THESIS

SENSORY GATING, HABITUATION, AND ORIENTATION OF P50 AND N100

EVENT-RELATED POTENTIAL (ERP) COMPONENTS IN NEUROLOGICALLY TYPICAL

ADULTS AND LINKS TO SENSORY BEHAVIORS

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ABSTRACT

SENSORY GATING, HABITUATION, AND ORIENTATION OF P50 AND N100 EVENT-
RELATED POTENTIAL (ERP) COMPONENTS IN NEUROLOGICALLY TYPICAL
ADULTS AND LINKS TO SENSORY BEHAVIORS

This thesis project used a novel electroencephalography (EEG) auditory paradigm, the orientation/habituation paradigm, to understand brain processing in response to multiple auditory stimuli. This paradigm allowed the exploration of several neurological processes within one task: sensory gating, orientation to deviant stimulus, and habituation and dishabituation. Sensory gating has been studied extensively in individuals with neurological disorders (Arnfred & Chen, 2004; Boutros, Belger, Campbell, D'Souza, & Krystal, 1999; Kisley et al., 2003) and there are a few studies that have examined habituation and orientation in individuals with epilepsy or schizophrenia (Rosburg et al., 2004; Rosburg et al., 2006; Viswanathan & Jansen, 2010). The construct of dishabituation, referring to the brain's processing of standard stimuli after the presentation of a deviant stimulus, has not been studied previously. In addition to exploring these neurological phenomena, this project investigated the relationship between brain processing and scores on sensory behavioral inventories, the Adolescent/Adult Sensory Profile (Brown & Dunn, 2002) and the Sensory Gating Inventory (Hetrick, Erickson, & Smith, 2012).

Participants were 38 neurologically typical adults (average age 19.6 ±1.46 years). These adults demonstrated significant sensory gating from stimulus 1 to stimulus 2 at all electrode sites ($p < .0005$). There was also a significant orientation effect of P50 and N100 to the deviant stimuli. There was no habituation of the P50 ERP component over time and there were mixed

results regarding whether or not the P50 was dishabituated when a deviant tone was presented. In contrast to the P50, there were significant linear trends found for N100 at four of the five electrode sites, demonstrating habituation. Additionally, when presented with a deviant stimulus in the middle of a series of standard stimuli, N100 was not dishabituated, and in some cases demonstrated significant increase in habituation after the deviant stimulus. These results indicate that there is some sort of cognitive control over the suppression of the N100 amplitude that is not seen for the suppression of P50. Finally, when correlated with sensory behavior tasks, sensory gating of N100 amplitude was significantly associated with Sensation Avoiding on the Adolescent/Adult Sensory Profile (A/ASP) (Brown & Dunn, 2002). Increase in P50 amplitude to the deviant stimulus, reflecting orientation, was significantly negatively correlated with both Over-Inclusion and Fatigue and Stress Vulnerability of the Sensory Gating Inventory (Hetrick, Erickson, & Smith, 2012) and positively with the Sensation Seeking quadrant of the A/ASP. Increase in N100 amplitude to the deviant stimulus, reflecting orientation, was significantly related to the Touch Processing subscale of the A/ASP.

ACKNOWLEDGEMENTS

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CHAPTER 1

This thesis project used a novel electroencephalography (EEG) auditory paradigm, which we termed the orientation/habituation paradigm and are using to understand brain processing in response to multiple auditory stimuli. This paradigm allows the exploration of several neurological processes within one task: sensory gating, orientation to deviant stimulus, and habituation and dishabituation. Studies using EEG have often investigated sensory gating by using a dual click paradigm in individuals who have neurological disorders compared to a group of control peers (Arnfred & Chen, 2004; Boutros, Belger, Campbell, D'Souza, & Krystal, 1999; Kisley et al., 2003). There are a few studies that have examined habituation and orientation in individuals with epilepsy or schizophrenia (Rosburg et al., 2004; Rosburg et al., 2006; Viswanathan & Jansen, 2010). The construct of dishabituation, which we are defining as the brain's response to standard stimuli after the presentation of a deviant stimulus, has not been studied previously. In addition to exploring these neurological phenomena, this project investigated the relationship between brain processing and scores on sensory behavioral inventories, the Adolescent/Adult Sensory Profile and the Sensory Gating Inventory. The following chapter reviews literature regarding the benefit of studying neurologically typical adults, explains electroencephalography (EEG) and event-related potential (ERP) components, outlines prior studies investigating sensory gating, habituation, and orientation, explores the brain areas involved in these phenomena, and describes background information on the sensory inventories used in the study.

Benefit of Studying Neurologically Typical Adults

Sensory processing phenomena, such as sensory gating and habituation, have often been studied in individuals who have neurological disorders including schizophrenia, autism, and

sensory processing disorder. Although studying specific disordered populations sheds light on much about brain processing, equally important is an understanding of typical brain responses to external stimuli. Persons (1986) suggested that there are several advantages to studying a specific psychological or neurological phenomenon in neurologically typical adults rather than a sample of individuals with neurological disorders. One of the advantages is that psychological symptoms are often experienced on a continuum from non-pathological to severe and may be found in populations other than a specific diagnostic group, so by studying a broad population, one may see more diversity and gain better understanding of the phenomenon. Hetrick, Erickson and Smith (2012) studied non-psychiatric samples because sensory gating difficulties occur frequently in typical individuals as well as those with neurological disorders. The knowledge gained from understanding neurological processes in typical individuals enriches information gathered about disordered populations by providing a foundation from which to interpret the results found.

It is well documented that individuals with neurological disorders such as schizophrenia, attention deficit hyperactivity disorder (ADHD), sensory processing disorders, and autism demonstrate different brain responses to auditory stimuli than their neurologically typical counterparts (Boutros, Belger, Campbell, D'Souza, & Krystal, 1999; Dunn, Gomes, & Gravel, 2008; Gavin et al., 2011; Jeste & Nelson, 2009; Kisley et al., 2003; Marco, Hinkley, Hill, & Nagarajan, 2011; Olincy et al., 2000; Sokhadze et al., 2009). This difficulty processing sensory information at the neural level leads to aberrant behaviors seen in these populations. For example, individuals with schizophrenia demonstrate abnormal perception and attention to stimuli, leading to the characteristic experiences of not being able to ignore stimuli in the environment and being flooded by sensory information (Hetrick, Erickson, & Smith, 2012).

Those with autism often display characteristic behavior patterns that also demonstrate sensory difficulties, such as tactile, oral, visual, and auditory defensiveness (Kern et al., 2006). Children with sensory processing disorder may be hyper- or hypo- sensitive to stimuli (Davies & Gavin, 2007; Dunn, 1997). By studying both the neurological response to stimuli and behavioral actions, neuroscientists expect to provide information that may lead to the development of interventions that will address the neurological differences that lead to aberrant behaviors. This study aims to use electroencephalography to better understand how mature brains of adults, who do not have neurological or sensory deficits, process auditory sensory information.

Electroencephalography

Electroencephalography (EEG) is a non-invasive brain imaging technique that measures the electrical activity of the extracellular fluid in the cortical regions of the brain as recorded by electrodes placed at specific locations on the scalp according to the International 10-20 system of electrode placement (Banaschewski & Brandeis, 2007; Stern, Ray, & Quigley, 2001). Other brain imaging techniques, such as functional magnetic resonance imaging (fMRI) and positron emission tomography (PET) scans, provide spatial information as to where brain activity occurs; however, they do not give the temporal resolution in milliseconds that EEG provides. This precise temporal resolution is important to understanding the neural processing that occurs during brain function (Banaschewski & Brandeis, 2007). For these reasons, EEG is the best tool for the study of brain processing.

EEG is used to measure brain activity at rest, when alert, when asleep, and during sensory, motor, and cognitive processing tasks (Stern et al., 2001). These processing tasks activate the brain and result in event-related potentials (ERPs). ERPs are derived from segments of the running EEG taken just around each presentation of a stimulus. These time-locked data are

averaged over many trials. This allows the random activity in the running EEG data to be cancelled-out leaving just the response to the stimulus, or the ERP, which shows a particular pattern of positive and negative deflections that researchers call components (Roach & Mathalon, 2008; Stern et al., 2001). Components are labeled based on the latency, or time since the onset of the stimulus in milliseconds, and the direction of the deflection (Coles & Rugg, 1995; Stern et al., 2001). For example, at approximately 50 ms after a stimulus, there is generally a positive deflection, labeled P50, and at 100 ms after a stimulus, a negative deflection is called N100 or sometimes N1. See Figure 1.1 for an image of an ERP with components labeled. The latency and amplitude of the components are generally reported in studies and compared between groups (Coles & Rugg, 1995).
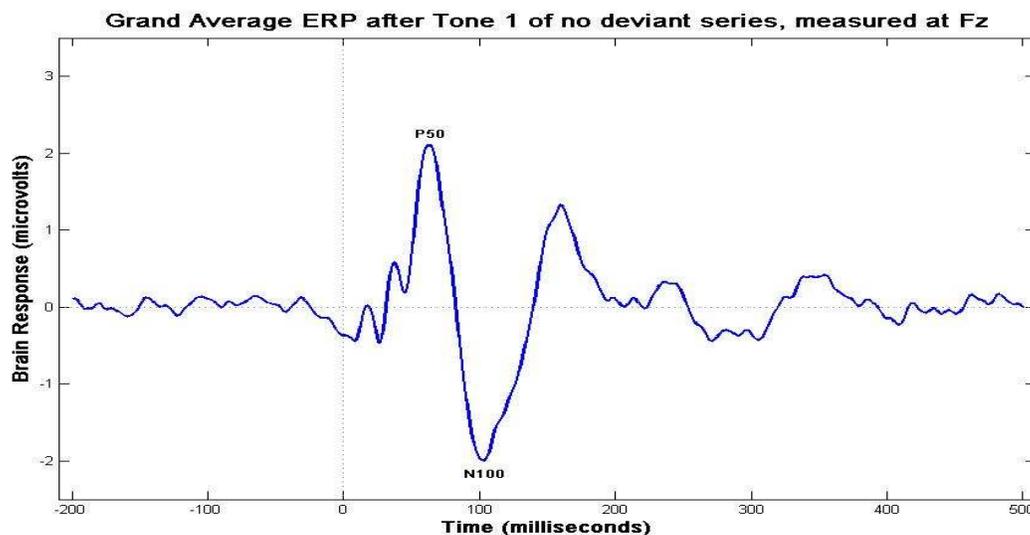
Figure 1.1: Labeled ERP components of P50 and N100. The vertical dashed line represents when the auditory stimulus occurred.

Each of the components in an ERP has been linked to specific aspects of brain processing. Early and mid-latency components (10 – 250 ms) are thought to be affected by exogenous information, meaning that they change in intensity or amplitude based on changes in information coming into the nervous system through the senses. They reflect sensory processing

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whereas later components (250 ms and later) reflect cognitive processing and are influenced by endogenous information (Boutros et al., 1999; Coles & Rugg, 1995; Olincy et al., 2000; Polich, 1993; Ponton, Eggermont, Kwong, & Don, 2000). For this study, analysis will focus on the P50 and N100 ERP components. The P50 component is thought to be representative of automatic processing (Olincy et al., 2000; Stern et al., 2001). However there is controversy whether or not the P50 is mediated by attention (Jerger, Biggins, & Fein, 1992; Lijffijt et al., 2009). It is thought that N100 is related specifically to triggering attention, the brain's orientation to a stimulus, as well as initiating working memory (Bomba & Pang, 2004; Boutros et al., 1999; Lijffijt et al., 2009). As we are interested in the intial sensory processing of repeated auditory stimuli, P50 and N100 are appropriate components to measure.

Sensory Gating

Sensory gating refers to the reduction in the amplitudes of ERP components, including the P50 and N100, to repetitive stimulus and is generally elicited with a paradigm that uses two auditory stimuli, typically clicks (Boutros et al., 1999; Kisley, Noecker, & Guinther, 2004; Kisley et al., 2003). Those with certain types of neurological deficits, such as schizophrenia, do not demonstrate sensory gating. For example, Kisley and colleagues (2003) used a sensory gating paradigm with 10 adults with schizophrenia compared to 10 typical adults both while awake and during REM sleep cycles. They found that the individuals with schizophrenia did not show gating at P50 in either state. Comparatively, the adults without schizophrenia did demonstrate P50 gating in both states. When comparing the N100, the groups differed during awake states, with typical adults showing greater gating. Olincy and colleagues (2000) compared sensory gating among 16 adults with schizophrenia, 16 adults with ADHD, and 16 typical adults. Similar to the Kisley et al. study, Olincy and colleagues (2000) found that adults with

schizophrenia did not gate auditory information, however adults with ADHD were not statistically significantly different than the normal adults with regard to sensory gating of the P50 component amplitude.

Habituation

To further explore how the brain processes sensory information, short term habituation paradigms have been used to analyze the ERP components of multiple stimuli to see what happens over a series of repetitive inputs. A key characteristic of habituation is that with each subsequent presentation of the same stimuli, the brain response should decrease (Budd, Barry, Gordon, Rennie, & Michie, 1998). There is current debate in the literature as to if the decrease in amplitude of ERP components is due to an inhibition phenomenon or a refractory period. An inhibition theory suggests that inhibitory signals are actively sent to reduce the firing of neurons to repeated stimuli (Boutros et al, 1999). A refractory period, or recovery cycle, is explained to be the time it takes for a single neuron to return to a resting state after the action potential; it cannot fire again until it is recovered (Budd et al., 1998). This process is considered passive, and the recovery involves clearing the synaptic space between the neurons through re-uptaking the neurotransmitters into the firing neuron or their absorption by other cells so that the next message will be able to be sent. Another aspect of recovery includes making sure that the firing neuron has enough neurotransmitters to fire; this is related to the reuptake of the neurotransmitters as well as the creation of new neurotransmitters as needed by the neuron (Widmaier, Raff, & Strang, 2011).

Several EEG researchers have attempted to study this cellular phenomenon by looking at the summed electrical activity of the brain through the manipulation of the inter-stimulus intervals (ISI) between repeated auditory stimuli. Coch, Skendzel, and Neville (2005) describe

"… an increase in ERP amplitude to the same stimulus presented with a longer ISI as compared to a shorter ISI is a reflection of the greater physiological recovery [refractory period] overtime of the neurons generating the response to that stimulus" (p. 2185). In auditory brain processing, Coch and colleagues (2005) summarize that it may take at least 3 seconds and possibly up to 10 seconds for full recovery. Although several EEG researchers investigating habituation interpret their results to indicate that the decrease in amplitude of components to multiple stimuli is due to a refractory period (Budd et al., 1998; Rosburg et al., 2006; Rosburg et al., 2004, Rosburg, Zimmerer, & Huonker, 2010), another possibility is an inhibitory response (Boutros et al., 1999; Sable, Low, Maclin, Fabiani, & Gratton, 2004). Sable and colleagues (2004) did not find that refractory periods were sufficient to explain the results of their study and suggested that for stimuli that are repeated within 400 ms of the initial stimulus, there is a latent inhibitory process whereby the N100 generators experience a negative feedback loop that inhibits their production of the next N100 response, but takes 300-400 ms after the initial stimulus to activate the inhibitory process.

In early studies of habituation, there was a focus on long-term habituation, that is, the decrease in amplitude of an ERP component over a session of stimuli (rather than a short train of a few stimuli, repeated over the session and averaged for analysis, which is considered short term habituation). Generally, long term habituation was found by the 3rd or 4th stimulus (Fruhstorfer et al., 1970; Ritter, Vaughan, & Costa, 1968). Ritter and colleagues (1968) studied 9 individuals and used a variety of habituation studies. In one experiment, which mirrors more closely the current short term habituation paradigms, the P200 habituated between the 2nd and 4th stimuli, finally stabilizing after the 4th stimulus. Fruhstorfer and colleagues (1970) studied 6 healthy adult males and used trains of 8 identical clicks of 1 ms in duration presented either at 1 click per

second or 1 click per 3 seconds. They also found that there was habituation in P100, N100, and P200 by the 3rd or 4th stimulus, with no further decrease noted.

More recently, Rosburg and colleagues (2004) collected intracranial ERP data from 29 patients with epilepsy using a short term habituation paradigm with a train of 5 clicks and a deviant 6th click. They found that from the first to second click, there was a reduction in amplitude in the P50 and N100 components, reflecting sensory gating as discussed in the previous section. Clicks 2-5 produced no additional decreases in either the P50 or N100 component which led the authors to suggest that there is no habituation, and the suppression of components was due to a refractory period. Rosburg and colleagues used a similar paradigm in 2006 when examining brain responses in 23 individuals with epilepsy. Their paradigm used 5 identical tones and 1 deviant tone that differed from the others in duration (100 ms as compared to standard of 50 ms), but not in pitch or intensity. The deviant was presented at positions 3, 4, or 5. The researchers collected data intracranially and at the scalp. As with other short term habituation studies, Rosburg and colleagues found a decrease in P50 and N100 from the first stimulus to the second stimulus and no other statistically significant decreases after the second stimulus. When recorded intracranially, N100 had a tendency to be smaller to the final stimulus than the second one; however, the findings only approached significance ($p = .074$). The amplitudes of P50 were consistent for the second through fifth stimuli.

Individuals with other neurological disorders have been studied using short term habituation paradigms as well. Boutros and colleagues (1999) studied 12 adults with schizophrenia as compared with 12 typical adults using 4 auditory gating paradigms including a short train paradigm where there were 5 clicks followed by a 6th deviant click. For the participants with schizophrenia, P50 gating from click 1 to click 2 was not statistically

significant. For P50 and N100, there was also no significant habituation from click 1 to click 5. Normal controls demonstrated decreases in amplitude, a gating response, of P50 and N100 for click 2, compared to the amplitude of click 1. When the authors compared the ratio of the first to second click and the ratio of the first to fifth click, there was no difference, suggesting no short term habituation beyond the initial gating response.

Rosburg, Zimmerer, and Huonker (2010) varied a short term habituation paradigm to investigate how the interstimulus interval (ISI), or time between the stimuli in the train, would impact the N100 and P200 gating and habituation. The paradigm included 3 short term habituation trains consisting of five 50 ms tones, 1000 Hz at 75dB. The only difference among the three trains was the length of ISI: 600, 1200, and 1800 ms. The participants were adults without neurological deficits. The authors found that for all 3 trains, the second stimulus, compared to the first stimulus, produced significantly smaller amplitudes and decreased latency for N100 and P200, a gating effect. They also noted that as the ISI increased from 600 ms to 1800 ms, there was a decrease in the amount of change from stimulus 1 to stimulus 2. The authors interpret this to give support to the concept of a refractory period, that when there is more recovery time between stimuli the cells recover more fully in preparation to fire again. As with the above studies, the responses for stimulus 2 through 5 were similar in nature with N100 demonstrating stabilization in amplitude after stimulus 2, suggesting no habituation after gating the second stimulus.

Prior habituation studies have not investigated the idea of dishabituation proposed in this study although they occasionally use deviant stimuli (to be discussed below in the orientation review). In the Orientation/Habituation paradigm, a series of 8 standard tones is interrupted by a deviant tone. If this deviant tone dishabituates the brain's response to the standard tones that

follow it, it would be expected that the amplitude to those tones would be larger than the ones that preceded the deviant. By looking at whether the deviant tone dishabituates the brain's response, we are better able to confirm if an inhibitory or refractory process may be responsible for habituation. This is important for understanding the neural mechanisms involved in auditory sensory processing.

Orientation

Orientation refers to the way the brain attends or orients to a novel or deviant stimulus. Viswanathan and Jansen (2010) took their short term habituation paradigm a step further than the prior studies and considered how a final deviant stimulus or knowledge of train length affected the amplitude of the P50 and N100 components for healthy adult participants to the final deviant tone. They called this dishabituation, rather than orientation; however, both the paradigm for the proposed study and the one Viswanthan and Jansen used address the brain's response to a deviant stimulus presented after a series of standard stimuli; therefore for this review, the results of Viswanathan and Jansen will be associated with the orientation phenomenon. The response to the deviant stimulus depended on which component the researchers were looking at and was impacted by several aspects of the train. For example, the P50 did not seem to be affected by the participant having prior knowledge of the train length, or type of deviant in the series (chirp versus tone). The N100 was significantly larger with a more complex stimulus (a chirp rather than a tone), and was significantly smaller when the participant had knowledge of how long the trains were going to be. The researchers concluded that the amplitude of P50 to a deviant stimulus is not affected by the complexity of the stimulus or expectancy/knowledge of the train length; however, the amplitude of N100 was larger for more complex stimulus or in response to the deviant when the trains were unpredictable.

Rosburg and colleagues (2004, 2006) also investigated brain responses to deviant stimuli in some of their short term habituation paradigms used with individuals with epilepsy. In 2004, the paradigm they used included a final deviant click, differing from the standard clicks in both frequency and duration. They found that for the deviant click, the P50 amplitude was greater than the previous click, but not as large in amplitude as the P50 to the first click. The deviant click elicited an N100 that was similar to the response to the first click. In 2006, Rosburg and colleagues used a short term habituation train of tones and found that the deviant, which only differed by length of tone, did not produce a statistically significantly orienting response, i.e., a larger amplitude, to the deviant as measured by P50 or N100. Boutros et al (1999) found that in their short term habituation paradigm that concluded with a deviant click, normal control subjects demonstrated an increase in amplitude of P50 and N100 to click 6, whereas those with schizophrenia did not.

Brain Regions Associated with Neural Phenomena

Researchers have used EEG and fMRI to determine which neural substrates are associated with various types of brain processing. At this point, the literature has addressed orientation to novel information and sensory gating. The neural mechanisms behind habituation have not been explored. Although knowing the brain areas associated with each neural phenomenon is not the focus of this study, it is important to note that different aspects of brain processing are performed in different brain areas.

Tregellas and colleagues (2007) used fMRI for the first time to assess the spatial aspects of sensory gating with those who have schizophrenia compared to typical adults. They modified sensory gating paradigm to be repeated clicks for 4 seconds because fMRI gives data in seconds rather than on the millisecond level (and therefore does not have the temporal sensitivity to

assess early attentive responses to stimuli), but also used EEG data with a typical gating

paradigm in order to associate the fMRI and EEG data. They found that individuals with

schizophrenia had greater activation of the hippocampus, dorsolateral prefrontal cortex, and

thalamus when compared to a control group of age matched adults for a repeated click paradigm

relative to a single click paradigm. Interneurons in the hippocampus and thalamus are thought to

be specifically involved in sensory gating. The authors suggest that the dorsolateral prefrontal

cortex may be involved when the hippocampus and thalamus "fail to inhibit afferent sensory

information" (p. 269).

Boutros and colleagues (2013) used EEG collected from cortical electrodes implanted on

64 patients with epilepsy undergoing pre-surgery evaluation. These participants listened to a

typical sensory gating two click paradigm and were asked to focus their attention, or listen, to the

clicks. The authors used the EEG data in combination with models created from MRI data for

source localization. The researchers located areas that demonstrated the highest P50 amplitude

(to click 1), or orientation, and the strongest P50 suppression (click 1 to click 2), or sensory

gating. They found that the involved brain regions for these two phenomena were different, with

the former being temporal (4 areas), parietal (3 areas), and cingulate (3 areas). For the

suppression measure, five of the top 10 areas were in the pre-frontal cortex. The researchers

suggest that perhaps there are three regions important to the auditory suppression phenomenon

based on the MRI data: the temporal neo-cortex, the prefrontal cortex, and the hippocampus,

with possible contributors being the parietal and cingulate regions. This demonstrates that there

are different neural networks for different aspects of brain processing. In this case, the temporal

lobe is important for processing initial stimulus input where the frontal lobe is activated to

suppress the response to subsequent identical stimuli, along with possibly temporal neo-cortex and hippocampus.

Although there are no studies that specifically address habituation, it is possible that the brain areas responsible for suppression may be responsible for habituation effects. Research on this topic would inform whether the mechanisms for gating and habituation are different. However, from the above information it may be assumed that there are a variety of brain regions involved in each aspect of sensory and cognitive processing. Therefore, it may be possible that sensory orientation, gating, and habituation occur with activation in different neural networks.

Unique Features of the Orientation/Habituation Paradigm

The orientation/habituation ERP paradigm used in this current study addresses several aspects of brain processing. The paradigm uses 3 trains, or series, of auditory stimuli, each composed of 8 tones, which are presented biaurally to the participant. For one series, the tones are identical. For the other two series, there is a deviant tone presented in the 4th or 5th position in the series of tones. This paradigm allows the examination of sensory gating from the first to the second tone, habituation to subsequent identical tones as the train goes on, orientation to a novel stimulus when the deviant tone is presented, and dishabituation of standard tones following a deviant tone. Although there are many studies on sensory gating in individuals across age or diagnostic groups, there is much less known about habituation and orientation, especially in the neurologically typical population. For habituation studies, researchers have looked at 23-29 participants with epilepsy (Rosburg et al., 2006; Rosburg et al., 2004), 12 individuals with schizophrenia compared with 12 normal participants (Boutros et al., 1999), and 17-18 healthy subjects (Rosburg, Zimmerer, & Huonker, 2010; Viswanathan & Jansen, 2010), all of which are smaller sample sizes than this current study. With the increased sample size to 38 individuals and

a more complex paradigm, a more detailed understanding of orientation and habituation brain responses in adults may be revealed.

<div align="center">**Sensory Inventories**</div>

Although understanding the physiological response to a stimulus is vastly important, it is understood that human experiences are not confined to a series of individual pieces of sensory information. A person experiences a multitude of sensory input at every second and the brain has to organize, filter, and attend to appropriate information. As mentioned above, it is likely that individuals who have neurological disabilities are not able to process all the sensory information in their environment and, therefore, exhibit characteristic behavioral responses to sensory input that is different than responses of their neurologically typical counterparts (Belmonte & Yurgelun-Todd, 2003; Hetrick et al., 2012; Tomchek & Dunn, 2007). For example, if a person is not able to process the auditory, visual, olfactory sensory input at a grocery store, he or she may easily become overwhelmed and be unable to buy groceries independently, an important task for most adults. A common way that sensory processing difficulties are measured is through behavior surveys. Two such surveys that can be used for adults are the Adolescent/Adult Sensory Profile (Brown, Tollefson, Dunn, Cromwell, & Filion, 2001) and the Sensory Gating Inventory (Hetrick et al., 2012).

Adolescent/Adult Sensory Profile

The Adolescent/Adult Sensory Profile (A/ASP) is based on Dunn's Model of Sensory Processing (1997). Dunn acknowledges that the central nervous system (CNS) modulates sensory input in order to interpret and respond accordingly. This modulation includes both habituation and sensitization. Habituation in Dunn's model is the way that the CNS stops sending repetitive information, such as the ambient sound in a room, to the brain. Sensitization is

similar to our definition of orienting and occurs when the CNS acknowledges something novel in the environment, such as a person opening the door to the room. The orientation/habituation paradigm used in this study addresses both of these concepts of sensory modulation on a neurological processing level. Dunn (1997) discusses the idea that habituation and sensitization have a give and take, and when there is a poor relationship between these factors, "maladaptive behaviors, such as being overly excitable or hyperactive (i.e., too much sensitization – low thresholds) or overly lethargic and inattentive (i.e., too much habituation – high thresholds)" occurs (p. 25). She describes these thresholds as being on a continuum, and that there are four quadrants in sensory modulation: low registration, sensory sensitivity, sensation seeking and sensation avoiding (see Figure 1.2). These are used in the Adolescent/Adult Sensory Profile (Brown et al., 2001). The quadrant of low registration occurs when a person has high neurological threshold and difficulty assessing their sensory environment; they act as though they are uninterested in the environment. An example from the profile is "I don't notice when my name is called." Those with sensory sensitivity have a low neurological threshold, that is, they seem to attend to too many things and behave hyperactively. For example, "I become bothered when I see lots of movement around me." Individuals who are sensation seeking have high thresholds but rather than being lethargic, they seek out stimulation to fill these needs, and

Neurological Threshold Continuum	Behavioral Response Continuum	
	responds in ACCORDANCE with threshold	responds to COUNTERACT the threshold
HIGH (habituation)	Low Registration	Sensation Seeking
LOW (sensitization)	Sensory Sensitivity	Sensation Avoiding

Figure 1.2: Relationships between behavioral responses and neurological thresholds (adapted from Figure 1 in Dunn, 1997, p. 24)

tend to be very busy. An example from the A/ASP is "I like to go barefoot." Finally sensation avoiding occurs when individuals have low thresholds and they seem to avoid activity because it is too overwhelming for them. For example, "I only eat familiar foods." The A/ASP has been used with individuals with schizophrenia (Brown, Cromwell, Filion, Dunn, & Tollefson, 2002), individuals with obsessive-compulsive disorder (Rieke & Anderson, 2009), adolescents with autism spectrum disorders (De la Marche, Steyaert, & Noens, 2012), and healthy adults (Engel-Yeger & Dunn, 2011). Brown et al (2001) reported that the A/ASP had good construct validity by showing that scores in the different quadrants were related to different physiological responses to skin conductance measures. They also reported the item reliability for the items in each quadrant and found that the internal consistency for the Sensation Seeking subscale was moderate (alpha = 0.60), and there was strong internal consistency for the other subscales (alpha = 0.78 for both Sensory Sensitivity and Low Registration, and alpha = 0.77 for Sensation Avoiding). The combination of good reliability and validity of the instrument as well as the frequent use in both research studies and practice makes the A/ASP an excellent choice for determining relationships to ERP data.

Sensory Gating Inventory

The Sensory Gating Inventory (SGI) created by Hetrick, Erickson, and Smith (2012) is also a self-report questionnaire that asks behavioral questions aimed at seeing how the neurological aspects of sensory gating may show up in the behaviors of typical or neurologically atypical individuals. In this model, Hetrick and colleagues found four factors that play a part in sensory gating. Perceptual Modulation refers to the ability to modulate stimulus intensity and "perceptual inundation" (p. 182). Distractibility refers to difficulties with attending. Over-Inclusion is an awareness of all aspects of an environment. And Fatigue-Stress Modulation refers

to how someone can modulate information even when fatigued. See Table 1.1 for examples of each factor from the inventory. Kisley and colleagues (2004) found that the typical adults who had difficulty with perceptual modulation (particularly with regard to filtering difficulties), as measured by a subset of the SGI, demonstrated less P50 gating. Additionally, those with difficulty in over-inclusion had less N100 suppression to the second click. These results may give support to the literature suggesting that P50 and N100 are unique aspects of sensory processing. The test-retest reliability for the SGI is between 0.86 and 0.88 as measured at 4.5, 6.5 and 9 weeks (Hetrick et al., 2012). Hetrick and colleagues found "substantial convergent validity evidence" (2012, p. 187) using a battery of other constructs. For example, the attentional "overload" by external stimuli subscale of the Test of Attentional and Interpersonal Style and the composite SGI score were strongly correlated ($r(219) = 0.79$). They also found discriminant validity of the four factors measured in the SGI. This inventory is appropriate to use for this study as it has been linked to ERP data and has moderate to strong validity and reliability.

Table 1.1: Sensory Gating Inventory Factors and Examples

Factor in Sensory Gating	Example Item from the Sensory Gating Inventory
Perceptual Modulation	"Every now and then colors seem more vivid to me than usual"
Distractibility	"I have more trouble concentrating than others seem to have"
Over-inclusion	"I notice background noises more than other people"
Fatigue-Stress modulation	"When I'm tired, the brightness of lights bother me"

Conclusion

In order to better understand the neurological phenomena of sensory gating, habituation, and orientation more fully, it is important to study a neurologically typical sample of individuals using this novel EEG paradigm. This will provide a baseline by which to compare adults with neurological disorders, assess the development of children, and eventually study children with neurological disorders. By determining the brain-behavior links using common behavior surveys,

this research will help explain what neurological phenomena may be related to a particular set of

sensory behaviors. This information may be helpful for researchers who either want to better

comprehend the nervous system or develop interventions based on the evidence found. The

information would also provide health practitioners valuable information in order to understand a

client and provide appropriate recommendations for that client as supported by best evidence.

CHAPTER 2

It is well documented that individuals with neurological disorders such as schizophrenia,

attention deficit hyperactivity disorder (ADHD), sensory processing disorders, and autism

demonstrate different brain responses to auditory stimuli than their neurologically typical

counterparts (Boutros, Belger, Campbell, D'Souza, & Krystal, 1999; Dunn, Gomes, & Gravel,

2008; Gavin et al., 2011; Jeste & Nelson, 2009; Kisley et al., 2003; Marco, Hinkley, Hill, &

Nagarajan, 2011; Olincy et al., 2000; Sokhadze et al., 2009). Differences in sensory processing

may lead to the characteristic behaviors in these diagnostic groups. A commonly studied group is

those with schizophrenia, who process each piece of auditory information as if it is novel. This

leads to an experience of being flooded by sensory information (Hetrick, Erickson, & Smith,

2012). Those with autism or sensory processing disorders respond to their sensory world

differently than their typical peers and often show behaviors of being hyper- or hypo-sensitive to

tactile, oral, visual and auditory sensory stimuli (Davies & Gavin, 2007; Dunn, 199; Kern et al.,

2006). By studying both the neurological response to stimuli and behavioral actions, we expect

to provide insights into the brain-behavior connections. This may pave the way for the

development of interventions that will address the neurological differences in sensory processing

that lead to aberrant behaviors.

The focus of this study is on three aspects of sensory processing: sensory gating,

habituation and dishabituation, and orientation, in neurologically typical adults. Persons (1986)

suggested that there are several advantages to studying a specific psychological or neurological

phenomenon rather than a sample of individuals with neurological disorders. One of the

advantages is that psychological symptoms often range on a continuum from non-pathological to

severe and may be found in populations other than a specific diagnostic group. Although there

are studies on sensory gating in many diagnostic populations (Kisley et al., 2003; Olincy et al., 2000), the majority of studies on habituation and orientation look primarily at samples of individuals with neurological disorders such as epilepsy or schizophrenia (Boutros et al., 1999; Rosburg et al., 2004; Rosburg et al., 2006). It is imperative that the understanding of typical brain processing is advanced in order to make sense of the information gathered from disordered populations.

This study used electroencephalography (EEG), a non-invasive brain imaging technique that provides temporal information about brain processing through the measurement of electrical activity of the extracellular fluid in the cortex, to explore the neurological responses to auditory stimuli (Banaschewski & Brandeis, 2007). From the running EEG data, event related potentials, or ERPs, are segmented just around the onset of a stimulus of interest and averaged over many trials. This allows the ERPs to show a particular pattern of positive and negative deflections, or components, which occur in response to that stimulus (Roach & Mathalon, 2008; Stern, Ray, & Quigley, 2001). Components are labeled based on the latency, or time since the onset of the stimulus in milliseconds, and the direction of the deflection (Coles & Rugg, 1995; Stern et al., 2001). For example, at approximately 50 ms after a stimulus, there is generally a positive deflection, labeled P50, and at 100 ms after a stimulus, a negative deflection is called N100 or sometimes N1.

Early and mid-latency components (10 – 250 ms) are thought to reflect sensory processing whereas later components (250 ms and later) reflect cognitive processing (Boutros et al., 1999; Coles & Rugg, 1995; Olincy et al., 2000; Polich, 1993; Ponton, Eggermont, Kwong, & Don, 2000). For this study, analysis will focus on the P50 and N100 ERP components. The P50 component is thought to be representative of automatic processing (Olincy et al., 2000; Stern et

al., 2001). N100 is related specifically to triggering attention, that the brain orients to a stimulus, as well as initiating working memory (Bomba & Pang, 2004; Boutros et al., 1999; Lijffijt et al., 2009).

Sensory gating refers to the reduction in amplitudes of ERP components, often the P50 and N00, to repetitive stimulus and is generally elicited with a paradigm that uses two auditory stimuli, typically clicks (Boutros et al., 1999; Kisley, Noecker, & Guinther, 2004; Kisley et al., 2003). Those with certain types of neurological deficits, such as schizophrenia, demonstrate significantly less sensory gating in P50 and N100 than do their typical peers (Kisley et al., 2003; Olincy et al., 2000).

Habituation refers to the idea that with each subsequent presentation of the same stimuli, the brain response, or amplitude of the ERP components, should decrease (Budd, Barry, Gordon, Rennie, & Michie, 1998). Research support for this phenomenon is mixed. Several current researchers suggest that the decrease in amplitude of ERP components is mostly due to a refractory period, or recovery cycle, which is a passive, automatic process. This is the time it takes for a single neuron to return to a resting state after the action potential; it cannot fire again until it is recovered (Budd et al., 1998). Others suggest that the decrease is due to an inhibitory process, at least in stimuli that occur within 400-500 ms of each other (Boutros et al., 1999; Sable, Low, Maclin, Fabiani, & Gratton, 2004). An inhibitory process is considered an active process where there is a cognitive control over the brain's response to multiple presentations of the same stimuli (Boutros et al., 1999). Some ERP studies have found habituation by the third or fourth stimulus with no further decrease in amplitude of components (Fruhstorfer et al., 1970; Ritter, Vaughan, & Costa, 1968), and others have not seen this habituation subsequent to a second stimulus (Boutros et al., 1999, Rosburg et al., 2004; Rosburg et al., 2006; alpha order).

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Dishabituation has not been previously researched. This phenomenon can be studied in a paradigm that uses a series of standard stimuli, in this case tones, and presents a deviant stimulus within the series. Dishabituation would be found if the amplitudes of the ERP components in response to a standard tone following the deviant are significantly larger than the one prior to the deviant. Dishabituation would imply the reduction in amplitude of response is due to a passive refractory period as the neurons would have twice the amount of time to regroup to fire after the deviant. A lack of dishabituation occurs when the ERP component amplitudes to the tone after the deviant are the same or smaller than the response to the tone before the deviant. This would support that habituation is related to an active inhibitory process, where working memory stores information about prior standard tones and sends a signal to supress the response to standard tones following the deviant. By studying this phenomena, we will gain information that supports whether it is an active inhibitory or passive refractory process that is responsible for any habituation of brain response to standard tones.

Orientation is the brain's response, or attention, to a novel stimulus. The novel stimulus could be to the first tone in a series or to a deviant tone at any position in a series of tones. In some habituation studies, researchers have attempted to understand this phenomenon by terminating their trains of standard stimuli with a deviant stimulus which results in an increase in amplitudes of P50 and N100 for neurologically typical adults (Boutros et al., 1999; Rosburg et al., 2004). In only one study were deviant tones placed in the middle of a train of tones; Rosburg and colleagues (2006) found that their deviant, which differed only by length of tone, did not produce a significant orienting response at P50 or N100. Other researchers have investigated orientation by using deviant tones at the end of a series of standard tones. Viswanathan and Jansen (2010) explored a variety of deviant stimuli at the end of a train of standard stimuli to

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determine if the participant having knowledge of the number of stimuli in the train or type of deviant would impact the response to the deviant stimuli. The results indicated that P50 did not seem to change with knowledge of the length of train or with different deviant sounds, but N100 was decreased when the participant knew the length of the train, and increased when the deviant was complex.

Human experiences are not confined to a series of individual pieces of sensory information. A person experiences a multitude of sensory input at every second and the brain has to organize, filter, and attend to appropriate information. Individuals who have neurological disabilities may not able be to process all the sensory information in their environment and, therefore, exhibit characteristic aberrant behavioral responses to sensory input (Belmonte & Yurgelun-Todd, 2003; Hetrick et al., 2012; Tomchek & Dunn, 2007). A common way that sensory processing difficulties are measured is through self-report behavior surveys. Two such surveys that can be used for adults are the Adolescent/Adult Sensory Profile (A/ASP) (Brown et al., 2001) and the Sensory Gating Inventory (SGI) (Hetrick et al., 2012). The A/ASP measures an individual's ability to modulate sensory information, has been used with many populations, both neurologically intact and otherwise, and has shown good construct validity and internal consistency for its subscales (Brown et al., 2001; Brown, Cromwell, Filion, Dunn, & Tollefson, 2002; De la Marche, Steyaert, & Noens, 2012; Engel-Yeger & Dunn, 2011; Rieke & Anderson, 2009). The A/ASP asks questions about taste/smell processing, movement processing, visual processing, touch processing, activity level, and auditory processing and scores from these questions are summarized into a four quadrant matrix (low registration, sensation seeking, sensory sensitivity, and sensation avoiding). The SGI explores four factors involved in sensory gating: perceptual modulation, distractibility, over-inclusion, and fatigue-stress modulation. The

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survey demonstrates good test-re-test reliability, "substantial convergent validity evidence" (p. 187), and discriminant validity of the factors (Hetrick et al., 2012).

Purpose of this Study

The purpose of this study is to gain a greater understanding of how mature brains process auditory information by examining the P50 and N100 ERP components obtained in response to stimuli in the Orientation/Habituation paradigm thought to reflect automatic sensory processing, as well as to determine if there is a correlation of the sensory gating, habituation, or orientation phenomena to reported sensory behavior. Prior studies in sensory gating have shown that there is a connection between gating and behavior (Hetrick et al., 2012; Kisley et al., 2004). Prior habituation and orientation studies had small sample sizes, focused on people with neurological diagnosis, and have not explored the relationships between performance on EEG paradigms and behavioral measures. By studying how typical adults perform, we will be able to better understand how the mature brain processes auditory information as well as to examine the brain and behavior relationship.

Research Questions and Hypotheses

1. **Sensory Gating.** What are the P50 and N100 sensory gating responses of neurologically typical adult brains and is there a relationship between sensory gating and a person's self-reported behavioral response to sensory information?

   1a. For trains of tones with no deviants, the findings will replicate previous results that show that there is a significant difference in amplitude of P50 and N100 from tone 1 to tone 2.

   1b. There will be a relationship between the amount of sensory gating of P50 and N100 and scores on and scores on the Perceptual Modulation and Over-Inclusion factors on the Sensory Gating Inventory.

2. **Habituation.** How does the typical adult brain process a series of repetitive tones, how is the response influenced by a deviant tone, and is there a relationship between P50 or N100 habituation/dishibituation and a person's self-reported behavioral response to sensory information?

    2a. For trains of tones with no deviants, this study will replicate previous results showing that there will be no significant difference in the amplitude of P50, however there will be a significant difference in the amplitude of N100 in response to tones 2-8.

    2b. In a train with a deviant tone, the tone that follows the deviant will elicit a P50 and N100 response that follows the trend of P50 and N100 amplitudes found for the tones prior to the deviant.

    2c. There will be a relationship between the difference of amplitudes of N100 from tone 2 to tone 8 of the no deviant trains and the scores the Sensation Avoiding and Sensory Sensitivity quadrants of the Adolescent/Adult Sensory Profile and the Perceptual Modulation factor of the Sensory Gating Inventory.

3. **Orientation.** What is the orienting response of P50 and N100 in typical adult brains and is there a relationship between orientation and a person's self-reported behavioral response to sensory information?

    3a. In a train with a deviant tone, the amplitudes of P50 and N100 for the deviant tone will be significantly different than the amplitudes of P50 and N100 for the tone prior to the deviant.

    3b. There will be a relationship between the difference of amplitudes of P50 and N100 from the deviant tone to the prior tone related to the scores on the Distractibility and Over-

Inclusion factors of the Sensory Gating Inventory and the Sensory Sensitivity and

Sensation Avoiding quadrants on the Adolescent/Adult Sensory Profile.

Methods

Participants

All procedures of this study were approved by the University's Institutional Review

Board. Participants in this study were 38 adults, average age of 19.6 years (SD 1.46 years),

39.6% male and 34/38 (89.5%) of the sample was white. Participants were recruited from an

undergraduate university via an online advertisement that listed exclusion criteria. Exclusion

criteria listed included: a history of traumatic brain injury with loss of consciousness (Kisley et

al., 2004), history of neurological disease, psychotic disorders, or bipolar disorder (Lijffijt et al.,

2009), smoking within an hour of the study (Adler, Hoffer, Griffith, Waldo, & Freedman, 1992),

or taking medications, such as antipsychotic medication, linked to affect sensory gating

(Nagamoto et al., 1996). None of the participants were excluded by the researchers; however, it

is unknown how many may have self-excluded based on the online advertisement. Participants

completed an informed consent form and demographic sheet prior to EEG collection.

Data Collection

Procedures. The data analyzed in this study was collected for prior research in the

Brainwaves Research Lab at Colorado State University. For the larger study, participants came

to the lab for two sessions on different days within approximately two weeks of each other. In

each session, EEG data were collected first followed by behavioral data. The EEG and sensory

behavioral data analyzed here were collected during the second lab session. Data that were

collected during the first session will be reported elsewhere. This study involved data analyses to

answer novel research questions. The following explains how the EEG and sensory inventories were collected from these participants.

EEG/ERP collection. For all data collection, the BioSemi ActiveTwo (BioSemi B.V., Amsterdam, Netherlands) EEG/ERP acquisition system was used. Data were collected through 32 channels, 2 reference electrodes placed on the earlobes, 2 electrodes placed over the mastoid bone, and 4 electrodes measuring eye movements. Sampling rate was 1024 Hz. Each participant was seated in a relaxed position and trained on the reduction of artifacts (eye blinks and muscle movement) prior to the collection of data. The tones of the paradigm were presented biaurally through the ER-3A inserted earphones (Etymotic Research) using E-Prime Software (Psychological Software Tools, Pittsburgh, PA, USA).

Orientation/habituation paradigm. The orientation/habituation paradigm consists of three different trains, or series, of stimuli. In each, there are 8 tones with an interstimulus interval (ISI), or time between the stimuli, of 500 ms. See Figure 2.1 for a visual diagram of the series. Standard tones were 1 kHz at 70 dB with a50 ms duration. Deviant tones were 3 kHz tones at 70 dB for 50 ms. The frequencies of 1 kHz for the standard tones and 3 kHz for deviant tones were chosen because in the human primary auditory cortex, neurons that process 1 kHz tones are different than those that process 3 kHz tones (Formisano et al., 2003). One series contained all standard tones, one had the deviant tone in the 4th position, and one had the deviant in the 5th position. The inter-trial interval (ITI), or time between the trains, is 9 seconds on average, with a random ITI between 8 to 10 seconds. Each of the three series was presented in a pseudo random order 80 times. During the presentation of the auditory paradigm, participants were visually distracted by watching a silent animated movie playing on a computer monitor and were not asked to attend to the auditory stimuli.
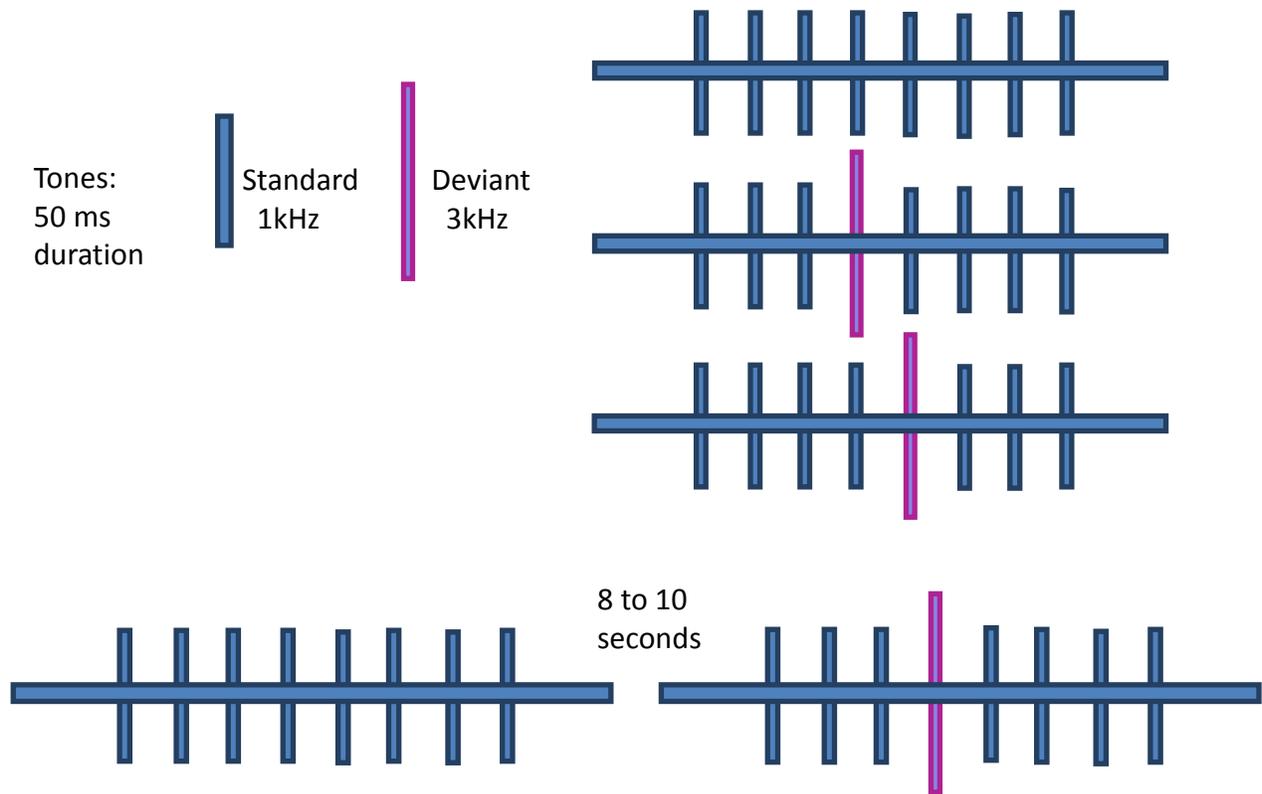
Figure 2.1: A visual representation of the 3 series of tones. Standard tones at 1kHz at 70 dB for 50 ms followed by an ISI of 500 ms. Deviant tones were 3kHz at 70 dB for 50 ms. ITI was 9 seconds on average.

EEG data reduction. EEG data were reduced to produce averaged ERP data using

BrainVision Analyzer2 (Brain Products GmbH, Gilching, Germany, 2002) and Matlab softwares

(The MathWorks, Inc, Natick, Massachusetts, USA). To reduce the ERPs out of the running

EEG data, the data were bandpass filtered appropriately for each component as the brainwave

frequencies associated with P50 and N100 vary. To measure the P50, the EEG data were filtered

from 10 - 75 Hz to capture the high frequency wavelengths expected for this early ERP

component (Chang, Gavin, & Davies, 2010). To measure the N100, the filter was set to .23 - 30

Hz to focus on the slower frequencies associated with early cognitive processing (Stern et al,

2001). For both the data for P50 and N100, the EEG data were then segmented around each

stimulus from 200 ms prior to onset of stimulus until 500 ms after the onset of the final stimulus

in the train. Each segment was baseline corrected from -200 ms to 0 ms, and this baseline taken before the series of tones was used to correct the responses to each stimuli. Artifacts, including eye blinks and muscle movement, were rejected. Then the segments were averaged for each individual. To select which of the 32 electrode sites recorded by the BioSemi to analyze further, t-maps were created in Matlab. The electrode sites that showed component amplitudes that are the most statistically different from zero were selected to continue the data analysis. These sites were Fz, Cz, Pz, C3 and C4. Finally, baseline to peak amplitudes for P50 and N100 were measured using a program in Matlab called PeakPicker (Gavin, Brainwaves Research Lab, Fort Collins, CO, 2009) which recorded the latency and amplitude of each peak into Microsoft Access for further data analysis. P50 amplitudes were recorded as the highest peak in a the 40-70 ms time window, and N100 amplitudes were the most negative trough in the 60-140 ms time window. Each component was then visually assessed to determine if the peak or trough selected was in fact the component of interest and was adjusted on an individual basis. Most peaks were within the above range, however some occurred earlier or later. For P50, there were 4530 data points, with 464 earlier than 40 ms (10.2%), and 539 later than 70 ms (11.9%). The range of P50 latency was 17.58 - 106.45 ms. For N100, there were 4520 data points, with 64 earlier than 60 ms (1.4%), and 151 later than 140 ms (3.3%). The range of N100 latency was 18.55-241.21 ms. Baseline-to-peak measurements were used for both P50 and N100 amplitudes rather than peak-to-peak measurements because there was great variation and unreliability in the N45 component which would have been used to determine the P50 amplitude had peak to peak measures been used. Using baseline-to-peak measurements is common in studies looking at adult brainwaves (Budd et al., 1998; Jerger, Biggins, & Fein, 1992) and has been found to be more reliable than peak to peak measures for P50 gating (Rentzsch, Jockers-Scherubl, Boutros, & Gallinat, 2008).

Sensory behavioral tests. Each participant filled out the Adolescent/Adult Sensory

Profile (A/ASP, 60 questions) (Brown et al., 2001) and the Sensory Gating Inventory (SGI, 36

Questions) (Hetrick et al., 2012) during their second visit to the Brainwaves Research lab. The

data collected from the A/ASP and the SGI were entered into a Microsoft Access file for further

data analysis.

Data Analysis

     Dependent measures. For P50 and N100 gating, amplitudes of the response to stimuli 1

and 2 in the all standard tones series were recorded and a difference (C-T difference) score,

where "C" refers to the conditioning response or response to stimulus 1 and "T" refers to testing

response or response to stimulus 2, was calculated. This dependent measure has been found to be

more reliable than the T/C ratio typically reported in sensory gating literature (Smith, Boutros, &

Schwartzkopf, 1994). For habituation, amplitudes for each component in response to stimuli 2

through 8 of the all standard tone series were recorded for analysis. The difference between the

response to stimulus 2 and stimulus 8 was calculated for correlation analysis with the behavioral

measures. To measure dishabituation, amplitudes for each component in response to stimulus 2

through 8 of the deviant trains were recorded. While orientation can be measured to the first tone

in the series or the deviant tone, this study looks just at orientation to a deviant tone. For the

orientation dependent measure, the amplitudes of each component for the deviant tone and the

prior tone were recorded. Then a difference score, D-P (deviant "D" stimulus minus prior "P"

stimulus), between these responses was calculated for use in correlation with sensory behavioral

measures.

     The dependent measures used for the behavior measures were the subscores on the

A/ASP and the SGI. For the A/ASP, dependent measures were the scores for each of the sensory

quadrants (Low Registration, Sensation Seeking, Sensory Sensitivity, and Sensation Avoiding) and the subscales (taste/smell processing, movement processing, visual processing, touch processing, activity level, and auditory processing). For the SGI, dependent measures were the subscores calculated for each of the four factors (Perceptual Modulation, Distractibility, Over-Inclusion, and Fatigue and Stress Modulation).

Statistical analysis. Descriptive statistics were run for both the ERP component and behavioral data. Most of these data were found to be normally distributed, and for the few that were skewed, non-parametric statistics were consistent with the results found through parametric statistic data analysis. Therefore, all statistics reported are results of the parametric statistics.

To test the hypotheses regarding sensory gating of P50 and N100 (1a), *t*-tests were used to compare amplitudes of P50 and N100 to stimulus 1 and to stimulus 2 at each electrode site (Fz, Cz, Pz, C3, and C4). To determine the relationship between P50 and N100 gating (as measured by the C-T score at each electrode site) and the Perceptual Modulation and Over-Inclusion factors on the SGI (hypothesis 1b), a Pearson product-moment correlation coefficient was calculated.

To test hypothesis 2a regarding habituation, a repeated measures ANOVA with tones as the within factor was run. Results were examined for a significant main effect for tones for P50 and N100 amplitudes. If significant sphericity was found, Greenhouse-Geisser correction was examined to confirm that the main effect remained significant. The tests of within subject contrasts results are reported. Least significant difference (LSD) pairwise comparisons of the amplitudes were calculated among the stimuli of the standard tone series. To address dishabituation (hypothesis 2b), a similar ANOVA analysis was conducted to examine the P50 and N100 amplitudes for stimuli 2-8 of the deviant series and the tests of within subject contrasts

are reported. LSD comparisons between amplitudes of components to the stimulus prior to the deviant and post-deviant were investigated using information from this analysis. Because the deviant stimulus was a significant contributor to the trend analysis results, the ANOVA analysis was repeated excluding the N100 amplitude response to the deviant stimulus to determine the trend of brain responses to just the standard stimuli. Pearson product-moment correlations were performed to identify associations between the brain's ability to habituate, using the difference in amplitude of N100 from stimulus 2 to stimulus 8 of the all standard tones series, and the performance on the Sensation Avoiding and Sensory Sensitivity quadrants of the A/ASP and the Perceptual Modulation factor of SGI (hypothesis 2c). After analysis of the amplitudes of N100 for tones 2 and 8 of the all standard tones series, it was noted there were no statistically significant differences between tone 2 and tone 8. However the trend analysis over tones 2-8 showed significant linear and sometimes cubic trends, with the greatest N100 amplitude difference between stimulus 3 and 7. Because of this, we also chose to run correlations between the difference from stimulus 3 to stimulus 7 and the behavioral measures.

To test orientation in hypothesis 3a, a *t*-test was used to compare P50 and N100 amplitudes to the deviant stimulus and the prior stimulus at each electrode site. Pearson product-moment correlations were used to see if there was an association between the orientation difference score and performance on the Distractibility and Over-Inclusion factors of the SGI and the Sensory Sensitivity and Sensation Avoiding quadrants on the (A/ASP).

<center>**Results**</center>

The Orientation/Habituation paradigm allowed the exploration of gating from stimulus 1 to stimulus 2, habituation over time, and orientation to a deviant stimulus. See Figure 2.2 for an image of the grand average brainwave responses during all three series.

<center>32</center>
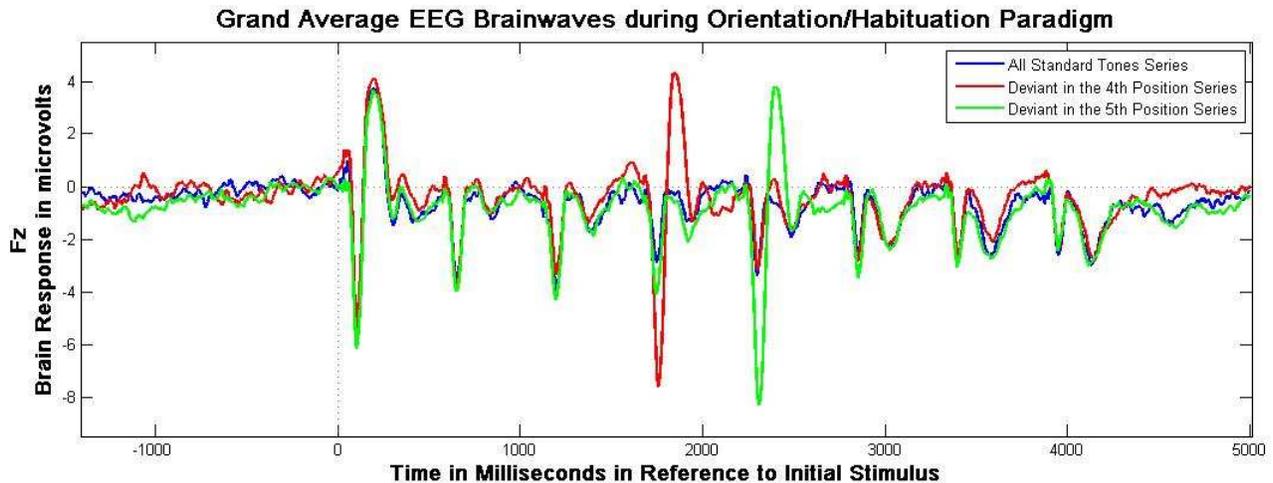
Figure 2.2: Brain responses throughout the Orientation/Habituation paradigm

Question 1: Sensory Gating

In addressing hypothesis 1a, sensory gating in P50 and N100, *t*-tests were performed to see if there was a significant reduction in amplitude of P50 and N100 to a second stimulus. Sensory gating for P50 and N100 was significant for all electrode sites at $p < .0005$. See Table 2.1 for amplitudes of P50 and N100 for tone 1 and tone 2, as well as the *t*-test statistics.

The C-T difference scores for P50 and N100 amplitudes were used as dependent measures of sensory gating to relate to sensory behavior data. There were no significant Pearson product-moment correlations between the C-T difference score at each site and the Perceptual Modulation or Over-Inclusion factors on the SGI. In an exploratory examination of the other behavior data, it was noted that the N100 C-T difference score showed a pattern of correlations (at 4 of the 5 electrode sites) with the Sensation Avoiding quadrant of the A/ASP at Cz ($r(35) = .34, p = .040$), Pz ($r(35) = .33, p = .049$), C3 ($r(35) = .33, p = .050$), and C4 ($r(35) = .33, p = .049$). This suggests that individuals who demonstrate greater gating also demonstrate fewer sensation avoiding behaviors.

Table 2.1: *t*-test Results for Sensory Gating at P50 (N=38) and N100 (N=37)

Electrode Site	Tone 1 Mean P50 amplitude (SD) in microvolts	Tone 2 Mean P50 amplitude (SD) in microvolts	Mean difference of P50 amplitude (SD) in microvolts	*t*-value
Fz	2.61(0.97)	1.49 (0.69)	1.13 (0.94)	7.37*
Cz	2.53 (1.05)	1.33 (0.73)	1.21 (0.96)	7.76*
Pz	1.58 (0.86)	1.01 (0.61)	0.57 (0.72)	4.89*
C3	2.32 (0.99)	1.41 (0.79)	0.90 (0.91)	6.12*
C4	2.20 (0.97)	1.27 (0.70)	0.92 (0.81)	7.08*
Electrode Site	Tone 1 Mean N100 amplitude (SD) in microvolts	Tone 2 Mean N100 amplitude (SD) in microvolts	Mean difference of N100 amplitude (SD) In microvolts	*t*-value
Fz	-7.27 (3.03)	-4.42 (2.66)	-2.84 (2.85)	-6.07*
Cz	-7.71 (3.36)	-3.96 (2.62)	-3.75 (2.89)	-7.89*
Pz	-5.14 (2.30)	-2.29 (2.25)	-2.85 (2.28)	-7.61*
C3	-6.85 (3.12)	-3.88 (2.10)	-2.97 (3.00)	-6.03*
C4	-6.20 (2.57)	-3.55 (2.21)	-2.65 (2.22)	-7.27*

*$p < .0005$

Question 2: Habituation/Dishabituation

The results of the repeated measures ANOVA trend analysis showed a lack of habituation of P50 amplitude over stimuli 2 through 8 during the all standard tones series. See Figure 2.3 for the amplitudes of P50 in response to stimuli 2 through 8 of the all standard tone series. There were no significant linear, quadratic, or cubic trends at any electrode site for the P50 component, however at sites Cz and C3, order four trends were significant. At Cz, $F (1, 37) = 4.27$, $p = .046$; however, there were no significant pairwise comparisons at this site. At C3, $F (1, 37) = 4.50$, $p = .041$, with one significant pairwise comparison between the amplitude of P50 for tone 2 and the amplitude of P50 for tone 7, mean difference = -.26, $p = .022$.

The results of the ANOVA trend analyses for N100 amplitudes showed habituation for Fz, Cz, C3 and C4 during the all standard tones series. See Figure 2.4 for trend analysis graphs and Table 2.2 for all pairwise comparisons. At the Fz electrode site, there were significant linear $(F(1, 36) = 4.70$, $p = .037)$ and cubic trends $(F(1, 36) = 6.12$, $p = .018)$. At Cz, there was a
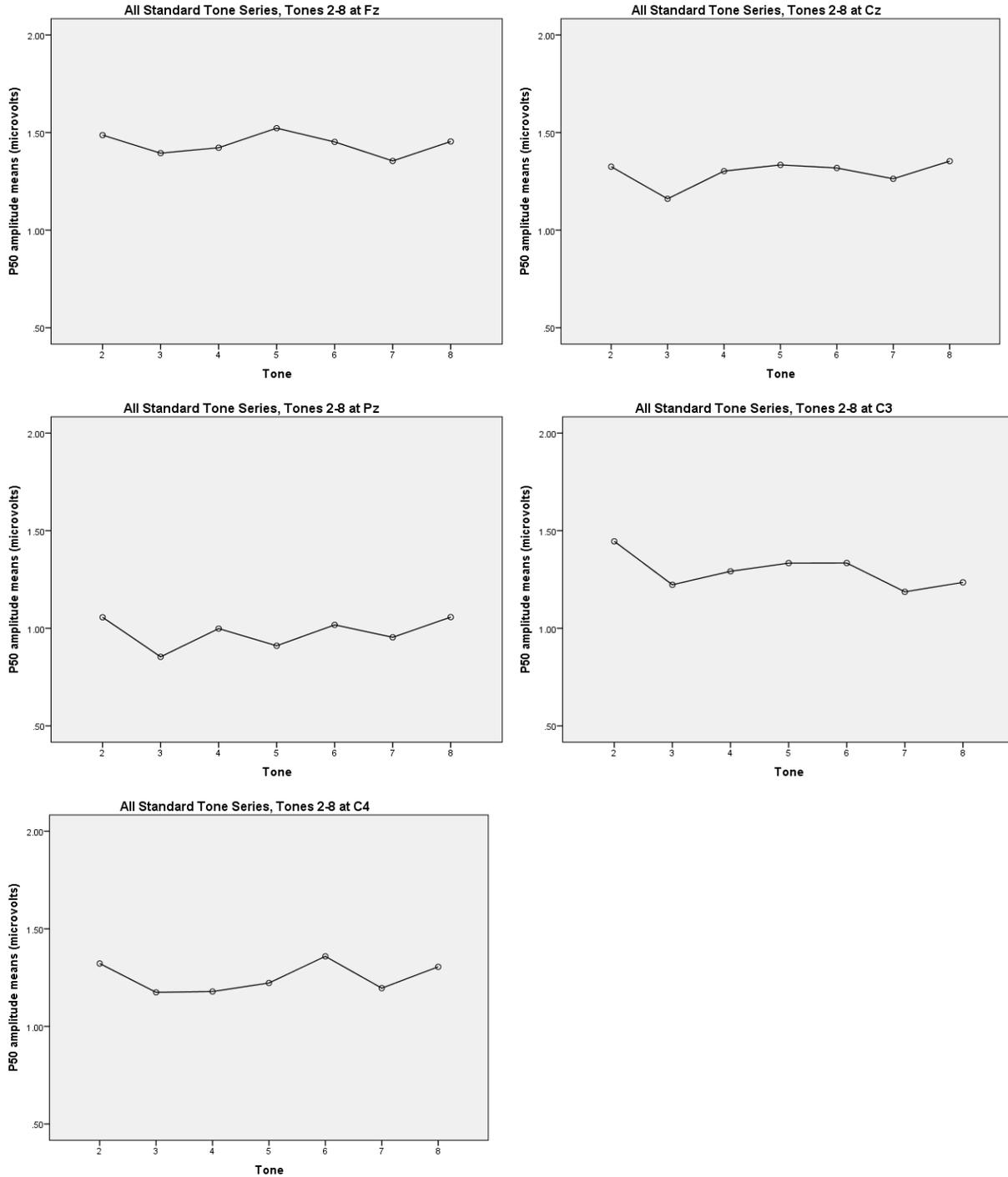
Figure 2.3: ANOVA trend analyses for P50 amplitudes in the all standard tones series, tones 2 through 8, at each of the electrode cites. No significant trends were found for any electrode site.
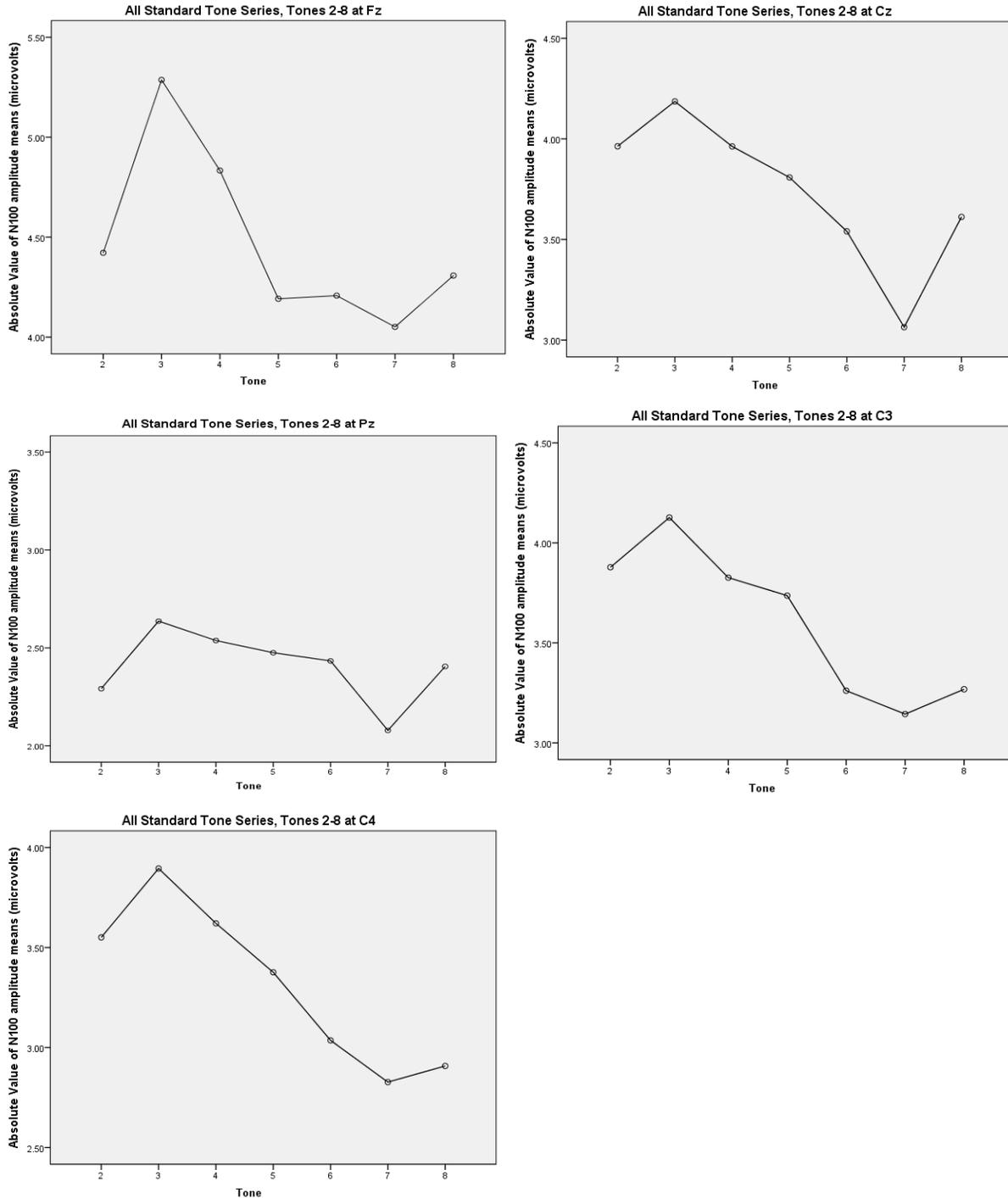
Figure 2.4: ANOVA trend analysis graphs for N100 amplitudes in the all standard tones series, tones 2 through 8, for each of the electrode cites. The N100 graphs depict the absolute value of the amplitude as this more clearly demonstrates the decrease in component amplitude. There is a significant linear trend for all sites except for Pz.

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Table 2.2: Pairwise comparisons of N100 amplitudes with significant mean difference for 4 electrode cites. Pz site is not included as there were not significant comparisons.

Site	Tones	Mean difference	p value	Site	Tones	Mean difference	p value
Fz	2&3	.87	.029	C3	2&7	-.73	.038
	3&5	-1.10	.021		3&6	-.87	.046
	3&7	-1.24	.002		3&7	-.98	.002
	3&8	-.98	.013		3&8	-.86	.014
	4&7	-.78	.029		4&7	-.68	.041
Cz	2&7	-.90	.016	C4	2&7	-.72	.030
	3&7	-1.12	.002		3&7	-1.07	.008
	4&7	-.90	.012		3&8	-.99	.008
	5&7	-.74	.014		4&7	-.79	.025
					4&8	-.71	.030
					5&7	-.55	.049

significant linear trend (F (1, 36) = 7.53, p = .009). Pz did not have any significant trends, nor were there any significant pairwise comparisons. At C3, there was a significant linear trend (F (1,36) = 8.39, p = .006). At C4, there was a significant linear trend (F (1,36) = 10.32, p = .003).

To address dishabituation for P50 (hypothesis 2b), LSD pairwise comparisons for the tone prior to the deviant tone and the tone after the deviant tone were calculated from the ANOVA trend analysis. For example, in the series of tones with the deviant in the 4th position, responses to stimulus 3 and stimulus 5 were compared. For the P50 component in the series of tones with the deviant in the 4th position, there were no significant differences between stimuli 3 and 5 at any electrode site. For the series of tones with the deviant in the 5th position, Cz, Pz, and C4 did not have significant differences between stimuli 4 and 6. These all support the hypothesis that the deviant tone did not dishabituate the brain's response to the standard tones. For the other two sites, there were significant differences between stimulus 4 and stimulus 6, which does not support the hypothesis because the amplitude for P50 at stimulus 6 was significantly greater than the amplitude of P50 at stimulus 4. At Fz, the mean difference between tones 4 and 6 = -.26, p =

.014. At C3, the mean difference between tones 4 and 6 = -.27, *p* = .033. See Figure 2.5 for examples of brain responses that demonstrate no disinhibition (support hypothesis 2b) and that demonstrate disinhibition (do not support hypothesis 2b).

For the N100 component, LSD pairwise comparisons in the repeated measures ANOVA showed no significant difference in amplitude to the stimulus prior to the deviant and the amplitude to the stimulus after the deviant for all electrode sites during the series of tones with the deviant in the 4th position. In the series of tones with the deviant in the 5th position, there

(a)

(b)

(c)

(d)
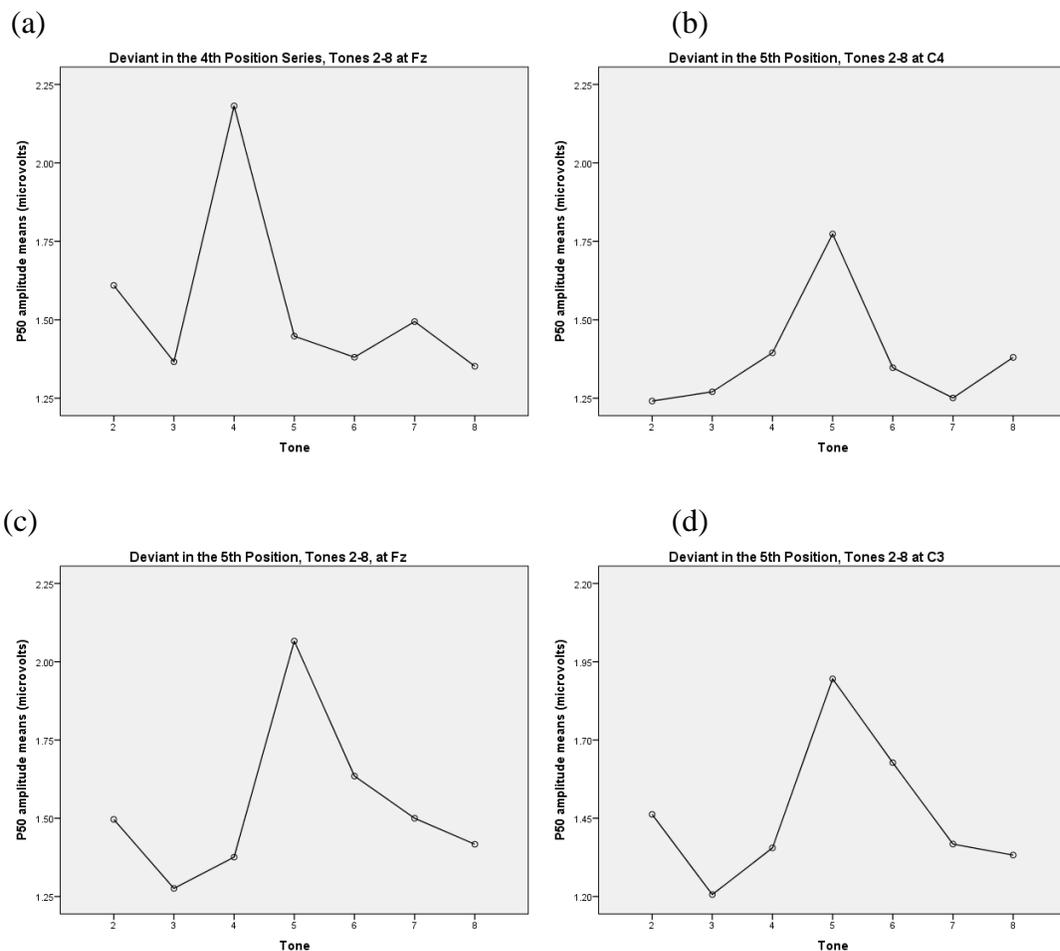
Figure 2.5: Graphs (a) and (b) illustrate examples of P50 amplitudes that show no significant difference between the tone prior to the deviant and after the deviant tone. Graphs (c) and (d) show a significant increase in amplitude to tone 6 from tone 4, which does not support hypothesis 2b.

were no significant difference in amplitude between stimulus 4 and stimulus 6 at electrode sites Pz and Cz. At Fz, Cz, and C4, however, there was a significant decrease in amplitude from stimulus 4 to stimulus 6, indicating significant further habituation after the deviant tone. At Fz, mean difference between stimuli 4 and 6 = -.74, *p* = .047. At Cz, the mean difference between stimuli 4 and 6 = -.94, *p* = .028. And at C4, the mean difference between stimuli 4 and 6 = -.94, *p* = .004. See Figure 2.6 for examples of brain responses that demonstrate no disinhibition, therefore supporting hypothesis 2b, and that demonstrate significant further habituation.

(a)

(b)

(c)

(d)
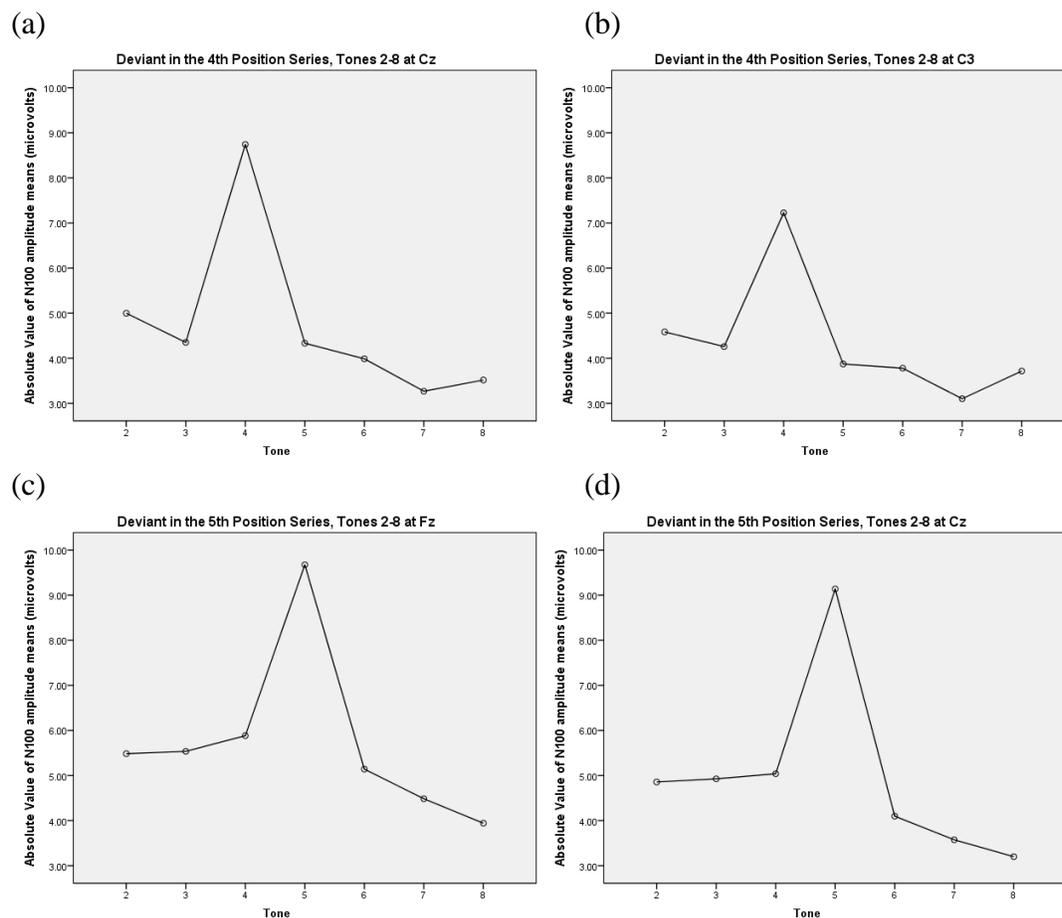
Figure 2.6: ANOVA trend graphs (a) and (b) show no disinhibition from tone 3 to tone 5 (no significant differences). Graphs (c) and (d) demonstrate significant further habituation after the deviant tone as the amplitude to stimulus 6 was significantly smaller than the amplitude to stimulus 4.

In the initial ANOVA trend analysis, there were a number of significant trends that were influenced by the amplitude of N100 to the deviant tone, resulting in each site and series demonstrating quadratic, order 4, and order 6 trends. Therefore, to gain a greater understanding of the behavior of the N100 to the standard tones among the series that contained deviant tones, ANOVA trend analyses were run again with the N100 response to the deviant tone removed. For every electrode site, and in both deviant series, there were at minimum significant linear trends found, see Table 2.3 for the results of the ANOVA trend analyses.

To address the final hypothesis regarding habituation, which asks if there is a relationship of habituation to sensory behavior inventories, Pearson product-moment correlations were run

Table 2.3: ANOVA trend analysis of N100 with deviant tone removed

	N100 LSD Comparisons from Prior- to Post- Deviant	N100 Significant Trend when Deviant Tone is Removed from ANOVA Analysis
Fz (Deviant 4th)	No significant difference	Linear: $F(1,37) = 9.658$, p=.004
Fz (Deviant 5th)	Significant decrease (further habituation)	Linear: $F(1,37) = 21.285$, p<.0005 Quadratic: $F(1,37) = 6.844$, p=.013
Cz (Deviant 4th)	No significant difference	Linear: $F(1,37) = 24.241$, p<.0005
Cz (Deviant 5th)	Significant decrease (further habituation)	Linear: $F(1,37) = 24.037$, p<.0005
Pz (Deviant 4th)	No significant difference	Linear: $F(1,37) = 5.853$, p=.021 Order 4: $F(1,37) = 10.431$, p=.003
Pz (Deviant 5th)	No significant difference	Linear: $F(1,37) = 10.910$, p=.002 Quadratic: $F(1,37) = 5.691$, p=.022
C3 (Deviant 4th)	No significant difference	Linear: $F(1,37) = 9.045$, p=.005
C3 (Deviant 5th)	No significant difference	Linear: $F(1,37) = 16.268$, p<.0005 Quadratic: $F(1,37) = 4.404$, p=.043
C4 (Deviant 4th)	No significant difference	Linear: $F(1,37) = 14.072$, p=.001 Order 4: $F(1,37) = 10.314$, p=.014
C4 (Deviant 5th)	Significant decrease (further habituation)	Linear: $F(1,37) = 17.827$, p<.0005 Quadratic: $F(1,37) = 9.349$, p=.039

using the N100 difference score from stimulus 2 to stimulus 8. The difference score was not

significantly associated with any of the sensory behavior categories hypothesized (Sensory

Sensitivity or Sensation Avoiding on the A/ASP or the Perceptual Modulation subscore of the

SGI). Additionally, after noting the significant linear trends above and that the biggest difference

scores for habituation was not between stimuli 2 and 8 (see Table 2.2 for pairwise differences), a

difference score of N100 between stimuli 3 and 7 was calculated for a more accurate

representation of the habituation phenomena. This difference score also did not correlate

significantly with the Sensory Sensitivity or Sensation Avoiding on the A/ASP or the Perceptual

Modulation subscore of the SGI.

Question 3: Orientation

The *t*-test results comparing the amplitudes of P50 and N100 of the deviant stimulus to

the stimulus prior to the deviant resulted a significant increase in amplitude of each component

to the deviant stimulus. For P50 in the series with the deviant in the 4th and 5th positions, the

orientation response was statistically significant with most pairs demonstrating significance of

$p < .0005$. For orientation in the N100 component, there was a significant difference between the

amplitude of N100 for the deviant stimulus to the prior stimulus at all sites ($p < .0005$). See

Table 2.4 for specifics.

Difference scores (deviant-prior) for P50 and N100 amplitudes were used as a dependent

measure of orientation to test hypothesis 3b which asks whether there is significant relationship

between orientation to the deviant tone and sensory behavior. Pearson product-moment

correlations were run between the orientation measure and the subscales of Distractibility and

Over-Inclusion on the SGI and the Sensory Sensitivity and Sensory Avoiding quadrants on the

A/ASP. The only statistically significant correlation was found in the deviant in the 4th position

Table 2.4: *t*-test Values for Orientation of P50 and N100 (N=38)

Electrode Site	Deviant Tone Mean P50 amplitude (SD) in microvolts	Prior Tone Mean P50 amplitude (SD) in microvolts	Mean difference of P50 amplitude (SD) in microvolts	*t*-value
Fz (deviant 4th)	2.18 (0.90)	1.37 (0.63)	0.82 (0.80)	6.26**
Fz (deviant 5th)	2.07 (0.86)	1.38 (0.66)	0.69 (0.77)	5.54**
Cz (deviant 4th) [#]	2.15 (0.96)	1.33 (0.60)	0.82 (0.76)	6.57**
Cz (deviant 5th)	2.07 (0.88)	1.37 (0.69)	0.69 (0.83)	5.15**
Pz (deviant 4th) [#]	1.33 (0.65)	1.04 (0.49)	0.30 (0.60)	3.02*
Pz (deviant 5th) [#]	1.35 (0.61)	0.96 (0.53)	0.39 (0.80)	2.95*
C3 (deviant 4th)	1.89 (0.87)	1.34 (0.87)	0.55 (0.82)	4.14**
C3 (deviant 5th)	1.89 (0.86)	1.29 (0.64)	0.60 (0.78)	4.77**
C4 (deviant 4th)	1.89 (0.76)	1.23 (0.56)	0.66 (0.84)	4.86**
C4 (deviant 5th)	1.75 (0.93)	1.36 (0.65)	0.39 (0.98)	2.45*

Electrode Site	Deviant Tone Mean N100 amplitude (SD) in microvolts	Prior Tone Mean N100 amplitude (SD) in microvolts	Mean difference of P50 amplitude (SD) in microvolts	*t*-value
Fz (deviant 4th)	-9.38 (3.09)	-4.84 (2.68)	-4.54 (2.26)	-12.39**
Fz (deviant 5th)	-9.67 (3.29)	-5.88 (2.69)	-3.79 (2.80)	-8.35**
Cz (deviant 4th)	-8.74 (3.46)	-4.35 (2.47)	-4.39 (2.27)	-11.90**
Cz (deviant 5th)	-9.14 (3.33)	-5.04 (2.46)	-4.10 (2.98)	-8.48**
Pz (deviant 4th)	-4.67 (2.49)	-2.47 (1.87)	-2.20 (1.84)	-7.38**
Pz (deviant 5th)	-5.93 (2.30)	-3.48 (2.46)	-2.44 (2.41)	-6.25**
C3 (deviant 4th)	-7.23 (3.06)	-4.26 (2.24)	-2.97 (2.58)	-7.10**
C3 (deviant 5th)	-8.09 (3.04)	-4.72 (2.16)	-3.37 (2.16)	-9.61**
C4 (deviant 4th)	-7.13 (2.73)	-3.54 (2.22)	-3.60 (2.06)	-10.79**
C4 (deviant 5th)	-7.49 (2.77)	-4.48 (2.22)	-3.01 (2.27)	-8.17**

N = 37; *p < .05 ** p < .0005

series between the P50 deviant-prior difference score at Cz and C4 with the Over-Inclusion subscale of the SGI. For P50 at Cz and Over-Inclusion, r (35) = -.34 (p = .038) and for P50 at C4 and Over-Inclusion, r (36) = -.37 (p = .024). This means if a person had greater P50 orientation, he or she were likely to experience less "over inclusion", that is, this person was less likely to notice every little thing in the environment.

An exploratory analysis of the orientation-behavior data resulted in several correlations that demonstrated a pattern of occurring minimally in 2 out of 10 opportunities. It is likely that these are not random due to the consistency across sites and condition, and results are as follows: Sensation Seeking on the A/ASP was correlated with 3 out of 10 possible P50 orientation

dependent measures. At Fz, during the series with the deviant in the 4th position, the deviant-prior score was correlated with Sensation Seeking (r (36) = .34, p = .039). At Fz during the series with the deviant in the 5th position (r (36) = .33, p = .042), and at Cz, during the series with the deviant in the 5th position, the deviant-prior score was correlated with Sensation Seeking (r (36) = .34, p = .040). This means that greater P50 orientation amplitude difference is correlated with higher sensation seeking behaviors. P50 orientation was negatively associated with the Fatigue and Stress Vulnerability (FSV) factor on the SGI for 2 of possible 10 dependent measure correlations. During the series of tones with the deviant in the 5th position, the FSV factor was associated with the orientation score at Fz (r (36) = -.36, p = .025) and at C4, (r (36) = -.37, p = .023). This indicates that greater P50 orientation is associated with less fatigue and stress vulnerability. The N100 orientation measure were found to correlate to the touch processing subscale of the A/ASP in 3 of 10 opportunities, at Fz, (r (36) = -.42, p = .009), at Cz, (r (36) = -.46, p = .004) and at C4, (r (36) = -.48, p = .002). This indicates that greater N100 orientation is associated with higher scores on touch processing. The items on the touch processing subscale indicate that a higher score (or marking "almost always") is related to a sensitivity to touch; therefore, larger N100 orientation is associated with greater sensitivity to touch.

Discussion

The results of this study provide information regarding the voltage changes in P50 and N100 ERP components during the neurophysiological phenomena of sensory gating, habituation, and orientation over time and in a novel paradigm - the first to address all of these phenomena in one ERP task. The results confirm that in neurologically typical adults there is significant sensory gating of P50 and N100 and significant orientation to a novel or deviant stimulus. The results also show significant decrease in the amplitude of N100 over time, with or without a

deviant tone present and the data suggest that a refractory period cannot be the major mechanism

for the decrease in amplitude as suggested by prior research. Finally, although there were limited

brain-behavior links, the ones found help demonstrate how neural processing may be manifested

in behaviors.

Sensory Gating

P50 and N100 sensory gating, or suppression of brain response as measured by voltage

changes in the amplitude of ERP components from stimulus one to stimulus two, was confirmed

by the data presented in this study. This would be expected based on the results of a variety of

previous sensory gating studies regarding neurologically typical adults (Kisley et al., 2003;

Rentzsch, Jockers-Scherübl, Boutros, & Gallinat, 2008).

Habituation and Dishabituation

N100 is thought to reflect attention and the initiation of working memory (Boutros et al.,

1999; Lijffijt et al., 2009), so theoretically, it was reasonable to predict that it may be affected by

a short term habituation type paradigm. While other researchers have not found N100 habituation

past the second stimulus in their short term habituation studies (Boutros et al., 1999; Rosburg et

al., 2006; Rosburg et al., 2004), the results of this study undeniably demonstrate significant

linear trend of amplitude reduction of N100 over the course of eight tones. The results that

suggest a lack of disinhibition of N100 subsequent to a deviant stimulus more strongly support

the idea that the brain habituates to standard stimulation even in the presence of a disorienting, or

novel, stimulus. For 7 conditions, there was continued suppression of the components after the

deviant tone, and for Fz, Cz, and C4 during the series of tones with the deviant in the fifth

position, there was even the demonstration of further habituation, that is, the brain responses to

the stimuli after the deviant stimulus were significantly smaller than the ones prior to the deviant

stimulus. Finally, there was, at minimum, a linear trend for all sites during both the deviant in the 4th and 5th position series when the deviant tone was removed for analysis, which supports the hypothesis that suggests the deviant tone will not interrupt the trend of decreasing brain response to the standard tones.

These results suggest that a refractory period could not be the major mechanism for suppression, or decrease in amplitude, of the auditory N100 ERP component. Rosburg, Zimmerer and Huonker (2010) propose that refractory periods are responsible for brain's response to multiple presentations of stimuli, and that if there are gradual decreases in component amplitude, it could be due to two possible explanations. First, it may be due to overlap of ERPs because stimuli are presented too closely together. This could not account for the results in this study for three reasons. One is that we baseline corrected each ERP to the pre-train baseline, which would remove any overlap of cognitive processing from the previous stimulus. Another reason is that our ISI was 500 ms, which was longer than the 400 ms Rosburg and colleagues (2010) reported to be responsible for this overlap. Finally, in the series of tones with deviants, the time between the standard stimuli before and after the deviant is 1050 ms, which is more than enough time to prevent overlap of ERPs. The other way that Rosburg and colleagues (2010) say that a decrease in amplitude could still be due to a refractory period is a processing negativity. Processing negativity indicates that over time, attention to the stimuli declines. Because we baseline corrected the response to each stimulus with the baseline from -200 to 0 ms prior to the first tone we were able to negate a negative drift. As we still showed a trend of decreased amplitude of N100 having corrected in this way, it is not possible for that to be a refractory period in conjunction with processing negativity.

Additionally, both the Rosburg et al. (2010) study and this one used 1000 Hz tones for 50 ms at similar sound pressure (70 dB in our study versus 75 dB in the Rosburg study). The ISI between our standard tones was 500 ms, however during the series with the deviant stimuli, this ISI between standard tones prior to after the deviant increased. For example, in the series of tones with the deviant in the 4th position, the ISI between standard tones at the 3rd and 5th positions was 1050 ms. Using the data reported in the Rosburg study, the response for the longer ISI should be approximately 1 microvolt larger than the 500 ms ISI; this was not seen in our results, further indicating that something other than a refractory period is responsible for the amplitude reduction.

Boutros and colleagues (2013) used EEG in combination with models created from MRI data to attempt to locate the brain regions associated with some neurological processing. They found that orientation to novel stimuli activated areas in the temporal, parietal, and cingulate areas, whereas auditory suppression was related to the pre-frontal cortex. As the pre-frontal cortex is involved in executive functioning, including inhibition, this further suggests that cognitive control may account for the decrease in N100 to multiple stimuli. In fact, Sable et al. (2004) suggest that for stimuli with less than 400 ms ISI, there is a latent inhibition that is responsible for the decrease in amplitude of N100. While that study used different methodology than this one, it is important to note that there may be other neural controls alongside a refractory period responsible for component suppression to multiple stimuli.

As hypothesized, P50, thought to reflect automatic sensory processing (Coles & Rugg, 1995), did not demonstrate habituation during the series of all standard tones, which replicates findings by Rosburg and colleagues (2004; 2006) and Boutros and colleagues (1999). These results do not provide the same strong evidence of a lack of refractory period being responsible

for the decrease in amplitude as found for N100. It may be possible that there is some sort of neural control which is responsible for the P50 suppression found for the post-deviant stimulus in 8 of the 10 deviant series, but as 2 of the 8 did show significant increase, these results do not provide strong evidence for or against any hypothesized mechanism for suppression.

Orientation

The results of this study confirm that both P50 and N100 show significant increases in amplitude to novel information as seen in prior studies (Rosburg et al., 2004; Viswanathan & Jansen, 2010). Because early ERP components are involved in the processing of sensory information, it is not surprising that this was supported (Coles & Rugg, 1995; Stern et al., 2001). The fact that our results demonstrated that our sample appropriately oriented to novel information was critical in helping us interpret the findings for habituation of the N100. Without knowing that there was indeed an orienting response, we would not have been able to say that a deviant did not dishabituate the brain's response to the standard tones.

There is only one other published study at this point that positioned a deviant tone in the middle of a short term habituation paradigm. Rosburg and colleagues (2006) found that when they used a deviant that differed by length of tone they did not find a statistically significant orienting response of P50 or N100. Viswanathan and Jansen (2010) reported that stimulus complexity affects ERP component amplitude, with more complex tones inducing a greater N100. Therefore, it may be possible that stimulus length is not as alerting as the change in frequency of a tone as was done for the current study.

Neural Processing and Sensory Behavior Links

The lack of correlations of the gating response in P50 or N100 to any of the factors of the SGI is surprising, as Hetrick and colleagues (2012) specifically developed the SGI based on the

theory that difficulty in sensory gating is due to difficulty in perceptual and attentional processes. They used factor analysis to confirm the factors involved resulting in the reduction of a 124 question survey to one of 36 questions. This tool has also been correlated with sensory gating using EEG. Kisley and colleagues (2004) found that in healthy adults, less P50 sensory gating ability was correlated with more difficulty with Perceptual Modulation factor, and less N100 sensory gating ability was related to Over-Inclusion factor. Some possible reasons this study did not replicate findings in the Kisley study are that the sample was smaller (38 in this study versus 52 in Kisley's), the Kisley study used an abbreviated 17 question SGI rather than the complete 36 question survey, and Kisley also correlated the behavior measures to a T/C ratio whereas we used a C-T dependent measure. Also, Kisley used a paired click paradigm, the most common sensory gating paradigm. There may be some difference in the brain's response to tones as compared to clicks, or some sort of attention or expectancy experienced by those who listened to the orientation/habituation paradigm in this current study which has eight stimuli instead of the traditional two stimuli for sensory gating. Even though both tones and clicks show gating, there have been no studies to compare gating for a click versus tone paradigms, so the amplitudes to different stimuli may relate to behavioral measures in different ways.

The lack of correlation between sensory behaviors as measured on the A/ASP and SGI and habituation is unexpected especially after changing the dependent measure to reflect the greatest amplitude difference from stimulus 3 to stimulus 7. One explanation may be that the difference score is not the best reflection or way to capture the habituation phenomena. Another may be that using a small sample of 38 neurologically typical adults may not have provided enough variation to truly capture a difference in either the sensory behavior or the EEG brain data, however as the data were normally distributed, it is difficult to determine if this was true.

Correlations between the P50 orientation measure and behaviors indicated that when someone does not appropriately orient to novel stimulus (has a smaller deviant-prior difference in amplitude), they are more likely to notice things in their environment, experience difficulty modulating sensory input when fatigued, and are less likely to seek out sensation. P50 orientation correlated negatively with Over-Inclusion (SGI), which is the idea that a person is aware of more things in their environment than the average person. For example, a person may be unable to select the things in his or her environment that are important to orient to even though he or she notices everything in the environment. Because this result was found with the P50 rather than the N100, this supports the idea that this awareness may be related to automatic processing rather than attention processing. P50 orientation was associated with higher Sensation Seeking behaviors on the A/ASP. What may be happening in this case is that a person who has smaller orientation brain responses does not seek out sensation because their nervous system does not recognize the new information as novel or interesting. They may not experience the pleasure average individuals derive from sensory experiences. P50 orientation was also negatively associated with the Fatigue and Stress Vulnerability factor of the SGI, indicating that the larger orientation to new stimulus, the less likely the person is to experience fatigue and stress vulnerability. On the SGI, an example question for this factor is "when I'm tired sounds seem amplified." It is possible that individuals who are better able to modulate their sensory information even when fatigued would also be more inclined to have greater attention to important stimuli in the environment.

Only one brain-behavior correlation was found for the N100 orientation measure. N100 orientation was associated with higher scores on touch processing on the A/ASP. As the touch processing subscale asks questions from all four sensory quadrants, it is not clear what this

correlation means clinically; however, upon closer look at the individual items, it appears that higher touch processing scores indicate a person is more sensitive to touch. Therefore, the more sensitive someone is to touch, the larger their orientation to novel auditory stimuli.

Overall, there is initial association between brain processing and sensory behaviors in neurologically typical individuals. Further research exploring these connections will be important for furthering the explanations of behaviors, especially for those who experience neurological disorders.

Limitations

Limitations of this study include the use of 38 undergraduate students and no baseline data. Many EEG researcher studies report brain activity in college age students, so our average age of 19.6 is not unusual (Davies, Segalowitz, & Gavin, 2004; Ponton et al, 2000). Other habituation, gating, and orientation studies used samples of individuals with neurological disorders whose average ages were between 34 and 39 years old (Olincy et al., 2000; Rosburg et al., 2004; Rosburg et al., 2006). It would have been a better comparison to those studies to have a larger age range in the current study. Another limitation is that with the multiple series of tones there were no baseline data as to what the brain does without deviant tones. In our results, the amplitude of N100 showed habituation throughout the series, however, demonstrated an increase in response to the final tone at every site. This increase was not statistically significant, however, was a trend that was unexpected and may be representative of some sort of expectation effect as the all standard tones series occurred only 1/3 of the time. This increase to the final tone was not seen in the deviant series. Without having a baseline data set of only standard tones it is difficult to determine what may have caused this phenomenon.

Further research is needed to replicate and fully understand the construct of N100 habituation. As there were only a few correlations that show the brain-behavior connection, this should continue to be an important aspect to include in future research.

Conclusion

In a novel orientation/habituation auditory EEG paradigm used with typical adults, this study showed sensory gating, habituation, and orientation in one data set. We found both P50 and N100 demonstrate sensory gating as well as orientation to novel stimuli and that the P50 does not habituate to stimuli across series of eight tones. For the first time in recent EEG studies, the study confirmed that the N100, an ERP component associated with attention, demonstrated habituation over a series of identical tones, and was not dishabituated when a deviant tone was presented. In fact, for the N100, there was additional habituation occurring following the deviant tone for some of the series analyzed. These results also support the idea that N100 habituation could not be due to a passive refractory period, but must be explained by an active mechanism, like inhibition.

When associated with sensory behavior data, N100 gating was correlated with Sensation Avoiding on the A/ASP, P50 orientation was associated with Over-Inclusion and Fatigue and Stress Vulnerability on the SGI as well as Sensation Seeking on the A/ASP, and N100 orientation was associated with the Touch Processing subscale of the A/ASP. These correlations suggest that the different brain phenomena are associated with different sensory behavior experiences and begin to lay the foundation for further studies on individuals who live with neurological disorders.

CHAPTER 3

Occupational therapists are interested in helping individuals who are limited in their ability to perform activities to engage in the things they need and want to do (American Occupational Therapy Association, 2008). Occupational therapists may work with individuals who experience physical, biological, psychological, or environmental barriers to participation. One type of biological barrier is the nervous system's response to sensory information. Difficulties in sensory processing, or in integrating sensory information within the brain, commonly occur in individuals with autism, schizophrenia, sensory processing disorders, and attention deficit/hyperactivity disorders and may be noticed when the individual displays aberrant behaviors (Belmonte & Yurgelun-Todd, 2003; Hetrick et al., 2012; Tomchek & Dunn, 2007). Individuals with these diagnoses are often referred to occupational therapy because they are not able to participate in their daily activities. Understanding the neural underpinnings of behavior is essential to understanding the "why" of behavior, and can support the development of more effective interventions.

The practice of occupational therapy is informed by a variety of scientific disciplines including occupational science, rehabilitation science, psychology, and exercise science (Yerxa et al., 1990). As such, it is a practice that applies the basic science unearthed by these other disciplines. One area that is important in occupational therapy is the knowledge of typical and atypical neurological development of individuals across the lifespan. Developmental psychologists primarily used behavior assessments to try to understand the brain development in children, but believe "purely behavioral measures are no longer considered adequate" and now explore the brain-behavior development through the use of brain imaging techniques along with behavioral measures (Segalowitz & Schmidt, 2008, p. 7). Bridging this gap is important to

understanding the phenomena, and also forms a base of information that will inform therapy with individuals who have difficulty doing activities because of neurological deficits. Occupational therapist and researcher Carolyn Baum (2009) stressed that individuals in the rehabilitation field fully embrace the idea of multimodal approaches to therapy; that an individual's participation is the ultimate goal of all researchers and practitioners, and this requires the understanding of many levels of rehabilitation. She suggests that improving participation requires the translation of knowledge along a continuum from cellular mechanisms to participation. If occupational therapists are more involved in the design, implementation, and interpretation of basic as well as applied research studies, it may be more likely that the findings will be applicable to occupational therapy practice.

In this research study, translation between the biomedical mechanisms, body function and structure, functional limitation and activity level were explored. Specifically, the biomedical mechanisms involved with the neurological phenomena of sensory gating, habituation, and orientation, as well as the individual's activity level as measured on sensory behavioral inventories. The sensory inventories themselves give more information about the body functions and functional limitations for each individual, but are explored when a person answers questions about their engagement in particular activities. In this controlled environment, the results begin to shed light onto some things an occupational therapist may see in practice.

The EEG results of this study are not specifically linked to what one might see in an occupational therapy clinic, but do provide some valuable information for therapists. This will be especially helpful once data on individuals with disorders is compared to this baseline data from neurologically typical adults. Especially interesting is the idea that typical adults experience a habituation of the N100, which is believed to be a part of the attention system, to multiple

stimuli, and this is not disturbed when a deviant stimuli is presented. This may look like an individual who is able to "habituate" to sound, for example the ambient noise in a coffee shop. When a new sound occurs and alerts the individual, he or she does not have to re-habituate to the ambient noise. Or that we habituate to our clothing, notice when someone or something touches us, but do not then also notice our clothing and have to re-habituate to it. Although we are not able to test such a "real life" experience with EEG, understanding this phenomenon in a controlled environment explains that real situation in a new way and allows us to better understand what is happening at a neurological level because we can limit confounding variables. As studies progress to look at the neurological phenomena of sensory gating, habituation, dishabituation, and orientation in disordered populations, it would not be surprising to find that individuals who have trouble attending, switching attention, or filtering sensory information would not show that same habituation in their ERPs as the group studied here. Those with neurological differences have been shown to process information differently, for example, it has been shown that children with sensory processing disorders process simple auditory stimuli in a different way than their typical peers do (Gavin et al., 2011).

Occupational therapists have long been interested in the brain-behavior relationship. In the case of sensory behaviors, the theory of sensory integration was developed by A. Jean Ayres, occupational therapist and psychologist, in the late 1960s (Parham & Mailloux, 2010). Ayres was interested in the neurobiological explanations for behaviors, and her research informs a practice framework used primarily in pediatric occupational therapy called Ayres Sensory Integration. The brain-behavior connection is important as it validates the theories in which therapists are grounded. For example, the idea that sensory differences exist and they are, at least in part, related to brain processing rather than an attitude or environmental influences.

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Other occupational therapy researchers have explored sensory processing. The Adolescent/Adult

Sensory Profile (A/ASP) was developed in occupational therapy from Winnie Dunn's model of

sensory processing (1997). Her four quadrant model of sensory modulation explains behavior as

being related to the amount of sensory input (neurological threshold) one needs, and the way one

responds to that information. Some of the results of this data correlate specifically with two of

these quadrants (See Figure 3.1). Individuals who are Sensation Seeking have high neurological

thresholds and they seek out stimulation to fill these needs; they tend to be very busy. P50

orientation is correlated with Sensation Seeking in that those who have low sensation seeking

have smaller P50 orientation. This may look like a person whose nervous system does not

recognize new information as novel or interesting, so he or she does not experience the pleasure

that average individuals derive from sensory experiences, and do not seek it out. Individuals who

fall into Sensation Avoiding experience low neurological thresholds and refuse to participate in

activities because they are overwhelmed. This behavior was correlated with the sensory gating of

N100, meaning that the better the individual gated information, the less likely he or she was to be

sensation avoiding. The opposite helps make this clearer: if a person is a

Neurological Threshold Continuum	Behavioral Response Continuum	
	responds in ACCORDANCE with threshold	responds to COUNTERACT the threshold
HIGH (habituation)	Low Registration "I don't notice when my name is called"	Sensation Seeking "I like to go barefoot" *Correlated with P50 orientation measure*
LOW (sensitization)	Sensory Sensitivity "I become bothered when I see lots of movement around me"	Sensation Avoiding "I only eat familiar foods" *Correlated with N100 sensory gating measure*

Figure 3.1: Dunn's Model of Sensory Processing, adapted from Figure 1 in Dunn, 1997, p. 24, with examples of survey questions and correlations to ERP data.

sensation avoider, he or she may have less sensory gating ability, that is, he or she may not be able to "ignore" the repeated stimulus. And if this is uncomfortable for this person, he or she may do whatever it takes to avoid the sensation. One brain-behavior correlation was found for a subscale of the A/ASP. The N100 orientation phenomenon was associated with touch processing. Although the scale asks questions from all four sensory quadrants, a closer look at the individual items reveals that a higher score on each item generally indicates someone is more sensitive to touch. So, it may be that when a person is sensitive to touch, he or she has greater orientation, and in this case, greater attention (because it was the N100 component) to novel stimuli.

Hetrick's (2012) Sensory Gating Inventory (SGI) is not a measure used by occupational therapists, but has been used in EEG research. It identifies four factors involved with sensory gating: perceptual modulation, distractibility, over inclusion, and fatigue and stress modulation (see Table 3.1 for examples of statements from the inventory). The negative association of P50 orientation with both Over-Inclusion and Fatigue and Stress Vulnerability may show up clinically. For example, an individual who is likely to "over-include," that is to notice environmental stimuli, is likely to have smaller P50 orientation. In this case, the individual may have difficulty picking out the important stimuli in an environment to attend to. Another

Table 3.1: Sensory Gating Inventory Factors and Correlations to ERP data

Factor in Sensory Gating	Example Item from the Sensory Gating Inventory	Negative correlation with ERP measure
Perceptual Modulation	"Every now and then colors seem more vivid to me than usual"	
Distractibility	"I have more trouble concentrating than others seem to have"	
Over-inclusion	"I notice background noises more than other people"	P50 orientation
Fatigue-Stress modulation	"When I'm tired, the brightness of lights bother me"	P50 orientation

relationship found was that individuals who are better able to modulate their sensory information even when fatigued would also be more inclined to greater attention to stimuli in the environment (or orientation).

For the occupational therapist, understanding that that there is a connection from the brain processing of sensory information to the behaviors seen is vital to support our general understanding of behavior and to influence our work with individual clients. The results from this study provide the basis for further research into populations of individuals with neurological disorders that are likely to be treated by occupational therapists. Because the brain processing of neurologically typical adults is correlating along the sensory continuum, it may be predicted that if individuals who fell a little further out on the continuum would tell us even more about the brain processing involved in these phenomena.

The demonstration of sensory gating, habituation, and orientation in a novel paradigm is showing promise as a way to understand these neurological phenomena. The understanding of underlying neurological mechanisms, in this case that neurologically typical adults experience sensory gating and orientation to novel stimuli, as well as the increased habituation to stimuli over time which is not disrupted by deviant information, is important for therapists to understand. Continued research through an occupational therapy lens into the specific neurological and behavioral difficulties experienced by their clients will advance the profession's basic understanding and support the development of effective interventions.

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