THESIS

SENSORY REGISTRATION IN CHILDREN WITH HIGH FUNCTIONING AUTISM

Submitted by

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In partial fulfillment of the requirements

For the Degree of Master of Science

Colorado State University

Fort Collins, Colorado

Spring 2015

Master's Committee:

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ABSTRACT

SENSORY REGISTRATION IN CHILDREN WITH HIGH FUNCTIONING AUTISM

Auditory processing is one of the most commonly reported sensory processing impairments in autism spectrum disorders. This study sought to determine whether children with high-functioning autism spectrum disorders (HFA) differ from typically developing children on neurophysiological measures of auditory information processing. We hypothesized that children with HFA would have significant different brain activity when listening to auditory stimuli compared to typically developing children. A cross-sectional quasi-experimental quantitative study design with convenience sampling procedures was employed to compare two groups. Nineteen children with HFA and 19 age- and gender-matched typically developing children, ages 5 to 12 years, participated in this study. Electroencephalography (EEG) recordings were made while participants watched a silent movie and heard random presentations of four auditory stimuli at two different frequencies (1 and 3 kHz) and at two different intensities (50 and 70 dB). The stimuli were presented in 4 blocks of 100 trials each, with 25 trials of each of the stimuli in random order with a 2-second inter-stimulus interval. Amplitude and latency measures were obtained for the P1, N1, P2, N2, and P3 components from the averaged event-related potentials (ERPs) for each of the four auditory stimuli.

An analysis of variance for the ERP components, revealed that children with HFA had significantly smaller N2 amplitudes for the low frequency low intensity tone, and significantly smaller P3 amplitudes to the high intensity at both frequencies stimuli compared to typically developing children. This finding suggests that children with HFA have increased difficulty in

automatic stimuli discrimination and reduced cognitive processing to these auditory stimuli. Children with HFA also had significantly longer P2 latencies for the high intensity high frequency tone compared to typically developing peers, suggesting delayed auditory processing.

In conclusion, this study shows that children with HFA display different brain processing mechanisms to auditory sensory stimuli compared to typically developing children. These differences suggest that the auditory processing deficits observed in children with HFA may arise from atypical neurophysiological functioning related to stimuli discrimination and processing. These results can help practitioners understand the neurophysiological basis of behavioral manifestations of ASD, especially those atypical behaviors that occur in response to sensory experiences in everyday activities. Understanding the specific aspects of sensory processing that are a challenge for children with HFA may provide guidance to the types of treatment strategies that will be most effective.

ACKNOWLEDGEMENTS

Firstly, I thank God Almighty for his unconditional love, abundant blessings and for giving me the wisdom and courage to pursue this research. Thank you Lord!

I am immensely grateful to Dr. Patti Davies for her patient teaching, valuable advice, and constant help from the very beginning. I am indeed blessed to have such a wonderful mentor whose encouragement and belief in me has made me a better researcher. I'd like to thank Dr. Gavin for his encouragement and enthusiasm throughout this research. Thanks to Dr. Blythe for her insightful suggestions and for all the help with recruitment.

I would like to acknowledge my heartfelt gratitude to all the members of the Brainwaves Research Lab. Thanks for all your help in data collection. I'd specially like to thank Brittany and Meiheng for their incredible support throughout and for making the lab such a fun place.

I would especially like to thank my family for believing in me and making it possible for me to study at CSU. Y'all are my inspiration!

Finally, I'd like to thank all the children who agreed to participate in my study and helped me accomplish it.

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CHAPTER ONE

Autism Spectrum Disorders

The prevalence of autism spectrum disorders (ASD) has continues to increase over the last few decades, which can be primarily attributed to wider case definition, better awareness, and earlier recognition (Fombonne, 2007). In the United States, the recent report from the Centers for Disease Control and Prevention (CDC, 2014) documented an ASD prevalence rate of 1 in 68 children. The report also stated that, 31% of children with ASD were classified as having IQ scores in the range of intellectual disability (IQ ≤70), 23% in the borderline range (IQ = 71–85), and 46% in the average or above average range of intellectual ability (IQ >85).

ASD is a neurodevelopmental disorder characterized by persistent deficits in social communication and social interaction as well as restricted, repetitive patterns of behavior, interests, or activities. Deficits in sensory processing, which includes hyper- or hyporeactivity to sensory input are part of the diagnostic criteria for children with autism in *The Diagnostic and Statistical Manual of Mental Disorders* (DSM-5: American Psychiatric Association, 2013). Previous studies suggest that 42% to 95% of the children with autism exhibit sensory processing disorders based on behavioral measures (e.g., Baranek, 2002; Liss, Saulnier, Fein, & Kinsbourne, 2006; Tomchek & Dunn, 2007; Walting et al., 2001). Additionally, several studies suggest auditory brain processing deficits in children with autism (Lincoln, Courchesne, Harms, & Allen, 1995). However, there is limited evidence identifying specific neuropathology underlying sensory processing dysfunction and connecting the neural processing to behavioral manifestations in children with ASD, which warrants further study. In this current study, differences in sensory processing, specifically to auditory stimuli are examined through a neurophysiological approach. A better understanding of the neuropathology underlying sensory

dysfunction can help therapists, parents, and teachers to gain a better understanding of behavioral and performance deficits in children with ASD.

In this chapter, I will first describe the DSM-5 diagnostic criteria of ASD, following which I will explain sensory processing dysfunction in children with ASD. I will then elaborate on the procedure used for data collection, namely electroencephalography (EEG), event-related potential (ERP), and the sensory registration paradigm. Following this, the conceptual description of the study, and the purpose of the study will be discussed.

DSM-5 diagnostic criteria of ASD. The DSM-5 lists five criteria for the diagnosis of ASD. The first criterion includes persistent deficits in social communication and social interaction across multiple contexts. This characteristic could include deficits in social-emotional reciprocity, in nonverbal communicative behaviors, and in developing, maintaining, and understanding relationships (American Psychiatric Association, 2013). The second criterion states a child must have restricted, repetitive patterns of behavior, interests or activities, which can consist of: 1) stereotyped or repetitive motor movements, use of objects, or speech, 2) insistence on sameness, rigidity of routines, ritualized pattern of verbal or nonverbal behavior, 3) highly restricted, fixated interests that are abnormal in intensity or focus, 4) hyper- or hyporeactivity to sensory input or unusual interest in sensory aspects of the environment. Lastly, these symptoms must be present in an early developmental period, cause clinically significant impairment in social, occupational or other areas of functioning, and are not better explained by other intellectual or developmental disabilities (American Psychiatric Association, 2013).

Sensory processing in ASD. Sensory processing refers to the way that sensory information is processed in the brain for the purpose of enabling an individual's engagement in occupation (Johnson-Ecker & Parham, 1999). This concept is synonymous with assumptions in

Ayres (1979) "sensory integration" theory. Ayres' theory postulates that the brain needs to successfully coordinate different sensory information to allow participation in everyday activities. It is postulated that efficient sensory integration results in adaptive behavior, learning, and coordinated movements (Bundy, Lane, Murray, & Fisher, 2002; Kranowitz, 1998). Although atypical behavioral responses to environmental sensory stimuli appear to be common to individuals across the spectrum, there exists a wide range of severity of sensory processing deficits (Baranek, 2002; Watling et al, 2001). These sensory processing deficits have been extensively studied and well documented in literature (Marco, Hinkley, Hill, & Nagarajan, 2011). Studies have also shown that sensory under- and over-responsivity may co-exist in children with ASD (Lane, Young, Baker & Angley, 2010). Sensory processing difficulties have been associated with social, emotional, and behavioral responsiveness in children with ASD (Baker, Lane, Angley, & Young, 2008). Specifically, sensory processing dysfunction can lead to aberrant behaviors in children, in an attempt to make sense of and regulate environmental stimulation (Iarocci & McDonald, 2006). Sensory processing deficits have been reported to occur across all sensory domains, including visual, tactile, vestibular, and auditory modalities (Harrison & Hare 2004; Rogers, 1998). Moreover, these deficits occur in the absence of known peripheral dysfunction such as a visual impairments or hearing loss (Baranek, 2002). In children with ASD, among the sensory domains affected, difficulties in auditory processing were one of the most commonly reported sensory processing impairments occurring around 77.6% of the time (Tomchek & Dunn, 2007).

Auditory processing in ASD. Children with ASD often have poor auditory processing compared to significantly better visual-spatial processing (Gomot, Giard, Adrien, Barthelemy, & Bruneau, 2002; O'Connor, 2012). Greenspan and Weider (1997) reported that in their sample, all

the participants with autism had impairments in auditory processing. Moreover, sensitivity to auditory stimuli in infancy was considered to be a powerful discriminator between children with autism and those without (Dahlgren & Gillberg, 1989). Researchers have found both, hypersensitivity (Lucker, 2013) and hyporeactivity (Guiraud et al., 2011) to auditory stimuli in ASD. Hyper-reactivity in the auditory system (i.e., hyperacusis) can cause abnormal sensitivity to sounds of low or moderate intensity and/or phonophobia which causes discomfort to certain sounds (Gomes, Pedroso, & Wagner, 2008). Hyporeactivity may manifest as a diminished response to name call, which has been found to be a behavioral red flag according to Courchesne, Redcay, Morgan, and Kennedy (2005).

There has been growing interest in understanding the neurophysiological processes underlying sensory processing in ASD and more specifically, understanding auditory processing (Kemner, Oranje, Verbaten, & van Engeland, 2002; Olincy et al., 2000; Orekhova et al., 2008; Perry, Minassian, Lopez, Maron, & Lincoln, 2007). Electrophysiological evidence suggests that children with ASD have impaired automatic detection of change in auditory stimulation. Children with ASD have been noted to have significant impairment in auditory discrimination and respond less to changes in environmental sounds than typically developing peers, with the exception of when they are involved in actively attending to a stimulus (Dunn, Gomes, & Gravel, 2008). Although several investigators have explored sensory processing impairments in ASD, further research aimed at understanding neurophysiological basis of specific aspects of auditory processing is warranted. Functional neurophysiological methods like electroencephalography (EEG) and event-related potentials (ERPs) are commonly used to examine real-time brain activation while the brain processes sensory stimuli (Davies & Gavin, 2007).

Understanding Electroencephalography (EEG)

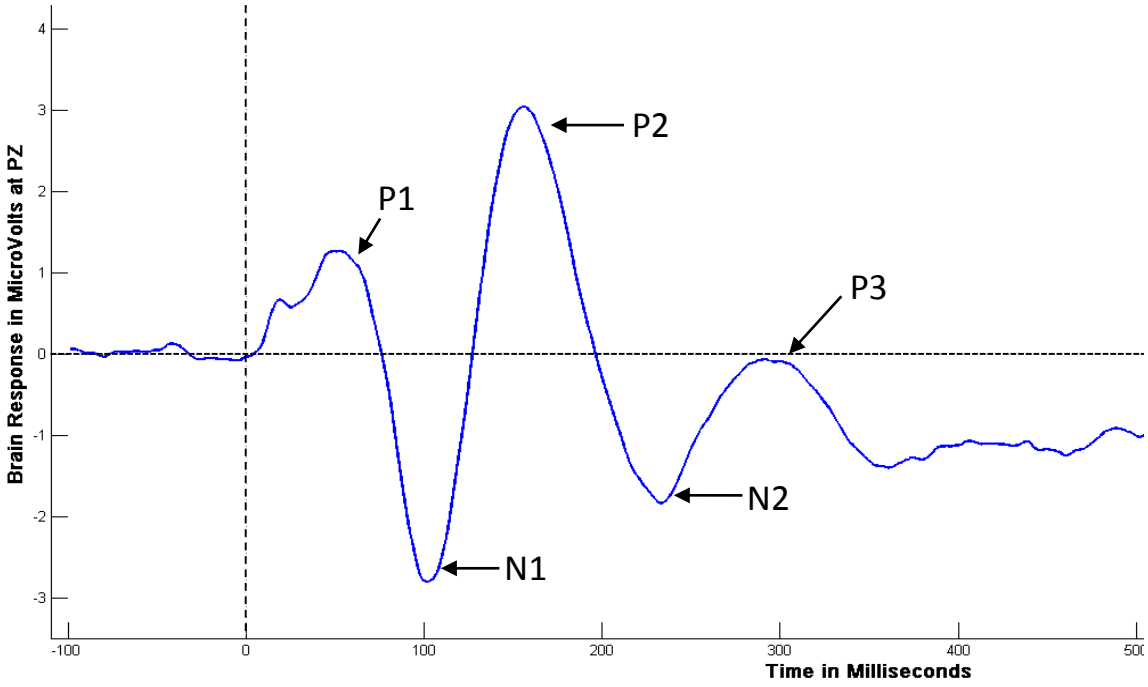
EEG is a non-invasive technique that can measure electrical activity of the brain by means of electrodes positioned on the scalp (Banaschewski & Brandeis, 2007; Davies, Chang & Gavin, 2010). These metallic sensors detect very small (10-50 microvolts) and continuous voltage changes across the scalp, which are then amplified and digitized (Davies & Gavin, 2007). EEG has been widely used for understanding brain functioning and behavior related to sensory processing skills of children with and without disabilities (Banaschewski & Brandeis, 2007; Davies & Gavin, 2007; Gavin & Davies, 2008; Key, Dove, & Maguire, 2005). EEG has also been successfully used to study auditory processing in individuals with ASD (Courchesne, Kilman, Galambos & Lincoln, 1984; Kemner et al, 2002; Olincy et al., 2000; Orekhova et al., 2008; Perry et al., 2007). During data collection researchers have been able to create positive environments for participants that minimize anxiety and fear in children, thus providing a means of maintaining compliance while simultaneously reducing fatigue. Creating a positive environment allows for participants to take breaks, and be comfortable seated alongside researchers and parents (Gavin & Davies, 2008).

Components of an ERP. A running EEG captures the brain response to various sensory and cognitive processing in response to stimuli being presented to the participant. When the running EEG is time locked to the occurrence of a specific stimulus, event related potentials (ERPs) are produced (Yordanova & Kolev, 2008). ERPs are described as graphical displays of changes in the brain's electrical activity associated with the defined event (Jeste & Nelson, 2009) and are obtained by averaging together the segments of the multiple presentations of the specified event (Segalowitz & Davies, 2004). This averaging helps to reduce environmental noise or other background brain processing, and results in a concise ERP associated with the

specified stimulus (Banaschewski & Brandeis, 2007; Luck, 2005; Segalowitz & Davies, 2004; Stern, Ray & Quigley, 2001). Thus, the resulting averaged ERP waveform provides information regarding the temporal aspects of information processing of stimulus events. Generally, the averaged ERP is used when scoring and interpreting ERP components. The aspects of the ERP waveform that can be analyzed include polarity, amplitude, and latency from stimulus onset. These features are associated with certain sensory or cognitive functions (Banaschewski & Brandeis, 2007; Davies et al., 2010; Trainor, 2008).

ERP components are labeled according to the sequence of when the peak occurs. Amplitude is measured in microvolts (μV) and can be positive or negative depending on its polarity, relative to a baseline of zero. Latency refers to the time from stimulus onset, and is usually measured in milliseconds (ms). The ERP components are labeled with a P for positive and an N for negative deflections (see Figure 1). The numbers following the letter represent the first, second, or third peak post-stimulus onset, such as P1 and N1. Additionally, the peaks can also be named to represent the duration in ms from onset, such as P100 and N100. For example, P1 refers to the first positive deflection and the N1 or N100 refers to the first negative deflection occurs about 100 ms after the stimulus presentation (Key et al., 2005; Segalowitz & Davies, 2004). In this study, the peaks will be referred to as P1, N1 and so forth. ERP components generated following an auditory stimulus typically form a positive-negative-positive-negative waveform, which are labeled as P1-N1-P2-N2 (Polich, 1993). Studies have shown that the initial ERP components recorded in response to a stimulus are often described as reflections of automatic or sensory processing, while later components are associated with cognitive processing of the stimulus (Banaschewski & Brandeis, 2007; Stern et al., 2001). More specifically, the P1 and N1 are greatly influenced by parameters of the stimulus, in contrast, the

P3 is known to reflect cognitive processing and has been shown to be larger when participants are told to respond to a stimulus than when they are told to ignore the stimulus (Stern et al., 2001). ERP components record very fine temporal resolutions that detect even the slightest change in patterns of brain activation (Key et al., 2005), which makes this method of data acquisition optimal for collecting measures related to sensory processing.



Studying Sensory Processing Using EEG/ERP Methodology

ERPs has been widely utilized for studying sensory processing in the general adult population and also in several disorders such as schizophrenia (Hasey, & Kiang, 2013), attention deficit hyperactivity disorder (ADHD; Olincy et al., 2000), sensory processing disorders (SPD; Davies et al., 2010), and autism (Kemner et al., 2002; Orekhova et al., 2008). Auditory stimulation has been used most frequently in these studies (Dawson et al., 2002; O'Connor, 2012), although few researchers have used visual or somatosensory (e.g., Arnfred & Chen, 2004) stimulation. Majority of studies investigating developmental changes in sensory processing in

children have used auditory stimuli (e.g., Ceponinené, Rinne, & Näätänen, 2002; Davies, Chang, & Gavin, 2009; Moore & Guan, 2001).

ERP measures provide precise temporal resolution from milliseconds to fractions of milliseconds. Hence, they are ideal measures of evaluating brain responses, because important aspects of sensory processing occur within a few hundred milliseconds. Magnetoencephalography (MEG) has this level of temporal capacity, however, the MEG equipment is often considered more daunting for children compared to EEG. Other types of brain imaging such as *f*MRI, PET, and DTI do not have such precise temporal resolution to observe the changes in brain activity occurring within the first few hundred milliseconds of activation of the central nervous system (Horwitz, & Poeppel, 2002). Thus, there exists sufficient evidence supporting the use of EEG/ERP paradigms in analyzing sensory processing in children with ASD. Individual ERP paradigms are uniquely designed to examine distinct aspects of brain processing. This study will incorporate the *sensory registration paradigm*.

Sensory registration paradigm. The paradigm that will be used in this study was previously used in our lab (Davies & Gavin, 2007) which had been modified from two studies involving children with autism (Bruneau, Garreau, Roux, & Lelord, 1987; Lincoln et al., 1995). This paradigm utilizes auditory tones which are presented at different frequencies and intensities. Four simple auditory stimuli differing in either the pure tone composition (1 kHz or 3 kHz frequency) or the presentation loudness (50 dB or 70 dB intensity) will be used in a manner replicating the procedures used by Lincoln et al. (1995). The term *registration* is used to describe the neurological phenomenon that occurs in response to the presentation of the different auditory stimuli in neuro-typical individuals. More specifically, distinct brain responses are elicited for each of the different auditory stimuli. Accordingly, each tone is uniquely "registered" in the

brain and results in an identifiable and dependable brain response or ERP waveform. Hence, this paradigm is termed as the *sensory registration* paradigm. In the sensory registration paradigm, two ERP components, namely the N1 (the negative deflection occurring about 100 ms post stimulus) and P2 (the positive deflection occurring about 200 ms post stimulus) have been studied due to their sensitivity to changes of stimulus intensity and frequency.

Davies et al. (2010) investigated the brain responses of adults and children with and without sensory processing disorders using the sensory registration paradigm. They demonstrated that adults have a very organized or systematic brain response to changes in the frequency and intensity of the four auditory tones presented in the sensory registration paradigm. In contrast, their study revealed that brain responses of typical children were less organized when compared to adults. Furthermore, the responses of children with SPD were even less organized when compared to typical children and adults.

Davies et al. (2010) also performed two discriminant analyses to determine the relative importance of each component and the nature of the relationship between the components in defining the groups. Their results revealed that 90.5% of the complete sample (adults, typically developing children, and children with SPD) were correctly classified on the basis of brain responses on ERP measures. The second discriminant analysis using only the two child groups, revealed a 95.6% correct classification rate. Davies et al. (2010) state that the results of their study have provided further evidence for the sensitivity of ERP data to detect individual differences and to successfully distinguish between children that are neuro-typical and children that have mild sensory processing deficits. Since sensory processing deficits are almost inherent in children with ASD, results from the Davies et al. (2010) study indicate the potential for use of ERP measures for discriminating this group from typically developing children. Other

researchers have also found that participants with autism did not demonstrate the normal increase in amplitude to increased intensity when compared to children without disabilities (Bruneau et al., 1987; Lincoln et al., 1995). Thus, the results of the above studies emphasize the potential to measure the organization of brain processing of auditory stimuli at different frequencies and intensities in children using the sensory registration paradigm.

ERP Findings in Children with Autism

Few researchers have reported that early ERP components (i.e. P1 and N2) are smaller in children with autism compared to healthy controls to auditory tones ((Bruneau, Bonnet-Brilhaut, Gomot, Adrien & Barthélémy, 2003; Ceponinené et al., 2003; Lepisto et al., 2005) while others have reported no difference in these components in children with autism compared to controls (Salmond, Vargha-Khadem, Gadian, de Haan, & Baldeweg, 2007; Whitehouse & Bishop, 2008). The ERP paradigm differences in these studies could account for some of the inconsistencies in these findings. Using a paradigm similar to the sensory registration paradigm, Lincoln et al. (1995) found no significant N1 and P2 peak amplitude or latency differences in children with autism compared to healthy controls regardless of stimulus type. However, compared to typical children, children with autism did not show an increase in N1 amplitude to increases in auditory stimulus intensity. Temporal auditory responses (N1c) have been reported to be smaller in amplitude with longer latency in children with autism compared to healthy children (Bruneau et al., 1999; 2003). Studies using middle and late-latency ERP components such as P2, N2, and P3 amplitudes and latency measures suggest atypical auditory processing. Smaller auditory N2 amplitudes (Jansson-Verkasalo et al., 2003, 2005; Orekhova et al., 2009) and attenuated P3 amplitudes in children, adolescents, and adults with autism has been reported in few studies (Dunn, Vaughan, Kreuzer, & Kurtzberg, 1999). Longer P2 latencies have also been found in

children with autism (Dunn et al., 1999; Jirsa & Clontz, 1990). In this study, group differences were examined for peak-to-peak amplitude measures of N1, P2, N2, and P3 and latency of P2 component.

Maturation of sensory processing. As mentioned above, researchers have found that brain responses to information processing of sensory stimuli of typical children are less organized and systematic when compared to the brain responses of adults. Maturation of the central auditory system using ERP components has been widely studied in healthy participants (Wunderlich, Cone-Wesson, & Shepherd, 2006). Baseline-to-peak measures of the ERP components were used in these studies (Mahajan & McArthur, 2012; Ponton, Eggermont, Kwong, & Don, 2000). Both amplitude and latency measures exhibit changes well into adolescence. Age-related changes in amplitude tend to be abrupt compared to a more gradual pattern of change in latency measures. In children and adolescents, the amplitude and latency of the auditory P1 appears to reduce with increasing age (Mahajan & McArthur, 2012; Ponton et al., 2000; Wunderlich et al., 2006). The auditory N1 increases in amplitude and decreases in latency until adulthood (Mahajan & McArthur, 2012; Ponton et al., 2000). Although some studies have shown no age related changes in P2 (Wunderlich et al., 2006), others have reported a decrease in amplitude and latency as a function of age (Oades, Dittmann-Balcar, & Zerbin, 1997; Ponton et al., 2000). The auditory N2 decreases in amplitude and latency with increasing age (Mahajan & McArthur, 2012; Ponton et al., 2000). P3 amplitudes increase with age and P3 latency decreases uniformly from 5 years till adolescence (Oades et al., 1997).

Scalp topography (pattern of activation across scalp electrodes) of ERP peaks have also shown to change as a result of maturation. The auditory P1 is relatively stable in children with a predominantly fronto-central distribution (Kurtzberg, Hilpert, Kreuzer, & Vaughan, 1984;

Mahajan & McArthur, 2012; Oades et al., 1997). The N1 has been found to have a diffuse pattern of activation over a large area of scalp with a few studies reporting strong fronto-central distribution pattern (Kurtzberg et al., 1984; Mahajan & McArthur, 2012; Oades et al., 1997). The P2 moves to a fronto-central distribution from a posterior distribution with age (Ponton et al., 2000). As with P1, the N2 also remains stable at fronto-central sites in children (Ponton et al., 2000).

There are numerous factors responsible for age-related ERP changes. Amplitude changes are assumed to reflect maturation of the neural generators of auditory processing. These developmental changes may arise due to non-linear synaptic pruning of cortical synapses, changes in grey and white matter tissue (Whitford et al., 2007) and rapid hormonal changes affecting neurotransmitter activity of the ERP-generating neurons (Mahajan & McArthur, 2012). Changes in ERP magnitude over time may also be influenced by changes in location and/or orientation of the neural processes generating the response (Wunderlich et al., 2006).

To understand auditory development in children with SPD, researchers have investigated developmental trends in sensory gating measures. Sensory gating is a neurological process that filters out irrelevant stimuli, thus preventing sensory overload of higher brain functions (Magnée, Oranje, van Engeland, Kahn, & Kemner, 2009). Typical children demonstrated improved detection of simple auditory stimuli as a function of being older. More specifically, sensory gating improved with increasing age. However, no such relationship between age and sensory gating was obtained for children with SPD (Davies et al., 2009). This suggests that neuro-typical children show maturation of brain processing of auditory stimuli, while children with SPD do not show a systematic change in brain processing as a function of age (Davies et al., 2009).

Functioning levels in children with ASD. Traditionally, researchers employing electrophysiological measures have studied children with high-functioning autism, who are more cooperative and can be easily trained to sit through EEG procedures (Cantor, Thatcher, Hrybyk, & Kaye, 1986). High-functioning autism can be described as having age-appropriate language abilities and an IQ above 80. This is synonymous with the DSM-IV category of Asperger's syndrome, which included social impairment and restricted and repetitive behaviors in the diagnostic criteria, with no history of significant delay in spoken language and self-help skills, adaptive behavior and curiosity about the environment in childhood (4th ed., text rev.; *DSM–IV–TR*; American Psychiatric Association, 2000). Few researchers have employed electrophysiological measures on children with low functioning autism. In the past, researchers have collected data while these children were either given drugs or restrained (Hermelin & O'Connor, 1970). Ferri et al. (2003) studied children with low functioning autism (diagnosis of autism and intellectual disability) using EEG and showed that significant ERP changes can be observed even in non-cooperative children with autism. Orekhova et al, (2008) examined sensory gating using EEG in children with high functioning autism, and children with autism who also had intellectual disability. They found that children with high functioning autism had similar sensory gating as typically developing peers but children with autism and intellectual disability has significantly poorer sensory gating. This study suggests that the functioning levels of children with autism have an impact the neurological phenomena being assessed (Orekhova et al., 2008). This present study examines auditory information processing in children with high functioning autism. Thus the results of this study may not be generalized to the entire spectrum of disorders in autism.

Obtaining feasibility data. Studies that are investigating novel phenomena are usually tested as pilot study methodology. A pilot or a feasibility study aims to determine the practicability of phenomena being studied (Porta, 2008) and whether a larger study is practical (Jeray & Tanner, 2012). Thus, they are usually designed as a small-scale version of a larger study that will be done in the future. To assess feasibility, researchers answer questions of data trends, effect sizes and conduct power analysis (LaGasse, 2013). The results obtained from power analyses and effect sizes can then be used in *a priori* sample size calculations for a larger study (Thabane et al., 2010) and can provide useful information about the clinical relevance of the study components (LaGasse, 2013). Researchers have suggested different estimates of a minimum sample size for feasibility studies ranging from a minimum of 12 per group (Julious, 2005) to a minimum of 30 participants. Due to the exploratory nature of the components being analyzed in this study, feasibility and power analysis will be conducted as in a pilot study. The effect sizes obtained will provide valuable information to calculate sample size for a larger study.

Purpose and Questions

Sensory processing is a very complex neurological process. The sensory registration paradigm has been successfully used to explore the fine intricacies of auditory sensory processing (Lincoln et al., 1995). The purpose of this study is to better understand auditory processing in children with ASD using electrophysiological measures. The study will examine group differences in auditory processing using ERP measures. These measures include differences in amplitudes, latencies and/or sites between groups for the four tones. Group differences in amplitudes would reflect differences in intensity of processing, while latency differences would imply differences in processing speed. Group differences for site would suggest differential activation patterns during processing, and allude to possible differences in

brain regions involved during processing. The data obtained will also be analyzed to examine whether a developmental trend exists in auditory processing. Furthermore, data will be analyzed using discriminant analysis to assess whether individual differences in ERP components can accurately classify children according to their diagnostic category (typically developing versus high functioning autism). Discriminant analysis is a form of multiple regression to predict a categorical dependent variable (grouping variable) by one or more continuous independent variables. Understanding the neuropathology underlying sensory processing can shed light on observed behavioral deficits in children with ASD, providing parents, teachers, and therapists with a greater understanding of how to best provide optimal learning and play environments for achieving desired outcomes.

Research Questions and Hypotheses

Question 1:

Can sensory registration be assessed using ERP components?

Hypothesis 1: Sensory registration can be assessed using ERP components.

Question 2:

Is there evidence of differences in brain processing of auditory stimuli, as measured by electroencephalography, in children with high functioning autism (HFA) compared to children who are typically developing?

Hypothesis 2: Children with HFA will have significantly different amplitudes for the P3 and different latencies for P2 components of the sensory registration paradigm compared to neuro-typical children.

Question 3:

Will neuro-typical children and children with HFA demonstrate a developmental trend in relation to information processing of auditory stimuli?

Hypothesis 3: Typical children will demonstrate a maturational trend, i.e. information processing of auditory stimuli will improve as a function of age, with larger N1 amplitudes and smaller N2 amplitudes with increasing age, while this trend will be absent in children in HFA.

Question 4:

Can individual differences in the ERP components collected using the sensory registration paradigm be used to accurately classify children according to their diagnostic category?

Hypothesis 4: The ERP components collected using the sensory registration paradigm will be able to correctly classify children according to their diagnostic category.

CHAPTER TWO

Autism spectrum disorder (ASD) is a neurodevelopmental disorder characterized by persistent deficits in social communication and social interaction as well as restricted, repetitive patterns of behavior, interests, or activities (DSM-5: American Psychiatric Association, 2013). Deficits in sensory processing, which includes hyper- or hyporeactivity to sensory input are part of the diagnostic criteria for children with autism in *The Diagnostic and Statistical Manual of Mental Disorders* (DSM-5: American Psychiatric Association, 2013). Previous studies suggest that 42% to 95% of the children with autism exhibit sensory processing disorders (e.g., Baranek, 2002; Liss, Saulnier, Fein, & Kinsbourne, 2006; Tomchek & Dunn, 2007; Walting et al., 2001). Evidence supporting deficits in processing auditory sensory information in children with autism exists (Lincoln et al., 1995). Children with ASD often have poor auditory processing compared to significantly better visual-spatial processing (Gomot et al., 2002; O'Connor, 2012). Greenspan and Weider (1997) reported that in their sample, all the participants with autism had impairments in auditory processing. Moreover, sensitivity to auditory stimuli in infancy was considered to be a powerful discriminator between children with autism and those without (Dahlgren & Gillberg, 1989).

There has been growing interest in understanding the neurophysiological processes underlying sensory processing in ASD and more specifically, understanding auditory processing (Kemner et al., 2002; Olincy et al., 2000; Orekhova et al., 2008; Perry et al., 2007). Electrophysiological evidence suggests that children with ASD have impaired automatic detection of change in auditory stimulation (Dunn et al., 2008). Although several investigators have explored sensory processing impairments in ASD, further research aimed at understanding neurophysiological basis of specific aspects of auditory processing is warranted. Functional

neurophysiological methods like electroencephalography (EEG) and event-related potentials (ERPs) are commonly used to examine real-time brain activation while the brain processes sensory stimuli (Davies & Gavin, 2007).

Electrophysiological Measures

EEG has been widely used for understanding brain functioning and behavior related to sensory processing skills of children with and without disabilities (Banaschewski & Brandeis, 2007; Davies & Gavin, 2007; Gavin & Davies, 2008; Gavin et al., 2011; Key, Dove, & Maguire, 2005). EEG has also been successfully used to study auditory processing in individuals with ASD (Kemner et al, 2002; Olincy et al., 2000; Orekhova et al., 2008; Perry et al., 2007). When the running EEG is time locked to the occurrence of a specific stimulus, event related potentials (ERPs) are produced (Yordanova & Kolev, 2008). ERPs are described as graphical displays of changes in the brain's electrical activity associated with the defined event (Jeste & Nelson, 2009) and are obtained by averaging together the segments of the multiple presentations of the specified event (Segalowitz & Davies, 2004). The aspects of the ERP waveform that can be analyzed include polarity, amplitude, and latency from stimulus onset. These are associated with certain sensory or cognitive functions (Banaschewski & Brandeis, 2007; Davies et al., 2010; Trainor, 2008). ERP components are labeled according to the sequence of when the peak occurs. Amplitude is measured in microvolts (μV) and can be positive or negative depending on its polarity, relative to a baseline of zero. Latency refers to the time from stimulus onset, and is usually measured in milliseconds (ms). The ERP components are labeled with a P for positive and an N for negative deflections (see Figure 1). The numbers following the letter represent the first, second, or third peak post-stimulus onset, such as P1 and N1. Additionally, the peaks can also be named to represent the duration in ms from onset, such as P100 and N100. For example,

P1 refers to the first positive deflection and the N1 or N100 refers to the first negative deflection occurs about 100 ms after the stimulus presentation (Key et al., 2005; Segalowitz & Davies, 2004). Studies have shown that the initial ERP components recorded in response to a stimulus are often described as reflections of automatic or sensory processing, while later components are associated with cognitive processing of the stimulus (Banaschewski & Brandeis, 2007; Stern et al., 2001). ERP components generated following an auditory stimuli typically form a positive-negative-positive-negative waveform, which are labeled as P1-N1-P2-N2 (Polich, 1993). ERP components record very fine temporal resolutions that detect even the slightest change in patterns of brain activation (Key et al., 2005), which makes this method of data retrieval optimal for collecting measures related to sensory processing.

Sensory Registration Paradigm

The paradigm used in this study was previously used in our lab (Davies & Gavin, 2007) which had been modified from two studies involving children with autism (Bruneau et al., 1987; Lincoln et al., 1995). This paradigm utilizes auditory tones which are presented at different frequencies and intensities. Four simple auditory stimuli differing in either the pure tone composition (1 kHz or 3 kHz frequency) or the presentation loudness (50 dB or 70 dB intensity) were used in a manner replicating the procedures used by Lincoln et al. (1995). The term *registration* is used to describe the neurological phenomenon that occurs in response to the presentation of the different auditory stimuli to neuro-typical individuals. More specifically, distinct brain responses are elicited for each of the different auditory stimuli. Accordingly, each tone is uniquely "registered" in the brain and results in an identifiable and dependable brain response or ERP waveform. Hence, this paradigm is termed as the *sensory registration* paradigm. In the sensory registration paradigm, two ERP components, namely the N100 (the

negative deflection occurring about 100 ms post stimulus) and P200 (the positive deflection occurring about 200 ms post stimulus) have been studied due to their sensitivity to changes of stimuli intensity and frequency.

Davies et al. (2010) investigated the brain responses of adults and children with and without sensory processing disorders using the sensory registration paradigm. They demonstrated that adults have a very organized or systematic brain response to changes in the frequency and intensity of the four auditory tones presented in the sensory registration paradigm. In contrast, their study revealed that brain responses of typical children were less organized when compared to adults. Furthermore, the responses of children with SPD were even less organized when compared to typical children and adults. When compared to adults, children demonstrated smaller peak-to-peak amplitudes in both N1 and the P2 components. In some cases, children showed less distinction between loud and soft auditory stimuli. In contrast, the peak-to-peak amplitudes in both N2 and P3 components were larger in children compared to adults, and children frequently demonstrated more distinction between loud and soft stimuli than compared to adults.

Davies et al. (2010) also performed two discriminant analyses to determine the relative importance of each component and the nature of the relationship between the components in defining the groups. Their results revealed that 90.5% of the complete sample (adults, typically developing children, and children with SPD) were correctly classified on the basis of brain responses on ERP measures. The second discriminant analysis using only the two child groups, revealed a 95.6% correct classification rate. Davies et al. (2010) state that the results of their study have provided further evidence for the sensitivity of ERP data to detect individual differences and to successfully distinguish between children that are neuro-typical and children

that have mild sensory processing deficits. Thus, the results of the above studies emphasize the potential to measure the organization of brain processing of auditory stimuli at different frequencies and intensities in children using the sensory registration paradigm.

ERP Findings in Children with Autism

Few researchers have reported that early ERP components (i.e. P1 and N2) are smaller in children with autism compared to healthy controls to auditory tones ((Bruneau, Bonnet-Brilhaut, Gomot, Adrien & Barthélémy, 2003; Ceponinené et al., 2003; Lepisto et al., 2005) while others have reported no difference in these components in children with autism compared to controls (Salmond et al., 2007; Whitehouse & Bishop, 2008). The ERP paradigm differences in these studies could account for some of the inconsistencies in these findings. Using a paradigm similar to the sensory registration paradigm, Lincoln et al. (1995) found no significant N1 and P2 peak amplitude or latency differences in children with autism compared to healthy controls regardless of stimulus type. However, compared to typical children, children with autism did not show an increase in N1 amplitude to increases in auditory stimulus intensity. Temporal auditory responses (N1c) have been reported to be smaller in amplitude with longer latency in children with autism compared to healthy children (Bruneau et al., 1999; 2003). Studies using middle and late-latency ERP components such as P2, N2, and P3 amplitudes and latency measures suggest atypical auditory processing. Smaller auditory N2 amplitudes (Jansson-Verkasalo et al., 2003, 2005; Orekhova et al., 2009) and attenuated P3 amplitudes in children, adolescents, and adults with autism has been reported in several studies (Dunn et al., 1999; Lincoln et al., 1995). Longer P2 latencies have also been found in children with autism (Dunn et al., 1999; Jirsa & Clontz, 1990). In this study, group differences were examined for peak-to-peak amplitude measures of N1, P2, N2, and P3 and latency of P2 component, with the hypothesis that children with autism

will have significantly different P3 amplitudes and P2 latency measures compared to typically developing children.

Several researchers have been using ERPs to assess auditory processing in children with autism and thus, an understanding of the development of auditory processing in this population is essential. Maturation of the central auditory system using ERP components has been widely studied in healthy participants (Wunderlich et al., 2006). Baseline-to-peak measures of the ERP components were used in these studies (Mahajan & McArthur, 2012; Ponton, Eggermont, Kwong, & Don, 2000). Both amplitude and latency measures exhibit changes well into adolescence. Age-related changes in amplitude tend to be abrupt compared to a more gradual pattern of change in latency measures. Developmental changes were largest for N1 and N2 amplitudes. The auditory N1 increases in amplitude while the auditory N2 decreases in amplitude as a function of age (Mahajan & McArthur, 2012; Ponton et al., 2000; Wunderlich et al., 2006). This study focused on the maturation of N1 and N2 amplitudes. Davies and Gavin (2007) reported that compared to typically developing children, children with SPD did not show a systematic change in brain processing as a function of age. Together, there exists evidence supporting auditory processing dysfunction in children with autism and further research exploring this mechanism, along with developmental effects is necessary.

The purpose of this study is to better understand auditory processing in children with ASD. The study will examine group differences in auditory processing using ERP measures. These measures include differences in amplitudes, latencies and/or sites between groups for the four tones. Group differences in amplitudes would reflect differences in intensity of processing, while latency differences would imply differences in processing speed. Group differences for site would suggest differential activation patterns during processing, and allude to possible

differences in brain regions involved during processing. The data obtained will also be analyzed to examine whether a developmental trend exists in auditory processing. Furthermore, data will be analyzed using discriminant analysis to assess whether ERP components can accurately classify children according to their diagnostic category (typically developing versus high functioning autism). Understanding the neuropathology underlying sensory processing can shed light on observed behavioral deficits in children with ASD, providing parents, teachers, and therapists with a greater understanding of how to best provide optimal learning and play environments for achieving desired outcomes. The study's first hypothesis is that sensory registration can be assessed using ERP components. The second hypothesis is that children with HFA will have significantly different amplitudes for the P3 and different latencies for P2 components of the sensory registration paradigm compared to neuro-typical children. The third hypothesis is that typical children will demonstrate a maturational trend, i.e. information processing of auditory stimuli will improve as a function of age, with larger N1 amplitudes and smaller N2 amplitudes with increasing age, while this trend will be absent in children in HFA. And the fourth hypothesis is that the ERP components collected using the sensory registration paradigm will be able to correctly classify children (above chance) according to their diagnostic category.

Methods

Participants

Thirty-eight children, ages 5 to 12 years (M = 8.71, SD = 2.01), participated in the study. Nineteen of these children (4 girls, 15 boys) had a medical or psychological diagnosis of high-functioning autism (HFA)/Asperger's disorder and were referred to the project from local clinics and support groups. The control group consisted of 19 age- and gender-matched typically

developing children. Parent reports were obtained for typical children as a screening questionnaire developed in our lab to ensure that the children participants were free of neurological injuries, disabilities, and family histories of psychological disorders. The children were recruited from the local community from girls and boys clubs, as well as advertisements at the local university and by word of mouth. Parents of children with HFA filled out the Asperger Syndrome Diagnostic Scale (Myles, Bock, & Simpson, 2001) which was used to confirm the diagnosis. Parent permission and child assent were obtained from all participants. After completing their first session, participants were compensated with a small thank you gift. Following the second session, participants received $15. All procedures used in this study were approved by the institutional review board of the local university.

Data Collection

Procedures. Upon volunteering, parents of the participants were mailed an information packet with consent forms and the Sensory Profile and were contacted to schedule two visits. The second visit was scheduled at least 3 days later but within 2 weeks of the first visit, and at the same time of day as the previous visit. This was done in an attempt to control for confounding performance factors. On the first visit, parent permission/consent, and child assent was obtained and testing procedures were reviewed. Time was allowed to build rapport with the children by answering any questions and sharing photos of previous child participants wearing the EEG cap and electrodes. One half of each visit was spent collecting EEG data (about 1 hour) and the other half was spent on behavioral assessments (about 1 hour). Data from the behavioral assessments are not used in this study. Only EEG data from the first visit will be used for this study and thus, the EEG data from the second visit will not be described.

On the first visit, the EEG data was collected while having each participant sit in a comfortable position in a chair, with pillows, and footstools if necessary. Once the EEG cap, and electrodes were applied, the child was given a brief training on strategies to reduce artifacts resulting from eye blinks, and other muscle activity. A brief click stimulus (3 ms) and a stepping procedure (Levitt, 1971) was used to assess the hearing threshold of the participants on the first visit. Each participant completed a series of three EEG paradigms. During the first visit each participant completed the sensory gating and the sensory registration paradigm. The data from the sensory registration paradigm was used in the current study. The presentation order of the two paradigms were counterbalanced. Each paradigm lasted around 20 minutes. Participants were given 2-3 minute breaks between the paradigms.

EEG/ERP data recording. All EEG data were collected using the BioSemi ActiveTwo EEG/ERP Acquisition System (BioSemi, Wg-Plein 129, 1054 SC Amsterdam, Netherlands). This system includes 32 Ag/AgCl sintered electrodes, with 8 additional flat electrodes. Four flat electrodes measured electro-oculograms (EOGs); two electrodes were placed on the left supraorbital and infraorbital region to record vertical eye movements, and two were placed lateral to the external canthus of each eye to measure lateral eye movement. Two flat electrodes were placed on the left and right earlobes and used as the offline reference. Additionally, two flat electrodes were placed on the left and right mastoids. A Common Mode Sense (CMS) active electrode and a Driven Right Leg (DRL) passive electrode served as the reference and ground (http://www.biosemi.com/faq/cms&drl.htm). For the sensory registration paradigm, tones were administered in both ears through the ER-3A inserted earphones (Etymotic Research) using E-Prime Software (Psychological Software Tools, Pittsburgh, PA, USA). Data was sampled at a rate of 1024Hz with a bandwidth of 0 to 268 Hz.

Sensory registration paradigm. In this paradigm, continuous EEG signals were recorded while the participant watched a silent animated movie (Wallace and Gromit) on a computer screen while the auditory stimuli were presented. The auditory stimuli (50 ms in duration with a 10 ms rise/fall time) consisted of pure tones (sinusoidal waves), two with frequencies at 1 kHz and two at 3 kHz, and each frequency was presented at either one of two intensity levels, 50 dB SPL or 70 dB SPL. The stimuli were presented in blocks of 100 trials, 25 trials of each of the stimuli, in random order with a 2-second inter-stimulus-interval. Four blocks of trials were presented with each block, taking about 3.5 minutes. At the conclusion of each block, the participant was given a 30-second break to rest his or her eyes, blink, or move about in the chair.

ERP Waveform and Component Analysis

Brain Vision Analyzer 2 (Brain Products GmbH, Gilching, Germany, 2002) and Matlab software (The MathWorks, Inc, Natick, Massachusetts, USA) were used for the analyses of the EEG and ERP data. Averaged ERPs were composed from the running EEG data. First, the four EOG channels were converted to a vertical and a horizontal bipolar EOG. Then data were filtered with a bandpass of .23 – 30 Hz. Following this, the EEG data were segmented about each of the four auditory stimuli with duration of 200 ms pre-stimulus onset to 800 ms post-stimulus onset. Baseline correction was performed on each segment using EEG data 200 ms prior to stimulus onset. Next, an eye regression technique designed to remove eye movement from trials (Segalowitz, 1996) was performed. Following this, an artifact rejection technique that eliminates segments with deviations greater than $\pm$ 100 µV on any of the EEG channels or the bipolar EOG channels was performed. The segments retained after eye regression and artifact rejection were averaged. Of the 32 channels, the central sites Fz, Cz, and Pz were analyzed based on previous

studies using the sensory registration paradigm (Davies et al., 2010). Peak amplitudes for the P1, N1, P2, N2, and P3 were identified using the Matlab software, PeakPicker program (Gavin, Brainwaves Research Lab, Fort Collins, CO, 2009). The window for determining the peaks was based on previous published research (Davies et al. 2010) and visual inspection of the grand average waveforms for the participants. The N1 component was scored between 70 and 170 ms and the P1 between 20 and 80 ms; the peak-to-peak amplitude of the N1 component was defined as the difference in μV between the N1 peak amplitude and the P1 peak amplitude. The P2 component was identified as the most positive peak between 130 and 270 ms after the stimulus onset and peak-to-peak amplitude was defined as the difference in μV between the N1 peak and the P2 peak. The N2 component was identified as the most negative peak between 200 and 375 ms after the stimulus onset and the peak-to-peak amplitude was defined as the difference in amplitude between the P2 peak and the N2 peak. The P3 component was identified as the most positive peak between 250 and 450 ms after stimulus onset. The peak-to-peak amplitude of the P3 component was defined as the amplitude difference between the N2 peak and the P3 peak. Microsoft Access was used to record and track the amplitudes and latencies of chosen peaks.

Data Analysis. To determine if brain processing of auditory stimuli differed significantly among children with HFA and typically developing children, peak-to-peak amplitudes of the N1, P2, N2, and P3 components were analyzed using a 2 x 3 x 2 x 2 repeated measures analysis of variance (ANOVA). The between subjects factor was group (2 levels: typical children and children with HFA). The three within factors were Site (Fz, Cz, Pz), Frequency (2 levels: 1 kHz and 3 kHz), and Intensity (2 levels: high and low). While averaging the ERP waveform, group differences in the temporal variability of ERP peak amplitudes and latency can cause unwanted attenuation of the ERP peak. To control for this effect, differences in the number of segments

between groups was tested in order to determine whether the amplitudes would need to be adjusted. When applicable, Greenhouse-Geisser corrections were used to adjust for violation of the assumption of homogeneity of variances as is reflected in the degrees of freedom. For the third hypothesis, Pearson's correlations between age and amplitudes of the N1 and N2 components (baseline-to-peak) were performed. Baseline to peak measurements were used here to be consistent with previous studies examining maturation of ERP components. For the fourth hypothesis, discriminant analysis was used to evaluate whether individual differences in ERP components can accurately classify children into their diagnostic category. Based on the results of second hypothesis, P3 amplitude measures to specific tones were used as variables for predicting diagnostic categories. All statistical analyses were performed using the Statistical Package for Social Sciences (SPSS), version 22.0. Alpha was set at 0.05 for the a priori hypotheses.

Results

Descriptive Data

The number of averaged segments for each of the four tones between the two groups were not significantly different (t (36) = -.90, p = .38) and hence, a correction for the number of segments was not considered necessary in the analyses. For typically developing children, N1 and P2 amplitude measures were missing from 8 children, 9 children had missing N2 peaks and 2 children had missing P3 peaks. For children with HFA, 5 children had missing N1, P2, and N2 peaks and 1 child had missing P3 peaks. Prior to the statistical analyses, the data were assessed for normality. The Kolmogorov-Smirnov test of normality was not significant for a majority of the peak-to-peak ERP component amplitudes for both groups indicating a normal distribution. Only 3 of the 24 measures violated the assumption of normality, i) P3 amplitude at Cz for low

frequency low intensity tone for typically developing children, ii) N1 amplitude at Cz for high frequency high intensity tone for both groups, iii) P2 amplitude at Fz for low frequency low intensity tone for children with HFA. Group difference of the amplitudes of these components were assessed using the ANOVA statistic, which is robust to violations of normalcy (Schmider, Ziegler, Danay, Beyer, & Bühner, 2010). Hence, parametric statistics were used for all of the analyses.

The grand averaged ERP waveforms for the four auditory stimuli were overlaid and are shown separately for typical children and children with HFA for the Fz (midline frontal), Cz (midline central), and Pz (midline parietal) sites in Figure 2. The mean and standard deviation of the peak-to-peak amplitudes of the N1, P2, N2, and P3 components for each group are reported in Table 1. Visual inspection of these ERP components indicate that typical children demonstrate a more organized brain response to changes in frequency and intensity of the auditory stimuli as compared to children with HFA. Children in both groups show larger brain responses to the high intensity tones compared to the low intensity tones, but this pattern is more distinct in typical children than children with HFA. Children with HFA appear to have smaller N1 and P2 amplitudes for all the four tones at Cz and Pz sites, and smaller P3 amplitudes at the Fz site compared to typically developing children.

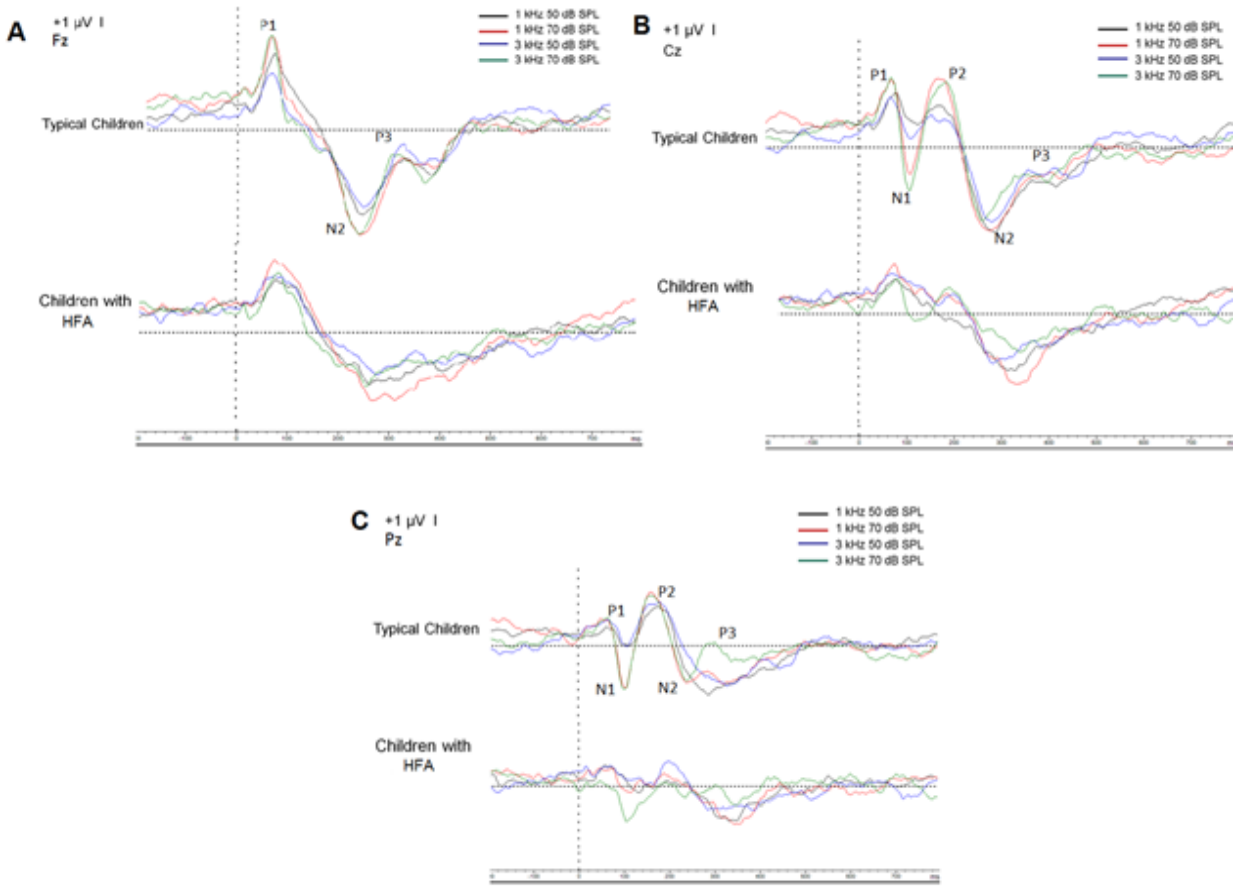


Figure 2. (A) Grand averages of the ERPs at Fz site (B) Grand averages of the ERPs at Cz site (C) Grand averages of the ERPs at Pz site.
The stimuli were filtered with a bandpass of 0.23-30 Hz with 200-ms baseline prior to the stimulus. The black line represents the auditory stimulus presented at 1 kHz 50 dB SPL. The red line represents the 1 kHz 70 dB SPL stimulus. The blue line represents the 3 kHz 50 dB SPL stimulus and the green line represents the 3 kHz 70 dB SPL stimulus. Positive voltage is up.

Table 1

Mean peak-to-peak amplitude (in μV) of the ERP components for each auditory stimulus for both groups. (Standard deviations are shown in parenthesis).

	Group					
Auditory	Typical Children			Children with HFA		
Stimulus	Fz	Cz	Pz	Fz	Cz	Pz
1 kHz 50 dB SPL						
N1	-6.16 (3.96)	-5.87 (3.33)	-4.17 (3.28)	-5.53 (3.01)	-4.93 (2.61)	-4.11 (2.25)
P2	4.10 (2.56)	6.69 (3.87)	6.19 (4.27)	3.93 (2.82)	4.76 (3.84)	4.44 (3.05)
N2	-10.38 (4.98)	-11.33 (4.24)	-8.59 (3.60)	-8.23 (3.53)	-7.87 (4.40)	-5.94 (2.71)
P3	7.20 (3.89)	6.88 (3.13)	4.89 (1.99)	5.59 (2.16)	5.41 (2.09)	4.76 (1.99)
1 kHz 70 dB SPL						
N1	-9.75 (4.96)	-8.72 (5.53)	-6.70 (3.66)	-7.25 (5.14)	-6.88 (4.89)	-5.76 (3.07)
P2	6.76 (3.11)	10.61 (8.12)	9.69 (4.54)	7.34 (3.78)	9.86 (5.95)	8.23 (3.86)
N2	-11.73 (4.43)	-13.82 (6.28)	-10.30 (3.53)	-12.64 (5.22)	-13.67 (3.81)	-9.26 (2.94)
P3	9.08 (3.47)	7.71 (3.36)	6.25 (2.12)	6.90 (2.44)	7.64 (2.75)	6.89 (3.01)
3 kHz 50 dB SPL						
N1	-8.35 (4.61)	-6.91 (3.91)	-4.56 (2.92)	-5.62 (3.50)	-6.16 (2.91)	-4.50 (2.50)
P2	4.75 (2.51)	6.74 (3.59)	5.99 (3.00)	5.70 (3.40)	6.94 (3.97)	5.29 (3.57)
N2	-8.05 (4.12)	-9.15 (4.07)	-8.62 (2.88)	-9.27 (3.70)	-9.73 (3.55)	-7.72 (3.09)
P3	7.60 (2.80)	6.43 (2.45)	4.92 (2.82)	5.90 (3.02)	5.99 (2.88)	5.42 (2.20)
3 kHz 70 dB SPL						
N1	-9.62 (3.74)	-9.74 (5.67)	-6.75 (2.88)	-8.70 (5.60)	-8.90 (4.96)	-6.07 (2.79)
P2	5.89 (3.41)	10.47 (8.82)	8.41 (4.62)	7.64 (4.62)	11.27 (7.75)	7.96 (4.62)
N2	-10.36 (4.57)	-12.92 (6.14)	-8.89 (4.01)	-9.71 (4.27)	-11.47 (4.84)	-7.66 (3.12)
P3	9.23 (2.71)	8.37 (3.08)	6.79 (2.89)	6.91 (2.52)	7.29 (3.22)	7.01 (3.91)

ERP Comparison Results

To answer hypothesis 2, group differences in peak-to-peak amplitude measures of N1, P2, N2, and P3, and latency of P2 between children with HFA and typically developing children are presented below.

The ANOVA evaluating the N1 component revealed significant main effects of site (F (2, 46) = 8.15, p = .001, η_p^2 = .26), and intensity (F (1, 23) = 25.62, p < .001, η^2 = .52). Post-hoc tests indicated that electrode sites Cz (M = -7.95) and Fz (M = -7.70) had significantly larger amplitudes than Pz (M =-6.04, p's < .006). Additionally, high intensity tones (70 dB) had larger N1 amplitudes (M = -8.58) compared to the low intensity tones (50 dB; M = -5.88, p < .001). Site x Intensity interaction approached significance (F (2, 46) = 3.03, p = .058, η^2 = .17). No other significant interaction effects were found. The effect size (η^2) for the between-subjects effect was 0.045 and observed power was .169.

The ANOVA evaluating the P2 component revealed significant main effects of site (F (1.5, 46) = 15.92, p < .001, η^2 = .41) and intensity (F (1, 23) = 55.46, p < .001, η^2 = .71). Post-hoc tests indicated that electrode sites Cz (M = 10.31) had significantly larger amplitudes than Fz (M = 6.56) and Pz (M =8.23, p's < .002). Similar to N1, high intensity tones had larger P2 amplitudes (M = 10.43) compared to the low intensity tones (M = 6.23, p < .001). A significant Site x Frequency interaction (F (2, 46) = 1.53, p = .02, η^2 = .16) and Site x Intensity interaction (F (1, 46) = 12.86, p < .001, η^2 = .36) was observed. No other significant effects were found. The effect size (η^2) for the between-subjects effect was 0.012 and observed power was .079.

The ANOVA evaluating the N2 component revealed significant main effects of site (F (1.5, 44) = 14.26, p < .001, η^2 = .39) and intensity (F (1, 22) = 16.54, p = .001, η^2 = .43). Post-hoc tests indicated that electrode sites Cz (M = -12.07) and Fz (M = -10.35) had significantly

larger amplitudes than Pz (*M* =-8.87, *p's* < .01). Similar to N1 and P2 amplitudes, high intensity tones had larger N2 amplitudes (*M* = -11.62) compared to the low intensity tones (*M* = -9.18, *p* = .001). A significant Site x Intensity interaction was observed (*F* (2, 44) = 7.73, *p* = .001, η^2 = .26). Frequency x Intensity interaction approached significance (*F* (1, 22) = 4.26, *p* = .051, η^2 = .16). No other significant effects were found. The effect size (η^2) for the between-subjects effect was 0.017 and observed power was .09. Post hoc *t* tests of N2 amplitude at the four tones revealed significant group differences for the low frequency, low intensity tone at sites Cz (*t* (33) = -2.37, *p* = 0.024) and Pz (*t* (35) = -2.53, *p* = 0.016).

The ANOVA evaluating the P3 component revealed significant main effects of site (*F* (1.6, 66) = 13, *p* < .001, η^2 = .28) and intensity (*F* (1, 33) = 13.79, *p* < .001, η^2 = .29). Post-hoc tests indicated that electrode sites Fz (*M* = 7.44) had significantly larger amplitudes than Pz (*M* = 5.93, *p* < .001) and Pz had significantly smaller amplitudes than Cz (*M* = 7.10, *p's* < .001). Similar to the other ERP components, high intensity tones had larger P3 amplitudes (*M* = 7.53) compared to the low intensity tones (*M* = 6.11, *p* = .001). A significant Group x Site interaction (*F* (2, 66) = 7.65, *p* = .001, η^2 = .19) was observed. Typically developing children had highest amplitudes for the P3 component at Fz whereas children with HFA had highest amplitude for P3 at Cz (See figure 3). The P3 component was further explored using a 2 x 2 x 2 analysis of variance at Fz site. The between subjects factor was group (2 levels: typical children and children with HFA). The two within factors were Frequency (2 levels: 1 kHz and 3 kHz) and Intensity (2 levels: high and low). A significant main effect of group (*F* (1, 35) = 9.13, *p* = .005, η^2 = .21) was observed. Post-hoc t tests revealed that children with HFA had significantly smaller P3 amplitudes to the high intensity tones at 1 kHz frequency (*t* (36) = 2.22, *p* = 0.03) and high intensity tones at 3 kHz frequency (*t* (36) = 2.73, *p* = 0.01).

Analysis of Latency of P2 Component

The ANOVA evaluating the P2 latency revealed a main effect of site approaching significance (F (2, 24) = 3.15, p = .06, η^2 = .21). A significant Frequency x Group interaction effect was observed (F (1, 25) = 7.39, p = .012, η^2 = .23). Typical children had longer latency for the high frequency (3 kHz) tones than low frequency (1 kHz) tones, whereas children with HFA had longer latency for the low frequency tone than high frequency tones. No other significant effects were found. Post-hoc t tests for P2 latency at Pz revealed significant group difference for the high frequency, high intensity tone (t (26.7) = -2.39, p = 0.024) with longer latency for children with HFA (M = 197.42 ms, SD = 45.73) than typically developing children (M = 169.25 ms, SD = 23.23).

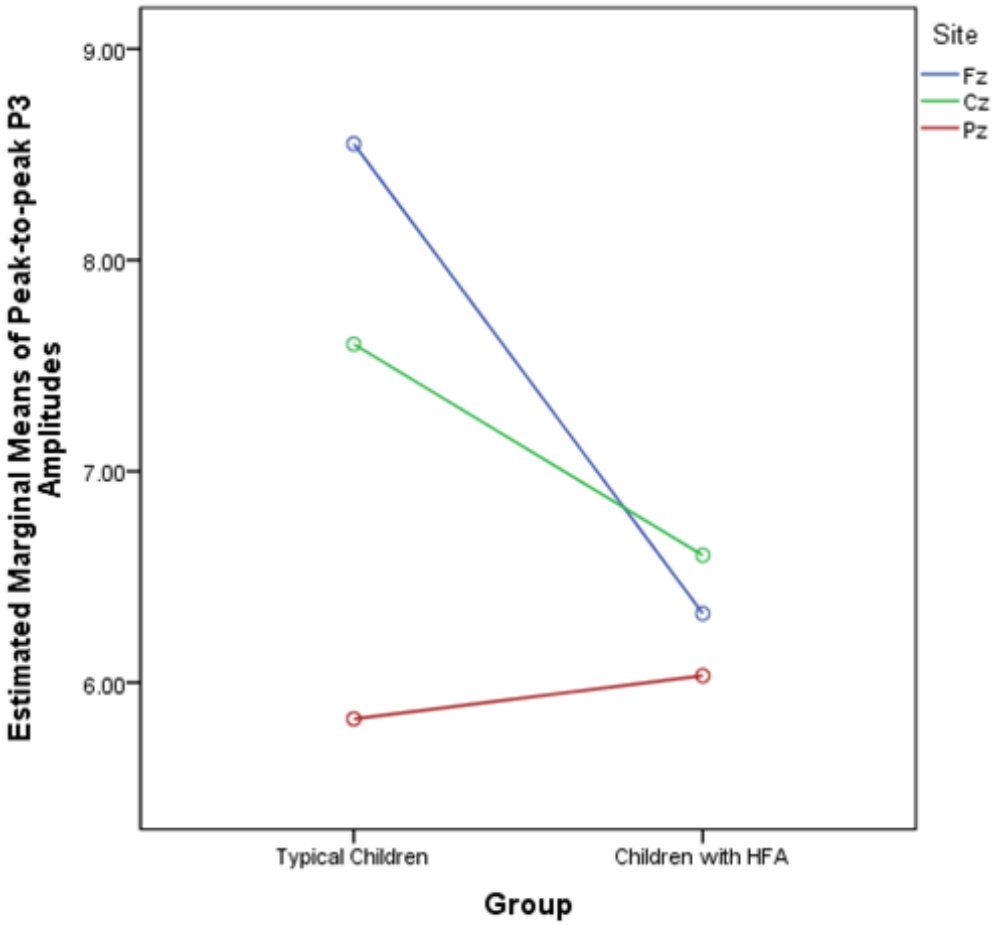


Figure 3: Site x group interaction for the peak-to-peak P3 amplitude

Maturation Analysis

In order to determine if typically developing children and children with HFA demonstrate a developmental trend in relation to information processing of auditory stimuli, Pearson's correlations of age with N1 and N2 amplitudes (baseline to peak) were performed. For the entire sample, a moderate negative correlation was found between age and N1 amplitudes at the high frequency high intensity tones at Fz (r = -0.43, p = 0.011). This indicated that as age increased, N1 amplitudes increased (See figure 4). The correlation coefficient here is negative, since more negativity in N1 amplitudes indicate larger amplitudes. N2 amplitudes were not significantly correlated with age (r = .044, p = 0.79). Separate correlations were performed for each group to further assess this developmental trend. For children with HFA, a significant moderate negative correlation was found between age and N1 amplitudes at the high frequency high intensity tones at Fz (r = -0.51, p = 0.038). This indicated that as age increased, N1 amplitudes increased. This relationship was not significant for typically developing children (r = -0.34, p = 0.18). For typical children, a moderate positive correlation was found between age and N2 amplitudes at the high frequency high intensity tones at Fz which approached significance (r = 0.45, p = 0.05). This suggests that N2 amplitudes reduce as age increases in typically developing children. This relation was not significant for children with HFA (r = -0.14, p = 0.57). In our sample, typically developing children had larger variation in N2 amplitudes (SD = 2.96) compared to children with HFA (SD = 2.02).

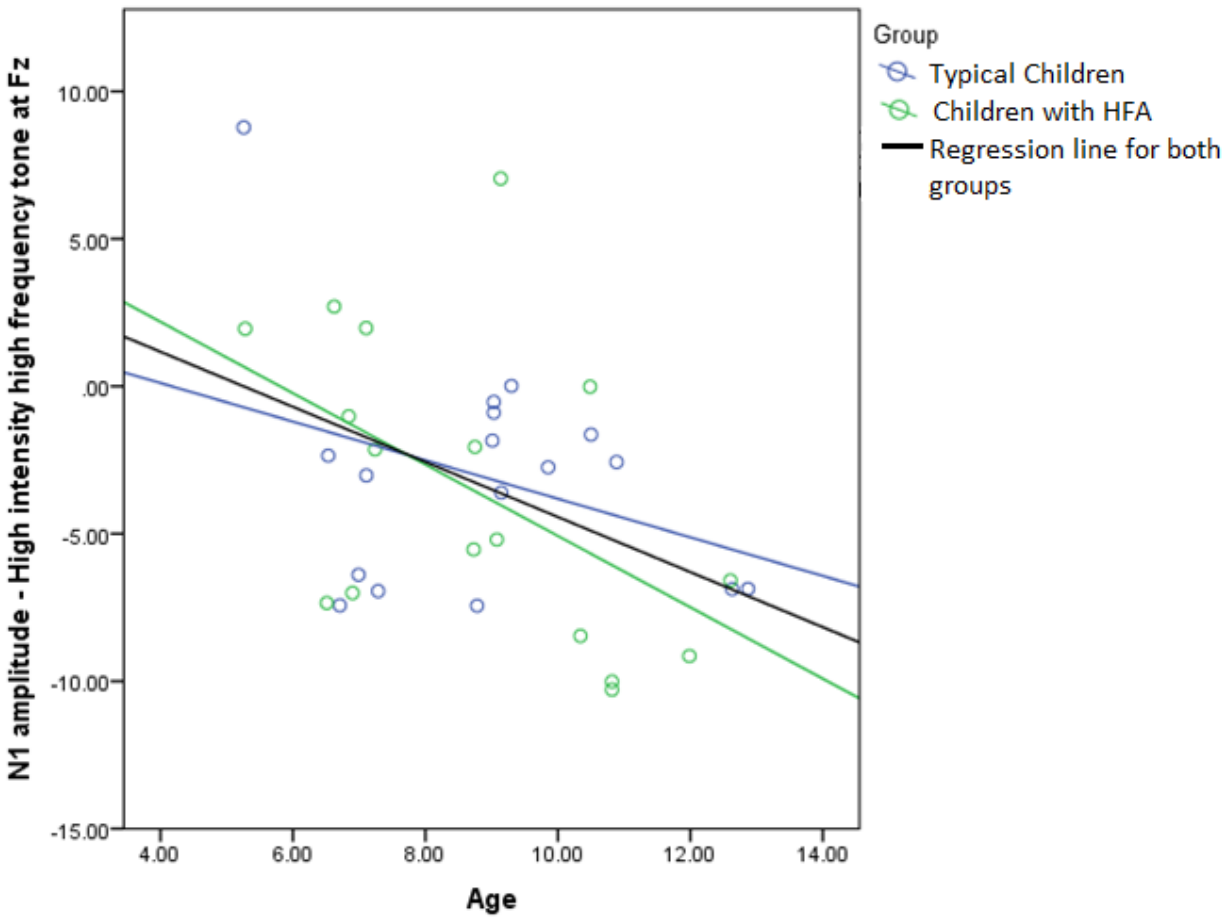


Figure 4: Correlation between age and N1 amplitude for the high intensity high frequency tones at Fz

Discriminant Analysis

A discriminant analysis was used to evaluate if individual differences in ERP components could be used to accurately classify children according to their diagnostic criteria. Because significant group differences were observed for the peak-to-peak P3 amplitudes, all four tones at sites Fz and Pz were used for this analysis. The discriminant function accounted for 38.44 % of the variance in the groups (Wilks $\lambda = 0.62$, $p = 0.08$). The low frequency low intensity tones at sites Fz and Pz were removed from the analysis to increase statistical power and due to poor loading on the standardized canonical discriminant function coefficients. The second

discriminant analysis using both of the high intensity tones and the high frequency low intensity tone was conducted. The discriminant function accounted for 23.33% of the variance in the groups (Wilks $\lambda = 0.63$, $p = 0.028$). The analyses revealed an 84.2 % probability to correctly classify children with HFA and 70.6 % probability to correctly classify typically developing children. The total classification accuracy was 77.8 %. Since the two groups had significantly different P3 amplitudes for the high intensity tones, a third discriminant analysis using only the high intensity tones at both frequencies was conducted. The discriminant function accounted for 32.38 % of the variance in the groups (Wilks $\lambda = 0.68$, $p = 0.012$). The analyses revealed an 84.2 % probability to correctly classify children with HFA and 66.7 % probability to correctly classify typically developing children. The total classification accuracy was 75.7 %. The standardized discriminant function coefficients for the three discriminant analyses are shown in Table 2.

Table 2

The discriminant analysis results of the peak-to-peak P3 ERP components

	All tones	**High intensity tones + High frequency low intensity tone**	**High intensity tones**
Variables	**Standardized canonical coefficients**		
P3 for 1 kHz 50 dB at Fz	-.021		
P3 for 1 kHz 70 dB at Fz	.291	.323	.542
P3 for 3 kHz 50 dB at Fz	.391	.488	
P3 for 3 kHz 70 dB at Fz	.851	.784	.946
P3 for 1 kHz 50 dB at Pz	.048		
P3 for 1 kHz 70 dB at Pz	-.616	-.543	-.318
P3 for 3 kHz 50 dB at Pz	-.060	-.103	
P3 for 3 kHz 70 dB at Pz	-.173	-.194	-.516
Overall classification accuracy	80 %	77.8%	75.7%

Discussion

This study sought to examine the differences in neural responses to auditory processing in children with HFA compared to age- and gender-matched typically developing peers using EEG and ERP methodology. The sensory registration ERP paradigm allowed us to demonstrate differences in ERP components to intensity and frequency changes. Peak-to-peak measures of the amplitudes were used to evaluate group differences. Children with HFA demonstrated significantly different brain processing to auditory stimuli of the peak-to-peak N2 and P3 amplitude and P2 latency components compared to age- and gender-matched typically developing children. A maturational trend was observed in relation to certain ERP components. Discriminant analysis using the peak-to-peak P3 amplitudes revealed a 78 % classification accuracy discriminating the two groups. These results are discussed in detail below.

Grand Averaged ERP waveform Pattern

Examination of the grand averaged ERP waveform indicated that typically developing children had more organized and larger brain responses to the four auditory stimuli compared to children with HFA (see Figure 2). ERP waveforms of both groups depicted the expected pattern following an auditory stimuli, i.e. P1-N1-P2-N2-P3 (Polich, 1993). At the Cz site, typically developing children demonstrated a clear distinction between the high intensity (70 dB) and low intensity (50 dB) tones for the N1 and P2 peaks. The low intensity tones had smaller ERP waveforms than the high intensity tones. This finding is consistent with existing literature (Adler & Adler, 1991; Davies et al., 2010). For children with HFA, this pattern was not clearly distinguishable. On the grand-average, it appeared as though children with HFA do not have the expected N1 deflection for the low intensity tones as compared to the high intensity tones.

Differences in Brain Processing of Auditory Stimuli

Peak-to-peak N1 amplitude. Although there were no significant group differences on the N1 amplitude in our sample, the means of the N1 amplitude were smaller in children with HFA compared to typically developing peers for all the four tones (see Table 1). The finding of larger N1 amplitudes for the high intensity tones compared to the low intensity tones is consistent with previous studies (Adler & Adler, 1991; Picton, Hillyard, Krausz, & Galambos, 1974; Polich, 1993; Ponton et al., 2000).

Peak-to-peak P2 amplitude. No significant group differences were found for the P2 amplitude. In our study, frontal and central sites had stronger responses than the posterior site, which is consistent with reported literature stating that P2 has a predominantly fronto-central scalp distribution (Wunderlich et al, 2006). Several studies have failed to find significant group differences between children with ASD and typical children on N1 and P2 amplitudes (Bruneau et al., 1987; Salmond et al., 2007; Whitehouse & Bishop, 2008).

Peak-to-peak N2 amplitude. N2 amplitudes also demonstrated sensitivity to the different intensities, consistent with existing literature (Ponton et al., 2000). Similar to the distribution of P2, N2 also showed larger fronto-central distribution, which has been reported previously (Ponton et al., 2000). In our study, we found smaller N2 amplitudes in children with HFA compared to typically developing children. This is consistent with research using pure tones, paired clicks, and speech stimuli that has demonstrated N2 attenuation in children with Asperger's syndrome (Jansson-Verkasalo et al., 2003, 2005; Orekhova et al., 2009). The N2 component is described as being influenced more by endogenous characteristics such as discrimination, recognition, perception, and classification of acoustic stimuli than exogenous stimulus features (McPherson, Ballachanda, Kaf, 2007; Picton, 2010). Smaller N2 amplitudes

suggest increased difficulty in automatic stimulus discrimination and deficits in sound encoding (Jansson-Verkasalo et al., 2003, 2005).

Peak-to-peak P3 amplitude. Results from this study indicated that children with HFA had significantly smaller peak-to-peak P3 amplitudes for the high intensity tones at both frequencies compared to typically developing children. Smaller P3 amplitudes in children, adolescents, and adults with autism has been reported in few studies (Dunn et al., 1999). Additionally, a significant site by group interaction was observed. Typically developing children had highest amplitudes for the P3 component at Fz whereas children with HFA had highest amplitude for P3 at Cz. This difference could be attributed to several factors. One possible explanation is that children with HFA have different neural activation patterns than typically developing peers. This could also allude to differences in brain regions involved during auditory processing. However, this difference could also be an artifact of the direction of the dipole. Since the current study was not designed to study source localization effects, the implications of differences in sites need further validation.

The sensory registration paradigm used in this study is a passive paradigm, which means that children were not instructed to actively attend or respond to the tones. Generally, a passive ERP paradigm does not elicit a large P3 response, because the P3 component is associated with cognitive processing of the stimuli (Polich, 1993). But researchers have found that the P3a component is reflective of involuntary attention to auditory stimuli (Samson et al., 2006). Smaller P3 amplitudes have been demonstrated in various clinical groups such as schizophrenia (Klein, Berg, Rockstroh, & Andresen, 1999), sensory processing dysfunction (Gavin et al., 2011), and attention deficit hyperactivity disorder (Tsai, Hung, & Lu, 2012). Smaller P3

amplitudes in individuals with disability reflect increased difficulty discriminating stimuli (Sugawara, Sadeghpour, De Traversay, & Ornitz, 1994).

P2 latency. In our study, children with HFA had significantly longer latencies for the high frequency high intensity tone compared to typically developing children. Dunn et al. (1999) had similar findings in children with autism to word stimuli, where children with autism also had delayed behavioral responses compared to a control group. Jirsa and Clontz (1990) also showed that children with auditory processing disorders had longer P2 latencies than age-, gender- and IQ-matched controls. ERP studies have shown prolonged latency of an ERP component - mismatch negativity (approximate latency window of the P2) in children with Asperger's syndrome than controls, indicating delayed processing and discrimination of auditory stimuli (Jansson-Verkasalo et al., 2005). Few studies have failed to show significant differences in P2 latency between children with autism and typical children (Lincoln et al., 1995; Salmond et al., 2007). Developmentally, P2 latencies decrease with increasing age suggesting faster processing (Oades et al., 1997). This could suggest delayed development of auditory processing skills in children with HFA compared to typically developing children.

Together, these results support our first hypothesis that ERP measures can be used to assess sensory registration. Our second hypothesis is also supported because there are significant differences in brain processing of auditory stimuli for the P3 amplitude and P2 latency, as measured by EEG, in children with HFA compared to typically developing peers. The effect sizes for the peak-to-peak amplitudes for the N1, P2, and N2 component suggest that with a larger sample size, we may find differences in these components as well.

Maturation of ERP Components

We hypothesized that as age increased, N1 amplitudes would increase and N2 amplitudes would decrease (Ceponiene et al., 2002; Davies et al., 2010; Mahajan & McArthur, 2012; Wunderlich et al., 2006). We also hypothesized that this developmental trend would be present in typically developing children but not in children with HFA. In our sample, for children with HFA, a developmental trend was observed for the N1 component, such that N1 amplitudes increased as age increased. However, this trend was not present in the group of typically developing children. The maturation of the N1 amplitude is associated with changes in the mean synaptic density and improved neural synchrony in the primary auditory cortex (Ponton et al., 2000). Age-related changes in amplitudes likely reflect maturation of the neural processes of the response generators (Wunderlich et al., 2006). Moreover, smaller N1's in younger children suggest that they may have fewer resources allocated to attending to incoming stimuli as compared to adults (Davies et al., 2010). The N1 is thought to reflect orienting and selective attention to incoming stimuli and smaller N1's in younger children suggest that they do not demonstrate mature proficiency in automatically registering sensory information (Sanders, Stevens, Coch, & Neville, 2006). The magnitude of N1 is reported to display a gradual developmental trend starting at infancy and extending to 12 -15 years (Ponton et al., 2000). It is possible that the group of typically developing children in our study had more stable and developed N1's compared to children with HFA. To summarize, the presence of a developmental trend in children with HFA and not in typically developing children could reflect a maturational delay in this group.

On the other hand, typically developing children demonstrated the developmental trend for the N2 component, such that N2 amplitudes decreased as a function of age. Declining

magnitude of N2 with increasing age has also been widely reported (Johnstone, Barry, Anderson, & Coyle, 1996; Ponton et al., 2000; Wunderlich et al., 2006). This trend was not present in the sample of children with HFA. Typically developing children had larger variability in N2 amplitudes compared to children with HFA. The increased variability could have allowed a clearer demonstration of the effect of age in typical children. This finding could also suggest that children with HFA do not display typical developmental maturation. This could help us understand certain behavioral manifestations to auditory processing.

Results from the above analyses, suggest that a developmental trend in auditory processing can be observed for children between the ages of 6-to-12 years supporting a part of our second hypothesis. The expected pattern of group differences in relation to developmental maturation of ERP components were not apparent in our study. Another possible explanation for this inconsistency could be that the N1 matures before the N2. This would mean that while typically developing children had a mature N1 and showed on-going development of the N2, this trend was delayed in children with HFA, who showed on-going development of the N1 but not of the N2. With a larger sample size, this trend may become clearer.

Discriminant Analysis

The discriminant analysis function incorporating both of the high intensity tones and the high frequency low intensity tone of the peak-to-peak P3 amplitude was able to correctly distinguish between typically developing children and children with HFA with an overall classification accuracy of 77.8%. The analyses revealed an 84.2 % probability to correctly classify children with HFA and 70.6 % probability to correctly classify typically developing children. This finding is consistent with Gavin et al. (2011) study, where they found that peak-to-peak P3 amplitudes and N2 latency measures were able to correctly classify children with the

modulation subtype of SPD from typically developing children with 79 % accuracy. Together, these findings support the fourth hypothesis that electrophysiological responses to simple auditory stimuli may be used to predict sensory registration difficulties in clinical groups demonstrating sensory processing dysfunction.

Implications of Differences in Sensory Registration

Neurophysiological abnormalities in auditory information processing abilities of children with HFA suggest that this population has difficulties in automatic stimulus discrimination, cognitive processing, and organization of stimuli. An inability to optimally regulate incoming sensory information early on (within the first 500 ms) in the brain could result in dysfunctional responses to environmental sensory information, resulting in maladaptive behaviors to everyday sensory information. Atypical behaviors to auditory sensory information often seen in children with autism include placing hands over ears to particular sounds and pre-occupation with certain sounds (Baranek et al., 2006; Tomchek & Dunn, 2007). Sensory processing dysfunction commonly observed in children with autism could be attributed to disorganized neurophysiological processing. Reduced cognitive processing to auditory stimuli suggests that the incoming information is not processed efficiently and this may lead to inefficient processing of decisions regarding whether the stimuli must be dismissed or processed further may be causing the sensory stimuli to be processed longer. Appropriate sensory experiences are crucial for neuro-developmental maturation of perceptual, cognitive, and social skills (Mottron et al., 2007). Dysfunction in early developmental stages could hamper development of appropriate neuronal circuitry (Hensch, 2004). Thus, therapeutic strategies targeting the physiological manifestations of sensory dysfunction could augment traditional behavioral sensory interventions.

Limitations

Due to convenience sampling methods in this study, generalizability of the results may be limited. This study sample consisted of children with high functioning autism. The implications of the study results to children on the low functioning spectrum of autism have to be empirically tested. A small sample size may have limited our ability to find differences between other ERP components such as the N1 and P2 due to reduced power.

Recommendations for Future Studies

Further research should involve children along the entire spectrum of autism to examine if auditory sensory processing differs based on functioning levels and behavioral phenotypes. The use of ERP data to classify other disability groups must be considered for future studies. ERP measures could be used as objective neural biomarkers that can aid in the diagnostic process in children with ASD but the potential of using ERPs to assist with early identification needs to be examined through systematic research. ERP measures could also be used to examine intervention effectiveness at the neurophysiological level. Comparison of auditory processing in ASD with other disorders that report auditory processing deficits such as dyslexia, ADHD and specific language impairment is also worthy of further investigation. With technological advancement in imaging and physiological measures, and use of behavioral correlates of daily functioning, the relationship between atypical auditory processing and everyday behavioral deficits should become clearer.

Conclusion

Together these findings demonstrate atypical neural processing of auditory information to be an inherent aspect of children with high functioning autism. Specifically, children with HFA manifest with difficulties in automatic stimulus discrimination and inefficient cognitive processing of auditory information than age-and gender-matched typically developing peers. These results can help practitioners understand the neurophysiological basis of behavioral manifestations of children with HFA, especially those atypical behaviors that occur in response to sensory experiences in everyday activities. Understanding the specific aspects of sensory processing that are a challenge for children with HFA could provide guidance to the types of treatment strategies that will be most effective. Further exploring the relationship between neurological measures of sensory processing and every-day behaviors can provide parents, teachers, and therapists with a greater understanding of how to best provide optimal learning and play environments for achieving desired outcomes. Additionally, ERP measures could be used to distinguish between children with HFA and typically developing children. Due to the relatively small number of subjects used in this study, these preliminary results should be confirmed by further testing on a larger group of children with high-functioning autism.

CHAPTER THREE

Studies suggest that 80% to 95% of the children with autism spectrum disorders exhibit sensory processing dysfunction (Baranek, 2002; Tomchek & Dunn, 2007). Zingerevich and LaVesser (2008) found that impairments in executive functions and sensory processing negatively impact participation patterns of children with ASD. Sensory processing refers to the way that sensory information is processed in the brain for the purpose of enabling an individual's engagement in occupation (Johnson-Ecker & Parham, 1999). In this context, sensory processing is synonymous with Ayres' (1979) "sensory integration", which is the brain's coordination of different sensory information to allow participation in everyday activities. Ayres, an occupational therapist, developed sensory integration theory to explain the relationship between the neurological processing of sensory information and the resultant adaptive behavior. Due to its focus on adaptive functioning and creating 'just-right-challenge', this approach has been extensively used by occupational therapists as a part of the therapeutic process (Bundy et al., 2002; Schaff & Miller, 2005). However, research understanding the underlying physiological mechanisms of sensory processing deficits and sensory-based interventions is warranted. Among the sensory domains affected, difficulties in auditory processing are one of the most commonly reported sensory processing impairments in children with autism (Tomchek & Dunn, 2007).

This study aimed to determine whether children with high-functioning autism spectrum disorders differ from typically developing children on neurophysiological measures of auditory information processing. The results indicated that children with HFA have significantly different neural responses, with reduced automatic discrimination and inefficient cognitive processing compared to age-and gender-matched typically developing peers. Additionally, our results show that ERP measures can distinguish children with HFA from typically developing children with

77.8 % accuracy. Results from this study can help therapists, practitioners, and parents understand the underlying neurological mechanisms of auditory information processing. Stein, Foran and Cermak, (2011) explain how parents of children with ASD experience decreased well-being due to lifestyle imbalance. The authors state that since the etiology of ASD remains unknown, parents often "question whether they are responsible for their child's disorder, producing feelings of confusion and guilt" (p.116). I believe that understanding the association between observable behavioral deficits and performance limitations, and abnormal neurological functioning can reduce these feelings of guilt and provide answers to parents and therapists.

Rehabilitation Science Perspectives

The discipline of rehabilitation science places significant emphasis on function, focusing on the mechanisms by which disability develops and the factors influencing it. It strives to develop a better understanding of the causes and factors contributing to disability to enable contribution towards improved and efficient treatments and technology for those with disabling conditions (Brandt & Pope, 1997). Baum (2013) emphasized the significance of the different levels of research in rehabilitation and occupational therapy. She stated that "science must be developed at all levels if we are to have knowledge to translate findings that will inform interventions to improve participation, health, and well-being" (p.172). This study fits within the realm of rehabilitation science.

On the International Classification of Functioning, Disability and Health framework (WHO, 2002), this study focuses on the domains of body structure and function and its relation to health. While this study's focus was restricted to basic neurological mechanisms underlying sensory processing in children with HFA, the results can be interpreted in light of common sensory behaviors that lead to participation limitations and occupational dysfunction.

Associations have been found between emotional and behavioral problems in ASD and sensory processing (Ashburner, Ziviani, & Rodger, 2008). However, it is not clear if behavioral outbursts (such as temper tantrums, covering ears during particular sounds, etc.) in children with ASD are due to behavioral issues or due to underlying sensory issues.

Impairment in the ability to automatically discriminate incoming sensory information, and delayed and reduced cognitive processing may hinder a child's ability to meaningfully integrate sensory information. This study revealed atypical neurological processing to simple auditory tones presented in a controlled laboratory environment in the group of children with HFA. These deficits may be further limiting in everyday environments where a tremendous amount of sensory information is being processed by the brain every moment. Children with autism often report the phenomenon of "sensory overload" in noisy and crowded environments like shopping malls (Pellicano & Burr, 2012). Deficits during very early neurological processing of incoming stimuli may shed light on understanding this phenomenon through the lens of a sensory processing impairment rather than a behavioral problem. Understanding the neurological underpinnings of sensory processing can help to distinguish behavioral problems from underlying neurological issues related to difficulties in processing sensory information. Many current interventions for children with ASD focus on behavior therapy. Other interventions focus on sensory based interventions. Researchers have found that there exists limited evidence to justify any specific treatment method for this population (May-Benson & Koomar, 2010). Further research examining the relationship between neurological mechanisms and observed behaviors can help determine the relevance of sensory based interventions.

One of the study hypotheses was to evaluate if ERP measures could distinguish between children with HFA and typically developing children. Currently, researchers are aiming to find

clinical (Botting, & Conti-Ramsden. 2003), biochemical (Correia et al., 2006), and biological (Smalley, & Asarnow, 1990) markers that can distinguish children with ASD from other developmental disorders and provide more objective tools to aid the behavioral diagnostic system. In 2008, the National Institute of Mental Health (NIMH) and subsequently the Research Domain Criteria project, or RDoC reported that one of its aim was to "Develop, for research purposes, new ways of classifying mental disorders based on dimensions of observable behavior and neurobiological measures" (http://www.nimh.nih.gov/research-priorities/rdoc/nimh-research-domain-criteria-rdoc.shtml). Further exploring the use of ERP to discriminate between groups could help validate neurophysiological biomarkers that could potentially aid in the process of diagnosis. Also, ERP measures could provide objective outcome measures of changes in neural processing post-interventions. The discovery of an efficient marker for any clinical condition can potentially have great impact on the screening, diagnosis process, and remediation. Moreover, it can serve to inform research about underlying mechanisms and provide clarity between differential diagnoses (Botting, & Conti-Ramsden. 2003).

Several studies have been using EEG techniques to examine the effects of various therapeutic interventions. Field et al., (1996) showed that EEG patterns of alertness improved after a massage therapy intervention. This finding corroborated with lower cortisol levels, lower depression and lower job stress scores. Similarly, another study used EEG to show better cortical connectivity and improved activation of the motor cortex following music-supported therapy for individuals with motor impairment following a stroke (Altenmüller, Marco-Pallares, Münte, & Schneider, 2009). Demonstrating the effects of interventions at the neurological level provides more convincing evidence of treatment efficacy complementing the traditional behavioral outcome measures. Although results of this study do not validate the use of EEG/ERP's as a

neural biomarker, they provide evidence for the feasibility of this approach. Future research with larger sample sizes would allow us to explore this promising methodology.

In summary, I would like to reiterate that research at every level of science can meaningfully contribute towards our understanding of participation, health, and well-being. Although research understanding sensory processing in ASD is currently in its infancy, it has great potential to contribute towards enhancing our knowledge about this vulnerable population and the development of our profession.

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