DISSERTATION

EXAMINING THE RELATIONSHIP BETWEEN SENSORY PROCESSING AND ATTENTION IN INDIVIDUALS WITH AUTISM SPECTRUM DISORDERS

Submitted by

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ABSTRACT

EXAMINING THE RELATIONSHIP BETWEEN SENSORY PROCESSING AND ATTENTION IN INDIVIDUALS WITH AUTISM SPECTRUM DISORDERS

Attention is a crucial element of our goal-directed, purposeful response to sensory information in our social and physical environments. Individuals with autism spectrum disorders (ASD) have significant deficits in sensory processing and attention. However, there is limited research examining the relationship between attention and sensory processing in individuals with autism spectrum disorders (ASD). The purpose of this dissertation was to examine the relationship between attention and sensory processing in individuals with autism spectrum disorders (ASD) and neurotypical individuals. Specifically, the objective was to examine if consciously directing attention to incoming information would result in more typical neural processing in individuals with ASD. To answer this question, study 1 was designed to understand how attention and distraction impacted sensory processing in neurotypical individuals. Studies 2 and 3 examined neural measures of sensory processing in individuals with ASD as compared to age-matched neurotypical controls during passive and active attentional states.

In Study 1, electroencephalography (EEG) data were recorded while 60 adults (18-35 years) heard random presentations of 4 auditory stimuli at 2 frequencies (1 and 3 kHz) each at 2 intensities (50 and 70 dB). Participants were randomly divided into 2 viewing conditions; one group watched a silent movie and the other viewed a fixation point during the recording. All participants completed 2 attention conditions, the passive condition involved only listening to the stimuli, followed by the active condition, wherein participants were instructed to press a button

to the 1 kHz 50 dB tone. Amplitude and latency measures were obtained for the N1, P2, N2, and P3 components for each of the auditory stimuli. The ANOVAs revealed a significant main effect of attention condition for the N1, P2, N2, and P3 amplitudes. There were also significant attention-by-viewing condition interaction effects at the P3 component. Results indicated that actively directing attention to the tones impacts auditory processing at all components. Additionally, manipulation of attention by changing the viewing environment significantly interacted with sensory processing, such that movie viewing resulted in larger P3 amplitudes compared with fixation viewing. Thus, viewing environment or distraction impacts sensory processing.

In study 2, we examined the effect of attention on auditory filtering using the sensory gating paradigm in individuals with ASD. EEG data were recorded during 2 attention conditions from 24 adults with ASD and 24 neurotypical individuals during the sensory gating paradigm. During the passive condition, participants were presented with single and paired clicks. For the active condition, participants made a motor response following the single click but not the paired click. Attending to the clicks resulted in larger P50 and N1 amplitudes, and reduced gating for all participants. Although, the ASD group had P50 and N1 gating during both attention conditions, they had significantly longer N1 latencies to the Click 1 during both the attention conditions, suggesting a delayed orienting response. However, click 2 latencies were delayed only in the passive condition and not the active condition for the ASD group compared to the neurotypical group. This finding suggests of attention-based amelioration of processing speed in individuals with ASD. Individuals with ASD also had significantly more deficits on behavioral measures of social responsivity, attention, sensory and perceptual processing. Additionally, neural measures of gating were associated with several behavioral measures of sensory processing as measured

by self-report questionnaires and a performance-based measure of attention, such that efficient neural processing was associated with more typical sensory processing and attention.

In study 3, we examined the effect of attention on auditory discrimination in individuals with ASD. EEG data were recorded from 24 individuals with ASD and 24 neurotypical individuals, while they heard random presentations of 4 auditory stimuli at 2 different frequencies (1 and 3 kHz) each at 2 different intensities (50 and 70 dB). All participants completed two attention conditions; the passive condition involved only listening to the stimuli, followed by the active condition, wherein participants were instructed to press a button to the 1 kHz 50 dB tone. Attention impacted N2, and P3 amplitudes, and P2 and N2 latencies. The ASD group had significantly longer N1, N2, and P3 latencies, suggesting delayed processing. N2 and P3 latency delays in the ASD group were present during the passive but not active condition, implying an attention-based amelioration of processing delay. Behavioral measures of sensory processing and attention correlated with neural measures of auditory processing.

Thus, through the series of studies, we found that actively directing attention to the tones impacts auditory processing, and may result in more typical processing in ASD. The study findings also suggest that sensory processing deficits observed in ASD may be associated with underlying deficits of attention. Study findings have significant implications related to understanding auditory discrimination in individuals with ASD and examining the impact of attention on sensory processing. Additionally, these results can help practitioners understand the neural basis of behavioral manifestations of ASD, especially those atypical behaviors that occur in response to sensory experiences in everyday activities.

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CHAPTER 1 – REVIEW OF LITERATURE

Our perception of everyday stimuli heavily relies on the amount of attention we devote to given sensory information. Our attention is also highly flexible, and constantly changing, sometimes consciously but mostly through unconscious mechanisms. When we focus our attention to a sensory stimulus, we can increase our perceptual sensitivity towards the object of our attention, while also simultaneously inhibiting or filtering out unimportant information. The manner in which the brain processes sensory stimuli and integrates that information with previously created templates and with novel environmental conditions is very complex. In addition, how other cognitive processes, such as attention influence the ongoing influx of multiple and sometime complex sensory stimuli are only recently beginning to be understood.

Attention

Although attention is a commonly used word in our everyday language, it has multiple meanings. We are able to pay *attention*, concentrate or become distracted. We are sometimes conscious of our own attention and are often able to observe attention in others. Attention is a crucial element of our goal-directed, purposeful response to sensory information in our social and physical environment. Attention is understood as a "broad cognitive concept that includes a set of mechanisms that determine how particular sensory input, perceptual objects, trains of thought, or courses of action are selected for further processing from an array of concurrent possible stimuli, objects, thoughts and action" (Talsma, Senkowski, Soto-Faraco, & Woldorff, 2010, p. 2). Attention is highly flexible and dynamically adjusts every moment depending on our goals, to focus on locations, visual features, or objects. Attention can be oriented reflexively

based on internal goals and desires of the observer (endogenous attention) or on our response to salient events in the environment (exogenous attention; Smith & Schenk, 2012).

Attention is a foundational element of human cognitive activity. Specifically, attention 1) increases the probability of learning, 2) improves detection of faint stimuli 3) reduces background noise (Carrasco, Penpeci-Talgar, & Eckstein, 2000), 4) improves feature discrimination (Lee, Itti, Koch, & Braun, 1999), and 5) affects stimulus appearance (Fuller, Liu, & Corrasco, 2006). Thus, attention filters out irrelevant stimuli and enables neural resources to focus on relevant information (Zhang et al., 2011). According to the information processing models of attention, information enters the sensory system and is then sent into memory via an attentional mechanism that operates independent of the sensory systems (Smith & Schenk, 2012). Thus, attention is conceived as a modular (anatomical and functional independence), domain-general higher-order cognitive function (Smith & Schenk, 2012).

Neural networks and brain structures involved in attention. Given the broad conceptualization of attention, researchers have attempted to organize attentional processes into a working taxonomy. Recent advances in neuroimaging have allowed scientists to understand the functional organization of the brain and the underlying networks regulating attention. Recent research has focused on applying principles of Graph Theory in neuroscience to examine neural networks related to functional connectivity of spatially distributed yet constantly communicating regions of the brain (Van Den Heuvel, & Pol, 2010). Functional connectivity has been defined as "the temporal dependency of neuronal activation patterns of anatomically separated brain regions" (Van Den Heuvel, & Pol, 2010, p. 519). Examining the integrative organization of functional neural networks can provide insights about large-scale neuronal communication, which can shed light on the relationship between functional connectivity and human behavior.

This knowledge can help researchers understand neuropathology and examine where and how this organization may be altered in neurological disorders like ASD (Bullmore, & Sporns, 2009). Most of the cognitive networks examined relate to a specific domain function such as memory, but attentional networks involve a mental function that is domain general (Fernandez-Duque, & Posner, 2001). Thus, we can pay attention to stimuli from the visual domain, the auditory domain, to the meaning of stimuli, etc. This domain generality allows attention the ability to influence and impact all areas of the brain. Neuroscientists examining attention related to different sensory inputs have identified different regions of the brain, however it is believed that the source of these influences is limited to a small number of functionally connected brain regions called networks (Fernandez-Duque, & Posner, 2001).

Attention networks proposed by Petersen and Posner. The classic neuroscience-based model by Posner and Petersen (1990) characterized attention in terms of three processes: 1) orienting to sensory stimuli, 2) detection of signals, and 3) maintenance of a vigilant state. Petersen and Posner (2012) showed support for their previously proposed tripartite organization of attention given recent advances in neuroscience. This model now includes the following functions, 1) alerting, 2) orienting, and 3) executive control (Petersen & Posner, 2012). Petersen and Posner (2012) have described the brain networks involved in each of these different forms of attention. Petersen and Posner (2012) categorized the attention system into the following three networks. The *orienting* network focusses on prioritizing sensory input by selecting specific modalities or locations. The *alerting* network focusses on brainstem arousal systems and is concerned with sustained vigilance. If a warning signal is presented prior to a target event, a phasic change in alertness ensues. This state allows preparation for target detection and increases the speed of target detection. The *executive* network is related to target detection and

focal attention. Greene et al. (2007) reported that these three networks are represented in each hemisphere separately and are largely comparable across both the hemispheres.

The orienting network. Orientation to a given sensory input can be driven from endogenous cues (voluntarily) or exogenous cues (environment). Imaging research revealed that both these cues activate similar areas in the frontal and parietal cortex. Functional magnetic resonance imaging (fMRI) studies have found that orienting activates the precentral gyrus of the frontal lobe and areas in the parietal lobe (Corbetta, 1998; Petersen & Posner, 2012). The cholinergic system arising in the basal forebrain is involved in the orienting network (Marocco & Davidson, 1998).

The alerting network. This network involves the ability to achieve and maintain an alert state. Warning tasks and continuous performance tasks are commonly used to examine this network. The reaction to an auditory warning signal has a strong exogenous component. Attentional processing is similar during continuous performance tasks that present either rare or frequent target stimuli. A vigilant state increases activation in the right fronto-parietal system (Pardo, Fox & Raichle, 1990; Petersen & Posner, 2012). The norepinephrine system arising in the locus coeruleus of the midbrain plays an important role in the alerting network (Marocco & Davidson, 1998).

The executive network. Executive attention involves effortful control or coordination, specifically, task switching, inhibitory control, conflict resolution, error monitoring, and allocation of attentional resources (Posner & Rothbart, 1998). The areas of the brain that are part of the executive attention network involve the anterior cingulate cortex, supplementary motor area, the orbitofrontal cortex, the dorsolateral prefrontal cortex, and portions of the basal ganglia, and the thalamus. The role of the anterior cingulate cortex has been widely investigated,

revealing its involvement in both emotional and cognitive self-regulation (Petersen & Posner, 2012). The mesocortical dopamine system is thought to be involved in the neuromodulation of the anterior cingulate cortex and the lateral prefrontal cortex (Marocco & Davidson, 1998). Based on functional magnetic resonance imaging (fMRI) studies, Corbetta and Shulman (2002) proposed the concept of two anatomically and functionally distinct attention systems composed of several brain regions. Numerous studies have shown that dorsal and ventral attention networks are supramodal attention systems, i.e., they function similarly across sensory modalities.

Dorsal and ventral attention networks. The dorsal attention network is assumed to mediate top-down voluntary allocation of attention, while the ventral attention system is proposed to be involved in detecting unattended or unexpected stimuli and triggering attention shifts (Corbetta & Shulman, 2002). The dorsal attention network is also responsible for 1) controlling spatial orienting by modulating the saliency of distractor stimuli according to task demands (Ptak & Schnider, 2010), 2) generating and maintaining endogenous signals related to current task demands (Corbetta, Kincade, Ollinger, McAvoy, & Shulman, 2000), and 3) linking stimuli to responses (Rushworth, Paus, & Sipila, 2001). Whereas, the ventral system is activated during 1) stimulus-driven attentional control (Corbetta & Shulman, 2002), 2) abrupt changes in sensory stimuli (Downar, Crawley, Mikulis, & Davis, 2000), and 3) at the end of a completed trial (Shulman et al., 2002). While several researchers have supported the functional roles of these networks, issues concerning their functional organization, and the interaction of the two networks remain debated.

The dorsal network comprises of the intraparietal sulcus and the frontal eye fields, and is organized bilaterally (Corbetta & Shulman, 2002). However, studies using concurrent

transcranial magnetic stimulation (TMS) and fMRI over left and right regions of the dorsal network have challenged the view of strictly symmetrical functions of both hemispheres (Ruff, et al, 2006; Ruff, et al, 2008). The ventral network comprises of the temporo-parietal junction (TPJ), and the ventral frontal cortex (Corbetta & Shulman, 2002). The ventral system is proposed to be lateralized to the right hemisphere (Corbetta & Shulman, 2002; Shulman et al., 2010). However, there are some inconsistencies in the literature regarding the specific role and lateralization of the TPJ. DiQuattro and Geng, (2011) demonstrated that the left TPJ is also involved in attention processes, and some others have shown bilateral TPJ activation during attentional tasks (Geng & Mangun 2011). Doricchi, Macci, Silvetti, and Macaluso (2009) demonstrated differences between left and right TPJ function such that the left TPJ responded during both bottom-up and top-down processing, while the right TPJ showed higher activity during bottom-up processing.

Although there are inconsistencies in the areas involved and lateralization of the networks, there is considerable consensus in the existence and general function of the two networks. Using fMRI, researchers have shown that the ventral and dorsal attention networks are distinguishable even during task-free conditions (Fox, Corbetta, Snyder, Vincent, & Raichle, 2006). A study by Umarova et al. (2009) also found white matter structural connectivity within the ventral and dorsal systems. The dorsal network has been found to inhibit activity in the ventral areas such as the TPJ during top-down guided attentional tasks (Shulman, Astafiev, McAvoy, d'Avossa, & Corbetta, 2007) and when no informative stimuli were present (DiQuattro & Geng, 2011). Thus, the dorsal network filters information sent to the ventral system allowing for efficient attentional regulation. Similarly, the ventral attention network dampened activity in the dorsal attention network to enable covert shifts of attention (Weissman & Prado, 2012). Fox

et al. (2006) have suggested that the right posterior middle frontal gyrus may allow for functional information transfer between the two systems, while Eckert et al. (2009) suggest that this interaction transfer occurs through the anterior insula.

Studies by Kincade, Abrams, Astafiev, Shulman, and Corbetta (2005) and Chica, Bartolomeo, and Valero-Cabré (2011) found that the right intraparietal sulcus (dorsal network) was involved in both top-down and bottom-up attention processing, while the right TPJ (ventral network) was associated with orienting of bottom-up but not top-down attention. These studies favor the notion of a *single* attention orienting network, which consists of the *dorsal* fronto-parietal system and the TPJ.

Frontoparietal control network. The fronto-parietal cortex is considered to be a domain-general attention control center (Scolari, Seidl-Rathkopf, & Kastner, 2015). This attention network, called the fronto-parietal control network is assumed to allow flexible coupling with either the dorsal or ventral attention networks based on exogenous versus endogenous goals (Spreng, Stevens, Chamberlain, Gilmore, & Schacter, 2010). This network is composed of the dorsolateral prefrontal cortex, middle frontal gyrus, anterior insula, dorsal anterior cingulate cortex, precuneus, and anterior inferior parietal lobule, and is anatomically interposed between the default mode network (see below for details) and dorsal attention networks (Vincent, Kahn, Snyder, Raichle, & Buckner, 2008). Several researchers have argued that this network is the mediator between the attention systems (Spreng et al., 2010; Vincent et al., 2008). However, others believe that attention control occurs within the dorsal system (Corbetta & Shulman, 2002).

Default mode network. Benedek et al. (2016) examined brain regions responsible for maintaining an internal focus of attention (such as during imagination or mental simulations).

The study showed that internal attention involved increased activation of the right anterior inferior parietal lobule (aIPL) and bilateral lingual gyrus compared to externally directed attention. These areas are associated with the parietal core of the fronto-parietal control network. These researchers also proposed that the right aIPL may be involved in the active suppression of sensory information processing during internally directed attention (Benedek et al., 2016). Internally directed attention has been commonly associated with the default mode network (Spreng et al., 2010). Brain regions implicated in this network include the medial prefrontal cortex, the posterior cingulate, the medial temporal lobes, and the posterior inferior parietal cortex (Raichle, 2015).

Additionally, researchers have found that the default mode network may be involved during increased attention demands (Popa, Popescu, & Paré, 2009). In contrast, others have found reduced activation of the default mode network during internally directed attention (Benedek et al., 2016). Researchers have shown differences in brain activation between a visuo-spatial attention task and an autobiographical planning task, wherein the former task engaged the dorsal attention network and the latter engaged the default mode network, and both tasks additionally activated the fronto-parietal control network (Spreng et al., 2010). Others have also found that increases in the dorsal attention network are accompanied by decreases in the default mode network and vice-versa (Fox, Zhang, Snyder, & Raichle, 2009).

Thus, there are still big gaps in our knowledge of the relationship between the default mode network, the dorsal and ventral attention networks, and the fronto-parietal control network. Presence of activity in the dorsal and ventral attention networks during attention-based tasks is ubiquitous across neuroimaging studies. Researchers have also shown that some areas of the frontal cortex serve as mediators for crosstalk between the two systems. However, there are still

gaps in literature determining the interactions that allow attentional systems to coordinate, for example, an orienting response.

Knowledge about the brain networks involved in attention along with the theories of attention suggest that attention is closely linked to our abilities to process sensory information. One's attention abilities impacts one's sensory processing abilities as well. Sensory processing is defined differently by different disciplines. For neuroscientists, sensory processing may deal with the neural mechanisms of information processing down to the neuron mechanisms, while for the discipline of occupational therapy (OT), it may include both neural and behavioral aspects of information processing.

Sensory Processing from an OT Perspective

Sensory processing refers to the way that sensory information is processed in the brain and perceived for the purpose of enabling an individual's experience of sensation and subsequent meaningful engagement with the environment (Kandel, Schwartz, & Jessell, 2000). Sensory processing is an encompassing mechanism which includes the reception, modulation, integration, and organization of incoming sensory stimuli and the behavioral response to the sensory information. These processes are fundamental to perception, learning, and functional abilities in behavioral, emotional, motoric, and cognitive domains. Sensory systems include the tactile, auditory, visual, gustatory, olfactory, proprioceptive, and vestibular systems. Occupational therapists have developed several theories of sensory processing and often use these theories to guide behavioral interventions to address sensory processing difficulties (Dunn, 2001). Several researchers have shown that difficulties with processing sensory information can lead to difficulties in meaningful engagement in everyday occupations (Ashburner, Ziviani, & Rodger, 2008; Baker, Lane, Angley, & Young, 2008; Dunn, 2001; Zingerevich & LaVesser, 2008).

Occupational therapists Johnson-Ecker and Parham (1999) refer to sensory processing as "brain's handling of sensory information for the purpose of enabling a person's engagement in occupations" (p. 495). The profession of OT is concerned with "helping people across the lifespan participate in the things they want and need to do through the therapeutic use of everyday activities (occupations)" (AOTA, 2017). Thus, numerous OT researchers (e.g., Dunn, 2001) have examined how sensory processing challenges affect everyday occupations. The discipline of OT has generated, and continues to generate, a wide knowledge-base about how individuals process sensory information and how this processing affects an individual's ability to meaningfully engage with the environment, not only during the typical course of a day but also how it might interfere with living a satisfying life (Dunn, 2001). Some studies have associated sensory processing with cognitive, behavioral, emotional, and psychosocial performance (Baranek, Foster, & Berkson, 1997; Parham, 1998; Kinnealey & Fuiek, 1999). OT research examining sensory processing has also shown how to support people with sensory processing deficits to be successful in their daily lives (e.g., Dunn, 2001). Occupational therapists (e.g., Dunn, 2001) have used a variety of measures, such as criterion measures, direct assessment of performance, open-ended interviews, surveys, parent-, teacher- and self-report questionnaires, and observations to characterize sensory processing. Inter-disciplinary teams, including OT researchers have also taken advantage of psychophysiological methods to investigate brain-behavior relationships examining attention and sensory processing as it impacts everyday behaviors (Brown, Tollefson, Dunn, Cromwell, & Filion, 2001; McIntosh, Miller, Shyu, & Dunn, 1999; Schaff & Davies, 2010).

The mechanisms of sensory processing are intertwined with several other neural functions. Most OT theories of sensory processing depend on assumptions about the underlying

brain processes associated with sensory processing. However, most of the research done by occupational therapists on this topic is based on behavioral measures that do not directly measure neural processing within the brain. Neuroscience literature is often incorporated to support these assumptions. Neuroscientists have reported on the brain's methods for mediating its own sensory input, with an emphasis on the role of attention (Kandel et al., 2000). Some OT researchers (e.g., Dunn, 2001) have also incorporated cognitive mechanisms such as attention as important constructs in understanding sensory processing. By studying the contributions and relationships of neural functions such as attention on sensory processing, we may be able to gain insights on the role of sensory processing in various clinical conditions.

Relationship between Sensory Processing and Attention.

The first step of sensory processing is the *detection* of incoming sensory stimuli in the CNS. Sensory stimuli are processed within multiple regions of the CNS. Depending on the stimuli, different processes such as facilitation, sensitization, habituation, suppression, inhibition, and summation can occur causing changes in the ongoing neuronal activity (Miller & Lane, 2000). Ayres noted that some children with sensory processing dysfunction fail to *register* incoming sensory input which leads to difficulties in modulating sensory information (Ayres, 1979). This *failure to register* is associated with difficulty in detection of sensory input. Registration of sensory stimuli has been alluded to as the complex process by which the CNS *pays attention to* or notices environmental information.

Relationship between attention and sensory processing from interdisciplinary psychophysiological studies. Several studies have shown that sensory processing abilities, as measured by psychophysiological measures, are dependent on attentional control (Talsma et al., 2010). McIntosh et al. (1999), examining sensory processing in pre-school children, and Brown

et al. (2001), examining adults, found that distinct patterns of noticing and habituation coincided with behavioral measures of sensory processing. Using positron emission tomography, researchers have demonstrated that spatial attention leads to stronger activation in the brain area responsible for processing the stimulus on the attended side compared to the unattended side (Corbetta, Miezin, Dobmeyer, Shulman, & Petersen, 1990; Heinze, et al., 1994; Hillyard, Vogel, & Luck, 1998). Additionally, blood flow in cortical areas processing characteristics that are the focus of attention (such as color, shape, velocity) was increased compared to when these characteristics were ignored (Corbetta et al., 1990). Researchers examining visual attention have shown that attention affects activity of brain areas that process stimulus characteristics, such as color, motion, form etc. A classic study by Motter (1993, 1994) demonstrated the effect of attention on neuronal behavior. Two conditions were compared: an attended condition, in which the monkey focused attention on a visual stimulus within the receptive field, and an unattended condition, wherein the monkey focused attention elsewhere in the presence of the same visual stimulus. The results of this experiment indicated that when attention was directed towards the given stimulus, there was an increase in the firing rate of neurons that respond to the attended stimulus.

Using implanted electrodes in rhesus monkeys, Reynolds and Desimone (2003) also showed that attention increases the activity in brain regions processing the attended location compared to visual stimuli at an unattended location. Such an enhancement of neural representation is thought to be due to an amplification of the intensity or magnitude of the attended stimulus, or due to the suppression of other irrelevant stimuli or environmental noise. Thus, attention appears to increase the gain of the stimulus for efficient processing (Borji & Itti,

2014). The aim of this increase in stimulus gain is an enhanced probability for that stimulus or event to be acted upon (Borji & Itti, 2014).

Theories Describing the Relationship between Attention and Sensory Processing

Sensory gain control theory. Researchers examining the effect of selective attention on stimulus-driven neural activity have suggested that sensory pathways can be modulated in amplitude based on attentional mechanisms. Hillyard et al. (1998) put forth the sensory gain control theory based on previous research by Corbetta and colleagues (1998). The researchers propose that "feature-specific increases in regional cerebral blood-flow may involve a 'sensory enhancement' whereby incoming visual information in attended sensory pathways would trigger stronger and more selective neuronal responses with a higher signal-to-noise ratio than in unattended pathways" (p. 1257; Hillyard et al., 1998). Thus, attention modulates sensory processing through an 'amplification' of neuronal activity within sensory processing areas of attended stimuli compared to unattended stimuli (Posner & DeHaene, 1994). For instance, attending to motion and ignoring color would result in an amplification of activity within motion processing areas of the brain.

Biased competition model of attention. With respect to visual attention, several researchers have proposed that there is competition for neural resources (Desimone & Duncan, 1995). Specifically, attending to a feature such as velocity may cause a 'bias signal' to be sent from higher cortical areas governing attention to the sensory areas specialized for motion processing. This bias signal might increase the baseline firing rate of neural activity without necessarily modulating sensory-evoked neural responses. Accordingly, neurophysiological researchers have put forth the "*biased competition hypothesis*" of the neural basis of attention. Attentional selection occurs by biasing an underlying competitive interaction between multiple

stimuli in the sensory receptive field toward one stimulus or another, such that behaviorally relevant stimuli are processed in the cortex whereas irrelevant stimuli are filtered out (Reynolds & Desimone, 1999). According to this hypothesis, attention appears as a nonlinear property that results from a top-down biasing effect that influences the competitive and cooperative interactions that work both within cortical areas and between cortical areas (Deco & Rolls, 2005).

Early and late selection theory of attention. The early selection view hypothesizes that focused attention can effectively prevent early perceptual processing of irrelevant distractors (Treisman, 1969), while the late selection view suggests that attention can only affect later post perceptual processes such as memory or response selection (Duncan, 1980). Researchers have found evidence supporting both these views and there is an on-going debate between the early versus late selection views of attention. To find a resolution to this debate, Lavie (2010) proposed the load theory of attention.

Load theory of attention. The load theory proposes two mechanisms of selective attention. The first includes a passive mechanism wherein irrelevant distractors are not perceived due to insufficient capacity of their processing under conditions of high perceptual load (Lavie, 1995, 2010). The second mechanism occurs during conditions of low perceptual load whereby an active mechanism rejects irrelevant distractors even when these are perceived. This second mechanism depends on higher cognitive functions to actively maintain processing priorities to ensure that low-priority stimuli do not drain resources. According to this theory, high perceptual load is hypothesized to reduce distractor interference while increasing cognitive control load is expected to increase distractor interference (Lavie, Hirst, De Fockert, & Viding, 2004). Thus, early selection is predicted for situations of high perceptual load, whereas late

selection is predicted for situations of low perceptual load (Lavie & Tsal, 1994). Lavoie, Hine, and Thornton (2008) compared different distraction tasks which included movie watching, reading, solving math, doing nothing eyes open, and doing nothing eyes closed while auditory stimuli were presented. The authors found that although the amplitude and latencies of event-related potentials (ERPs) were not affected, pre-stimulus activity (signal-to-noise analysis) was significantly different for the distraction conditions (Lavoie et al., 2008).

Although most of the above mentioned the research examining sensory processing is based on neurotypical functioning, researchers have examined sensory processing in clinical conditions as well. This dissertation examines sensory processing in one such condition, namely autism spectrum disorders.

Autism Spectrum Disorders (ASD)

ASD are neurodevelopmental disorders characterized by persistent deficits in social communication and social interaction as well as restricted, repetitive patterns of behavior, interests, or activities. The Diagnostic Statistical Manual-5 (DSM-5) lists five criteria for the diagnosis of ASD (DSM-5: American Psychiatric Association, 2013). 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. 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 hypo-reactivity 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 (DSM-5: American Psychiatric Association, 2013). ASD is commonly classified based on the level of intellectual dysfunction. Children functioning in the average or above average range of intelligence are often called high-functioning ASD.

There is strong evidence establishing neuropathological dysfunction in individuals with ASD, which has its origin in abnormal brain development early in prenatal life (Courchesne, 2004). Although ASD is typically diagnosed around 3 years of age, there is compelling evidence suggesting abnormality in early development and behavior. In a longitudinal study examining early signs in infants with a high-risk of developing ASD, Zwaigenbaum et al. (2005) found that infants who were later diagnosed with ASD could be distinguished from a comparison group of low-risk infants based on the following characteristics: 1) atypical patterns in eye contact and sensory oriented behaviors, 2) prolonged latency to disengage visual attention, 3) marked passivity and decreased activity level, and 4) delayed expressive and receptive language.

Deficits in sensory processing, which includes hyper- or hypo-reactivity to sensory input are part of the diagnostic criteria for children with ASD in the DSM-5 (American Psychiatric Association, 2013). Previous studies suggest that 42% to 95% of the children with ASD exhibit sensory processing disorders based on behavioral measures (e.g., Baranek, 2002; Liss, Saulnier, Fein, & Kinsbourne, 2006; Tomchek & Dunn, 2007; Walting, Deitz, & White, 2001). Additionally, several studies suggest auditory brain processing deficits in children with ASD (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.

Attention difficulties in ASD. Deficits in joint attention and social attention, are considered a hallmark characteristic of the core manifestation in ASD. Despite limited research examining attention in individuals with ASD, some researchers have found significant attention deficits in individuals with ASD using both behavioral and neuroimaging methods (Christakou et al., 2013; Corbett, Constantine, Hendren, Rocke, & Ozonoff, 2009; Geurts, Verte, Oosterlaan, Roeyers, & Sergeant, 2004). Evidence suggests that an early disruption in basic attention regulation (such as atypical orienting patterns) may be responsible for development of later deficits in social attention. Impairments in visual attention and orienting have been consistently reported even during infancy in individuals with ASD (Zwaigenbaum et al., 2005). Researchers examining ERPs have also shown that the attention-related late positivity (LPC) is compromised in individuals with ASD during attention orienting compared to neurotypical controls (Townsend et al., 2001). Using both behavioral measures of target detection and auditory ERP amplitudes, researchers have found that individuals with ASD have impairments in focusing their attention to target stimuli (Teder-Sälejärvi, Pierce, Courchesne, & Hillyard, 2005).

In a sample of ninety-one children with Asperger's syndrome, Sturm, Fernell, and Gillberg (2004) found that 95% of the participants had attentional problems using behavioral reports from clinicians. Using the Continuous Performance Test, researchers have documented deficits in sustained attention (Garretson, Fein, & Waterhouse, 1990). Using a comprehensive battery of behavioral measures, Corbett et al. (2009) found that children with ASD (7-12 years) had significant deficits in vigilance, and cognitive flexibility/switching. Deficits in shifting and disengaging attention are also commonly observed among individuals with ASD. Researchers

found that individuals with ASD take longer to disengage from a central target to orient toward a peripheral event when compared to neurotypical controls (Elsabbagh et al., 2009).

Neural basis of attention deficits in ASD. During a task of visual spatial attention in adults with ASD using electroencephalography (EEG; Belmonte, 2000) and fMRI (Belmonte & Yurgelun-Todd, 2003), attended and unattended sensory inputs evoked equally abnormal large activations in the ASD group compared to the control group. Additionally, there was a reduction in activation for brain regions serving integrative functions in the ASD group. In another study, integrative regions in the prefrontal and medial temporal cortices showed abnormally low activations compared to stronger activations in parietal cortex during suppression of distractors in individuals with ASD compared to neurotypical controls (Belmonte & Baren-Cohen, 2004). Researchers have found anatomic hypoplasia and reduction in number of Purkinje cells in the cerebellum, which have been associated with selective attention and orienting difficulties (Allen & Courchesne, 2003; Harris, Courchesne, Townsend, Carper, & Lord, 1999). Structural abnormalities in the inferior parietal lobe have been shown to correlate with attentional deficits observed in both ASD and attention-deficit hyperactivity disorder (ADHD; Brieber et al., 2007). Although several studies have implicated deficits in the attention networks in ASD, others have found intact organization of the task-positive network a.k.a. dorsal attention network, involved in performance of externally directed cognitively demanding tasks (Kennedy & Courchesne, 2008). It is noteworthy, that most of the imaging studies have examined the end result of the pathology of ASD rather than the etiological changes taking place during neural development.

Sensory processing in ASD. For the most part, since sensory organs in individuals with ASD are known to function normally, the deficits of under- and over-responsive processing may reflect modulatory mechanisms of information processing in cortical networks. Assessing

behavioral indicators, Tomchek and Dunn (2007) reported that children with ASD had differences in 92% of the sensory behaviors compared to typically developing controls. Under-responsivity (86%) and deficits in auditory filtering (78%) were the most consistent issues in children with ASD compared to controls (Tomchek & Dunn, 2007). Researchers examining sensory processing subtypes in ASD have found distinct profiles (Lane, Young, Baker, & Angley, 2010). Based on a model-cluster analysis, three distinct sensory processing subtypes were reported: 1) Sensory-based inattentive seeking – this profile correlates with deficits in attention and milder sensory processing deficits, 2) Sensory modulation with movement sensitivity – this subtype is characterized by deficits across all sensory domains, with both under- and over-responsivity. This was the only group to experience atypical performance in movement sensitivity coupled with an extremely low score in low energy/weak domain (weak muscles, poor endurance), 3) Sensory modulation with taste/smell sensitivity – this profile is characterized with deficits across all sensory domains except low energy and movement sensitivity, and with an extreme dysfunction in taste/smell sensitivity. Other researchers have reported similar profile patterns (Ben-Sasson, et al., 2009; Miller et al., 2007).

Auditory processing in ASD. Children with ASD often have more auditory processing difficulties compared to significantly better visual-spatial processing (Gomot, Giard, Adrien, Barthelemy, & Bruneau, 2002; O'Connor, 2012). Moreover, sensitivity to auditory stimuli in infancy was considered to be a powerful discriminator between children with autism and those without later in childhood (Dahlgren & Gillberg, 1989). Researchers have found both, hypersensitivity (Lucker, 2013) and hypo-reactivity (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). Hypo-reactivity 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). 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).

Theories describing attention and sensory processing in ASD. Although numerous theories have attempted to explain the constellation of seemingly unrelated symptoms of ASD and match them with observed neuroanatomical deficits, there is no consensus on a unifying theory. In the past, autism research was dominated by theories identifying dysfunction in individual brain regions, such as the amygdala (Baron-Cohen et al., 2000), prefrontal cortex (Courchesne et al., 2011), superior temporal sulcus (Redcay, 2008), or the fusiform gyrus (van Kooten et al., 2008). However, these localizing studies were fraught with inconsistencies in study findings and the inability to explain the spectrum of ASD. Recent conceptualizations have adopted a systems-level approach, and proposed that ASD may be explained by abnormalities in the mirror neuron system, and the connections between the limbic, and autonomic systems (Oberman & Ramachandran, 2007).

Mirror neuron theory. This theory proposes dysfunction in the fronto-parietal mirror neuron networks in individuals with ASD (Oberman et al., 2005). Mirror neurons are visuo-motor neurons that fire both when voluntarily performing a task, and observing a goal-directed action (Perkins, Stokes, McGillivray, & Bittar, 2010). Mirror neurons play a crucial part during

development and allow children to learn numerous skills such as language, emotional empathy, play behavior, and the ability to infer the goals of others for predicting their behavior (Brang & Ramachandran, 2010). Since these are some of the abilities compromised in ASD, dysfunction in mirror neuron system explains at least in part, the neurological basis for this condition (Oberman et al., 2005). Several studies have shown evidence of mirror neuron dysfunction in ASD using fMRI, TMS, electroencephalography (EEG), and magnetoencephalography (MEG; Hamilton, 2013). However, certain deficits including sensory sensitivities, and unpredictable emotional outbursts have not been explained by mirror neuron dysfunction. To explain some of these inconsistencies, Ramachandran and Oberman (2006) proposed the salience landscape theory.

Salience landscape theory. According to this theory, in neurotypical children, information from the brain's sensory areas are relayed to the amygdala, which is the gateway to the emotion-regulating limbic system. Using input from stored knowledge, the amygdala determines how the child should respond to incoming information. Information from the amygdala is sent to the rest of the limbic system and the autonomic nervous system. The autonomic activity, in turn, feeds back into the limbic system. Thus, the amygdala creates a *salience landscape* of the environment. Ramachandran and Oberman (2006) propose that children with ASD have a distorted salience landscape, either due to altered connections between the cortical areas that process sensory stimuli and the amygdala or between the limbic system, and the frontal lobes that regulate resulting behavior. These abnormal circuitries can explain unexpected autonomic arousal in children with ASD to otherwise trivial stimuli. This hypothesis can also explain avoidance of eye contact, sensory processing disturbances, and self-injurious behavior (Ramachandran & Oberman, 2006).

These researchers also propose that temporal lobe epilepsies, commonly occurring in children with ASD may cause disturbances in the ventro-dorsal pathway, which carries information from the visual cortices to the TPJ (Brang & Ramachandran, 2010). This pathway is rich in mirror neurons, especially those involved in emotional empathy. Additionally, researchers suggest accompanying dysgenesis or agenesis of the olfactory bulbs and projection zones of the brain, which can cause dysregulation of oxytocin and vasopressin functioning, resulting in emotional disturbances (Brang & Ramachandran, 2010). In summary, the researchers propose a combination of temporal lobe epilepsies, olfactory bulb dysgenesis, mirror neuron system deficits, and hypothalamic/autonomic dysregulation as probable causes of ASD (Brang & Ramachandran, 2010). Dysfunction in sensory processing (due to distorted salience landscapes) and attention (TPJ involvement) can be explained using this theory. However, while the salience landscape theory and its updates explain a wide range of symptoms in individuals with ASD, it lacks the rigor of empirical research. Additionally, this theory proposes a set of different neuropathology's to explain the spectrum, whose etiologies are not clearly connected. Another theory that aimed to explain the spectrum of symptoms using a single common pathology was proposed by Markram, Rinaldi, and Markram (2007) using the valproic acid animal model of ASD.

The intense world theory. This theory proposes a unifying model of neuropathology of hyper-functioning local neural microcircuits. These hyper-functional microcircuits are assumed to become autonomous and memory-trapped resulting in the core cognitive consequences of hyper-perception, hyper-attention, hyper-memory mediated by the neocortex, and hyper-emotionality mediated by the limbic system (Markram & Markram, 2010). The authors have used these four dimensions to explain the full spectrum of symptoms in ASD, depending on the

severity of the microcircuit pathology in different brain regions. On a perceptual level, the excessive functioning of local neuronal circuits may lead to an intensely perceived world, which may become stressful and aversive if the amygdala and the limbic system are also affected (Markram & Markram, 2010). The strengths of this theory lie in its ability to explain the disorder from molecular, cellular, and circuit changes to affective-cognitive behavioral levels. The local hyper-reactivity in the neocortex and amygdala can account for sensory sensitivity, and aversion to everyday sensory stimuli observed in ASD. Additionally, hyper-functioning microcircuits in the neocortex may lead to increased perception of fragments of the sensory environment, causing hyper-focusing on details and difficulties in shifting attention (Markram & Markram, 2010). A strength of this theory is that this model helps to explain weak central coherence theory (Happé & Frith, 2006), and the enhanced perceptual functioning theory (Mottron, Dawson, Soulieres, Hubert, & Burack, 2006), which state that individuals with ASD have enhanced detailed-focused processing and impaired gestalt processing.

Under-connectivity theory. Researchers using fMRI in individuals with ASD established that signs and symptoms of ASD were attributable to dysfunction in several recognizable neural regions. Thus, ASD was classified as a disorder of distributed neural systems resulting in deficits in higher order functioning (Minshew & Keller, 2010). More recent research focused on functional connectivity using fMRI, which revealed that ASD is a disorder of underconnectivity among brain regions participating in long-range cortical networks. However, there is still considerable heterogeneity in network disturbances or the extent of brain regions affected. A common finding across studies using fMRI was that of fronto-parietal underconnectivity. This white matter dysfunction is thought to be associated with attention deficits in ASD (Velazquez et al., 2009). Along with reduced long-range connectivity,

researchers have found increased local connectivity of posterior regions such as parietal-occipital circuitry. This local over-connectivity is assumed to account for the enhanced visuo-spatial abilities in individuals with ASD. There is mixed evidence regarding functional connectivity in the default mode network in ASD and its implications. Some researchers have found reduced connectivity in the default network, suggesting a lack of introspective and self-reflective thinking (Kennedy & Courschesne, 2008).

Several fMRI studies have demonstrated that long-range connections between brain regions are under-developed in ASD (Just, Cherkassky, Keller, Kana, & Minshew, 2007; Mottron et al., 2006). Under-connectivity has been demonstrated between fronto-temporal and occipital lobes (Castelli, Frith, Happé, & Frith, 2002), superior temporal and inferior frontal lobes (Just et al., 2007), parietal and frontal lobes (Just et al., 2007), as well as amygdala and parahippocampal gyrus (Welchew et al., 2005). Thus, researchers proposed the Under-Connectivity Theory which states that ASD is associated with hypo-connectivity of integrative circuitry, resulting in impairments of complex information processing at neural and cognitive levels (Just, Keller, Malave, Kana, & Varma, 2012). Based on this unifying theory, most of the co-occurring deficits in ASD such as attention, sensory processing, social and emotional functioning can be explained (Just et al., 2012). Although, Herbert and colleagues examining white-matter connectivity found that while long-range fibers were not affected in ASD, the more short- and middle-range connections were increased (Herbert et al., 2004). The under-connectivity theory also suggests that functional connectivity among posterior regions may be higher in ASD than controls because of the decrease in fronto-posterior connectivity. This local over-connectivity with long-range under-connectivity explains savant skills and enhanced perceptual functions along with impairments in executive control and attention (Just et al., 2007).

Belmonte et al. (2004) stated that similar to individuals with ASD who have difficulty in central coherence, the field of autism research has had difficulty in synthesizing fragmented research theories into an identifiable pattern. The three major theories reviewed, the 'Salience landscape theory', 'Intense world theory', and the 'Underconnectivity theory' have several similar assumptions. A common key feature is the recognition of a systems-level impairment affecting functional connectivity and communication between multiple brain regions. Additionally, each of these theories has been able to explain the spectrum of symptoms in ASD ranging from impairments in socio-emotional functioning to sensory sensitivities, and deficits in executive functioning. Moreover, findings of abnormal neural connectivity have been integrated with neurophysiology and behavior to provide a coherent explanation of the underlying pathology of ASD. However, most of the assumptions in these theories have not yet been empirically validated. The etiology of ASD and abnormal connectivity is still debated and ranges from heredity and genetics to environmental factors. Additionally, correlations between brain irregularities and symptoms do not necessarily translate directly into cause and effect relationships. Thus, more research is required to test the theoretical assumptions and understand cause and effect relationships.

Impact of Attention and Sensory Processing Issues on Everyday Behaviors

Sensory processing deficits result in the inability to discriminate, modulate, coordinate, and organize incoming sensory information adaptively (Lane, Miller, & Hanft, 2000). According to some authors, attentional processes are subsumed within the neurological ability to integrate sensory information. More recently researchers have begun to focus on *attention* and *arousal deficits* in ASD with the notion that these deficits may precede social symptoms and represent the earliest signs of ASD in infants at risk of developing ASD (Elison et al., 2013;

Elsabbagh et al., 2013; Zwaigenbaum et al., 2005). Ben-Sasson et al. (2007) suggested that co-occurrence of sensory under- and over-responsive behaviors in ASD may result from abnormal *arousal* regulation. Additionally, Liss et al. (2006) and Allen and Courchesne (2001) proposed that both sensory and behavioral under- and over-responsivity may be linked to the child's *attention* deficit. Liss et al. (2006) suggested that the over-focused attention style in ASD may be the result of hyperarousal. Others have hypothesized that atypical behavioral regulation in everyday activities may result from early impairment in shifting and disengaging *attention* (Keehn, Muller, Townsend, 2013). To summarize, several researchers have posited that impairments in sensory processing, and social and behavioral regulation in individuals with ASD may be associated with a common underlying neurophysiological mechanism of attention.

In the auditory domain, researchers examining attention and sensory processing using neurophysiological measures suggest that processing of attended stimuli is either normal or increased in ASD, while processing of unattended stimuli is usually decreased (Orekhova & Stroganova, 2014). In a review of findings of mismatch negativity, Orekhova and Stroganova (2014) found that individuals with ASD are usually able to detect changes in the stimuli presentation when these stimuli are the focus of their attention. However, in the presence of distractors or in the case of unattended stimuli, processing issues arise. When competition for attention is higher, detection of change and associated cognitive processing are reduced in ASD compared to typical controls. Thus, sensory processing appeared to be dependent on the context of stimulus presentation, which suggests deficits in early orienting and attentional mechanisms.

Preliminary Research Examining Sensory Processing and Attention in ASD

The Brainwaves Research Lab has conducted several studies to examine attention and sensory processing in neurotypical and clinical populations using both behavioral and

neuropsychological measures, such as EEG and ERPs. EEG is a non-invasive technique that can measure electrical activity of the brain by means of electrodes positioned on the scalp. These metallic sensors detect very small (10-50 microvolts) and continuous voltage changes across the scalp, which are then amplified and digitized. EEG has been widely used for understanding neurophysiological functioning, and behavior related to sensory processing skills of children and adults with and without disabilities. EEG/ERP technologies 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. The Brainwaves Research Lab had focused on two auditory ERP paradigms, sensory gating and sensory registration.

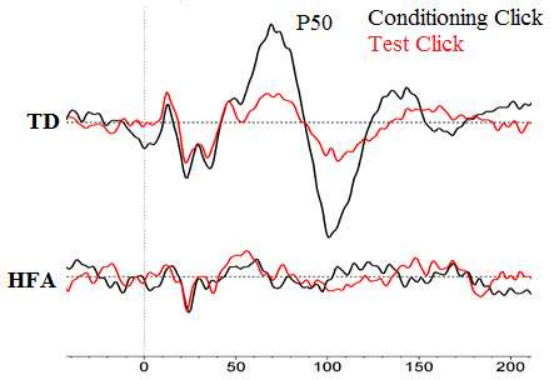

Figure 1. Grand-averaged ERP waveforms of the sensory gating paradigm in children with HFA and TD peers.

Sensory gating literature. Previous research in our lab manipulated attention during a sensory gating paradigm. The sensory gating paradigm consists of repeated presentations of paired-click stimuli. During my master's, I examined sensory gating in children with high-functioning ASD (HFA) as compared to age- and gender-matched typically-developing (TD) peers. The results indicated that children with HFA have significantly poorer gating compared to the control group (See Figure 1; Dungan, Crasta, Davies, & Gavin, 2015). Participants completed

two sensory gating paradigms, one wherein their attention was directed towards a silent movie, and the other wherein their attention was directed to the click stimuli. In this second paradigm, paired clicks were interspersed with single click stimuli. In the focused attention condition participants were asked to press a button to the single click (Gavin, Bulwan, & Davies, 2011). In the focused attention condition, this study demonstrated a difference in early brain processing to the auditory stimuli that required a motor response compared to the auditory stimuli that were asked to be ignored, with all other parameters remaining constant. While the passive attention condition (no motor response required) activates the orienting network, it is assumed that the focused attention condition (motor response required) activates the alerting system.

Additionally, adults and children had larger N1 amplitudes for the focused attention paradigm compared to the gating with movie watching condition. Thus, the effects of attention manipulation and distraction were evident in processing of auditory click stimuli. Understanding the neurological mechanisms underlying how the brain processes information in light of attention manipulations and distractions in neurotypical and clinical populations can shed light on the different attention theories and the attentional networks.

Another study in our lab examining sensory processing in children with SPD found contrasting results related to cognitive processing of auditory information in active versus passive attention conditions. Compared to typically developing peers, children with SPD had reduced cognitive processing to simple auditory stimuli while they watched a silent movie. In contrast, children with SPD had increased cognitive processing for the same paradigm when they stared at a fixed symbol on a computer screen as compared to the typically-developing control group. The other parameters of the two studies were the same and hence this difference in cognitive processing was attributed to the methodological difference of movie watching versus

staring at a fixed symbol. The authors inferred that the increase in cognitive processing in children that were not distracted by the movie, could be due to more resource allocation for processing the auditory stimuli (Gavin et al., 2011).

These findings are in line with the load theory of attention (Lavie et al., 2004). The *early selection* view of attention suggests that perceptual processing capacity is limited. Thus, individuals who are fully engaged in a perceptual task are unable to perceive unattended distractors due to insufficient capacity for their processing. This view also suggests that early perceptual processing of irrelevant distractors is reduced while one is actively focusing attention to a given sensory stimulus. EEG research on children often involves the use of a silent movie while auditory EEG paradigms are being presented. According to the attention theories mentioned previously, if a participant is actively engaged in watching a movie, processing of the auditory stimuli is significantly reduced, while the absence of a movie would allow for unobstructed processing of the stimuli.

Sensory registration literature. For my master's thesis, I also examined the ability to discriminate between different auditory stimuli using the sensory registration EEG paradigm in children with and without HFA. This paradigm utilizes four auditory tones which are presented at different frequencies (1 kHz or 3 kHz) and intensities (50 dB or 70 dB). Results indicated that children with HFA had significantly smaller P300 ERP amplitudes to all the four tones. The P300 is an ERP component that occurs around 300 ms post-stimulus onset and is associated with cognitive processing of the stimuli. Smaller P300s in the HFA group compared to the TD group suggest increased difficulty discriminating between stimuli (See Figure 2; Crasta, 2015).

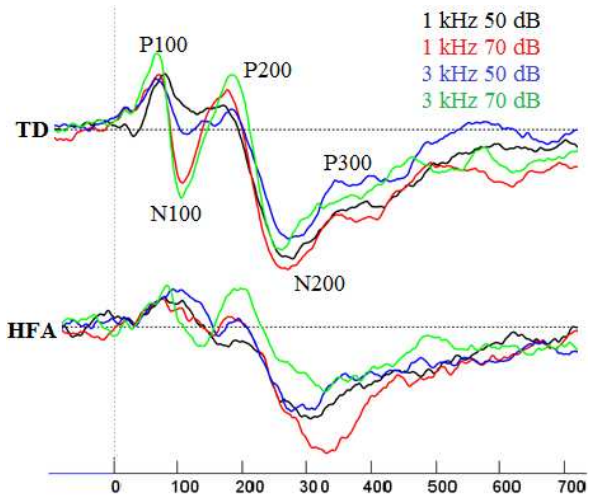

Figure 2. Grand-averaged ERP waveforms of the sensory registration paradigm in children with HFA and TD peers.

Attention measured by Test of Everyday Attention for Children (TEA-Ch). The TEA-Ch is a standardized and well-normed assessment that provides raw- and age-corrected scaled-scores for each of its nine subtests. The subtests measure three attention subgroups, namely selective, sustained, and attention control/shift which correspond to Petersen and Posner's (2012) attention networks (Manly et al., 1999). In a study examining attention abilities in children with high-functioning ASD (n=27) and age- and gender-matched typically-developing controls, we found that children with ASD had significant deficits in selective, sustained, and control/shift attention compared to typically-developing controls (Crasta, 2015).

Sensory processing measured by the Sensory Profile. The Short Sensory Profile is a parent-report, norm-referenced screening tool frequently utilized by occupational therapists (Dunn, 1999). The seven subscales assess auditory filtering, low energy-weak, under-responsive-seeks sensation, sensitivity to movement, tactile, taste-smell, and visual-auditory. Responses are scored on a 5-point Likert scale, with higher scores indicating more functional and adaptive behaviors. Adaptive behavior is defined as purposeful, goal-directed behavior in

response to sensory information (Ayres & Robbins, 2005). We examined sensory processing in 27 children with high-functioning ASD as compared to age- and gender-matched typically-developing peers using the Short Sensory Profile. The results indicated that children with high-functioning ASD had significantly more sensory processing issues in all domains except movement sensitivity compared to the control group.

Modified Approach towards Understanding Attention and Sensory Processing in ASD

Using information from attention theories, OT theories and research, ASD research, and my master's research, I propose a more comprehensive model for understanding ASD. OT research has shown that there is a relationship between sensory processing and effective participation (Dunn, 2014; Miller et al., 2007). This revised model, suggests that *active* attentional processes are essential for efficient sensory processing (See Figure 3 below). The premise for this dissertation stems from the assumption that attention deficits in ASD may prevent automatic neural attentional allocation to relevant sensory information. The neurological theories explaining ASD have clearly demonstrated impairments in integration of sensory information across brain regions. Thus, I hypothesize that for efficient sensory processing in individuals with ASD, active attentional processes are required. Active allocation of attention to relevant sensory information may result in enhanced neural processing of sensory information. Thus, while passive processes are sufficient in neurotypical individuals, due to deficits in neural connectivity, individuals with ASD may require to actively focus or attend to sensory stimuli to efficiently process sensory information. Due to deficits in gating, passive processing may be impacted by distractors, which may hamper the stream of sensory processing. According to the Intense World Theory, passive processing may result in hyper-focusing, leading to sensory overload. Anecdotal reports of sensory overload in individuals with ASD have been documented

by several researchers (for review see Pellicano, 2013). According to the proposed model, active attentional regulation of sensory information may bolster neural processes and aid in effective gating and information processing, leading to effective participation. This dissertation empirically tests this model and examines the mediating role of attention on sensory processing.

Since auditory processing is the most commonly reported sensory processing deficit in ASD (Tomchek & Dunn, 2007), this dissertation research focused on auditory processing, and the impact of attention during auditory processing. This dissertation research hypothesizes that integration of attention in understanding sensory processing provides a holistic explanation of the neurophysiological and behavioral mechanisms at play in individuals with ASD.

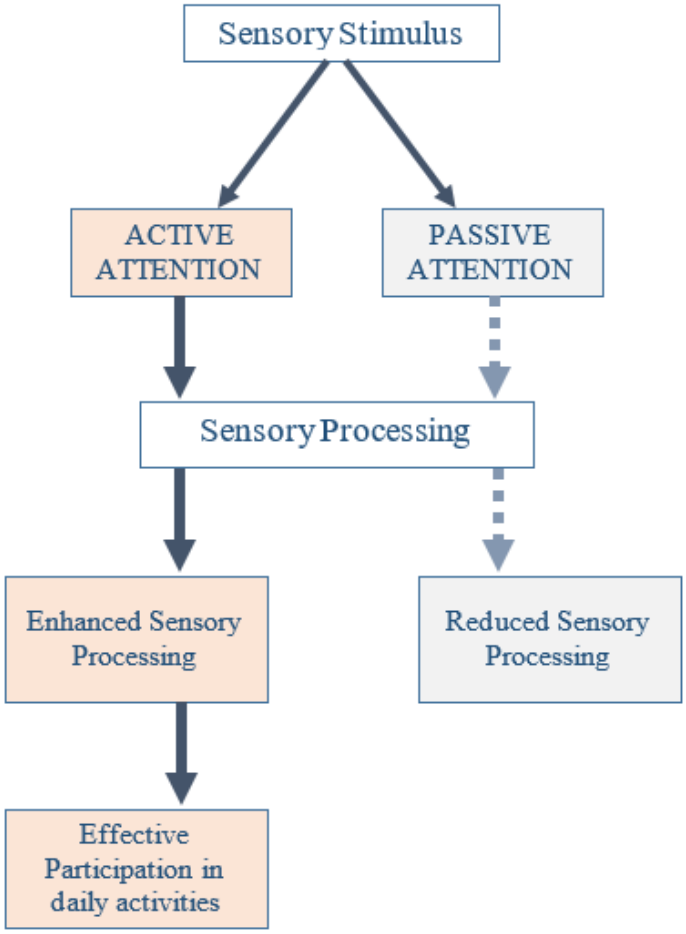

Figure 3. Proposed model depicting the relationship between attention and sensory processing.

Through the following three studies, we aimed to empirically examine the impact of attention on auditory processing using established EEG paradigms, namely the sensory gating paradigm and the sensory registration paradigm (See Table 1). The first study involved examining the feasibility of the task demands which involves performing either passive or active tasks in the presence of a distractor (movie-watching). This first study was conducted in neurotypical individuals. The second and third study examined sensory gating and sensory registration respectively in 24 individuals with ASD and a control group of 24 age- matched neurotypical controls. Thus, overall the three studies provide information about different stages of information processing. Using behavioral measures of sensory processing and attention along with ERP measures, we explored brain-behavior relationships in ASD and controls.

Table 1. Paradigms involved in the dissertation studies.

Study 1		**Study 2**	**Study 3**
Neurotypical (n = 60)		ASD (n=24) and neurotypical (n=24)	ASD (n=24) and neurotypical (n=24)
Group 1: Movie	Group 2: No Movie		
Registration (Passive)		No movie – Gating (Passive)	No movie – Registration (Passive)
Registration (Active)		No Movie – Gating (Active)	No Movie – Registration (Active)

CHAPTER 2 – STUDY 1

Attentional demands and environmental distraction differentially affect the sensory registration of the frequency and loudness of tones measured with ERPs

Attention is a crucial element of our goal-directed, purposeful response to sensory information in our social and physical environment. Attention is understood as a "broad cognitive concept that includes a set of mechanisms that determine how particular sensory input, perceptual objects, trains of thought, or courses of action are selected for further processing from an array of concurrent possible stimuli, objects, thoughts and action" (Talsma, Senkowski, Soto-Faraco, & Woldorff, 2010, p. 2). According to the feature-integration theory of attention, without focused attention, stimulus features cannot be related to one another (Treisman & Gelade, 1980). Thus, attention is necessary for the accurate perception and integration of information. Studies have shown that sensory processing abilities are dependent on attentional control (Corbetta, Miezin, Dobmeyer, Shulman, & Petersen, 1990; Talsma et al., 2010). How selective attention and distraction impact sensory processing, in the visual and auditory domain has gained considerable interest in recent years. Several theories have been posited to provide a framework to understand the influence of attention on visual processing (Borji & Itti, 2014; Corbetta et al., 1990; Hillyard, Vogel, & Luck, 1998; Lavie, 2010; Reynolds & Desimone, 2003).

The perceptual load theory of selective attention, one of the most prominent theoretical framework, proposed two mechanisms of selective attention (Lavie, 2010). The first includes a passive mechanism wherein irrelevant distractors are not perceived due to insufficient capacity of their processing under conditions of high perceptual load (Lavie, 2010). The second

mechanism occurs during conditions of low perceptual load whereby an active mechanism rejects irrelevant distractors even when these are perceived. This second mechanism depends on higher cognitive functions to actively maintain processing priorities to ensure that low-priority stimuli do not drain resources. According to this theory, high perceptual load is hypothesized to reduce distractor interference while increasing the cognitive demand (i.e., cognitive load) of a task is expected to increase distractor interference (Lavie, Hirst, De Fockert, & Viding, 2004). A fundamental aspect of this theory, regardless of the attention mechanism involved, is that it proposes that our perceptual system has limited processing capacity, and implies that the perceptual demand of the relevant task that we are engaged with determines our success in ignoring irrelevant information.

Using EEG and event-related potentials (ERPs), researchers have examined the effect of attention and distraction on auditory processing (Herrmann & Knight, 2001). The initial ERP components recorded in response to a stimulus are often described as reflections of automatic processing of sensory characteristics, while later components are associated with cognitive processing of the stimulus (Polich, 1993; Stern et al., 2001). More specifically, the P1 and N1 are greatly influenced by parameters of the stimulus such as intensity and frequency, and reflect exogenous processes which are modulated by physical stimulus attributes but not by cognitive processing (Rugg & Coles, 1995). 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). However, attending to tones can enhance the N1 amplitude (Hillyard, Hink, Schwent & Picton, 1973). Thus, the N1 is thought to represent the orienting of attention towards task-relevant stimuli (Luck, Heinze, Mangun & Hillyard, 1990).

Fewer researchers have studied the effects of attention on the P2 and N2 components. The P2 represents stimulus classification and leads to the N2-P3 response (Crowley & Colrain, 2004). García-Larrea, Lukaszewicz and Mauguiére (1992) noted that P2 occurred in response to non-targets in an auditory oddball, in order to assess if the stimulus was a target. Based on P2's stimulus classification, if the stimulus was a target, then there would be a P3, else the P3 would not be elicited. Thus, P2 is proposed to be involved in protection against needlessly processing irrelevant stimuli, which may lead to protection from processing distractors (García-Larrea et al., 1992). The N2 component, was previously measured in association with the P3, and referred to as the N2-P3 complex. Recent research has shown that the N2 is functionally distinct from the P3 with regards to cognitive processing (Folstein & Van Petten, 2008) and is associated with a general alerting system (Suwazono, Machado & Knight, 2002). The N2 to auditory stimuli has been shown to be larger during difficult than easy discrimination tasks (Senkowski & Herrmann, 2002).

Researchers examining attention effects at the P3 component have found a discernible P3 during passive listening states, albeit smaller in amplitude compared to the active attention states (Polich, 1987). The P3 is elicited when subjects attend to a stimulus and when they discriminate stimulus features (Polich & Bondurant, 1997). The P3 amplitude reflects the probability and task relevance of a stimulus while the P3 latency reflects the duration of stimulus evaluation (Donchin & Coles, 1988). Additionally, researchers have found that the P3 amplitude may decrease and latency increase with increased level of difficulty and distractibility introduced. Robust intensity discrimination has been found in N1, P2, N2 and P3 auditory ERP components, such that loud tones generate larger amplitudes and shorter latencies than soft tones (Harris et al., 2007; Martin & Boothyord, 2000). With regards to frequency discrimination, low-frequency

sounds produce larger amplitudes than high-frequency sounds at the same intensity (Wunderlich & Cone-Wesson, 2001). Specifically, the researchers found that N1 amplitude and latency decreased as frequency increased, while P2 amplitude, but not latency, decreased as frequency increased (Wunderlich & Cone-Wesson, 2001). Thus, stimulus characteristics such as intensity and frequency are expected to impact the amplitude and latency of ERP components following the presentation of auditory stimuli.

The auditory paradigm used in the present study has been modified from two studies involving children with autism (Bruneau, Garreau, Roux, & Lelord, 1987; Lincoln, Courchesne, Harms & Allen, 1995) and was previously used in our lab (Davies, Chang & Gavin 2010). 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 in neurotypical 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 ERP waveform. Hence, this paradigm is termed as the *sensory registration* paradigm. Davies et al. (2010) investigated the brain responses of adults using the sensory registration paradigm and 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.

Researchers have found that the ERPs generated from tasks that had a distraction element still contained at least one ERP component time-locked to the task-relevant tasks

(Escera, Alho, Schröger, & Winkler, 2000). For example, researchers have shown that working memory and task-related processes may be reflected in ERP components that are time-locked to auditory or visual stimuli in a paradigm that also includes a distraction protocol (Berti, 2008; Roeber, Berti, Widmann, & Schröger, 2005). To examine the effects of attention and distraction without the confounding effects of other executive functions, a simpler discrimination-based paradigm was used in the present study. We chose watching a silent movie as the distraction stimulus since several researchers use silent movies during auditory ERP paradigms. However, the effect of movie viewing on auditory processing and discrimination is unclear. Additionally, since attention is not modality specific and because strong cross-modal links exist between vision and audition, it is very likely that the visual viewing condition would influence auditory processing (Kanwisher & Wojciulik, 2000). Manipulation of the environment to change a participant's attention, such as adding a distractor element to a task, has been shown to affect sensory processing as measured by ERP component amplitude (Roeber et al., 2005). Additionally, as discussed above, manipulation on the participant's internal state of attention by requiring a response to a particular stimulus has also shown to influence sensory processing.

In the present study, participants were presented with two attention conditions, a passive condition, wherein participants were asked to only listen to the stimuli, and an active condition, wherein participants were asked to respond with a button press to a target stimulus. Thus, the design of the present study manipulates both the environment by the presence or absence of a distractor and the participant's internal attentional state by whether or not a response to a target stimulus is required. The aim of the present study was to examine the effects of attention (passive versus active) with and without a visual distractor during a simple auditory detection

task. An additional aim was to replicate the effects of stimulus characteristics of intensity and frequency on amplitude and latency of ERP components.

Research Questions:

1. How does manipulating stimulus characteristics impact auditory processing?

Hypothesis: Robust intensity and frequency discrimination will be observed at the N1, P2, N2 and P3 components regardless of attention and viewing conditions. Loud tones and low frequency tones will have larger amplitudes and shorter latencies than soft tones and high frequency tones.

2. How does manipulating the environment impact auditory processing?

Hypothesis: Participants in the movie-viewing group will have smaller N1, P2, N2, and P3 amplitudes and longer latencies than participants who view a fixation point.

3. How does manipulating the participant's internal attention state impact auditory processing?

Hypothesis: During the active condition, participants will have smaller N1, P2, and N2 amplitudes, and larger P3 amplitudes compared to the passive condition.

Methods

Participants were 60 neurotypical individuals, ages 18 – 35 years (M = 24.66, SD = 3.9; 31 females and 29 males) recruited via convenience sampling. All participants were screened using a self-report screening questionnaire developed in our lab to ensure that they are free of neurological injuries, disabilities, and family histories of psychological disorders. All the procedures performed in the research involving human participants were in accordance with the ethical standards of the institutional review committee at the local university and with the 1964 Helsinki declaration and its later amendments. All participants signed a written informed consent

prior to the study. Participants were randomly assigned to the movie-viewing or fixation viewing group (viewing condition). Participants in the movie viewing condition watched a silent animated movie (Shaun the Sheep), while the fixation viewing group stared at a star symbol on a computer screen. Both groups were presented the passive condition followed by the active condition described in detail below.

EEG/ERP data recording. EEG data were collected in a sound attenuated and electrically shielded room. Once the EEG cap, and electrodes were applied, the participant was given a brief training on strategies to reduce artifacts resulting from eye blinks, and other muscle activity. All EEG data were collected using the BioSemi ActiveTwo EEG/ERP Acquisition System (BioSemi, Wg-Plein 129, 1054 SC Amsterdam, Netherlands). This system included 64 Ag/AgCl sintered scalp electrodes. The electrodes were located in accordance with the modified 10–10 system (Klem, Lüders, Jasper, & Elger, 1999; Oostenveld & Praamstra, 2001). EEG was recorded with the Common Mode Sense active electrode as the reference and the Driven Right Leg passive electrode as the ground (http://www.biosemi.com/faq/cms&drl.htm). Electrooculograms (EOGs) were recorded from individual electrodes placed on the left and right outer canthus for horizontal movements and on the left supraorbital and infraobital region for vertical movements. Two more individual electrodes were placed on the left and right earlobes and used as the offline reference. 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 were sampled at a rate of 2048 Hz with a bandwidth of 0 to 417 Hz.

Sensory Registration EEG paradigm. The four auditory stimuli (50 ms in duration with 10 ms ramping of intensity up at onset and down at offset) consisted of pure tones, 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 sound pressure level (SPL) or 70 dB SPL. For each attention condition, the stimuli were presented in two blocks of 160 trials each, with a total of 80 trials of each tone in pseudo-random order with a two-second inter-stimulus interval. Each block lasted about five minutes with short breaks of about 1 minute between blocks.

Passive attention condition. Participants were instructed to stare at the fixation point or watch the movie while they heard the auditory stimuli. No motor response was required.

Active attention condition. Participants were instructed to respond with a button press to the low frequency soft tone (1 kHz, 50 dB SPL stimuli) and ignore the other 3 auditory stimuli. The participants were instructed to stare at the fixation point or watch the movie while they listened to the tones and pressed the button. Based on previous research, the low frequency soft tone was chosen as the target tone since it has the smallest ERP amplitude compared to the other tones in the passive condition (Crasta, 2015; also See Figure 4), which allows us to determine the influence of focused attention. At the start of the paradigm, participants went through a brief practice session with feedback. During the session, no feedback was provided.

ERP waveform and component analysis. Averaged ERPs for each participant were composed from the running EEG data using Brain Vision Analyzer 2.0. 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 with a 12 dB/octave rolloff using casual phase-shift free butterworth filter settings. 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 was

performed (Segalowitz, 1996). Following this, the artifact rejection technique built into the Brain Vision Analyzer software 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 to create the averaged ERP. Of the 64 channels, the central-midline site Cz was analyzed based on previous studies using auditory paradigms (Davies et al., 2010; Lincoln et al., 1995). Peak amplitudes for the N1, P2, N2, and P3 were identified using the Matlab software, PeakPicker program (Gavin, 2009). The window for determining the peaks is based on previous published research (Davies et al. 2010; Lincoln et al., 1995) and visual inspection of the grand average waveforms for the participants. The N1 component was scored between 65 and 150 ms. The P2 component was scored between 130 and 325 ms after the stimulus onset. The N2 component was scored between 185 and 400 ms after the stimulus onset and the P3 component was scored between 250 and 500 ms after stimulus onset

Data analysis. To determine if brain processing of auditory stimuli differed significantly between the two groups with different viewing conditions across the two different attention conditions, amplitudes of the N1, P2, N2, and P3 components were analyzed using a 2 x 2 x 2 x 2 repeated measures analysis of variance (ANOVA). The between subject's factor was viewing condition (2 levels: movie and fixation). The three within factors were Attention (Passive and Active), Frequency (2 levels: 1 kHz and 3 kHz), and Intensity (2 levels: high and low). Testwise alpha was set at 0.0063 for the *apriori* hypotheses (ANOVAs), with Bonferroni correction for the 4 ERP components and two ANOVAs examining amplitude and latency measures for each ERP component, (.05/8 = .0063). Effect sizes for η^2 are interpreted as follows, .04 – small, .25 – medium, and .64 – large (Ferguson, 2009). *A posteriori* Tukey's honestly significantly difference

(HSD) post-hoc *t* tests were calculated to examine interaction effects (Kirk, 1968, p. 265-269). All statistical analyses were performed using the Statistical Package for Social Sciences (SPSS), version 24.0

Results

The grand-averaged ERP waveforms for the four auditory stimuli are shown separately for the two viewing groups and attention conditions at site Cz in Figure 4. The means and standard deviations of the N1, P2, N2, and P2 amplitudes are reported in Table 2. Visual inspection of the ERP components indicates that the loud tones (70 dB) have larger amplitudes than the soft tones (50 dB) at the early N1 and P2 components. Additionally, the active condition appears to have larger amplitudes at the mid-latency N2 and P3 components (see Figure 4).

Table 2. Means and standard deviations for the ERP components for the sensory registration paradigm.

	Viewing group			
	Movie		Fixation	
Stimulus	Passive	Active	Passive	Active
1 kHz 50 dB SPL	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)
N1	-7.66 (3.09)	-7.48 (2.56)	-6.61 (2.03)	-7.39 (2.4)
P2	3.85 (2.71)	2.03 (2.91)	4.27 (2.61)	2.17 (2.73)
N2	-2.67 (2.33)	-2.00 (3.20)	-1.79 (2.13)	-1.07 (2.49)
P3	1.27 (1.86)	3.18 (3.36)	1.00 (1.64)	4.88 (4.15)
1 kHz 70 dB SPL				
N1	-10.51 (3.26)	-9.5 (3.29)	-9.07 (2.61)	-8.7 (2.63)
P2	8.07 (2.65)	4.73 (3.11)	7.24 (3.47)	5.14 (3.48)
N2	-2.95 (2.65)	-1.85 (2.97)	-1.72 (2.41)	-.73 (3.44)
P3	2.11 (2.33)	2.47 (3.12)	1.51 (2.77)	4.31 (3.99)
3 kHz 50 dB SPL				
N1	-7.47 (3.02)	-6.57 (3.04)	-6.68 (2.21)	-6.29 (2.43)
P2	3.66 (2.27)	4.06 (3.12)	4.01 (2.68)	5.63 (2.46)

N2	-2.97 (1.93)	-1.63 (3.21)	-2.1 (2.59)	-1.19 (3.34)
P3	1.47 (1.52)	1.67 (2.74)	.57 (2.53)	2.75 (2.93)
3 kHz 70 dB SPL				
N1	-10.35 (3.39)	-8.58 (3.85)	-8.91 (2.51)	-8.19 (2.72)
P2	7.58 (2.89)	6.67 (3.21)	6.65 (3.16)	7.59 (3.06)
N2	-3.14 (2.14)	1.07 (2.72)	-1.52 (2.28)	1.78 (3.38)
P3	2.31 (2.36)	4.92 (2.79)	2.31 (2.75)	6.04 (3.65)

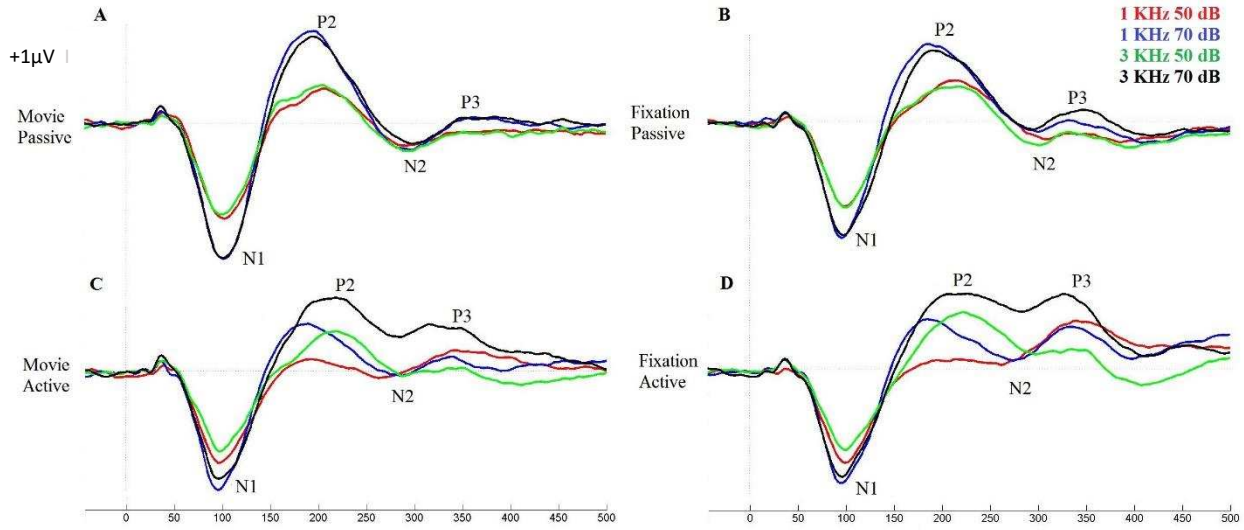

Figure 4. Grand averages of the ERPs at site Cz. A. Movie viewing group during the passive condition. B. Fixation viewing group during the passive condition. C. Movie viewing group during the active condition. D. Fixation viewing group during the active condition. Positive voltage is up.

For the active condition, we examined the response times to determine if the viewing environment (i.e., distraction) affected the behavior of the participants. Analysis of the behavioral data revealed that the means of the response times for the active condition for both viewing conditions (fixation viewing: $M = 581.53$, $SD = 98.98$ and movie viewing: $M = 601.62$, $SD = 79.05$) were not significantly different, $t_{(58)} = .86$, $p = .39$. To answer the research questions, group differences in amplitude and latency measures of N1, P2, N2, and P3 components were separately analyzed using repeated measures ANOVAs.

Stimulus Characteristics: Intensity and Frequency Discrimination

For **N1 amplitude**, the main effects of intensity, $F_{(1, 58)} = 190.17$, $p < .0005$, $\eta^2 = .77$ and frequency, $F_{(1, 58)} = 8.64$, $p = .005$, $\eta^2 = .13$ were significant. As expected, high intensity loud tones had larger N1 amplitudes than the soft tones across attention and viewing conditions. Low frequency tones had larger N1 amplitudes than high frequency tones across attention and viewing conditions. For **N1 latency, the** ANOVA revealed a main effect for intensity, $F_{(1, 58)} = 6.63$, $p = .013$, $\eta^2 = .10$ with a small to medium effect size but was not significant at the alpha level set for this study. Loud tones, *M (SE)* = 99.46 ms (.88), had shorter N1 latencies than the soft tones, *M (SE)* = 101.44 ms (1.11), across attention and viewing conditions.

For **P2 amplitude,** significant main effects for intensity, $F_{(1, 58)} = 206.78$, $p < .0005$, $\eta^2 = .78$ and frequency, $F_{(1, 58)} = 31.06$, $p < .0005$, $\eta^2 = .35$, were revealed. As expected, loud tones had larger P2 amplitudes than the soft tones across attention and viewing conditions. Unexpectedly, high frequency tones had larger P2 amplitudes than low frequency tones across attention and viewing conditions. The **P2 latency** revealed a significant main effect for intensity, $F_{(1, 58)} = 13.41$, $p = .001$, $\eta^2 = .19$, such that loud tones (*M (SE)* = 198.03 ms (2.43)) had shorter P2 latencies than the soft tones (*M (SE)* = 207.19 ms (2.76)) across attention and viewing conditions. A significant main effect for frequency, $F_{(1, 58)} = 20.63$, $p < .0005$, $\eta^2 = .26$ revealed that the low frequency tones (*M (SE)* = 196.90 ms (2.62)) had shorter latencies than the high frequency tones (*M (SE)* = 208.32 ms (2.59)) across attention and viewing conditions.

For **N2 amplitude**, main effects for intensity, $F_{(1, 58)} = 19.62$, $p < .0005$, $\eta^2 = .25$, and frequency, $F_{(1, 58)} = 12.41$, $p < .0005$, $\eta^2 = .18$, were significant. Contrary to our hypothesis, soft tones had larger N2 amplitudes than the loud tones across attention and viewing conditions. Low frequency tones had larger N2 amplitudes than high frequency tones across attention and

viewing conditions. The ANOVA evaluating **N2 latency** revealed a significant main effect of frequency, $F_{(1, 58)} = 13.67$, $p < .0005$, $\eta^2 = .19$, such that the low frequency tones (*M (SE)* = 285.29 ms (2.88)) had shorter latencies than the high frequency tones (*M (SE)* = 300.05 ms (3.96)) across attention and viewing conditions.

For P3 amplitude, significant main effect for intensity, $F_{(1, 58)} = 27.47$, $p < .0005$, $\eta^2 = .32$ was revealed. As expected, high intensity loud tones had larger P3 amplitudes than the soft tones across attention and viewing conditions. The main effect for frequency was not significant. The **P3 latency** ANOVA revealed no significant main effects for intensity or frequency.

Environmental Manipulation: Movie-viewing versus Fixation-viewing

For the **N1 amplitude**, there was no significant main effect of viewing condition, $F_{(1, 58)} = 1.51$, $p = .22$, $\eta^2 = .03$. In addition, the attention by viewing interaction effect, $F_{(1, 58)} = 6.49$, $p = .014$, $\eta^2 = .11$, though close with a small to medium effect size, did not meet the significance level for the study. The **N1 latency** main effect of viewing condition, $F_{(1, 58)} = 4.24$, $p = .04$, $\eta^2 = .07$, was not significant with the testwise alpha set for this study. For the **P2 amplitude**, no significant main effect of viewing condition was found, $F_{(1, 58)} = .20$, $p = .66$, $\eta^2 = .003$. There was an attention by viewing interaction effect, $F_{(1, 58)} = 4.37$, $p = .041$, $\eta^2 = .11$, which did not meet the significance level for the study. There was no effect of viewing condition on **P2 latency**, $F_{(1, 58)} = .71$, $p = .40$, $\eta^2 = .012$.

For the **N2 amplitude**, while the movie-viewing group had larger N2 amplitudes than the fixation group, the main effect of viewing condition, $F_{(1, 58)} = 4.16$, $p = .046$, $\eta^2 = .07$, was not significant at the alpha level set for the study. **N2 latency** was not significantly different between viewing conditions, $F_{(1, 58)} = 1.24$, $p = .27$, $\eta^2 = .02$. For the **P3 amplitude,** there was no main effect of viewing condition. However, there was an attention by viewing interaction effect, $F_{(1,}$

$_{58)}$ = 9.86, p = .003, η^2 = .15. *A posteriori* tests indicated that there was no difference in P3 amplitudes between the two attention conditions for the movie viewing group ($q_{(1, 58)}$ = 2.27, p > .01). However, for the fixation-viewing group, P3 amplitudes were significantly larger in the active condition compared to the passive condition ($q_{(1, 58)}$ = 5.61, p < .01; See Figure 4). The **P3 latency** revealed a significant attention condition by viewing condition interaction effect, $F_{(1, 58)}$ = 9.98, p = .003, η^2 = .15. *A posteriori* tests indicated that there was no significant difference between the latencies of the active and passive condition for the movie viewing ($q_{(1, 58)}$ = 2.18, p > .01) or the fixation viewing group ($q_{(1, 58)}$ = 1.26, p > .01). However, the means indicate that for the fixation viewing group, the passive condition had shorter P3 latencies than the active

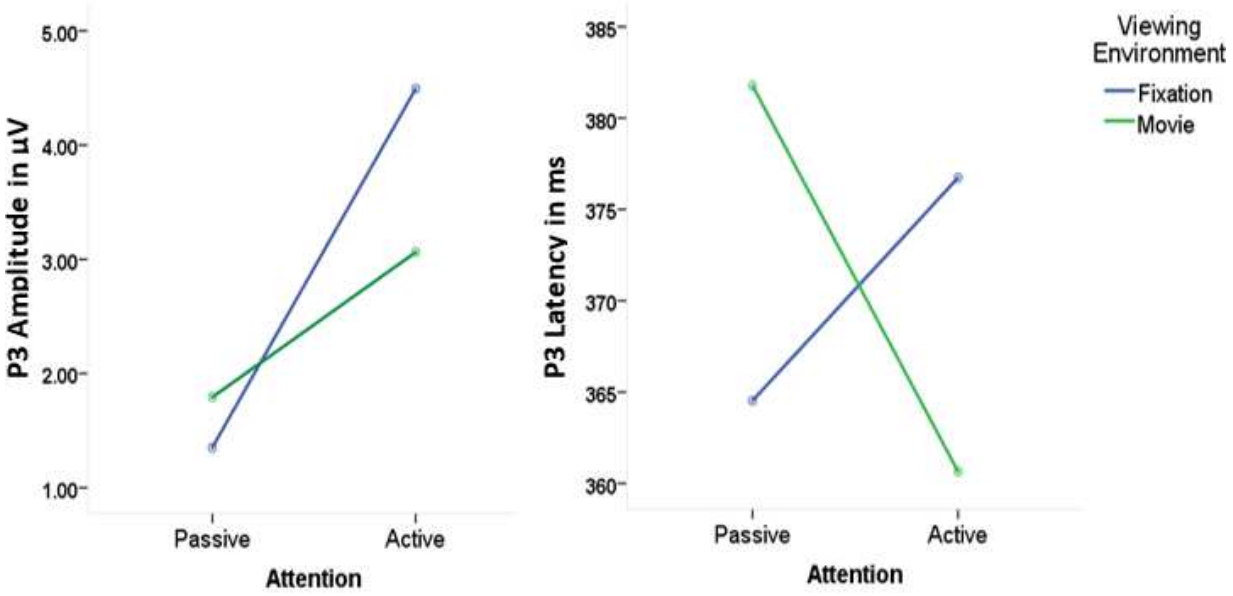

Figure 5. Plot of interaction effects of attention condition and viewing environments for both P3 amplitude and latency as measured at site Cz.

condition, while for the movie viewing group, the active condition had shorter latencies than the passive condition (See Figure 5).

Attentional State Manipulation: Passive versus Active Attention

The **N1 amplitude** revealed significant main effect of attention condition, $F_{(1, 58)}$ = 13.71, p < .0005, η^2 = .19. N1 amplitudes had significantly larger amplitudes in the passive

condition compared to the active condition across all tones regardless of the viewing group. **N1 latency** also revealed a significant main effect of attention condition, $F_{(1, 58)} = 12.51$, $p = .001$, $\eta^2 = .18$, such that the active condition (*M (SE)* = 99.03 (1.08)) had shorter latencies than the passive condition (*M (SE)* = 101.87 (.93)) across all tones and viewing conditions.

For N1 amplitude, there was also a significant attention by frequency interaction, $F_{(1, 58)} = 8.85$, $p = .004$, $\eta^2 = .13$, and an attention by intensity interaction, $F_{(1, 58)} = 11.61$, $p = .001$, $\eta^2 = .17$. *A posteriori* tests indicated that the low frequency tones had significantly larger amplitudes than the high frequency tones in the active condition ($q_{(1, 58)} = 3.8$, $p < .01$), but not in the passive condition ($q_{(1, 58)} = .48$, $p > .01$). *A posteriori* tests examining the attention by intensity interaction revealed that the loud tones had significantly larger amplitudes than the soft tones during the passive condition ($q_{(1, 58)} = 11.67$, $p < .01$) as well as the active condition ($q_{(1, 58)} = 8.13$, $p < .01$).

For the **P2 amplitude,** a significant main effect of attention condition, $F_{(1, 58)} = 14.31$, $p < .0005$, $\eta^2 = .20$ revealed that the amplitudes were significantly larger in the passive condition compared to the active condition across all tones regardless of the viewing group. Similarly**, P2 latency** revealed a significant main effect of attention condition, $F_{(1, 58)} = 13.25$, $p = .001$, $\eta^2 = .19$, such that the passive condition (*M (SE)* = 198.09 ms (2.49)) had shorter latencies than the active condition (*M (SE)* = 207.13 ms (2.7)) across all tones and viewing conditions.

For the P2 amplitude, there was also a significant attention by frequency interaction, $F_{(1, 58)} = 52.12$, $p < .0005$, $\eta^2 = .47$, and an attention by intensity interaction, $F_{(1, 58)} = 9.24$, $p = .004$, $\eta^2 = .14$. *A posteriori* tests indicated that the low frequency tones were significantly smaller than the high frequency tones in the active condition ($q_{(1, 58)} = 8.05$, $p < .01$), but not in the passive condition ($q_{(1, 58)} = 1.25$, $p > .01$ *A posteriori* tests examining the attention by intensity

interaction revealed that the loud tones were significantly larger than the soft tones during the passive condition ($q_{(1, 58)} = 10.77$, $p < .01$) as well as the active condition ($q_{(1, 58)} = 8.0$, $p < .01$). P2 latency also revealed a significant attention by frequency interaction effect, $F_{(1, 58)} = 18.6$, $p < .0005$, $\eta^2 = .24$. *A posteriori* tests revealed that there was no significant difference between P2 latencies for the low and high frequency tones for the passive condition ($q_{(1, 58)} = .82$, $p > .01$). However, for the active condition, the low frequency tones had a significantly shorter latency than the high frequency tones ($q_{(1, 58)} = 5.65$, $p < .01$).

The **N2 amplitude** revealed a significant main effect of attention condition, $F_{(1, 58)} = 37.31$, $p < .0005$, $\eta^2 = .39$. N2 amplitudes had significantly larger amplitudes in the passive condition compared to the active condition across all tones regardless of the viewing group. For **N2 latency**, the main effect of attention was not significant, $F_{(1, 58)} = 3.77$, $p = .057$, $\eta^2 = .06$ based on the testwise alpha set for this study.

For the N2 amplitude, there was also a significant attention by frequency interaction, $F_{(1, 58)} = 13.03$, $p = .001$, $\eta^2 = .18$, and an attention by intensity interaction, $F_{(1, 58)} = 17.93$, $p < .0005$, $\eta^2 = .24$. *A posteriori* tests indicated that the low frequency tones had significantly larger amplitudes than the high frequency tones in the active condition ($q_{(1, 58)} = 4.38$, $p < .01$), but not in the passive condition ($q_{(1, 58)} = .47$, $p > .01$). *A posteriori* tests examining the attention by intensity interaction revealed that the soft tones had significantly larger amplitudes than the loud tones during the active condition ($q_{(1, 58)} = 4.74$, $p < .01$) but not during the passive condition ($q_{(1, 58)} = .15$, $p > .01$). The N2 latency also revealed a significant attention by frequency interaction effect, $F_{(1, 58)} = 24.96$, $p < .0005$, $\eta^2 = .30$. *A posteriori* tests revealed that there was no significant difference between N2 latencies for the low and high frequency tones for the passive

condition ($q_{(1, 58)} = .79$, $p > .01$). However, for the active condition, the low frequency tones had a significantly shorter latency than the high frequency tones ($q_{(1, 58)} = 6.26$, $p < .01$).

The **P3 amplitude** revealed significant main effects of attention condition, $F_{(1, 58)} = 54.71$, $p < .0005$, $\eta^2 = .49$. P3 amplitudes were significantly larger in the active condition compared to the passive condition across all tones regardless of the viewing group. The **P3 latency** revealed a significant attention by frequency interaction effect, $F_{(1, 58)} = 12.42$, $p = .001$, $\eta^2 = .18$. *A posteriori* tests revealed that there were not significant differences between P3 latencies for the low and high frequency tones for the passive condition ($q_{(1, 58)} = 1.36$, $p > .01$) or the active condition ($q_{(1, 58)} = 2.82$, $p > .01$). The means indicated that for the active condition, the low frequency tones had a shorter latency than the high frequency tones, while the opposite effect was observed for the passive condition.

Discussion

The purpose of this study was to examine the effects of focused attention and visual distraction on auditory neural processing using the sensory registration paradigm. This auditory ERP paradigm allowed us to demonstrate differences in processing auditory intensities and frequencies across mid-latency ERP components based on environmental and internal attention demands. Each ERP component reflects a functionally discrete stage of neural processing, and understanding how these components are differentially impacted by attention demands can provide insight into understanding neural sensory processing. The grand averaged ERP waveforms of all conditions depicted the expected pattern following auditory stimuli, i.e. N1-P2-N2-P3 (Polich, 1993). Answering research question 1, robust intensity discrimination was found at the N1, P2, N2, and P3 components across all conditions, although the N2 was not in the expected direction, with soft tones eliciting larger N2 amplitudes than loud tones. Frequency

discrimination was observed at the N1, P2, and N2 components but not at the P3 component. Supporting hypothesis 1, these results confirmed that manipulating stimulus characteristics do influence mid-latency phases of sensory processing i.e., N1, P2, N2, and P3 ERP components. Answering research question 2, manipulation of the environment resulted in no significant main effects, however, there were interactions effects of viewing (movie versus fixation) and attention (passive versus active) conditions for the N1, P2, and P3 components. However, except the P3 component, other interaction effects were not significant at the alpha level set for this study. Answering research question 3, there were significant differences between the active and passive attention conditions for all the ERP components, demonstrating that altering the participant's internal attentional state by requiring the participant to actively respond to stimuli, also influences the mid-latency phases of sensory processing.

Effects of stimulus characteristics on auditory ERPs. The expected finding of larger N1, P2, and P3 amplitudes to loud tones compared to soft tones obtained is the present study has been shown numerous times in the literature (Adler & Adler, 1991; Crowley & Colrain, 2004; Paiva et al., 2016; Picton, Hillyard, Krausz, & Galambos, 1974; Polich & Kok, 1995; Ponton, Eggermont, Kwong & Don, 2000). Intensity discrimination did not differ between viewing conditions or attention conditions, which further supports the robust nature of intensity effects at the ERP components. Researchers have suggested that the intensity dependence of the N1 and P2 components reflects low central seratonergic neurotransmission, which "sets the tone" and adjusts levels of sensory processing (Hegerl & Juckel, 1993). In contrast to the other ERP components, the N2 amplitude was larger for the soft tones compared to the loud tones. This could be because the target tone was the soft tone. Szmalec et al. (2008) suggested that an N2 amplification is observed in trials with high perceptual overlap, when the target cannot be easily

discriminated. A larger N2 amplitude to the target tone in the present study could therefore be attributed to the difficulty in discerning the target tone from the other tones. However, more research is required to understand this effect.

In terms of frequency discrimination, researchers have found that N1and P2 amplitudes decrease as frequency increases (Wunderlich & Cone-Wesson, 2001). This finding can be explained by results from a study using fMRI which showed that a larger area of the transverse temporal gyrus was activated for the 1 kHz tone compared to a 4 kHz tone (Strainer et al., 1997). We found a similar effect in our study across the viewing and attention conditions. Additionally, the target tone consisted of a low frequency stimulus, which could contribute to the higher amplitude of the low frequency tone. The P3 is considered to be relatively immune to the effects of stimulus characteristics such as frequency and pitch (Polich, 2007). In line with this theory, we found no discrimination of frequencies at the P3 component.

Effect of viewing environment on auditory ERPs. There were no significant effects of viewing environment at the N1, P2 and N2 components. This is consistent with previous studies (Lavoie, Hine & Thornton, 2008, Yadon et al., 2015). The significant attention and viewing interactions effects at P3 amplitude indicate that P3 amplitudes were larger in the fixation viewing group than the movie viewing group. Theoretically, the P300 amplitude is elicited in tasks requiring the maintenance of working memory (Polich, 2007). A larger P3 in the fixation condition may suggest more efficient working memory processes towards stimuli processing compared to the movie viewing condition. The P3 latency interaction effect revealed that for the movie group, the passive condition had shorter latency than the active condition, while for the fixation viewing group, the active condition had shorter latency than the passive condition.

Effect of Attention on Auditory ERPs

N1 component. The N1 represents a sensory filter which is activated by auditory events and represents stimulus encoding (Näätänen & Picton, 1987). The N1 amplitude was significantly larger for the passive condition compared to the active condition for both the viewing conditions. A larger N1 for the passive condition can be attributed to a greater attention shift required during this condition compared to active condition. Due to the nature of the active condition, participants sustained attention to all auditory stimuli since they were anticipating a tone. Researchers have shown that expectations which induce prediction processes result in decreased N1 amplitudes (Lange, 2013). N1 latencies were shorter for the active condition compared to the passive condition, which is consistent with most existing literature (Folyi, Feher, & Horvath, 2012; Mondor & Zatorre, 1995). Interestingly, we found that frequency discrimination was greater during the active condition compared to the passive condition across viewing conditions. This is consistent with literature which states that stimuli presented during attended states are detected faster and discriminated more accurately than stimuli presented during unattended states (Mondor & Zatorre, 1995).

P2 component. The P2 component is assumed to represent at least partially an exogenous response following stimuli and is believed to play a role in stimulus classification (Crowley & Colrain, 2004). In the present study, the P2 amplitude was smaller for the active condition compared to the passive across viewing conditions. This is consistent with previous findings (Tong, Melara & Rao, 2009). In a review of the P2 component, Crowley and Colrain (2004) noted that an increase in the level of attentiveness results in larger N1 amplitudes but smaller P2 amplitudes (Crowley & Colrain, 2004). Additionally, P2 latencies were longer for the

active condition compared to the passive condition in the present study. This is consistent with previous research (Morris, Steinmetzger & Tøndering, 2016).

N2 component. The auditory N2 is considered to reflect attentional allocation (Tomé, Barbosa, Nowak & Marques-Teixeira, 2014), and cognitive processes associated with stimulus evaluation (Michalewski, Prasher & Starr, 1986). In the present study, N2 amplitudes were larger for the passive condition compared to the active condition regardless of the viewing condition. Smaller N2 amplitudes in the active condition could be due to better attention allocation during the active condition compared to the passive condition. Nieuwenhuis, Yeung and Cohen (2004) found that the N2 component is reduced when stimuli can be easily discriminated during an auditory go/no-go task. Our findings have indicated better stimulus discrimination at the N1 and P2 components during the active condition compared to the passive condition. This ability to better discriminate the auditory stimuli during the active condition could have led to smaller N2 amplitudes compared to the passive condition. Consistent with the N1 and P2 components, we also found interactions effects between attention condition and intensity, and frequency, such that low frequency tones were better discriminated from high frequency tones during the active condition than the passive condition.

Interestingly, the attention by intensity interaction revealed that the soft tones had larger amplitudes than the loud tones during the active condition. This contrasts with the N1 and P2 components, wherein the loud tones had larger amplitudes. This reversal could be explained by the fact that the target tone for the active condition consisted of a low intensity stimulus. Since the N2 is involved in cognitive processing, we can assume that the target tone had greater processing than the non-targets at the N2 component. Previous research has also shown that target stimuli elicit a larger N2 amplitude compared to non-targets in the auditory modality

(Folstein & Van Petten, 2008). For our active condition, low frequency tones had shorter latencies than the high frequency tones, suggesting more efficient processing of the target frequency.

P3 component. The P3 or the P300 component is perhaps the most extensively studied ERP component with reliable consensus that the P3 occurs when an individual consciously detects an informative task-relevant stimulus (Huang, Chen & Zhang, 2015). In accordance with existing literature, our study elicited larger P3 amplitudes for the active condition compared to the passive condition regardless of viewing condition. In addition, for the active condition, low frequency tones had shorter P3 latencies than the high frequency tones, which suggests that the low frequency target tones were processed faster than the non-target tones (Polich, 2007).

Impact of attention on intensity versus frequency. In this study, we found differential effects of attention on processing of intensity versus frequency. We found robust intensity dependency in all components, i.e., N1-P2-N2-P3, such that high intensity tones generated larger amplitudes than soft tones regardless of the viewing and attention condition, except the N2 component had larger amplitude for soft tones than loud tones. In contrast, we found that there was no frequency discrimination during the passive condition regardless of the viewing condition. Harris, Mills, and Dubno (2007) used 500 and 3000 Hz stimuli and found that the young adults (ages 18 – 30) showed no difference between the N1 and P2 across the two frequencies during a passive listening task. However, they did find the expected robust intensity discrimination at the N1 and P2 components (Harris et al., 2007). In contrast to these previous studies, during the active condition, we found significant frequency discrimination at the N1, P2, and N2 components. This is consistent with studies examining mismatch negativity, wherein the amplitude of N1 and P2 decreased as frequency increased (Wunderlich & Cone-Wesson, 2001).

To summarize, this suggests that intensity discrimination is more robust than frequency discrimination during passive attention states. A study by Dimitrijevic et al. (2009) also demonstrated that intensity and frequency discrimination employ distinct neural processes. However, when actively directing attention to stimuli, frequency discrimination is evident in the mid-latency ERP components.

Viewing environments during auditory paradigms. During the past decade, researchers have increased the use of playing a silent/close-captioned movie during auditory EEG paradigms. Several researchers studying auditory processing in children with and without disabilities use a movie to help participants remain engaged throughout the EEG testing (Carroll & Seeley, 2013). Often, results from studies with a movie have been compared to results with studies without a movie, without considering the effects of the movie viewing on overall processing. The results of this study indicated that movie viewing significantly interacts with attentional states during an auditory paradigm, such that movie viewing results in use of additional neural resources demonstrated by larger amplitudes compared to participants viewing a fixation point. This finding has implications not only from a theoretical and methodological standpoint but also has implications for research in clinical populations with attention deficits.

Theoretically, watching a movie during an auditory paradigm can be considered a low perceptual load, such that an active mechanism is involved in processing the distraction (Lavie, 2010). Thus, in accordance with the load theory of attention, we found that the movie viewing group had smaller P3 amplitudes than the fixation viewing group. Additionally, supporting the "sensory gain theory", attention led to enhanced stimulus discrimination ((Hillyard et al., 1998). These attention effects seem to echo the work of Carrasco, Ling and Read (2004) that demonstrated that attention alters stimulus appearance by increasing visual contrast sensitivity

and spatial resolution (sensory gain). Methodologically, researchers must consider the impact of the perceptual load (movie viewing) while comparing results of study paradigms that use a movie versus studies that use a fixation during an auditory paradigm to accurately interpretation of sensory processing. Clinically, there has been growing interest in using auditory ERPs as objective biomarkers of neuropsychiatric conditions. Understanding the impact of attention on auditory processing is crucial especially in people with diagnostic conditions that may have exhibit attention deficits.

Conclusion

The results from this study have shown that attention and distraction significantly impact auditory processing at the N1, P2, N2, and P3 ERP components. Intensity discrimination was significant at all components across attention and viewing conditions. Frequency discrimination was significant only during the active condition at the N1, P2, and N2 components. The results indicate that actively directing attention to the tones impacts auditory processing at all components, and that discrimination is more robust during active than passive tasks that influence attentional states. Additionally, movie viewing and fixation viewing differentially impacts auditory processing. Findings from this study have significant implications related to theoretical, methodological, and clinical applications of ERP research examining the impact of attention on auditory processing.

CHAPTER 3 – STUDY 2

Examining the effect of attention on sensory gating in adults with autism spectrum disorders

The capacity of the human brain to process information is limited. To deal with this, certain stimuli or aspects of stimuli are prioritized at the expense of dealing less efficiently with other stimuli (a.k.a., selective attention). Additionally, irrelevant information is filtered out (i.e., sensory gating), to prevent sensory overload of higher cognitive functions. Sensory gating in the auditory modality has been extensively examined using the paired-click paradigm (Adler et al., 1982; Freedman et al., 1996; Dalecki et al., 2016). For the sensory gating electroencephalography (EEG) paradigm, the participant listens to repeated presentations of a pair of identical click sounds, presented within a short period from each other. In the resulting averaged event-related potential (ERP), the P50 component presents as a positive deflection that occurs around 50 - 65 milliseconds (ms) after stimulus presentation. The P50 develops as a neural orienting response to the first click while simultaneously activating inhibitory pathways (Freedman, Adler, & Waldo, 1987). The reduction in amplitude of the P50 to the second click (a.k.a., test click) compared to the first click (a.k.a., conditioning click) represents gating, which is also described as suppression. One explanation for the gating mechanism is that when the second click is presented immediately thereafter, the active inhibitory pathways are believed to suppress the P50 potential in response to the second click stimulus (Freedman et al., 1987).

Deficits in sensory gating have been associated with difficulties in organizing sensory information, and with the development of severe behavioral aberrations (Freedman, Waldo, Bickford-Wimer, & Nagamoto, 1991). The P50 ERP component has been widely used to

evaluate sensory gating in people with schizophrenia (Clementz, Geyer, & Braff, 1998; Freedman et al., 1996). Due to the pervasive and quantifiable nature of gating, impaired P50 suppression is considered an endophenotype for schizophrenia (Calkins et al., 2007). Some researchers have proposed that gating deficits observed in schizophrenia could be due to two mechanisms; 1) less consistent complete responses or reduced responsiveness to the first click leading to smaller amplitudes to click 1, and 2) reduced gating of click 2 (Jansen, Hu, & Boutros, 2010). Thus, the reduced responsiveness to the conditioning click (i.e., click 1) in schizophrenia suggests deficits in orientation to a novel stimulus and basic attentiveness. Studies have found that P50 (Wan, Friedman, Boutros, & Crawford, 2008) and N1 gating (Lijffijt et al., 2009) have been associated with behavioral measures of attention.

Attention is understood as a "broad cognitive concept that includes a set of mechanisms that determine how particular sensory input, perceptual objects, trains of thought, or courses of action are selected for further processing from an array of concurrent possible stimuli, objects, thoughts and action" (Talsma, Senkowski, Soto-Faraco, & Woldorff, 2010, p. 2). The P50 component was initially thought to be unaffected by attentional modulations (Adler et al., 1982; Jerger, Biggins, & Fein, 1992). The early latency (around 40-60 ms) of the P50 component was thought to reflect sensory processing of the stimulus, while the mid-latency ERPs (such as the N1 and P2) were thought to reflect endogenous components such as attention (Boutros, Korzyukov, Jansen, Feingold, & Bell, 2004). However, recent research has brought this notion into question. There have been mixed results regarding the influence of attention on sensory gating abilities in neurotypical individuals. Some studies have shown that although directing attention towards the clicks (button press to high intensity pairs) resulted in greater amplitude of the N1, there was no effect of attention on P50 gating (White & Yee, 1997).

Dalecki, Green, Johnstone, and Croft (2016) examined the influence of attention versus non-attention states on a modified P50 gating paradigm. The authors designed the paired-click paradigm with the addition of randomly interspersed louder clicks in certain pairs. In the attention condition, the researchers asked participants (healthy controls and individuals with schizophrenia) to respond with a button press only to the pairs with the louder click. In the non-attention condition participants were instructed to ignore the auditory stimuli. In both conditions, participants watched a silent movie during the EEG recording. The findings from this study revealed that the control group of healthy adults had enhanced P50 suppression during the attention condition compared to the non-attention condition. However, the attention condition did not affect gating in individuals with schizophrenia (Dalecki et al., 2016). Others have found that directing attention towards the clicks resulted in attenuation of P50 gating (Guterman, Josiassen, Bashore, 1992; Yee et al., 2010).

Yee et al. (2010) found that while schizophrenia patients had significant deficits in P50 suppression during standard gating testing compared to healthy controls, the group difference was not significant when attention was directed towards either the first or the second click. Thus, schizophrenia patients exhibited substantial improvements in gating when voluntary attention was directed towards the stimuli (Yee et al., 2010). Additionally, Hutchison et al. (2013) examined sensory gating in 40-month-old infants and found that P50 suppression deficits significantly predicted attention symptoms three years later. The authors concluded that attentional dysfunction may relate to altered neural sensory gating.

The changes in P50 gating due to attentional states indicate that this early component captures not only pre-attentive sensory aspects but is also influenced by attentional states. However, the impact of an individual's attention state on sensory gating during the EEG

recording is still unclear. Understanding the influence of attention on sensory gating is crucial since gating abnormalities may be associated with deficits in attention rather than deficits in sensory processing (Rosburg et al., 2009). Abnormalities in P50 gating have now been demonstrated in several clinical groups besides schizophrenia such as attention deficit hyperactivity disorders (Olincy et al., 2000), sensory processing disorders (Davies, Chang & Gavin, 2009) and autism spectrum disorders (ASD; Orekhova et al., 2008). Sensory processing deficits, which include hyper- or hypo-reactivity to sensory input are part of the diagnostic criteria for children with ASD in *The Diagnostic and Statistical Manual of Mental Disorders* (5th ed.; *DSM–5*; American Psychiatric Association, 2013). Auditory processing is one of the most commonly reported sensory processing impairment in ASD. Research examining brain-behavior relationships has shown that behavioral deficits in auditory processing have been associated with impairments in neural inhibition and filtering of sensory input (Orekhova et al., 2008). Additionally, individuals with ASD are known to have deficits in attention (Allen & Courchesne, 2001). However, controversy exists in the identification of specific neuropathology underlying dysfunction in sensory processing and attention, which warrants further study of brain-behavior relationships.

Researchers examining gating deficits in ASD have found mixed results. While some studies have shown that children with ASD have significant deficits in P50 and N1 suppression (Crasta, LaGasse, Gavin, & Davies, 2016; Madsen et al., 2015) and sensorimotor gating (McAlonan et al., 2002; Perry, Minassian, Lopez, Maron & Lincoln, 2007) compared to neurotypical peers, others have found no difference in gating abilities in ASD and controls (Kemner et al., 2002; Magnée, Oranje, van Engeland, Kahn, & Kemner, 2009). Some of the inconsistencies in the study findings may be related to differences in the methods employed to

study gating, such as the presence of a silent movie versus starring at a fixation point, and the individual's attention state.

Neural and behavioral attention mechanisms may work differently towards suppression, inhibition, and filtering information in individuals with ASD and neurotypical controls. When no instructions have been given towards the direction of attention, individuals without attention deficits, such as neurotypical controls, usually have stronger gating compared to clinical populations who show reduced gating. Thus, since individuals with ASD have impaired attention, the attention-based enhancement on P50 suppression (as seen in the study by Yee et al., 2011) may explain underlying mechanisms of gating dysfunction, which may be attributed to attention deficits. The purpose of this study was to investigate whether attentional manipulations would produce differences in sensory gating (P50 and N1 amplitude and suppression) in neurotypical controls and individuals with ASD. Since research have shown that individuals with ASD have delayed N1 latencies to auditory stimuli (Edgar et al., 2015), a second objective was to also examine auditory latencies in individuals with ASD. Additionally, behavioral measures assessing sensory processing, perceptual processing, attention, and social responsivity were included to not only to validate the group differences but also to examine brain-behavior relationships.

Research Questions

1. How does active versus passive attentional states affect sensory gating?

Hypothesis: All participants will have more robust gating during the passive condition compared to the active condition. All participants will have shorter latencies in the active compared to the passive condition.

2. Do individuals with ASD have deficits in sensory gating at the P50 and N1 component compared to neurotypical controls during the passive or active condition?

Hypothesis: Individuals with ASD will have less robust sensory gating during the passive condition but not active compared to the neurotypical group. Individuals with ASD will have longer P50 and N1 latencies to the click stimuli compared to neurotypical individuals.

3. Are there group differences between neurotypical individuals and individuals with ASD on behavioral measures of attention and sensory processing?

Hypothesis: The ASD group will have significantly more deficits on behavioral measures of attention and sensory processing compared to neurotypical individuals.

4. How do behavioral measures of attention and sensory processing relate to neural measures of sensory gating?

Hypothesis: Across all participants, more typical scores on the behavioral assessments will be associated with more robust gating.

Methods

Participants. This study included a total of 48 participants recruited via convenience sampling. Twenty-four participants (M = 23.31 years, SD = 3.77; 17 males, 7 females) had a confirmed diagnosis of high-functioning ASD. The control group consisted of twenty-four age-matched neurotypical individuals (M = 23.7 years, SD = 3.51; 12 males, 12 females). There was no group difference in age ($t_{(46)} = .41$, $p = .69$). The diagnosis of ASD was confirmed using the ADOS-2 (Rutter, DiLavore, Risi, Gotham, & Bishop, 2012) administered by the primary author prior to initiating the EEG portion of the study. All participants with ASD met the cut-off criteria for ASD based on the ADOS. All participants in the control group were screened using a questionnaire designed by our lab to ensure via self-report that they are free of neurological

injuries, disabilities, and family histories of psychological disorders. All the procedures performed in the research involving human participants were in accordance with the ethical standards of the institutional review committee at the local university and with the 1964 Helsinki declaration and its later amendments. All participants signed a written informed consent prior to the study.

Procedures. Once the EEG cap, and electrodes were applied, the participant was given a brief training on strategies to reduce artifacts resulting from eye blinks, and other muscle activity. EEG data were collected in a sound-attenuated and electrically shielded room during the sensory gating paradigm. Participants in both groups completed two conditions of the sensory gating paradigm followed by behavioral testing of attention. The EEG, and the behavioral testing took around 1 hour each.

Sensory gating EEG paradigm. The sensory gating paradigm was presented using E-Prime software (Psychological Software Tools, Pittsburg, PA) running on a laptop computer. A modified sensory gating paradigm was used which consists of presentations of 80 pairs of click stimuli and 40 pseudo-randomly interspersed single clicks. The click stimuli were binaurally presented through the ER-3A inserted earphones (Etymotic Research). The stimuli were presented at 85 dB SPL. Each click had a 3 ms duration. The paired click stimuli were presented with a 500 ms stimulus onset asynchrony (SOA), and an 8 second inter-trial-interval between pairs. The single clicks were presented with an inter-trial-interval of 8 seconds. The study consisted of two conditions:

The passive condition. In this condition, participants were asked to watch at a fixation point (star symbol) on a computer screen while they were being presented with click sounds.

The active condition. In this condition, participants were asked to selectively respond to single clicks with a button press and ignore the paired-clicks while watching at a fixation point (star symbol) on a computer screen.

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 included 64 Ag/AgCl sintered scalp electrodes. The electrodes were located in accordance with the modified 10–10 system (Klem, Lüders, Jasper, & Elger, 1999; Oostenveld & Praamstra, 2001). EEG was recorded with the Common Mode Sense active electrode as the reference and the Driven Right Leg passive electrode as the ground (http://www.biosemi.com/faq/cms&drl.htm). Electrooculograms (EOGs) were recorded from individual electrodes placed on the left and right outer canthus for horizontal movements and on the left supraorbital and infraobital region for vertical movements. Two more individual electrodes were placed on the left and right earlobes and used as the offline reference. Data were sampled at a rate of 2048 Hz with a bandwidth of 0 to 417 Hz.

Electrophysiological Data Reduction. Brain Vision Analyzer software (Brain Products GmbH, München, Germany) was used to conduct all offline EEG analyses. Baseline-to-peak measures for the P50 and N1 component were obtained based on previously established procedures (e.g., Boutros et al., 2004; Davies et al., 2009). Averaged ERPs were composed from the running EEG data. First, the four EOG channels were converted to a vertical and a horizontal bipolar EOG. For the P50 component, data were filtered offline from the continuous EEG with a band pass setting of 10 to 75 Hz with a 24 dB/octave rolloff using casual phase-shift free butterworth filter settings (Chang, Gavin, & Davies, 2012). Time-frequency analysis of evoked power indicated that this filter setting best captures the gamma activity of the P50

response (See Figure 6). Following this, data were segmented time-locked to the stimulus onset into epochs representing either the click 1 (conditioning) or click 2 (test) with a duration of 100 ms pre-stimulus onset to 200 ms post-stimulus onset.

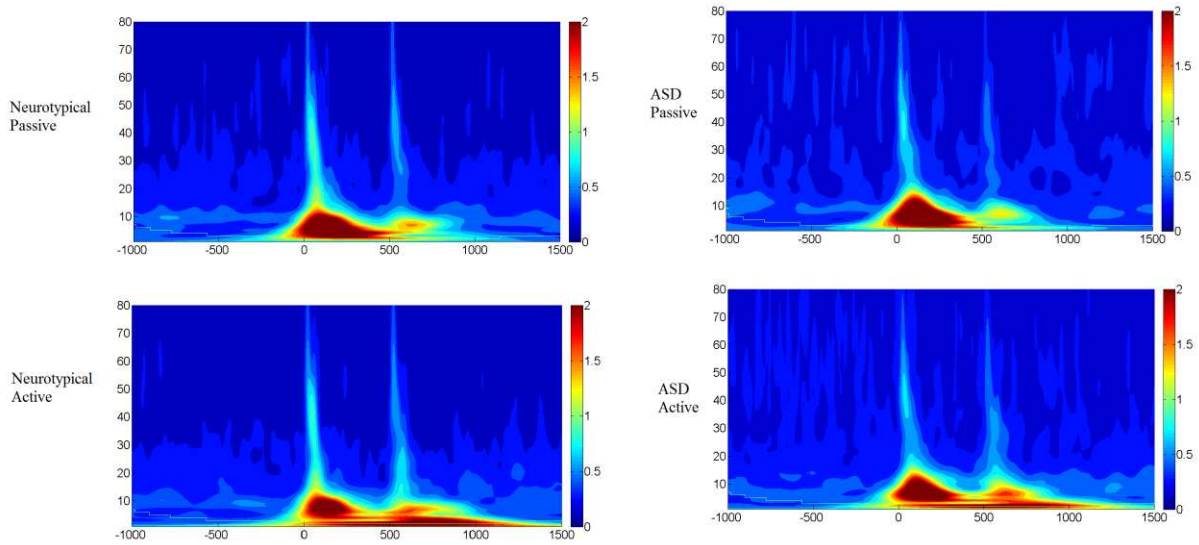

Figure 6. Time-frequency analysis of evoked power for neurotypical participants and participants with ASD. As seen in the figure, a filter setting of 10 – 75 Hz best captures the P50 gamma response.

For the N1 component, data were filtered offline from the continuous EEG with a band pass setting of .1 to 30 Hz with a 12 dB rolloff using casual phase-shift free butterworth filter settings (Boutros et al., 2004; Lijffijt et al., 2009). Following this, data were segmented time-locked to the stimulus onset into epochs representing either click 1 or click 2 with a duration of 100 ms pre-stimulus onset to 500 ms post-stimulus onset. Baseline correction relative to a baseline of -100 ms to 0 ms was performed. Next, specific for processing the N1 component, an eye regression technique designed to remove eye movement artifacts from each segment was performed (Segalowitz, 1996). Baseline correction was performed again relative to a baseline of -100 ms to 0 ms for the non-rejected segments. For P50 and N1 data reduction, segments with voltage deviations greater than ±100 microvolts (μV) on any of the EEG channels or the bipolar

EOG channels were eliminated after final baseline correction. Segments were then averaged to create averaged ERP waveforms separately for the click 1 and 2 in order to measure the P50, and N1 components for each participant.

The P50 peak was identified as the most positive peak between 40 and 80 ms after the stimulus onset. The N1 peak was identified as the most negative peak between 70 and 180 ms after the stimulus onset. The test/conditioning (T/C) ratio and difference scores were computed to quantify gating abilities. A T/C ratio approaching 0 is indicative of robust gating and the T/C ratio approaching 1 indicates less gating (Cromwell, Mears, Wan, & Boutros, 2008). Difference scores were calculated by subtracting P50 amplitude of Click 2 from the P50 amplitude of Click 1, and N1 amplitude of click 2 from the N1 amplitude click 1. For the P50 component, a large positive difference score indicates better gating than a small score. For the N1 (a negative ERP component), a large negative difference score indicates better gating compared to a small score. Of the 64 channels, the central site Cz was analyzed, to maintain consistency with previous research.

Behavioral Measures. To validate group differences and assess the relationship between neural measures of sensory processing and behavioral measures of attention and sensory processing, the Test of Everyday Attention (TEA) was administered to all participants. Additionally, participants were asked to fill out the Adolescence and Adults Sensory Profile, the Sensory Gating Inventory. Participants with ASD also filled out the Social Responsiveness Scale-2, which is a measure of ASD severity.

Social responsiveness scale – 2 (SRS-2). The SRS-2 Adult form is a 65-item self-report rating scale measuring deficits in social behavior associated with Autism Spectrum disorder, as outlined in the Diagnostic and Statistical Manual of Mental Disorders. Items are scored on a 4-

point Likert scale, ranging from 1 “not true”, 2 “sometimes true”, 3 “often true” to 4 “almost always true”. Results are reported as *T*-scores for the treatment subscales: Social Awareness (8 items), Social Cognition (12 items), Social Communication (22 items), Social Motivation (11 items), and Restricted Interests and Repetitive behavior (12 items) and the overall total score. *T*-scores of 76 or higher are considered severe suggesting that an individual has clinically significant deficits in social functioning that interfere with interactions with others. Scores that fall between 66 and 75 are considered moderate, signaling some clinically significant social deficits. The mild range includes *T*-scores of 60 to 65, which indicate mild to moderate deficiencies in social behavior. *T*-scores of 59 and below indicate an individual probably does not have social difficulties indicative of a possible ASD diagnosis (Constantino & Gruber, 2012; Frazier et al., 2014). The scale takes approximately 15 minutes to complete. The scale has strong internal consistency (.94 - .96) across gender, age, and clinical subgroups within the spectrum. The adult form appears to have less predictive validity compared to the school-age forms, with a specificity level of .60 and a sensitivity of .86. No concurrent validity data were reported for the Adult Form. Confirmatory factor analysis demonstrated good fit for the two-symptom clusters measuring social communication and interaction domain and the restricted interested and repetitive behavior domain (Bruni, 2014; Mandell et al., 2012).

Sensory gating inventory (SGI). The SGI is a measure of perceptual anomalies related to sensory gating. Participants respond with a 6-point Likert ratings (from 0 “never true” to 5 “always true”) to the 36 item self-report questionnaire. The questionnaire yields 4 factors: Perceptual Modulation (16 items), Distractibility (8 items), Over-Inclusion (7 items), and Fatigue-Stress Vulnerability (5 items). An overall SGI score is also obtained by computing the sum of all the Likert responses (Hetrick, Erickson & Smith, 2012). A higher score indicates

more deficiencies. The scale has moderate to strong internal consistency reliability (Cronbach's alpha ranging from .75 to .92), with convergent validity coefficients ranging from .53 - .79. The authors report discriminant validity as well (Hetrick et al., 2012).

Adolescent/Adult sensory profile (AASP). The AASP is a self-report questionnaire consisting of 60 items that relate to everyday sensory experiences. The AASP is validated for individuals 11 or older. Each item is scored on a 5-point Likert scale indicating how frequently the behavior is performed (from 1 "almost never" to 5 "almost always"). The 60 items are organized into six categories of taste or smell, movement, visual, touch, activity level, and auditory sensitivities. The questionnaire takes about 10-15 minutes to complete. The AASP scores are categorized into 4 quadrants based on Dunn's (1997) model of sensory processing, which classifies sensory behaviors based on neurological thresholds (high or low) and behavioral responses (passive or active). Neurological thresholds refer to the amount of stimuli needed for the nervous system to respond to sensory stimuli, and behavioral responses relate to the way in which a person responds to their sensory thresholds. The four quadrants are, 1) *Low registration* (passive behavioral responses with a high neurological threshold), 2) *Sensation seeking* (active behavioral responses with a high neurological threshold), 3) *Sensory sensitivity* (passive behavioral responses with a low neurological threshold and, 4) *Sensation avoiding*: refers to active behavioral responses with a low neurological threshold. Quadrant scores are classified as "much less than most people" (-2 SD from mean), "less than most people", "similar to most people", "more than most people", and "much more than most people" (+2 SD from mean). Extreme sensory processing is defined as scores falling in either "much less than most people" or "much more than most people". The AASP has reported item reliability (r = .64 - .78) and construct validity (Brown & Dunn, 2002).

Test of everyday attention. TEA is a standardized and normed clinical battery that has been validated for ages 18 to 80 years. The TEA is based largely on everyday materials with real-life scenarios to ensure that participants find it relevant to their problems of adjustment in everyday life. The eight subtests, with a four-factor structure, correspond to the attentional model presented by Petersen and Posner (2012). Subtests assess selective, sustained attention, attentional switching, and divided attention. The TEA takes around 45-50 minutes to complete. Higher scores indicate better attention abilities. For this study, raw scores were used in the analysis since all participants were within the same age-range for the standardized scores, and raw scores preserved individual variability. The reliability of the subtests of the TEA range from good to excellent for clinical populations and healthy controls (r = .34 – 64; Ward, Ridgeway & Nimmo-Smith, 1994).

Statistical analyses. Group differences on the behavioral assessments were conducted using independent samples t tests. Discriminant analyses were performed to identify which assessment would best distinguish between neurotypical individuals and individuals with ASD. Group differences on the P50 and N1 ERP component amplitudes and latencies were examined using a 2 (Group) x 2 (Attention) x 2 (Clicks) repeated measures ANOVA. The main effect of clicks was used to determine whether there was a statistically significant difference between click 1 and click 2 representing gating. The main effect of attention used to determine the impact of attention on processing. The clicks by group by condition interaction was used to determine whether the effect of attention on gating differed between the control group and the group of individuals with ASD. *A posteriori* tests were conducted to examine the interaction effects. *A posteriori* Tukey's honestly significantly difference (HSD) post-hoc t tests (reported as q values) were calculated to examine interaction effects (Kirk, 1968, p. 265-269). Testwise alpha was set

at 0.013 for the *apriori* hypotheses (ANOVAs), with Bonferroni correction for the 2 ERP components and two ANOVAs examining amplitude and latency measures for each ERP component, (.05/4 = .013). Effect sizes for η^2 are interpreted as follows, .04 – small, .25 – medium, and .64 – large (Ferguson, 2009). Effect sizes for Cohen's *d* can be interpreted as follows, .41 – small, 1.15 – moderate, 2.7 – strong (Ferguson, 2009). Pearson product-moment correlations were used to identify the relationship between gating and the behavioral assessments of attention, sensory processing, perceptual processing, and social responsivity. All statistical analyses were performed using the Statistical Package for Social Sciences (SPSS) for Windows software, 24.0 version.

Results

Analysis of Behavioral Measures Validating Group Differences

Social Responsiveness Scale 2. The means and standard deviation of the 5 treatment subscales and the total score of the SRS 2 are shown in Table 3. All neurotypical individuals scored within normal limits on the SRS 2 based on the T score. Six individuals with ASD scored within normal limits, three scored in the mild range, six scored in the moderate range, and seven scored in the severe range. Independent samples *t* tests revealed significant group differences in all domains. Specifically, individuals with ASD had significantly higher scores in the Social Awareness subscale, Social Cognition, Social Communication, Social Motivation, Restricted and Repetitive behaviors, and the SRS 2 total score.

Sensory Gating Inventory. The means and standard deviation and *t* tests of the 4 factors and the total score of the SGI are shown in Table 3. The SGI scores were compared between groups using independent samples *t* tests. The ASD group had significantly higher scores than

the neurotypical group on all domains, namely Perceptual modulation, Over-inclusion, Distractibility, the effects of Fatigue and Stress, and the SGI total score.

Adolescent/Adult Sensory Profile. The means and standard deviations of the four sensory quadrants are shown in Table 3. The ASD participants had more sensory issues in all the four domains compared to neurotypical peers. Specifically, the ASD group had significantly higher scores in the Low registration quadrant, Sensation seeking, Sensory sensitivity, and Sensation avoiding. Analysis of each sensory domain indicated that the ASD group had significantly higher scores than the neurotypical group, in Auditory processing ($t_{(46)} = 4.46$, $p < .0005$, $d = 1.29$), Activity level ($t_{(46)} = 4.79$, $p < .0005$, $d = 1.38$), Touch processing ($t_{(46)} = 3.0$, $p = .004$, $d = .87$), and Visual processing ($t_{(35.6)} = 2.45$, $p = .02$, $d = .7$). There were no group differences in the Taste/Smell processing ($t_{(46)} = .86$, $p = .4$, $d = .25$), and the Movement processing domains ($t_{(46)} = .23$, $p = .82$, $d = .07$). For participants with ASD, for the low registration category, 29.2% met the criteria for extreme sensory processing deficits (±2 SD from mean), 33.3% met this criterion for the sensory sensitivity quadrant, 37.5% met this criterion for the sensation avoiding quadrant, and 4.2% met the criteria for the sensation seeking quadrant. Of all the ASD participants, 62.5 % reported extreme levels of sensory processing on at least one sensory quadrant. None of the participants in the neurotypical group reported quadrant scores that met the criteria for the extreme sensory processing category.

Table 3. Means and standard deviations for the behavioral assessments along with group comparisons using *t* tests.

Behavioral assessments & domains	Neurotypical *M* (*SD*)	ASD *M* (*SD*)	*t*	*p*	*d*
SRS 2					
Social Awareness	6.46 (2.7)	10.79 (4.31)	4.16	**< .0005**	1.2
Social Cognition	6.29 (3.4)	14.5 (6.9)	5.24	**< .0005**	1.5
Social Communication	10.58 (7.5)	29.67 (11.5)	6.81	**< .0005**	2.0
Social Motivation	8.42 (4.2)	17.88 (6.2)	6.16	**< .0005**	1.8
Restricted & Repetitive Behaviors	6.17 (4.1)	19 (8.19)	6.79	**< .0005**	2.0
Total Raw Score	37.92 (18.4)	91.83 (33.5)	6.54	**< .0005**	2.0
SGI					
Perceptual Modulation	15 (10.3)	39.42 (20.4)	5.24	**< .0005**	1.5
Over-Inclusion	11.08 (7.9)	22.67 (7.7)	5.11	**< .0005**	1.5
Distractibility	14.21 (7.8)	25.29 (8.9)	4.58	**< .0005**	1.3
Fatigue and Stress Vulnerability	8.88 (4.5)	13.46 (7.8)	2.49	**.018**	.71
Total score	49.17 (26.8)	100.8 (40.4)	5.22	**< .0005**	1.5
AASP					
Quadrant 1: Low Registration	29.92 (5.6)	39.38 (8.7)	4.46	**< .0005**	1.3
Quadrant 2: Sensation Seeking	50.46 (7.1)	41.21 (8.8)	4.0	**< .0005**	1.2
Quadrant 3: Sensory Sensitivity	31.83 (5.7)	40.96 (11.8)	3.40	**.002**	1.0
Quadrant 4: Sensation Avoiding	34.13 (6.2)	46.08 (11.9)	4.35	**< .0005**	1.3
TEA					
Map Search 1 minute	61.88 (9.3)	51.96 (11.7)	3.24	**.002**	.94
Map Search 2 minutes	78.48 (1.3)	76.33 (3.2)	3.0	**.005**	.88
Elevator Count	6.96 (.2)	6.92 (.3)	.59	.56	.16
Elevator Count Distraction	9.52 (.8)	8.38 (2.2)	2.41	**.022**	.69
Visual Elevator: Raw Accuracy	8.63 (.9)	8.25 (1.4)	1.07	.29	.32
Visual Elevator: Timing Score	2.92 (.4)	3.5 (.7)	3.53	**.001**	1.0
Elevator Counting with Reversal	7.79 (1.9)	6.83 (2.7)	1.39	.17	.41
Telephone Search	2.39 (.5)	2.87 (.9)	2.35	**.025**	.66
Telephone Search while Counting	.52 (.9)	1.86 (3.4)	1.86	.07	.54
Lottery	9.46 (.9)	8.13 (2.3)	2.36	**.026**	.76

Analysis of Neural Measures of Gating

The grand-averaged ERP waveform shows P50 gating in neurotypical group and ASD group during the passive condition, and less robust gating during the active condition (See Figure

7). The means and standard deviations of the P50 and N1 amplitudes and latencies are shown in Table 4.

Table 4. Means and standard deviations for the P50 and N1 ERP amplitude and latencies.

		Neurotypical		ASD	
		Passive	Active	Passive	Active
		M (*SD*)	*M* (*SD*)	*M* (*SD*)	*M* (*SD*)
Amplitude	P50 Click 1	3.8 (1.66)	3.89 (1.77)	3.28 (1.5)	3.23 (1.13)
	P50 Click 2	1.57 (.84)	2.15 (1.06)	1.46 (.86)	2.21 (1.0)
	N1 Click 1	-7.55 (2.29)	-6.36 (2.46)	-8.12 (5.03)	-7.69 (4.57)
	N1 Click 2	-3.5 (2.23)	-6.49 (2.79)	-3.15 (2.84)	-6.44 (4.07)
Latency	P50 Click 1	63.37 (6.1)	60.6 (3.36)	65.12 (7.75)	66.10 (9.0)
	P50 Click 2	61.58 (4.96)	59.85 (5.93)	64.16 (9.93)	63.03 (11.7)
	N1 Click 1	99.81 (10.3)	98.69 (10.9)	109.78 (11.9)	110.6 (11.9)
	N1 Click 2	91.51 (13.6)	101.97 (22.2)	102.95 (20.5)	105.6 (17.7)

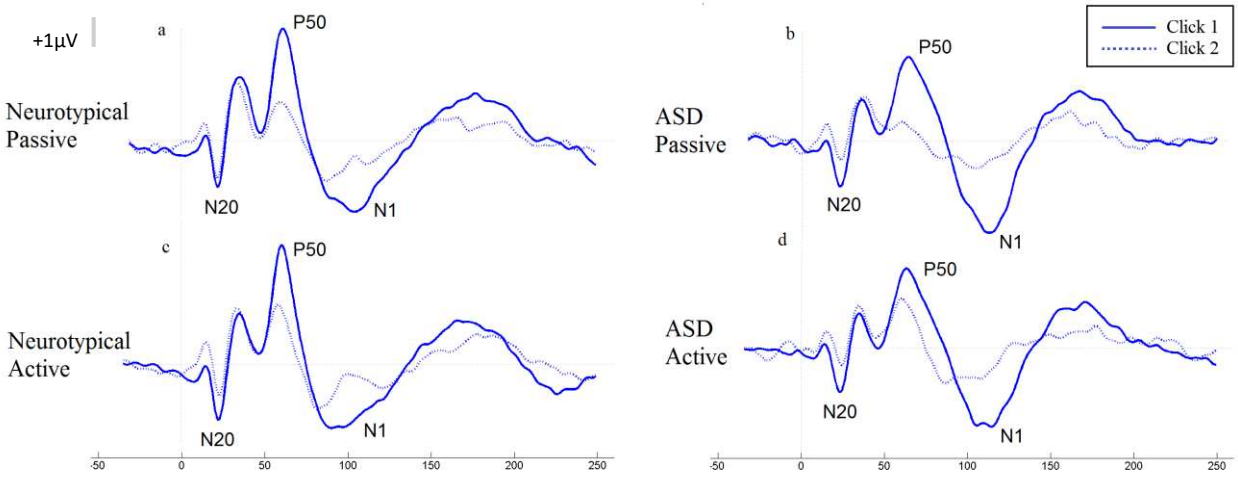

Figure 7. Grand averages of the ERPs at site Cz. A. ERP for the neurotypical group during the passive condition. B. ERP for the ASD group during the passive condition. C. ERP for the neurotypical group during the active condition. D. ERP for the ASD group during the active condition. Positive voltage is up.

P50 Component

The P50 amplitude ANOVA indicated a main effect of attention, ($F_{(1, 46)} = 10.28$, $p = .002$, $\eta^2 = .18$). P50 amplitudes in the active condition were significantly larger than the passive condition, for both clicks across both groups. There was also a significant main effect of clicks, ($F_{(1, 46)} = 105.73$, $p < .0005$, $\eta^2 = .70$) such that the first click had significantly larger P50 amplitudes than the second click across attention conditions for all participants. This indicates gating at the P50 component on average for both groups. There was a significant attention by clicks interaction effect, ($F_{(1, 46)} = 10.82$, $p = .002$, $\eta^2 = .19$). *A posteriori* tests indicated that there was no difference in click 1 between the active and passive condition ($q_{(1, 46)} = .09$, $p > .05$), however, click 2 was significantly larger in the active condition compared to the passive condition, ($q_{(1, 46)} = 4.77$, $p < .01$). There was no main effect of group, ($F_{(1, 46)} = 1.09$, $p = .30$, $\eta^2 = .02$), indicating that there was no statistically significant difference at the P50 component between the neurotypical group and the ASD group.

The T/C ratio for the passive condition for the neurotypical group ($M = .48$, $SD = .32$) and the ASD group ($M = .50$, $SD = .33$) indicated gating at the P50 component. The means for the T/C ratio for the active condition for the neurotypical group ($M = .57$, $SD = .25$) and the ASD group ($M = .74$, $SD = .40$) indicated less gating at the P50 component compared to the passive condition for both groups. An independent samples *t* test examining the P50 T/C Ratio revealed no significant group differences for the passive ($t_{(46)} = .24$, $p = .81$) and active ($t_{(46)} = 1.79$, $p = .08$) condition. However, using P50 difference scores, although no group differences were found for the passive condition ($t_{(46)} = .97$, $p = .34$); significant group differences were found for the active condition ($t_{(46)} = 2.14$, $p = .03$). This indicates that the ASD group ($M = 1.02$, $SD = 1.1$) had less gating than the neurotypical group ($M = 1.74$, $SD = 1.21$) for the active condition.

A paired samples *t* test examining differences in T/C ratios between the active and passive condition for the neurotypical group revealed no significant difference ($t_{(23)} = 1.1$, $p = .28$), suggesting gating during both conditions. However, the paired samples *t* test examining differences in T/C ratios between the active ($M = .74$, $SD = .4$) and passive condition ($M = 50$, $SD = .33$) for the ASD group revealed a significant difference ($t_{(23)} = 2.9$, $p = .007$), suggesting significantly less gating at the P50 component during the active condition compared to the passive condition. For the passive condition, none of the neurotypical participants had a T/C ratio at or above 1, while 4.2 % (n = 1) of the ASD group had a T/C ratio at or above 1. For the active condition, 4.2 % (n = 1) of the neurotypical group had a T/C ratio at or above 1, while 20.8% (n = 5) of the ASD group had a T/C ratio at or above 1.

The P50 latency ANOVA showed no significant main effects or interaction effects. The between-subject group effect indicated a small effect although not significant, ($F_{(1, 46)} = 3.59$, $p = .06$, $\eta^2 = .07$), such that the ASD group had delayed latencies (M (SE) = 64.61 (1.2)) compared to the neurotypical group (M (SE) = 61.35 (1.2)).

N1 Component

The N1 amplitude ANOVA indicated a main effect of attention, ($F_{(1, 46)} = 21.23$, $p < .0005$, $\eta^2 = .32$). N1 amplitudes in the active condition were significantly larger than the passive condition, for both clicks across both groups. There was also a significant main effect of clicks, ($F_{(1, 46)} = 44.75$, $p < .0005$, $\eta^2 = .50$) such that the first click had significantly larger N1 amplitudes than the second click across attention conditions across both groups. This indicates gating at the N1 component. There was a significant attention by clicks interaction effect, ($F_{(1, 46)} = 57.95$, $p < .0005$, $\eta^2 = .56$). *A posteriori* tests indicated that there was no difference in click 1 between the active and passive condition ($q_{(1, 46)} = 2.58$, $p > .05$), however, click 2 was

significantly larger in the active condition compared to the passive condition, ($q_{(1, 46)} = 10.58$, $p < .01$). There was no main effect of group, ($F_{(1, 46)} = .19$, $p = .66$, $\eta^2 = .004$), indicating that there was no statistically significant difference at the N1 component between the neurotypical group and the ASD group.

The T/C ratio for the passive condition for the neurotypical group ($M = .46$, $SD = .26$) and the ASD group ($M = .40$, $SD = .45$) indicated gating at the N1 component for both groups, and no significant group differences were found for the passive ($t_{(46)} = .60$, $p = .55$) and active ($t_{(46)} = 1.38$, $p = .17$) condition. The means for the T/C ratio for the active condition for the neurotypical group ($M = 1.01$, $SD = .34$) and the ASD group ($M = .88$, $SD = .58$) indicated less gating at the N1 component compared to the passive condition for both groups. A paired samples *t* test examining differences in T/C ratios between the active and passive condition for the neurotypical group revealed significant difference between the two conditions ($t_{(21)} = 7.05$, $p < .0005$), suggesting less gating during the active condition compared to the passive. Similarly, the paired samples *t* test examining differences in T/C ratios between the active and passive condition for the ASD group revealed a significant difference ($t_{(22)} = 3.4$, $p = .003$), suggesting significantly less gating at the N1 component during the active condition compared to the passive condition. For the neurotypical group, 41.7% (n = 10) had a T/C ratio at or above 1, while for the ASD group, 20.8% (n=5) had a T/C ratio at or above 1. As expected for the passive condition, none of the neurotypical participants had a T/C ratio at or above 1, while 4.2% (n=1) of the ASD group had a T/C ratio at or above 1 during the passive condition.

The N1 latency ANOVA, showed a significant main effect of click ($F_{(1, 46)} = 5.06$, $p = .03$, $\eta^2 = .10$), such that Click 2 had significantly shorter N1 latencies than Click 1 across attention conditions for all participants. There was also a significant group difference ($F_{(1, 46)} =$

8.92, $p = .005$, $\eta^2 = .16$), such that the ASD group had significantly longer N1 latencies than the neurotypical group. Post-hoc tests revealed that, for the ASD group, Click 1 had significantly longer latencies than the neurotypical peers during the passive ($t_{(46)} = 3.1$, $p = .003$), and active condition ($t_{(46)} = 2.28$, $p = .027$). For the active condition, ASD group had longer latencies than the neurotypical group for Click 1 ($t_{(46)} = 3.62$, $p = .001$) but not Click 2 ($t_{(46)} = .63$, $p = .53$). This suggests a delay in orienting to the first click stimuli for the ASD group compared to neurotypical group, regardless of the attention manipulation. However, there appears to be an attention-based reduction in the latency delay for Click 2 in the ASD group.

Brain-behavior relationships. To answer research question 3, the relationship between sensory gating as assessed by the T/C ratio with the behavioral measures of attention, sensory processing, and social responsivity were examined using Pearson's correlations. Additionally, since there were significant group differences in N1 latency, this measure was used to examine brain-behavior relationships. There was a significant correlation between the P50 T/C ratio of the active condition and the total TEA score ($r_{(48)} = -.36$, $p = .012$), such that better attention abilities were associated with more robust gating during the passive condition. Click 1 N1 latency of the passive condition was positively associated with 3 domains of the AASP, namely low registration ($r_{(47)} = .33$, $p = .024$), sensory sensitivity, ($r_{(47)} = .33$, $p = .023$), and sensation avoiding ($r_{(47)} = .3$, $p = .04$), such that a longer latency was associated with more sensory processing issues. Additionally, click 1 N1 latency of the passive condition also positively correlated with the SRS -2 ($r_{(47)} = .43$, $p = .003$), such that delayed processing was associated with greater social difficulties. The association between Click 1 N1 latency and the SGI total score also approached significance ($r_{(48)} = .29$, $p = .05$), suggesting that delayed processing may be associated with more deficits on behavioral sensory gating deficits.

Discussion

The paired-click sensory gating paradigm has been widely used to assess neural filtering of redundant information in neurotypical individuals as well as several clinical groups. The purpose of this study was to examine sensory gating in young adults with high functioning ASD as compared to neurotypical controls, and to examine the impact of attention on sensory gating in both these groups. As per hypothesis 1, directing attention towards the click stimuli during the active condition led to less gating at the P50 and N1 component compared to the passive condition for all participants. Specifically, click 2 had greater P50 and N1 amplitudes during the active condition compared to the passive condition, indicating reduced filtering or suppression. However, contrary to our hypothesis 2, there was no difference in gating between the ASD group and the neurotypical group at the P50 and N1 amplitudes during both the passive and active attention conditions. However, using P50 difference scores, the ASD group had reduced gating in the active condition compared to neurotypical peers. The ASD group had significantly longer N1 latencies to click 1 during the passive and active conditions compared to the neurotypical group. Additionally, the ASD group had significantly delayed click 2 N1 latencies in the passive condition but not the active condition.

Analysis of the behavioral data suggested that compared to neurotypical controls, the ASD group had significantly more deficits in social responsivity as measured by the SRS 2, sensory processing as measured by the SGI and AASP, and attention as measured by the TEA. Additionally, as per hypothesis 3, several behavioral measures were associated with N1 latency, such that faster processing was associated with better sensory processing, and social responsivity. P50 gating correlated with attention, such that more typical gating was associated with more typical attention abilities.

Attention Impacts P50 and N1 Gating

Traditionally. although the P50 and N1 component have been considered as pre-attentive, automatic, and unaffected by attentional manipulations (Boutros et al., 2004), more recent research has led to a consensus that focused attention can impact these early ERP components (Jones et al., 2016). In our study, we found that both, the neurotypical group and the ASD group had less gating at the P50 and N1 component during the active condition compared to the passive condition. Specifically, click 2 had significantly larger P50 and N1 amplitudes during the active condition compared to the passive condition. Several researchers have found that focusing attention to the click stimuli results in reduced suppression (Guterman et al., 1992; Rosburg, Trautner, Elger, & Kurthen, 2009; Yee et al., 2010). White and Yee (1997), and Rosburg et al. (2009) found that directing attention towards the clicks resulted in reduced suppression at the N1 component but not the P50. Contrary to the findings mentioned above, we found reduced suppression in the active attention condition at both the P50 and the N1 component.

Gating in Individuals with ASD

Research regarding gating in young adults with ASD has been mixed. In our study, we found no difference between the ASD and control group. Individuals with ASD had gating as measured by the T/C ratio at the P50 and N1 component during the passive condition. However, individuals with ASD had less gating in the active condition than the neurotypical group as measured by difference scores. This difference was not statistically significant using T/C ratios. Hence, this finding must be interpreted with caution. Additionally, for the ASD group, the number of non-gaters (T/C ratio >.99) at the P50 and N1 component remained the same in the passive and active condition. However, for the neurotypical group, there were more instances of failure to gate in the active condition than the passive condition at both the P50 and N1

component. This implies that self-directed attention differentially impacts information filtering in the ASD group compared to the neurotypical group. Specifically, the impact of self-directed attention is stronger in the neurotypical group, especially for the N1 component. Orekhova et al. (2008) showed that P50 suppression improved with age in individuals with ASD. Similarly, no P50 suppression deficits were found in a study with adult males with ASD (Magnee et al., 2009). Although some studies have shown gating deficits in children with ASD (Madsen et al., 2015; Orekhova et al., 2008), studies examining adults with ASD have reported typical P50 and N1 suppression. Individuals with ASD had larger standard deviations for the P50 and N1 amplitudes than neurotypical participants, indicating more variability in the ASD group, however, this difference was not statistically significant. This is an expected finding due to the nature of the spectrum of symptoms in ASD. Moreover, this could be a possible reason for the inconsistencies in the gating literature in ASD populations. Our results showed that gating abilities are associated with attention abilities as measured by a performance-based behavioral assessment of attention, the TEA. Including measures of attention and examining the relationship between gating and attention may provide valuable insights into understanding the inconsistencies in the neural measures of gating.

An interesting finding in this study was that compared to the control group, individuals with ASD had significantly longer Click 1 N1 latencies during both attention conditions and longer Click 2 N1 latencies in the passive but not active condition. Since the Click 1 is an orienting stimulus, a longer latency suggests a delayed orienting response. Similar findings of delayed latencies of the early component, M100 (corresponding to N1 in EEG) were found in a magnetoencephalography (MEG) study of auditory processing in children with ASD (Edgar et al., 2015). Longer N1 latencies are linked to decreased neural synchrony or temporal jitter within

the auditory pathway (Harris et al., 2007). In the active condition, a lack of group difference in Click 2 suggests improved processing speed for the ASD group relative to the passive condition. In the auditory domain, researchers examining attention and sensory processing using neurophysiological measures suggest that processing of attended stimuli is either normal or increased in ASD, while processing of unattended stimuli is usually decreased (Orekhova & Stroganova, 2014). Thus, more typical N1 latencies in the active but not passive condition in the ASD group suggest an attention-based enhancement of sensory processing. Further research is required to validate this finding.

Sensory Processing in ASD

Our results indicated that our sample of young adults with ASD had significantly more sensory processing deficits than the control group. Specifically, the ASD group had significantly lower scores on all four sensory quadrants. Sensory processing deficits are part of the diagnostic criteria for ASD (*DSM–5*; American Psychiatric Association, 2013). In line with our findings, researchers have found that sensory deficits persist into adulthood in ASD (Billstedt, Gillberg, & Gillberg, 2007; Crane, Goddard, & Pring, 2009). In a study of 18 adults with ASD (18-65 years), and an age- gender- and IQ-matched control group, Crane et al. (2009) found significant sensory deficits in the four quadrants of the AASP compared to the control group. Additionally, 94.4% of the ASD participants reported extreme levels of sensory processing on at least one sensory quadrant (Crane et al., 2004). In our study, 62.5% of the ASD sample reported with extreme sensory processing on at least one sensory quadrant. Our findings are contrary to the findings of Kern et al. (2007), who reported that abnormal sensory processing in ASD tends to dissipate with increasing age. However, in the study by Kern et al., most questionnaires were completed by the caregivers, which could result in underestimation of the sensory challenges faced by the adults.

Attention in ASD

In our study, individuals with ASD had significant deficits in attention as measured by the TEA. Of the 8 subtests, individuals with ASD had significantly lower scores on Map search (1 and 2 minutes), visual elevator distraction, visual elevator timing score, telephone search, and lottery. The Map search and telephone search tasks assess visual selective attention, while the visual elevator task assess attentional switching, and lottery assesses divided attention. These subtypes of attention were categorized based on Petersen and Posner (2012). Of the 24 participants with ASD in this sample, ten participants (41.7%) reported a dual-diagnoses of attention-deficit hyperactivity disorder (ADHD), and eight (33%) reported being diagnosed with a learning disorder as a child. This is an expected finding since ADHD is one of the most common comorbid conditions with ASD (Matson, Rieske, & Williams, 2013). Moreover, several researchers have shown that children with ASD have significant deficits in all the three subtypes of attention, selective, sustained, and shifting (Allen & Courchesne, 2011).

An attention model of autism was proposed by Gold and Gold (1975), which has been supported by recent research (Williams, Minshew & Goldstein, 2015). However, there is a lack of research examining attention in adults with ASD. Minshew, Goldstein, and Siegel (1997) proposed the complex information processing model of ASD which suggests that individuals with ASD do not have deficits in a specific modality or cognitive domain, but rather present with a generalized deficit involving multiple modalities and domains that are supported by distributed cortical networks responsible for higher order functions (Minshew, Muenz, Goldstein & Payton, 1992; Williams et al., 2015). Based on the model, the researchers suggested intact or superior simple attention abilities, but deficits in complex memory, concept formation and reasoning. It is

possible that the tasks of the TEA simulate these complex skills, since most of these subtests measure everyday functioning which can be complex.

Social Responsivity in ASD

The Social responsiveness scale is a widely-used tool to assist in the diagnosis of ASD, and has been shown to be highly associated with ASD symptoms (Chan, Smith, Hong, Greenberg, & Mailick, 2017). Persistence of deficits in social responsivity in adults has been extensively documented (Billstedt et al., 2007). Thus, our finding of significantly more social deficits in the ASD group compared to the neurotypical group validates our study sample of ASD participants. Moreover, the ASD group had significantly higher scores in all sub-categories of the SRS 2, namely, social awareness, social cognition, social communication, social motivation, and restricted interests and repetitive behavior.

Sensory Gating Phenomenology

The SGI was developed to assess the perceptual and attentional phenomenology associated with sensory gating deficits, commonly observed in Schizophrenia (Hetrick et al., 2012). In our study, young adults with ASD had significantly more deficits on all four factors, namely perceptual modulation, distractibility, over-inclusion, and fatigue-stress vulnerability compared to the neurotypical control group. To our knowledge, the SGI has not been used in young adults with ASD before. However, research using several other self-report sensory and perceptual inventories have demonstrated that children and adults with ASD have more pervasive and frequent perceptual anomalies than neurotypical individuals (Crane et al., 2009; Baranek et al., 2014).

Brain-Behavior Relationships in ASD

Gating abilities at the N1 component were associated with better attention skills, better social responsivity, and better sensory registration. Gating abilities at the P50 component were associated with better attention abilities. Researchers have found similar relationships, such that deficits in gating were associated with difficulties in sensory processing, perceptual, and severe behavioral deficits (Croft, Lee, Bertolot, & Gruzelier, 2001; Freedman et al., 1991, Hutchison et al., 2013, Potter, Summerfelt, Gold, & Buchanan, 2006). In a sample of 60 neurotypical individuals, researchers found that gating was associated with several measures of cognitive functioning, such as fluid intelligence and working memory (Jones, Hills, Dick, Jones, & Bright, 2016). In a review of gating in schizophrenia, researchers found that P50 suppression was associated with measures of attention (Potter et al., 2006). Similarly, Wan et al. (2007) found that sensory gating positively correlated with performance on the Attention Network Test and a Stroop task, indicating better alerting, less conflict between stimuli, and greater accuracy. Moreover, Croft et al. (2001) found that sensory gating was associated with perceptual deficits. Additionally, sensory gating abnormalities have been shown to correlate with positive symptoms in schizophrenia (Potter et al., 2006). In our study, we found a significant correlation between gating at the SRS 2 total score. In the current sample, although the ASD group did not demonstrate significant gating deficits, the correlation between gating and autism severity as measured by the SRS 2 warrants further investigation. Contrary to some previous research in schizophrenia, we found no significant relationship between gating at the P50 or N1 component with the SGI total score or the 4 factors (Micoulaud-Franchi et al., 2014). This could be due to the difference in the clinical group, and the lack of gating deficits in ASD compared to the schizophrenia sample. To summarize, gating at the P50 and N1 component is strongly associated

with measures of attention, sensory processing, and social responsivity. Further research investigating the potential use of gating as an objective measure of attention and sensory processing is warranted.

One of the study limitations is that while the ASD group and the neurotypical controls were matched on age, they were not matched on gender. However, there were no gender differences in either groups on gating ERP measures or the TEA. For the neurotypical participants, significant gender differences were only found for the SRS-2 scale, such that females had better social responsivity than males. However, for the ASD group, there were no gender differences for the SRS-2 scale. For the ASD group, females had significantly higher scores on the SGI total score and the AASP total score compared to males. However, this finding must be interpreted with caution since out of 24 participants with ASD, 17 were males. To summarize, the gender differences in the ASD group and neurotypical group do not seem likely to confound any of the study findings. A second possible limitation is that nearly half of our ASD participants had a comorbid diagnosis of ADHD. Since ADHD is one of the most commonly occurring comorbid diagnosis, we believe that this validates our sample as being representative of the general ASD population.

CHAPTER 4 – STUDY 3

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 hypo-reactivity to sensory input are part of the diagnostic criteria for children with ASD (DSM-5: American Psychiatric Association, 2013). There has been growing interest in understanding the neurophysiological processes underlying sensory processing in ASD and more specifically, understanding auditory processing (Orekhova et al., 2009). Researchers have documented atypical development of the central auditory system in children with ASD (Yoshimura et al., 2016).

Using electrophysiological measures such as electroencephalography (EEG) and event-related potentials (ERPs), several researchers have shown differences in neural processing of auditory information in individuals with ASD as compared to neurotypical individuals (Ludlow et al., 2014). Researchers have shown that ERP measures of auditory processing are related to behavioral measures of sensory processing, such that higher sensory sensitivities are associated with reduced neural activation of auditory stimuli (Ludlow et al., 2014). ERPs provide a non-invasive and accurate neural measure of the timing and stages of auditory processing (Luck, 2005). An ERP waveform to an auditory stimulus consists of N1, P2, N2, and P3 components (Polich, 1993). Each of these responses reflect different stages of sensory processing, orienting, attention, and cognitive processing of the stimulus (Luck, 2005).

The N1 component, occurring around 100 ms post-stimulus onset, is thought to reflect automatic catching of attention to auditory stimulus (Näätänen & Picton, 1987). Research

examining the auditory N1 response in ASD has been highly variable (Bomba & Pang, 2004). Some researchers have found smaller N1 amplitudes in children with ASD (Bruneau et al., 1999; Orekhova et al., 2009) while Oades et al. (1988) reported that the N1 component was larger and had a shorter latency in 5-7 year olds with ASD compared to neurotypical controls. Several studies have reported delays in auditory response in individuals with ASD, at the N1 and the N2 time-period (around 100-200 ms post-stimulus onset; Edgar et al., 2015; Gandal et al., 2010). Others have demonstrated the absence of significant differences in the N1 component between ASD and neurotypical controls (Dunn et al., 2008; Ferri et al., 2003). Although, Brandwein et al. (2014) showed that the N1 ERP component significantly predicted autistic symptom severity, and was associated with behavioral measures of sensory processing.

With regards to the P2 amplitude, a positive ERP component around 200 ms post-stimulus onset, several researchers have failed to find a significant difference between ASD and neurotypical controls (Salmond et al., 2007; Whitehouse & Bishop, 2008). Several studies have consistently reported that individuals with ASD have attenuated N2 amplitudes to pure tones, paired clicks, and speech stimuli (Donkers et al., 2013; Jansson-Verkasalo et al., 2003, 2005). The N2 is a negative ERP occurring around 200 ms post-stimulus onset (Folstein & Van Petten, 2008). Researchers suggest that smaller N2 amplitudes imply increased difficulty in automatic stimulus discrimination and deficits in sound encoding (Jansson-Verkasalo et al., 2003, 2005). Donkers et al. (2013) reported that smaller N2 amplitudes in children (4-12 years) with ASD to standard auditory tones in an oddball paradigm were associated with greater sensory seeking behaviors. Several researchers have reported attenuated P3 amplitudes in ASD compared to controls (Donkers et al., 2015). The P3 is a positive ERP occurring around 300 ms post-stimulus onset (Polich, 1993). Lepisto et al. (2005) reported that children with ASD had deficits in sound

encoding, discrimination of duration changes, and involuntary orienting to sound changes as reflected by smaller P3a ERP components than controls. Others have shown no group differences in the auditory P3 amplitude and latency in adults with ASD and healthy controls (Andersson et al., 2013).

While there are inconsistencies in the literature regarding specific ERP dysfunction, some of the differences in findings can be attributed to differences in participant characteristics (e.g., age, level of functioning) and experimental parameters (inter-stimulus interval, tone characteristics, active versus passive tasks). Specifically, instructions regarding the direction of attention towards or away from the auditory stimulus may play an important role in understanding the study findings. Studies have shown that sensory processing abilities are dependent on attentional control (Talsma et al., 2010). Researchers have also argued that atypical responses to auditory information in children with auditory processing disorders may be due to underlying deficits in attention (Moore et al., 2010). Attention is a crucial element for goal-directed, purposeful response to sensory information in our social and physical environment. Attention is understood as a "broad cognitive concept that includes a set of mechanisms that determine how particular sensory input, perceptual objects, trains of thought, or courses of action are selected for further processing from an array of concurrent possible stimuli, objects, thoughts and action" (Talsma et al., 2010, p. 2).

Impairments in orienting (Zwaigenbaum et al., 2005), sustained attention (Christakou et al., 2013), vigilance, cognitive flexibility/switching (Corbett et al., 2009), shifting and disengaging attention (Elsabbagh et al., 2009) have been consistently reported in individuals with ASD. According to the feature-integration theory of attention, without focused attention, stimulus features cannot be related to one another (Treisman & Gelade, 1980). Thus, deficits in

attention may be one of the possible causes of behavioral under-responsiveness to auditory information in ASD.

The sensory registration paradigm used in this study 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). Strong intensity discrimination has been found in N1, P2, N2 and P3 auditory ERP components, such that loud tones have larger amplitudes and shorter latencies than soft tones (Harris et al., 2007; Martin & Boothyord, 2000). With regards to frequency discrimination, low-frequency sounds generate larger N1 and P2 amplitudes than high-frequency sounds at the same intensity (Wunderlich & Cone-Wesson, 2001). Although there are inconsistencies in findings, most research seems to agree that individuals with ASD have enhanced pitch perception, however with impaired processing of acoustic change when complex stimulus paradigms are used (O'Connor et al., 2012).

The aim of the present study is to examine the effects of attention (passive versus active) in a simple auditory detection task in neurotypical individuals and individuals with ASD. The paradigm in this study consisted of two conditions. In the passive condition, the participants were asked to listen to the tones while staring at a fixation point. In the active condition, the participants were asked to respond with a button press to the low frequency soft tone (1 kHz, 50 dB) and ignore the other tones while staring at a fixation point. Additionally, we examined intensity and frequency discrimination between groups. To examine brain-behavior relationships of attention and sensory processing, a self-report measure of sensory processing and a performance-based measure of attention were also used.

Research Questions:

1. How do stimulus characteristics impact auditory processing?

Hypothesis: Robust intensity and frequency discrimination will be observed at the N1, P2, N2, and P3 components for both groups regardless of attention condition. Loud tones and low frequency tones will have larger amplitudes and shorter latencies than soft tones and high frequency tones.

2. How does active versus passive attentional states affect sensory registration?

Hypothesis: During the active condition, participants will have smaller N1, P2, and N2 amplitudes, and larger P3 amplitudes compared to the passive condition.

3. Are there differences in N1, P2, N2, and P3 amplitude and latency measures in individuals with ASD as compared to neurotypical individuals?

Hypothesis: Participants with ASD will have smaller N1, P2, N2, and P3 amplitudes and longer latencies compared to neurotypical controls. However, these differences will be more prominent in the passive compared to the active attention condition.

4. Are there group differences between neurotypical individuals and individuals with ASD on behavioral measures of attention and sensory processing?

Hypothesis: Individuals with ASD will have significantly more deficits in attention and sensory processing compared to neurotypical individuals.

5. How do behavioral measures of attention and sensory processing relate to neural measures of attention and sensory processing?

Hypothesis: Individuals with better attention or sensory processing scores on the behavioral assessments will have faster N1 latencies of the target tone during the active attention condition.

Methods

This study included a total of 48 participants recruited via convenience sampling. Twenty-four participants (M = 23.31 years, SD = 3.77; 17 males, 7 females) had a confirmed diagnosis of high-functioning ASD. The control group consisted of twenty-four age-matched neurotypical individuals (M = 23.7 years, SD = 3.51; 12 males, 12 females). There was no group difference in age ($t_{(46)} = .41$, $p = .69$). The diagnosis of ASD was confirmed using the ADOS-2 administered by author JEC prior to the initiation of the study (Rutter et al., 2012). All control participants were screened using a self-report screening questionnaire developed in our lab to ensure that they were free of neurological injuries, disabilities, and family histories of psychological disorders. All the procedures performed in the research involving human participants were in accordance with the ethical standards of the institutional review committee at the local university and with the 1964 Helsinki declaration and its later amendments. All participants signed a written informed consent prior to the study.

Procedures. Once the EEG cap, and electrodes are applied, the participant were given a brief training on strategies to reduce artifacts resulting from eye blinks, and other muscle activity. Participants in both groups completed a series of two attention conditions during the EEG recording followed by behavioral testing of attention. Both groups were presented the passive condition first followed by the active condition described in detail below. Participants also completed a second EEG task but these data are not reported here. The EEG recording and the behavioral assessment lasted approximately 45 minutes each.

Sensory registration EEG paradigm. EEG data were collected in a sound-attenuated electrically shielded room. For the sensory registration paradigm, the four auditory stimuli (50 ms in duration with a 10 ms rise/fall time) consisted of pure tones, two with frequencies at 1000

Hz and two at 3000 Hz, and each frequency was presented at either one of two intensity levels, 50 dB sound pressure level (SPL) or 70 dB SPL. For each attention condition, the stimuli were presented in two blocks of 160 trials each, with a total of 80 trials of each tone in pseudo-random order with a two-second inter-stimulus interval. Each block lasted about five minutes with short breaks of about 1 minute between blocks. 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).

*Passive attention condition***.** Participants were instructed to stare at the fixation point while they heard the auditory stimuli. No motor response was required.

*Active attention condition***.** Participants were instructed to respond with a button press to the low frequency soft tone (1 kHz, 50 dB SPL stimuli) and ignore the other 3 auditory stimuli. The participants were instructed to stare at the fixation point while they listened to the tones and pressed the button. The low frequency soft tone was chosen as the target tone since it produces ERP components with the smallest amplitudes compared to the other tones in the passive condition (See figure 8), which allowed us to determine the influence of focused attention. At the start of the paradigm, participants went through a one-minute practice session with feedback. During the session, no feedback was provided.

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 included 64 Ag/AgCl sintered scalp electrodes. The electrodes were located in accordance with the modified 10–10 system (Klem, Lüders, Jasper, & Elger, 1999; Oostenveld & Praamstra, 2001). EEG was recorded with the Common Mode Sense active electrode as the reference and the Driven Right Leg passive electrode as the ground

(http://www.biosemi.com/faq/cms&drl.htm). Electrooculograms (EOGs) were recorded from individual electrodes placed on the left and right outer canthus for horizontal movements and on the left supraorbital and infraobital region for vertical movements. Two more individual electrodes were placed on the left and right earlobes and used as the offline reference. 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 were sampled at a rate of 2048 Hz with a bandwidth of 0 to 417 Hz.

ERP waveform and component analysis. Averaged ERPs were composed from the running EEG data using Brain Vision Analyzer 2.0. First, the four EOG channels were converted to a vertical and a horizontal bipolar EOG. Then data were filtered with a bandpass of .1 – 30 Hz with a 12 dB/octave rolloff using casual phase-shift free butterworth filter settings. 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 was performed (Segalowitz, 1996). 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 artifact rejection were averaged. Of the 64 channels, the central sites Cz was analyzed based on previous studies using the sensory registration paradigm (Bomba & Pang, 2004; Davies et al., 2010). Peak amplitudes for the N1, P2, N2, and P3 were identified using the Matlab software, PeakPicker program (Gavin, 2009). The window for determining the peaks was based on previous published research (Bomba & Pang, 2004; Davies et al., 2010) and visual inspection of the grand average waveforms for the participants. The N1 component was scored

between 80 and 200 ms after the stimulus onset. The P2 was scored between 130 and 300 ms; however, 6 peaks of participants with ASD and 1 peak of a neurotypical participant were scored between 300-340 ms. The N2 was scored between 175 and 475 ms. The P3 was scored between 250 and 550 ms; however, 2 peaks of neurotypical participants were scored between 230-250ms.

Behavioral Measures

To assess the relationship between neural measures of sensory processing and behavioral measures of attention and sensory processing, the Test of Everyday Attention (TEA) was administered to all participants. Additionally, participants were asked to fill out the Adolescent/Adult Sensory Profile.

Adolescent/Adult sensory profile (AASP). The AASP is a self-report questionnaire consisting of 60 items that relate to everyday sensory experiences. The AASP is validated for individuals 11 or older. Each item is scored on a 5-point Likert scale indicating how frequently the behavior is performed (from 1 "almost never" to 5 "almost always"). The 60 items are organized into six categories of taste or smell, movement, visual, touch, activity level, and auditory sensitivities. The questionnaire takes about 10-15 minutes to complete. The AASP scores are categorized into 4 quadrants based on Dunn's (1997) model of sensory processing, which classifies sensory behaviors based on neurological thresholds (high or low) and behavioral responses (passive or active). Neurological thresholds refer to the amount of stimuli needed for the nervous system to respond to sensory stimuli, and behavioral responses relate to the way in which a person responds to their sensory thresholds. The four quadrants are:

1. Low registration: refers to passive behavioral responses with a high neurological threshold. These items identify behaviors such as missing stimuli or responding slowly. Ex: "I don't smell things that other people say they smell".

2. Sensation seeking: refers to active behavioral responses with a high neurological threshold, i.e., actively pursuing sensory input. Ex: “I like how it feels to get my hair cut”
3. Sensory sensitivity: refers to passive behavioral responses with a low neurological threshold, i.e., experiencing discomfort with regular sensory stimuli. Ex: “I startle easily to unexpected or loud noises”.
4. Sensation avoiding: refers to active behavioral responses with a low neurological threshold, i.e., deliberately reducing exposure to sensory stimuli. Ex: “I only eat familiar foods”.

Quadrant scores are classified as “much less than most people” (-2 SD from mean), “less than most people”, “similar to most people”, “more than most people”, and “much more than most people” (+2 SD from mean). Extreme sensory processing is defined as scores falling in either “much less than most people” or “much more than most people”. The AASP has good reliability (r = .64 - .78) and validity (Brown & Dunn, 2002).

Test of everyday attention. TEA is a standardized and normed clinical battery that has been validated for ages 18 to 80 years. The TEA is based largely on everyday materials with real-life scenarios to ensure that participants find it relevant to their problems of adjustment in everyday life. The TEA is developed based on an imaginary trip to Philadelphia in the US. Participants are required to perform various simulated daily activities with familiar materials in the scenarios of each subtest, such as searching for restaurants on a map. Eight subtests with a four-factor structure correspond to the attentional model presented by Petersen and Posner (2012). Subtests assess selective, sustained attention, attentional switching, and divided attention. The TEA takes around 45-50 minutes to complete. Higher scores indicate better attention abilities. For this study, raw scores were used in the analysis since all participants were within the same age-range for the standardized scores, and raw scores preserved individual variability.

The reliability of the subtests of the TEA range from good to excellent for clinical populations and healthy controls (r = .34 – 64; Ward et al., 1994).

Data analysis

To determine if brain processing of auditory stimuli differed significantly between the two groups across the different attention conditions, baseline-to-peak amplitudes of the N1, P2, N2, and P3 components were analyzed using a 2 (Group) x 2 (Condition) x 2 (Intensity) x 2 (Frequency) repeated measures analysis of variance (ANOVA). The between subject's factor was group, neurotypical controls and ASD group. The three within factors were attention (2 levels: Passive and Active), Frequency (2 levels: 1 kHz and 3 kHz), and Intensity (2 levels: high and low). Group differences on the behavioral assessments were examined using independent samples *t* tests. Pearson's product moment correlation analyses were used to assess the relationship between ERP components and behavioral measures of attention and sensory processing. *A posteriori* Tukey's honestly significantly difference (HSD) post-hoc *t* tests were calculated to examine interaction effects (Kirk, 1968, p. 265-269). Testwise alpha was set at 0.0125 for the *apriori* hypotheses (ANOVAs), with Bonferroni correction for the 4 ERP components, (.05/4 = .0125). Effect sizes for η^2 are interpreted as follows, .04 – small, .25 – medium, and .64 – large (Ferguson, 2009). Effect sizes for Cohen's *d* can be interpreted as follows, .41 – small, 1.15 – moderate, 2.7 – strong (Ferguson, 2009). All statistical analyses were performed using the Statistical Package for Social Sciences (SPSS), version 24.0.

Results

The number of correct responses during the active condition were not significantly different between neurotypical participants (M (SD) = 77.96 (3.93)) and the participants with ASD (M (SD) = 75.87 (5.65)), $t_{(46)}$ = 1.48, p = .15. Similarly, the means of the response times

for the active condition for the neurotypical participants (*M* (*SD*) = 579.3 (102.6)) and the participants with ASD (*M* (*SD*) = 601.8 (113)) were not significantly different, $t_{(46)} = .72$, $p = .48$. The grand-averaged ERP waveforms for the four auditory stimuli are shown separately for the two groups and attention conditions at site Cz in Figure 8. The means and standard deviations of the N1, P2, N2, and P2 amplitudes and latencies are reported in Table 5. Visual inspection of the ERP components indicates that the loud tones (70 dB) have larger amplitudes than the soft tones (50 dB) at the early N1 and P2 components. Additionally, the active condition appears to have larger amplitudes at the mid-latency N2 and P3 components.

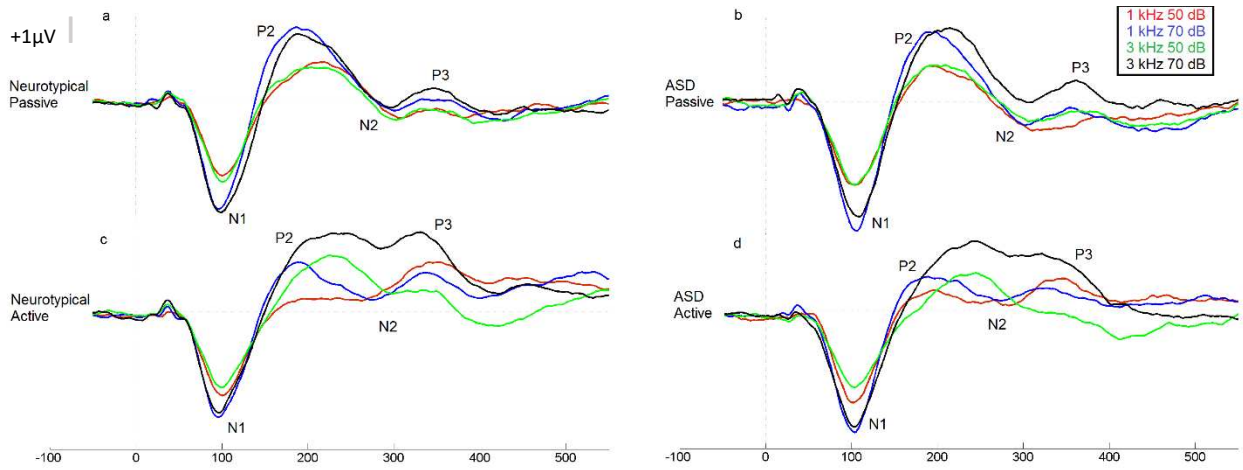

Figure 8. Grand average ERP waveforms for the sensory registration paradigm. a. ERP waveform for the passive condition for the neurotypical group. b. ERP waveform for the active condition for the neurotypical group. c. ERP waveform for the passive condition for the ASD group. d. ERP waveform for the passive condition for the neurotypical group. Positive voltage is up.

Table 5. Means and standard deviations for the ERP component amplitudes for the sensory registration paradigm

	Neurotypical		ASD	
Stimulus	Passive	Active	Passive	Active
1 kHz 50 dB SPL	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)
N1 amplitude	-6.24 (1.9)	-6.88 (2.2)	-7.29 (2.78)	-7.45 (2.25)
N1 latency	100.7 (8.7)	100.8 (10.0)	104.2 (11)	102.9 (8.7)

P2 amplitude	4.02 (2.64)	2.4 (2.8)	3.98 (4.15)	2.67 (3.03)
P2 latency	209.9 (32.6)	199.1 (40.6)	206.5 (28.4)	212.3 (39.3)
N2 amplitude	-1.79 (2.28)	-.68 (2.36)	-3.54 (2.82)	-2.03 (2.68)
N2 latency	261.6 (50.1)	382.8 (70.5)	311.7 (41.1)	280.5 (48.7)
P3 amplitude	1.06 (1.72)	5.1 (4.21)	2.52 (.78)	4.15 (4.19)
P3 latency	382.8 (70.5)	354.3 (57.6)	397.3 (58.9)	377 (73.7)
1 kHz 70 dB SPL				
N1 amplitude	-8.87 (2.62)	-8.42 (2.4)	-10.56 (3.49)	-9.9 (2.98)
N1 latency	97.4 (8.2)	95.3 (6.7)	104.6 (7.2)	103.3 (8)
P2 amplitude	6.86 (3.49)	5.04 (3.83)	7.02 (4.79)	4.76 (5.32)
P2 latency	187.9 (22.3)	193.2 (31.5)	197.9 (30.9)	195.9 (35.5)
N2 amplitude	-1.86 (2.53)	-.76 (3.5)	-3.94 (2.81)	-1.38 (3.41)
N2 latency	293.9 (42.4)	277.7 (48.3)	319.3 (46.6)	265.6 (61.5)
P3 amplitude	1.59 (3.05)	4.09 (4)	.8 (2.59)	3.53 (3.58)
P3 latency	367.8 (62.4)	340.6 (26.5)	399.4 (70.9)	359.9 (65.8)
3 kHz 50 dB SPL				
N1 amplitude	-6.77 (2.26)	-6.2 (2.54)	-7.1 (2.88)	-6.4 (2.51)
N1 latency	102.4 (10.1)	101.6 (9.9)	107.8 (11.2)	116.7 (30.1)
P2 amplitude	3.84 (2.8)	5.34 (2.57)	4.6 (3.76)	4.74 (3.43)
P2 latency	199.9 (28.8)	223.8 (41.3)	305.6 (30.5)	232.4 (37.3)
N2 amplitude	-1.95 (2.79)	-1.13 (3.57)	-3.04 (2.32)	-2.33 (2.88)
N2 latency	299.1 (38.5)	339.1 (70.8)	314.2 (37.8)	316.9 (66.5)
P3 amplitude	.62 (2.74)	2.77 (2.96)	.75 (2.36)	1.6 (2.96)
P3 latency	347.5 (45.4)	427.1 (100.8)	381.9 (50.2)	403.5 (97.8)
3 kHz 70 dB SPL				
N1 amplitude	-9.06 (2.39)	-8.11 (2.71)	-9.47 (3.6)	-9.27 (3.23)
N1 latency	100 (9.9)	97.5 (8.6)	107.3 (11.9)	104.6 (11)
P2 amplitude	6.24 (3.24)	7.12 (3.09)	7.44 (4.93)	7.44 (5.26)
P2 latency	200.9 (24)	218.3 (39.5)	209 (29.7)	225.4 (51.2)
N2 amplitude	-1.67 (2.27)	2.05 (3.41)	-2.03 (3.31)	1.07 (4.6)
N2 latency	285.9 (33.3)	294.2 (73.2)	312 (44.1)	297.6 (91)

P3 amplitude	2.19 (3.01)	6.58 (3.74)	2.93 (2.71)	4.7 (4.2)
P3 latency	360.8 (67.4)	363.6 (79.1)	387.9 (49.8)	366 (75.5)

Stimulus characteristics: intensity and frequency discrimination. For **N1 amplitude**, intensity, $F_{(1, 46)} = 157.73$, $p < .0005$, $\eta^2 = .77$, and frequency, $F_{(1, 46)} = 15.62$, $p = .025$, $\eta^2 = .11$, main effects were significant. As expected, high intensity loud tones had larger N1 amplitudes than the soft tones across attention conditions for both groups. Low frequency tones had larger N1 amplitudes than high frequency tones across attention conditions for both groups. Similarly, for **N1 latency**, intensity, $F_{(1, 46)} = 8.66$, $p = .005$, $\eta^2 = .15$, and frequency, $F_{(1, 45)} = 10.02$, $p = .003$, $\eta^2 = .18$, main effects were significant. Loud tones had shorter N1 latencies than the soft tones across attention conditions for both groups. Low frequency tones had shorter latencies than the high frequency tones across both attention conditions for both groups.

For **P2 amplitude**, main effects of intensity, $F_{(1, 46)} = 73.98$, $p < .0005$, $\eta^2 = .62$ and frequency, $F_{(1, 46)} = 25.15$, $p < .0005$, $\eta^2 = .36$ were significant. As expected, high intensity loud tones had larger P2 amplitudes than the soft tones across attention conditions for both groups. High frequency tones had larger P2 amplitudes than low frequency tones across attention conditions for both groups. Similarly, **for P2 latency**, the main effect of intensity was significant, $F_{(1, 46)} = 6.05$, $p = .018$, $\eta^2 = .12$, such that loud tones had shorter P2 latencies than the soft tones across attention conditions for both groups. Similarly, the main effect of frequency was also significant, $F_{(1, 46)} = 18.69$, $p < .0005$, $\eta^2 = .29$, such that the low frequency tones had shorter latencies than the high frequency tones across attention conditions for both groups.

For **N2 amplitude**, intensity, $F_{(1, 46)} = 17.69$, $p < .0005$, $\eta^2 = .28$, and frequency, $F_{(1, 46)} = 13.75$, $p = .001$, $\eta^2 = .23$, main effects were significant. Unexpectedly, soft tones had larger N2 amplitudes than the loud tones across attention conditions for both groups. Additionally, low

frequency tones had larger N2 amplitudes than high frequency tones across attention conditions for both groups. For **N2 latency**, intensity effect was not significant, but the frequency effect was significant, $F_{(1, 45)} = 7.77$, $p = .008$, $\eta^2 = .15$, such that the low frequency tones had shorter latencies than the high frequency tones across attention conditions for both groups.

For **P3 amplitude**, the main effect for intensity was significant, $F_{(1, 46)} = 21.66$, $p < .0005$, $\eta^2 = .32$. As expected, high intensity loud tones had larger P3 amplitudes than the soft tones across attention conditions for both groups. The main effect for frequency was not significant, $F_{(1, 46)} = .35$, $p = .56$, $\eta^2 = .007$. Frequency and intensity main effects were not significant for **P3 latency**.

Effects of attention condition: passive versus active. For **N1 amplitude**, the main effect for attention was not significant, $F_{(1, 46)} = 2.97$, $p = .09$, $\eta^2 = .06$. Similarly, for **N1 latency**, the main effect for attention was not significant, $F_{(1, 46)} = .004$, $p = .95$, $\eta^2 = .00$. For **P2 amplitude**, although the main effect for attention was not significant, $F_{(1, 46)} = 3.85$, $p = .05$, $\eta^2 = .08$, there was a significant attention by frequency interaction, $F_{(1, 46)} = 23.5$, $p < .0005$, $\eta^2 = .34$. *A posteriori* tests indicated that the low frequency tones had significantly smaller P2 amplitudes than the high frequency tones in the active condition ($q_{(1, 46)} = 6.97$, $p < .01$), but not in the passive condition ($q_{(1, 46)} = .36$, $p > .01$). This indicates that frequency discrimination was significantly better in the active compared to the passive condition at the P2 component. **P2 latency** revealed a significant main effect for attention condition, $F_{(1, 46)} = 11.64$, $p = .001$, $\eta^2 = .20$, such that the passive condition had shorter latencies than the active condition across all tones and for both groups. There was a significant attention by frequency interaction effect for P2 latency, $F_{(1, 46)} = 17.19$, $p < .0005$, $\eta^2 = .27$. *A posteriori* tests revealed that there was no significant difference between P2 latencies for the low and high frequency tones for the passive

condition ($q_{(1, 46)} = .75$, $p > .01$). However, for the active condition, the low frequency tones had a significantly shorter latency than the high frequency tones ($q_{(1, 46)} = 5.6$, $p < .01$). Thus, the task requiring attention resulted in faster brain responses for the P2 component for low frequency tones than high frequency tones only in the active condition, not the passive condition, demonstrating better frequency discrimination in the active condition.

The **N2 amplitude** revealed a significant main effect for attention condition, $F_{(1, 46)} = 34.96$, $p < .0005$, $\eta^2 = .43$, such that N2 amplitudes were significantly larger in the passive condition compared to the active condition across all tones for both groups. There was an attention by intensity interaction, $F_{(1, 46)} = 11.66$, $p = .001$, $\eta^2 = .21$. *A posteriori* tests revealed that the soft tones had significantly larger N2 amplitudes than the loud tones during the active condition ($q_{(1, 46)} = 3.62$, $p < .01$) but not during the passive condition ($q_{(1, 46)} = .57$, $p > .01$). This indicates that intensity discrimination was also significantly better during the active condition compared to the passive condition at the N2 component.

The **N2 latency** revealed a significant main effect for attention, $F_{(1, 45)} = 8.76$, $p = .005$, $\eta^2 = .16$, such that active condition had significantly shorter latencies than the passive condition. There was a significant attention by frequency interaction effect, $F_{(1, 45)} = 24.23$, $p < .0005$, $\eta^2 = .35$. *A posteriori* tests revealed that there was no significant difference between N2 latencies for the low and high frequency tones for the passive condition ($q_{(1, 45)} = .73$, $p > .01$). However, for the active condition, the low frequency tones had a significantly shorter latency than the high frequency tones ($q_{(1, 45)} = 5.09$, $p < .01$). This result is similar to what was revealed for the P2 component latency.

The **P3 amplitude** revealed a significant main effect for attention condition, $F_{(1, 46)} = 60.74$, $p < .0005$, $\eta^2 = .57$. P3 amplitudes were significantly larger in the active condition

compared to the passive condition across all tones for both groups. For **P3 latency**, the main effect of attention was not significant, $F_{(1, 42)} = .21$, $p = .65$, $\eta^2 = .005$. However, there was a significant attention by frequency interaction effect, $F_{(1, 42)} = 11.27$, $p = .002$, $\eta^2 = .21$. *A posteriori* tests revealed no significant difference between P3 latencies for the low and high frequency tones for the passive condition ($q_{(1, 42)} = 1.69$, $p > .01$) or the active condition ($q_{(1, 42)} = 2.51$, $p > .01$).

Group differences: individuals with ASD and neurotypical peers. There was no main effect for group at the **N1 amplitude**, $F_{(1, 46)} = 1.67$, $p = .20$, $\eta^2 = .04$. However, for **N1 latency**, the main effect for group was significant, $F_{(1, 45)} = 9.75$, $p = .003$, $\eta^2 = .18$, such that individuals with ASD (*M (SE)* = 106.43 (1.58)) had significantly longer N1 latencies across all tones compared to the neurotypical participants (*M (SE)* = 99.39 (1.6)). This effect was present in both the passive and active attention conditions. There was a significant frequency by group interaction effect, $F_{(1, 45)} = 6.21$, $p = .016$, $\eta^2 = .12$. *A posteriori* tests revealed significant group difference for the high frequency tones ($q_{(1, 45)} = 3.76$, $p > .01$), with the ASD group having significantly longer N1 latencies than the neurotypical group. There was no group difference for the low frequency tones ($q_{(1, 45)} = 1.87$, $p > .01$).

There was no main effect for group at **P2 amplitude**, $F_{(1, 46)} = .04$, $p = .85$, $\eta^2 = .001$, and at **P2 latency**, $F_{(1, 46)} = 1.04$, $p = .31$, $\eta^2 = .02$. The main effect for group at the **N2 amplitude** had a small effect but was not significant, $F_{(1, 46)} = 3.71$, $p = .06$, $\eta^2 = .08$, the ASD group had larger N2 amplitudes than the neurotypical group. For **N2 latency**, the main effect for group was not significant, $F_{(1, 45)} = 1.14$, $p = .29$, $\eta^2 = .03$. However, there was an attention by group interaction effect, $F_{(1, 45)} = 4.41$, $p = .04$, $\eta^2 = .09$. A post-hoc ANOVA for the passive condition, revealed a significant main effect for group, such that the N2 latency was significantly longer in

the ASD group than the neurotypical group, $F_{(1, 45)} = 5.21$, $p = .027$, $\eta^2 = .1$. However, in the ANOVA for the active condition, the main effect for group was not significant $F_{(1, 45)} = .07$, $p = .78$, $\eta^2 = .002$, suggesting that latency delay in the ASD group was present only during the passive condition.

For the **P3 amplitude**, there was no main effect for group, $F_{(1, 46)} = 1.03$, $p = .32$, $\eta^2 = .02$. For **P3 latency**, the main effect for group had a small effect, but was not significant, $F_{(1, 42)} = 3.84$, $p = .057$, $\eta^2 = .08$. The means for the P3 latency of the neurotypical participants *(M (SE)* = 361.69 (7.37)) were shorter than the means for the participants with ASD *(M (SE)* = 381.67 (7.04)). Although the attention by group interaction effect was not significant, post-hoc ANOVAs for each attention condition were conducted. As expected, there was a significant group effect for the P3 latency in the passive condition, $F_{(1, 46)} = 5.67$, $p = .02$, $\eta^2 = .11$, such that the ASD group has longer P3 latencies than the neurotypical group. However, this effect was not significant for the P3 latency in the active condition, $F_{(1, 42)} = .57$, $p = .45$, $\eta^2 = .01$.

Test of Everyday Attention (TEA). The 10 scores obtained from the six subtests along with the total score were compared between the groups using independent samples *t* tests. The total score was significantly lower for individuals with ASD compared to neurotypical peers, ($t_{(46)} = 3.9$, $p < .005$, $d = 1.13$). See table 6 for means and standard deviations and *t* test comparisons for the subtests. Significant group differences were found for four of the eight TEA subtests. To summarize, individuals with ASD had significant deficits in attention compared to neurotypical peers.

Adolescent/Adult sensory profile. The means and standard deviations of the four sensory quadrants are shown in Table 6. Individuals with ASD had significantly more sensory issues in all the four domains compared to neurotypical peers. Specifically, the ASD group had

significantly higher scores in the Low registration quadrant, Sensation seeking, Sensory sensitivity, and Sensation avoiding. Analysis of each sensory domain indicated that individuals with ASD had significantly higher scores than the neurotypical group, in Auditory processing ($t_{(46)} = 4.46$, $p < .0005$, $d = 1.29$), Activity level ($t_{(46)} = 4.79$, $p < .0005$, $d = 1.38$), Touch processing ($t_{(46)} = 3.0$, $p = .004$, $d = .87$), and Visual processing ($t_{(35.6)} = 2.45$, $p = .02$, $d = .7$). There were no group differences in the Taste/Smell processing ($t_{(46)} = .86$, $p = .4$, $d = .25$), and the Movement processing domains ($t_{(46)} = .23$, $p = .82$, $d = .07$). For participants with ASD, for the low registration category, 29.2% met the criteria for extreme sensory processing deficits (±2 SD from mean), 33.3% met this criterion for the sensory sensitivity quadrant, 37.5% met this criterion for the sensation avoiding quadrant, and 4.2% met the criteria for the sensation seeking quadrant. Of all the ASD participants, 62.5 % reported extreme levels of sensory processing on at least one sensory quadrant. None of the participants in the neurotypical group reported quadrant scores that met the criteria for the extreme sensory processing category.

Table 6. Means and standard deviations for the behavioral assessments along with group comparisons using *t* tests.

Behavioral assessment & domains	Neurotypical M (SD)	ASD Mean (SD)	*t*	*p*	*d*
AASP					
Quadrant 1: Low Registration	29.92 (5.6)	39.38 (8.7)	4.46	**< .0005**	1.3
Quadrant 2: Sensation Seeking	50.46 (7.1)	41.21 (8.8)	4.0	**< .0005**	1.2
Quadrant 3: Sensory Sensitivity	31.83 (5.7)	40.96 (11.8)	3.40	**.002**	1.0
Quadrant 4: Sensation Avoiding	34.13 (6.2)	46.08 (11.9)	4.35	**< .0005**	1.3
TEA					
Map Search 1 minute	61.88 (9.3)	51.96 (11.7)	3.24	**.002**	.94
Map Search 2 minutes	78.48 (1.3)	76.33 (3.2)	3.0	**.005**	.88
Elevator Count	6.96 (.2)	6.92 (.3)	.59	.56	.16
Elevator Count Distraction	9.52 (.8)	8.38 (2.2)	2.41	**.022**	.69
Visual Elevator: Raw Accuracy	8.63 (.9)	8.25 (1.4)	1.07	.29	.32
Visual Elevator: Timing Score	2.92 (.4)	3.5 (.7)	3.53	**.001**	1.0

Elevator Counting with Reversal	7.79 (1.9)	6.83 (2.7)	1.39	.17	.41
Telephone Search	2.39 (.5)	2.87 (.9)	2.35	**.025**	.66
Telephone Search while Counting	.52 (.9)	1.86 (3.4)	1.86	.07	.54
Lottery	9.46 (.9)	8.13 (2.6)	2.36	**.026**	.76

Brain-behavior relationships. There was a moderate negative relationship between the N1 latency of the target tone in the active condition and the sensory sensitivity quadrant ($r_{(48)}$ = -.32, p = .028), and low registration quadrant ($r_{(48)}$ = -.31, p = .03), indicating that a shorter latency was associated with more typical sensory processing. Additionally, there was a significant relationship between N1 latency for the target tone in the active condition and the total score of the TEA ($r_{(48)}$ = -.35, p = .016), such that a shorter latency correlated with higher attention scores.

Discussion

The purpose of this study was to examine the impact of attention on auditory registration and discrimination in young adults with ASD and a neurotypical control group. Answering research question 1 examining the effect of stimulus characteristics, our results indicated that intensity discrimination was evident at all the components, while frequency discrimination was present at the N1, P2 and N2 components. Additionally, intensity discrimination was more robust than frequency discrimination. However, there were significant attention by frequency interactions effects, such that frequency discrimination was more robust during the active attention condition compared to the passive condition. Answering research question 2 examining the effect of active and passive attention states on sensory registration, we found that directing attention to the tones resulted in amplitude and latency differences at the P2, N2, and P3 mid-latency components. Answering research question 3 examining group differences on ERP measures, there were no group differences in amplitudes of the ERP components, namely N1-P2-

N2-P3 following the auditory stimuli. However, there were significant latency differences at the N1, N2, and P3 components, such that the responses of individuals with ASD were significantly delayed responses compared to the neurotypical group. For N1 latency, the ASD group displayed a delayed response in both the passive and active conditions. Moreover, latency differences at the N2 and P3 components were present during the passive condition and not the active condition. This implies that latency delays in the ASD group were offset when participants were asked to direct their attention to the tones. Answering research question 4 examining group differences on behavioral measures of sensory processing and attention, we found that that the ASD group had significantly more deficits in sensory processing and attention. Finally, answering research question 5, analysis of the behavioral data suggested that compared to neurotypical controls, individuals with ASD had significantly more deficits in sensory processing as measured by the AASP, and attention as measured by the TEA. Additionally, these behavioral measures were associated with ERP components, such that shorter latencies were associated with more typical sensory processing as measured by the AASP and attention as measured by the TEA.

Stimulus Characteristics Impacting Auditory Processing

N1 component. The N1 has been associated with both stimulus-specific and stimulus-nonspecific components, and is described as an "initial orienting response to acoustic stimuli" (Näätänen & Picton, 1987). Consistent with literature, both N1 amplitude and latency measures showed strong frequency and intensity discrimination. The N1 amplitudes were larger and latencies shorter for the low frequency tones than high frequency tones for both groups. This is consistent with literature indicating that N1 amplitude decreases as frequency increases (Wunderlich & Cone-Wesson, 2001). This finding can be attributed to greater activation of the area of the transverse temporal gyrus to a 1 kHz tone compared to a 4 kHz tone measured using

fMRI (Strainer et al., 1997). In terms of intensity discrimination, N1 amplitudes were larger and latencies shorter for the loud tones than the soft tones. This finding of intensity dependence has been extensively documented in the literature (Ponton et al., 2000).

P2 component. The P2 component represents an exogenous response, which is sensitive to stimulus intensity and frequency changes (Crowley & Colrain, 2004). P2 amplitudes were smaller and latencies shorter for the low frequency tones compared to the high frequency tones. Similar to the N1 component and existing literature, loud tones had larger P2 amplitudes and shorter latencies than the soft tones (Crowley & Colrain, 2004; Paiva et al., 2016).

N2 component. Frequency and intensity effects were also observed at the N2 component, such that the N2 amplitude was larger and latency shorter for the low frequency stimuli than the high frequency stimuli. However, the N2 amplitude was larger with longer latencies for the soft tone compared to the loud tone. Post-hoc analyses revealed that this effect was significant for the active condition but not the passive condition. Since the low frequency soft tone was the target tone, larger amplitude for the low frequency tones and soft tones imply greater processing of the target tone compared to the non-target tones. This finding supports the function of the N2 reflecting attention allocation and discrimination (Folstein & Van Petten, 2008).

P3 component. Intensity effects were also observed at the P3 component, such that the loud tones had larger amplitudes and shorter latencies than the soft tones. This is also consistent with literature demonstrating intensity-sensitivity of the P3 component (Polich & Kok, 1995). There were no frequency effects at the P3, which aligns with existing research (Polich & Kok, 1995).

Attention Impacts Auditory Processing

N1 component. The N1 represents a sensory filter which is activated by auditory events and represents stimulus encoding (Näätänen & Picton, 1987). In this study, we failed to show an attention effect at the N1 component. The means indicate that the passive condition had larger amplitudes than the active condition for all the tones except the target tone (1 kHz 50 dB). Additionally, the small effect size for the attention main effect for N1 amplitude ($\eta^2 = .06$), implies that the lack of attention effect could be a power issue.

P2 component. There was an interaction effect of attention condition and frequency for both, P2 amplitude and latency measures, revealing better frequency discrimination between the 1 kHz and 3 kHz tones during the active condition compared to the passive condition. This is consistent with literature which states that stimuli presented during attended states are detected faster and discriminated more accurately than stimuli presented during unattended states (Mondor & Zatorre, 1995). Additionally, consistent with previous research, P2 latencies were shorter for the passive condition compared to the active condition (Morris et al., 2016).

N2 component. The N2 component is associated with auditory discrimination, recognition, perception, and discrimination (Picton, 2010). Attention significantly impacted the N2 amplitude, such that the passive condition had larger N2 amplitudes than the active condition. Smaller N2 amplitudes in the active attention condition could be due to better attention allocation during the active condition compared to the passive condition. Researchers have found that the N2 component is reduced when stimuli can be easily discriminated during an auditory go/no-go task (Nieuwenhuis et al., 2004). At the N1 and P2 components, stimulus discrimination was better during the active condition compared to the passive condition. This ability to better discriminate the auditory stimuli during the active condition could have led to smaller N2

amplitudes compared to the passive condition. Consistent with the N1 and P2 components, we also found interactions effects between attention condition and frequency, such that low frequency tones were better discriminated from high frequency tones during the active condition than the passive condition.

P3 component. The P3 or the P300 component is perhaps the most extensively studied ERP component with reliable consensus that the P3 is attention-dependent, and occurs when an individual consciously detects an informative task-relevant stimulus (Huang et al., 2015). Attention significantly impacted auditory processing of the P3 amplitude, such that the active condition had larger P3 amplitudes than the passive condition. This is in accordance with existing literature (Huang et al., 2015).

Neural Processing in individuals with ASD

N1 component. Individuals with ASD had longer N1 latencies across all tones and attention conditions compared to neurotypical individuals. Longer latencies suggest delayed processing, slower transmission of information in neural pathways, and a delayed orienting response. Several studies have reported longer N1 latencies to auditory stimuli in individuals with ASD (Bruneau et al., 1999; Jeste & Nelson, 2009; Gandal et al., 2010). Gandal and colleagues (2010) showed that children with ASD, and valproic acid- (VPA) exposed mice demonstrated significant latency delay in the N1/M100 response. Using magnetoencephalography (MEG), researchers found that the M100 (corresponds to N1 in EEG) latency delays in children with ASD provided accurate ASD classification (Roberts et al., 2010). Longer N1 latencies are linked to decreased neural synchrony or temporal jitter within the auditory pathway (Harris et al., 2007). Additionally, N1 latencies decrease with aging at Cz, which could imply a maturational lag in auditory processing in the ASD participants (Tomé et

al., 2015). There have been mixed results examining N1 amplitude differences in ASD, with some showing no difference and others showing amplitude increases and decreases (for review see Bomba & Pang, 2004). In our study, we failed to find a difference in N1 amplitudes between the ASD group and the neurotypical controls.

P2 component. The P2 amplitude and latency was not significantly different between the neurotypical and ASD group. Similar studies of no P2 amplitude differences in children with ASD have been reported previously (Lincoln et al., 1995).

N2 component. There was a significant attention condition by group interaction effect for N2 latency, such that individuals with ASD had delayed N2 latencies compared to neurotypical peers during the passive condition but not the active condition. This suggests that directing attention to the auditory stimuli may have led to an improvement in processing speed in the ASD group. Researchers have proposed that auditory processing deficits may stem from underlying attention deficits (Marco et al., 2011; Moore et al., 2010). In the auditory domain, researchers examining attention and sensory processing using neurophysiological measures suggest that processing of attended stimuli is either normal or increased in ASD, while processing of unattended stimuli is usually decreased (Orekhova & Stroganova, 2014). In a review of findings of mismatch negativity, Orekhova and Stroganova (2014) found that individuals with ASD are usually able to detect changes in the stimuli presentation when these stimuli are the focus of their attention. However, in the presence of distractors or in the case of unattended stimuli, processing issues arise. When competition for attention is higher, detection of change and associated cognitive processing are reduced in ASD compared to typical controls. Collectively these results demonstrate that auditory processing appears to be dependent on the

context of stimulus presentation and that individuals with ASD have delayed and reduced neural processing which may reflect deficits in early orienting and attentional mechanisms.

P3 component. While there were no group differences of the P3 amplitude, there were significant latency differences. Similar to the N2 latency results, P3 latencies were significantly delayed in the passive condition but not in the active condition. This further supports the hypothesis of an attention-based improvement in processing speeds at mid-latency components. Similar results of longer P3 latencies to auditory stimuli in children with ASD have been documented before (Oades et al., 1988; Čeponienė et al., 2003). However, our findings are contrary to some studies failing to find a group difference in P3 latencies (Andersson, et al., 2013; Kohls et al., 2011). With regards to P3 amplitude, studies have found similar results, with no P3 abnormalities in the visual or auditory domain in adults with ASD (Hoeksma et al., 2006). In the study by Hoeksma et al. (2006), the group of children with ASD had significantly reduced P3 amplitudes, while the adolescents with ASD had "normal" P3 amplitude responses. Additionally, the authors found significant deficits in behavioral measures of selective attention in the adolescents with ASD (Hoeksma et al., 2006).

Sensory Processing in ASD

Our results indicated that our sample of young adults with ASD had significantly more sensory processing deficits than the control group. Specifically, the ASD group had significantly higher scores on all four sensory quadrants. Sensory processing deficits are part of the diagnostic criteria for ASD (*DSM–5*; American Psychiatric Association, 2013). In line with our findings, researchers have found that sensory deficits persist into adulthood in ASD (Billstedt et al., 2007; Crane et al., 2009). In a study of 18 adults with ASD (18-65 years), and an age- gender- and IQ-matched control group, Crane et al. (2009) found significant sensory deficits in the four

quadrants of the AASP compared to the control group. Additionally, 94.4% of the ASD participants reported extreme levels of sensory processing on at least one sensory quadrant. Our findings are contrary to the findings of Kern et al. (2007), who reported that abnormal sensory processing in ASD tends to dissipate with increasing age. However, in the study by Kern et al., most questionnaires were completed by the caregivers, which could result in underestimation of the sensory challenges faced by the adults.

Attention in ASD

In our study, individuals with ASD had significant deficits in attention as measured by the TEA. Of the eight subtests, individuals with ASD had significantly lower scores on Map search (1 and 2 minutes), visual elevator distraction, visual elevator timing score, telephone search, and lottery. The Map search and telephone search tasks assess visual selective attention, while the visual elevator task assess attentional switching, and the lottery task assesses sustained attention. These three subtypes of attention were categorized by Petersen and Posner (2012). Several researchers have shown that children with ASD have significant deficits in all the three subtypes of attention, selective, sustained, and shifting (Allen & Courchesne, 2001). It must be noted that of the 24 participants with ASD in this sample, ten participants (41.7%) reported a dual-diagnoses of attention-deficit hyperactivity disorder (ADHD), and eight (33%) reported being diagnosed with a learning disorder as a child. ADHD is one of the most common comorbid conditions with ASD (Matson et al., 2013).

An attention model of autism was proposed by Gold and Gold (1975), which has been supported by recent research (Williams et al., 2015). However, there is a lack of research examining attention in *adults* with ASD. The complex information processing model suggests that individuals with ASD do not have deficits in a specific modality or cognitive domain, but

rather present with a generalized deficit involving multiple modalities and domains that are supported by distributed cortical networks responsible for higher order functions (Minshew et al., 1992; Williams et al., 2015). Based on this model, the researchers suggested intact or superior simple attention abilities, but deficits in complex memory, concept formation and reasoning. It is possible that the tasks of the TEA simulate these complex skills, since most of these subtests mimic everyday functioning which can be complex.

Brain-Behavior Relationships of Attention and Sensory Processing

N1 latency was associated with sensory processing domains, such that faster processing was related to more typical sensory processing as measured by the ASSP. Additionally, N1 latency of the target tone was also associated with attention, implying that faster processing was related to better attention abilities as measured by the TEA. Since the N1 component is considered a both a measure of neural sensory orientation and initial attention, we would expect this relationship between its latency and behavioral measures of sensory processing and attention (Näätänen & Picton, 1987). Moore et al. (2010) proposed that auditory processing deficits in children with auditory processing disorders were due to underlying deficits in attention.

There is a relative lack of research examining the relationship between neural and behavioral measures of sensory processing in ASD. Ludlow et al. (2014) found a significant relationship between the MMN (mismatch negativity) in children with ASD and sensory sensitivity of the AASP. The authors proposed that the expression of sensory behaviors in ASD may result in impaired psychophysiological mechanisms underlying automatic language processing (Ludlow et al., 2014). Thus, our study finding of a relationship between N1 latency with a self-report measure of sensory processing suggests that sensory processing deficits observed in individuals with ASD may be associated with underlying deficits in neural

processing. Researchers have proposed that sensory processing challenges in ASD may cause core symptoms in ASD including social and emotional communication (Marco et al., 2011). The relationship of sensory processing to ASD symptomatology must be studied beyond the traditional correlational research studies to further examine causation.

Latency Delays in ASD

While several studies have documented latency delays to auditory ERPs in ASD, the underlying neural mechanism is still unknown. Recent studies have proposed that latency delays may be related to disturbances of white-matter integrity, specifically, poorly myelinated acoustic radiations and associated auditory processing pathways (Gandal et al., 2010; Stufflebeam et al., 2008). Researchers have even proposed using delayed auditory responses as translational biomarkers of ASD (Gandal et al., 2010; Roberts et al., 2010). Maziade et al. (2000) showed that delayed early auditory-evoked responses were not only evident in individuals with ASD, but also in a sample of unaffected first-degree relatives of individuals with ASD. In our study, we found significant latency delays in the N1, N2, and P3 components. Although the latency delay in the N1 component was evident in both the active and the passive condition, the N2 and P3 latency delays were only present in the passive condition. This potentially implies that directing attention to the auditory stimuli may ameliorate latency differences during auditory processing. Additionally, this suggests that latency delays in ASD may reflect an underlying neural attentional deficit. Since the N1 is often considered pre-attentive, the impact of attention at the N2 and P3 components, which are exogenous attention-dependent components, suggests that conscious allocation of attention may result in more typical auditory processing. This finding of an attention-based amelioration of auditory processing neural delay needs to be further investigated.

Age Effects in ASD

When mature, high-functioning young adults with ASD continue to present with deficits in neural and behavioral measures of attention and sensory processing, one might also expect to find equal or worse deficits in younger and lower functioning individuals with ASD. The implication of the present study is that young adults with ASD experience deficits in both behavioral attention and sensory processing performance and well as neural measures of attention and auditory processing. Most research in ASD has focused on children, and there is limited research examining the pervasiveness of deficits in young adults with ASD. A study examining outcomes in young adults with ASD found that at the mean age of 24 years, 46% of the sample reported poor outcome while the rest reported good-to-fair outcome (Eaves & Ho, 2008). Researchers have argued that services for adults with ASD do not appear to have kept pace with the increases in services for children (Eaves & Ho, 2008).

One of the study limitations is that while the ASD group and the neurotypical controls were matched on age, they were not matched on gender. However, there were no gender differences in either groups on ERP measures or the TEA. For the ASD group, females had significantly higher scores on the AASP total score compared to males. However, this finding must be interpreted with caution since out of 24 participants with ASD, 17 were males. To summarize, the gender differences in the ASD group and neurotypical group do not seem likely to confound any of the study findings. A second possible limitation is that nearly half of our ASD participants had a comorbid diagnosis of ADHD. Since ADHD is one of the most commonly occurring comorbid diagnosis, we believe that this validates our sample as being representative of the general ASD population.

Conclusion

Results of this study have shown that young adults with ASD have delayed N1, N2, and P3 latencies to auditory processing compared to neurotypical peers. Amplitude measures of the N1, P2, N2, and P3 ERP components were not significantly different between individuals with ASD and neurotypical controls. Additionally, N2 and P3 latency delays in the ASD group were present during the passive listening condition, and were not present during the active attention condition, when participants were asked to focus their attention to the tones, suggesting that focused attention may assist in ameliorating delayed neural sensory processing. Neural measures of auditory processing were associated with behavioral measures of attention and sensory processing. These findings suggest that attention significantly impacts auditory processing in ASD. Further research is required to validate the findings of an attention-based improvement of neural processing in ASD.

CHAPTER 5 – DISCUSSION

Overall Goal of the Dissertation

The primary goal of this dissertation was to examine the relationship between attention and sensory processing in individuals with autism spectrum disorders and neurotypical individuals. Specifically, the objective was to examine if consciously directing attention to incoming information would result in more typical neural processing in individuals with ASD. To answer this question, the first step was to find evidence that directing attention to stimuli compared to passive processing resulted in detectable changes in neural processing. Thus, study 1 was designed to understand how distraction and attention impacted sensory processing in neurotypical individuals. The next step was to identify if the target population of young adults with ASD had significant deficits in neural measures of sensory processing during passive attentional states. Thus, study 2 and 3 examined neural measures of sensory processing in individuals with ASD as compared to age-matched neurotypical controls during passive attentional states. Study 2 examined filtering of information while study 3 examined the registration and discrimination of auditory stimuli.

The third step was to examine if directing attention to stimuli resulted in more typical sensory processing in individuals with ASD by offsetting the deficits observed during the passive condition. Thus, study 2 and 3 involved an active attention condition wherein participants were asked to respond with a button press to a target stimulus. This ensured that participants were actively directing their attention to the auditory stimuli during the active condition. Finally, to examine the relationship between neural measures of sensory processing and behavioral

measures of sensory processing and attention, study 2 and 3 involved specific research questions that examined these brain-behavior relationships.

These series of studies used EEG/ERP methodology to examine brain processing since this method provides a direct measure of the brain's response to sensory information with identifiable transitions across the temporal processing stream, with each ERP component reflecting successive and distinct phases of processing (Luck, 2005). The high temporal resolution of EEG allows examination of the impact of attention at the different phases, namely the early cortical sensory orientation phase (reflected by the P50 and N1), sensory registration phase (N1 and N2), sensory-perceptual processing phase (P2), and later cognitive stages of processing (P3; Naatanen & Picton 1987).

Summary of Findings

The results from Study 1 showed that directing attention to click stimuli resulted in increased amplitudes of the ERP components throughout the stream of processing. Attention effects were observed even at the N1 component, which occurs around 100 ms post-stimulus onset, and which has been historically been considered as pre-attentive. Additionally, the viewing environment impacted sensory processing; specifically watching a silent movie during the EEG paradigms resulted in an increased effort to process stimuli, as demonstrated by larger amplitudes and longer latencies of the mid-latency ERP components compared to a viewing environment of watching a fixation point. Although frequency and intensity discrimination were evident in the passive condition, these discrimination effects were more robust during the active condition. Thus, study 1 provided evidence indicating that attention, both internal attentional states and environmental distraction, impacts neural processing and these effects can be measured by changes in the amplitude and latency of ERP components.

Contrary to our hypothesis, results from study 2 demonstrated that young adults with ASD had gating at the P50 and N1 components during the passive condition, and were comparable to gating in neurotypical individuals. However, individuals with ASD had significantly delayed click 1 responses at the N1 component during both the active and passive attention conditions. However, N1 click 2 responses were delayed only during the passive condition and no group differences were found in the active condition. Thus, study 2 findings provided preliminary evidence supporting an attention-based amelioration of neural sensory processing. Supporting our hypothesis, all participants showed less robust gating during the active condition compared to the passive condition. This lack of suppression was an expected finding, since participants were focusing their attention to Click 2 during the active condition. Thus, these results suggest that directing attention to click stimuli could impact neural processing as early as 50 ms post-stimulus onset. As expected, individuals with ASD had significantly more deficits than neurotypical controls on behavioral measures of attention, sensory processing, and social responsivity. These behavioral measures positively correlated with each other, such that better attention was associated with better sensory processing, and both these were associated with better social responsivity. Moreover, with a decent sample size of 48 participants, there were significant relationships between neural measures of gating and behavioral measures of attention, sensory processing, and social responsivity. Thus, efficient filtering of information at 100 ms was associated with better every day functioning.

Results from study 3 indicated that individuals with ASD had significantly delayed processing of click stimuli during the sensory registration paradigm at the N1, N2, and P3 components. As hypothesized, the latency delay observed at the N2 and P3 components were only present during the passive condition and not during the active condition. Thus, directing

attention towards the stimuli resulted in more typical processing in individuals with ASD. It is worth noting that, for the sensory registration paradigm this attention-based improvement was not present at the N1 component. There are a few possible explanations for this finding in the sensory registration paradigm. Since the N1 is an early pre-attentive component, the effects of consciously directing attention may not influence N1 latency in individuals with ASD since there is an existing processing delay. However, attention can impact processing at the mid-latency exogenous attention-dependent components, which demonstrated more typical processing in our study. Another possible explanation is that the neural generators of N1, which are more wide-spread may not be optimally functioning in individuals with ASD and areas with specialized auditory *cognitive* functions may be compensating for this early deficit. As in study 2, behavioral measures of attention and sensory processing were associated with neural measures of sensory registration.

Theoretical Implications

The dissertation findings provide evidence to support several theoretical concepts proposed by researchers examining attention, sensory processing, and autism spectrum disorders. Additionally, these results also provide preliminary evidence supporting the model proposed in Chapter 1. (See Figure 3 below).

Attention theories. The finding of larger P3 amplitudes and smaller N1, P2, and N2 amplitudes during the active condition, when participants were required to press a button to a target tone, imply that actively directing attention to stimuli results in neural changes while processing auditory stimuli. These results support the "sensory gain control" theory which suggests that sensory pathways can be modulated by increased intensity of brain activity based on attentional mechanisms (Hillyard et al., 1998). The sensory gain theory also suggests that

attention modulates sensory processing through an 'amplification' of neuronal activity within sensory processing areas of attended stimuli compared to unattended stimuli (Posner & DeHaene, 1994). Similarly, these findings align with the assumptions of the "biased competition model of attention" which states that attention is as a nonlinear property that results from a top-down biasing effect (Deco & Rolls, 2005). Thus, the findings from this dissertation align with the theoretical assumptions of the sensory gain theory and the biased competition model. However, these findings contrast with the "late selection theory" of attention which suggests that attention can only affect later post perceptual processes such as memory or response selection (Duncan, 1980).

The finding of significant interaction effects between the viewing environments and attention condition, suggest that distraction leads to an additional load on neural processing. Our study findings support the "load theory of attention" which states that in conditions of low perceptual load, an active mechanism rejects irrelevant distractors to actively maintain processing priorities (Lavie, 2010). However, in the absence of distraction, passive processes are sufficient for perceptual processing. This is evident in the neurotypical group as seen in findings from studies 2 and 3. However, the ASD group may have deficits in neural connectivity such that they require active strategies for efficient sensory processing even in the absence of distractors. The results also indicated better intensity and frequency discrimination during the active condition compared to the passive condition, in both neurotypical individuals and individuals with ASD. These attention effects also seem to echo the work of Carrasco, Ling and Read (2004) that demonstrated that attention alters stimuli appearance by increasing neuronal contrast sensitivity of visual stimuli. These authors suggested that "attention changes the strength of a stimulus by enhancing its effective contrast or salience" (Carrasco et al., 2004, p.5).

Autism theories. Evidence of abnormal neural activity in ASD is ubiquitous. Several theories have tried to explain the spectrum of ASD, albeit failing to provide a unifying solution. Bridging neurological findings with observable behavioral phenotypes is crucial to succeed in deciphering the neurobiology of ASD. There is growing literature expanding on brain-behavior relationships in ASD, however, more work is required to establish these relationships.

Functional connectivity theories of ASD. The long-range underconnectivity theory states that fronto-parietal underconnectivity can lead to deficits in higher order functioning (Minshew & Keller, 2010). The deficits observed in behavioral measures of sensory processing, along with the delayed processing of auditory information align with this theory. Researchers have shown that attention networks involve several distributed regions of the brain, including the fronto-parietal control systems. Additionally, researchers have shown that sensory processing requires multiple brain regions and shares some brain regions such as the insula, which is also involved in the attention system (Menon & Uddin, 2010). Others have proposed that since sensory processing is dependent on rapid information transfer between distinct cortical and subcortical regions, disruptions in long-range connectivity play a causal role in sensory processing dysfunction (Marco et al., 2011). Since we have data from 64 channels of the EEG system, using source localization techniques, we can examine how different brain regions and networks are at play in individuals with ASD compared to neurotypical controls. Using source-localization analyses, brain regions implicated in early auditory processing, namely the superior temporal gyrus, can be analyzed. Additionally, it would be worthwhile to examine regions of the fronto-parietal network as well. Brock, Brown, Boucher and Rippon (2002) proposed that underconnectivity between brain regions might be reflected in a lack of EEG phase synchrony of the gamma band (30-80 Hz). Using time-frequency analysis, phase synchronization and evoked

power can be examined in the paradigms used in this study. Time-frequency analysis will provide a holistic understanding and a confirmation of ERP findings observed in this study.

A proposed model of ASD. A key finding of this study was the attention-based improvement in neural auditory processing. The findings from this dissertation indicated that when attention is directed to auditory stimuli it can modulate or change sensory processing at early stages soon after an auditory stimulus enters the stream of processing to the more cognitive stages of processing. This is compared to when the participant hears the same stimuli but are not directed to attend to the stimuli. This finding supports the model that was proposed to understand the relationship between sensory processing and attention in ASD (See figure 3). Specifically, it was hypothesized that sensory processing is dependent on attention abilities at the neural level, which in turn impacts participation in daily activities. Recent research has attempted to decipher this relationship. Research has proposed that aberrant sensory processing contributes to ASD symptoms (Brandwein et al., 2015). Moreover, others have hypothesized that sensory processing deficits in ASD may be related to underlying attention deficits (Marco et al., 2011).

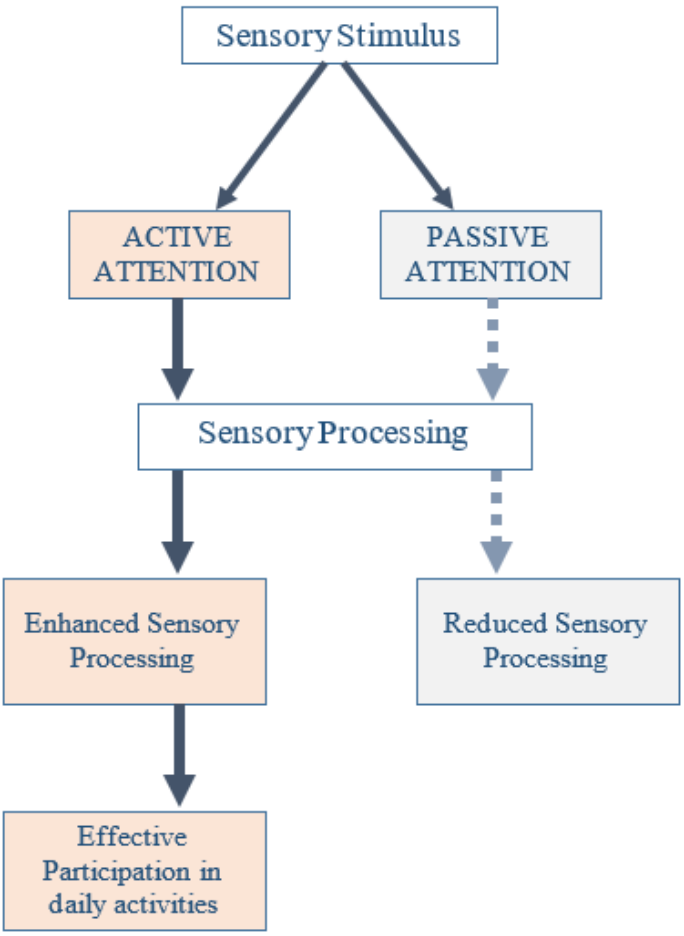

Figure 3. Proposed model depicting the relationship between attention and sensory processing.

To our knowledge, this is the first study to examine how attention deficits can lead to sensory processing deficits which are associated with social challenges in ASD. The Social Responsiveness Scale – 2 (SRS 2) measures social reciprocity and has often been used to examine ASD severity. The relationship between the neural processing of auditory stimuli (as measured by ERPs) and the SRS 2 indicate that neural sensory processing is associated with social challenges observed in ASD, and relate to ASD severity. Gold and Gold (1975) proposed an attentional model in ASD postulating that increased and/or decreased sensitivity and attention to novel stimuli resulted in ASD symptoms. However, most of the research examining this theory has focused on social and joint attention.

ASD as a disorder of attention. Attentional deficits have been documented in infants at-risk for ASD (Elsabbagh et al., 2009; Zwaigenbaum et al., 2005), and may be one of the earliest features that distinguish infants who later receive an ASD diagnosis (Zwaigenbaum et al., 2005). Moreover, non-social attentional strengths (e.g., visual search) and weaknesses (e.g., novelty detection) in ASD and their psychophysiological correlates have also been linked with increased ASD symptomatology (Belmonte et al., 2010; Gomot et al., 2008; Keehn et al., 2010). Keehn, Müller, and Townsend (2013) posited that "early deficits in disengaging attention result in cascade of impairments and ultimately contribute to the emergence of the ASD phenotype" (p.165). While attention has traditionally been considered as a secondary deficit in ASD, there is overwhelming research indicating that attention plays a significant role in ASD symptomatology throughout the course of this neurodevelopmental spectrum disorder (Courschesne et al., 2005; Elsabbagh et al., 2013; Keehn et al., 2010; Gold & Gold, 1975; Minshew & Keller, 2010). Gold and Gold (1975) stated that "using attentional mechanisms as our fulcrum, we may be able to understand the global nature of autism and appreciate the clinical manifestations of this disease" (p. 76).

Methodological Implications

This study used two separate attention conditions (passive and active) to examine the impact of attention on sensory processing. Several studies examining auditory processing in ASD have used a silent movie to facilitate participant engagement through the EEG recording (Carroll & Seeley, 2013). Additionally, the results of studies using a movie versus those using a blank screen or a fixation point are often compared without concern of the viewing environment.

Use of a movie during EEG studies. The results of this dissertation indicated that movie viewing significantly interacts with attentional states during an auditory paradigm, such that

movie viewing results in use of additional neural resources or larger amplitudes compared to participants viewing a fixation point. Thus, researchers should consider the methodology used in the paradigm while comparing study findings. We found robust distraction effects of movie viewing in a population of neurotypical young adults. These effects may be even more pronounced in younger populations and in clinical conditions with attention deficits. While the use of a silent movie in children and clinical populations allows for easier data collection efforts, one must consider the impact of this added visual distraction on auditory processing.

Phases of processing. The results of this study revealed that attention states differentially impact ERP components across the temporal domain following the onset of auditory stimuli. These differences suggest that the corresponding neural generators likely play different roles during stimulus detection and perception. Often researchers focus on single ERP components which results in a reductionist approach. For a holistic understanding, researchers must focus on the entire stream of processing, incorporating the N1-P2-N2-P3 components elicited during an auditory paradigm. Additionally, understanding the differential impact of study manipulations on these ERP components provides valuable insight into the underlying neurophysiology.

Clinical Implications

The findings from this dissertation indicated that young adults with ASD had significant deficits in neural measures of auditory processing, and that when attention was directed towards the auditory stimuli, we found more typical performance in the ASD group as compared to an age-matched group of neurotypical individuals. Data from behavioral measures indicated that individuals with ASD had significantly more deficits in attention, sensory processing, and social reciprocity as compared to neurotypical peers. Additionally, the relationship between neural

measures of sensory processing and behavioral measures of attention suggested that sensory processing deficits observed in ASD may be associated with deficits of attention.

OT theory and practice. Results from this dissertation can help therapists, researchers, and parents understand the underlying neurological mechanisms impacting auditory processing in ASD. Future research examining brain-behavior relationships of sensory processing in clinical conditions may provide valuable insight into advancing not only theory but also practice. Using behavioral measures, Stein, Foran and Cermak (2011) explain how parents of children with ASD often experience decreased quality of life. The authors mention that since ASD etiology remains unknown, parents often "question whether they are responsible for their child's disorder, producing feelings of confusion and guilt" (Stein et al., 2011; p. 116). Firstly, further understanding of the abnormal neurological functioning underlying some of the behavioral manifestations of ASD may reduce these feelings of guilt and provide guidance to parents and therapists to understand the child's processing challenges. Consistent with previous literature, the results from this dissertation showed that young adults with high-functioning ASD had significantly delayed neural responses to simple auditory stimuli in a controlled laboratory environment. These abnormal neural responses may be further amplified in real-life contexts wherein individuals deal with a multitude of sensory information, in lower-functioning individuals, and in younger individuals with ASD. An understanding that abnormal behaviors observed in ASD may be due to deficits at the neural level, some of which occur prior to conscious processing, may help therapists recognize the underlying difficulties resulting in abnormal behavior. Additionally, in my personal experience as an OT, better understanding the neural functioning underlying some of the behavior problems in ASD, provides a different lens of viewing ASD behavior.

Secondly, ASD has traditionally been viewed as a socio-behavioral condition rather than a cognitive condition (Gold & Gold, 1975). Although previous research has shown that there are neuroanatomical abnormalities in individuals with ASD (for e.g. Belmonte & Baren-Cohen, 2004; Belmonte & Yurgelun-Todd, 2003), the findings from this dissertation demonstrated direct brain and behavior associations in adults with ASD. By directly manipulating attention (i.e. requiring a behavioral response), we observed that attention changed the way the brain processed auditory stimuli. Furthermore, the findings from this dissertation demonstrated that individuals with ASD have significant deficits in attention, both at the neural and behavioral levels. Several researchers have suggested that behavioral manifestations of ASD may be related to a neurobehavioral driven distractibility or attention deficit (Marco et al., 2011). Allen and Courchesne (2001) suggested that sensory hyper-reactivity and restricted and repetitive behaviors in ASD may be associated with deficits in attention. As stated earlier in the discussion, several researchers view ASD as a disorder of attention. Marco et al. (2011) suggested that the multidirectional flow of information processing which is required for efficient sensory processing is impaired in individuals with ASD, and that this disruption in brain connectivity underlies the individuals' inability to meaningfully attend to and interact with the environment. A goal of future research would be examining if attention deficits aid in early identification of children with ASD. A review by Rogers (2009) demonstrated that, contrary to popular belief, early social functioning may not be the best tool for identifying ASD in infants at-risk for ASD. If attentional deficits are one of the first characteristics that can be used to distinguish infants who are later diagnosed with ASD, incorporating attentional measures in diagnostic tools may result in an earlier diagnosis, ultimately leading to successful early interventions (Elison et al., 2013; Elsabbagh et al., 2013; Keehn et al., 2013).

Lastly, the novel finding of an attention-based improvement in neural measures of auditory processing in ASD suggests that actively directing attention towards sensory stimuli may ameliorate some of the neural delay. This information can help both practitioners and researchers understand that attention and cognition may be important aspects of ASD assessment and intervention. Based on this finding, one goal of future research would be to examine if this finding of an attention-based improvement is replicable with other sensory modalities or with multi-sensory integration, and in individuals across the spectrum. Moreover, if attention is a primary impairment in ASD, the development of attention-based interventions may improve socio-behavioral functioning as well. For example, Posner and Rothbart (2005) have proposed that early attentional interventions may be a vital tool for promoting cognitive and social development, and that training attention also generalizes to aspects of intelligence. Similarly, Koegel, Shirotova, and Koegel (2009) demonstrated that use of individualized orienting cues during intervention resulted in an increase in word-use in three children with ASD.

Furthermore, a study examining attentional training interventions in 42 typically-developing infants (11-months old) demonstrated improvements not only in attention but also in play behavior, such that the infants engaged in more spontaneous looking behaviors towards novel objects, with more attentional shifts from object to person (Wass, Porayska-Pomsta, & Johnson, 2011). Future research examining what types of attentional manipulations might be most effective for improving sensory processing and meaningful engagement with the environment in children with ASD is warranted. An additional goal for future research would be to examine how an attention manipulation impacts processing at the neural level and affects everyday performance in ASD. When we can identify how attention impacts both neural and

behavioral functioning, we may be able to develop effective interventions for this vulnerable population.

Biomarker development. Clinical diagnosis of ASD is currently made based on behavioral signs and symptoms which may be highly subjective and often require tremendous amounts of clinical expertise. On the other hand, biomarkers (genetic, neuroanatomical, or psychophysiological) can be measured objectively and systematically. Biomarkers may prove invaluable in sub-grouping this incredibly heterogeneous spectrum, and assisting in developing targeted, customized therapeutic interventions that are tailored to the individual's specific strengths and challenges. Several researchers have proposed the use of neurophysiological indices of sensory processing as biomarkers of the clinical phenotype of ASD (Brandwein et al., 2015; Gandal et al., 2010). Brandwein and colleagues (2015) found the auditory N1 component to be the strongest neurophysiological predictor of autistic symptom severity. Researchers have even proposed using delayed auditory N1 responses as a translational biomarker of ASD (Gandal et al., 2010; Roberts et al., 2010). Maziade et al. (2000) showed that delayed early auditory-evoked responses were not only evident in individuals with ASD, but also in a sample of unaffected first-degree relatives of individuals with ASD.

Sensory gating deficits are considered an endophenotype in schizophrenia (Calkins et al., 2007). However, results from this dissertation and other similar studies suggest that sensory gating deficits may not be present across the lifespan and across the spectrum in ASD. However, it appears that auditory processing delays measured by early ERPs such as the N1 and N2 components may serve as potential candidates for a larger biomarker study. Although there is much ground to be covered in terms of identifying the right biomarkers of ASD, the hope is that

combining robust neurophysiological indices of basic sensory processing with well-established clinical measures of ASD, will help get us closer to the goal.

Limitations and Future Directions

While this dissertation has several strengths, there were also a few limitations that must be acknowledged. The study included a sample of young adults with high functioning ASD. Since ASD is a wide spectrum, the generalizability of the study findings to individuals across the spectrum must be done cautiously. Moreover, there are limited studies with adults with ASD. Most of the existing research in ASD is with children, and comparing these findings with adults is not be ideal. A second limitation is in terms of the statistical methods used to examine brain-behavior relationships. While simple correlational analyses with a decent sample size provide valuable directions towards the existence of brain-behavior relationships, they do not provide causal information. With a larger sample size, future research could include elaborated modelling methods such as structural equation modelling linking ERP measures to performance-based observable behaviors. Modelling out these brain-behavior relationships of attention and sensory processing will provide us with more accurate causal pathways and help in identifying how attention impacts sensory processing.

Another unexpected finding in this study was the absence of gating deficits in individuals with ASD. Using the same sensory gating paradigm, we found that children with ASD (ages 6 – 12 years) had significantly reduced gating compared to typically-developing peers (Crasta et al., 2015). Since this is not a longitudinal study, we cannot assume that gating improves with age. ASD is a neurodevelopmental disorder, but research has been restricted to school-aged years. Longitudinal research examining maturation of neural functions is very crucial to understand

how the brain processing may change allowing individuals to cope and deal with everyday functioning.

Relation to the Occupation and Rehabilitation Science Framework

The International Classification of Functioning, Disability, and Health (ICF), a model proposed by the World Health Organization is often used to examine health and well-being through impairment of body function and structure, activity limitation, and participation restriction through contextual factors of the environment and personal factors (WHO, 2002). In the ICF, health is described as an interaction between the changes in body function and structure, what a person with a health condition can do in a standard environment as well as what they actually do in their usual environment. Utilizing the biopsychosocial model, the ICF explains disability as a dysfunction at one or more of levels of body function and structure impairments, activity limitations and participation restrictions through the contextual factors of the external environment and internal personal factors. Thus, "disability is characterized as the outcome or result of a complex relationship between an individual's health condition and personal factors, and of the external factors that represent the circumstances in which the individual lives" (WHO, 2001, p. 17). This also means that problems with performance arise when there is a mismatch between one's functioning levels and one's environmental contexts. For example, Dunn (2001) stated that "sensory processing patterns are a reflection of who we are: these patterns are not a pathology that needs fixing" (p. 641). Dunn (2001) proposed that intervention must address the interference that sensory processing challenges cause to our desired life and that hinder current performance. Research examining sensory processing can provide insight on ways to narrow this gap between current and desired performance, thereby affording a satisfying life (Dunn, 2001).

The discipline of rehabilitation science places significant emphasis on function, focusing on the mechanisms by which disability develops and the factors influencing it. Occupational science is committed to enhancing the understanding of occupation in context (Yerxa, 1990). Rehabilitation science 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). Rehabilitation science views functional restoration of pathological and physiological impairments as the end goal of the therapeutic process. While occupational science views meaningful engagement in occupation as the end goal of the therapeutic process. Baum (2011) emphasized the significance of the different levels of research in rehabilitation and occupational therapy. Baum 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).

Findings from this dissertation have shed light on neural and behavioral aspects of sensory processing and attention dysfunction in individuals with ASD. These findings also provide insight into brain-behavior relationships in neurotypical individuals and those with ASD. Additionally, these results can help practitioners understand the neural basis of some of the behavioral manifestations of ASD, especially those atypical behaviors that occur in response to sensory experiences in everyday activities. Researchers have shown that sensory processing is vital to occupational performance. Dunn (2001) stated that OT knowledge provides a unique contribution to sensory processing research in that OT attaches understanding and meaning to sensory experiences. While most disciplines only allude to daily life applications, OT research bridging brain-behavior relationships can serve as a translator and stand in the space between abstract concepts and clinical applications, communication with other disciplines what each

group has to add to the knowledge-base and ultimately advance both science and practice (Dunn, 2001).

In this dissertation, the behavioral measures of sensory processing, attention, and social responsiveness provided information about areas of performance that may lead to occupational dysfunction in ASD. Additionally, using EEG, this dissertation provided insight on deficits at the neural level of processing. Understanding the neural mechanisms of performance areas impacting occupational performance may lead researchers to develop interventions that ameliorate this dysfunction to improve everyday performance and participation. Findings from this dissertation have shown that neural sensory processing is associated with behavioral performance areas of attention and sensory processing. Bridging basic research at the neural mechanism level to research examining behavioral performance is an important step to holistically understand a clinical condition. Thus, I believe that this dissertation aligns with the philosophy of occupation science and rehabilitation science.

Conclusion

The goal of this dissertation was to examine how attention impacts sensory processing in neurotypical individuals and individuals with ASD. The dissertation findings revealed that attention modulates early neural auditory processing, and that directing attention towards sensory stimuli results in more efficient processing in individuals with ASD compared to passive processing. These findings support a model of ASD wherein attention is a vital element to understanding ASD symptomatology. However, interpreting "the attentional model" as a unitary explanation for the entire spectrum of ASD would be deceptive. Rather, one aim of future research understanding the role of attention in ASD is to assess if neurophysiological measures of attention can be used as biomarkers to aid in early diagnosis for ASD, and to examine whether

early interventions emphasizing attention can improve occupational performance and participation in individuals with ASD.

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