hour post recovery as well as the sleep deprived and 6 hour post recovery statistics when amplitudes were taken from the Cz generation site and measured from peak to trough. Thus the research conducted showed a trend for a steady decline in P300 amplitude from baseline to 6 hour post recovery. A picture of the P300 waveforms showing this decline can be seen in Figure 3 which depicts the declination of the grand averages of the P300 amplitudes taken at the Cz generation site for each of the following conditions: baseline, sleep deprived, recovery, three hours post recovery and six hours post recovery. Notice the slow decline of P300 amplitude as time progresses through each test period.

Due to the trend seen of a downward decline in P300 amplitude over a 32 hour period with only 110 minutes of rest, it can be said that a nap may not have beneficial effects for an extended period of time. In a study conducted by Brooks and Lack, (2006) for the purpose of evaluating a three hour period following 5, 10, 20 and 30 minute naps, researchers found that after a five minute nap there was a general trend of improvement for at least an hour after the nap. The 10 minute nap showed a pronounced increase in performance (almost twice that of the 5 minute nap) immediately after napping and through the majority of the three hour period following the nap. However, improvement declined by the end of the 3 hour testing period following the naps. Interestingly, the 20 and 30 minute naps produced some significantly improved performance but not until approximately 35 minutes after the nap, which shows effects of sleep inertia following the 20 and 30 minute naps. After the sleep inertia wore off, improvements in performance were similar to that of the 10 minute nap.

Due to the effects of sleep inertia discovered by Brooks and Lack, (2006) after a 20 and 30 minute nap and the decline in improvement toward the end of the three hour test period following the naps, it could be said that 30 minutes of wait time before post recovery testing in this study, was not enough time to allow sleep inertia to wear off. It could also be concluded that testing 3 hours after the recovery period was just enough time to miss the possible improvements in amplitude and latency of the P300 that may have been seen after the 110 minute recovery period. This also supports the findings of a downward decline in P300 amplitude 3 hours and 6 hours post recovery.

Given the above information, there may have been a significant difference discovered in sleep deprived conditions and recovery conditions as well as recovery and post recovery conditions if enough time was allotted to recover from sleep inertia prior to testing after the 110 minute recovery period. This should be taken into consideration when further research is conducted in this area.

Implications of the Stanford Sleepiness Scale

In this study, as with other sleep deprivation studies, participants were asked to rate their level of alertness by using the Stanford Sleepiness Scale (SSS). This scale provides responses rated from 1 (maximum alertness) to 7 (sleep onset). In research conducted by Jain et al. (2010), Panjwani et al. (2010), and Zukerman et al. (2007) participant reports resulted in a significant increase in SSS levels after a period of sleep deprivation. In the present study, similar results were found after sleep deprivation (refer to Table 26). The mean level of sleepiness increased from baseline condition (1.79 ± .70)

to the sleep deprived condition (4.5 ± 1.79) which means that participants subjectively believed that they felt less alert and active as compared to the baseline reports.

Interestingly, reports of sleepiness with the SSS were lower than expected given the significant decline in P300 amplitude during the 6 hour post recovery condition when compared to the baseline and sleep deprived conditions. Participant reports showed a slow decrease in sleepiness from the recovery period (3.85 ± 1.83) to the 3 hour post recovery period (2.36 ± .93). Then there was a slight increase in sleepiness reports during the 6 hour post recovery period (2.43 ± .94). Similarly, Panjwani et al. (2010) reported a significant decrease in SSS levels proceeding a recovery period of 30 minutes, indicating that a 30 minute recovery period is adequate to overcome subjective effects of sleepiness brought on by sleep deprivation. However, this study objectively shows the opposite results with a steady decline in cognition as measured by the P300 amplitudes from baseline to the 6 hour post recovery conditions. Therefore it can be concluded that subjective reports of alertness are not always in line with the reality of cognitive decline.

Conclusion

The results of this study provided valuable insight on the subjective and objective reports of the effects of recovery and post recovery periods following sleep deprivation. Subjectively, participants reported an improvement in alertness after a 110 minute recovery and a continued improvement after the 3 hour post recovery period. Objectively, it appears that a recovery period of 110 minutes is may not be enough rest to recover from 24 hours of sleep deprivation. At least not for very long. Even if P300 amplitude and latency were measured more than 35 minutes after the recovery period to avoid sleep

inertia and before three hours post recovery to actually see the effects of the recovery (Brooks & Lock, 2006), it is apparent that the recovery can only last a short time before cognitive decline sets in again. Though this study did not show a significant difference in the sleep deprived and the 110 minute recovery period, it clearly indicated a continued decline in P300 amplitude over the duration of the 3 and 6 hour post recovery periods. Despite the insight gained throughout the duration of this study, more research is needed to answer the following questions:

1. How long should an individual wait after the recovery period before testing to avoid sleep inertia during a sleep deprivation study?
2. What would the effects of P300 amplitude and latency be if testing was conducted 45 minutes, 60 minutes and 90 minutes after the 110 minute recovery period?
3. Would the recovery effects last longer given a stimulant such as caffeine?
4. How long would recovery be effective if participants were allowed to have twice the recovery period following 24 hours of sleep deprivation?
5. How can the P300 be implemented clinically to evaluate and monitor sleep deprivation.

The answers to these questions can only serve to generate an unquenchable thirst for knowledge for the clinical application of late auditory evoked responses such as the ones derived from the P300.

Table 26. Stanford Sleepiness Scale ratings for each condition.

Participant	Baseline	Sleep Deprived	Recovery	3 Hrs Post Recovery	6 Hrs Post Recovery
1	3	6	6	2	2
2	2	6	3	1	2
3	2	6	5	3	2
4	2	5	3	3	3
6	1	2	3	3	1
7	2	4	3	2	2
8	2	6	5	4	3
10	3	4	5	3	3
11	2	6	5	3	2
12	1	2	3	1	1
13	1	2	3	2	4
14	2	6	5	2	4
15	1	6	2	1	3
16	1	2	3	3	2
M	1.79	4.5	3.85	2.36	2.43
SD	.70	1.79	1.23	.93	.94

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APPENDICES

Appendix A: Case History

Name:_____

Date of Birth:_____ **Gender: Male/Female**

Email:_____ **Phone #:**_____

Please answer the following question to the best of your knowledge:

On average, how many hours of sleep do you get on weeknights?

a) 4 hours or less
b) 5 - 6 hours
c) 7 - 9 hours
d) 10 - 12 hours
e) More than 12 hours

Do you typically wake up feeling rested?

a) Yes
b) No

Do you take sleep medication to help you fall asleep?

a) Yes
b) No

What time do you wake up on weekdays?

a) Earlier than 6:00 am
b) 6:00 - 6:29 am
c) 6:30 - 6:59 am
d) 7:00 - 7:29 am
e) 7:30 - 7:59 am
f) 8:00 - 8:29 am
g) 8:30 - 8:59 am
h) 9:00 - 9:29 am
i) 9:30 am or later

How often do you take a nap during the week?

a) Daily
b) A few days a week
c) Once a week
d) Once every 2 weeks
e) Once a month
f) Rarely
e) Never

How long do you tend to nap?

a) Less than 10 minutes
b) 10 - 20 minutes
c) 21 - 30 minutes
d) 31- 45 minutes
e) 46 minutes to an hour
f) More than 1 hour
g) I don't nap

Have you been diagnosed with a sleep disorder?

a) Yes
b) No

Have you been diagnosed with a neurological disorder?

a) Yes
b) No

Have you been diagnosed with a psychiatric disorder?

a) Yes
b) No

On average, how much caffeine do you consume daily?

a) 0 glasses
b) 1 glass
c) 2 - 3 glasses
d) 4 - 5 glasses
e) 6 or more glasses

On average, how much alcohol do you consume daily?

a) 0 glasses
b) 1 glass
c) 2 - 3 glasses
d) 4 - 5 glasses
e) 6 or more glasses

Please list the medications (both prescription and over the counter) you are currently taking:

_____
_____
_____

Appendix B: Sleep Logs

Name:_____

2 mornings before testing:

Please record the:

Time you went to bed_____
Time you fell asleep_____
Time you woke up _____

1. How many times did you wake up during the night? (Circle the correct response)

None (proceed to question 4) 1 2 3 4 5 6 more than 6

2. Why did you wake up during the night?

a) To use the restroom
b) Dreams or nightmares
c) External noise
d) Other: _____

3. When you woke up during the night how long was it before you fell back asleep? (Please record approximate tie in minutes)

_____minutes

4. Did you sleep with any devices on? (Circle all that apply)

a) Television
b) Computer
c) Lights
d) Cell phone
e) Music
f) Other: _____

5. How did you feel 30 minutes after waking in the morning?

a) Feeling active, vital, alert, or wide awake
b) Functioning at high levels, but not at peak; able to concentrate
c) Awake, but relaxed; Responsive but not fully alert
d) Somewhat foggy, let down
e) Foggy; losing interest in remaining awake; slowed down
f) Sleepy, woozy, fighting sleep; Prefer to lie down
g) No longer fighting sleep, sleep onset soon; having dream-like thought

Name:_____

1 morning before testing:

Please record the:

Time you went to bed _____
Time you fell asleep _____
Time you woke up _____

1. How many times did you wake up during the night? (Circle the correct response)

None (proceed to question 4) 1 2 3 4 5 6 more than 6

2. Why did you wake up during the night?

a) To use the restroom
b) Dreams or nightmares
c) External noise
d) Other: _____

3. When you woke up during the night how long was it before you fell back asleep? (Please record approximate tie in minutes)

_____minutes

4. Did you sleep with any devices on? (Circle all that apply)

a) Television
b) Computer
c) Lights
d) Cell phone
e) Music
f) Other: _____

5. How did you feel 30 minutes after waking in the morning?

a) Feeling active, vital, alert, or wide awake
b) Functioning at high levels, but not at peak; able to concentrate
c) Awake, but relaxed; Responsive but not fully alert
d) Somewhat foggy, let down
e) Foggy; losing interest in remaining awake; slowed down
f) Sleepy, woozy, fighting sleep; Prefer to lie down
g) No longer fighting sleep, sleep onset soon; having dream-like thoughts

Name:_____

Morning before testing:

Please record the:

Time you went to bed _____
Time you fell asleep _____
Time you woke up _____

1. How many times did you wake up during the night? (Circle the correct response)

None (proceed to question 4) 1 2 3 4 5 6 more than 6

2. Why did you wake up during the night?

a) To use the restroom
b) Dreams or nightmares
c) External noise
d) Other: _____

3. When you woke up during the night how long was it before you fell back asleep? (Please record approximate tie in minutes)

_____minutes

4. Did you sleep with any devices on? (Circle all that apply)

a) Television
b) Computer
c) Lights
d) Cell phone
e) Music
f) Other: _____

5. How did you feel 30 minutes after waking in the morning?

a) Feeling active, vital, alert, or wide awake
b) Functioning at high levels, but not at peak; able to concentrate
c) Awake, but relaxed; Responsive but not fully alert
d) Somewhat foggy, let down
e) Foggy; losing interest in remaining awake; slowed down
f) Sleepy, woozy, fighting sleep; Prefer to lie down
g) No longer fighting sleep, sleep onset soon; having dream-like thoughts

Appendix C: Informed Consent Form

Sleep Deprivation and Recovery Time:
The Effects on P300 Two, Four and Six Hours Post Recovery

Investigators: Dr. Thomas C. Franklin (clayfranklin@missouristate.edu)
Kimberly Brauer (kimberly623@live.missouristate.edu)

1. Introduction

You are invited to take part in a research study. Before you decide to be a part of any study, you need to evaluate any potential risks and benefits associated with it. This consent form provides information about the research study. As the investigators conducting this study, we will be available to answer your questions and provide further explanations. If you agree to take part in the research study, you will be asked to sign this consent form. This process is known as informed consent.

Your decision to take part in this study is voluntary. You are free to choose whether or not you will take part in the study.

2. Research Purpose

The goal of this research is to determine how sleep deprivation affects auditory evoked cortical potentials, specifically the P300. By examining the changes in latency and amplitude, we hope to determine whether or not auditory awareness declines due to sleep deprivation. The research design will also allow a recovery period of 110 minutes which will allow the P300 to return closer to baseline measures. Additions tests will be given two, four and six hours post recovery to help determine when the P300 will diminish again due to sleep deprivation.

3. Procedures

You will be subjected to the following screening procedurews prior to selection candidacy for the experimental protocol: a) otoscopic examination, flash-light to visualize your ear canal and ear drum to exclude presence of occluding wax, eardrum perforation or infection, b) standard hearing test to ensure within normal hearing sensitivity (hearing thresholds should be 25 dB HL or lower at frequencies 500 to 4000 Hz), and c) Tympanometry, a probe-tip will be placed in your ear canal and air pressure will be varied, to ensure normal middle ear function. The above tests take approximately 20 - 30 minutes.

You must also report no history of neurological, psychiatric, chemical dependency, or sleep related disorders. Prior to electrophysiological testing, you will fill out a questionnaire that assesses your perceived level of fatigue before and after sleep deprivation, and after an assigned period of rest. If you meet the pre-determined criteria for inclusion in the study, following the above screening tests, you will be eligible to participate in the experiments, wherein your brain response to tonal stimuli will be assessed to study your auditory cortical function six times: 1) prior to sleep deprivation (baseline), 2) after being sleep deprived for 24 hours, and 3) after a 110 minute rest period, 4) two hours post recovery, 5) four hours post recovery and 6) six hours post

recovery. It is anticipated that each participant will spend a total of 30-32 hours participating, including the 24 hours of sleep deprivation and testing time. Data collection is anticipated to take approximately 20 minutes per trial (120 minutes total, not including the nap time to examine the effect of recovery or each of the two hour periods between trials.

4. Benefits

There is no monetary compensation for participation, but you will receive a free test of hearing sensitivity, middle ear function, and function of the central auditory pathway. Results of the study are likely to be beneficial to employers, teachers, students, military personnel, medical professionals and to any other individuals who often function on low amounts of sleep. This study will help determine the effects of sleep deprivation on cognitive processing of auditory information. Additionally, researchers will assess how long it takes an individual to reenter a sleep deprived state after a 110 minute nap (one full sleep cycle).

5. Possible Risks

The preliminary screening tests are non-invasive standard tests that involve minimal risk. For the experimental procedure, a small risk of discomfort exists due to the tightness of the electrode cap. Also, minor skin irritation could result from the preparation of the skin for testing through the use of abrasive skin cleansers. It is possible that you may experience some physical; and psychological risk, such as fatigue and frustration, during the 24-hour sleep deprivation period. You may be too fatigued to operate a vehicle when the study is completed. To avoid conflicts with class, the study will be conducted during weekends at your convenience. The potential benefits and implications are believed to outweigh any possible risk.

6. Costs

Aside from your time, approximately 30 - 32 hours of participation, there are no costs associated with taking part in this study.

You will complete the relevant sleep deprivation period in a comfortable, controlled environment. We will provide caffeine free beverages and snacks to minimize the fatigue and hunger during sleep deprivation. Games and movies will also be provided; and one of the student researchers will observe you to ensure that you will stay awake and are safe.

Transportation before and following the experiment will be arranged for you to eliminate the possible danger and strain of driving while sleep deprived. Again, the study will be conducted during the weekend to avoid any conflict with class and give you a change to recovery before continuing work or school.

7. Right to Withdraw from this Study

Your participation in this research study is completely voluntary. Upon participation, we will provide you with beverages, snacks, and rides to ensure your safety before and after participation in this study. You do not have to take part in this research study, and should

you change your mind, you can WITHDRAW from the study at any time without any penalty. You may refuse to participate in this study or in any part of this study. You may withdraw at any time without effect to your relations with the university. You're are encouraged to ask questions about this study at the beginning or any time during the research study.

8. Confidentiality of Research Records

Your records will be confidential. You will not be identified (e.g., by name or social security number) in any reports or publications about this study. It is possible that representatives of regulatory agencies and the University may review your information to make sure that the study is being conducted carefully. If this happens, copies of the relevant parts of your records will be released with all identifying information removed. Apart from this study, your records will remain confidential unless you authorize their release or if the records are required by law (i.e., court subpoena). Your records will only be used for the purpose of this study. All records and data gathered will be kept in a locked cabinet by the investigators. At the end of the study, unless you authorized differently, your data will be shredded.

9. Questions

If you have any questions about the procedures of this research study, please contact Dr. Franklin (clayfranklin@missouristate.edu) or Kimberly Brauer (kimberly623@live.missouristate.edu)

10. Signatures

By signing this consent form, you affirm that you have read this informed consent form, this study has been explained to you, all questions have been answered, and you agree to take part in this study. You do not give up any legal rights by signing this informed consent form. You will receive a copy of this form.

_____

Participant's Name (Please print name)

_____

Participant's Signature

_____

Date

11. Investigator Statement

I certify that the research study has been explained to the above individual by one of the investigators including the purpose, the procedures, the possible risks, and the potential benefits associated with the participation in this research study. Any questions raised have been answered to the individual's satisfaction.

_____

Investigator (Please print name)

_____

Signature of Investigator

_____

Date

Appendix D. Stanford Sleepiness Scale

How do you feel?

1. Feeling active, vital, alert, or wide awake
2. Functioning at high levels, but not at peak; able to concentrate
3. Awake, but relaxed; Responsive but not fully alert
4. Somewhat foggy, let down
5. Foggy; losing interest in remaining awake; slowed down
6. Sleepy, woozy, fighting sleep; Prefer to lie down
7. No longer fighting sleep, sleep onset soon; having dream-like thoughts

Appendix E: Debriefing Form

Sleep Deprivation and Recovery Time:
The Effects on P300 Two, Four and Six Hours Post Recovery

Thank you for participating in this study. Your time and effort are greatly appreciated. This experiment investigated how sleep deprivation affects auditory evoked cortical potentials, specifically the P300. By examining the changes in latency and amplitude, we hope to determine whether or not auditory awareness declines due to sleep deprivation. The procedure included a first phase during which participants were asked to sleep at least 8 hours prior to testing, a second phase in which participants remained awake for approximately 24 hours prior to testing, a third phase 30 minutes after a set recovery period of 110 minutes and a fourth and fifth and phase to conduct testing three and six hours post recovery.

You are reminded that your original consent document included the following information: you are to plan to nap on the day following the study.

This study has received ethics clearance through the Missouri State University Institutional Review Board. If you have any questions or concerns about your participation in this study, you can contact Dr. Thomas C. Franklin at clayfranklin@missouristate.edu or Kimberly Brauer at 417-489-4286 or kimberly623@live.missouristate.edu.

Please again accept our appreciation for your participation in this study.

_____
Investigator (Please print name)

_____
Signature of Investigator

_____
Date