

**ELECTROPHYSIOLOGICAL AND BEHAVIORAL MEASURES OF  
TACTILE AND AUDITORY PROCESSING IN CHILDREN WITH  
AUTISM SPECTRUM DISORDER**

by

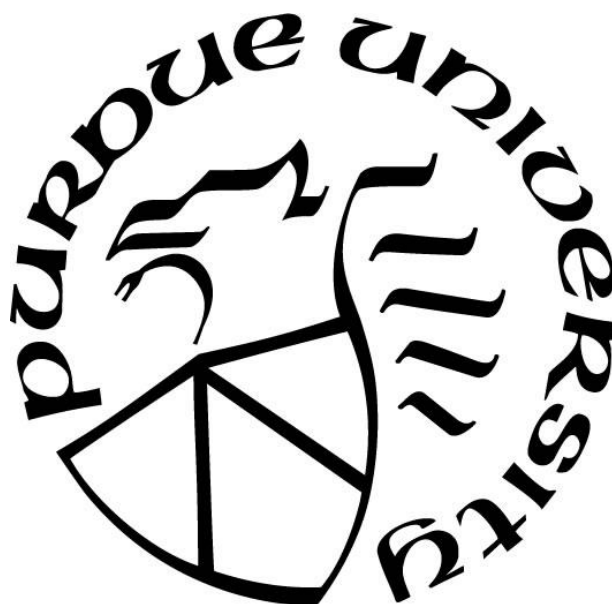
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*Dedicated to my parents:*  
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## ABBREVIATIONS

ABA	Applied Behavior Analysis
ABR	Auditory Brainstem Responses
ADOS	Autism Diagnostic and Observation Schedule
AEP	Auditory Evoked Potentials
ANOVA	Analysis of Variance
ANS	Autonomic Nervous System
ANT	Attention Network Test
ASD	Autism Spectrum Disorder
CT	C-tactile
DAS	Differential Ability Scale
dB	Decibel
DD	Developmental Disorders
DSM	Diagnostic and Statistical Manual of Mental Disorders
EDA	Electrodermal Activity
EEG	Electroencephalography
EHI	Edinburgh Handedness Inventory
EOG	Electrooculography
ERF	Event-Related Fields
ERP	Event-Related Potential
EVT	Expressive Vocabulary Test
fMRI	Functional Magnetic Resonance Imaging
Hz	Hertz
ICA	Independent Component Analysis
ISI	Interstimulus Interval
IQ	Intelligence Quotient
KCl	Potassium Chloride
k $\Omega$	Kiloohm
M	Mean

MEG	Magnetoencephalography
MMF	Mismatch Field
MMN	Mismatch Negativity
$\mu\text{V}$	Microvolt
N	Negative
NVIQ	Nonverbal Intelligence Quotient
P	Positive
PPVT	Peabody Picture Vocabulary Test
ROI	Regions of Interest
RRB	Restricted and Repetitive Behaviors
RT	Reaction Time
SA	Social Affect
SASICA	Semi-Automated Selection of Independent Components of the electroencephalogram for Artifact correction
SCI	Social Communication and Interaction
SCP	Sensory Challenge Protocol
SCQ	Social Communication Questionnaire
SD	Standard Deviation
SE	Standard Error
SEQ	Sensory Experiences Questionnaire
SLI	Specific Language Impairment
SNS	Sympathetic Nervous System
SOA	Stimulus Onset Asynchrony
SP	Sensory Profile
SPA	Sensory Processing Assessment
SPM	Sensory Processing Measure
SPS	Sensory Processing Scale
SRS	Social Responsiveness Scale
SS	Severity Score
TD	Typically Developing
TP	Transitional Probabilities

TDDT-R	Tactile Defensiveness and Discrimination Test-Revised
VIQ	Verbal Intelligence Quotient
WASI	Wechsler Abbreviated Scale of Intelligence

## ABSTRACT

Touch plays a key role in facilitating social communication and is often presented in conjunction with auditory stimuli such as speech. Individuals with autism spectrum disorder (ASD) frequently show atypical behavioral responsivity to both tactile and auditory stimuli, which is associated with increased ASD symptomatology. However, as discussed throughout Chapter 1, the neural mechanisms associated with responsivity to tactile and auditory stimuli in ASD are not fully understood. For example, some have argued that differences in responding to tactile and auditory stimuli may be attributed to sensory and perceptual factors, whereas others suggest that these differences could be related to atypicalities in allocation of attention to incoming stimuli. In Chapter 2, I address these competing hypotheses by examining early and late ERP components (indicative of perceptual and attentional processing respectively) in response to tactile and auditory stimuli. Next, despite the evidence suggesting that touch plays a role in modulating attention in typical development (TD), it is unclear whether touch cues affect the response of the phasic alerting network – a subcomponent of attention – in ASD and TD, and whether the alerting response may be atypical in children with ASD. In Chapter 3, I address this gap in the literature by examining whether tactile cues presented at different intervals before auditory targets facilitate reaction times differently in children with ASD and TD. Lastly, because prior research has shown associations between sensory and attentional processes and ASD symptomatology, in Chapters 2 and 3, I examine the associations of neural and behavioral indices of tactile and auditory processing with ASD symptomatology and language skills in children with ASD and TD.

In Chapter 2, I show that children in both the ASD and TD groups do not exhibit differences in both early and later neurological responses to tactile and auditory stimuli, suggesting that under certain experimentally-controlled conditions, behavioral differences to tactile and auditory stimuli may not be attributable to atypicalities in perceiving or attending to the incoming sensory input. However, neural responsivity to tactile and auditory stimuli is linked with sensory responsivity and social skills in all children. Specifically, reduced early contralateral activation to tactile stimuli is related to increased tactile symptoms, and reduced early amplitudes to auditory oddball stimuli are associated with impairments in reciprocal social communication in children with ASD as well as when examined across all children, and greater tendency of overall sensory hyper-reactivity. Additionally, in the TD group, greater later amplitudes to touch and auditory oddball stimuli are

related to differences in reciprocal social communication and sensory reactivity respectively, indicating that patterns of allocation of attention may be related to ASD-like traits in typical development. Lastly, there is an association between greater sensitivity to changes to a stream of auditory stimuli and expressive language skills in all children. These results suggest that, although there are no group differences between neurological responses to tactile and auditory stimuli in ASD and TD, individual neural differences may be related to sensory and socio-communicative skills in all children.

In Chapter 3, I show that although children with ASD responded more slowly than children with TD, both groups displayed faster reaction times as a result of tactile cues before auditory targets, suggesting equivalent phasic alerting in response to tactile stimuli. Longer intervals between cues and targets benefitted children in both groups resulting in faster reaction times. Contrary to my hypotheses, touch-related behavioral facilitation was not associated with ASD symptomatology and language skills.

Taken together, the results of these studies suggest that, at least in certain contexts and with certain cues, children with ASD may show typical neurological processing in response to tactile and auditory stimuli, and that touch may facilitate the response of the alerting network similarly in ASD and TD. Therefore, everyday behavioral differences in response to tactile and auditory stimuli may be related to the specific nature of the stimuli as well as social contexts in which such stimuli are more likely to be encountered. Differences between processing rich and dynamic sensory stimuli experienced in the outside world vs experimentally-controlled sensory stimuli presented in the laboratory settings are discussed in Chapter 4. Additionally, I argue that individual responses expected in social vs non-social experimental settings may affect neural and behavioral responses in individuals with ASD. Finally, future research directions are discussed.

# 1. INTRODUCTION

## 1.1 Sensory processing

From birth, we are constantly exposed to a variety of sights, sounds, tastes, smells, and textures. For instance, take a typical example of a North American 6-month-old interacting with her mother during mealtime. She may be exposed to (1) the sight of her mother sitting in front of her, the food on her plate, her spoon (2) the sound of her mother's voice saying, "here's some applesauce!", (3) the taste and smell of the food that she is eating, (4) the texture and shape of a spoon in her hands, and (5) a gentle affectionate touch delivered by her mother on her arm. Additionally, the infant may also be experiencing a variety of other sensory stimuli present in the periphery. For instance, she may be exposed to the sight of her father cooking dinner in the kitchen, her brother playing a videogame in the living room, non-speech sounds coming from the videogame, the family dog barking in the front hall, and food smells coming from the kitchen.

Using her senses, this 6-month-old is able to experience her surrounding environment. For instance, the sense of hearing helps her to learn about the sounds in her language presented by her parents (e.g., the French learning infant hears fewer interdental fricatives than the English learning infant) and to localize sources of sounds (e.g., sounds coming from her mother vs sounds coming from the videogame). Touch initiated by the infant enables her to explore objects, whereas, maternal touches to the infant may convey affect. Further, stimulation of each of these senses does not occur independently, but very often overlaps as in the example above, in which, e.g., touches and sounds occur together. Crucially, these co-occurrences may simplify the learning problem, as maximal learning can occur when the infant also calculates co-occurrences across sensory experiences (e.g., the infant is more likely to hear "applesauce" and smell applesauce when she tastes it).

But how does the infant learn to make use of these sorts of informational streams? The question of how human beings process sensory information and in what way sensory processing impacts development has been a topic of interest for decades (Bremner, Lewkowicz, & Spence, 2012). Using a variety of methodologies (discussed below), researchers are able to understand behavioral manifestations of typical and atypical sensory processing, as well as the underlying physiological and neurological mechanisms that govern the processing of everyday sensory



information. The majority of research in this area, however, has focused on visual and auditory channels of sensory processing due to their obvious role in the development of language and socio-communicative skills (Bremner et al., 2012). Nonetheless, recent research has also highlighted links between the ability to process tactile information presented with speech and word learning skills in typically developing infants (Seidl, Tincoff, Baker, & Cristia, 2015). Such findings motivate researchers to explore how individuals process touch, and its role in typical and atypical development. In this thesis, I will primarily focus on auditory and tactile processing skills in children with and without Autism Spectrum Disorder (ASD). I will begin by briefly outlining the role of hearing and touch in typical development with a focus on how these modalities affect language and socio-communicative development.

### **1.1.1 Hearing**

In humans, the sense of hearing begins to function during the second trimester of gestation (Hall, 2000). Prenatal functional development of hearing is determined by behavioral and physiological responses to auditory stimuli observed in the fetus (Bremner et al., 2012). For example, evidence has shown that the fetus can behaviorally respond (measured in fetal movements) to auditory information at as early as 26 weeks (Hepper & Shahidullah, 1994; Ruben, 1992). This prenatal hearing ability impacts infants' postnatal auditory responses. Specifically, newborn infants have been shown to have a preference for their mothers' voice compared to another female voice (DeCasper & Fifer, 1980) or music (Standley & Madsen, 1990). A preference for listening to the mother's voice is relevant as it can have survival consequences for a newborn infant. For instance, a newborn, when hungry, may produce sounds upon encountering her mother's voice to express hunger, and hence get fed. Identification of the maternal voice, thus, becomes a crucial part of newborns' ability to thrive.

This sense of hearing that aids in survival also provides infants with a 'kick-start' to learn and attend to meaningful sounds in their environments. For example, recent research has revealed that newborn infants are specifically attuned to attend to the auditory perceptual characteristics of speech. Specifically, infants as young as 1-to-4 days show a preference for listening to speech over complex non-speech auditory stimuli (Vouloumanos & Werker, 2007). This preference for speech is important for human infants because the skill to learn a language is largely dependent on infants' ability to attend to language-relevant signals in their surroundings. Language-relevant signals (in

the auditory domain) can be defined as signals that carry communicative content (Vouloumanos & Werker, 2007). Speech is one such stimulus and is more relevant to language than non-speech sounds because it carries communicative information and helps the infant hone in on the language-specific properties of her language. For example, attention to speech will help her to learn whether her language contrasts retroflex d and alveolar d (Werker & Tees, 1984) which will enable her to become a language-specific listener by 12 months of age. The ability to discriminate between sounds in a language-specific way is important as it enables infants to distinguish between words such as *bat* and *pat*, which have different meanings.

Yet, selectively attending to communicatively relevant auditory stimuli can be challenging because infants are surrounded by rich sensory environments that include a variety of sounds; both speech and non-speech (e.g., sound of a doorbell, birds chirping, telephone ringing, etc...; Aslin & Hunt, 2001). For instance, in our example above, the infant is exposed to speech sounds coming from her mother (e.g., “here’s some applesauce!”) as well as non-speech sounds coming from a videogame. In such situations, if the infant equally attends to both types of sounds or attends more to the non-speech sounds, she may not learn the name of the food that she is eating, and consistently missed opportunities such as this may result in a delay in her language learning.

The importance of selectively attending to relevant auditory information is highlighted in neurophysiological research examining auditory attentional processing in response to narrative stories in children with Specific Language Impairment (SLI; Stevens, Sanders, & Neville, 2006). Findings from this study indicate that children with SLI show deficits in the neural mechanisms underlying auditory attention when listening to narrative stories, and this deficit has been suggested to impact their later language skills. A correlation between selectively listening to speech and later language skill has also been shown in typically developing children, suggesting that infants’ ability to selectively attend to speech compared to non-speech sounds during early development predicts their later language outcomes (Vouloumanos & Curtin, 2014). This correlation may be explained through reference to statistical learning (Saffran, Aslin, & Newport, 1996). For example, a myriad of studies show that infants are able to track transitional probabilities (TPs) between syllables. A lack of attention to speech may therefore result in fewer TPs to learn from. Thus, in our example, if the mother says to her infant, “do you like applesauce?”, “here’s some applesauce”, and “let’s eat applesauce”, the syllable *ap* is preceded by three different syllables, but it is always followed by the syllable sequence *plesauce*. Therefore, the transitional

probability of *plesauce* appearing after *ap* is greater than the transitional probability of *ap* appearing after syllable sequences such as *like*, *some*, and *eat*. Thus, these statistical cues provide information to the infant that the probability of hearing the syllable sequence *applesauce* is greater than hearing syllable sequences such as *likeapple*, *someapple*, and *eatapple*, suggesting that, *ap* may be the onset of a word and *applesauce* may be a word. Thus, in this case, if the infant fails to selectively attend to speech during the interaction and the child only has applesauce once a month, she may miss out on opportunities to learn transitional probabilities between neighboring speech sounds relevant to the discovery of this word. Therefore, the infant may not learn this particular word, until it is spoken to her again in the future. This would not be a problem if the infant misses out on learning just a word or two, but could be detrimental if the infant does not selectively attend to speech on a regular basis, resulting in missed opportunities to learn many other words. In addition, failure to selectively attend to speech may also impact mapping between sounds and accompanying sights, tastes, smells and textures which also exploit similar statistical properties of the input (Smith & Yu, 2008). Thus, the probability of infants learning a greater number of words based on the statistical relationships is higher if they attend more to speech sounds compared to non-speech sounds.

### **1.1.2 Touch**

Tactile processing comes online earlier than either hearing or vision, as it is first experienced at around 4 to 7 weeks of gestation (see, Bremner et al., 2012; Bremner & Spence, 2017, for a review). As the first sense to develop, it has been suggested that touch may lay the foundation for other senses. For example, some have theorized that separate timings of the emergence of different sensory systems in the prenatal period may actually be beneficial during the early stages of development, as it decreases the total quantity of the sensory input the fetus has to process at a given time (Turkewitz, 1994). Thus, touch, being the first sense to develop, can be seen as a foundation on which the development of future multisensory processing is built (Bremner & Spence, 2017).

Postnatally, touch serves as a primary source of contact for young infants with their external world. Additionally, receptive touch plays an important role in early social interactions (Dunbar, 2010; Hertenstein, Verkamp, Kerestes, & Holmes, 2006) by facilitating secure attachment (Weiss, Wilson, Hertenstein, & Campos, 2000), bonding (Field, 2001), and reducing

infant distress (Hertenstein, 2002). Furthermore, because maternal touch occurs frequently and affects the quality of mother-child dyadic interactions, for example, by increasing positive affect and attention in infants (Stack & Muir, 1992), it may facilitate the development of early social communication skills. For instance, returning to our example of the mother-infant mealtime interaction, it is possible that the gentle affectionate touch delivered by the mother on the infant's arm conveys the mother's positive affect during that interaction, which could then elicit a social response from the infant. Support for this hypothesis comes from evidence suggesting that a greater amount of maternal affectionate touch in early typical development is associated with an increase in infant smiles and vocalizations (Stack & Muir, 1992); skills typically used in social communication.

Not only do infants get touched, but they also use touch themselves during social interactions. For instance, in a still-face paradigm, young infants used more active forms of touch when their mothers were emotionally unavailable, whereas they used more passive forms of touch when their mothers were emotionally available (Moszkowski & Stack, 2007). Additionally, touch has been associated with infants' exploration abilities (Kravitz, Goldenberg, & Neyhus, 1978; Morange-Majoux, Cougnot, & Bloch, 1997; Streri, 1987). For example, infants use their hands to actively explore and manipulate their own body parts as well as objects around them, thereby allowing them to experience and learn about the world. For instance, the infant in our example is holding a spoon in her hands which would provide her information about the haptic characteristics of that particular utensil, such that it is smooth and round. Using touch for object exploration, therefore, provides an additional source of information as opposed to just seeing or hearing the name of that object.

Last, touch may also play a role in early language learning because (1) infants' language input is often coupled with caregivers' touches (e.g., mother talks about the infant's arm while delivering a gentle touch on the arm; Abu-Zhaya, Seidl, & Cristia, 2017; Nomikou & Rohlfing, 2011), and (2) touch has been shown to facilitate infants' speech perception skills (Seidl et al., 2015). Together these findings suggest that touch is a ubiquitous signal that is available to infants, and that typical processing of this input may shape social and language development.

## **1.2 Motivation for examining sensory processing in Autism Spectrum Disorder**

Processing of sensory information is vital to the acquisition of socio-communicative skills. For example, in the auditory domain, typical hearing abilities enable young infants to listen to a variety of sounds in their environments, thereby building a foundation for infants' ability to distinguish between language-relevant and non-relevant sounds; a skill important for language and socio-communicative development (Vouloumanos & Werker, 2007). Similarly, in the tactile domain, presentation of caregiver touch has been suggested to impact the quality of caregiver-infant social interactions (Dunbar, 2010; Stack & Muir, 1992), and has also been associated with infants' language learning skills in typical development (Abu-Zhaya et al., 2017; Nomikou & Rohlfsing, 2011; Seidl et al., 2015). Therefore, differences in processing sounds or touches may impact the development of infants' early socio-communicative skills. In our earlier example, if the infant fails to process her mother's auditory input, "here's some applesauce", she may not learn the name of the food that she is eating during this exposure, resulting in a reduced opportunity for learning this word. Similarly, if the mother talks about the infant's arm (e.g., "where is your arm? Here is your arm!") while delivering her gentle affectionate touch on that arm, and the infant fails to perceive or attend to her mother's touch on her arm, she may not make the connection between the auditory label (i.e. arm) and her body part. Again, this would result in a reduced word learning opportunity when compared with another infant who is attentive to these cues. In sum, differences in typical auditory and tactile processing may hinder individuals' early word learning.

One condition associated with differences in processing sensory information is Autism Spectrum Disorder (ASD). In particular, recent estimates have suggested high prevalence rates of sensory differences, varying from 42 to 96%, in individuals with ASD (Baranek, David, Poe, Stone, & Watson, 2006; Ben-Sasson et al., 2009; Lane, Dennis, & Geraghty, 2011; Leekam, Nieto, Libby, Wing, & Gould, 2007; Marco, Hinkley, Hill, & Nagarajan, 2011; Tomchek & Dunn, 2007). These observed differences in sensory processing may put individuals with ASD at high risk for developing delays in their language and socio-communicative skills (Baranek, 1999; Watson et al., 2011); primarily as a result of missed opportunities that may arise because of atypical processing of incoming sensory inputs. Prior research investigating sensory impairments in ASD has mainly focused on auditory and visual modalities, as these have long been considered as the primary routes that enable social communication (Lundqvist, 2015). However, as discussed above, touch is also an important sensory channel that plays a role in facilitating social communication (Dunbar, 2010),

and language when paired with speech in typical development (Seidl et al., 2015). Additionally, aforementioned high prevalence rates of sensory differences in ASD have also been reported in the tactile modality (Mikkelsen, Wodka, Mostofsky, & Puts, 2018; Puts, Wodka, Tommerdahl, Mostofsky, & Edden, 2014), and these differences in processing tactile stimuli have been associated with social skills and overall ASD symptomatology (see Thye, Bednarz, Herringshaw, Sartin, & Kana, 2018 for a review). Therefore, examination of tactile processing in individuals with ASD becomes a crucial topic in the field of ASD. However, we know that touch in everyday life is rarely presented in isolation. For example, Kadlaskar, Seidl, Tager-Flusberg, Nelson, and Keehn (2020) showed that caregivers of infants at high- and low-risk for ASD often use auditory stimuli while presenting touches to their infants. Specifically, caregivers in this study used greater amounts of touch-speech stimuli compared to touch-only stimuli while interacting with their infants. Therefore, despite the important role that touch plays in facilitating social communication, examining touch in the context of auditory stimuli, mainly speech, may provide a more comprehensive understanding of tactile processing in ASD.

### **1.3 Autism Spectrum Disorder**

Autism spectrum disorder (ASD) is a neurodevelopmental disorder that is diagnosed on the basis of deficits in social communication and social interaction, and the presence of restricted and repetitive behaviors (DSM-5; American Psychiatric Association, 2013). To receive a clinical diagnosis of ASD, individuals must display impairments in all three areas included within the social communication and social interaction domain (i.e., deficits in social-emotional reciprocity, deficits in non-verbal communicative behaviors, and deficits in developing, maintaining, and understanding relationships). In addition to this, two of the four criteria under restricted and repetitive patterns of behaviors (i.e., stereotyped or repetitive motor movements, insistence on sameness, restricted interests, and hyper- or hyperreactivity to sensory input or unusual interests in sensory aspects of the environment) must be present. These symptoms must be present early in the development, and they should significantly impact individual's daily functioning. Last, these symptoms should not be better explained by the presence of intellectual disability or a global developmental delay (DSM-5; American Psychiatric Association, 2013).

The prevalence of ASD has increased dramatically since the earliest epidemiological reports of this disorder in the 1960s. During that time, the prevalence of ASD was estimated to be

under .5 in 1000 children (Gillberg & Wing, 1999). By the early 2000s the prevalence was estimated to be 1 in 150, which later increased to 1 in 68 in 2012. The most recent report based on data collected in 2016 provides an estimated prevalence of 1 in 54 children aged 8 years (Maenner, Shaw, & Baio, 2020).

Given the drastic increase in the prevalence of ASD, many researchers have focused on studying early markers of ASD with an aim of assisting with early diagnoses. In the domain of tactile and auditory processing, differences in orienting to touch (e.g., air puff/shoulder tap) and sounds (name call) have been observed during the early years of development in children with ASD (Baranek et al., 2013). In line with this literature, recent evidence has shown that infants at high risk for ASD (because they have an older sibling diagnosed with the disorder) who later receive a diagnosis of ASD are less likely to respond to maternal touch and this failure to respond to touch is predictive of their ASD symptom severity (Kadlaskar, Seidl, Tager-Flusberg, Nelson, & Keehn, 2019). Although these studies provide us with information regarding behavioral manifestations of differences in sensory processing in ASD, they do not shed light on underlying mechanisms that may govern individual responses to sensory information. Understanding these mechanisms may be useful in identifying objective tools or strategies aimed at improving early diagnoses as well as targets for more efficacious interventions.

To date, researchers have used a combination of questionnaires and observational methods to report sensory differences in ASD (Baranek et al., 2006; Baranek et al., 2013). This research has been supplemented with physiological, psychophysical, and neurological studies that examine covert factors that may explain overt sensory behaviors in ASD (Marco et al., 2011). Consideration of a variety of research methods while reviewing the literature on sensory processing in ASD may provide us with a holistic understanding of this condition. For example, as mentioned before, an observational study may highlight sensory *behaviors* that distinguish individuals with and at high risk for ASD from those without ASD, but studies using physiological, psychophysical, and neurological measures may help us to investigate underlying factors such as neural responsivity, sensory thresholds, functioning of the Autonomic Nervous System etc...that might contribute to these observable sensory patterns in ASD. In the section below, I discuss several methodologies that researchers have used to study sensory processing in ASD. This review will provide the reader with information regarding how each method is used, and how selection of research methods impacts our understanding of sensory processing in ASD.

## 1.4 Methodologies for examining sensory processing in ASD

In the past decades, researchers have assessed sensory processing in individuals with ASD using a variety of methods such as, self- and parent-report questionnaires, direct behavioral observations, psychophysiological and psychophysical measures, and neuroimaging techniques. Each of these methods bring a unique perspective to the study of sensory differences in ASD. For instance, reports of lack of responses to stimuli in observational studies give us an example of a behavioral manifestation of what *appears* to be hypo-reactivity (e.g., lack of behavioral orienting in response to name or a shoulder tap), whereas, examining neural correlates underlying a lack of a response might provide us with evidence of either neural under-responsivity (in support of the behavioral example) or even neural over-responsivity (in contrast to behavioral responses). In the latter case, lack of a behavioral response could be explained as a defense mechanism that individuals with ASD might use to cope with their hyper-reactivity. Specifically, it has been suggested that, excessive neural processing in response to sensory stimuli in ASD may result in individuals perceiving the world as too intense (Markram, Rinaldi, & Markram, 2007). This may lead to social withdrawal that behaviorally may seem like hypo-reactivity. Thus, it is possible that, the behavioral response of hypo-reactivity in ASD may be a result of either neural under- or over-responsivity. Alternately, it is also possible that, behavioral hypo- and hyper-reactivity observed in ASD may be associated with unique neurofunctional sources. For example, in the tactile modality, greater neural responsivity approximately 220-270 ms post stimulus presentation was found to be related to less hypo-reactivity, in other words, typical tactile processing in the ASD group (Cascio, Gu, Schauder, Key, & Yoder, 2015). Neural responses around 200-400 ms post stimulus are related to attentional processes (Polich, 2003). Thus, hypo-reactivity generally observed in ASD may be a result of reduced neural responsivity in higher-order attentional processes observed around 200-400 ms post stimulus rather than being related to lower level sensory processing. On the other hand, greater hyper-reactivity was found to be associated with increased neural responsivity in earlier stages (Cascio et al., 2015). Different timings of neural responses to tactile stimuli suggest that hypo- and hyper-reactivity in ASD may follow different neural mechanisms (Cascio et al., 2015). Therefore, examining underlying mechanisms along with behavioral manifestations of sensory processing may provide us with a more comprehensive understanding of sensory profiles in ASD.



Another challenge to methods used to examine sensory responsivity in ASD is that behavioral manifestations of sensory processing in ASD have been suggested to change with age. For instance, Ben-Sasson et al. (2009) reported that hyper-reactivity and sensory seeking responses measured using questionnaire data seem to increase until age 9, after which they steadily decline. Yet, the underlying mechanisms for this developmental trajectory of sensory processing remains unclear. There is a general consensus that no single method of data collection will provide us with a comprehensive understanding of sensory processing in ASD. Therefore, researchers often use a combination of methods to examine processing of sensory information in ASD. Therefore, methods of data collection as well as the age range we focus on can greatly influence our understanding of sensory processing in ASD. The current thesis will focus on sensory processing in pre-school and young-school age children with ASD. In the following section, I will briefly discuss five methods of data collection that are often used to examine sensory processing in ASD.

#### **1.4.1 Self- and parent-report questionnaire**

There are a number of standardized tools available to assess sensory symptoms in ASD. A few of the most widely used questionnaires include the Sensory Profile (SP; Dunn, 2014), Short Sensory Profile (SSP; McIntosh, Miller, Shyu, & Dunn, 1999), Infant/Toddler Sensory Profile (Dunn, 2002), and the Sensory Experiences Questionnaire (SEQ; Baranek et al., 2006). Such standardized questionnaires measure behavioral responses to everyday sensory events and take about 20-30 minutes to complete. Questionnaire-based methods are one of the most commonly used methods to examine sensory processing in ASD and generally focus on answering two primary questions: (1) Do individuals with ASD respond differently to sensory stimuli compared to typically developing individuals measured across different sensory modalities and lifespan? and (2) Are impairments in sensory processing skills in ASD related to core features of ASD and other areas of daily functioning (Schuder & Bennetto, 2016)? Questionnaire-based methods have been successful in the past to distinguish atypical sensory processing from typical sensory processing and show high reliability in examining sensory issues in ASD (Ben-Sasson et al., 2009).

However, there are a few disadvantages of examining sensory processing in ASD using *only* questionnaires. First, sensory questionnaires are primarily based on the reports of parents or individuals with ASD. This subjectivity may result in data that are biased due to inaccurate perception of behavioral responses by parents or individuals with ASD. Second, questionnaires

often collapse across sensory modalities. As a result, the final scores may fail to capture differences in sensory reactivity in response to single sensory input (or even pairs of inputs). Third, although some questionnaires score modality specific sensory responses separately (Baranek et al., 2006; Dunn, 2014), only a few of them independently examine responsivity to social and non-social stimuli (SEQ; Baranek et al., 2006). Consideration of the type of the stimuli is important because, although individuals with ASD show differences in responding to both social and non-social sensory stimuli, these differences may be larger in response to social than non-social stimuli (Dawson et al., 2004). Fourth, self-report questionnaires are primarily completed by high-functioning individuals with ASD (i.e., individuals with an  $IQ \geq 70$ ). The complexity of the items and the minimum language requirements needed to complete the questionnaires may restrict data collection using self-reports from low-functioning individuals with ASD. Last, questionnaires provide information regarding observable behaviors in response to sensory stimulation (e.g., fails to orient to a name call). However, they do not provide us with underlying information regarding whether children have high or low sensory thresholds that may affect stimulus detection or whether children were able to perceive a particular stimulus but failed to direct their attention towards that stimulus and so on. For these reasons, a common practice has been to use questionnaires in combination with other methods of data collection that focus on underlying mechanisms of sensory processing.

#### **1.4.2 Direct behavioral observation**

A number of coding schemes have been developed to observe sensory responses in structured and non-structured settings. The most widely used structured observational coding schemes include the Tactile Defensiveness and Discrimination Test-Revised (TDDT-R; Baranek, 2010) and the Sensory Processing Assessment (SPA; Baranek, Boyd, Poe, David, & Watson, 2007). Both these tests are designed to observe sensory responses in structured play-based settings. Such measures are used in lab-based play sessions and may provide us with insights regarding individuals' natural behavioral responses to sensory stimulation. However, there can be a few challenges in using such measures: (1) Both of these tools do not have published clinical norms which makes it difficult to use them in clinical practice, and (2) given that these observations are measured during play-sessions, they can only be used with young individuals with ASD (Schauder & Bennetto, 2016). In addition to these observational tools, a few researchers have also used the

Sensory Processing Scale (SPS; Schoen, Miller, & Sullivan, 2014). This scale consists of structured games that involve responding to sensory inputs that are encountered in our daily life. Given the nature of the tasks, this observational measure has been used with older children (aged 4-19 years) with ASD.

In non-structured observational studies, caregivers are asked to interact with their children in naturalistic settings. Caregivers are instructed to play as they would at home, while being video-recorded for later analysis. The primary aim of such studies is to examine how participants respond to sensory inputs in naturalistic settings. Experimenters then code infant behaviors such as looking at the mom in response to her/his name or orienting to maternal touches using frame-by-frame analysis. In longitudinal studies, observational analyses conducted at different stages is often used to identify early behavioral markers of ASD (Kadlaskar et al., 2019). Retrospective reports using early home-videos of participants who are now diagnosed with ASD are analyzed to examine red flags that were present before receiving their diagnosis (Baranek, 1999). Both these methods provide information about individuals' behavioral responses to sensory stimulation in natural settings. Although valuable, these methods of data collection can pose challenges as coding of some participant behaviors may involve coder subjectivity especially when looking for eye gaze (e.g., it might be difficult to assess which object the child is looking at if two objects are in close proximity). Similar to questionnaire data, this type of analysis also focuses on overt behaviors and does not provide information about covert physiological and neural mechanisms that may govern these behaviors. Nonetheless, because of the possibility of direct behavioral observations of sensory responses in natural settings, such coding schemes are often used in combination with other methodologies.

### **1.4.3 Psychophysiological measures**

Psychophysiological studies provide a non-invasive objective measure to examine the body's natural responses to sensory information. Specifically, they focus on the functioning of the Autonomic Nervous System (ANS) in response to sensory stimuli. The ANS is responsible for regulating an individual's ability to adapt to surrounding environment via its sympathetic and parasympathetic branches. Psychophysiological studies are motivated by two main hypotheses proposing that an individual's physiological arousal level may be an underlying factor for observable differences in sensory processing in ASD. The first hypothesis suggests that individuals

with ASD show a general state of under-arousal of the Sympathetic Nervous System (SNS) – a part of the ANS –, and that this reduced arousal is manifested as lack of responses to sensory stimulation (DesLauriers & Carlson, 1969; Rimland, 1964). The second hypothesis proposes that the over-arousal of the SNS may be responsible for differences in sensory processing in ASD (Dawson, 1989; Hirstein, Iversen, & Ramachandran, 2001; Hutt, Hutt, Lee, & Ounsted, 1964). According to this hypothesis, over-arousal of the SNS hinders habituation to sensory information resulting in sensory overload that may be followed by extreme behavioral responses as coping mechanisms.

One of the paradigms used to examine arousal levels is the Sensory Challenge Protocol (SCP; Miller, Reisman, McIntosh, & Simon, 2001; Schaaf, Benevides, Leiby, & Sendekki, 2015). In this paradigm, participants are systematically presented with sensory stimuli across five modalities: tactile, auditory, visual, vestibular, and olfactory. During the experiment, ANS measures such as electrodermal activity (EDA) or skin conductance, and heart rate are collected in response to stimulus presentation (Schoen, Miller, Brett-Green, & Nielsen, 2009). Any changes observed in skin conductance or heart rate may be indicative of an individual's internal arousal state. Therefore, even though not directly related to sensory processing, measurements of EDA and heart rate may shed light on underlying arousal levels that may contribute to behavioral manifestations of sensory responsivity in ASD.

#### **1.4.4 Psychophysical measures**

Psychophysical studies provide another objective measure to examine individual responses to sensory stimulation. These studies examine perceptual experiences of sensory stimuli by measuring detection thresholds. (Schauder & Bennetto, 2016). For example, while studying tactile perception, participants may be presented with basic tactile stimuli (e.g., a 50 Hz vibrotactile stimuli) and they would be asked to report whether or not they detect the vibration. In other tasks, participants may be presented with two or more stimuli that differ in their intensity (e.g., 50 Hz and 100 Hz vibrations in the tactile modality or high- and low-pitched beeps in the auditory modality) and they would be asked to respond when they detect a change in stimuli.

Psychophysical studies are designed in a way that they may represent patterns of neurological thresholds to sensory stimulation. For example, neurological thresholds denote the overall quantity of sensory stimuli required for the nervous system to notice or react to that input.

Therefore, low threshold to sensory input results in an individual requiring less stimulation to register incoming sensory information and to produce a behavioral response. On the other hand, high thresholds to sensory input may result in individuals needing a greater amount of sensory input to produce a behavioral response (Dunn, 1997). Consideration of neurological thresholds is essential as they suggest that typical amounts of sensory input that individuals receive in their daily life, might produce atypical behavioral responses. For instance, individuals may show hyper-reactivity if they have low thresholds and hypo-reactivity if they have high thresholds.

Last, similar to other methodologies, the use of psychophysical studies may also present some challenges. Stimuli used in lab-based psychophysical studies (e.g., tactile vibrations, pure tone stimuli) are not always representative of the rich multisensory information that is experienced in the outside world (e.g., affectionate touch while hearing a name call). Nonetheless, psychophysical studies are important as they enable researchers to examine how processing of most basic forms of sensory stimuli may map onto higher-order perceptual capacities (Cascio, Woynaroski, Baranek, & Wallace, 2016; Schauder & Bennetto, 2016).

#### **1.4.5 Neuroimaging measures**

Neuroimaging techniques offer a unique perspective in sensory processing studies as they allow us to focus on covert brain responses to sensory stimulation. Examination of neural responses provides additional information regarding underlying factors that may impact behavioral responses to sensory input. The most commonly used neuroimaging methods in ASD are event-related potentials (ERP) measured using electroencephalography (EEG), functional magnetic resonance imaging (fMRI) and event-related fields (ERF) measured using magnetoencephalography (MEG). All these techniques measure the timing of neural responses as well as location while examining sensory processing (Schauder & Bennetto, 2016). The current study utilizes EEG for studying sensory processing in ASD.

One of the major strengths of studies using EEG is the high temporal resolution of neural responses. Many studies that use EEG, examine individual components that are related to specific sensory events (event-related potentials; ERP). ERP components can measure covert information processing in the presence or absence of overt behavioral responses. ERP waveforms typically consist of peaks and valleys, and they are named based on their polarity (e.g., P for positive and N for negative) as well as on the time between the peaks and the onset of the stimulus (i.e., P300,

indicating a positive peak at 300 ms after stimulus onset). Subset of ERP components are called Auditory Evoked Potentials (AEP), and they are divided into short, middle, and long latency responses. Short latency responses include involuntary brainstem responses that occur within 10 ms after the onset of the stimulus. Mid latency responses are measured between 10 and 50 ms post stimulus onset. Late latency responses are measured after 50 ms post stimulus onset (Eggermont, 2007). In electrophysiological research, early ERP components (0 -150 ms) are indicative of modality specific processing (Eggermont, 2007), whereas, later ERP components are reflective of attention and memory functions (Polich, 2003; Samson, Mottron, Jemel, Belin, & Ciocca, 2006). One of the most common paradigms used to study these components is the oddball paradigm, during which participants are repeatedly presented with standard stimuli (e.g., 80 Hz pure tone stimuli around 80% of total stimuli) with occasional deviant (e.g., 200 Hz pure tone stimuli around 10% of total stimuli) and/or novel stimuli (e.g., speech sound /a/ around 10% of total stimuli) embedded within the stream of standard stimuli. In the oddball paradigm, researchers often examine if individuals are involuntarily able to shift their attention to a deviant or a novel stimulus by looking at later occurring ERP components. Studies examining sensory processing using neuroimaging methods also study mismatch negativity (MMN) or the mismatch field (MMF). These components are seen around 100 – 250 ms after stimulus onset and are elicited when a deviant stimulus is encountered during a stream of standard stimuli (Rinne, Alho, Ilmoniemi, Virtanen, & Näätänen, 2000; Samson et al., 2006).

High temporal resolution of ERP, enables researchers to study both bottom-up and top-down processing of stimuli (Jeste & Nelson, 2009). ERP components corresponding to bottom-up processing provide information regarding basic perceptual abilities, whereas top-down processing sheds light on complex cognitive functions such as attention that may impact processing of sensory stimuli. Therefore, by examining the timing of ERP components we may be able to determine if, for example, behavioral observation of lack of response to a touch (e.g., hypo-reactivity) is a result of differences in *perceiving* a stimulus or *attending* to that stimulus. In sum, examining associated brain responses (using any of the above methods) is beneficial as it can provide an objective explanation for observable differences in sensory processing that are reported via behavioral measures.

## **1.5 Sensory processing in ASD**

### **1.5.1 From Kanner to DSM 5**

In the first account of autism, Kanner (1943) described certain associated sensory behaviors that may now be considered as defining diagnostic features of ASD. For example, he stated that children with ASD may be hyper-reactive to sounds in their environment and yet be under-reactive to their parents' verbal attempts of engaging their attention. Although these behaviors were present in the majority of his cases, Kanner (1943) only discussed these behaviors as secondary features of ASD and did not include them in his diagnostic criteria of ASD. However, in the past three decades researchers have systematically focused on sensory behaviors that distinguish individuals with ASD from typically developing (TD) controls (Rogers & Ozonoff, 2005). For example, toddlers and young children with ASD are often found to be behaviorally less responsive to their name (Baranek et al., 2013); high-responsivity to name is a skill that typically developing children master before the age of 12 months (Bortfeld, Morgan, Golinkoff, & Rathbun, 2005; Mandel, Jusczyk, & Pisoni, 1995). Further, researchers have also reported differences in responding to other sensory modalities in ASD manifested as reduced response to pain, avoidance of touch, and aversion to fluorescent light (Baranek et al., 2006). Similar findings emerge from recent studies focusing on sensory processing in infants (Ben-Sasson et al., 2008), children (Leekam et al., 2007), and adults with ASD (Crane, Goddard, & Pring, 2009), extending the earlier reports of atypical sensory processing in this population (see Rogers & Ozonoff, 2005, for a review).

These differences in processing sensory stimuli in ASD are associated with social, linguistic, and adaptive skills (Baranek et al., 2013; Lane, Young, Baker, & Angley, 2010) and may also present as early markers of ASD, especially in infants at high risk for ASD (i.e., infants with an older sibling with ASD; Germani et al., 2014). Given the almost universal nature of sensory processing differences in ASD, the most recent edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-5; American Psychiatric Association, 2013) has now included "hyper-or-hypo-reactivity to sensory input or unusual interests in sensory aspects of the environment" as one of the four types of restricted and repetitive behaviors.

### 1.5.2 Three subtypes of sensory behavioral differences

Differences in processing sensory information have been characterized into three behavioral response patterns; *hyper-reactivity*, *hypo-reactivity*, and *sensory seeking* (Ausderau et al., 2014; Baranek et al., 2006; Ben-Sasson et al., 2009; Miller, Anzalone, Lane, Cermak, & Osten, 2007). Hyper-reactivity refers to exaggerated behavioral responses to sensory stimuli (e.g., aversion to sounds, avoidance of touch, covering of eyes in response to light; Baranek et al., 2006). Hyper-reactivity has been alternatively described as *hyper-responsivity* and *sensory defensiveness* defined as negative reactions to sensory stimuli (Boyd et al., 2010; Pfeiffer & Kinnealey, 2003). Hypo-reactivity, on the other hand, refers to a lower level of behavioral response to sensory stimuli (e.g., lack of orienting to touch or novel sounds, failure to respond to pain; Baranek et al., 2006). Hypo-reactivity has been alternatively described using terms such as *sensory under-responsivity* or *hypo-responsivity* that have also been defined as slower responses to sensory stimuli (Ben-Sasson et al., 2009). Sensory differences are usually interpreted based on normative data. Sensory responses that fall within one standard deviation (SD) from the mean are categorized as ‘typical’. Whereas, behaviors that fall outside the range of one standard deviation from the mean may be classified as ‘probable’ (between 1-2 SDs from the mean) or ‘definite’ differences (more than 2 SDs from the mean; Dunn, 2014). Use of a variety of terms while studying sensory processing in ASD may lead to confusion across the field. Thus, in this thesis, I have used the same terminology (i.e., hyper/hypo-reactivity) used in DSM 5 to maintain consistency within the study of sensory processing in ASD.

Although, the above-mentioned behavioral response patterns to sensory stimuli in ASD have been described as distinct behavioral profiles, patterns of hyper- and hypo-reactivity have been observed to co-exist in individuals with ASD (Baranek et al., 2006). For example, Baranek et al. (2006) found that 38% of children with ASD show both hyper- and hypo-reactivity to sensory stimuli. These findings suggest that there may be heterogeneity in the manifestation of sensory differences across and within individuals with ASD. Last, sensory seeking is characterized by excessive interest in sensory experiences that are prolonged and intense (Dunn, 1997), or repetitive in nature (Liss, Saulnier, Fein, & Kinsbourne, 2006). Dunn (1997) has indicated a relationship between having high thresholds and sensory seeking behaviors. For example, it has been suggested that individuals with high thresholds for sensory stimulation may engage in seeking behaviors in



order to increase their sensory experience. In the current study, I will primarily focus on hyper- and hypo-reactivity to auditory and tactile modalities in children with ASD.

In the following section, I will discuss several theories that may explain sensory differences in ASD. However, it should be noted that, explaining sensory profiles observed in ASD with any one theory has many challenges, primarily because, ASD is a heterogeneous disorder. This heterogeneity is often observed in the core symptoms of ASD and is manifested in socio-communicative deficits, and restricted and repetitive patterns of behaviors in individuals with ASD (Masi, DeMayo, Glozier, & Guastella, 2017). For example, in the socio-communicative domain, individuals with ASD may show a diverse range of behaviors from a complete lack of social skills to little difficulties in interacting with others, or from using very little spoken language to mild or moderate difficulties in spoken language usage. Similar trends of variability are also found in the domain of sensory processing skills in individuals with ASD, with some individuals showing extreme hyper-reactivity to certain stimuli, while others showing hypo-reactivity to the similar kinds of stimuli (Baranek et al., 2006). In addition to the heterogeneity in behavioral patterns of responsivity in ASD, there have also been reports of heterogeneity in the neural (Salmond, Vargha-Khadem, Gadian, de Haan, & Baldeweg, 2007) and genetic (Abrahams & Geschwind, 2008; Betancur, 2011) basis of ASD, which may account for some of the behavioral variability in ASD. Nonetheless, these challenges are problematic only if we try to find a single explanation underlying all symptoms of ASD. Therefore, in the following section, I discuss several sensory processing theories of ASD that may account for at least some of the sensory profiles that are observed in ASD.

## **1.6 Theories of sensory processing in ASD**

### **1.6.1 Sensory specific theories**

#### ***1.6.1.1 Over-and under-arousal theories***

Over-arousal theories of ASD are based on two primary hypotheses: 1) individuals with ASD show greater physiological arousal in response to sensory input compared to individuals without ASD, and 2) individuals with ASD may show difficulties in habituating to environmental stimuli compared to their peers (Rogers & Ozonoff, 2005). Habituation refers to attenuation of physiological responses after repeated presentation of stimuli. The central argument behind the

over-arousal theory is that an individual's internal state of physiological arousal may affect processing of sensory stimuli that are present in the environment (see Rogers & Ozonoff, 2005).

Over-arousal theory was first put forward by Hutt et al. (1964) by discussing the overstimulation of the sensory receptors measured in an EEG experiment and their link to reduced behavioral responses to incoming stimuli, social withdrawal, and repetitive behaviors in individuals with ASD. This theory has been explored using a variety of methods and has received substantial support since then (Chang et al., 2012; James & Barry, 1984; Woodard et al., 2012). Specifically, evidence has shown that individuals with ASD show increased physiological arousal in response to auditory, tactile, visual, kinesthetic, gustatory and olfactory stimuli (Chang et al., 2012; James & Barry, 1984; Woodard et al., 2012). For example, Chang et al. (2012) measured electrodermal activity (EDA) and showed that, 5- to 12-year-olds with ASD had a significantly higher skin conductance response in response to auditory stimuli compared to typically developing children. Additionally, higher EDA arousal was associated with behavioral difficulties in the auditory modality measured using the Sensory Processing Measure-Home Form (SPM; Parham, Ecker, Miller-Kuhaneck, Henry, & Glennon, 2007). Other studies have supported the over-arousal theory by reporting heightened arousal in response to sensory stimulation using heart rate; a measure of the sympathetic nervous system (Woodard et al., 2012), as well as by providing evidence of failure to habituate to repeated stimuli in the ASD group (James & Barry, 1984).

A model of over-arousal may help in explaining underlying factors that may impact hyper- and/or hypo-reactivity in ASD. For example, McDonnell et al. (2015) argue that, an attempt to regulate internal physiological levels may impact behavioral responses to incoming sensory inputs. Specifically, the authors suggest that, individuals try to maintain a state of homeostatic equilibrium, which is the optimum physiological arousal level needed to typically respond to surrounding inputs. Therefore, if individuals with ASD show heightened levels of physiological arousal in response to stimulation, they may constantly engage in certain behaviors aimed at maintaining their typical arousal levels. For example, extreme levels of over-arousal may lead individuals to become less responsive (i.e., hypo-reactive) to stimulation, which might be a defense mechanism to block the outside world, thereby controlling their heightened arousal. Evidence in support of this hypothesis comes from Goodwin et al. (2006), who showed that individuals with ASD had higher levels of baseline heart rate, and showed overall less responsivity to sensory stimulation, suggesting that over-arousal was related to how individuals with ASD responded to their environments. Therefore,

a hypo-reactive behavior in ASD such as lack of a response to own name or to a caregiver touch may result from physiological over-arousal as a way of modulating dysregulated arousal levels. Other researchers have suggested that individuals with ASD may engage in stereotypical or repetitive sensory behaviors in order to regulate their physiological over-arousal (Hirstein et al., 2001). Last, it is possible that, individuals with ASD who are unable to self-regulate their over-arousal levels, may display hyper-reactivity (e.g., covering of ears to sounds, orienting away from shoulder taps, etc...) to get away from the sensory information that is perceived to be over-arousing.

The premise of the over-arousal theory is further strengthened by studies suggesting that individuals with ASD may show heightened baseline arousal levels on physiological measures such as EDA and heart rate (see, Lydon et al., 2016 for a review). Nonetheless, over-arousal theory has not been universally accepted due to equally compelling evidence indicating that not all individuals with ASD display heightened physiological arousal levels (see, Lydon et al., 2016 for a review). For example, past research has failed to find a significant difference between physiological arousal levels between individuals with and without ASD (McCormick et al., 2014). Additionally, other research has indicated that individuals with ASD may show under-arousal in response to sensory stimuli (Schoen et al., 2009). This has led researchers to also explore an under-arousal theory of ASD.

The under-arousal theory of ASD was first discussed by (Rimland, 1964) and (DesLauriers & Carlson, 1969). Rimland (1964) hypothesized that impairments in the reticular activating system impact how individuals with ASD connect past experiences with present ones, affecting their typical learning and generalization. Rimland argues that deficits in the reticular activating system may lead to observable differences in reacting to surrounding information, mainly resulting in under-responsivity to incoming stimuli in individuals with ASD. DesLauriers and Carlson (1969) also noted deficits in the reticular activating system resulting in under-arousal of the limbic system. Their results indicated that, under-arousal of the limbic system was related to experiences of sensory deprivation in individuals with ASD, which impacted their typical perception of sensory information. Thus, individuals with ASD may be more likely to show hypo-reactivity if they fail to perceive incoming sensory stimuli.

The under-arousal theory of ASD has also been supported by studies that have used a variety of physiological and neurological measures to help explain underlying factors impacting sensory processing in ASD. For example, using the Sensory Challenge Protocol, Schoen et al.

(2009) showed that, compared to typically developing controls, children with ASD had significantly lower EDA during baseline and reduced EDA in response to sensory stimulation, which are indicative of reduced arousal levels in ASD. Evidence of reduced arousal has also been corroborated in neurophysiological studies using ERP paradigms. Bruneau, Bonnet-Brilhault, Gomot, Adrien, and Barthélémy (2003) observed smaller amplitudes and delayed latencies of the early ERP components in response to pure tones in 4- to 8-year-olds with ASD compared to typically developing controls indicating under reactivity to basic auditory stimuli. In sum, these results suggest that, under-arousal of physiological or neurological systems may underlie behavioral manifestations of hypo-reactivity in ASD. Together, evidence supporting over- and under-arousal theories suggest alternate hypotheses underlying sensory processing differences in ASD. These alternate theories indicate that, the amount of dysregulation of arousal in ASD may be heterogeneous, with subtypes displaying different arousal levels in individuals with ASD (Hirstein et al., 2001; Schoen, Miller, Brett-Green, & Hepburn, 2008). Therefore, if individuals with ASD fail to modulate physiological arousal in response to sensory stimulation, their behavioral responses that follow may appear as hypo- or hyper-reactive to that stimulus.

#### ***1.6.1.2 Enhanced perceptual functioning theory***

Enhanced perception is defined as heightened acuity in awareness of specific sensory stimuli and attention to specific parts of the stimuli (Mottron, Dawson, Soulieres, Hubert, & Burack, 2006). One possible explanation underlying sensory processing differences in ASD could be attributed to the enhanced perceptual capacities of individuals with ASD. For example, in the auditory modality, Bonnel et al. (2003) examined pitch discrimination and categorization abilities in 12 individuals with high functioning ASD and 12 typically developing (TD) controls. During the pitch discrimination task, participants were presented with a “same-different” task, where they were asked to determine if pairs of tones were same or different. During the pitch categorization task, participants were asked to judge each tone as high or low in terms of its pitch. During both of these tasks, participants in the ASD group showed higher pitch sensitivity compared to controls suggesting enhanced pitch perception at least in high-functioning individuals with ASD. These results have been supported by more recent studies using similar tasks in the auditory domain (Bonnel et al., 2010; O’Riordan & Passetti, 2006) and suggest that enhanced perceptual abilities consistently seen in basic visual tasks (e.g., embedded figures task, visual search task; O’Riordan,

2004; O’Riordan, Plaisted, Driver, & Baron-Cohen, 2001) are also extended to other modalities such as hearing. Findings in the auditory modality suggest that enhanced perception may underlie at least some differences in processing auditory information in ASD. Evidence for this comes from Ausderau et al. (2014) in that the authors report a strong association of hyper-reactivity with enhanced perception in individuals with ASD. It is possible that, enhanced perception of slight changes in the auditory sequences in individuals with ASD (Mottron, Peretz, & Menard, 2000), may result in distressful reactions to certain sounds (O’Riordan & Passetti, 2006) contributing to hyper-reactivity in the auditory domain.

Evidence supporting the enhanced perceptual functioning theory in the tactile modality is mixed. O’Riordan and Passetti (2006) studied tactile perception in high functioning children with ASD and compared their performance with typically developing children. Their results indicated no significant group differences in children’s abilities to discriminate roughness of tactile stimuli presented on the arm. The authors, therefore concluded that, contrary to the findings in the auditory and visual modalities (Bonnell et al., 2010; Mottron & Burack, 2001), there is no strong evidence for enhanced perception in the tactile modality in ASD. In contrast to these results, Blakemore et al. (2006) showed that individuals with ASD demonstrated superior detection abilities in response to 200 Hz (but not 30 Hz) vibrotactile stimuli presented to the fingertip compared to controls. These results indicate enhanced tactile perception to at least one class of stimuli in individuals with ASD. Consistent with these findings, Cascio et al. (2008) demonstrated that, although individuals with ASD showed similar thresholds while detecting light touch compared to typically developing controls, they showed heightened sensitivity in response to tactile vibrations presented on the forearm as well as increased sensitivity to thermal pain on the forearm and palm.

A possible reason underlying heightened tactile sensitivity in ASD could be attributed to the type of somatosensory receptors that are innervated as a result of touch. One of the widely studied tactile receptors are known as CT-afferents. Typically, CT-afferents are low-threshold unmyelinated tactile mechanoreceptors that are primarily found in the hairy skin of the human body such as the forearm and face, and they preferentially respond to light and slow moving strokes and textures (Olausson et al., 2002). Innervation of the CT-afferents is associated with feelings of pleasantness (Vallbo, Olausson, & Wessberg, 1999; Wessberg, Olausson, Fernström, & Vallbo, 2003). Most common somatosensory receptors found in the glabrous (non-hairy) skin are myelinated tactile mechanoreceptors known as Meissner’s corpuscles (stimulated by low-

frequency tactile stimuli) and Pacinian corpuscles (stimulated by high-frequency tactile stimuli). Furthermore, Pacinian corpuscles are associated with tactile discrimination (Kakuda, 1992). Given that CT-afferents preferentially respond to slow stroke stimuli, they may not explain heightened sensitivity observed in response to tactile vibrations presented on the forearm in Cascio et al. (2008), however, lower thresholds for high-frequency tactile stimuli in Blakemore et al. (2006) may be explained by stimulation of the Pacinian corpuscles that are innervated by high-frequency tactile stimuli. In sum, these results indicate that, while there may be instances of typical tactile perception in individuals with ASD, there are also instances of enhanced perception which may lead to hyper-reactivity to tactile stimuli.

### ***1.6.1.3 Intense world theory***

Hyper-reactivity to sensory stimulation has also been discussed using the intense world theory in ASD. The intense world theory states that ASD is a result of a molecular syndrome that sensitizes gene expression pathways resulting in excessive neuronal information processing and storage of microcircuits in the brain (Markram et al., 2007; Markram & Markram, 2010). In other words, the authors of the intense world theory of ASD propose that behavioral difficulties observed in ASD are a result of hyper-reactivity of certain neural systems that are responsible for managing flow of incoming information and selective attention. According to this theory, the abnormality lies in the local microcircuits. The local microcircuits are connected to neighboring as well as distant cells. In individuals with ASD, there may be too many connections within the local microcircuits compared to those without ASD. Hence, when a new stimulus is encountered, it results in stronger excitation in any given microcircuit. This overexcitation of the microcircuits causes individuals to perceive the outside world as too intense.

The evidence in support of this theory comes from an animal model in which rats were exposed to valproic acid in order to explore changes in their synaptic, microcircuit, and behavioral levels (Markram et al., 2007; Markram & Markram, 2010). The decision to use valproic acid was based on previous evidence showing that, valproic acid, when taken during pregnancy, has been associated with the development of ASD in the offspring (Christianson, Chester, & Kromberg, 1994; Rasalam et al., 2005; Williams et al., 2001). Additionally, many of the deficits associated with *in utero* exposure to the valproic acid in humans are also present in rodents (Binkerd, Rowland, Nau, & Hendrickx, 1988; Ehlers, Stürje, Merker, & Nau, 1992). Markram et al. (2007) argued that,

rats exposed to valproic acid spent less time socializing with their peers, were more anxious, and engaged in more repetitive behaviors. Additionally, the neural systems in rats exposed to the valproic acid were found to be hyper-active in response to stimulation. Specifically, rats exposed to valproic acid showed hyper-reactivity and hyper-plasticity in the neocortex and amygdala, which may have been a result of hyper-connectivity of the neurons in these regions (Markram, Rinaldi, La Mendola, Sandi, & Markram, 2008; Silva et al., 2009). These hyper-active systems indicate excessive processing of incoming information in the nervous system. Further, the authors suggest that hyper-reactivity of the microcircuits, mainly in frontal and temporal regions as well as in amygdala and thalamus may make perception of the outside world overly intense. This may result in regression in neurodevelopment as the brain actively tries to avoid or block out excessive stimulation (Markram & Markram, 2010) through hyper-reactivity (e.g., covering of ears to sounds, avoidance of touch). Thus, according to the intense world theory, hyper-reactivity of specific neural systems may cause hyper-perception, hyper-attention, and hyper-memory, which may be the basis of most ASD-like symptoms (Markram et al., 2007).

Although this theory explains hyper-reactivity in ASD, there are some areas of concern that need to be addressed. First, the primary support for this theory comes from rat models, and it still needs to be proven using human participants. Further, the ASD-like characteristics in the rats were a result of an *in utero* exposure to the valproic acid. However, not all cases of ASD are a result of such chemical exposures. Thus, the conclusions drawn in the studies regarding the causes of the observed ASD-like features may not be generalizable to other cases of ASD. Second, we know that evidence of sensory differences in ASD is well established in ASD (Rogers & Ozonoff, 2005), however, unlike the consistent evidence of hyper-reactivity in the valproic acid rat models, the data in human participants is much more mixed. For example, there is evidence suggesting that individuals with ASD may display hyper-reactivity (e.g., covering of ears to sounds), hypo-reactivity (e.g., lack of a response to shoulder tap), as well as sensory seeking (e.g., a need for more sensory stimulation; Baranek et al., 2006; Ben-Sasson et al., 2009). To some extent, the intense world theory may explain hypo-reactivity in ASD. It is possible that individuals with ASD may withdraw from the surrounding environment to deal with the intense nature of the stimuli. This behavioral withdrawal may appear as hypo-reactivity to incoming input. However, the exact role of the intense world theory in explaining hypo-reactivity in ASD needs further exploration.

Therefore, given the heterogeneity of ASD, intense world theory may only partially explain factors that underlie sensory processing in ASD.

## **1.6.2 Alternate theories explaining sensory processing differences in ASD**

### ***1.6.2.1 Social motivation theory***

Social motivation theory states that social motivation is a guiding force for everyday human behaviors, and any deficits in the social motivation may contribute to behavioral differences such as hypo-reactivity observed in ASD (Chevallier, Kohls, Troiani, Brodtkin, & Schultz, 2012). In typical development, shared socio-communicative experience motivates individuals to participate in social acts (Dawson et al., 2004). However, individuals with ASD may find it difficult to form stimulus-reward contingencies for social stimuli, which could result in reduced attention directed towards such stimuli (Chevallier et al., 2012).

Although social motivation theory is not a sensory processing theory, it may still account for sensory processing differences at least to social stimuli or to a variety of stimuli occurring in social settings. Support in favor of the social motivation theory comes from a previous study by Dawson et al. (2004), in that they examined orienting behaviors of 3- to 4-year-olds with ASD in response to social and non-social auditory stimuli. Auditory social stimuli consisted of a human presenting sounds such as calling the child's name, humming, patting hands on thighs and snapping fingers. Whereas, non-social stimuli consisted of sounds that were produced using a mechanical device such as sounds of a telephone ringing and timer beeping. Results suggested that children with ASD were less likely to orient to sounds in general, but showed more profound differences for the social stimuli, further supporting the idea that it might be the social nature of the stimuli that may play a role in sensory processing differences in ASD. Therefore, hypo-reactivity in ASD may be viewed as a domain-specific deficit in social motivation and social orienting (Dawson et al., 2004). For more results in support of the social motivation theory, see Dawson, Meltzoff, Osterling, Rinaldi, and Brown (1998); Swettenham et al. (1998). Results from Kadlaskar et al. (2019) may support the argument that social settings may impact sensory responsivity in ASD. Specifically, the authors in this study showed that infants at risk for ASD who later received a diagnosis of ASD (HRA+) were less responsive to caregiver touches presented in naturalistic social interactions compared to low-risk infants. It is possible that, failure



to orient to caregiver touches in HRA+ infants was a result of reduced motivation to participate in social interactions. Together, these studies suggest that differences in processing sensory stimuli could be related to the social nature of the stimuli or to social settings in which a variety of stimuli may be presented.

Although the social motivation theory provides compelling evidence to explain reduced orienting to social stimuli in ASD, it faces challenges in explaining differences in sensory processing triggered by non-social stimuli. For example Baranek et al. (2013) examined orienting to social and non-social stimuli in three groups of children aged 11-105 months with ASD, Developmental Delay, and typical development. Their results indicated that children with ASD showed deficits in orienting to both social and non-social stimuli (although with larger effects for social stimuli in younger infants). The authors, thus, argue that hypo-reactivity to sensory stimuli may be a domain-general process in sensory processing occurring in both social and non-social contexts. These findings also indicate that the social motivation theory may not be mutually exclusive from other theories mentioned in this section. For example, it is possible that hypo-reactivity to both social and non-social stimuli may be a result of under-arousal in response to sensory stimulation (Schoen et al., 2009), however, these effects might be more prevalent in reactions to social stimuli (in support of the social motivation hypothesis). Nonetheless, more research is needed to understand how different theories relate to one another while explaining sensory processing differences in ASD.

#### ***1.6.2.2 Atypical attentional processing theory***

Many researchers argue that, complex attentional processes are fundamental for the development of typical socio-communicative skills, and that any deficit in early attentional processes may contribute to the emergence of the core behavioral symptoms observed in ASD (Keehn, Müller, & Townsend, 2013). Although atypical attentional processing theory is not primarily a sensory processing theory, it may explain at least some of the differences in responding to sensory information in ASD. For example, it is possible that individuals with ASD are able to *perceive* a stimulus like TD individuals but are unable to *direct their attention* to that stimulus in a typical manner. Therefore, we may observe behavioral manifestations of hypo-reactivity in ASD despite the possibility that the individual with ASD may have perceived that stimulus like a TD individual.

Evidence for this theory in the domain of sensory processing comes from Čeponienė et al. (2003). Čeponienė et al. used ERP to examine early and later occurring ERP components of auditory sensory processing in children with and without ASD. In particular, the participants were presented with simple tones, complex tones, and vowels in an oddball paradigm. In this paradigm, the same tones were presented repeatedly (standard stimuli) with occasional deviant tones (oddball stimuli) embedded in that sequence. Inclusion of the deviant stimuli enabled researchers to examine involuntary attentional orienting to those stimuli. Results of this study showed intact perception of tones and vowels in individuals with ASD measured by no differences in early ERP components compared to TD individuals. Late occurring responses were examined by looking at the P3a; an ERP component indicating involuntary attentional orienting to deviant stimuli. Results indicated that in the ASD group, involuntary attentional orienting was most affected in response to vowels compared to simple and complex tones. These findings suggest that, early exogenous responses are similar in ASD for all stimuli, but that individuals with ASD may fail to *attend* to those sounds in a typical manner, especially to speech-sounds. These results suggest that deficits in attentional processes may contribute to behavioral manifestations of hypo-reactivity in ASD.

Atypical attentional processing theory may also explain differences to tactile stimulation in individuals with ASD. Specifically, Cascio et al. (2015) examined neural responsivity to tactile stimulation (air puffs presented on the fingertip) in individuals with and without ASD. The results indicated that later ERP components (indicative of cognitive processes, such as attention) were associated with hypo-reactivity whereas, earlier ERP components (indicative of basic sensory processing) were associated with hyper-reactivity in the ASD group. These findings suggest that behavioral manifestation of tactile hypo-reactivity may be a result of attentional processes rather than differences in merely perceiving the tactile stimuli, further supporting the atypical attentional processing theory.

Despite studies supporting the importance of attentional processes in sensory processing, there also lies some evidence suggesting that there may be deficits in basic perceptual processing in ASD (Bruneau et al., 2003; Fujikawa-Brooks, Isenberg, Osann, Spence, & Gage, 2010; Marco et al., 2012; Rosenhall, Nordin, Brantberg, & Gillberg, 2003). Together, these findings suggest two possible explanations underlying differences in sensory processing in ASD. First, sensory processing differences may have its roots in basic perceptual differences that are measured by looking at early ERP components. If this is true, then individuals with ASD may perceive sensory

stimuli differently. This difference at the basic perceptual level may also contribute to differences in attending to those stimuli. Second, sensory differences in ASD may be associated with attentional processes measured during later ERP components. It is possible that the basic perceptual abilities in ASD are intact, and the main difference lies in the cognitive capacities while processing the correctly perceived input. Since there is evidence to indicate differences at both stages of neural processing (basic perceptual and cognitive processing) in response to sensory stimulation, this area of research warrants further exploration.

### **1.6.3 Summarizing theories of sensory processing in ASD**

In sum, it is safe to argue that no one theory may explain all differences in sensory processing in ASD. First, given that ASD is a heterogeneous condition, it makes sense to simultaneously consider several competing theories to account for the combination of any given sensory deficits in individuals with ASD. For example, even though the domain-specific social motivation theory may explain hypo-reactivity to *social* sensory stimuli (e.g., name call, shoulder tap), it may not explain differences in responding to *non-social* sensory stimuli, which are equally evident in ASD. Such differences may be better explained using domain-general theories of impairments in basic attentional or perceptual processes. Second, not all theories of sensory processing in ASD complement each other. For example, in dysregulation of arousal, instances of both over- and under-arousal have been observed in response to incoming sensory inputs, with some studies even suggesting no difference in arousal levels in individuals with ASD compared to TD controls (Rogers & Ozonoff, 2005). Similarly, although the intense world theory may explain behavioral and neural hyper-reactivity in ASD (Markram et al., 2007), it may fall short of explaining diminished amplitudes of neural responses to sensory stimulation in ASD (Bruneau et al., 2003). Last, it is possible that these theories are not mutually exclusive. For example, there may be fundamental differences in basic attentional processes while responding to sensory stimuli, and these differences may be more evident to social stimuli (e.g., speech) than to non-social stimuli, supporting both the atypical attentional processing theory and the social motivation theory. Evidence for this comes from Lepistö et al. (2006), in that individuals with ASD had diminished P3a (an ERP component indicating involuntary attentional orienting to novel stimuli) in response to speech pitch and phoneme changes, but not to non-speech changes, indicating that the social nature of the speech stimuli may have contributed to the diminished amplitude in the P3a.

Therefore, consideration of multiple theories of sensory processing is essential as it provides us with a more complete understanding of differences in sensory profiles in ASD.

### **1.7 Auditory and tactile sensory processing in ASD**

As discussed in the beginning of this section, the processing of auditory and tactile modalities is the focus of this dissertation. Therefore, below I review the literature on basic auditory and tactile sensory processing differences in ASD, how these align with the behavioral patterns reviewed above, and how they may contribute to the development of socio-communicative skills in individuals with ASD. Discussion of auditory and tactile sensory processing will follow an order based on temporal processing. Thus, I will first review studies investigating sensory evoked brainstem responses that are measured within 10 ms for auditory stimuli (Fujikawa-Brooks et al., 2010; Talge, Tudor, & Kileny, 2018) and 30 ms for tactile stimuli (Miyazaki et al., 2007). Responses recorded within 10 or 30 ms after stimulus presentation are reflective of involuntary brainstem activity and may help us to identify differences in fundamental processing of auditory and tactile sensory information in ASD. Next, I will review literature that examines later cortical responses of sensory stimulation. Neuroimaging techniques such as electroencephalography (EEG) and magnetoencephalography (MEG) have been used to investigate both evoked and endogenous neural activities in response to sensory stimuli using event-related potentials (ERP) and event-related fields (ERF), respectively. Examining early and later cortical responses are important as they can help tease apart whether sensory processing differences are a result of differences in perception and threshold detection or they are a result of differences in cognitive functions such as attending to a stimulus. I will try to disentangle these notions to get a clear understanding of mechanisms underlying differences in auditory and tactile processing in ASD. Last, I will discuss how differences in perceptual and cognitive processing of sensory inputs may impact behavioral manifestations of sensory differences in individuals with ASD.

#### **1.7.1 Auditory processing in ASD**

Processing auditory information is essential for the development of language and socio-communicative skills. Therefore, examination of auditory processing becomes a crucial topic while studying deficits in language and socio-communicative skills in ASD. Common clinical

complaints of atypical responsivity to auditory stimuli in individuals with ASD have been shown in behaviors of hypo- and/or hyper-reactivity to incoming sounds. Hypo-reactivity to auditory stimuli has often been reported as reduced orientation to own name (Baranek, 1999; Osterling & Dawson, 1994; Werner, Dawson, Osterling, & Dinno, 2000), whereas, instances of hyper-reactivity have been observed as adverse reactions to surrounding sounds and covering of ears in response to sounds in individuals with ASD (Kern et al., 2006; Tomchek & Dunn, 2007).

One way of examining auditory processing has been to investigate the earliest subcortical responses to auditory stimulation in individuals with ASD. A widely used subcortical measure to examine auditory processing is involuntary auditory brainstem responses (ABRs). ABRs are electrophysiological responses reflecting activations of the auditory pathway in response to acoustic information (Moore, 1987). ABR consists of 7 waves, that occur within 10 ms after the onset of the auditory stimulus with 1-2 ms intervals between two peaks. Processing of ABRs in individuals with ASD have been mainly studied by presenting simple ‘clicks’ that result in excitation of nerve fibers from cochlea to the brainstem (Fujikawa-Brooks et al., 2010; Källstrand, Olsson, Nehlstedt, Sköld, & Nielzén, 2010; Talge et al., 2018).

The research examining ABR in individuals with ASD have yielded mixed results with evidence suggesting both typical (Courchesne, Courchesne, Hicks, & Lincoln, 1985) and atypical (Magliaro, Scheuer, Assumpção Júnior, & Matas, 2010; Rosenhall et al., 2003) auditory brainstem responses. Specifically, studies reporting differences in ABR have shown prolonged interpeak latencies of waves I-V in children and adolescents with ASD compared to TD controls (Kwon, Kim, Choe, Ko, & Park, 2007; Magliaro et al., 2010; Rosenhall et al., 2003). Interpeak latencies in ABR are indicative of the speed of auditory information processing. Therefore, any delay in interpeak latency may indicate slower processing of information. Contrary to previous findings of atypical brainstem responses to click stimuli, Russo, Nicol, Trommer, Zecker, and Kraus (2009) have reported typical auditory brainstem responses to click stimuli, but reduced magnitudes of brainstem responses to speech stimuli in 21 children with ASD suggesting that, differences in early auditory responsivity to speech may contribute to language deficits in ASD.

Although none of these studies directly measure the association between diminished early subcortical auditory brainstem responses and sensory profiles, it is possible that delayed ABR latencies and reduced amplitudes may account for some differences in hypo-reactivity in individuals with ASD. For instance, if auditory information (e.g., name call) is processed

atypically at a subcortical level, it may affect the timing and the magnitude with which this information is subsequently processed in the cortical regions of the brain, resulting in hypo-reactivity to auditory stimuli (e.g., reduced or slower responsivity to name call). Therefore, differences in subcortical auditory processing may be considered as one of the mechanisms underlying auditory hypo-reactivity in ASD. Nonetheless, differences in auditory processing at a subcortical level is not a *necessary* condition for ASD, because as mentioned before, there exists equally compelling evidence of intact subcortical auditory responsivity in ASD (Courchesne et al., 1985).

Beyond the brainstem, processing of auditory stimuli in cortical areas has been studied by examining initial auditory responses (e.g., N1, P1, M50, M100), sound discrimination responses (e.g., MMN and MMF), and attentional processes (e.g., P3, P3a). The majority of the studies examining these neural components have used pure tones, complex tones and/or speech stimuli in a variety of experimental paradigms. However, similar to evidence in the subcortical regions, research investigating auditory processing in cortical areas is equivocal. For example, using oddball paradigms, some have reported shorter latencies of the N1 ERP component in response to pure tone stimuli in children with ASD (Ferri et al., 2003; Oades, Walker, Geffen, & Stern, 1988), which may possibly imply faster processing of basic auditory information. These results may support the intense world theory since faster processing of auditory information may be indicative of excessive processing of information resulting in hyper-reactivity to incoming stimuli. On the contrary, others have reported prolonged latencies and smaller amplitudes of the earlier ERP (e.g., P1) and ERF components in response to pure and complex tones (Donkers et al., 2015; Jansson-Verkasalo et al., 2003; Jansson-Verkasalo et al., 2005; Lepistö et al., 2005; Roberts et al., 2010) in children with ASD, indicative of slower processing of auditory information in ASD. Evidence of smaller amplitudes and delayed latencies have also been reported in response to speech stimuli (Lepistö et al., 2005; Russo, Zecker, Trommer, Chen, & Kraus, 2009; Whitehouse & Bishop, 2008). These results indicate deficits in auditory perceptual processes to both simple and complex stimuli in individuals with ASD. Additionally, reduced amplitudes of early ERP and ERF components suggest higher thresholds of detecting a stimulus, which may result in hypo-reactivity to that stimulus.

Studies examining MMN have also yielded contradictory results. For example, Ferri et al. (2003) and Gomot, Giard, Adrien, Barthelemy, and Bruneau (2002) have reported reduced MMN

latencies in response to pitch changes in 10 and 15 children with ASD respectively. Reduced MMN latencies suggest heightened pitch perception in individuals with ASD. These results support the enhanced perceptual functioning theory of ASD. However, on the other hand, Jansson-Verkasalo et al. (2003) have shown delayed MMN latencies in 10 children with ASD suggesting differences in discrimination of auditory information. Such inconsistencies in auditory processing literature in ASD may be a result of differences in participants' ages, cognitive abilities, small sample sizes, and type of tasks used during the experiment (e.g., active vs passive). For example, in Whitehouse and Bishop (2008), the tendency to show smaller amplitudes to speech sounds disappeared when participants were asked to actively attend to those sounds. Therefore, although atypical responsivity in subcortical and cortical components suggest differences in perceptual mechanisms underlying both hypo- and hyper-reactivity, they may not be sufficient to explain atypical auditory processing in *all* individuals with ASD.

It follows that another possible explanation underlying differences in sensory profiles of individuals with ASD could be differences in cognitive processes. For example, Čėponienė et al. (2003) used ERP to examine earlier and later components of auditory sensory processing in children with ( $n = 9$ ) and without ( $n = 10$ ) ASD. Results of this study showed intact processing of tones and vowels in individuals with ASD measured by no differences in ERP components P100 and N200 compared to typically developing individuals. Cognitive processing was examined by looking at the P3a component; an ERP component indicating involuntary attentional orienting to deviant stimuli. Results indicated that, in the ASD group, involuntary attentional orienting was most affected in response to vowels compared to simple and complex tones. These findings suggest that early exogenous responses are similar in ASD for all stimuli, but that individuals with ASD may fail to *attend* to those sounds in a typical manner, especially for speech-sounds. Whitehouse and Bishop (2008) have reported contradictory findings regarding cognitive processes underlying orienting to speech in 15 children with ASD. Specifically, in an oddball paradigm, children with ASD showed reduced orienting to novel tones (as measured by P3a) embedded in a stream of speech sounds, but showed intact orienting to novel speech sounds embedded in a stream of tones, indicating that individuals with ASD are able to attend to speech sounds, but they may use top-down processing to attenuate responses to repeated presentations of speech sounds (Whitehouse & Bishop, 2008). Together these results suggest that there may be some differences in *attending*

to sounds in certain contexts that may be an underlying factor explaining hypo-reactivity in individuals with ASD.

Differences in processing auditory stimuli at subcortical and cortical levels may have implications in individuals' daily functioning in ASD. Using observational and questionnaire data past research has shown evidence of hypo- and/or hyper-reactivity to auditory input in individuals with ASD (Baranek et al., 2006; Dawson et al., 2004). For example, previous retrospective analyses of home videos showed that infants with ASD were less likely to respond to their name between 8 to 12 months of age compared to typically developing controls (Baranek, 1999; Werner et al., 2000). It is possible that hypo-reactivity observed in these studies could be a result of differences in subcortical or cortical regions of the brain, and/or it could also be due to the social nature of the interactions that were measured in these studies. For instance, lack of social motivation may have been an essential factor resulting in lack of responsivity to name in individuals with ASD. A few researchers have examined the effects of social and non-social stimuli on auditory responsivity in individuals with ASD (Baranek et al., 2013; Dawson et al., 2004). For example, Dawson et al. (2004) examined auditory orienting behaviors of 3-to-4-year-olds with ASD ( $n = 72$ ) in response to social and non-social auditory stimuli. Results of this study suggested that children with ASD were less likely to orient to sounds in general, but with more profound differences observed in the social stimuli. On the contrary, Baranek et al. (2013) reported deficits in responding to both social and non-social stimuli in 63 children with ASD indicating a domain-general impairment in orienting to auditory information. A number of fundamental sensory processing patterns can help explain differences in non-social auditory processing environments in individuals with ASD. For example, reduced responsivity to basic auditory stimuli such as tones and clicks may suggest differences in processing of the auditory input at a fundamental level and indicates that behavioral manifestations of hypo-reactivity (such as lack of response to own name) may not just be a result of the social nature of the stimuli. Together these results suggest that, there may be fundamental differences in perceiving and/or attending to auditory stimuli in general and that, although present in response to both social and non-social stimuli, these differences may be more salient in response to social stimuli.

It is essential to examine auditory processing in ASD not just because it could be a distinguishing feature of the disorder (Germani et al., 2014), but because differences in auditory processing could be related to core and associated symptoms of ASD. For example, Donkers et al.



(2015) showed that attenuated early ERP amplitudes (e.g., N2) and reduced P3a were associated with heightened sensory seeking behaviors in the ASD group, indicating that early sensory as well as attention components may contribute to the development of features associated with ASD. Additionally, there was a marginally significant trend for auditory ERP components to predict hyper-reactivity in children with ASD. Surprisingly, hypo-reactivity was not predictive of any neural measures examined in this study. It is important to note that, the ERP measures in Donkers et al. (2015) were based solely on the auditory modality, whereas the behavioral sensory measures were examined across multiple modalities. Future research could examine the relationship between auditory ERP components and behavioral sensory measures only in the auditory modality, which might be more directly impacted by differences in auditory processing at a neural level.

Findings indicating a relationship between neural and behavioral sensory responses are strengthened by results suggesting significant associations between early ERP components and autism symptom severity scores obtained using the Autism Diagnostic Observation schedule (ADOS) in 43 children and adolescents with ASD (Brandwein et al., 2015). Similar associations have been reported with respect to language skills in ASD. For example, delayed latencies of early neural components have been correlated with poorer language functioning in children with ASD (Cardy, Flagg, Roberts, & Roberts, 2008; Riva et al., 2018). In the domain of observational and parent report measures, auditory filtering difficulties obtained via SSP (McIntosh et al., 1999) in children with ASD were found to be associated with hyper-activity, inattention and academic underachievement (Ashburner, Ziviani, & Rodger, 2008). On the other hand, in adults with ASD, poorer performance on auditory discrimination abilities have been associated with severity of restricted and repetitive behaviors (Kargas, López, Reddy, & Morris, 2015). In sum, differences in auditory processing, both at neural and behavioral level may have detrimental consequences for everyday functioning in individuals with ASD. Additionally, associations between auditory functioning and language skills in ASD may have direct implications for individuals' socio-communicative skills, because processing auditory information as well as age equivalent language abilities are fundamental skills required to participate in a variety of social interactions.

### **1.7.2 Tactile processing in ASD**

Tactile processing has received far less attention especially in the neuroscience literature compared to auditory processing in ASD (Schauder & Bennetto, 2016). Common clinical

symptoms reported in ASD in the tactile domain are avoidance of touch, reduced responsivity to touch etc... One way of examining tactile processing in ASD has been to study early somatosensory evoked potentials (SEP) in individuals with ASD (Azouz, Khalil, El Ghani, & Hamed, 2014; Hashimoto, Tayama, & Miyao, 1986; Miyazaki et al., 2007). For example, Miyazaki et al. (2007) examined somatosensory evoked potentials within 30 ms after the electrical stimulation of the median nerve in 24 children with ASD. Result of this study showed delayed peak latency of N20, as well as prolonged interpeak latency of P13/14-N20 in 10 of 24 children with ASD (for similar results, see Azouz et al., 2014). Prolonged interpeak latency of P13/14-N20 suggests central conduction slowing of the somatosensory pathway that carries signals between the brainstem and the sensory cortex (Azouz et al., 2014). Authors of both these studies (Azouz et al., 2014; Miyazaki et al., 2007) argue that, differences in somatosensory functioning in ASD may be due to the dysfunction of the cerebral cortex, and not the brainstem. However, in sharp contrast to these findings Hashimoto et al. (1986) have shown prolonged interpeak latency of earlier components (i.e., P11-P14) in 11 children with ASD following median nerve stimulation, suggesting that differences in somatosensory processing in ASD could be a result of a brainstem dysfunction. These delayed interpeak latencies of both P13/14-N20 and P11-P14 may act as underlying mechanisms of hypo-reactivity to tactile stimuli in ASD.

Additionally, Miyazaki et al. (2007) have also showed enhanced somatosensory evoked potential of N20-P25 in the right hemisphere, which was indicative of hyper-reactivity in the right primary somatosensory area. Association between differences in somatosensory evoked potentials and behavioral manifestations of somatosensory symptoms in children with ASD have been reported in Azouz et al. (2014). Specifically, it was shown that, 11 out of 30 children with ASD displayed hyper- ( $n = 2$ ) and hypo-reactivity ( $n = 4$ ) to touch, as well as hyper- and hypo-reactivity to pain ( $n = 4$ ) and temperature ( $n = 3$ ). Children with hypo-reactivity to touch, pain and temperature also showed delayed interpeak latency of P13/14-N20, whereas children with hyper-reactivity to touch showed enhanced amplitude of N20-P25. However, there was no relationship between deficits in somatosensory evoked potentials and ASD symptom severity (Azouz et al., 2014; Ververi, Vargiami, Papadopoulou, & Tryfonas, 2010). Together, these studies suggest that differences in somatosensory evoked potentials may be an underlying factor for behavioral manifestations of tactile hypo- and/or hyper-reactivity, however, they may not impact symptom severity of ASD. Nonetheless, findings of Azouz et al. (2014) need replication in bigger samples

as association between differences in somatosensory evoked potentials and behavioral manifestations of hypo- and hyper-reactivity to touch in children with ASD were based on just a very small subgroup of children in the entire sample.

In addition to somatosensory evoked potentials, early responsivity to touch has been studied in psychophysical studies with children as well as with adults with ASD. For example, Güçlü, Tanidir, Mukaddes, and Ünal (2007) examined tactile detection thresholds to 40 and 250 Hz vibrotactile stimuli in 6 children with and without ASD. The results of this study indicated no significant differences between the ASD and the control groups in detection thresholds, indicating that children with ASD show typical perception of tactile information. They did, however, report an association between tactile and emotional subscales of the Sensory Profile (Dunn, 2014) and the Touch Inventory for Elementary School Aged children (Royeen & Fortune, 1990). Therefore, the authors argue that hypo- and/or hyper-reactivity to touch may be a result of emotional difficulties rather than being related to differences in perceiving tactile stimuli. Nevertheless, it is possible that lack of a difference in detection thresholds between groups in Güçlü et al. (2007) may have been a result of low statistical power. Specifically, this study only had 6 participants in each of their ASD and control groups, and this low sample size might have failed to produce significant group differences which may be observed in a larger sample.

Additional support in favor of intact tactile perception comes from O’Riordan and Passetti (2006) in that, they examined 13 high-functioning children with ASD compared to 13 TD controls on their ability to discriminate the texture of different grades of sandpaper presented to the hand, and to detect touches presented with synthetic fibers on the arm. Findings of this study indicated no differences in the detection and discrimination abilities between the two groups, suggesting typical tactile perception in children with ASD. On the contrary, Puts et al. (2014) showed higher static detection thresholds for 25 Hz stimuli in 32 children with ASD compared to age and IQ-matched TD controls. However, the two groups did not differ in their detection thresholds when the stimuli were presented dynamically (i.e., stimuli increasing from zero amplitude). Higher static thresholds (i.e., hypo-reactivity) in children with ASD ( $n = 21$ ) were also reported in Tavassoli et al. (2016). Additionally, Tavassoli et al. (2016) showed that children with ASD who had higher static detection thresholds also had greater ASD traits as measured using the autism spectrum quotient scores.

Differences in tactile perception have also been observed in adults with ASD. For example, in Blakemore et al. (2006) detection thresholds were examined in response to 30 and 200 Hz vibrotactile stimuli presented on the fingertip in 16 adults with ASD. The results showed that adults with ASD had lower detection thresholds for 200, but not for the 30 Hz stimuli, indicating hyper-reactivity in response to high-frequency (200 Hz) tactile stimuli. Cascio et al. (2008) examined tactile perception of light touch and vibrations as well as thermal sensations on the palm and the forearm in adults with ( $n = 8$ ) and without ( $n = 8$ ) ASD. Touch presented on the forearm is innervated by the low threshold unmyelinated tactile mechanoreceptors called the CT-afferents (associated with social/affiliative touch; Olausson et al., 2002; Wessberg et al., 2003), whereas, touch on the palm is innervated by myelinated tactile mechanoreceptors. Participants in both the groups displayed similar detection thresholds to light touch on both the locations. Additionally, the groups did not differ in their hedonic ratings of the pleasantness of textures. However, adults with ASD did show lower detection thresholds (heightened sensitivity/hyper-reactivity) to vibrations presented on the forearm, as well as greater sensitivity to thermal pain presented on both sites. Together, psychophysical studies with children and adults suggest evidence of both, intact and altered tactile processing in ASD.

Beyond the somatosensory evoked potentials and psychophysical measures, tactile processing has been studied by examining early cortical functioning in response to touch. Using MEG, Marco et al. (2012) recently showed that 7 male participants with ASD showed smaller cortical responses to slow-rate tactile stimuli (presentation of just the deviant stimuli at the same rate as the deviant presented in an oddball paradigm). Post-hoc analyses showed that amplitudes of cortical responses were directly correlated with scores on the tactile sensory profile. This suggests that early cortical differences in processing touch may be an underlying factor for observable differences in response to tactile stimulation.

Another possible explanation underlying differences in tactile processing in ASD could be attributed to the cognitive processes in ASD. This hypothesis was tested in Cascio et al. (2015) in that 21 high-functioning children with ASD were presented with air puffs on their fingertips while they were asked to attend to the stimuli. Results of this study showed that the timing of ERP responses were associated with parental measures of tactile hypo- and hyper-reactivity in ASD. For instance, earlier ERP responses were related to measures of hyper-reactivity, whereas, later ERP components (indicative of attentional capture) were related to hypo-reactivity. The authors,

therefore, concluded that behavioral manifestations of hypo-reactivity in ASD may be more related to cognitive functions such as allocation of attention rather than being related to tactile perception. These findings may provide additional understanding regarding the contradictory results of the psychophysical studies. It is possible that although individuals with ASD have intact tactile perceptual abilities (i.e., no differences in detection thresholds compared to controls), their atypical responsivity to touch could be a result of later cortical processes such as attending to that perceived touch.

Differences in tactile processing at neurological and psychophysical levels may have consequences at a behavioral level in individuals with ASD. For example, using tactile stimuli (shoulder tap, air puff), Baranek et al. (2013) showed that children with ASD ( $n = 63$ ) were less responsive to both kinds of tactile stimuli compared to TD controls. Differences in processing tactile information have also been observed in 13 infants at high risk for ASD (Kadlaskar et al., 2019). Specifically, it was shown that infants at high risk for ASD were less responsive to touch, and when they did respond, they were more likely to respond away from touch. Additionally, responsivity to touch was correlated with participants' ASD symptom severity measured using the Autism Diagnostic and Observation Schedule (ADOS). Other empirical studies have also shown associations between tactile responsivity and core features of ASD (Foss-Feig, Heacock, & Cascio, 2012; Hilton et al., 2010). For example, Foss-Feig et al. (2012) recently showed that tactile hypo-reactivity is associated with greater impairments in social communication in children with ASD ( $n = 34$ ). Surprisingly, tactile hyper-reactivity was not related to any of the core features of ASD (Foss-Feig et al., 2012). One possibility for this surprising finding could be that, any social impairments associated with hyper-reactivity to touch may have been characteristic of just a small subgroup of children with ASD who participated in this study. Therefore, the overall heterogeneity of sensory profiles may have impacted these results. Hilton et al. (2010) have added to this literature by showing significant relationships between atypical responsivity to touch and social impairments in children with ( $n = 36$ ) and without ( $n = 26$ ) ASD. Associations between hyper-reactivity to touch and social functioning have been reported in 143 adults with ASD (Lundqvist, 2015). These results indicate that differences in responding to touch may impact individual's social skills throughout the development. In sum, differences in tactile processing are evident in behavioral, psychophysical and neurological observations in ASD, and these differences may affect social functioning in individuals with ASD.

## 1.8 Research objectives

The pattern of hypo- and hyper-reactivity to auditory and tactile stimuli is commonly observed in individuals with ASD and may reflect poor modulation of incoming sensory information. There have been several competing theories underlying differences in auditory and tactile processing in individuals with ASD. For instance, these differences have been associated with atypical physiological arousal levels in ASD (DesLauriers & Carlson, 1969; Hutt et al., 1964; Rimland, 1964), intense sensory surroundings (Markram et al., 2007), lack of social motivation (Chevallier et al., 2012) to name a few. As discussed throughout the first chapter, the literature in sensory processing in auditory and tactile modalities is mixed. One of the common themes observed in both these modalities is the presence of both intact and altered perceptual skills in individuals with ASD. These inconsistent findings have led researchers to theorize that differences in auditory and tactile processing are a result of deficits in early sensory responses (Bruneau et al., 2003; Marco et al., 2012; Puts et al., 2014; Tavassoli et al., 2016), or, alternatively, that these differences may be attributed to atypical attentional processing in ASD (Cascio et al., 2015; Čeponienė et al., 2003). In this dissertation using ERP, I aim to examine neural indices of both perceptual and attentional functioning underlying tactile and auditory processing in children with ASD compared to TD controls. I hypothesize that, if differences in behavioral sensory profiles in ASD are related to atypical perceptual abilities then there would be differences in early ERP components in children with ASD. On the other hand, if differences in tactile and auditory processing are related to attentional components, then there would be differences in later ERP components that are indicative of involuntary attentional capture in children with ASD compared to TD children.

Next, given that touch facilitates learning and attention in typical development (Hertenstein, 2002; Jean & Stack, 2009; Stack & Muir, 1992), I will examine if tactile cues improve behavioral performance in children with ASD compared to TD controls. I hypothesize that, if children with ASD show differences in behavioral sensory profiles in the tactile domain, then they will demonstrate reduced touch-related facilitation compared to TD children. Last, because differences in processing tactile and auditory stimuli could impact the emergence of social communication skills, the present studies will examine the relationship of neural and behavioral indices of tactile and auditory processing with socio-communicative impairments, language, and overall symptom severity in ASD. I hypothesize that neurological differences underlying perceptual and/or

attentional processing of tactile and auditory stimuli as well as decreased touch-related facilitation will be associated with greater socio-communicative impairments, reduced language skills, and greater overall symptom severity in children with ASD.

## 2. ELECTROPHYSIOLOGICAL MEASURES OF TACTILE AND AUDITORY PROCESSING IN CHILDREN WITH ASD

### 2.1 Abstract

**Introduction:** Touch plays a key role in facilitating social communication in humans. Many individuals with autism spectrum disorder (ASD) often show atypical tactile responsivity, which is associated with increased ASD symptomatology. However, the neural mechanisms associated with responsivity to touch in ASD remain unknown with contrasting theories suggesting differences in both perceptual and attentional processes underlying atypical tactile responsiveness. Given the importance of touch in everyday life and that touch is mostly presented in conjunction with speech, the current study investigates neural indices of perceptual and attentional factors underlying tactile and auditory processing in children with and without ASD.

**Objectives:** I examined (1) whether atypical processing of tactile and auditory information in ASD is related to differences in early sensory or later attentional processes compared to TD children, and (2) the relationship between neural indices of tactile and auditory processing and ASD symptomatology and (3) language skills in children with and without ASD.

**Methods:** Participants included 14, 6-to-12-year-olds with ASD and 14 age- and non-verbal IQ matched typically developing (TD) children. During the experiment, children participated in an ERP oddball paradigm during which they watched a silent video while being presented with tactile and auditory stimuli (i.e., 80% standard speech sound /a/; 10% oddball speech sound /i/; 10% novel vibrotactile stimuli on the fingertip with standard speech sound /a/). The task contained 1200 trials in total, which were divided into 4 blocks of 300 trials each. Children's early and later ERP responses to tactile and auditory stimuli were examined.

**Results:** Repeated measures ANOVAs were calculated separately for each of the early and later ERP components to novel tactile and auditory oddball stimuli. Findings indicated that children with ASD showed similar early as well as later ERP amplitudes in response to both tactile and auditory stimulation compared to their TD peers, suggesting equivalent neural responsivity to touch and speech sounds in the ASD group. Correlational analyses suggested that smaller early ERP amplitude to novel touch was related to increased tactile symptoms in all participants. Additionally, smaller early amplitudes to auditory oddball stimuli were related to increased differences in social communication skills and greater levels of hyper-reactivity in all children.



Larger late ERP amplitudes to touch and auditory stimuli were associated with poorer reciprocal social skills and increased hyper-reactivity respectively in TD children. Finally, larger late ERP responses to auditory oddball stimuli were related to better language skills in all children.

**Conclusion:** Children with ASD may display typical early and later neural responses to tactile and auditory stimuli, suggesting equivalent perceptual and attentional processing of incoming sensory stimuli compared to TD children. Widely reported differences in behavioral responses to sensory stimuli could be attributed to social contexts in which sensory stimuli are more likely to be encountered in everyday life. Additionally, for the tactile modality, location of the touch could play a significant role in determining children's responsivity to touch. Finally, neural responsivity to tactile and auditory stimuli may be linked with sensory responsivity and social skills in all children.

## 2.2 Introduction

Processing sensory information is important for the development of socio-communicative skills (Bundy, Lane, & Murray, 2002). From birth, perception of sensory information enables individuals to recognize various sources of information as well as to extract meaningful information coming from different sensory modalities. Additionally, perception of sensory information allows the child to notice patterns from which she/he can calculate statistical regularities essential to socio-communicative learning (Saffran, 2003; Saffran et al., 1996; Smith & Yu, 2008). For example, in the auditory modality, infants have been shown to use sequential statistics to segment word boundaries from continuous speech (Saffran et al., 1996). Evidence of extracting meaningful patterns from sensory information using visual and tactile inputs has also been observed in typical development (Bulf, Johnson, & Valenza, 2011; Kirkham, Slemmer, & Johnson, 2002; Seidl et al., 2015). Processing sensory information, therefore, lays the foundation for extracting meaningful information, as well as for generalizing these meanings to novel category members (Lany & Saffran, 2010); skills required during social communication. Therefore, perception of sensory information becomes an important skill that impacts our learning and the development of socio-communicative abilities.

However, between 42 – 96% of individuals with ASD display some form of differences in responding to sensory information compared to typically developing individuals (Baranek et al., 2006; Ben-Sasson et al., 2009; Lane et al., 2011; Leekam et al., 2007; Marco et al., 2011; Tomchek

& Dunn, 2007) as well as individuals with other developmental disorders (DD; Rogers, Hepburn, & Wehner, 2003; Watson et al., 2011; Wiggins, Robins, Bakeman, & Adamson, 2009). These differences in sensory processing are manifested in at least three unique behavioral response patterns (Ausderau et al., 2014; Baranek et al., 2006; Ben-Sasson et al., 2009; Dunn, 1997; Miller et al., 2007): (a) hyper-reactivity (e.g., exaggerated behavioral responses to sensory stimuli), (b) hypo-reactivity (e.g., reduced or slowed responses to sensory stimuli), and (c) sensory seeking (e.g., sensory experiences that are prolonged and intense). Differences in sensory processing have been observed in infants (Ben-Sasson et al., 2008), children (Leekam et al., 2007), and adults with ASD (Crane et al., 2009), and are associated with social, linguistic, and adaptive skills (Baranek et al., 2013; Lane et al., 2010) making them an important area to explore in the field of ASD.

A review of the past literature suggests that different patterns of sensory responsivity are present across all modalities in individuals with ASD (Dudova et al., 2011; Kern et al., 2007). Nonetheless, the majority of prior studies examining sensory processing in ASD have primarily focused on auditory and visual modalities due to their role in language and socio-communicative development (Bremner et al., 2012). However, the tactile modality, a channel exploited frequently during human interactions (Stack & Muir, 1990), is also used as a communicative signal (Dunbar, 2010; Hertenstein, Verkamp, et al., 2006). Furthermore, recent research has also shown links between the ability to process tactile information presented with speech and finding word boundaries in typically developing infants (Seidl et al., 2015). These findings suggest that, similar to auditory and visual modalities, tactile processing may be important for the development of socio-communicative skills in humans.

Acknowledging the importance of touch in social communication, a few researchers have examined tactile processing in children with ASD using observational (Baranek et al., 2013; Foss-Feig et al., 2012; Kadlaskar et al., 2019), psychophysical (O’Riordan & Passetti, 2006; Puts et al., 2014; Tavassoli et al., 2016), and neuroimaging methods (Cascio et al., 2015; Marco et al., 2012; Miyazaki et al., 2007). For example, using observational measures, Baranek et al. (2013) showed that children ( $n = 63$ ) with ASD were less responsive to both social (shoulder tap) and non-social (air puff) tactile stimuli compared to TD controls. Similar differences in responding to tactile stimuli were observed in infants at high risk for ASD (Kadlaskar et al., 2019). In particular, Kadlaskar et al. showed that infants at high risk for ASD (i.e., infants who had an older sibling with ASD) were overall less responsive to maternal touch during natural interactions, and that

when they did respond, they were more likely to orient away from the interaction. Both these observational studies suggest atypical responsivity to touch in children with ASD. However, studies using psychophysical measures have yielded mixed results suggesting both intact (Güçlü et al., 2007; O’Riordan & Passetti, 2006) and atypical (Puts et al., 2014; Tavassoli et al., 2016) tactile processing in children with ASD. Together, these studies indicate that differences in responding to tactile information may be present at behavioral and perceptual levels in at least *some* individuals with ASD. However, they do not highlight underlying mechanisms that may regulate individual responses to tactile information.

Few studies to date have addressed this issue by using neuroimaging methods to examine tactile processing in children with ASD (Cascio et al., 2015; Marco et al., 2012; Miyazaki et al., 2007). Neuroimaging methods provide a unique opportunity to examine neural processes underlying atypical sensory responsivity. For example, Marco et al. (2012) used three different conditions to examine early cortical functioning in response to touch in 7 male children (aged 7-11 years) with and without ASD. In condition one, participants were presented with an oddball paradigm that included a stream of tactile stimulations on the tip of the second (standard; 83% of times) and third digits of the hand (deviant; 17% of times). Conditions two and three involved presentation of just the deviant stimuli at the same rate as the deviant (slow rate) and standard (fast rate) stimuli in the oddball paradigm. The results indicated that children with ASD showed smaller amplitudes of early (S1) cortical responses in the left somatosensory cortex in response to slow and deviant tactile stimuli. Additionally, participants’ cortical activity was directly correlated with scores on the Tactile Sensory Profile (Dunn & Westman, 1997) suggesting a relationship between behavioral and neural indices of tactile processing. Similar to studies in the psychophysical literature, research in the neuroimaging field has yielded mixed results. For instance, unlike Marco et al. (2012), a recent study (Miyazaki et al., 2007) showed enhanced somatosensory processing in even earlier components (N20-P25) in the right hemisphere, indicating hyper-reactivity in the right primary somatosensory area. Together these results suggest that differences in tactile responsivity may be related to early differences in somatosensory processing.

An alternate explanation underlying differences in tactile processing in ASD could be attributed to the cognitive processes in ASD. This argument was tested in Cascio et al. (2015). Here, 21 high-functioning children with ASD (aged 5-17 years) were presented with air puffs on their fingertips while they were asked to attend to the sensory stimuli. Results indicated that the

timing of ERP responses were associated with parent-report measures of tactile hypo- and hyper-reactivity in both the ASD and TD groups. Specifically, earlier ERP responses (approximately 120-220 ms post-stimulus) were related to measures of hyper-reactivity in both the ASD and TD groups, whereas, later ERP components (220-270 ms post-stimulus; indicative of attentional capture) were related to hypo-reactivity in the ASD group. The authors, therefore, concluded that behavioral manifestations of hypo-reactivity in ASD may be more related to cognitive functions such as allocation of attention rather than being related to differences in tactile perception. These findings support the atypical attentional processing theory, indicating that, domain-general impairments in basic attentional processes (Keehn et al., 2013) may explain at least some of the differences in responding to sensory information in ASD. This argument may provide additional understanding regarding the contradictory results in the field of tactile processing. It is possible that, although, some individuals with ASD have intact tactile perceptual abilities (no differences in detection thresholds compared to controls; Güçlü et al., 2007; O’Riordan & Passetti, 2006), their atypical behavioral responsivity to touch could be a result of later cortical processes such as attending to that perceived touch.

At present, there exists only one ERP study (Cascio et al., 2015) that has examined attentional processes underlying tactile stimuli in individuals with ASD, making it challenging to generalize across individuals with similar conditions. Nonetheless, findings indicating atypical attentional processing in the tactile modality are in agreement with research examining sensory processing in the auditory modality in individuals with ASD. For example, using an oddball paradigm, Čeponienė et al. (2003) reported that children with ASD showed typical early exogenous responses to auditory stimuli, but failed to *attend* to those stimuli in a typical manner (measured by later ERP components), suggesting that impairments in basic attentional processes may underlie atypical responsivity to auditory sensory stimuli. However, findings regarding underlying attentional processes in the auditory modality are not uniform. In particular, Whitehouse and Bishop (2008) showed that individuals with ASD *are able* to attend to certain sounds, but they may use top-down processing to attenuate responses to repeated presentations of these sounds (Whitehouse & Bishop, 2008). Additionally, similar to the findings in the tactile modality (Marco et al., 2012; Miyazaki et al., 2007), there also exists evidence in the auditory modality suggesting differences in basic perceptual sensory processing in ASD (Bruneau et al., 2003; Fujikawa-Brooks et al., 2010; Rosenhall et al., 2003). Together, these findings suggest two

possible explanations underlying differences in sensory processing in ASD: (1) sensory processing differences may have their roots in basic perceptual differences, and/or (2) differences in sensory responsivity may be related to differences in basic attentional processes.

In sum, given the paucity of neuroimaging research in the tactile modality, and contrasting neuroimaging findings in the available tactile processing literature in ASD (Cascio et al., 2015; Marco et al., 2012), the current study sought to investigate neural mechanisms underlying tactile processing in children with ASD. However, we know that, the majority of human interactions are multimodal in nature, and that, touch is rarely presented in isolation. For instance, (Kadlaskar et al., 2020) showed that, during mother-infant naturalistic interactions the majority of maternal communication that involved touch also included speech that was directed towards infants at high and low risk for ASD. Thus, in order to increase the ecological validity of this study, I examined how children with ASD process touch in the context of processing speech sounds. Therefore, my first objective was to examine neural indices of perceptual and attentional factors (measured by early and late ERP components respectively) underlying tactile and auditory processing in children with ASD compared to TD controls. I predicted that, if differences in behavioral sensory patterns in ASD are related to atypical perceptual abilities then there may be differences in early ERP components in children with ASD. On the other hand, if differences in auditory and tactile processing are related to attentional components, then there may be differences in later ERP components that are indicative of involuntary attentional capture in children with ASD compared to TD children.

Next, because prior research has provided evidence suggesting an association between differences in tactile and auditory responsivity and core features of ASD (Foss-Feig et al., 2012; Hilton et al., 2010; Kadlaskar et al., 2019; Kargas et al., 2015; Linke, Keehn, Pueschel, Fishman, & Müller, 2018), my second objective was to examine the association between neural indices of tactile and auditory processing and ASD symptomatology measured by the Autism Diagnostic Observation Schedule-2 (ADOS-2; Lord et al., 2012), the Social Responsiveness Scale-2 (SRS-2; Constantino, 2012), and the Sensory Profile-2 (SP-2; Dunn, 2014). Last, given that early linguistic input is often coupled with caregiver touches (Abu-Zhaya et al., 2017; Nomikou & Rohlfsing, 2011), and that touch may also support early speech perception skills (Seidl et al., 2015), my third objective was to examine the relationship between neural indices of tactile and auditory processing and receptive and expressive language skills measured using the Peabody Picture Vocabulary Test-

4 (PPVT-4; Dunn & Dunn, 2007) and the Expressive Vocabulary Test-2 (EVT-2; Williams, 2007), respectively. I predicted that, atypical neural amplitudes for attention and/or perception underlying touch-speech processing may be associated with greater ASD symptomatology and reduced language skills in children with ASD.

## **2.3 Methods**

### **2.3.1 Participants**

Participants in this study included 14 children with ASD (11 males) and 14 age-, sex- and nonverbal IQ-matched TD children (11 males) with no reported history of ASD (Table 2.1). In order to reduce the total testing time and to increase participant compliance, IQ-based matching was determined by using just the Verbal and Nonverbal scales of the Wechsler Abbreviated Scale of Intelligence (ASD 10, TD 8; WASI-II; Wechsler, 2011) or the Differential Ability Scale II (ASD 4, TD 6; DAS-II; Elliott, 2007). Verbal and Nonverbal IQ scales of the WASI-II are highly correlated with Verbal and Nonverbal scales of the DAS-II ( $r = .69$  to  $.70$ ; Elliott, 2007). Clinical diagnoses for the ASD group were confirmed using the Autism Diagnostic Observation Schedule, Second Edition (ADOS-2; Lord et al., 2012), and the Social Communication Questionnaire (SCQ; Rutter, Bailey, & Lord, 2003). All children in the ASD group were administered the ADOS-2 Module 3. Additionally, the presence or absence of clinically significant ASD symptomatology was confirmed for participants in both the groups using the parent reported Social Responsiveness Scale-2 (SRS-2; Constantino, 2012).

Participants with ASD were recruited from local Applied Behavior Analysis (ABA) therapy centers, departmental registry, and community sources. TD participants were recruited from the departmental registry and community sources. Out of 28 participants, 24 (11 ASD, 13 TD) were right-handed as measured by the Edinburgh Handedness Inventory (EHI; Oldfield, 1971). All participants and their caregivers provided written assent and consent prior to participating in the study. All study procedures were conducted in accordance with the Purdue University Institutional Review Board. No children in the ASD group reported the presence of other ASD-related medical conditions (e.g., fragile-X syndrome, tuberous sclerosis). Lastly, 3 additional participants in the ASD group were excluded from the final sample due to refusal to participate in the EEG task ( $n = 2$ ) or due to excessively noisy EEG data ( $n = 1$ ).

Table 2.1. Participant demographics

	ASD	TD	Statistic	<i>p</i>
N (M:F)	14 (11:3)	14 (11:3)	$X^2(1) = .00$	1.0
Age (years)	10.13 (1.9); 6.17-12.58	9.95 (1.36); 7.78-12.53	$t(26) = .29$	.77
Handedness (R:L)	11:3	13:1	$X^2(1) = 1.16$	.28
Verbal IQ	98 (21); 67-126	117 (11); 94-135	$t(26) = -2.97$	.006
Nonverbal IQ	108 (18); 74-136	117 (16); 89-144	$t(26) = -1.46$	.15
ADOS-2				
Social Affect	10 (5); 4-20	-	-	-
Repetitive Behavior	3 (2); 1-6	-	-	-
Severity Scores	8 (2); 4-10	-	-	-
Sensory Profile-2				
Touch Raw Score	24 (9); 5-41	10 (5); 0-15	$t(26) = 4.96$	<.001
Auditory Raw Score	28 (7); 15-38	12 (4); 2-21	$t(26) = 7.41$	<.001
Sensitivity Index	13 (14); -3-46	4 (15); -33-34	$t(26) = 1.62$	.11
Usable Trials (N)				
Standard	552 (150); 368-857	654 (161); 405-871	$t(26) = -1.73$	.09
Oddball	71 (21); 46-107	83 (21); 49-112	$t(26) = -1.45$	.15
Novel	69 (21); 36-108	84(20); 49-109	$t(26) = -1.99$	.06

*Note.* IQ determined using the Wechsler Abbreviated Scale of Intelligence, Second Edition (WASI-II; Wechsler, 2011) or the Differential Ability Scale, Second Edition (DAS-II; Elliott, 2007).

Mean (SD); range

## **2.3.2 Standardized measures**

### ***2.3.2.1 Autism Diagnostic Observation Schedule-2 (ADOS-2)***

The ADOS-2 (Lord et al., 2012) is a widely used semi-structured play-based interaction designed to measure autism symptoms in five domains: Language and communication, reciprocal social interaction, play, stereotyped behaviors and restricted interests, and other abnormal behaviors. The ADOS-2 consists of five modules, which can be administered to children and adults based on their developmental and language levels. In the present study, all children in the ASD group were administered Module 3 which is typically used with children and adolescents with fluent speech. Severity scores from the ADOS-2 diagnostic algorithm were used as symptom measures while addressing Objective 2 with higher ADOS-2 scores reflecting greater severity (Gotham, Pickles, & Lord, 2009).

### ***2.3.2.2 Social Responsiveness Scale (SRS-2)***

The SRS-2 (Constantino, 2012) is a 65-item caregiver-report questionnaire that provides a quantitative measure of autism-related traits in children. The SRS-2 is used as a measure of children's social impairments and focuses on their behaviors during the past 6 months. Caregivers respond to each item using a four-point Likert scale with a score of 1 indicating a behavior that is not present and 4 indicating a behavior that is almost always present. This scale offers three forms; Preschool (ages 2.5 to 4.5 years), School-Age (ages 4 to 18), and Adult (ages 19 and up; this form is administered as a self-report questionnaire). The present study administered the School-Age form to participants in both the groups. The SRS-2 Standard scores as well as Social Communication and Interaction (SCI) and Restricted Interests and Repetitive Behavior (RRB) scores were used as measures of ASD symptom severity, with higher scores reflecting greater severity, while examining the association between neural correlates of tactile and auditory processing and ASD symptomatology (Objective 2).

### ***2.3.2.3 Sensory Profile-2 (SP-2)***

The SP-2 (Dunn, 2014) is a caregiver-report questionnaire designed to assess everyday sensory processing in 3- to 14-year-olds. It consists of 86 items that are divided into six sensory categories (auditory, visual, touch, movement, body position, and oral), three behavioral categories



(conduct, social emotion, and attention), and four quadrants (seeking, avoiding, sensitivity, and registration). Parents respond to each item using a five-point Likert scale with a score of 1 indicating a behavior that is present almost never and 5 indicating a behavior that is present almost always. Scores from the Touch and Auditory Sensory Profile were used as measures of tactile and auditory sensory processing respectively. Additionally, scores from four quadrants were used to calculate a sensitivity index score while examining the association between neural correlates of tactile and auditory processing and ASD symptomatology (Objective 2).

#### ***2.3.2.4 Peabody Picture Vocabulary Test- 4 (PPVT-4)***

The PPVT-4 (Dunn & Dunn, 2007) was administrated to examine the association between neural correlates of tactile and auditory processing and receptive language skills in children with and without ASD. The PPVT-4 (Dunn & Dunn, 2007) is a standardized assessment that measures single word receptive language skills in children and adults. It is conducted in a structured format where the examiner orally presents a target word along with four pictures, and the participant is instructed to select the picture that best represents the meaning of the target word. PPVT-4 standard scores were used as measures of receptive language skills with higher scores reflecting greater receptive language skills (Objective 3).

#### ***2.3.2.5 Expressive Vocabulary Test (EVT-2)***

The EVT-2 (Williams, 2007) was administrated to examine the association between neural correlates of tactile and auditory processing and expressive language skills in children with and without ASD. The EVT-2 (Williams, 2007) is a standardized assessment that measures single word expressive language skills in children and adults. It is conducted in a structured format where the participant is instructed to name pictures that are presented one at a time. EVT-2 standard scores were used as measures of expressive language skills with higher scores reflecting greater expressive language skills (Objective 3).

### **2.3.3 Experimental stimuli**

#### **2.3.3.1 Auditory stimuli**

Auditory stimuli consisted of two vowels (/a/ and /i/) generated using the Praat software (Boersma & Weenink, 2019). Stimuli were created in Praat to maintain a fundamental frequency of 140 Hz (as it fits within the pitch range of a typical male speaker; Goy, Fernandes, Pichora-Fuller, & van Lieshout, 2013), and to set the duration of these vowels as 200 ms (similar to the duration of stimuli used in Whitehouse & Bishop, 2008). Auditory stimuli were presented at a comfortable listening level (60 dB) using a speaker located approximately 60 cm from the participant.

#### **2.3.3.2 Tactile stimuli**

A customized tactor was used to deliver vibrotactile stimuli to participants' index fingertip of the non-dominant hand (Figure 2.1a). Vibrotactile stimuli were delivered on the fingertip to be consistent with the location of the tactile stimuli in past studies that have examined touch responsivity in individuals with ASD (Blakemore et al., 2006; Cascio et al., 2015; Marco et al., 2012). Vibrotactile stimuli were presented to the non-dominant hand because participants were instructed to respond using their dominant hand in a separate experiment (please refer to Chapter 3 for more details). Tactile stimuli consisted of vibrotactile stimulation presented at a frequency of 290 Hz. A vibrotactile frequency of 290 Hz was chosen because individuals with ASD have shown differences in tactile responsivity to high-frequency, but not low-frequency, vibrations (Blakemore et al., 2006) that stimulate Pacinian corpuscles; a type of mechanoreceptor that is sensitive to vibrotactile stimuli ranging from 100 – 300 Hz (Johnson, 2001). Participant's hand was covered with a white cloth to mask the sound coming from the tactor, and also because seeing somatosensory stimulation have been shown to modulate somatosensory cortical responses (Taylor-Clarke, Kennett, & Haggard, 2002). Last, similar to the duration of the auditory stimuli, tactile stimuli also lasted for 200 ms.

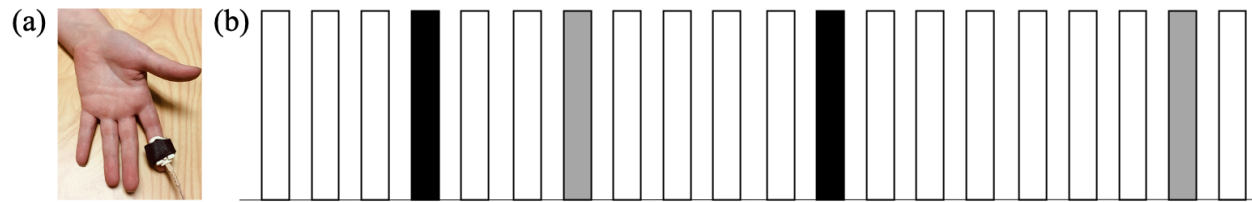


Figure 2.1. (a) Mechanical tactor used to deliver the vibrotactile stimuli. (b) Illustration of the oddball paradigm. White bars represent the standard stimuli /a/ (80%), black bars represent the oddball stimuli /i/ (10%), and grey bars represent the novel vibrotactile stimuli on the fingertip along with the speech sound /a/ (10%). Each stimulus lasted for 200 ms (ISI = 1400 ms).

### 2.3.4 Procedure

To ensure the cooperation of all participants, the total testing time was divided into two sessions. Session 1 included consenting the individual and his/her family, and standardized testing. Session 2 included data collection using EEG.

Session 1 was conducted in a brightly lit room with child sized furniture. After an experimenter explained the procedure, caregivers and participants provided their written informed consent and assent respectively. Next, a trained examiner administered the ADOS-2 (Lord et al., 2012) only to participants in the ASD group. Finally, all participants were administered standardized cognitive and language measures along with the Edinburgh Handedness Inventory (Oldfield, 1971), while the caregivers completed the SCQ (Rutter et al., 2003), the SRS-2 (Constantino, 2012), and the SP-2 (Dunn, 2014). Session 2 was conducted within a month after completing session 1.

During session 2, EEG data were collected in a dimly lit room. Participants were seated at a conformable viewing distance of approximately 60 cm from a computer monitor. Prior to applying the EEG net, the child's head was measured, and a small mark was made at the top of the participant's head to allow proper placement of the net. Before the net was placed over the participant's head, the sponges were soaked in a salt-water solution (distilled water + potassium chloride (KCl) + baby shampoo). The elastic tension structure allowed the net to be quickly and easily stretched over the participant's head. No cleaning or abrasion of the scalp was necessary, and there were no gels or creams to clean up afterwards. This procedure was consistent with previous ERP studies that used similar EEG equipment (McPartland, Dawson, Webb, Panagiotides, & Carver, 2004; Shuffrey et al., 2018). After the net application, the tactor was placed on the participants' index fingertip of the non-dominant hand and was covered using a hand towel to

mask the sound coming from the tactor. Participants were instructed to sit still throughout the duration of the experiment. A trained research assistant sat behind the participant to ensure that participants were following the instructions. Next, a passive auditory oddball paradigm was employed. Participants watched a silent video of their choice on the computer monitor and were presented with auditory stimuli consisting of 80% of the standard stimuli (the speech sound /a/), 10% of the oddball stimuli (the speech sound /i/), and 10% of the novel stimuli (vibrotactile stimulation on the fingertip of the index finger along with the standard speech sound /a/; Figure 2.1b). The task contained 1200 trials in total, which were divided into 4 blocks of 300 trials each. The stimuli were presented randomly (ISI = 1400 ms) with at least two standard stimuli prior to every oddball and novel stimuli. In all four blocks, participants were instructed to watch the movie and ignore the sounds and the “tingles”.

### **2.3.5 Electroencephalography (EEG)**

#### ***2.3.5.1 EEG acquisition***

EEG data were recorded using 124 or 128-channel HydroCel Geodesic Sensor Nets (HCGSN, Electrical Geodesics, Inc., Eugene, OR) with NetAmps 400 amplifier. Electrooculography (EOG) electrodes (i.e., 125, 126, 127, 128) in a 128-channel net were excluded from data collection because EOG electrodes that are usually placed on participant’s face may reduce compliance in participants. EEG data were recorded in Net Station 5.2 software (HCGSN, Electrical Geodesics, Inc., Eugene, OR). The continuous EEG data were digitized at 500 Hz and referenced online to the vertex (electrode Cz). Impedances were kept below 100 k $\Omega$ . A 0.1 Hz high-pass filter was applied to the raw data, which was subsequently segmented into 1100 ms epochs (100 ms pre- and 1000 ms post-stimulus onset).

#### ***2.3.5.2 EEG pre-processing***

EEG data processing was completed offline using a MATLAB-based toolbox EEGLAB (Delorme et al., 2011). First, the raw EEG data were digitally filtered using a 0.5 – 50 Hz bandpass filter. Epochs in each channel were marked bad if they had amplitude values exceeding  $\pm 150$   $\mu$ V. Subsequently, channels were marked bad if they had more than 25% of epochs rejected. Manual artifact detection was then carried out on continuous EEG data to reject non-stereotyped artifacts.

After filtering and removal of non-stereotyped artifacts, Independent Component Analysis (ICA; Jung et al., 2000) was carried out in EEGLAB. SASICA was then used to identify artifacts associated with eye movements, saccades, muscle contractions, and bad channels (Chaumon, Bishop, & Busch, 2015). After removing artifactual independent components, bad channels were replaced using spherical interpolation, and data were re-referenced to the average reference. Finally, epochs in ICA-corrected data with extreme amplitudes ( $\pm 150 \mu\text{V}$ ) were rejected and any remaining channels with more than 25% of bad epochs were interpolated.

Before analyses, participants ( $n = 1$ ; ASD) with fewer than 20 usable trials in each of the stimulus types (standard, oddball, novel) were excluded. The decision to exclude participants with fewer than 20 usable trials was based on past research requiring a minimum of 10 usable trials in each condition to be included in the final sample (Wagner, Hirsch, Vogel-Farley, Redcay, & Nelson, 2013).

### ***2.3.5.3 Event-related potential (ERP) processing***

ERP data processing was completed using ERPLAB toolbox (Lopez-Calderon & Luck, 2014) in MATLAB. Following filtering, artifact correction and rejection, and re-referencing to average reference, averaged ERPs from accepted epochs were created for each stimulus type (standard, oddball, novel). Next, regions of interest (ROIs) were generated using 9 clusters of EGI HydroCel GSN electrodes in the left-frontal (32, 26, 33, 27), left-central (35, 40, 41, 36), left-posterior (51, 58, 59, 52), mid-frontal (11, 4, 19, 16), mid-central (129, 55, 106, 7), mid-posterior (62, 67, 72, 77), right-frontal (1, 2, 123, 122), right-central (104, 103, 109, 110) and right posterior (92, 97, 91, 96) regions (Figure 2.2). In order to examine tactile sensory components, I primarily focused on left-central and right-central ROIs. These ROIs were chosen to examine ipsi- and contralateral activation in response to tactile stimulation. Auditory sensory components were examined by analyzing mid-frontal, mid-central and mid-posterior ROIs. These ROIs were chosen based on previous evidence showing that early auditory responses are observed over the midline in the frontocentral regions (Donkers et al., 2015; Picton, Hillyard, Krausz, & Galambos, 1974; Whitehouse & Bishop, 2008). Next, in order to examine attentional components, I primarily focused on mid-frontal, mid-central, and mid-posterior ROIs. These ROIs were chosen based on past evidence showing that involuntary attentional capture to novel stimuli is observed in the

frontocentral regions, whereas, attentional capture to oddball stimuli is observed over the posterior region (Katayama & Polich, 1998; Polich, 2003).

Selection of specific time windows for analyzing ERP components was based on past research showing that early ERP components reflect basic sensory processing (Ponton, Eggermont, Kwong, & Don, 2000) as well as conscious perception (P100; Schubert, Blankenburg, Lemm, Villringer, & Curio, 2006), whereas later components are more likely to be affected by attention (Novelty N2; Schomaker & Meeter, 2014) and may reflect cognitive processing underlying deviant (P3b) stimuli (Polich, 2003). Early and late ERP components were identified by visually inspecting the grand-averaged waveforms to novel and oddball stimuli. Mean amplitude was calculated for P1 (100-200 ms), N2 (250-400 ms), and P3b (500-700 ms).

Lastly, I calculated difference waves to examine the changes in amplitudes as a result of receiving novel and oddball stimuli in a stream of standard stimuli. Difference waves were calculated by subtracting ERP amplitudes underlying standard stimuli from novel and oddball stimuli. Mean amplitudes of the difference wave were then calculated for N2 between 250-400 ms post stimulus and for P3b between 500 and 700 ms post stimulus.

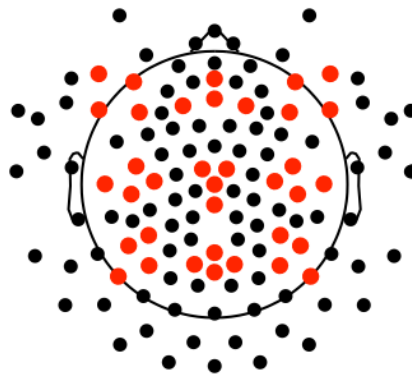


Figure 2.2. Nine regions of interest (ROI) marked in red. Grand averaged ERPs were calculated for standard, oddball, and novel conditions in each of the nine ROIs.

### 2.3.6 Analysis

Statistical analyses were conducted in SPSS software version 25 (IBM SPSS Statistics 25; Chicago, IL). First, independent sample t-tests were conducted (1) to explore parent reported behavioral differences in responding to tactile and auditory input in children with ASD and TD and (2) to examine any differences in the number of usable trials for each of the three stimulus types (standard, oddball, novel) in the two groups. In order to examine sensory differences in

response to novel tactile stimulation, a repeated measures ANOVA with between-subject factor Group (ASD, TD) and within-subjects factor ROI (ipsilateral, contralateral) was conducted. In order to examine sensory differences in response to oddball stimuli, a repeated measures ANOVA with between-subject factor Group (ASD, TD) and within-subjects factor ROI (mid-frontal, mid-central, mid-posterior) was conducted. Next, a mixed-model repeated-measures ANOVA with between-subject factor group (ASD, TD) and within-subject factors Stimulus Type (standard, oddball, novel) and ROI (mid-frontal, mid-central, mid-posterior) was conducted to evaluate differences in attending to infrequent tactile and auditory stimuli. Separate analyses were performed for mean amplitudes for each of the tactile (P1, N2) and auditory ERP components (P1, P3b). When significant differences were observed in ANOVAs, follow-up t-tests were subsequently conducted to examine simple effects. To supplement results examining differences in tactile and auditory ERPs between ASD and TD groups, I also conducted one-way ANOVAs on difference waves obtained for frontal N2 and posterior P3b components.

Finally, correlational analyses examined the association of neural indices of tactile and auditory processing with ASD symptomatology and language skills. Specifically, correlations were conducted to examine the association between mean amplitudes of tactile (P1, N2) and auditory (P1, P3b) components and ADOS-2, SRS-2, tactile and auditory subscales of SP-2, PPVT-4, and EVT-2 scores. Additionally, correlations were examined between the four ERP components and a sensitivity index score that indicated a tendency of hypo- or hyper- reactivity in each participant based on the SP-2. Sensitivity index score was calculated by first combining average quadrant scores that suggested hyper-reactivity (avoiding + sensitivity) and hypo-reactivity (seeking + registration). These two scores were then entered into the following equation:  $((\text{hyper-reactivity} - \text{hypo-reactivity}) / (\text{hyper-reactivity} + \text{hypo-reactivity})) \times 100$ . Resulting positive scores indicated a tendency for hyper-reactivity, whereas, negative scores indicated hypo-reactivity.

## 2.4 Results

Independent sample t-tests were conducted to explore parent reported behavioral differences in responding to tactile and auditory input in children with ASD and TD. As expected, children with ASD showed a greater number of sensory symptoms in the tactile and auditory domains compared to TD children as measured by parental report (touch,  $t(26) = 4.96, p < .001, d = 1.92$ ; audition;  $t(26) = 7.41, p < .001, d = 2.80$ , (Table 2.1). These results confirmed the presence of aberrant behavioral responses to tactile and auditory input in children with ASD.

Independent sample t-tests were conducted to explore whether the number of usable trials differed in the ASD and TD groups across the four blocks. Results revealed that the two groups did not differ significantly in the amount of usable trials for standard ( $t(26) = -1.73, p = .09, d = .65$ , oddball ( $t(26) = -1.45, p = .15, d = .55$ ), and novel ( $t(26) = -1.99, p = .06, d = .75$ ) stimuli (Table 2.1).

### 2.4.1 Neural responses to novel tactile stimuli

#### 2.4.1.1 Early ERP responses

Perceptual differences in processing tactile stimulation were examined by evaluating mean P1 amplitudes to novel stimuli between 100 and 200 ms post stimulus onset in the ipsilateral and contralateral stimulation sites. I hypothesized that, if differences in tactile processing in ASD are related to atypical perceptual abilities then there may be differences in early ERP components in children with ASD. A repeated measures ANOVA was conducted with between-subject factor Group (ASD, TD) and within-subjects factor ROI (ipsilateral, contralateral). Results indicated that there was a significant within-subjects main effect of ROI,  $F(1, 26) = 12.68, p = .001, \eta_p^2 = .32$ . As expected, ERP amplitudes were greater in the contralateral ( $M = .80 \mu V$ ;  $SD = 2.73$ ) compared to the ipsilateral ( $M = -1.18 \mu V$ ;  $SD = 1.61$ ) regions (Figure 2.3). However, there was no significant main effect of Group  $F(1,26) = 1.38, p = .25, \eta_p^2 = .05$ , nor was there a significant interaction between Group and ROI  $F(1,26) = 1.41, p = .24, \eta_p^2 = .05$ , indicating similar early processing of novel tactile stimuli in ASD and TD groups.



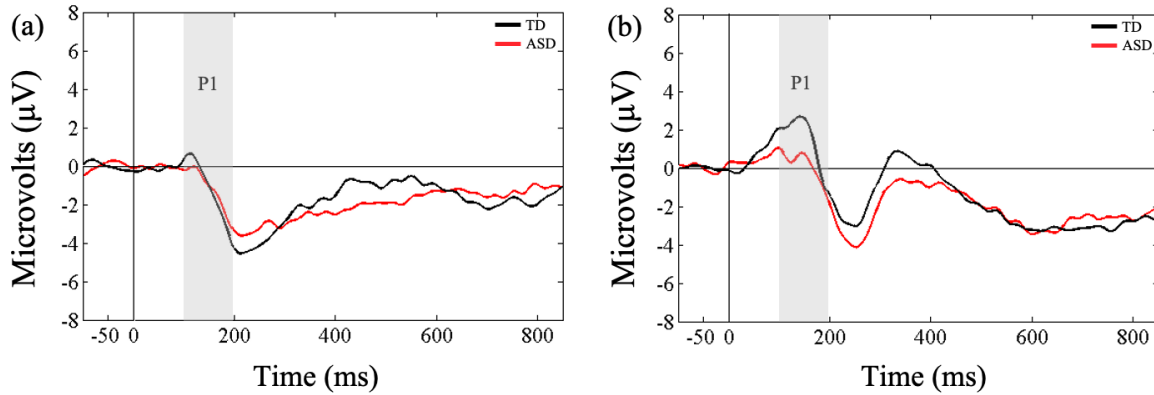


Figure 2.3. Grand averaged ERPs from (a) ipsilateral and (b) contralateral stimulation sites for novel tactile stimuli.

#### 2.4.1.2 Late ERP responses

Attentional processing of tactile stimulation was examined by evaluating mean N2 amplitudes to novel tactile stimuli between 250 and 400 ms post stimulus onset. I hypothesized that, if differences in tactile processing are related to atypical attentional processes, then there may be differences in late ERP components that are indicative of involuntary attentional capture in children with ASD compared to TD children. A mixed-model repeated-measures ANOVA was conducted with between-subject factor group (ASD, TD) and within-subject factors Stimulus Type (standard, oddball, novel) and ROI (mid-frontal, mid-central, mid-posterior). As expected, results showed a significant main effect of Stimulus Type  $F(2,52) = 6.37, p = .003, \eta_p^2 = .19$  and ROI  $F(2,52) = 86.04, p < .001, \eta_p^2 = .76$ . In addition, there was a significant interaction between Stimulus Type and ROI  $F(4,104) = 8.24, p < .001, \eta_p^2 = .24$ , suggesting that mean amplitudes to standard, oddball and novel stimuli between 250 and 400 ms differed depending on the ROIs. Follow-up paired samples t-tests revealed that both groups showed greater amplitudes in response to the novel stimuli in the frontal ( $M = -3.69 \mu V$ ;  $SD = 2.13$ ) compared to the central ( $M = -.68 \mu V$ ;  $SD = 2.20, t(27) = 5.62, p < .001, d = 1.06$ ) and posterior ( $M = 2.72 \mu V$ ;  $SD = 2.14, t(27) = 9.27, p < .001, d = 1.75$ ) ROIs. However, there was no main effect of Group  $F(1,26) = 2.38, p = .13, \eta_p^2 = .08$ , nor was there any significant interaction between Group and Stimulus Type  $F(2,52) = 1.14, p = .32, \eta_p^2 = .04$  or ROI  $F(2,52) = 2.35, p = .10, \eta_p^2 = .08$ , indicating similar novelty processing in the two groups (Figure 2.4).

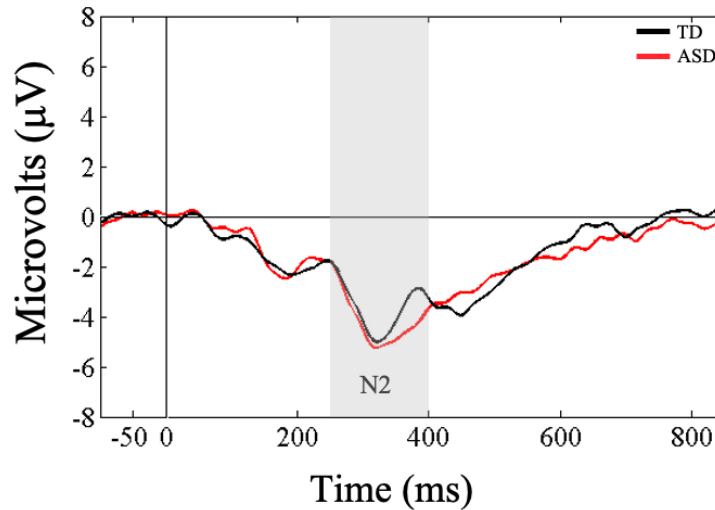


Figure 2.4. Grand averaged ERPs from frontal regions of interest for novel tactile stimuli.

These results were further supported by my difference wave analysis. One-way analysis of variance showed that frontal N2 magnitude was not significantly different in ASD ( $M = -1.10 \mu V$ ,  $SD = 2.22$ ) and TD ( $M = -.40 \mu V$ ,  $SD = 2.39$ ,  $F(1, 26) = .65$ ,  $p = .42$ ,  $d = .02$ ) groups, suggesting that children in the ASD group showed similar processing of novel tactile stimuli compared to their TD peers.

## 2.4.2 Neural responses to auditory oddball stimuli

### 2.4.2.1 Early ERP responses

Perceptual differences in processing auditory stimuli were examined by evaluating mean P1 amplitudes to oddball stimuli between 100 and 200 ms post stimulus onset in the mid-frontal, mid-central and mid-posterior regions of interest. I hypothesized that, if differences in auditory processing in ASD are related to atypical perceptual abilities then there may be differences in early ERP components in children with ASD. A repeated measures ANOVA was conducted with between-subject factor Group (ASD, TD) and within-subjects factor ROI (mid-frontal, mid-central, mid-posterior). Results indicated that, there was no significant within-subjects main effect of ROI,  $F(2,52) = .92$ ,  $p = .40$ ,  $\eta_p^2 = .03$ , nor was there a significant interaction between ROI and Group  $F(2,52) = 2.93$ ,  $p = .06$ ,  $\eta_p^2 = .10$ . Additionally, there was no significant main effect of Group  $F(1,26) = 3.66$ ,  $p = .06$ ,  $\eta_p^2 = .12$ , suggesting that the two groups showed similar early ERP responses to oddball stimuli (Figure 2.5).

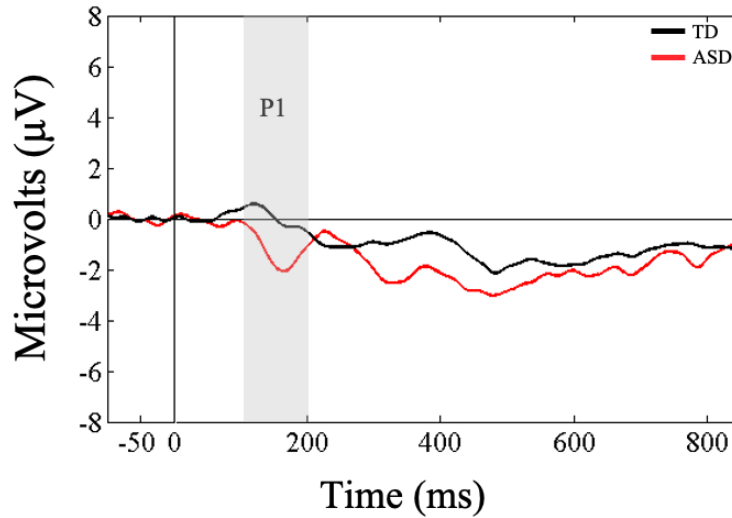


Figure 2.5. Grand averaged ERPs from central regions of interest for auditory oddball stimuli.

#### 2.4.2.2 Late ERP responses

Attentional orienting to auditory stimuli was examined by evaluating mean P3b amplitudes to oddball stimuli between 500 and 700 ms post stimulus onset. I hypothesized that, if differences in auditory processing are related to attentional components, then there may be differences in late ERP components that are indicative of involuntary attentional capture in children with ASD compared to TD children. A mixed-model repeated-measures ANOVA with between-subject factor group (ASD, TD) and within-subject factors Stimulus Type (standard, oddball, novel) and ROI (mid-frontal, mid-central, mid-posterior) was conducted. As expected, there were significant main effects of Stimulus Type  $F(2,52) = 8.15, p = .001, \eta_p^2 = .23$  and ROI  $F(2,52) = 64.64, p < .001, \eta_p^2 = .71$ . In addition, there was a significant interaction between Stimulus Type and ROI  $F(4,104) = 11.47, p < .001, \eta_p^2 = .30$ , suggesting that mean amplitudes to standard, oddball and novel stimuli differed depending on the ROIs. As expected, follow-up paired samples t-tests showed that mean P3b amplitude to oddball stimuli was greater in the mid-posterior ROI ( $M = 2.14 \mu V, SD = 1.45$ ) compared to mid-frontal ( $M = -2.87 \mu V, SD = 1.98, t(27) = 9.29, p < .001, d = 1.75$ ) and mid-central ROIs ( $M = -1.84 \mu V, SD = 1.24, t(27) = 10.14, p < .001, d = 1.91$ ). However, there was no main effect of Group  $F(1,26) = .75, p = .39, \eta_p^2 = .02$ , nor was there any significant interaction between Group and Stimulus Type  $F(2,52) = 1.46, p = .24, \eta_p^2 = .05$  or ROI

$F(2,52) = .55, p = .57, \eta_p^2 = .02$ , suggesting that children in the ASD group showed similar attentional orienting to auditory oddball stimuli compared to their TD peers (Figure 2.6).

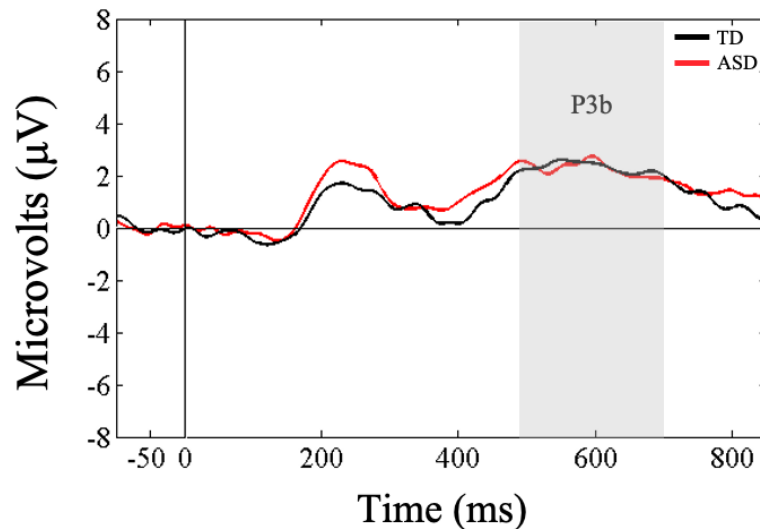


Figure 2.6. Grand averaged ERPs from posterior regions of interest for auditory oddball stimuli.

These results were further supported in my difference wave analysis. One-way ANOVA showed that posterior P3b amplitudes between the ASD ( $M = 1.69 \mu V, SD = 1.69$ ) and TD ( $M = 1.68 \mu V, SD = 1.22$ ) groups did not differ,  $F(1, 26) = .001, p = .97, d = .00$ , suggesting that both groups showed similar attentional response to oddball stimuli compared to their TD peers.

## 2.4.3 Correlations

### 2.4.3.1 Early neural responsivity to touch and ASD symptomatology, and language

Pearson correlations were calculated to examine whether early neural responsivity to novel tactile stimulation (measured by P1) was related to participants' ASD symptomatology as well as their language abilities. I hypothesized that, atypical neural amplitudes underlying tactile P1 may be associated with greater ASD symptomatology and reduced language skills in children with and without ASD. For all children, mean P1 amplitude in the contralateral site of the tactile stimulation was negatively correlated with scores on the tactile section of the SP-2 ( $r(28) = -.38, p = .04$ ; Figure 2.7). These results suggested that greater activation in early ERP components was associated with reduced tactile impairments as measured by parental reports.

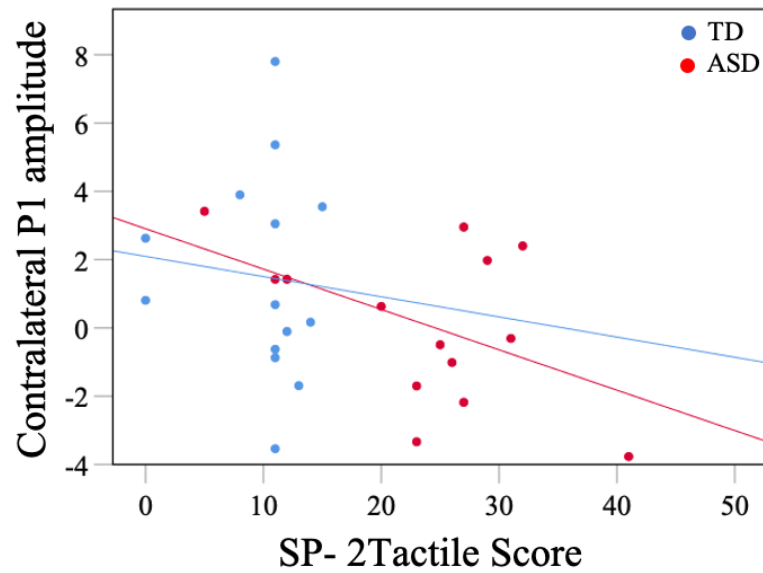


Figure 2.7. Mean contralateral P1 amplitudes in response to novel stimuli and SP-2 tactile scores for TD and ASD groups.

There were no significant correlations between mean amplitudes of P1 and any of the other behavioral measures of ASD symptomatology when examined across all children (all  $ps > .1$ ; Table 2.2). For the ASD group, contrary to my hypotheses, there were no significant correlations between mean P1 amplitudes and measures of ASD symptomatology including scores on the ADOS-2, (all  $ps > .29$ ), SRS-2 (all  $ps > .38$ ) and SP-2 ( $ps > .05$ ; Table 2.2). For the TD group, there were no associations between early neural responsivity to touch and ASD symptomatology (all  $ps > .16$ ; Table 2.2).

Mean P1 amplitude in the contralateral site of the tactile stimulation was not associated with language skills for all children as well as for children in individual groups (all  $ps > .28$ ; Table 2.2).

Table 2.2. Correlations between tactile mean P1 amplitude and ASD symptomatology

Group	ADOS-2				SRS-2		SP-2			
	SA	RRB	SS	SCI	RRB	Total	Touch	Sensitivity Index	PPVT-4	EVT-2
All (n = 28)	-	-	-	-.30	-.31	-.30	-.38*	-.03	.18	.21
ASD (n = 14)	.16	.01	.30	-.25	-.12	-.22	-.48	.24	-.004	.01
TD (n = 14)	-	-	-	-.11	-.39	-.20	-.08	-.09	.20	.27

*Note.* SA, Social Affect; RRB, Restricted and Repetitive Behaviors; SS, Severity Score; SCI, Social Communication and Interaction; RRB, Restricted Interests and Repetitive Behaviors; Touch SP-2, Touch section of Sensory Profile-2; PPVT-4, Peabody Picture Vocabulary Test-4; EVT-2, Expressive Vocabulary Test-2.

\*  $p < .05$

#### 2.4.3.2 Late neural responsivity to touch and ASD symptomatology, and language

Pearson correlations were calculated to examine whether late neural responsivity to novel tactile stimulation (measured by frontal N2) was related to participants' ASD symptomatology as well as their language abilities. I hypothesized that, atypical neural amplitudes underlying frontal N2 may be associated with greater ASD symptomatology and reduced language skills in children with and without ASD. Results showed that, for all children, as well as for children in the ASD group, mean frontal N2 amplitudes were not significantly associated with measures of ASD symptomatology (all  $ps > .05$ ). However, for children in the TD group, there was a significant negative correlation between mean frontal N2 amplitudes and social communication and interaction domain of the SRS-2 ( $r(14) = -.62, p = .02$ ) as well as the total composite score of the SRS-2 ( $r(14) = -.54, p = .04$ ; Table 2.3) with larger negative amplitudes of N2 being associated with greater SRS-2 scores.

For all children as well as for children in the ASD and TD groups, frontal N2 amplitude was not associated with language skills (all  $ps > .15$ ; Table 2.3).

Table 2.3. Correlations between mean N2 amplitude and ASD symptomatology

Group	ADOS-2				SRS-2			SP-2		
	SA	RRB	SS	SCI	RRB	Total	Touch	Sensitivity Index	PPVT-4	EVT-2
All (n = 28)	-	-	-	-.36	-.25	-.35	-.13	.13	.24	.25
ASD (n = 14)	.37	.33	.18	-.35	-.19	-.37	-.04	.28	.04	.11
TD (n = 14)	-	-	-	-.62*	.01	-.54*	.20	.17	.40	.30

*Note.* SA, Social Affect; RRB, Restricted and Repetitive Behaviors; SS, Severity Score; SCI, Social Communication and Interaction; RRB, Restricted Interests and Repetitive Behaviors; Touch SP-2, Touch section of Sensory Profile-2; PPVT-4, Peabody Picture Vocabulary Test-4; EVT-2, Expressive Vocabulary Test-2.

\*  $p < .05$ .

#### 2.4.3.3 Early neural responsivity to oddball stimuli and ASD symptomatology, and language

Pearson correlations were calculated to examine whether early neural responsivity to oddball stimuli (measured by P1) was related to participants' ASD symptomatology as well as their language abilities. I hypothesized that, atypical neural amplitudes underlying auditory P1 may be associated with greater ASD symptomatology and reduced language skills in children with and without ASD. For all children, mean P1 amplitudes to oddball stimuli were negatively correlated with total scores on the SRS-2 ( $r(28) = -.47$ ,  $p = .01$ ) suggesting that reduced P1 amplitudes were associated with greater impairments in reciprocal social behavior. Additionally, for all children, mean P1 amplitudes to oddball stimuli were also negatively correlated with both the subscales of the SRS-2 (Table 2.4; Figure 2.8).

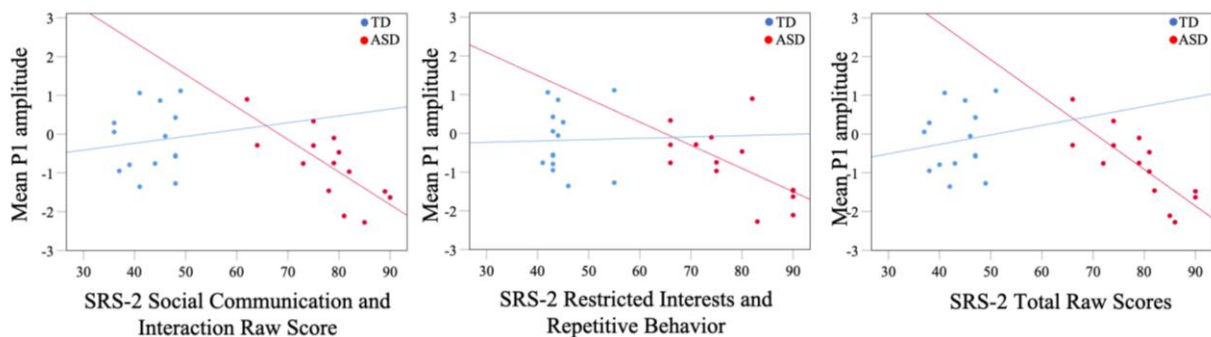


Figure 2.8. Mean P1 amplitudes to oddball stimuli and SRS-2 scores for TD and ASD groups.

Similar relationship between P1 amplitudes to oddball stimuli and SRS-2 scores was observed for children in the ASD, but not in the TD groups (Table 2.4). Additionally, for all children, a significant negative correlation was obtained between mean P1 amplitudes and participants' sensitivity index score of the SP-2 ( $r(28) = -.47$ ,  $p = .01$ ; Figure 2.9) indicating that reduced P1 amplitudes to auditory oddball stimuli were associated with greater hyperresponsivity<sup>1</sup>.

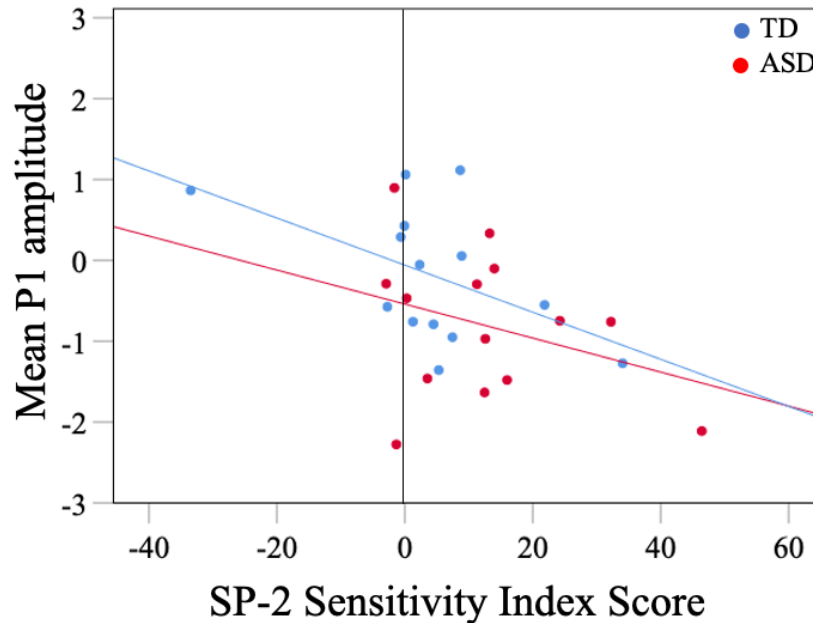


Figure 2.9. Mean P1 amplitude to oddball stimuli and SP-2 sensitivity index score. Participants with positive scores indicate hyper-reactivity, whereas, those with negative scores indicate hypo-reactivity.

Finally, mean P1 amplitudes to oddball stimuli in all three regions were not correlated with scores on the ADOS-2 as well as on both the language measures across all children as well as children in individual groups (all  $ps > .24$ ; Table 2.4).

<sup>1</sup> Because there were two clear outliers (1 TD, 1 ASD) based on the SP-2 sensitivity index score, I reanalyzed the correlation between auditory mean P1 amplitude and SP-2 sensitivity index score to examine whether the results were impacted by outliers. Correlation did not remain significant after removing the two outliers ( $r(26) = -.25$ ,  $p = .21$ ).



Table 2.4. Correlations between auditory mean P1 amplitude and ASD symptomatology

Group	ADOS-2				SRS-2		SP-2			
	SA	RRB	SS	SCI	RRB	Total	Auditory	Sensitivity Index	PPVT-4	EVT-2
All (n = 28)	-	-	-	-.46*	-.47*	-.47*	-.34	-.47*	.17	.23
ASD (n = 14)	-.21	.16	-.14	-.73**	-.61*	-.80**	-.14	-.32	-.05	.06
TD (n = 14)	-	-	-	.10	.02	.12	-.04	-.50	.10	.20

*Note.* SA, Social Affect; RRB, Restricted and Repetitive Behaviors; SS, Severity Score; SCI, Social Communication and Interaction; RRB, Restricted Interests and Repetitive Behaviors; Touch SP-2, Touch section of Sensory Profile-2; PPVT-4, Peabody Picture Vocabulary Test-4; EVT-2, Expressive Vocabulary Test-2.

\*  $p < .05$ . \*\*  $p < .01$ .

#### 2.4.3.4 Late neural responsivity to oddball stimuli, and ASD symptomatology, and language

Pearson correlations were calculated to examine whether late neural responsivity to oddball stimuli (measured by P3b) was related to participants' ASD symptomatology as well as their language abilities. I hypothesized that, atypical neural amplitudes underlying P3b may be associated with greater ASD symptomatology and reduced language skills in children with and without ASD. For all children, as well as for children in the ASD group, mean P3b amplitude was not significantly associated with ASD symptomatology. However, for children in the TD group, there was a significant positive association between P3b amplitude and sensitivity index score of the SP-2 ( $r(14) = .63$ ,  $p = .01$ ), suggesting that patterns of attentional processing in response to oddball stimuli were related to greater hyperresponsivity.

Pearson correlations between mean P3b amplitudes and language scores indicated that, for all children, there was a positive correlation between late ERP responses to oddball stimuli and EVT-2 scores ( $r(28) = .39$ ,  $p = .04$ ), suggesting that greater attentional orienting to oddball stimuli was associated with greater expressive vocabulary skills (Table 2.5; Figure 2.10).

	ADOS-2			SRS-2			SP-2			
Group	SA	RRB	SS	SCI	RRB	Total	Auditory	Sensitivity Index	PPVT-4	EVT-2
All (n = 28)	-	-	-	.17	.22	.17	.23	.25	.31	.39*
ASD (n = 14)	-.26	.15	-.19	.42	.46	.44	.40	-.12	.46	.47
TD (n = 14)	-	-	-	.22	.39	.23	.20	.63*	.32	.44

*Note.* SA, Social Affect; RRB, Restricted and Repetitive Behaviors, SS, Severity Score SCI, Social Communication and Interaction; RRB, Restricted Interests and Repetitive Behaviors; Auditory SP-2, Auditory section of Sensory Profile-2; PPVT-4, Peabody Picture Vocabulary Test-4; EVT-2, Expressive Vocabulary Test-2.

\*  $p < .05$ .

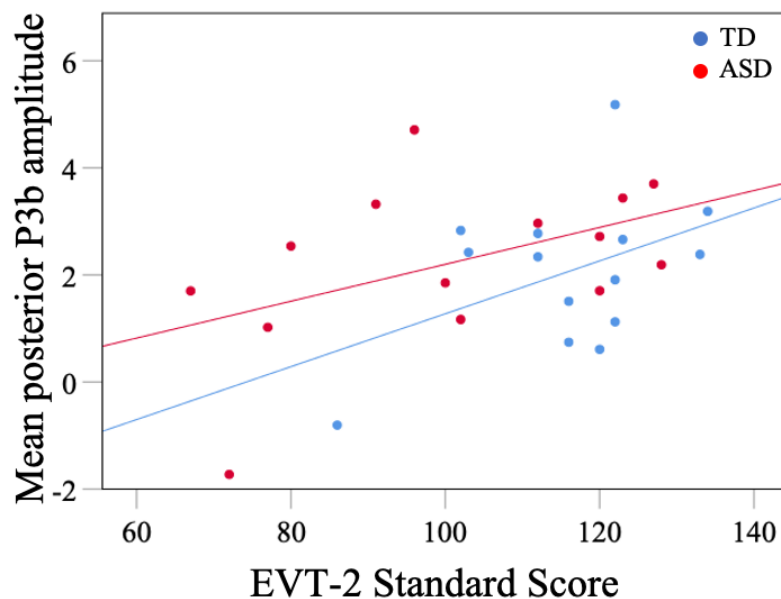


Figure 2.10. Mean posterior P3b amplitudes to oddball stimuli and EVT-2 scores for TD and ASD groups.

## 2.5 Discussion

The goal of this study was to assess neural indices of perceptual and attentional factors underlying tactile and auditory processing in children with ASD. Specifically, I examined (1)

whether atypical processing of tactile and auditory information in ASD is related to differences in early perceptual or later attentional processing of the stimuli compared to TD children, and (2) the relationship between neural indices of tactile and auditory processing and ASD symptomatology and (3) language skills in children with and without ASD. I hypothesized that, if differences in tactile and auditory processing in ASD are related to atypical perceptual abilities, then there may be differences in early ERP components in children with ASD. Alternatively, if differences in tactile and auditory processing are associated with attentional components, then there may be differences in later ERP components that are indicative of involuntary attentional processing in children with ASD compared to TD children. Additionally, I hypothesized that neural differences in processing tactile and auditory stimuli would be related to ASD symptomatology and language skills in children with and without ASD.

My results indicated that, as expected for the tactile modality, both groups showed increased activation at P1 in the contralateral location of the stimulation compared to the ipsilateral location. This finding is similar to previous studies that have shown neural activation in response to touch in contralateral stimulation sites in children with and without ASD (Cascio et al., 2015; Russo et al., 2010). Additionally, as expected, both groups showed a later neural response to perceptual novelty (indicated by increased N2) in the frontal region of the brain. However, contrary to my hypotheses, children with ASD showed similar early as well as later ERP amplitudes in response to tactile stimulation compared to their TD peers, suggesting equivalent neural responsivity to touch in the ASD group. This finding stands in contrast to previous neuroimaging studies (Marco et al., 2012; Russo et al., 2010), that have suggested diminished early cortical responses to tactile stimulation in individuals with ASD. One possible reason for these contradictory findings could be attributed to methodological differences between studies. For example, in Marco et al. (2012), both standard and oddball tactile stimuli consisted of pneumatically driven pulses, whereas in the current study tactile stimuli consisted of a vibration that was presented only as novel stimuli embedded in a stream of standard and oddball auditory sounds. It is possible that the change in modality in my novel stimuli may have facilitated neural responsivity in individuals with ASD.

Additionally, tactile stimulation in my study was always presented together with an auditory stimulus. Although there are differences in auditory-somatosensory integration in children with ASD (Russo et al., 2010), it is possible that the presentation of bimodal input may

have facilitated early as well as later neural responsivity to novel stimuli. Support for this argument comes from previous research that has shown diminished amplitudes in response to unimodal somatosensory input starting around 70 ms post stimulus onset in children with ASD compared to TD children; however, the authors do not present a detailed discussion on amplitude differences between unimodal and bimodal stimuli (Russo et al., 2010). The impact of bimodal input on tactile responsivity as measured by orienting responses is observed in a behavioral study (Kadlaskar et al., 2020), where infants at risk for ASD showed more attentional orienting to bimodal touch-speech input compared to unimodal touch-only input presented by their mothers. However, further research is needed to investigate whether the presentation of tactile input along with auditory input facilitated neural responsivity in the ASD group.

My results related to auditory stimuli followed a similar trend to those in the tactile modality. As expected, participants in both the groups showed early responsivity to oddball stimuli distributed over the midline and later attentional orienting to oddball stimuli distributed over the posterior region of the brain. Results pertaining to the location of neural activation were similar to those in previous neuroimaging studies examining auditory processing (Lepistö et al., 2005; Polich, 2003; Whitehouse & Bishop, 2008). However, contrary to my hypotheses, children with ASD showed similar early as well as later ERP amplitudes underlying oddball stimuli compared to TD children, suggesting intact neural processing of auditory stimuli. These findings contradict previous studies that found attenuated early as well as later neural responses to auditory stimulation for individuals with ASD (Donkers et al., 2015; Lepistö et al., 2005; Whitehouse & Bishop, 2008). Differences among results could be attributed to differences in participant characteristics (e.g., in Lepistö et al. (2005) mean VIQ for the ASD group was 59, whereas in the current study it was 98), nature of the stimuli (e.g., speech vs. tones) etc...These results indicate that, under certain conditions children with ASD may show typical neural responsivity to auditory stimuli.

Although the current study did not find neurological differences in processing tactile and auditory stimuli in the ASD group as compared to the TD group, these differences were still present at a behavioral level as measured by the SP-2. Similar behavioral differences in everyday sensory response patterns are also reported in previous studies in individuals with ASD (Baranek et al., 2006; Ben-Sasson et al., 2009). A possible reason for the discrepancy between my neural and parent report measures underlying sensory stimuli could be attributed to differences between

processing controlled experimental stimuli as opposed to responding to stimuli encountered in the outside world which is often social and dynamic.

Responding to sensory stimuli – particularly touch – in the outside world often involves responding to the social aspects of the stimuli. The reward value associated with our social responsiveness (including to sensory stimuli) facilitates our participation in future social communication. Individuals with ASD, however, may find it challenging to naturally form stimulus-reward contingencies for social stimuli, resulting in reduced motivation to typically respond to such stimuli (Chevallier et al., 2012). While social motivation theory is not primarily a sensory processing theory, it may account for some sensory differences observed in everyday social contexts in individuals with ASD. For example, deficits in social orienting were reported in Dawson et al. (2004) suggesting that although children with ASD showed reduced orienting to both social and nonsocial stimuli, this impairment was more profound in response to social stimuli. In the present study, my tactile stimuli consisted of highly controlled non-social vibrations which are not representative of the rich tactile input that is experienced in the outside world (e.g., a loving touch presented by a caregiver). Additionally, touch presented in social contexts can be of various types (e.g., tap, brush, tickle) and often carries communicative intent (e.g., touch to reduce distress, get attention, convey affect; Ferber, Feldman, & Makhoul, 2008; Field, 2001; Hertenstein, 2002). Individuals presented with social touch are therefore required to respond to social aspects of that interaction in addition to responding to the touch alone. Therefore, it is possible that everyday challenges in responding to tactile information may stem from differences in social motivation in individuals with ASD, and as a result could be more robustly observed in response to social stimuli or in social contexts involving dynamic touches compared to non-social controlled experimental settings with mechanical touches.

Social motivation theory may also explain current results for the auditory modality. Although, in the current study, participants were presented with speech stimuli (considered to be inherently social), they were synthesized non-words presented in a non-social context with no communicative intent, making them less social. This type of presentation of experimentally-controlled speech sounds does not mirror everyday speech input that often involves a communicative partner and listening to communicatively relevant utterances. Behavioral differences in responding to auditory information in ASD could be more related to social aspects that are associated with surrounding auditory information rather than just the underlying

neurological differences. Nevertheless, I do acknowledge previous empirical evidence indicating that children with ASD may also show atypical responses to non-social stimuli presented in controlled settings (Baranek et al., 2013; Bruneau et al., 2003; Lepistö et al., 2005; Marco et al., 2012; Miyazaki et al., 2007), and suggest that differences in sensory processing in ASD may be *more* evident in social contexts or specifically in response to social-stimuli compared to experimental settings. However, further electrophysiological research is warranted to examine whether individuals with ASD respond differently to social and non-social stimuli presented in both social and non-social contexts.

Additionally, for the tactile modality, afferent mechanoreceptors involved in processing touch as well as the location of the touch may have impacted current results. In the present study, participants received high-frequency tactile stimulation on their fingertip which stimulates Pacinian corpuscles; mechanoreceptors involved in discrimination of fine textures or other stimuli with high-frequency vibrations (Johnson, 2001). Whereas, a social touch might often involve tactile stimulation on non-glabrous (hairy) skin that is innervated by C-touch or CT afferents; low-threshold unmyelinated afferent fibers (Olausson, Wessberg, McGlone, & Vallbo, 2010). CT afferents primarily respond to gentle, caress-like stroking that is delivered at typical human skin temperatures, thereby promoting interpersonal tactile interaction (Ackerley et al., 2014). Previous research with individuals with ASD has shown elevated levels of defensiveness to touch presented on CT-innervated regions such as face and arm compared to non-CT-innervated regions such as the palm (Cascio, Lorenzi, & Baranek, 2016), indicating that that deficits in responding to touch could be more apparent at CT-innervated regions compared to touches on the glabrous skin (such as palm or fingertip) that is not innervated by the CT afferents.

Correlational analyses partially supported my second and third hypotheses that neural correlates of tactile and auditory processing would be related to ASD symptomatology and language skills in children with and without ASD. Particularly, for the tactile modality, early contralateral responses were negatively associated with tactile raw score of the SP-2 for all children with reduced neural response being related to increased tactile symptoms. Additionally, in the auditory modality, reduced early amplitudes were associated with impairments in reciprocal social communication, and greater tendency of overall sensory hyper-reactivity for all children. Significant relationship between early auditory ERP responses and social communication was also

present for the ASD group. These findings support previous research that has reported associations between sensory symptoms and ASD symptomatology (Foss-Feig et al., 2012; Watson et al., 2011).

Later ERP responses to touch were associated with TD, but not the ASD group. Specifically, greater amplitudes at N2 were associated with higher SRS-2 total and social communication and interaction scores, suggesting that patterns of allocation of attention could be associated with individual differences in reciprocal social skills. Additionally, greater sensitivity to changes in the auditory stimuli were associated with increased tendencies of hyper-reactivity in the TD group. These findings extend previous research that has suggested possible links between neural hyper-reactivity to novel stimuli and ASD-related traits (Gomot, Belmonte, Bullmore, Bernard, & Baron-Cohen, 2008). My results suggest that links between patterns of allocation of attention to novel and oddball stimuli and ASD-like traits may represent a more dimensional characterization of ASD. In other words, although TD participants may not receive a categorical diagnosis of ASD, the association between neural responses and ASD-like traits in TD may follow a similar pattern observed in ASD. Next, for all children greater P3b amplitudes to oddball stimuli were linked with greater expressive language scores, indicating an association between attention to changes in the auditory stream and language skills. Finally, contrary to my hypotheses, both early and late neural responses to tactile and auditory stimuli were not associated with ADOS-2 scores.

This study is not without limitations. First, my sample was relatively small given limited data collection due to COVID-19 and included high-functioning children with ASD, and as a result may not be adequately representative of a heterogeneous sample of ASD. Second, my paradigm did not include presentation of tactile-only input to examine whether neural responsivity to touch observed in my study was impacted by the presence or absence of accompanying auditory input. Future studies could consider examining neural responsivity to touch using both unimodal and bimodal input.

In sum, the present study revealed that despite differences in parent report sensory measures, under certain conditions, children with ASD may show typical early and late neural responses to tactile and auditory stimuli. Differences in behavioral patterns of sensory processing in ASD could therefore be attributed to social contexts in which sensory stimuli are more likely to be encountered in everyday life. Finally, both early and late ERP responses were associated with behavioral measures of sensory responsivity and social skills in children with and without ASD.

Therefore, examining early and late neural processing to sensory stimuli presented in both social and non-social contexts could be beneficial in future research that aims to study sensory processing using dimensional characterization of ASD.



### 3. BEHAVIORAL MEASURES OF TACTILE AND AUDITORY PROCESSING IN CHILDREN WITH ASD

#### 3.1 Abstract

**Introduction:** Attending to surrounding sensory information facilitates the development of cognitive and socio-communicative skills. The alerting network, a subcomponent of attention, plays a vital role in everyday functioning by enabling humans to recognize novel information. Past evidence has shown equivalent alerting in individuals with ASD when presented with auditory and visual stimuli. However, touch is also an important channel used for communication in our everyday life and it is still unclear whether children with ASD show equivalent alerting when presented with touch. Given the importance of touch, and that touch is most often embedded in speech, I investigated whether the presentation of tactile cues before an auditory target facilitates behavioral performance in children with and without ASD.

**Objectives:** I examined (1) whether tactile cues affect accuracy and reaction times in children with ASD and TD, (2) whether the duration between the presentation of tactile cues and the target impacts accuracy and reaction times of behavioral responsivity in children with ASD and TD, and whether behavioral responses in the tactile-cueing task are associated with (3) ASD symptomatology including sensory responsivity to touch, and (4) language.

**Methods:** Participants included 15, 6-to-12-year-olds with ASD and 15 age- and non-verbal IQ matched typically developing (TD) children. During the experiment, participants were instructed to respond with a button press to a target speech sound /a/. Tactile cues were presented at 200, 400, and 800 ms (25% each) prior to the target speech sound. The remaining trials (25%) were presented without the tactile cues. The task included a total of 96 trials divided into 3 blocks of 32 trials each. Children's accuracy and reaction times for each trial were examined.

**Results:** Present findings indicated that the presence or absence of tactile cues before the auditory target impacted accuracy in all children. All participants displayed higher accuracy in trials without tactile cues and at 200 ms SOA compared to trials with longer touch-cue intervals. Additionally, the presentation of tactile cues facilitated reaction times in all children with longer touch-cue intervals resulting in faster reaction times. Finally, there were no associations between behavioral facilitation to touch cues and measures of ASD symptomatology and language skills in ASD and TD children.

**Conclusion:** Children with and without ASD display equivalent phasic alerting in response to tactile cues. Longer cue-target intervals may be beneficial resulting in faster reaction times in all children while responding to auditory targets. However, children with ASD show overall slower reaction times compared to their TD peers. Finally, touch-related behavioral facilitation is not linked with ASD symptomatology and language skills.

### 3.2 Introduction

Autism spectrum disorder (ASD) is a neurodevelopmental disorder that is diagnosed on the basis of deficits in social communication and social interaction, and the presence of restricted and repetitive behaviors (DSM-5; American Psychiatric Association, 2013). In addition to these core behavioral features, differences in attention have also been associated with the disorder ever since it was first reported by Kanner (1943). Attending to surrounding information is important as it can impact the development of cognitive and socio-communicative skills (Colombo, Richman, Shaddy, Follmer Greenhoot, & Maikranz, 2001; Salley et al., 2016; Wagner, Luyster, Yim, Tager-Flusberg, & Nelson, 2013). For example, shifting attention to surrounding auditory, visual, and tactile inputs enables individuals to recognize different sources of information, extract meaningful information from their environment, as well to engage in joint attention; a skill necessary during social interaction (Mundy & Newell, 2007). Nonetheless, individuals with ASD typically show early and pervasive impairments in attention (Allen & Courchesne, 2001; Baranek, 1999; Zwaigenbaum et al., 2005). Furthermore, these deficits in attention are often associated with their ASD symptomatology (Dawson et al., 2004; Zwaigenbaum et al., 2005), and have been argued to play a key role in the emergence of the ASD phenotype (Keehn et al., 2013).

The study of attention has been divided into three subcomponents: alerting, orienting, and executive control networks (Posner & Petersen, 1990; Posner & Rothbart, 2007). The alerting network is defined as achieving and maintaining a state of heightened sensitivity to incoming stimuli. The alerting network is further classified into tonic (intrinsic arousal) and phasic alerting (transient alertness as a result of a warning before the presentation of a target). The orienting network is responsible for selecting the information from the surrounding sensory input whereas the executive control network involves mechanisms responsible for conflict resolution and cognitive functions. Differences in each of these attentional networks have been reported in the

past literature, and may contribute to the development of ASD (see Keehn et al., 2013, for a review). The current study focuses on the alerting network in children with ASD.

The alerting network plays an important role in human attention as it helps humans to recognize new information. For example, in typical development, presentation of transient auditory cues either slightly before or simultaneously with visual targets have been shown to impact perception resulting in faster behavioral responses (Diederich, Schomburg, & Colonius, 2012; Keetels & Vroomen, 2011; Zou, Müller, & Shi, 2012). These findings regarding differences in reaction times between cue and no-cue conditions have been shown to reflect both phasic and tonic alerting. Specifically, transient sensory inputs stimulate alerting responses thereby improving the processing speed of incoming sensory information after salient events. Equivalent phasic alerting has also been observed in individuals with ASD. For example, in an implicit learning task, Kleberg, Thorup, and Falck-Ytter (2017) reported that children with ASD showed behavioral facilitation, measured by reduced saccadic reaction times, in a visual disengagement task when transient auditory cues were presented before the visual targets. The authors thus concluded that, intact phasic alerting may play a key role in facilitating behavioral responses in children with ASD.

Evidence of similar alerting in ASD has received support in other studies using auditory (Raymaekers, van der Meere, & Roeyers, 2006) and visual cues (Keehn, Lincoln, Müller, & Townsend, 2010; Landry, Mitchell, & Burack, 2009). For instance, using the Attention Network Test (ANT; Fan, McCandliss, Sommer, Raz, & Posner, 2002), Keehn et al. (2010) showed that both children with ASD and TD exhibited reduced reaction times when the target visual stimuli were preceded by visual cues indicating equivalent phasic and tonic alerting. Specifically, the Attention Network Test (ANT; Fan et al., 2002) is an explicit learning task that measures the three attentional networks (alerting, orienting, and executive control) in children and adults. The efficiency of the alerting network is measured by looking at differences in reaction times (RTs) resulting from the presentation of warning cues before the target. The orienting network is measured by examining the changes in RTs resulting from cues indicating the location of the target. Finally, the executive control network is measured by instructing the participant to indicate the direction of the arrows (left or right) that are surrounded by one of the three flanker conditions (congruent, incongruent, neutral). Additionally, in Keehn et al. (2010) an association was observed between alerting score and the Social Domain score on the ADOS (Lord, Rutter, DiLavore, & Risi, 1999), with reduced efficiency of the alerting network being associated with greater social

impairments in children with ASD (Keehn et al., 2010). Together, these findings suggest that children with ASD are able to use auditory and visual cues to facilitate attentional responses within (i.e., visual cues preceding visual targets; Keehn et al., 2010; Landry et al., 2009) and across (i.e., auditory cues preceding visual targets; Kleberg et al., 2017; Raymaekers et al., 2006) modalities, and that differences in alerting network efficiency may be related to the socio-communicative impairments observed in ASD.

Landry et al. (2009) have further added to our understanding of how individuals with and without ASD may use transient cues (presented at different times) to facilitate their behavioral performances. In particular, using an implicit learning task, Landry et al. (2009) examined children's behavioral performances in two cue conditions – the variable cue exposure condition i.e., cues lasting for 100, 300, 600 or 1000 ms, and the constant cue exposure condition i.e., cues always lasting for 100 ms. Additionally, by manipulating the response preparation time (100, 300, 600, 1000 ms) in the constant cue exposure conditions, Landry et al. (2009) showed that, while children with ASD exhibited facilitation effect in response to all stimulus onset asynchronies (SOAs), TD children only showed facilitation at shorter SOAs. This facilitation effect was observed in both groups and in both the cue conditions. These findings further support the evidence of similar efficiency of alerting in children with ASD and TD children. Last, these results also indicate that different SOAs might differently impact behavioral performances in the two groups, warranting further exploration to understand the role of SOAs in behavioral cueing tasks in both ASD and TD children.

Together, the studies utilizing transient visual and auditory cues have shown equivalent alerting in children with ASD compared to TD children. With respect to the tactile modality, there exists some evidence showing that the presentation of touch-cues facilitates behavioral responses in typically developing adults. For example, in Turatto, Galfano, Bridgeman, and Umiltà (2004) participants were asked to respond to auditory, visual, and tactile targets that were preceded by transient cues that were of the same or different sensory modality. The results of this study revealed that participants were faster to respond to the tactile targets when they were preceded by tactile cues compared to visual or auditory cues, suggesting typical alerting responses, at least, within the tactile modality. Although this study suggests within-modality touch-related behavioral facilitation in adults, it remains unclear whether touch (presented both within and across modalities) facilitates behavioral performance in children, and whether these results can be extended to individuals with

ASD. The present study addresses this gap in the literature by examining the role of tactile cues in facilitating behavioral responses in a cross-modal task in children with ASD compared to TD controls.

The current study primarily focuses on processing tactile cues as they relate to alerting because touch has been shown to modulate attention in early typical development (Jean & Stack, 2009; Stack & Muir, 1992). Additionally, although touch is a frequent channel of communication during the first couple of months of life (Stack & Muir, 1990), past research has reported a systematic decline in the overall amounts of touch produced by caregivers as infants get older (Ferber et al., 2008). Ferber et al. (2008) argue that with growing mobility and cognitive abilities of the child, caregivers may use other forms of communication (such as speech) with greater frequency compared to touch (also see Herrera, Reissland, & Shepherd, 2004). Although growing mobility associated with age provides infants more opportunities to tactually explore their surroundings, thereby increasing the amount of tactile contact they initiate, the frequency of caregiver-initiated tactile input decreases with age as a result of adapting to children's growing autonomy (Ferber et al., 2008). In contrast to the overall decrease in the amount of caregiver touch, Bergelson et al. (2019) showed an increase in infant-directed speech with children's age. Therefore, given that the frequency of caregivers' infant-directed speech is linked with growing age (Bergelson et al., 2019), and the fact that children are constantly receiving visual input in their surroundings while they are awake (e.g., continuous exposure to surrounding objects and people), caregiver touch becomes less frequent compared to these two modalities as children get older.

Because incoming tactile input becomes relatively less frequent with age, I reasoned that the novelty associated with touch may modulate alerting responses resulting in behavioral facilitation. Support for this argument comes from previous electrophysiological research examining the impact of novelty on attention regulation. For example, large number of studies have shown increased neurological responses to infrequent/novel stimuli encountered in a stream of repeatedly presented stimuli indicating involuntary attentional orienting (for a review, see Friedman, Cycowicz, & Gaeta, 2001). Therefore, I propose that if relative cue frequency and novelty impacts attention, then touch, a relatively less frequent cue in everyday life should impact alerting.

However, we know that individuals with ASD often show hypo- and/or hyper-reactivity in response to tactile stimulation (see Mikkelsen et al., 2018, for a review). These differences to

tactile stimuli might neutralize the significance of tactile cues in ASD. For example, hypo-reactivity to touch might result in missing out on transient tactile cues, whereas, hyper-reactivity might result in perceiving too much tactile stimulation either making touch no longer a novel stimulus or overlearning the relationship between tactile cues and corresponding targets. In the latter case, children in the ASD group may show rigidity in applying the rule when tactile cues are present and may display even greater delays in behavioral responses when tactile cues are absent compared to the TD group. To explore this topic further, using a tactile-cueing task, the present study sought to investigate (1) whether tactile cues presented before auditory targets affect accuracy and reaction times in children with ASD and TD, (2) whether increasing the duration between the presentation of tactile cues and auditory targets impacts accuracy and reaction times in children with ASD and TD, and (3) whether behavioral responses in the tactile-cueing task are associated with ASD symptomatology including sensory responsivity to touch, and (4) language.

In the current experiment, tactile cues were presented prior to auditory targets making this task cross-modal in nature. I designed a cross-modal task to increase the ecological validity of this study. We know that the majority of information humans receive in everyday life, comes from multiple sensory modalities which may be presented simultaneously (e.g., seeing an apple while hearing the name apple) or in close temporal intervals (e.g., receiving a tap on the shoulder slightly before hearing one's name). In such multimodal situations, especially when related cross-modal stimuli are presented in close temporal intervals, if one fails to attend to any of the stimuli or if there are impairments in learning the relationship between two or more stimuli coming from different modalities (e.g., shoulder taps preceding one's name may indicate upcoming verbal or nonverbal communication), they may miss out on an opportunity to receive new information or show slower attentional shifts in response to informative stimuli, which may be detrimental for the course of typical development.

In the current task, participants were required to shift their attentional focus between tactile and auditory stimuli to implicitly learn the relationship between tactile cues and auditory targets (i.e., tactile cues always lead to auditory targets). Examining alerting responses as they relate to cross-modal stimuli is particularly important for individuals with ASD, because past research has shown evidence of less efficient patterns of attentional set shifting between sensory modalities in ASD (Courchesne et al., 1994; Reed & McCarthy, 2012; Williams, Goldstein, & Minshew, 2013). For example, Reed and McCarthy (2012) reported that children with ASD displayed greater

challenges in cross-modal attentional-switching tasks compared to within-modality switching task. These findings have implications in everyday multimodal interactions where individuals are required to effectively switch their attentional focus between stimuli and use information from one modality to facilitate the processing of other modality in their surroundings. Therefore, any differences in attentional set shifting, including non-spatial shifting of attention, in ASD may impact the use of transient cues to facilitate behavioral responses in ASD.

For Objectives 1 and 2, in line with previous research (Raymaekers et al., 2006), I hypothesized that, the presentation of tactile cues before the target will be associated with an increase in anticipatory responses in all children. Additionally, variable cue-target interval may affect accuracy especially at longer cue-target intervals where participants will be required to wait for a longer period of time to submit their responses. Next, if equivalent alerting response to auditory and visual cues is extended to the tactile modality in children with ASD and TD, then children in both groups should show faster reaction times as a result of tactile cues irrespective of the duration between cues and targets. On the other hand, if children with ASD are hypo-reactive to tactile information, then they should show reduced touch-related behavioral facilitation compared to TD children as measured by decreased changes in reaction times (RT) in response to tactile cues across all duration-gaps between cues and targets. Alternatively, if children with ASD are slower to attend to tactile inputs then they would mainly benefit from longer touch-cue intervals. In other words, children with ASD may show greater differences in responding to targets at shorter touch-cue intervals compare to TD children, but show similar touch-related behavioral facilitation at longer-touch intervals.

Finally, given that differences in alerting efficiency and sensitivity to novel information may be related to socio-communicative deficits in ASD (Keehn et al., 2010; Keehn et al., 2013), and that there exists an association between processing touch and the development of social communication (Dunbar, 2010; Hertenstein, Verkamp, et al., 2006) and language (Abu-Zhaya et al., 2017; Seidl et al., 2015), I hypothesize that, reduced touch-related facilitation will be related to greater ASD symptomatology and reduced socio-communicative (Objective 3) and language skills in both ASD and TD children (Objective 4).

### 3.3 Methods

#### 3.3.1 Participants

Fifteen 6- to 12-year-old children with ASD (12 male) and fifteen (12 male) age-, sex- and nonverbal IQ matched TD children participated in the study (Table 3.1). Verbal and Nonverbal scales of the Wechsler Abbreviated Scale of Intelligence (11 ASD, 8 TD; WASI-II; Wechsler, 2011) or the Differential Ability Scale II (4 ASD, 7TD; DAS-II; Elliott, 2007) were used to determine IQ-based matching; this resulted in reduced total testing time and increased participant compliance. Verbal and Nonverbal IQ scales of the WASI-II are highly correlated with Verbal and Nonverbal scales of the DAS-II ( $r = .69$  to  $.70$ ; Elliott, 2007). Clinical diagnoses for the ASD group were confirmed using the Autism Diagnostic Observation Schedule, Second Edition (ADOS-2; Lord et al., 2012), and the Social Communication Questionnaire (SCQ; Rutter et al., 2003). All children in the ASD group were given ADOS-2 Module 3, Out of 30 participants, 26 (12 ASD, 14 TD) were right-handed as measured by the Edinburgh Handedness Inventory (EHI; Oldfield, 1971). Participants in the TD group reported no family history of ASD. The Social Responsiveness Scale-2 (SRS-2; Constantino, 2012), a 65-item caregiver-report questionnaire, was used to confirm the presence or absence of clinically significant ASD symptomatology.

Participants with ASD were recruited from local ABA therapy centers, a departmental registry, and other community sources. TD participants were recruited from a departmental registry and community sources. All participants and their caregivers provided written assent and consent prior to participating in the study. All study procedures were conducted in accordance with the Purdue University Institutional Review Board. No children in the ASD group reported the presence of any other ASD-related medical conditions (e.g., fragile-X syndrome, tuberous sclerosis). Finally, two additional participants in the ASD group were excluded from the final sample due to the refusal to participate in the tactile-cueing task.



Table 3.1. Participant demographics

	ASD	TD	Statistic	<i>p</i>
N (M:F)	15 (12:3)	15 (12:3)	$X^2(1) = .00$	1.0
Age (years)	10.03 (1.88); 6.17-12.58	9.79 (1.45); 7.55-12.53	$t(28) = .38$	.70
Handedness (R:L)	12:3	14:1	$X^2(1) = 1.15$	.28
Verbal IQ	96 (22); 67-126	117 (11); 94-135	$t(28) = -3.40$	.002
Nonverbal IQ	105 (20); 70-136	116 (16); 89-144	$t(28) = -1.63$	.11
ADOS-2				
Social Affect	11 (5); 4-20	-	-	-
Repetitive Behavior	3 (2); 1-6	-	-	-
Severity Score	8 (2); 4-10	-	-	-
Sensory Profile-2				
Touch Raw Score	23 (9); 5-41	10 (4); 0-15	$t(28) = 5.15$	<.001
Auditory Raw Score	27 (7); 15-38	12 (4); 2-21	$t(28) = 7.66$	<.001
Sensitivity Index	13 (14); -3-46	4 (14); -33-34	$t(28) = 1.73$	.093

*Note.* IQ determined using the Wechsler Abbreviated Scale of Intelligence, Second Edition (WASI-II; Wechsler, 2011) or the Differential Ability Scale, Second Edition (DAS-II; Elliott, 2007).

Mean (SD); range

### **3.3.2 Standardized measures**

#### ***3.3.2.1 Autism Diagnostic Observation Schedule-2 (ADOS-2)***

The ADOS-2 (Lord et al., 2012) is a widely used semi-structured play-based interaction designed to measure autism symptoms in five domains: Language and communication, reciprocal social interaction, play, stereotyped behaviors and restricted interests, and other abnormal behaviors. The ADOS-2 consists of five modules, which can be administered to children and adults based on their developmental and language levels. In the present study, all children in the ASD group were administered Module 3 which is used with children and adolescents with fluent speech. Severity scores from the ADOS-2 diagnostic algorithm were used as symptom measures while addressing Objective 3 with higher ADOS-2 scores reflecting greater severity (Gotham et al., 2009).

#### ***3.3.2.2 Social Responsiveness Scale (SRS-2)***

The SRS-2 (Constantino, 2012) is a 65-item caregiver-report questionnaire that provides a quantitative measure of autism-related traits in children. The SRS is used as a measure of children's social impairments and focuses on their behaviors during the past 6 months. Caregivers respond to each item using a four-point Likert scale with a score of 1 indicating a behavior that is not present and 4 indicating a behavior that is almost always present. Of the three available SRS-2 forms, the present study administered the School-Age form to participants in both the groups. The SRS-2 Standard scores as well as Social Communication and Interaction (SCI) and Restricted Interests and Repetitive Behavior (RRB) scores were used as measures of ASD symptom severity, with higher scores reflecting greater severity, while examining the association between reaction times on the tactile-cueing task and ASD symptomatology (Objective 3).

#### ***3.3.2.3 Sensory Profile-2 (SP-2)***

The SP-2 (Dunn, 2014) is a caregiver-report questionnaire designed to assess everyday sensory processing in 3- to 14-year-olds. It consists of 86 items that are divided into six sensory categories (auditory, visual, touch, movement, body position, and oral), three behavioral categories (conduct, social emotion, and attention), and four quadrants (seeking, avoiding, sensitivity, and registration). Parents respond to each item using a five-point Likert scale with a score of 1

indicating a behavior that is present almost never and 5 indicating a behavior that is present almost always. Scores from the Touch Sensory Profile were used as measures of tactile sensory processing. Additionally, scores from four quadrants were used to calculate a sensitivity index score while examining the association between reaction times on the tactile-cueing task and ASD symptomatology (Objective 3).

#### ***3.3.2.4 Peabody Picture Vocabulary Test- 4 (PPVT-4)***

The PPVT-4 (Dunn & Dunn, 2007) was administrated to examine the association between reaction times on the tactile-cueing task and receptive language skills in children with and without ASD. The PPVT-4 (Dunn & Dunn, 2007) is a standardized assessment that measures single word receptive language skills in children and adults. It is conducted in a structured format where the examiner orally presents a target word along with four pictures, and the participant is instructed to select the picture that best represents the meaning of the target word. PPVT-4 standard scores were used as measures of receptive language skills with higher scores reflecting greater receptive language skills (Objective 4).

#### ***3.3.2.5 Expressive Vocabulary Test (EVT-2)***

The EVT-2 (Williams, 2007) was administrated to examine the association between reaction times on the tactile-cueing task and expressive language skills in children with and without ASD. The EVT-2 (Williams, 2007) is a standardized assessment that measures single word expressive language skills in children and adults. It is conducted in a structured format where the participant is instructed to name pictures that are presented one at a time. EVT-2 standard scores were used as measures of expressive language skills with higher scores reflecting greater expressive language skills (Objective 4).

### **3.3.3 Experimental stimuli**

#### ***3.3.3.1 Auditory stimuli***

Auditory stimuli consisted of the vowel sound /a/ generated using the Praat software (Boersma & Weenink, 2019). The /a/ sound was created with four lowest frequencies of 140, 800, 1290, and 2080 Hz (as it fits within the pitch range of a typical male speaker; Goy et al., 2013),

and the duration of the vowel was set as 200 ms (similar to the duration of stimuli used in Whitehouse & Bishop, 2008). Auditory stimuli were presented at a comfortable listening level (60 dB) using a central speaker located approximately 60 cm from the participant.

### **3.3.3.2 Tactile stimuli**

A custom tactor was used to deliver vibrotactile stimuli to participants' index fingertip of the non-dominant hand (Figure 3.1a). Vibrotactile stimuli were delivered on the fingertip to be consistent with the location of the tactile stimuli in the past studies that have examined touch responsivity in individuals with ASD (Blakemore et al., 2006; Cascio et al., 2015; Marco et al., 2012). Vibrotactile stimuli were presented to the non-dominant hand because participants were instructed to respond with a button press using their dominant hand. Tactile stimuli consisted of vibrotactile stimulation presented at a frequency of 290 Hz. A vibrotactile frequency of 290 Hz was chosen because individuals with ASD have shown differences in tactile responsivity to high-frequency, but not low-frequency, vibrations (Blakemore et al., 2006) that stimulate Pacinian corpuscles; a type of mechanoreceptor that is sensitive to vibrotactile stimuli ranging from 100 – 300 Hz (Johnson, 2001). Last, similar to the duration of the auditory stimuli, tactile stimuli also lasted for 200 ms.

### **3.3.4 Procedure**

The total testing time was divided into two sessions to ensure the cooperation of all participants. Session 1 included consenting procedure and standardized testing and session 2 included the tactile-cueing task. Session 1 was conducted in a brightly lit room with child sized furniture. After an experimenter explained the procedure, caregivers and participants provided their written informed consent and assent respectively. Next, a trained examiner administered the ADOS-2 (Lord et al., 2012) only to participants in the ASD group. Finally, all participants were administered standardized cognitive and language measures along with the Edinburgh Handedness Inventory (Oldfield, 1971), while the caregivers completed the SCQ (Rutter et al., 2003), the SRS-2 (Constantino, 2012), and the SP-2 (Dunn, 2014). Session 2 was conducted within a month after completing Session 1.

During Session 2, participants completed a tactile-cuing task in which they were instructed to respond with a button press to the target speech sound /a/. On 75% of the trials, participants received a tactile cue before the target speech sound. Tactile cues were presented at 200, 400, and 800 ms (25% each) prior to the onset of the target speech sound (Figure 3.1b). The remaining 25% of the trials were presented without the tactile cues (Figure 3.1c). Participants were informed that on some trials they would feel a ‘tingle’ before the sound, and on some they would not. They were instructed to press the button as quickly as they could *only* in response to the speech sound.

Participants first completed a practice round which included a total of 16 trials. During the practice session, all participants received immediate feedback on the computer after each button press informing them about the accuracy of their response (e.g., ‘correct’ if the button was pressed within 3 seconds after the speech sound; ‘incorrect’ if the button was pressed before the speech sound or if the button was not pressed at all). In case the participants pressed the button before the sound, the computer feedback reminded them to wait for the speech sound. Participants did not receive feedback regarding their reaction times during practice. Completing the practice session ensured the experimenter that the participants were able to follow the instructions. The experiment proper followed the practice session and included a total of 96 trials divided into 3 blocks of 32 trials each. Participants did not receive any feedback during test trials.

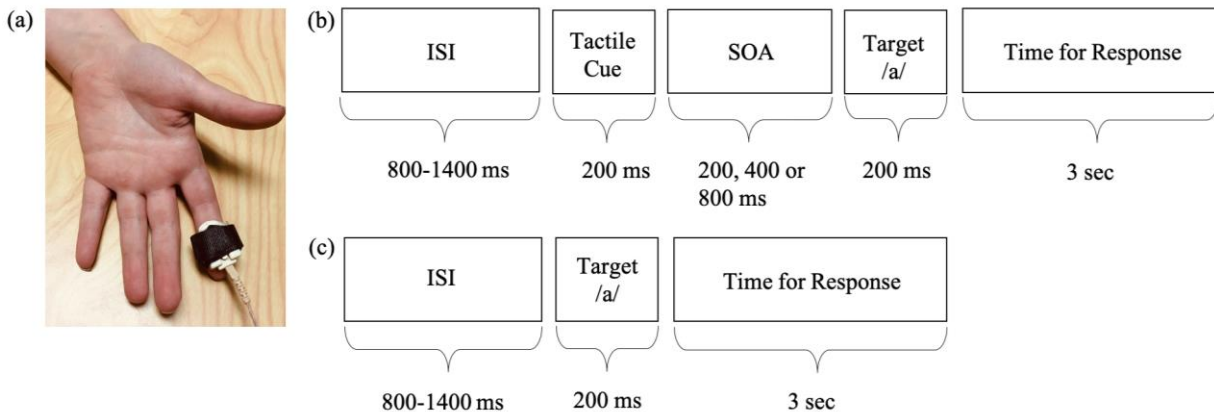


Figure 3.1. (a) Mechanical tactor used to deliver the tactile cues. Illustration of trials with (b) and without (c) tactile cues. ISI, Interstimulus Interval; SOA, Stimulus Onset Asynchrony

### 3.3.5 Analysis

First, independent sample t-tests were conducted to explore parent reported behavioral differences in responding to tactile and auditory inputs in children with ASD and TD. Next,

measures of accuracy and median reaction time (RTs) were calculated for trials with and without touch cues. Accuracy was defined as any response that occurred within 3 seconds after the presentation of the speech sound. Reaction time was defined as the duration between the presentation of the target speech sound and the first button press within 3 seconds after the speech sound. Finally, anticipatory responses (i.e., button presses before or 100 ms after the speech sound) were excluded from further analyses.

Statistical analyses were conducted in SPSS software version 25 (IBM SPSS Statistics 25; Chicago, IL). A separate repeated measures ANOVA with Group (ASD, TD) as between-subjects factor and Interval (no cue, 200, 400, 800 ms SOA) as within-subjects factor was conducted to examine differences in percentages of (1) accuracy (2) and anticipations as well as (3) median RTs between ASD and TD groups. When significant differences were observed in ANOVAs, follow-up t-tests were subsequently conducted to examine simple effects. Results related to reaction time were followed up with exploratory analyses to investigate the percentage of RT facilitation at various touch-cue intervals. The percentage of facilitation was calculated by entering median reaction time values into the following formula:  $((RT_{\text{No Cue}} - RT_{200 \text{ SOA}})/RT_{\text{No Cue}}) * 100$ . The same formula was used to calculate percentage facilitation at 400 and 800 ms touch-cue intervals. A repeated measures ANOVA with Group (ASD, TD) as a between-subjects factor and Cue Interval (200, 400, 800 ms SOA) as a within-subjects factor was conducted to examine the percentage of behavioral facilitation as a result of tactile cues.

Correlational analyses examined the association between performance on the tactile-cueing task (measured using the mean difference score), and ADOS-2 severity scores along with SRS-2, tactile SP-2, PPVT-4, and EVT-2 standard scores. Difference scores were calculated by subtracting median RTs in each of the three tactile-cueing intervals from median RTs in the no-cue condition (i.e.,  $RT_{\text{No Cue}} - RT_{200 \text{ SOA}}$ ;  $RT_{\text{No Cue}} - RT_{400 \text{ SOA}}$ ;  $RT_{\text{No Cue}} - RT_{800 \text{ SOA}}$ ). The mean of the three difference scores was used as a measure of performance facilitation on the tactile-cueing task.

Last, correlations were examined between the mean difference score and SP-2 sensitivity index score that indicated a tendency of hypo- or hyper- reactivity in each participant. Sensitivity index score was calculated by first combining average quadrant scores that suggested hyper-reactivity (avoiding + sensitivity) and hypo-reactivity (seeking + registration). These two scores were then entered into the following equation:  $((\text{hyper-reactivity} - \text{hypo-reactivity}) / (\text{hyper-}$

reactivity + hypo-reactivity)) X 100. Resulting positive scores indicated a tendency for hyper-reactivity, whereas, negative scores indicated hypo-reactivity.

### 3.4 Results

Independent sample t-tests were conducted to explore parent reported behavioral differences in responding to tactile and auditory input in children with ASD and TD. As expected, children with ASD showed a greater number sensory symptoms in the tactile and auditory domains compared to TD children as measured by parent report (touch,  $t(28) = 5.15$ ,  $p < .001$ ,  $d = 1.86$ ; audition,  $t(28) = 7.66$ ,  $p < .001$ ,  $d = 2.63$ ; Table 3.1). These results confirmed the presence of aberrant behavioral responses to tactile and auditory stimuli in children with ASD.

#### 3.4.1 Accuracy

Accuracy results were entered into a 2 (Group: ASD, TD) X 4 (Interval: no cue, 200, 400, 800 ms SOA) repeated measures ANOVA to examine if the two groups differed in their percentages of accurate responses as a result of cue interval. Results revealed that there was a significant within-subjects main effect of Interval on the amount of accurate responses in ASD and TD groups,  $F(3,84) = 16.07$ ,  $p < .001$ ,  $\eta_p^2 = .36$ . Accuracy was most affected in trials with 800 SOA compared to 400 SOA,  $t(29) = -3.52$ ,  $p = .001$ ,  $d = .64$ , 200 SOA,  $t(29) = 4.06$ ,  $p < .001$ ,  $d = .74$ , and no cue interval,  $t(29) = 4.48$ ,  $p < .001$ ,  $d = .83$  (800 SOA < 400 SOA < 200 SOA & no cue; Table 3.2). There was no main effect of Group,  $F(1,28) = 4.12$ ,  $p = .052$ ,  $\eta_p^2 = .12$ , nor was there an interaction between Group and Interval  $F(3, 84) = .87$ ,  $p = .459$ ,  $\eta_p^2 = .03$ . Additionally, because percentages of accuracy at no cue, 200, 400, and 800 SOA were not normally distributed (Shapiro-Wilk test: all  $ps < .001$ ), data were log transformed in SPSS. Results of ANOVA using log-transformed data remain unchanged. These results indicated that both groups showed greater accuracy in no cue and at shorter SOAs compared to longer SOAs.

Table 3.2. Percentage of accurate trials in ASD and TD groups

Interval (Max. trials)	ASD	TD	Statistic	<i>p</i>
No touch cues (24)	93 (11); 63-100	98 (3); 88-100	$t(28) = -1.71$	.098
Touch cue 200 ms prior (24)	93 (9); 75-100	98 (3); 92-100	$t(28) = -1.94$	.062
Touch cue 400 ms prior (24)	83 (13); 67-100	91 (11); 67-100	$t(28) = -1.62$	.115
Touch cue 800 ms prior (24)	70 (30); 8-100	84 (17); 46-100	$t(28) = -1.53$	.135
Mean (SD); range				

### 3.4.2 Anticipatory responses

A 2 (Group: ASD, TD) X 4 (Interval: no cue, 200, 400, 800 ms SOA) repeated measures ANOVA was conducted to examine if the two groups differed in their percentages of anticipatory responses at different cue intervals. Anticipatory responses were defined as button presses that occurred before the presentation of a target speech sound or within 100 ms after the speech sound. Results revealed that there was a significant within-subjects main effect of Interval on the amount of anticipatory responses in ASD and TD groups,  $F(3,84) = 19.51$ ,  $p < .001$ ,  $\eta_p^2 = .41$ . The percentage of anticipatory responses were greater in trials with 800 SOA compared to 400 SOA,  $t(29) = -4.06$ ,  $p < .001$ ,  $d = .74$ , 200 SOA,  $t(29) = -4.49$ ,  $p < .001$ ,  $d = .82$ , and no cue interval,  $t(29) = -4.45$ ,  $p < .001$ ,  $d = .81$  (800 SOA > 400 SOA > 200 SOA & no cue; Table 3.3). There was no significant main effect of Group,  $F(1,28) = 1.44$ ,  $p = .240$ ,  $\eta_p^2 = .04$ , nor was there an interaction between Group and Interval  $F(3, 84) = .37$ ,  $p = .376$ ,  $\eta_p^2 = .03$ .



Table 3.3. Percentage of anticipatory responses in ASD and TD groups

Interval (Max. trials)	ASD	TD	Statistic	<i>p</i>
No touch cues (24)	1 (3); 0-8	.2 (1); 0-4	$t(28) = 1.34$	.19
Touch cue 200 ms prior (24)	1 (3); 0-13	1(3); 0-8	$t(28) = .00$	1
Touch cue 400 ms prior (24)	12 (12); 0-33	7 (9); 0-21	$t(28) = 1.36$	.18
Touch cue 800 ms prior (24)	25 (30); 0-92	16 (17); 0-54	$t(28) = 1.05$	.29

Mean (SD); range

### 3.4.3 Reaction time

I examined whether behavioral facilitation was affected by touch cue intervals by entering median RTs into a repeated measures ANOVA with Group as a between-subjects factor (ASD, TD) and Interval as a within-subjects factor (no cue, 200, 400, 800 SOA). Results suggested that there was a significant within-subjects main effect of Interval  $F(3, 84) = 47.79, p < .001, \eta_p^2 = .63$ . Compared to no cue trials, median RTs were reduced for 200 SOA,  $t(29) = 7.56, p < .001, d = 1.38$ , 400 SOA,  $t(29) = 7.50, p < .001, d = 1.36$ , and 800 SOA,  $t(29) = 9.19, p < .001, d = 1.67$ . Both groups showed greater facilitation in response to longer SOAs. Particularly, compared to 200 SOA, median RTs were reduced for 400 SOA  $t(29) = 2.57, p < .01, d = .47$ , and 800 SOA  $t(29) = 4.12, p < .001, d = .75$ . There were, however, no differences between median RTs between 400 and 800 SOA  $t(29) = .05, p < .95, d = .01$  (Table 3.4; Figure 3.2). Additionally, there was a significant main effect of Group  $F(1, 28) = 4.55, p = .04, \eta_p^2 = .14$ . However, there was no interaction between Group and Interval  $F(3, 84) = .35, p = .78, \eta_p^2 = .01$ . Because median RTs at no cue, 200, 400 and 800 SOA were not normally distributed (Shapiro-Wilk test:  $ps < .001$ ), data were log transformed in SPSS. Results of an ANOVA using log-transformed data remain unchanged. These results suggested that, although both groups showed evidence of facilitation as a result of tactile cues, especially at longer SOAs, children with ASD were overall slower to respond to the target speech sound compared to TD children.

Table 3.4. Median RTs for ASD and TD Groups

Interval	ASD	TD	Statistic	<i>p</i>
Touch cue absent	801.14 (303.95); 268.71-1186.74	633.78 (150.44); 462.81-1048.18	$t(28) = 1.91$	.07
Touch cue 200 ms prior	619.38 (304.53); 310.78-1378.74	433.37 (127.87); 296.58-805.88	$t(28) = 2.18$	.04
Touch cue 400 ms prior	549.36 (274.91); 246.53-1300.50	395.06 (128.97); 251.51-771.30	$t(28) = 1.96$	.06
Touch cue 800 ms prior	540.62 (242.14); 238.98-1079.30	401.87 (143.15); 232.72-772.67	$t(28) = 1.91$	.07

Mean (SD); range

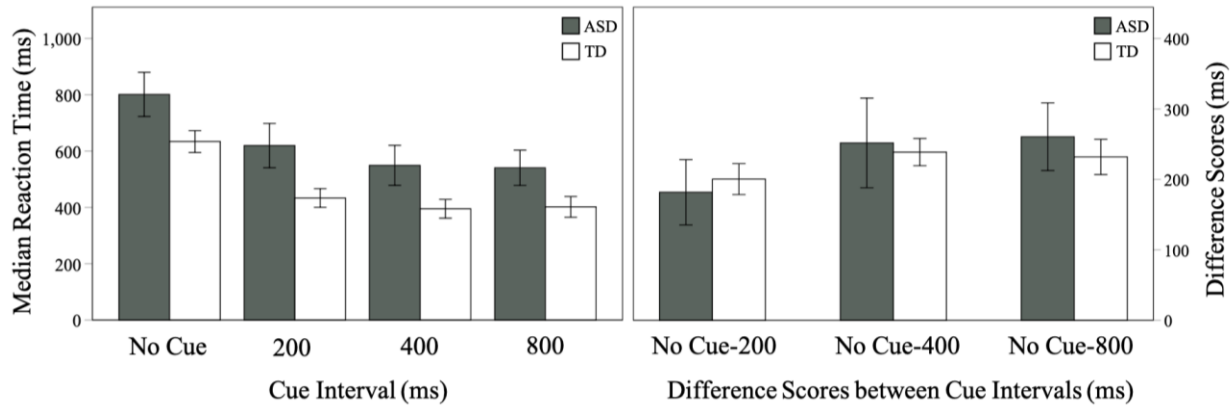


Figure 3.2. Median RTs showing both groups are faster to respond when tactile cues are present. Error bars represent  $\pm 1$  SE.

### 3.4.3.1 Exploratory analyses for reaction time

Because the current results showed a main effect of Group and a main effect of Interval for reaction time, I followed these up with exploratory analyses investigating the percentage of facilitation in reaction times at different touch-cue intervals. The repeated measures ANOVA revealed that there was a within-subjects main effect of Cue Interval  $F(2, 56) = 8.07, p = .001, \eta_p^2 = .22$ . When presented with touch cues, percentage facilitation was greater at 400  $t(29) = 3.11, p < .004, d = .56$  and 800 ms  $t(29) = 4.36, p < .001, d = .79$  compared to the 200 ms interval.

However, there was no main effect of Group  $F(1, 28) = 1.32, p = .259, \eta_p^2 = .04$ , nor was there an interaction between Group and Interval  $F(2, 56) = .388, p = .68, \eta_p^2 = .01$  (Table 3.5).

Table 3.5. Percentage facilitation for ASD and TD Groups

Interval	ASD	TD	Statistic	<i>p</i>
Touch cue 200 ms prior	24 (19); 12-48	31 (11); 17-56	$t(28) = 1.41$	.16
Touch cue 400 ms prior	31 (24); 14-59	38 (10); 25-56	$t(28) = 1.06$	.29
Touch cue 800 ms prior	32 (19); 3-60	37 (14); 17-59	$t(28) = .76$	.45

*Note.* Values represent percentage facilitation in reaction times when presented with touch-cues compared to no-cue condition. For instance, children with ASD showed a 24% facilitation in their reaction times when touch cues were presented 200 ms prior to the target sound. Mean (SD); range

These exploratory results confirm that although children with ASD were overall slower to respond to target speech sounds (as shown in Table 3.4), both groups showed equivalent amounts of percentage facilitation when presented with touch cues before the auditory targets.

#### **3.4.4 Correlation between behavioral facilitation, and ASD symptomatology and language**

Pearson correlations were conducted to examine if behavioral facilitation as a result of touch cues presented before the target sound was associated with ASD symptomatology as well as language. In order to reduce the number of correlations run, I used the mean of the three difference scores as a measure of performance facilitation on the tactile-cueing task. Results suggested that, behavioral facilitation to touch cues was not significantly correlated with measures of ASD symptomatology and language scores for all children (all  $ps > .37$ ) as well as for children in ASD (all  $ps > .32$ ) and TD (all  $ps > .09$ ) groups (Table 3.6).

Table 3.6. Correlations between behavioral facilitation to tactile cues and ASD symptomatology

Group	ADOS-2			SRS-2			SP-2			
	SA	RRB	SS	SCI	RRB	Total	Tactile	Sensitivity Score	PPVT- 4	EVT- 2
All (n = 30)	-	-	-	.02	.03	.02	.09	-.11	-.01	-.02
ASD (n = 15)	.20	.26	.27	.08	.08	.08	.03	-.16	.02	.002
TD (n = 15)	-	-	-	-.32	-.21	-.30	.44	-.08	-.12	-.09

*Note.* SA, Social Affect; RRB, Restricted and Repetitive Behaviors, SS, Severity Score SCI, Social Communication and Interaction; RRB, Restricted Interests and Repetitive Behaviors; Tactile SP-2, Tactile section of Sensory Profile-2; PPVT-4, Peabody Picture Vocabulary Test-4; EVT-2, Expressive Vocabulary Test-2.

### 3.5 Discussion

The goal of this study was to investigate the response of the alerting network by presenting tactile cues before auditory targets in children with and without ASD in a tactile-cueing paradigm. Past research has revealed that children with ASD may show equivalent alerting in behavioral tasks where target stimuli are preceded by cues that fall within (Keehn et al., 2010; Landry et al., 2009) or outside (Kleberg et al., 2017; Raymaekers et al., 2006) the modality of the target stimuli. These studies showing similar alerting in ASD and TD have mainly used a variety of auditory and visual cues to investigate the response of the alerting network within and across modalities. I designed a task that specifically included tactile cues because of the role that touch plays in facilitating attention (Jean & Stack, 2009; Stack & Muir, 1992). Additionally, although touch is one of the frequently presented channels in early social interactions (Stack & Muir, 1990), it may still be relatively less frequent given the high amount of exposure to speech (Bergelson et al., 2019) and surrounding visual stimuli, making it more novel. Therefore, I reasoned that the relatively low frequency and novelty associated with touch may be beneficial in facilitating behavioral responses in everyday life. However, given that individuals with ASD often show differences in processing tactile stimuli (Mikkelsen et al., 2018), they may show atypicalities in effectively using informative tactile cues to benefit their behavioral responses compared to TD individuals.

Therefore, it becomes essential to systematically examine the role of tactile cues in facilitating behavioral responses in typical and atypical development.

To the best of my knowledge, no study to date has examined whether the presentation of tactile cues before an auditory target facilitates behavioral performance in children with ASD indicating efficiency of the alerting network across audio-tactile modalities. I explored this topic by examining (1) whether transient tactile cues presented before an auditory target impact behavioral responses measured by accuracy and reaction time in children with and without ASD, and (2) whether changes in the duration (SOAs) between tactile cues and auditory targets impact accuracy and reaction time of behavioral responses in children with and without ASD. Additionally, because previous research has shown links between the alerting network and ASD symptomatology (Keehn et al., 2010), in my third objective I sought to investigate whether behavioral responses in the tactile-cueing task are associated with ASD symptomatology in children with ASD and TD. Finally, given the role that touch plays in language acquisition (Abu-Zhaya et al., 2017; Nomikou & Rohlfsing, 2011; Seidl et al., 2015), my fourth objective was to determine the association between touch related behavioral facilitation and language skills in ASD and TD.

It has been shown that, at least in studies using audio-visual stimuli, the presentation of auditory cues before visual targets results in increased anticipatory responses (Fernandez-Duque & Posner, 1997; Raymaekers et al., 2006). Given these findings, I hypothesized that, the presentation of tactile cues before the target will be associated with an increase in anticipatory responses in all children that may be dependent on the cue-target interval with more anticipatory errors occurring at longer intervals affecting overall accuracy. Next, similar to auditory and visual cues, if alerting responses to tactile cues are equivalent in ASD and TD, then children in both groups should display behavioral facilitation after receiving tactile cues irrespective of the duration between tactile cues and auditory targets. However, if processing of touch is atypical in children with ASD, then they should show reduced touch-related facilitation compared to TD children as measured by diminished changes in reaction times in trials with and without tactile cues. Alternatively, if children with ASD show differences in attending to the tactile input (i.e., slower attentional orienting to touch), then they should mainly benefit from longer touch-cue intervals compared to shorter intervals. Finally, I hypothesized that reduced touch-related facilitation will

be associated with greater ASD symptomatology and language related impairments in ASD and TD.

The current results indicated that, not just the presence of tactile cues, but the duration between tactile cues and auditory targets impacted accuracy in both the ASD and TD groups. Specifically, all children exhibited higher accuracy in conditions with no touch-cues and at 200 ms SOA. Participants were more likely to make errors (i.e., anticipatory responses or no responses) when touch-cue intervals were longer. Especially, anticipatory responses were most common in both groups with longer touch-cue intervals. However, the percentages of accuracy and anticipatory responses did not differ between children with and without ASD at any of the intervals, suggesting similar error patterns in ASD and TD at all SOAs.

My finding of increased error rate in conditions with longer touch-cue intervals is partially consistent with the findings of Raymaekers et al. (2006) who showed increased anticipatory errors when salient auditory cues were presented before visual targets in children with and without ASD. However, it should be noted that the current paradigm differed slightly from that of Raymaekers et al. (2006). In the current study, I systematically examined the effect of variable cue-target interval on participants' responses, whereas in Raymaekers et al. (2006) differences in interstimulus interval in relation to error rate have not been discussed. As observed in Raymaekers et al. (2006), if accuracy and anticipatory responses were merely affected as a result of presenting cues before the target, then there would have been a uniform increase in error rate at all three touch-cue intervals. However, this was not the case; anticipatory errors were more likely at 400 and 800 ms SOA, but not at 200 ms SOA. Given the evidence, I extend the findings of Raymaekers et al. (2006) to an audio-tactile paradigm, suggesting a modality-independent anticipatory effect that may be dependent on the duration between cues and targets. In sum, anticipatory errors may reflect sudden increase in alerting/arousal levels as a result of encountering cues that systematically indicate upcoming targets, and may be more prominent when participants are required to wait a long time to be presented with a target and submit their responses.

Presentation of transient tactile cues before auditory targets resulted in faster reaction times in children in both groups, suggesting similar alerting in ASD and TD. These findings are consistent with previous studies that have shown evidence of faster reaction times when within or across-modality cues are presented shortly before the target stimuli (Keehn et al., 2010; Keetels & Vroomen, 2011; Kleberg et al., 2017; Raymaekers et al., 2006). I extend these findings to audio-

tactile modality and suggest that efficient phasic alerting may also be observed in multimodal settings in ASD and TD. My findings also revealed that variable touch-cue intervals affected reaction times in both groups. Specifically, the percentage of facilitation in reaction times was greater at 400 and 800 ms SOA compared to 200 ms SOA. Additionally, the facilitation effect plateaued after 400 ms SOA in both groups. These results are similar to those in previous research by Landry et al. (2009) in which children with and without ASD showed attenuated reaction times as SOAs between cues and targets increased. I argue that, longer intervals between cues and targets may have provided children with more time to prepare for a response resulting in enhanced performance following the presentation of the target compared to shorter cue-target intervals.

My results showing touch-related behavioral facilitation in all children could be attributed to the efficient response of the phasic alerting network. Phasic alerting is associated with improved response readiness and faster processing speed of incoming sensory information (Posner & Rothbart, 2007; Sturm & Willmes, 2001). Given these results, I argue that, similar to visual and auditory modalities, tactile cues may also impact the alerting network similarly in children with ASD and TD. Additionally, it is possible that the predictable nature of events in touch-cue trials (i.e., presentation of touch cues → waiting period lasting between 200 to 800 ms → presentation of auditory target followed by response) facilitated behavioral performance in all children. Although the present task included variable cue-target intervals as well as 25% of trials with no cues introducing some level of uncertainty regarding the onset of the target, just the presence of cues *always* indicated impending targets making trials with tactile cues more predictable compared to no-cue trials. For instance, every time a participant encountered a tactile cue, it signaled to the participant that a target sound was about to be presented in a brief period of time. This predictable course of events in cued trials may have assisted participants in learning the temporal relationship between cues and targets (i.e., a target will always be presented after a 200 to 800 ms window following the cue). Therefore, along with the efficiency of the alerting network, implicitly learning the temporal pattern between cues and targets may have increased response readiness in all children resulting in faster reaction times in cued trials compared to no-cue trials. The argument in favor of predictability of events facilitating behavioral responses is consistent with previous findings suggesting possible links between predictive events and efficient cognitive processing (for a review, see Bubic, Von Cramon, & Schubotz, 2010).

To my knowledge, this is the first study to examine how touch may serve as an informative cue to facilitate behavioral performance in ASD. As mentioned in the introduction, differences in tactile processing are a common feature in individuals with ASD (Baranek et al., 2006; Mikkelsen et al., 2018), which may affect how touch is perceived and used in various settings. Current results allow me to argue against an impairment in sensory or attentional processing of tactile stimuli in ASD. In particular, present findings do not indicate hypo-reactivity to tactile cues in ASD, as a disruption at this level would have resulted in no facilitation effects in any of the three touch-cue intervals. However, this was not the case. Similarly, my results do not suggest an impairment in attending to tactile cues, because if attention to touch were impaired in ASD, then children in this group would have benefitted only from longer touch-cue intervals. However, present results showed that facilitation effects were present even at the shortest SOA in children with ASD.

In the present study, although children in both groups learned the association between tactile cues and the auditory targets, children with ASD were overall slower in their responses compared to TD children. This main effect of Group on reaction times may be related to differences in attentional set shifting in ASD. For instance, previous research has reported greater differences in attentional switching in tasks requiring shifting of attention across modalities in ASD compared to TD controls (Courchesne et al., 1994; Reed & McCarthy, 2012; Williams et al., 2013). Given the nature of the present task, participants were required to non-spatially shift their attentional focus between tactile cues and auditory targets and to use information from the tactile modality to facilitate processing of the auditory modality. Therefore, although there was equivalent touch-related facilitation effect in children with ASD, set shifting between modalities may have resulted in slowed reaction times compared to TD children. Future research should examine this further by providing unimodal vs cross-modal cues that require shifting of attention within and across modalities respectively.

Finally, contrary to my hypotheses, my correlational analyses did not reveal significant associations between behavioral facilitation to touch cues and measures of ASD symptomatology and language skills in ASD and TD children. My correlational analyses are not consistent with past research that reported links between alerting in response to non-social visual cues and ASD symptomatology (Keehn et al., 2010). These contradictory results could be related to the nature of the modality. For example, the association between alerting responses to non-social cues and ASD symptomatology could be more prevalent in the visual modality compared to the tactile modality.



Because touch is inherently a social signal (Dunbar, 2010; Hertenstein, 2002) and that social touch has been shown to facilitate learning (Lew-Williams, Ferguson, Abu-Zhaya, & Seidl, 2019), future studies should aim to examine the links between alerting in response to social touch and ASD symptomatology and language skills; as this correlation may be more robust compared to examining the association between non-social tactile vibrations on the fingertip and ASD symptomatology.

This study is not without limitations. My sample was relatively small as a result of limited data collection due to COVID-19. Further, the sample was limited in diversity/severity due to task related demands and included only high-functioning children with ASD and TD. My sample, therefore, may not be adequately representative of a heterogeneous sample of ASD. Additionally, although I improved ecological validity by presenting a cross-modal tactile-cueing task, the nature of the tactile cues in my study do not represent the heterogeneity of touches experienced in the outside world. For instance, my tactile stimuli were experimentally controlled non-social vibrations on the fingertip. Whereas, touches used to facilitate alerting in real-world settings may include a variety of touches (e.g., tap, brush, tickle), locations (e.g., touch on the shoulder, arm, leg), and may also show a range of communicative intents and are more dynamic (e.g., touch to get attention, convey affect; Ferber et al., 2008; Field, 2001; Hertenstein, 2002). Moreover, although caregivers frequently use touch during early social interactions (Stack & Muir, 1990), given the overall high frequency of caregivers' infant-directed speech (Bergelson et al., 2019), and the constant exposure to surrounding visual stimuli, it is possible that touch is a less frequent stimulus compared to these two modalities, making it more salient and special. Individuals presented with touch in non-experimental settings are therefore required to respond to a variety of aspects of that touch while learning cross-modal links between touch and other modalities that are presented during that interaction. The crucial difference between the quality of experimentally controlled non-social touch and novel and dynamic touch experienced in the outside world, therefore, warrants further exploration to understand how touch-related alerting in everyday life may contribute to the ASD phenotype.

In sum, the present study revealed that children in both the ASD and TD groups show equivalent phasic alerting in response to transient tactile cues. However, overall reaction times might be generally slower in children with ASD compared to TD children. These results have

implications in everyday social interactions, where novel and dynamic touches are naturally used as cues to facilitate alerting before a variety of auditory or visual stimuli are presented.

## 4. GENERAL DISCUSSION

Touch is an important channel that modulates social communication (Cascio, Moore, & McGlone, 2019; Gliga, Farroni, & Cascio, 2019). For example, touch conveys affect (Field, 2010; Hertenstein, Holmes, McCullough, & Keltner, 2009; Hertenstein, Keltner, App, Bulleit, & Jaskolka, 2006), and increases infant attention (Jean & Stack, 2009; Stack & Muir, 1992), smiles and vocalizations (Stack & Muir, 1992) thereby improving the quality of interpersonal social communication. Touch also forms the basis of early caregiver-child interactions (Stack & Muir, 1990) and may aid in language learning (Abu-Zhaya et al., 2017; Seidl et al., 2015). For example, typically developing (TD) infants can use tactile cues to find linguistic units in continuous speech (Seidl et al., 2015) and infants' early vocabularies include words that are frequently associated with caregiver touches (Abu-Zhaya et al., 2017). Therefore, perceiving and attending to relevant tactile input is vital during social interactions, and any impairment in responding to touch may be detrimental for the development of social and linguistic skills.

Behavioral responses to tactile stimuli, however, are often an area of concern for individuals with ASD (Mikkelsen et al., 2018). Atypical patterns of tactile responsivity are well documented from first-person accounts of individuals with ASD (Cesaroni & Garber, 1991; Grandin, 1992), parental reports (Baranek et al., 2006; Leekam et al., 2007), and clinical observations (Baranek, 1999; Baranek & Berkson, 1994). These differences in responding to touch in ASD have been linked with core and associated clinical symptoms of the disorder (Foss-Feig et al., 2012). Additionally, we now know that atypical responsivity to touch is present in infancy and can be related to later diagnosis and symptom severity of ASD (Kadlaskar et al., 2019). For example, Kadlaskar et al. (2019) showed that 12-month-olds at high risk for ASD who later received a diagnosis of ASD were overall less responsive to caregiver touch, and when they did respond, they were more likely to orient away from that interaction. Moreover, in the high-risk group, infants' responsivity to touch was related to later ASD symptomatology. Because differences in responding to touch are frequently observed in ASD (Mikkelsen et al., 2018), and that atypical responsivity to touch (observed as early as 12 months) has been linked with later ASD symptom severity (Kadlaskar et al., 2019), it becomes important to examine whether touch is processed differently in individuals with ASD compared to their TD peers.

Although touch plays an important role in facilitating social interactions, it is rarely presented in isolation. Specifically, when experiencing caregiver touches, infants are also exposed to caregivers' speech and other visual stimuli that are constantly encountered when the child is awake (e.g., objects in the surrounding area). Abu-Zhaya et al. (2017) support this argument by showing that, in a book reading scenario with TD infants, caregivers often align their touches with spoken language. This study confirmed that infants are often exposed to auditory (i.e., mother's speech) as well as surrounding visual stimuli (i.e., pictures in a book) while experiencing touches in naturalistic settings. Evidence of caregiver touch presentation along with speech has also been reported in infants at risk for ASD. For example, Kadlaskar et al. (2020) showed that caregivers of infants at high- and low-risk for ASD communicated with their infants using a greater number of touch-speech stimuli compared to touch-only stimuli. As a result, examining touch in the context of speech and other constantly existing surrounding visual stimuli may provide a more ecologically valid perspective of tactile processing in both children with ASD and TD.

As previously mentioned, differences in responding to tactile and auditory inputs (including speech) have been widely reported in individuals with ASD (for reviews, see Mikkelsen et al., 2018; O'Connor, 2012); however, the underlying mechanisms that may explain these behavioral differences still remain unclear. For example, using neuroimaging measures some have argued that there may be differences in how individuals with ASD *perceive* tactile and auditory inputs as evidenced by atypical early neural responses to such inputs (Bruneau et al., 2003; Marco et al., 2012; Rosenhall et al., 2003), whereas, others have argued that differences in tactile and auditory processing may be more related to atypical *attentional* processing of incoming stimuli which is manifested in later neural responses to sensory stimuli (Cascio et al., 2015; Čeponienė et al., 2003). In order to examine this further, I designed a study that investigated neural indices of perceptual and attentional factors (measured by early and late ERP components respectively) underlying tactile and auditory processing in children with and without ASD. Given the mixed evidence, I hypothesized that if differences in sensory response profiles in ASD are related to impairments in perception of the stimuli, then there should be differences in early neural responses compared to TD children. On the other hand, if behavioral manifestations of sensory symptoms in ASD are related to atypical allocation of attention, then there should be differences in later ERP components that are indicative of attentional functioning compared to TD children.

Contrary to these hypotheses, my results indicated that, children with ASD showed equivalent early as well as later neural responses to tactile and auditory stimuli compared to their TD peers. These findings are in contrast to past studies that have suggested that tactile and auditory differences in ASD may be related to early (Marco et al., 2012; Russo et al., 2010) and later (Cascio et al., 2015; Čeponienė et al., 2003) neural components. These inconsistencies in the results could be related to methodological differences among studies. For example, in Marco et al. (2012), participants were presented with pneumatically driven pulses as tactile stimuli, whereas, in the current experiment, tactile stimuli consisted of high-frequency vibrations.

Additionally, it is possible that the bimodal nature of my novel tactile stimuli (i.e., vibration along with a speech sound) may have facilitated early and later neural responsivity in the ASD group compared to the presentation of unimodal tactile stimuli that yielded neurological differences in previous research (Marco et al., 2012). Support for this argument comes from Russo et al. (2010) who showed attenuated neural amplitudes in response to unimodal somatosensory input starting around 70 ms post-stimulus onset in children with ASD compared to TD children. The facilitative effect of bimodal input has also been reported in Kadlaskar et al. (2020), where infants at risk for ASD were more likely to orient to maternal bids for communication when they were presented with bimodal touch-speech input compared to unimodal touch-only input. Therefore, it is possible that in the current study additive effects of multimodal cues may have aided in processing of the novel stimuli. However, because there was no touch-only condition in the present study, more research is needed to determine whether it was bimodal nature of the stimuli that modulated processing of the novel tactile stimuli. Given these mixed results, I argue that under certain conditions, children with ASD may show equivalent neural responsivity to tactile and auditory stimuli compared to their TD peers indicating typical perceptual as well as attentional processing of incoming sensory stimuli.

Given the links between differences in sensory responsivity and ASD symptomatology (Foss-Feig et al., 2012; Watson et al., 2011), I hypothesized that neural indices of tactile and auditory processing would be associated with ASD symptomatology and language skills in children with and without ASD. My correlational analyses partially supported this hypothesis. In particular, early tactile and auditory neural responses were related to parent-reported tactile sensory symptoms in all children and impairments in reciprocal social communication in children with ASD as well as in all children respectively. Additionally, attenuated early auditory responses

were related with greater tendency of hyper-reactivity for all children. Next, later ERP components indicating attentional processing of tactile and auditory stimuli were associated with impairments in reciprocal social skills and tendencies of hyper-reactivity respectively only in the TD group, suggesting that patterns of allocation of attention to specific stimuli may be linked with differences in social and sensory response patterns in the TD group. These findings are consistent with a previous study suggesting that hyper-reactivity to novel stimuli may be associated with ASD-related traits (Gomot et al., 2008). My results, therefore, indicate a dimensional characterization of ASD suggesting that even though TD participants do not receive a categorical diagnosis of ASD, there may be a similar association between ASD-like traits in TD and patterns of neural responsivity as one might predict in the ASD group. Finally, contrary to my hypothesis, both early and late neural responses to tactile and auditory stimuli were not associated with ADOS-2 scores.

Next, because of the role that touch plays in facilitating attention in typical development, (Jean & Stack, 2009; Stack & Muir, 1992), in my second study, I specifically examined whether touch cues presented before auditory targets modulate the response of the alerting network in both typical and atypical development. Previous studies investigating the efficiency of the alerting network have reported equivalent alerting in individuals with ASD and TD controls in tasks where target stimuli are preceded by auditory or visual cues that fall within (Keehn et al., 2010; Landry et al., 2009) or outside (Kleberg et al., 2017; Raymaekers et al., 2006) the modality of the target stimuli. Using visual stimuli Landry et al. (2009) have added to this literature by showing that variable intervals between cues and targets may affect the response of the alerting network (i.e., faster reaction times as a result of increased cue-target intervals). In the tactile modality, however, there exists limited evidence showing impact of the tactile cues on behavioral performance. For example, Turatto et al. (2004) reported that tactile cues presented before tactile targets facilitated the response of the alerting network in TD adults. However, it is still unclear whether tactile cues facilitate behavioral performance in children, and if yes, whether touch-related facilitation is observed in cross-modal tasks with variable cue-target intervals in typical and atypical development.

The current study sought to address this gap in the literature by investigating the role of tactile cues (presented at variable cue-target intervals before auditory targets) in facilitating behavioral responses in children with ASD compared to TD children. Specifically, I examined (1) whether transient tactile cues presented before an auditory target impact behavioral responses

measured by accuracy and reaction time in children with and without ASD, and (2) whether changes in the duration between tactile cues and auditory targets impact accuracy and reaction time of behavioral responses in children with and without ASD. In line with previous findings (Raymaekers et al., 2006), I hypothesized that, in all children, the presentation of tactile cues will be linked with an increase in anticipatory responses that may be dependent on the cue-target interval with more anticipatory errors occurring at longer intervals affecting overall accuracy. Next, similar to auditory and visual modalities (Keehn et al., 2010; Kleberg et al., 2017; Landry et al., 2009; Raymaekers et al., 2006), if alerting responses to tactile cues are equivalent in ASD and TD, then children in both groups should display behavioral facilitation after receiving tactile cues irrespective of the duration between tactile cues and auditory targets. However, if processing of touch is atypical in children with ASD, then they should show reduced touch-related facilitation compared to TD children as measured by diminished changes in reaction times in trials with and without tactile cues. Alternatively, if children with ASD are slower to attend to the tactile input, then they should mainly benefit from longer cue-target intervals compared to shorter intervals (i.e., greater differences at shorter SOAs and more ‘typical’ responses at longer SOAs where there is more time to prepare for a response).

My results showed equivalent behavioral responses in children with and without ASD. First, anticipatory responses were more prevalent in trials with touch cues in all children, and as hypothesized, they were dependent on variable cue-target intervals (i.e., anticipatory errors were more likely at 400 and 800 ms SOA, but not at 200 ms SOA). The presentation of touch cues before targets also resulted in faster reaction times in all children indicating efficient alerting in ASD and TD. My findings are consistent with previous studies that have shown similar alerting responses in individuals with ASD and TD (Keehn et al., 2010; Keetels & Vroomen, 2011; Kleberg et al., 2017; Raymaekers et al., 2006). Additionally, in agreement with Landry et al. (2009), my results showed faster reaction times at longer cue-target intervals compared to shorter intervals in all children. It is possible that longer cue-target intervals may have provided participants more time to prepare for a response resulting in faster reaction times compared to shorter cue-target intervals.

Findings related to faster reaction times in all children could be attributed to the efficient response of the alerting network. Contrary to my hypotheses, the present results argue against an impairment in sensory or attentional processing of tactile stimuli in children with ASD.

Specifically, my results do not suggest hypo-reactivity to tactile cues in ASD, because a disruption at a perceptual level might have resulted in reduced touch-related facilitation at all touch-cue intervals. However, this was not observed in the current study. My results also do not indicate slower attentional responses to touch. If this were the case, then children with ASD would have shown more difficulties in using touch cues primarily at the shortest, but not the at the longest, cue-target intervals. However, touch-related behavioral facilitation was shown even at the shortest cue-target interval. My results are in agreement with previous studies showing similar alerting responses to auditory and visual cues in individuals with ASD and TD (Keehn et al., 2010; Kleberg et al., 2017; Landry et al., 2009; Raymaekers et al., 2006), and extend to the tactile modality.

Despite the fact that both groups learned the relationship between tactile cues and auditory targets, children with ASD showed overall slower reaction times compared to TD children. One possible reason underlying the overall slower reaction times in children with ASD could be attributed to widely reported difficulties in cross-modal attentional set shifting in ASD (Courchesne et al., 1994; Reed & McCarthy, 2012; Williams et al., 2013). The present task required participants to constantly shift their attention between tactile and auditory modalities to make use of tactile cues while responding to auditory targets. Therefore, despite implicitly learning the association between tactile cues and auditory targets, the constant need of attentional set shifting may have impacted overall reaction times in children with ASD. Future studies should examine this argument further by presenting cues in unimodal and cross-modal tasks to compare within vs across modality attentional shifting in individuals with ASD.

Based on previous research showing significant links between the alerting network and ASD symptomatology (Keehn et al., 2010), I hypothesized that touch-related behavioral facilitation would be associated with ASD symptomatology in children with and without ASD. Last, because of evidence showing links between touch and language learning (Lew-Williams et al., 2019; Seidl et al., 2015), I hypothesized that touch-related behavioral facilitation would be significantly associated with language skills in ASD and TD. Contrary to my hypotheses touch-related behavioral facilitation was not related to ASD symptomatology or language skills in ASD and TD. These results could be related to the type of stimuli used in the present study. For instance, I used non-human tactile cues, however, tactile input that has been shown to facilitate interpersonal communication in everyday life is often social. Future studies should examine the association between social touch-related alerting and ASD symptomatology and language skills.



Together both of my studies indicate typical perceptual as well as attentional processing of tactile and auditory stimuli in children with ASD. Although there were significant group differences in ASD and TD children in behavioral sensory profiles as measured by parent report, my results did not reveal differences in how these stimuli are processed at a neurological level. Additionally, typical neurological processing of tactile stimuli was supported in my tactile-cueing paradigm, where children with ASD showed equivalent touch-related behavioral facilitation. Specifically, my results of the tactile-cueing paradigm allowed me to argue against an impairment in sensory or attentional processing of tactile stimuli, as differences at these levels would have resulted in overall reduced touch-related facilitation irrespective of variable cue-target intervals due to hypo-reactivity to touch or facilitation effects only at longer cue-target intervals as a result of slower attentional processing of tactile cues at shorter intervals. Next, although neural responsivity to tactile and auditory stimuli were related to sensory responsivity and social skills in all children, contrary to my hypotheses, neural as well as behavioral indices of tactile processing were not associated with ADOS-2 scores. In sum, both my studies indicate that behavioral sensory differences in ASD may not always be due to impairments in perceiving or attending to the sensory stimuli as previously suggested.

Although the two studies discussed here have yielded consistent results regarding tactile and auditory processing in children with ASD, they do not shed light on underlying mechanisms that may explain behavioral differences in responding to sensory inputs in ASD; a characteristic that has been consistently reported in the past literature (Baranek et al., 2006; Ben-Sasson et al., 2009) and also observed in the current studies based on parent report. I discuss three possible explanations that may help us understand the discrepancy among my findings and parent and observational reports. First, I argue that everyday differences in responding to sensory stimuli in ASD may be related to the context in which the stimuli are presented. For example, tactile and auditory stimuli experienced in the outside world may often involve other social aspects that are a part of that interaction. Individuals are therefore required to not only process the sensory characteristics of those stimuli, but also understand and respond to the social nature of those stimuli (e.g., shoulder tap or a name call may indicate upcoming interaction). We know that responding to sensory inputs in social contexts is inherently rewarding to typically developing individuals, thereby increasing their probability of engaging in future social interactions. However, individuals with ASD may find it challenging to naturally form stimulus-reward contingencies during social

interactions (Chevallier et al., 2012), which may result in atypical responses to stimuli presented in such contexts. I acknowledge that social motivation theory may not be used to explain widely observed differences in sensory processing in ASD (especially in non-social contexts), however, it may account for some sensory processing differences that are observed primarily in social settings.

Support for this argument comes from Kadlaskar et al. (2019), where infants at high risk for ASD who later received a diagnosis of ASD showed hypo-reactivity to caregiver touches in naturalistic interactions. However, this study did not examine touch responsivity in non-social contexts to compare any differences in hypo-reactivity dependent on social and non-social contexts. In both of my studies, tactile and auditory stimuli were presented in non-social contexts, and participants were only required to process the physical characteristics of the stimuli. For example, in the ERP study participants were presented with auditory and tactile stimuli in an experimentally-controlled passive task. Unlike in typical social settings, successful participation in this study did not require children to understand the communicative intent of any of the stimuli. In the tactile-cueing task, although participants implicitly learned the relationship between tactile and auditory stimuli, they did not have to engage in any social task.

Additionally, our caregiver-report measure of sensory reactivity – for which there were between-group differences – primarily focused on social contexts (e.g., becomes anxious when standing close to others, shows distress during grooming [for example, fights or cries during haircutting, face washing, fingernail cutting]). Moreover, we know that individuals with ASD may often display increased physiological arousal in response to surrounding stimuli (Chang et al., 2012; James & Barry, 1984; Woodard et al., 2012). Further, it is also possible that the stress associated with the dynamic and unpredictable nature of social interactions may impact arousal levels in individuals with ASD, thereby affecting their behavioral responses to sensory stimuli in social settings. Another challenge associated with responding to sensory stimuli in social settings could be related to the high task demands of social vs non-social settings. Specifically, in typical social settings individuals are required to carry out a number of calculations to participate and respond in various interactions. For example, while communicating with her mother during mealtime, a child may calculate that the probability of her mother producing reliable information about food (e.g., mom says apple while showing apple) may be higher than the information coming from her brother. However, the source of accurate information may change in a different context

(e.g., while playing with video games) in which reliable information may come from her brother instead of her mother. This type of dynamic social context requires individuals to calculate contingencies based on the communicative partner. Whereas, in the current non-social experiment, the tactor and the speaker always produced reliable information thereby reducing the task demands associated with processing those stimuli. Therefore, the discrepancy between my results and caregiver-reported behavioral difficulties in responding to tactile and auditory input could be related to the social contexts in which such stimuli are more likely to occur.

Second, the discrepancy among results could also be attributable to the nature of the stimuli used. Support for this argument comes from Dawson et al. (2004) where children with ASD showed differences in responding to both social and non-social stimuli compared to children with delayed and typical development; however, this impairment was more prominent in response to social stimuli. These findings suggest that the social nature of the stimuli may have a greater impact while responding in children with ASD. In my studies, tactile stimuli consisted of high-frequency vibrations that were always presented on the fingertip. This type of tactile stimulation is rarely experienced in the outside world. We know that touch presented in everyday life, at least in social settings, consists of various types (e.g., tap, brush, tickle, kiss) and may carry a variety of communicative intents (e.g., touch to reduce distress, get attention, convey affect; Ferber et al., 2008; Field, 2001; Hertenstein, 2002). Additionally, touch in everyday life is more dynamic and can be presented to various body locations depending on the context. This unpredictable nature of stimuli can pose challenges for individuals with ASD (Gomot & Wicker, 2012). In both of my studies, participants always received the same type of touch on the exact same location. My tactile stimuli therefore do not represent the rich, heterogeneous nature of touches one might experience in everyday life. With respect to my auditory stimuli, although participants were presented with speech sounds (which may be considered inherently social), they were not actual words and were synthesized using a software package with no communicative intent making them less social. As a result, these speech sounds did not mirror the qualities of dynamic human speech input that involves a human communicative partner. Therefore, the predictable, non-social nature of tactile and auditory stimuli may have impacted the results in both of my studies.

Third, because tactile stimuli in the current study were only presented to the fingertip, it primarily stimulated the Pacinian corpuscles; mechanoreceptors present on the glabrous (non-hairy) skin of the body that are involved in discrimination of fine textures or other stimuli with high-

frequency vibrations (Johnson, 2001). Whereas, social touch often presented on the non-glabrous (hairy) skin (such as on the arm, back or shoulder) primarily innervates the CT afferents; low-threshold unmyelinated afferent fibers (Olausson et al., 2010). There exists some evidence showing that experimenter-initiated touch presented to children with ASD may display more defensive reactions in CT-innervated regions compared to non-CT-innervated regions (Cascio, Lorenzi, et al., 2016). Given these results I argue that everyday differences in responding to tactile stimuli may be related to the specific mechanoreceptors involved during the given stimulation and may be more evident at CT-innervated regions compared to non-CT innervated regions such as the fingertip.

The arguments discussed above only partially explain behavioral differences in responding to sensory information in ASD. We know that children with ASD also show atypical responsivity to non-social stimuli (Baranek et al., 2013; Bruneau et al., 2003; Lepistö et al., 2005; Marco et al., 2012; Miyazaki et al., 2007). My results fall short of explaining mechanisms that may be responsible for sensory processing differences in non-social settings and with non-social stimuli. Given the current results showing typical processing of sensory stimuli in non-social contexts and previous findings showing differences in responding to sensory stimuli in social settings (Dawson et al., 2004; Kadlaskar et al., 2019; Kadlaskar et al., 2020), I speculate that sensory processing differences may be more robustly observed in social contexts with dynamic stimuli compared to controlled experimental settings. Future research directions have been proposed in the section below that may help us elucidate this argument in greater detail.

#### **4.1 Future directions**

Sensory processing patterns observed from the studies presented in this dissertation highlight a number of interesting topics that need systematic exploration in future research. First, in Chapter 2 it was observed that children with and without ASD showed equivalent neural processing in response to the novel tactile stimuli (i.e., tactile vibration along with speech sound /a/). Because my tactile stimuli were always presented with an auditory sound, I argued that the bimodal nature of stimuli may have facilitated neural responsivity in both the ASD and TD groups. Future research should therefore examine neural responsivity to unimodal and bimodal touch to investigate the impact of multimodal sensory stimuli on information processing in ASD and TD.

Second, in Chapters 2 and 3, participants were presented with touch that consisted of high-frequency vibrations presented on the fingertip. Although this kind of tactile stimulation allowed me to control for the duration, intensity, and the amount of touches participants received, it does not mirror the dynamic nature of everyday tactile input one may experience in the outside world. It might be beneficial in future to examine tactile processing in ASD and TD using touches delivered by a human being making the experimental setup more ‘social’. Throughout this discussion I argue that sensory processing differences may be more prominent in social settings. Adding experimenter/caregiver-delivered touches would help us determine how touch is processed in social settings compared to non-social settings where touches are delivered using a mechanical factor.

Finally, equivalent processing of tactile stimuli in children with ASD compared to TD children could be related to the location of touch and the underlying tactile mechanoreceptors. For example, as mentioned before participants in my studies always received touches on the fingertip (a non-CT-innervated region). There is now some evidence showing different degrees of defensive reactions in response to touch presented to CT-innervated (arm, face) vs non-CT-innervated regions (palm) in individuals with ASD (Cascio, Lorenzi, et al., 2016). Future research should examine neural responses to touch presented in both CT- and non-CT-innervated regions in children with ASD.

## **4.2 Conclusion**

The research in this dissertation explored whether behavioral differences in responding to tactile and auditory stimuli in ASD are related to perceptual and/or attentional mechanisms (measured by early and later neural components respectively) underlying sensory processing, and whether tactile cues before auditory targets facilitate behavioral performance in children with ASD compared to TD controls. Additionally, the studies discussed above sought to investigate the relationship of neural and behavioral indices of tactile and auditory processing with ASD symptomatology and language skills in ASD and TD children. The results showed that, under certain contexts, children in both the ASD and TD groups displayed similar early and later ERP amplitudes to tactile and auditory inputs, indicating equivalent perceptual as well as attentional processing of tactile and auditory stimuli in children with ASD compared to their TD peers.

Next, correlations revealed that, in all children, reduced early activation in response to tactile and auditory stimuli was linked with deficits in sensory reactivity and reciprocal social communication. Additionally, patterns of allocation of attention were linked with differences in reciprocal social communication and sensory reactivity respectively in TD children, suggesting a dimensional characterization of ASD-like traits. Last, there was an association between greater sensitivity to changes to a stream of auditory information and expressive language in all children. These results suggested that, although there were no group differences in neural responsivity to tactile and auditory stimuli, individual differences to incoming sensory stimuli were associated with sensory responsivity and social skills in all children.

Although children with ASD were overall slower in their reaction times compared to TD children, the presentation of tactile cues before auditory targets resulted in similar patterns of behavioral facilitation in both the ASD and TD groups, suggesting equivalent alerting responses to tactile cues as well as efficiency of the phasic alerting network in ASD and TD. Touch-related behavioral facilitation was not related to ASD symptomatology or language skills in ASD and TD groups. Given these results, I argue that widely reported differences in behavioral patterns of responding to tactile and auditory stimuli in ASD could be attributed to social contexts in which these stimuli are more likely to be encountered in everyday life.

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## VITA

### RESEARCH INTERESTS

Identification of early risk markers for ASD; sensory processing in infants at risk for and young children diagnosed with ASD; early caregiver-infant dyadic interactions and their association with sensory responsivity and later social communication in ASD and TD; the use of observational and electrophysiological measures to examine sensory processing in children with ASD and TD.

### EDUCATION

Ph.D., Speech, Language, and Hearing Sciences Purdue University	Aug15-Present
M.S., Applied Child Psychology Nottingham Trent University	Aug 2013
M.A., Clinical Psychology University of Pune	May 2012
B.A., Psychology University of Pune	May 2010

### RESEARCH EXPERIENCE

Graduate Research Assistant, <i>AtteND</i> Lab, Purdue University Director: Brandon Keehn, Ph.D.	2016 - Present
Graduate Research Assistant, Infant Speech Lab, Purdue University Director: Amanda Seidl, Ph.D.	2015 - Present
Research Assistant, Neonatology Lab, University College London Director: Neil Marlow, D.M.	2013 - 2015

### TEACHING EXPERIENCE

Teaching Assistant SLHS 309; Language Development), Purdue University	Aug 2016 - May 2018
Teaching Assistant Crabtree Farm Primary School, Nottingham	Sept 2012 - July 2013
Teaching Assistant Akanksha Foundation: NGO, Pune	Oct 2008 - April 2010

### PUBLICATIONS

**Kadlaskar, G.,** Seidl, A., & Waxman, S. R. (in revision). More than words: Touch facilitates object categorization in 6-month-old infants.

Lory, C., **Kadlaskar, G.,** Keehn, R. M., Francis, A. L., & Keehn, B. (2020). Brief Report: Reduced Heart Rate Variability in Children with Autism Spectrum Disorder. *Journal of Autism and Developmental Disorders*, 1-8. [\[PDF\]](#)

- Kadlaskar, G.,** Seidl, A., Tager-Flusberg, H., Nelson, C.A., & Keehn, B. (2019). Caregiver touch-speech communication and infant responses in 12-month-olds at high risk for autism spectrum disorder. *Journal of Autism and Developmental Disorders*. [\[PDF\]](#)
- Keehn, B., **Kadlaskar, G.,** McNally Keehn, R., & Francis, A. (2019). Auditory attentional disengagement in children with autism spectrum disorder. *Journal of Autism and Developmental Disorders*, 49(10), 3999-4008. [\[PDF\]](#)
- Kadlaskar, G.,** Seidl, A., Tager-Flusberg, H., Nelson, C.A., & Keehn, B. (2019). Atypical response to caregiver touch in infants at high risk for autism spectrum disorder. *Journal of Autism and Developmental Disorders*, 49(7), 2946-2955. [\[PDF\]](#)

## PRESENTATIONS

- Kadlaskar, G.,** Bergmann, S., McNally Keehn, R., Seidl, A., & Keehn, B. (2019, November). Electrophysiological study of tactile processing in children with autism spectrum disorder. Poster presented at HHS Fall Research Day, Purdue University, USA.
- Keehn, B., **Kadlaskar, G.,** & McNally Keehn, R. (2019, October). Measures of tonic and phasic activity of the locus coeruleus – norepinephrine system in children with autism spectrum disorder. Poster presented at Society for Neuroscience, Chicago, IL.
- Pierce, S., **Kadlaskar, G.,** & Keehn, B. (2019, October). Associations between resting-state EEG alpha-band power and atypical sensory processing and social communication impairments in children with autism spectrum disorder. Poster presented at Society for Neuroscience, Chicago, IL.
- Kadlaskar, G.,** Seidl, A., Tager-Flusberg, H., Nelson, C.A., & Keehn, B. (2019, May). Caregiver-infant tactile communication in infants at-risk for autism spectrum disorder. Poster presented at the International Society for Autism Research Meeting, Montreal, Canada.
- Keehn, B., **Kadlaskar, G.,** & McNally Keehn, R. (2019, May). Attentional disengagement and the locus coeruleus – norepinephrine system in children with autism spectrum disorder. Poster presented at the International Society for Autism Research Meeting, Montreal, Canada.
- Kadlaskar, G.,** Seidl, A., Tager-Flusberg, H., Nelson, C.A., & Keehn, B. (2019, April). Caregiver-infant tactile communication in infants at-risk for autism spectrum disorder. Talk presented at the Brown Bag Seminar of the Speech, Language and Hearing Sciences Department, Purdue University, West-Lafayette, IN, USA.
- Kadlaskar, G.,** Seidl, A., Tager-Flusberg, H., Nelson, C.A., & Keehn, B. (2018, October). Atypical response to caregiver touch in infants at risk for autism spectrum disorder. Poster presented at the Purdue Autism Research Conference, Purdue University, USA.
- Kadlaskar, G.,** Seidl, A., & Waxman, S. R. (2018, June). Does touch facilitate object categorization? Poster presented at the International Congress of Infant Studies, Philadelphia, PA, USA.
- Kadlaskar, G.,** Seidl, A., Tager-Flusberg, H., Nelson, C.A., & Keehn, B. (2018, May). Atypical response to caregiver touch in infants at risk for autism spectrum disorder. Poster presented at the International Society for Autism Research Meeting, Rotterdam, Netherlands.
- Kadlaskar, G.,** Seidl, A., Tager-Flusberg, H., Nelson, C.A., & Keehn, B. (2018, April). Atypical response to caregiver touch in infants at risk for autism spectrum disorder. Talk presented at the Brown Bag Seminar of the Speech, Language and Hearing Sciences Department, Purdue University, West-Lafayette, IN, USA.
- Kadlaskar, G** & Sawarkar, A (2012, February). The efficacy of REBT as a group therapy in dealing with emotional maladjustment among underprivileged adolescents. Talk presented at

National Conference on Research: Interdisciplinary Approaches in Management, Humanities, Social Sciences and Languages, Nasik, India.

**Kadlaskar, G** & Sawarkar, A (2012, January). The efficacy of REBT as a group therapy in dealing with emotional maladjustment among underprivileged adolescents. Talk presented at 38<sup>th</sup> National Annual Conference of the Indian Association of Clinical Psychologists, Pune, India.

## **INVITED TRAINING**

Conducted research training on caregiver touch coding scheme Vanderbilt University	Sept 2018
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## **GUEST LECTURES**

“Tactile Processing in Infants at Risk for ASD” Purdue; SLHS 444: Introduction to Research in Communication Sciences and Disorders Instructor: Dr. Ji Yeon Lee	Feb 2020
“Introduction to Speech, Language, and Communication Disorders” Purdue; EDPS 265: The Inclusive Classroom Instructor: Jasmine Begeske	Apr 2020

## **CLINICAL TRAINING**

Training course in Autism Diagnostic Observation Schedule-2 by WPS, USA	Dec 2017
Introduction to Good Clinical Practice (GCP) in research, UCL, UK	Aug 2013
Psychological Assessment Workshop, NTU, UK	May 2013
Intensive Certificate Course in Autism, Positive Steps Clinic, India	Apr 2012
Play Therapy, Positive Steps Clinic, India	Aug 2011
Bayley Scales of Infant Development, Antarang Clinic, India	Oct 2011

## **GRANTS AND FELLOWSHIPS**

Bilsland Fellowship (\$17,583), Purdue University, USA	Aug 2019 - July 2020
Purdue Research Foundation Grant (\$17,645), Purdue University, USA	Aug 2018 - July 2019
Ross fellowship, (\$16,386) Purdue University, USA	Aug 2015 - July 2016

## **AWARDS AND HONORS**

Student Research Award in Autism (\$5000), Purdue University, USA	2020
Compton Research Travel Award (\$500), Purdue University, USA	2019
Purdue Graduate Student Government Travel Award (\$250), Purdue University, USA	2019
Lions Clinical Research Award (\$400), Purdue University, USA	2018
Best poster at the Purdue Research Conference (\$120), Purdue University, USA	2018
Wilson Scholarship (\$2,355), Purdue University, USA	2018 - 2019
Compton Graduate Research Travel Award (\$500), Purdue University, USA	2018
Purdue Graduate Student Government Travel Award (\$500), Purdue University, USA	2018
Wilson Scholarship (\$9,242), Purdue University, USA	2017 - 2018
Graduate Tuition Scholarship (\$10,758), Purdue University, USA	2017 - 2018
Compton Professional Development Award (\$500), Purdue University, USA	2017
Wilson Scholarship (\$12,828), Purdue University, USA	2016 - 2017
Graduate Tuition Scholarship (\$7,171), Purdue University, USA	2016 - 2017



Wilson Scholarship (\$3614), Purdue University, USA	2015 - 2016
Tuition scholarship (£5650), MSc Applied Child Psychology, NTU, UK	2012 - 2013
Ranked 1st at MSc Applied Child Psychology, NTU, UK	2013
Ranked 2nd at MA Clinical Psychology, University of Pune, India	2012

### **TESTING/TECHNICAL SKILLS**

Neuropsychological Testing: ADOS-2 (in the process of achieving research reliability); Differential Ability Scale-2, Peabody Picture Vocabulary Test-4; Expressive Vocabulary Test-2; Wechsler Abbreviated Scales of Intelligence-2; Mullen Scales of Early Learning, Bayley Scales of Infants and Toddler Development-3

Software: SPSS, JMP, Praat, ELAN, NetStation, MATLAB