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Auditory Brainstem Response in Autistic Children: Potential Implications for

Sensory Processing

Madelyn Cate

A thesis submitted to the faculty of Brigham Young University in partial fulfillment of the requirements for the degree of

Master of Science

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ABSTRACT

Auditory Brainstem Response in Autistic Children: Potential Implications for Sensory Processing

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Autistic people frequently experience sensory processing difficulties. For many on the autism spectrum, such difficulties can significantly impact important functions and quality of life. We are only beginning to understand the neural mechanisms of atypical sensory processing. However, one established way to measure certain levels of auditory processing is with auditory brainstem responses (ABR). While ABR has been primarily hypothesized in the current literature as a means of early detection/diagnosis in autism, additional research is needed to determine the ABR's utility in examining sensory processing in this population. Thus, we evaluated ABR in 19 young children with autism during various stimulus (click and tone burst) and intensity conditions by comparing ABR waveform characteristics, such as absolute peak latencies and amplitudes, inter-peak latencies (IPL), inter-aural latency differences (IAD) between agematched groups of autistic and typically developing children. We also examined within ear waveform cross correlations and inter-aural cross correlations (IACC) to assess replicability and synchrony of participants' auditory brainstem responses. Though we observed longer peak latencies (esp. wave III and V) and IPLs in both the autism and typically developing groups in different conditions, there were no statistically significant results in cross correlation or IACC. These results indicate that at the level of the brainstem, auditory processing may differ slightly, but is mostly similar between autistic and typically developing children. In terms of sensory processing in autism, future studies should examine the connection between ABR responses and behavioral measures of sensory processing, as well as function at more central levels of the auditory system.

Keywords: auditory brainstem response, autism, auditory processing, sensory processing

ACKNOWLEDGMENTS

Firstly, I would like to thank my thesis advisor, Dr. Cardon, for his tireless guidance, encouragement, and patience throughout this thesis project. Without his support, this thesis would not be possible. Thank you to my committee members, Dr. Cabbage and Dr. Harmon, for their feedback and encouragement. I would also like to thank Dr. Sarah Cordingley, AuD, CCC-A, PASC and Dr. Brittany Bown, (AuD, CCC-A, PASC) at Peak ENT in Provo, UT for providing the de-identified participant demographics, waveform data, and calculating the cross correlations. Finally, I would like to thank my family and friends for their patience and support in helping me reach personal and academic goals while receiving my education at BYU.

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DESCRIPTION OF THESIS STRUCTURE AND CONTENT

This thesis, *Auditory Brainstem Response in Autistic Children: Potential Implications for Sensory Processing*, was written in a hybrid format to adhere to both traditional thesis requirements and journal publication formats. The initial pages observe traditional university thesis requirements. The body of the paper follows journal submission length and style requirements by following American Psychological Association (APA) guidelines. This article may by adapted for submission in a peer-reviewed journal with the primary author listed as a contributor. The annotated bibliography is included in Appendix A. This retroactive study contained only de-identified data and was approved by the Institutional Review Board at BYU. Identity-first language (e.g., "autistic children") will be used in this paper as it is becoming the preference of many autistic individuals (Bottema-Beutel et al., 2021; Kenny et al., 2015), though we acknowledge and respect those who prefer person-first language.

Introduction

Sensory Processing in Autism

While Autism Spectrum Disorder (ASD; henceforth *Autism/autistic*, Bottema-Beutel et al., 2021; Kenny et al., 2015) is characterized as a developmental disorder recognized by difficulties in social interaction and communication as well as repetitive behaviors and restricted interests (5th ed.; DSM–5; American Psychiatric Association, 2013), sensory processing difficulties are also very common among those in this population (ASD; Marco et al., 2011; Crane et al., 2009). In fact, some accounts indicate that as many as 96% of autistic children report difficulty with sensory processing (Marco et al., 2011; Shah et al., 2015; Tomchek & Dunn, 2007).

Sensory processing refers to the manner in which an individual's brain receives, organizes, and processes information received from their peripheral senses, and may also involve perception; it is fundamental to how people interact with the world (Ahn et al., 2004; Suarez, 2012). Three main categories of sensory processing difficulties that have been shown in autistic individuals are over-responsiveness, under-responsiveness, and sensory seeking (Ben-Sasson, Hen, et al., 2009; Dunn, 1997; Hilton et al., 2010). Over- responsivity (also referred to as hyper-responsiveness), is an amplified, extended, or rapid behavioral reaction in response to sensory input. Under-responsivity (also referred to as hypo-responsivity or hyporesponsiveness) refers to a delayed or lack of response to sensory input. Sensory seeking is when an individual seeks out extreme or intense sensory input (Baranek et al., 2006; Ben-Sasson, Hen, et al., 2009; Dunn, 1997). Difficulties in any of these three areas of sensory processing can interfere with an individual's ability to participate in social, educational environments, and many other common everyday activities (Ahn et al., 2004).

Sensory processing can considerably impact the quality of an individual's life by limiting participation in common activities (Suarez, 2012). For instance, one longitudinal study found that children with sensory over-responsivity (SOR) exhibited a higher rate of social-emotional difficulties and dysregulation than neurotypical peers (Ben-Sasson, Carter, et al., 2009). Additionally, higher rates of anxiety and other social-emotional disorders have been regularly associated with atypical sensory processing (Aron & Aron, 1997; Ben-Sasson, Carter, et al., 2009; Engel-Yeger & Dunn, 2011; Suarez, 2012). On the other hand, some have related that atypical sensory processing can enhance sensory perception and can lead to special talents and abilities (Dakin & Frith, 2005; Heaton et al., 2008; Stevenson et al., 2021).

Auditory Processing

While autistic people can present with atypical sensory processing in any sensory modality (Marco et al., 2011; Tomchek & Dunn, 2007), it has been shown that between 50- 86.7% experience difficulties with auditory processing (Azouz et al., 2014; Demopoulos & Lewine, 2016). Thus, the auditory system is of particular interest when considering sensory processing in autism. Many autistic people frequently have increased sensitivity to auditory stimuli—i.e., 37% more than typically developing (TD) peers (Demopoulos & Lewine, 2016). While loud or noxious sounds are commonly distressing to autistic people (e.g., sirens, alarms, etc.); other, less threatening sounds (e.g., fans, hairdryers, lights, etc.) can also cause difficulties to individuals on the autism spectrum. Overall, increased sensitivity to sound can cause everyday sounds to be distracting, uncomfortable, or worse (Grandin, 2019).

Another way auditory processing impacts autistic peoples' lives is difficulty understanding speech in the presence of competing sounds (Alcántara et al., 2004; Thye et al., 2018). Autistic people frequently experience auditory over-responsivity which makes selectively attending to speech or social cues challenging (Thye et al., 2018). For instance, Temple Grandin, a well-known autistic author, speaker, and self-advocate, reported difficulties speaking on the phone in noisy environments, indicating that if she tried to tune out the background noise, she would also tune out the conversation. She further described how difficult it was to attend to instruction in a classroom because of the constant bombardment of surrounding sounds (Grandin, 2019). However, in the right context increased sensory sensitivity and its related skills can be very beneficial. For example, autistic people demonstrate strengths in tasks relating to attention to detail or visual thinking, such as computer programing, engineering, or photography (Grandin, 1999). Employers and employees are taking advantage of these special talents by specifically recruiting autistic individuals for these types of jobs (Szczerba, 2015).

Auditory Brainstem Response

There are both behavioral and physiologic ways to measure auditory processing. Among these physiologic methods is the auditory brainstem response (ABR; Demopoulos & Lewine, 2016). ABR measures the function of the cochlea, auditory nerve, and auditory brainstem neural pathways by placing electrodes on the scalp and recording electroencephalographic (EEG) responses. EEG is made up of voltage fluctuations on the scalp that correspond to groups of neurons being activated (Light et al., 2010). Large fluctuations (i.e., "peaks" and "valleys") represent the activity of large groups of synchronously activated neurons, often associated with auditory brainstem nuclei (See Figure 1; Källstrand et al., 2010). Both clinical and research ABRs are frequently done by presenting several thousand click stimuli and then averaging the electrical responses to each stimulus across trials, resulting in one averaged waveform. Most often, at least two averaged waveforms are acquired for each condition (e.g., stimulus type, intensity) and ear to assess replicability of these responses. ABRs using click stimuli are

frequently used because the results are robust, responses represent activity from neurons responsible for coding a wide range of frequencies and can be collected quickly (Gorga et al., 2006). Tone burst stimuli can be used in a similar way, but allow for enhanced information about the auditory brainstem's response to specific frequencies. Typical ABRs consist of 5 peaks that correspond roughly to anatomical features (e.g., nuclei) along the canonical auditory brainstem pathway (See Figure 1; Hall, 1992; Katz, 1972). ABRs are attractive in research because they consist of an obligatory response, making them possible to measure across the lifespan, regardless of attention to stimuli, and even during sleep (Hall, 1992). Thus, their most common use is auditory threshold estimation in young children and newborn hearing screenings (Miron et. al., 2020). Additionally, the auditory brainstem processes early timing and pitch discrimination, which is important for speech processing (Russo et al., 2008). Therefore, ABR can be indicative of speech processing because speech processing begins in the auditory brainstem (Russo et al., 2008). In practice, ABR testing is widely available and relatively low cost, which increases its desirability as a diagnostic or evaluation tool.

Auditory Brainstem Response and Autism

ABRs have also been hypothesized in numerous studies as a possible diagnostic tool for autism. Unfortunately, the results of these studies have varied. For instance, several studies have indicated that autistic people have prolonged ABR I, III, and V waves (Azouz et al., 2014; Kwon et al., 2007; Miron et al., 2015; Miron et al., 2018; Ramezani et al., 2019) Additionally, autistic people have been shown to have notably reduced amplitudes (ElMoazen et al., 2020; Ramezani et al., 2019). These results have been found in young children as well as adults (Miron et al., 2020). In contrast, there are several studies that disagree with the previous claims (Fujihira et al., 2021; Rumsey et al., 1984; Russo et al., 2009; Tharpe et al., 2006). For example, Russo and

colleagues (2009) found the Wave V latencies from click-ABR in their autistic participants to be consistent with the established normal range for latencies (Russo et al., 2009). The reason(s) for this apparent discrepancy across the literature is yet unknown. However, inconsistencies in ABR findings could be due to the heterogeneity of the autism population or methodological differences between studies, including recording parameters, analysis techniques, and/or sampling differences, among other less recognized factors.

While an absolute consensus has not been reached regarding ABR characteristics in those on the autism spectrum, there appear to most often be notable latency results in this population. In fact, significant links between atypical ABR results and autism diagnosis have been observed (Cohen et al., 2013; Miron et al., 2020; Roth et al., 2012). However, it is important to recognize that the ABR is not a definitive test for autism because delayed latencies of ABR peaks can also be indicative of tumors, hearing loss, brainstem dysfunction, among other neurologic conditions (Hall, 1992). Due to this variability, as presently constituted, ABR cannot be used as a definitive test to establish a diagnosis of ASD. Indeed, if there is a characteristic ABR pattern associated with autism, it is yet to be recognized. On the other hand, we submit that the ABR could potentially be used as an indicator of atypical sensory processing and added as a complimentary assessment to other diagnostic procedures for ASD. Currently, receiving an ASD diagnosis can be a complicated process based largely on patient observation, involving data from assessments such as the ADOS-2 (Lord et al., 2012) or DSM-5 (American Psychiatric Association, 2013) as well as reports from parents, the schools, and SLPs. Often, children in the process of receiving an ASD diagnosis are sent to an audiologist to rule out hearing loss, which makes adding ABR to diagnostic procedures achievable.

The ABR provides great insight into the neural underpinnings of audition because it evaluates how auditory information travels through and is processed by the auditory brainstem, (Rosenhall et al., 2003) and, thus, could be used as a physiologic measure of sensory processing in autism. While some studies have included measures of ABR as well as of sensory processing separately, these results have not been directly compared (Azouz et al., 2014). Azouz and colleagues (2014) collected data on ABRs, cortical evoked potentials, language measures, and behavioral measures in autistic children. Unfortunately, behavioral measures were only correlated with cortical auditory evoked potentials (CAEP), and not ABR. CAEPs indicated a greater right hemisphere dominance in auditory processing in the ASD group whereas the typically developing (TD) group demonstrated a left hemisphere dominance. Additionally, 40% of the ASD group were over-responsive to sound on behavioral measures. Azouz and colleagues also concluded that prolonged ABR latencies and inter-peak latencies were indicative of an immature auditory brainstem in autistic individuals. While the authors of this study did not directly connect ABR and sensory processing results, this demonstrates the ABR's potential in providing valuable information about autism's neural foundations.

By understanding the relationship between sensory processing difficulties and autism, all could gain a clearer understanding of autism as a whole and its various dimensions, as well as promote increased empathy for those who experience sensory processing and/or autistic traits. Such understanding also underscores the importance of maintaining a therapeutic and educational environment that does not exacerbate sensory dysregulation, especially as sensory dysregulation can interfere with accurate assessment of skills during testing and learning throughout therapeutic intervention and teaching (Khalfa et al., 2004; Thye et al., 2018). This impacts how clinicians might prepare the therapeutic environment to be a supportive setting

(Khalfa et al., 2004). For example, clinicians could build sensory support into treatment, thereby improving therapy outcomes, and ultimately quality of life. Additionally, documenting the relationship between sensory processing difficulties and autism could lead to an earlier, more accurate diagnosis by using an objective measure of sensory processing. ABR has the potential to indicate specific areas of sensory processing difficulties from the auditory brainstem. For example, speech discrimination deficits and auditory skill development have been seen in disorders in which ABRs are typically abnormal, such as Auditory Neuropathy Spectrum Disorder (ANSD; Cardon & Sharma, 2013; De Siati et al., 2020; Nash-Kille & Sharma, 2014; Sharma et al., 2011).

The Role of Neural Synchrony

ABR might be an effective research tool by offering more information about neural functioning in autism. For instance, it is hypothesized that autism is caused by an imbalance in the ratio of excitation/inhibition (E/I) in sensory as well as other neural systems (Rubenstein $\&$ Merzenich, 2003). Neurons naturally oscillate at various frequencies (Patel & Joshi, 2013). Additionally, when disparate parts of the brain are active together, they synchronize their oscillations (Mathalon & Sohal, 2015). Whether working together or separately, groups of neurons cannot achieve regular oscillations without typically functioning inhibitory mechanisms (Mathalon & Sohal, 2015). Additionally, E/I imbalance has possible connotations for neuro maturation because previous studies have also shown that the advent of inhibition is associated with developmental events, such as the opening and closing of sensitive periods (Cardin, 2018; Sohal & Rubenstein, 2019). Furthermore, without typical inhibition and precise synchrony, recording typical ABR waveforms is highly unlikely (Cardin, 2018). That is, due to the rapid time course of the ABR, high temporal precision is needed for ABR recording—i.e., because

ABR peaks and latencies are so close to each other in time, any jitter around the peaks causes the waveform to lose its shape when sweeps are averaged together. Timing and synchrony must be very precise to yield a typical ABR waveform. Taking the above notions together suggests that ABR has great potential as an instrument to measure the level of synchrony and maturation in the auditory brainstem (Hall, 1992).

ABR testing presents an opportunity to measure an individual system's synchronization in processing sound. One evidence of decreased neuro maturation in autism is an immature auditory brainstem as indicated by prolonged ABR latencies and inter-peak latencies (Azouz et al., 2014). Further, it is theorized that longer ABR wave V latencies in ASD groups could be caused by decreased synchronization in processing speech stimulus in the brainstem (Ramezani et al., 2019). While the synchrony of ABR has not been studied in autistic individuals, it has been studied, albeit on a different time course, in MRI studies concerning those on the autism spectrum. For instance, it was found that autistic children demonstrated decreased neural synchrony while watching a movie compared to same-aged, typically developing peers (Lyons et al., 2020). While EEG and fMRI techniques have vastly different temporal resolutions, based on the above, it may be useful to further investigate neural synchrony via ABR in autistic persons.

Another possible, though indirect, measure of synchrony is intra-individual variability, such as evaluating the similarities and differences between ABR recording runs within or between ears for a single stimulus condition. As previously defined, intra-individual variability is a fluctuating, within-individual behavioral change in performance that can reflect neurologic dysfunction such as schizophrenia, a traumatic brain injury, or age-related cognitive degeneration (MacDonald et al., 2006). Intra-individual variability has been utilized in a variety of studies as a measure of cognitive processing, neurologic performance, performance stability,

and indicator of neurodegenerative diseases such as dementia; for example, intra-individual variability has been found to be a more reliable measure of neurologic functioning than meanlevel performance in a study on multiple sclerosis (MacDonald et al., 2006; Wojtowicz et al., 2012). In another study, intra-individual variability in response time was used as a measure in attention deficit hyperactive disorder (ADHD), autism, and Tourette's syndrome (Geurts et al., 2008). It was found that both the ADHD and autism group had variable response times, which could suggest deficits in inhibitory control (Geurts et al., 2008). While intra-individual variability has not been used in ABR studies of autistic individuals, borrowing the reasoning from the above and other studies, we submit that this technique could provide important knowledge about synchrony and neurologic functioning if used in this context because of its past use as a measure of neurologic functioning in other contexts.

Research Aim

Given the availability and low cost of ABR and all of the above arguments for its use as a measure of aspects of sensory processing and autism, the purpose of this study was to examine ABRs in autistic children as a measure of sensory (esp. auditory) function. By learning more about sensory processing in autism we may eventually gain the ability to better support autistic people struggling with sensory processing difficulties and aid in their therapy goals, educational outcomes, and general quality of life, if needed. To this end, we used ABR results in young children from two separate groups: those with an official autism diagnosis and typically developing children. Statistical comparison of waveform characteristics allowed us to examine correlates of auditory processing among those on the autism spectrum. We hypothesized that autistic children would have delayed latencies, decreased amplitudes, and decreased synchrony,

compared to typically developing participants. Such results might suggest an immature auditory brainstem and possible atypical sensory processing in autism.

Methods

Participants and Data

Participants for this retrospective study were children who had undergone clinical ABR testing at a local audiology clinic from two distinct groups: (a) autistic children with a diagnosis of autism spectrum disorder (ASD) and (b) typically developing children (TD). The ASD group had 11 participants and a mean age of 34 months. The TD group had 8 participants and a mean age of 38 months. Only children with typical hearing were included in this study; as such, the TD group was smaller than the ASD group because it is less frequent for typically developing children without a hearing loss to be referred for audiological testing. By all accounts, no participant had been diagnosed with any additional neurological disorder. Data were shared between the aforementioned local audiology clinic and the research team via a data sharing agreement. All data were de-identified prior to sharing. Shared information included ABR recording parameters, waveform characteristics (esp. latency and amplitude), and raw waveform data. All data sharing and analysis was approved by the Institutional Review Board of Brigham Young University.

Auditory Brainstem Response Recording Procedures and Parameters

ABRs were recorded by a comprehensive local audiology clinic and ENT practice staffed by trained doctoral level, state and federally certified pediatric audiologists. During recordings, unsedated patients were seated in their parent's lap in a chair or on a couch; sedated patients were typically given Propofol through an IV or Sevo which is a gas. Previous studies have shown that sedation does not significantly affect latency or amplitude. Thus, we will not consider sedation a confound in the present study (Mokotoff et al., 1977; Palaskas et al., 1989; Sohmer & Student, 1978). Click and pure tone ABRs were elicited by placing ground and alternating electrodes on the forehead and non-innervating electrodes on the test ear. Clicks were presented at 70 dB HL at a presentation rate of 37.7s. 2000 sweeps were collected and averaged. Pure tone ABRs were collected at a variety of intensities and frequencies. The ABRs were initially analyzed by Vivosonic, a software designed to analyze ABRs and other audiological measures. Subsequent analysis of waveform characteristics was carried out in Microsoft Excel (version 16.60) and SPSS (IBM Corp., 2022).

Data Analysis

After data was collected, several variables were extracted from ABR waveforms in both research groups and agreed upon by three experienced clinical audiologists. First, the absolute latencies for waves I, III, and V at the intensity of 70 dB HL. Second, amplitudes for waves I, III, and V at the 70 dB HL and wave V at various frequencies and intensities. Third, interpeak latencies (IPL) were calculated for the peaks I-III, III-V, and I-V. The means and standard deviations of each group's variables were computed and statistically compared. Fourth, we measured inter-aural difference (IAD) by comparing latencies and IPL between the right and left ear. Fifth, we measured synchrony through cross-correlation analysis which is a measure of consistency over trials, yielding an r-value that is an indication of the similarity of the timing and amplitude of the waveform oscillations. This was done by dividing the sweeps into two separate runs, which were then averaged and compared with one another via cross-correlation. Finally, we measured inter-aural cross correlation (IACC) by computing the correlation coefficient for ABR waveforms between the right and left ear.

Statistical Analysis

All data (absolute latencies, amplitudes, IPL, IAD, cross correlations, and IACC) were collected for both groups (ASD and TD) and compared between groups using non-parametric (Mann-Whitney U) tests. All statistics will be computed using the Vivosonic proprietary software and/or SPSS (IBM Corp., 2022).

Results

Absolute Latencies

In general, when latencies were different between groups, the autistic children tended toward having longer latencies and greater IPL difference than neurotypical children, though this was not the case in every instance. For example, the wave III latency for the autistic children (mean $= 4.24$, SD $= 0.23$) was significantly longer than that of the neurotypical children (mean $=$ 3.98, $SD = 0.14$; U=13.50, p=0.009) at 70 dB HL in response to click stimuli in the left ear (See Table 1). Similarly, the wave V latency for autistic participants (mean = 6.29 , SD = 0.36) was significantly longer than that of the TD group (mean = 6.02 , SD = 0.25 ; U= 20.50 , p= 0.05) at 70 dB HL in response to click stimuli in the left ear (See Figure 3; See Figure 2; See Table 1). Also, wave V latencies in the right ear of autistic children (right: mean $= 6.30$, SD $= 0.39$) trended toward statistical difference, compared to the TD group (right: mean $= 5.99$, SD $= 0.23$; right comparison: $U=22.00$, $p=0.075$) at 70 dB HL to clicks (See Table 1).

In contrast, we also identified differences in which the TD group had longer latencies. For instance, the wave V latency for the autistic individuals (mean = 12.63 , SD = 0.93) was significantly shorter than that of the TD group (mean = 13.80 , SD = 1.04 ; U=61.50, p=0.035) in the right ear at 500 Hz and 40-45 dB HL (See Table 1). Additionally, for pure tone stimuli of 500 Hz at 45 dB HL, the wave V latency showed a similar trend when compared between the autistic

(mean = 12.52, SD = 0.96) and TD groups (mean = 13.16, SD = 1.03, U=17.50 p=0.06) (See Table 1).

Interpeak Latencies (IPL)

We similarly identified differences in IPL between the groups. For example, the wave I-III IPL in autistic children (mean $= 2.51$, SD $= 0.42$) was significantly longer than that of the neurotypical children (mean = 2.2250 , SD = 0.23719 ; U=19, p=0.041) at 70 dB HL in the left ear in response to click stimuli (See Table 1). The wave I-V IPL in the right and left ears of autistic children (right: mean = 4.59, SD = 0.34; left: mean = 4.57, SD = 0.46) though not statistically significant, was approaching significance compared to the TD group (right: mean $= 4.29$, SD $=$ 0.31, left: mean = 4.26, SD = 0.31; right comparison U=22.50, p=0.075, left comparison U=22.00, $p=0.075$) at 70 dB HL with click ABR (See Table 1).

Inter-Aural Differences (IAD)

We also observed differences in IAD between autistic individuals and the neurotypical children. That is, the inter-aural difference for wave I-V IPL for the autistic participants (mean = 0.1055, $SD = 0.1876$) was significantly smaller than that of the neurotypical group (mean = 0.1500, SD = 0.06969; U=69, p=0.041) at 70 dB HL click ABR (See Table 1).

Cross Correlations and Inter-Aural Cross Correlations

We found no statistically significant difference between groups upon cross-correlation analysis. In the ten cross correlation analyses we completed, the autism group had a larger mean in five and the typically developing group had a larger mean in five (See Table 1). The typically developing group tended to have smaller standard deviations in seven out of the ten cross correlation analyses. While these descriptive observations were notable, there were no statistically significant differences between the groups (See Figure 2; See Figure 3). We also

found no statistically significant difference between groups upon inter-aural cross correlation analysis. The autism group and typically developing group had fairly similar results across all five test conditions.

Discussion

The aims of the current study were to investigate auditory neurophysiology at the level of the brainstem through measuring absolute latencies, inter-peak latencies, inter-aural differences, and cross-correlations of the ABRs of autistic individuals in comparison to their typically developing peers. We observed significantly longer wave III and V latencies in autistic individuals to click stimuli and longer wave V latencies at a low frequency and intensity. In IPL, we observed significantly longer wave I-III and I-V latencies. Results also revealed a smaller IAD for wave I-V IPL in autistic children compared to typically developing children. Finally, we found no significant differences between groups in cross correlation or inter-aural cross correlation analysis. The following paragraphs will discuss these findings in light of the existing literature and implications for the future.

Absolute Latencies

In terms of absolute latencies, we found significantly longer wave III and V latencies for some (esp. click) stimuli in autistic children. Our findings are somewhat consistent with previous literature, in which autistic children had longer latencies (Azouz et al., 2014; Kwon et al., 2007; Miron et al., 2015; Miron et al., 2018; Ramezani et al., 2019). For example, using similar stimuli and presentations levels, Miron and colleagues (2015) found longer wave V latencies in both autistic toddlers and infants later diagnosed with autism, compared to typically developing peers. We also found significantly longer wave III and V latencies in autistic children with click stimuli at relatively high intensities. Wave V latency delays have been shown to be associated with

lower verbal intelligence scores (Fujikawa-Brooks et al., 2010) and delayed language acquisition (Roth et al., 2012). Thus, while we do not have behavioral data to correlate with waveform characteristics in this study, given previous findings, it's possible that the delayed wave V latencies connected with these clinically detectable differences in language and behavior in autistic children.

Since click stimuli are complex sounds comprised of many frequencies, longer latencies in response to such stimuli, but not simple pure tones, may also suggest that the brains of autistic people struggle to process more complex sounds compared to simple sounds (Boddaert et al., 2004; Ceponiene et al., 2003; Key & D'Ambrose, 2021; Mamashli et al., 2017; Otto-Meyer et al., 2018). Another possible interpretation is that the increase in response time for more complex sounds could be related to under-responsiveness (Thye et al., 2018; Williams et al., 2021). Many autistic individuals experience under-responsiveness to sound (Baranek et al., 2006; Ben-Sasson, Hen et al., 2009; Glod et al., 2015; Hilton et al., 2010). Delayed latencies in brainstem evoked potentials, such as those reported here, could represent some of the neural correlates of those sensory processing difficulties; that is, if neurons are not responding as readily to sounds (esp. complex sounds), this may translate to delayed latencies (Azouz et al., 2014; Baranek et al., 2006; Ben-Sasson, Hen et al., 2009; Miron et al., 2018; Ramezani et al., 2019). On the other hand, perhaps the longer response latencies to relatively high intensity signals (e.g., 70 dB HL) are related to sensory overload. That is, it is possible that louder sounds "clog" the system, causing sensory overload and longer latencies (Baranek et al., 2013; Miron et al., 2018; Ramezani et al., 2019; Williams et al., 2021).

In contrast, we also found the neurotypical children to have significantly longer wave V latency in the right ear at 500 Hz and 40-45 dB HL. A number of studies have found no

significant difference between autistic wave V latencies and neurotypical wave V latencies (Fujihira et al., 2021; Rumsey et al., 1984; Russo et al., 2009; Tharpe et al., 2006). For example, Russo and colleagues (2009) found Wave V latencies from click-ABR in their autistic participants to be consistent with the established normal range for latencies (Russo et al., 2009). It is possible that the variability in results could in part be due to the difference in type of sound and intensity. 500 Hz is a much simpler sound than a click, and 40-45 dB HL is much softer than 70 dB HL. That autistic children have shorter latencies in these simpler, softer sounds, could imply that autistic brains are more efficient at processing simple sounds than complex sounds (Boddaert et al., 2004; Ceponiene et al., 2003; Key & D'Ambrose, 2021; Mamashli et al., 2017; Otto-Meyer et al., 2018). Additionally, or alternatively, this finding could be an indication the sound systems of autistic individuals are processing quiet sounds as if they were louder $-$ i.e., louder sounds typically result in shorter waveform peak latencies (Baranek et al., 2013; Danesh et al., 2015; Khalfa et al., 2004; Williams et al., 2021). Ultimately, to investigate these ideas further, future ABR studies in autistic individuals should include behavioral measures of sensory processing to investigate the relationship between ABR waveform latencies and functional sensory processing (esp. hypo- and hyper-sensitivity).

The variability of the above results could be due to the heterogeneous nature of the autism population (Hassan & Mokhtar, 2019). Autistic individuals present with sensory processing difficulties in a variety of ways. For example, some present with over-sensitivity and others with under-sensitivity (Baranek et al., 2006; Ben-Sasson, Hen et al., 2009; Ramezani et al., 2019). Thus, the variety of responses observed in this study could be indicative of the variation in sensory characteristics across the autism population (Crane et al., 2009; Demopoulos & Lewine, 2016; Marco et al., 2011). Furthermore, because of the heterogeneity among those on

the autism spectrum, the current results may need to be interpreted cautiously, because of the study's small sample size.

Interpeak Latencies (IPL)

In our inter-peak latency analysis, we found significantly longer wave I-III IPL in the left ears of autistic participants and trending towards statistically different wave I-V IPL in both right and left ears in the autistic participants. These results are consistent with previous literature that found longer IPL in autistic individuals compared to neurotypical participants. (Azouz et al., 2014; Miron et al., 2015; Roth et al., 2012). For example, in an ABR study with click ABR at 85 dB HL by Roth and colleagues (2012), the investigators found significantly prolonged I to III and I to V IPLs in suspected autistic participants; notably, in their study IPL III-V was not prolonged in the autism group, findings that were similar to those of the current study (Roth et al., 2012). Increased IPLs suggest processing delays between nuclei along the central auditory pathway. These observed delays could be important when considering brainstem functions related to timing, which is extremely important to complex auditory processing, such as localization, speech processing, and hearing in noise (Alcántara et al., 2004; Banai et al., 2005; Thye et al., 2018). Additionally, timing plays an important role in localization and understanding speech in noise.

It is important to recognize that in this study we only had IPLs from click ABR results at higher intensities. As previously stated, autistic children tended to have longer latencies in these testing conditions. This is certainly a contributing factor in finding prolonged IPLs in the autism group consistently compared to the difference of results observed between high-intensity complex sounds and low-intensity simple sounds.

Inter-Aural Differences (IAD)

In the present study, inter-aural differences for wave I-V IPL for the autistic children were significantly shorter than in neurotypical children. This might support the notion that, while autistic children have longer latencies and IPL than the neurotypical children in both left and right ears, their ears are processing sounds at similar speeds. The fact that there is such a small difference between ears in the autistic participants supports the notion that wave V click latencies are longer-overall, thus lending support to our original absolute latencies results.

Cross Correlations and Inter-Aural Cross Correlation

We found no statistical significance difference between typically developing and autistic participants in our cross-correlation analysis or inter-aural cross correlation analysis. This may be an indication that at the level of the brainstem, synchrony in auditory processing is relatively similar for autistic and neurotypical people. Auditory processing differences between many autistic and neurotypical people seem to exist at the level of the brainstem, as evidenced by shifted latencies. However, synchrony does not appear to be a contributing factor to such auditory processing differences. Given this notion, and the fact that auditory difficulties are common in autism, it could be that the major neurological differences occur in levels of the central auditory pathway more central than the brainstem (Demopoulos & Lewine, 2016; Edgar et al., 2015). Additionally, sensory differences may be mediated by processing in supramodal brain regions that are connected to all sensory systems and modulate the activity therein (Levine & Schwarzbach, 2018; Rosenblum et al., 2017; Cardon, 2018; Cardon et al., 2017). Ultimately, these novel cross-correlation-based findings suggest that brainstem synchrony may be typical in autism. Ruling out areas and functions that have the potential to affect sensory processing in

autism is a useful step in the quest to discover the neurobiological underpinnings of such differences in this population.

Interesting comparisons may be drawn between the behavioral results of autistic individuals and individuals with auditory neuropathy spectrum disorder (ANSD)—a disorder of the synchrony of the VIII cranial nerve (Cardon & Sharma, 2013; De Siati et al., 2020; Miron et al., 2015; Ramezani et al., 2019). That is, both populations often present with abnormal ABR results and difficulty processing speech and understanding signals in noise (Alcántara et al., 2004; Azouz et al., 2014; Cardon & Sharma, 2013; De Siati et al., 2020; Miron et al., 2015; Ramezani et al., 2019; Zeng & Liu, 2006). However, unlike our autistic participants, ANSD patients do not have high degrees of synchrony at the level of the brainstem (Cardon & Sharma, 2013; Kraus et al., 2000) though cortical synchrony can be good enough to elicit evoked potentials from the auditory cortex in ANSD (Cardon & Sharma, 2013; De Siati et al., 2020; Nash-Kille & Sharma, 2014). Overall, while ANSD patients and autistic individuals share some behaviors, the underlying physiology appears to be different. Since both populations exhibit similarities in behavioral auditory function, yet autistic individuals seem to have strong auditory brainstem synchrony, it is reasonable to believe that atypical neurobiology may be occurring in higher order brain regions in autism (Demopoulos & Lewine, 2016; Edgar et al., 2015).

Limitations of Current Study

It is important to note that there is a great deal of heterogeneity in autism (Hassan $\&$ Mokhtar, 2019). Because of the small size of our study, it would be difficult to separate groups into subgroups with similar traits. It is possible that there are autistic individuals who do not have good auditory processing at the level of the brainstem. Future studies should investigate this with larger sample sizes to subdivide into different subgroups with similar traits. Furthermore, this

study had no behavioral data, meaning that sensory processing implications are grounded in current literature. Thus, future studies correlating ABR responses with behavioral data would strengthen this area of inquiry. Finally, as this is a retroactive study, the data was collected clinically instead of in a lab. Thus, it is possible that unknown confounds impacted the results.

Clinical Implications

Because of the variety of ABR responses present in autism population, ABR may not provide absolute clarity in the autism diagnosis process; it is unclear if there is anything from the ABR that can definitively diagnose autism. However, as researchers continue to look at biomarkers connected to certain aspects of autism, ABR and other auditory evoked potentials may still be considered. For example, synchrony seems to be similar at the level of the brainstem for those on the autism spectrum, compared to undiagnosed individuals. Given this similarity, future research may need to look to more central portions of the nervous system, such as through cortical auditory evoked potentials (Azouz et al., 2011; Marco et al., 2011). From a clinical (esp. SLP and audiology) standpoint, the ABR continues to have potential to evaluate differences in neural responses to complex sounds versus simple sounds, possibly contributing a physiologic measure to our understanding of speech processing and hearing in noise in autism (Kraus et al., 2000). Additionally, studying the correlation between atypical ABRs and behavioral differences (i.e., sensory seeking or sensory avoidant) could contribute to better clinical practice by recognizing sensory needs and their neurophysiologic underpinnings.

Conclusion

In this study, the ABR was used to investigate auditory brainstem function in children through comparing absolute latencies, IPL, IAD, cross correlation, and IACC between agematched groups of autistic and typically developing children. We observed significantly longer

latencies in the autism group in some conditions, and in the typically developing group in others. We found no statistically significant results between the ASD group and TD group in either the cross correlation or IACC. These results suggest function and synchrony are very similar with some possible differences at the level of the brainstem; thus, differences may be more central in the auditory system. Future studies should investigate the correlation between various ABR responses and behavioral measures because of the varied responses due to the heterogeneity in the autism population.

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Tables

Table 1

| | ASD $(n=11)$ | $NT(n=8)$ | |
|----------------------------------|--------------|-------------|-------------|
| | mean(SD) | mean(SD) | U; p |
| Age in Months | 34.53(10) | 38.22(8.86) | |
| Sex | M:9, F:2 | M:6, F:2 | |
| | | | |
| Click R 70 dB HL Wave V Amp | 0.54(0.17) | 0.57(0.06) | 40.0; 1 |
| Click L 70 dB HL Wave V Amp | 0.54(0.18) | 0.48(0.10) | 31.0; 0.31 |
| 2000 Hz R 30 dB HL Wave V Amp | 0.29(0.12) | 0.29(0.08) | 39.5; 0.425 |
| 2000 Hz L 30 dB HL Wave V Amp | 0.24(0.1) | 0.26(0.06) | 47.5; 0.93 |
| 500 Hz R 40-45 dB HL Wave V Amp | 0.21(0.07) | 0.22(0.03) | 44.5; 0.596 |
| 500 Hz L 40-45 dB HL Wave V Amp | 0.19(0.07) | 0.22(0.08) | 51.0; 0.6 |
| 4000 Hz R 25 dB HL Wave V Amp | 0.25(0.09) | 0.28(0.08) | 44.0; 0.659 |
| 4000 Hz L 25 dB HL Wave V Amp | 0.23(0.09) | 0.22(0.07) | 39.5; 0.93 |
| 1000 Hz R 35 dB HL Wave V Amp | 0.28(0.09) | 0.23(0.06) | 25.5; 0.203 |
| 1000 Hz L 35 dB HL Wave V Amp | 0.25(0.09) | 0.21(0.05) | 29.5; 0.36 |
| | | | |
| Click R 70 dB HL Wave I Lat | 1.70(0.30) | 1.7(0.29) | 43.0; 0.968 |
| Click L 70 dB HL Wave I Lat | 1.73(0.42) | 1.76(0.20) | 57.0; 0.31 |
| Click R 70 dB HL Wave III Lat | 4.21(0.37) | 4.03(0.17) | 32.5; 0.351 |
| Click L 70 dB HL Wave III Lat* | 4.24(0.23) | 3.98(0.14) | 13.5; 0.009 |
| Click R 70 dB HL Wave V Lat | 6.29(0.36) | 5.99(0.23) | 20.5; 0.051 |
| Click L 70 dB HL Wave V Lat* | 6.3(0.39) | 6.02(0.25) | 22.0; 0.075 |
| 2000 Hz R 30 dB HL Wave V Lat | 8.83(0.43) | 8.48(0.34) | 20.0; 0.104 |
| 2000 Hz L 30 dB HL Wave V Lat | 8.10(0.45) | 8.71(0.31) | 27.5; 0.328 |
| 500 Hz R 40-45 dB HL Wave V Lat* | 12.63(0.93) | 13.80(1.04) | 61.5; 0.035 |
| 500 Hz L 40-45 dB HL Wave V Lat | 12.88(1.05) | 13.61(1.06) | 56.0; 0.351 |
| 4000 Hz R 25 dB HL Wave V Lat | 8.06(0.41) | 7.7(0.38) | 22.0; 0.151 |
| 4000 Hz L 25 dB HL Wave V Lat | 8.09(0.51) | 7.81(0.38) | 28.5; 0.375 |
| 1000 Hz R 35 dB HL Wave V Lat | 10.58(0.53) | 10.70(0.75) | 42.0; 0.897 |
| 1000 Hz L 35 dB HL Wave V Lat | 10.70(0.45) | 11.01(1.02) | 46.0; 0.633 |
| | | | |
| IPL Click R I-III | 2.51(0.19) | 2.33(0.26) | 27.0; 0.177 |
| IPL Click R III-V | 2.08(0.31) | 1.96(0.19) | 37.0; 0.6 |
| IPL Click R I-V | 4.59(0.34) | 4.29(0.31) | 22.5; 0.075 |
| IPL Click L I-III* | 2.51(0.43) | 2.23(0.24) | 19.0; 0.041 |

Summary of Demographics and Waveform Characteristics

 $Amp =$ amplitude; Lat = latency; IPL = inter-peak latency; IAD = inter-aural difference; CC =

cross correlation; IACC=inter-aural cross correlation.

* for significant results

Figures

Figure 1

Sample Auditory Brainstem Response

Note. A sample picture of an Auditory Brainstem Responses (ABR) with each wave and its corresponding anatomical landmark labeled.

Creel, D. J. (1995). Visual and auditory anomalies associated with albinism: Figure 24: Auditory brainstem response (ABR) recorded from pigmented human being at click intensity of 70 dB HL and rate of 11.9 per second. In H. Kolb, E. Fernandez, R. Nelson, (Eds.), *Webvision: The organization of the retina and visual system*. University of Utah Health Sciences Center.

https://www.ncbi.nlm.nih.gov/books/NBK303985/figure/CreelAlbinism.F24/

Figure 2

Auditory Brainstem Responses for Autistic Children (A) and Typically Developing Children (B)

Note. Auditory Brainstem Responses (ABR) to click stimuli at 70 dB HL for right (left panels) and left (right panels) from Autistic Children (A) and typically developing children (B). Dashed and dotted lines indicate ABR recording runs one and two, respectively. Bold lines indicate the average of these runs.

Figure 3

Children

Auditory Brainstem Response Comparison Between Autistic Children and Typically Developing

Note. This figure compares Auditory Brainstem Responses to click stimuli at 70 dB HL for autistic children (solid line) and typically developing children (dashed line) in the right ear (left panel) and left ear (right panel).

 $*_{p<0.05}$

APPENDIX

Annotated Bibliography

Alcántara, J. I., Weisblatt, E. J., Moore, B. C., & Bolton, P. F. (2004). Speech-in-noise perception in high-functioning individuals with autism or Asperger's syndrome. *Journal of Child Psychology and Psychiatry, and Allied Disciplines*, *45*(6), 1107–1114. https://doi.org/10.1111/j.1469-7610.2004.t01-1-00303.x

Purpose: Three purposes: first, to verify that autistic individuals and individuals with Asperger's syndrome struggle to understand speech in noise. Second, to quantify the extent of difficulties. Third, to propose the underlying mechanism behind why these individuals struggle to understand speech in noise.

Summary: Speech-in-noise (SNRTs) were measured in 11 ASD/HFA (high functioning autism) and 9 controls with various background noises. SRTs were higher (worse) in the HFA/AS group than the control, indicating greater difficulty understanding speech in noise. Results were only statistically significant if the background noise included temporal or spectral dips. This could potentially mean that speech-in-noise perception difficulties in autism could be caused by trouble integrating information from temporal dips in noise.

Relevance: Very relevant to our study because it demonstrates a real-world impact of sensory processing difficulties.

Unique Features: Figure 3 is a great comparison of speech reception thresholds in ASD and the control groups.

Research methodology: Causal-Comparative Research Study

The strengths, weaknesses or biases in the material: Small sample size, however the groups were age and IQ matched.

Azouz, H. G., Kozou, H., Khalil, M., Abdou, R. M., & Sakr, M. (2014). The correlation between central auditory processing in autistic children and their language processing abilities. *International Journal of Pediatric Otorhinolaryngology*, *78*(12), 2297–2300. https://doi.org/10.1016/j.ijporl.2014.10.039

Purpose: To study the auditory profile of children with ASD and find out if (central) auditory processing disorder is a crucial component of ASD, or frequently co-morbid with ASD. Additionally, to study the correlation between CAP findings and language delay.

Summary: In this study, 30 autistic children received thorough history taking and comprehensive neurological examination. Autism was established using the Criteria of the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV-TR and Autism Diagnostic interview- revised (ADI-R). Their hearing was then assessed using ABR thresholds. Finally, subjects were given the Test of Acquired Communication Skills (TACS) to evaluate the pre-linguistic and communication skills and a sensory checklist for auditory/listening skills was performed. There was a control of 20 typically developing children. They concluded that central auditory processing disorder is an essential component of ASD. It was found that autistic children had an immature or dysfunction in the central auditory nervous system. Typically, the right hemisphere is the central hemisphere in processing auditory information, but in the autistic subjects in this study auditory information is being processed in the left hemisphere. There was a

correlation between lower language scores and more severe differences in the Cortical Auditory Evoked Potential (CAEP).

Its relevance to the topic: Discusses prevalence of central auditory processing disorder in children with autism, using ABR to identify central processing disorder.

Any special or unique features about the material: I really liked the chart showing the correlation between cortical auditory evoked potentials and lower language scores.

Research methodology: 30 children with a confirmed diagnosis of autism and were assessed using a thorough case history, language assessment using the Test of Acquired Communication Skills (TACS), sensory checklists for auditory skills, and cortical evoked potentials and ABR.

The strengths, weaknesses or biases in the material: Methods section was very brief, making replication difficult.

Ben-Sasson, A., Carter, A. S., & Briggs-Gowan, M. J. (2009). Sensory over-responsivity in elementary school: Prevalence and social-emotional correlates. *Journal of Abnormal Child Psychology*, *37*(5), 705–716.<https://doi.org/10.1007/s10802-008-9295-8>

Purpose: Examine the impact of sensory over-responsivity (SOR) in children and find the prevalence of social-emotional difficulties in this group.

Summary: 925 children were followed by researchers from infancy to elementary school. 16% of parents reported at least four tactile or auditory sensations bothered their children. Participant measures include Sensory Over-Responsivity Scales, Child Behavior Checklist, The Infant Toddler Social and Emotional Assessment, and Adaptive Social Behavior Ratings. Parents of children with higher SOR scores reported higher frequencies of dysregulation problems and lower levels of adaptive social behaviors.

SOR was associated with higher levels of social-emotional problems, especially anxiety, depression, and withdrawal. Additionally, children with higher SOR had lower levels of social competence.

Relevance: This study underscores the importance of studying sensory processing because of the huge impact it can have on an individual's quality of life.

Unique Features: Clear definitions of sensory over responsiveness, extensive tables with participant details.

Research methodology: Longitudinal Study with 925 children from infancy until ages 7-11.

The strengths, weaknesses or biases in the material: This study has a large sample size (925) which is a strength. A limitation would be that information was collected via parent questionnaire and the questionnaires focused largely on auditory and tactile processing, so this is not a comprehensive picture of all sensory processing considerations.

Bottema-Beutel, K., Kapp, S. K., Lester, J. N., Sasson, N. J., & Hand, B. N. (2021). Avoiding ableist language: Suggestions for autism researchers. *Autism in Adulthood, 3*(1), 18-29. <https://doi.org/10.1089/aut.2020.0014>

Purpose: Instruct researchers on how to avoid ableist language and what terms are preferred by the autistic community.

Summary: This paper first establishes the importance of avoiding ableist language and how these steps will help autistic people. Second, it summarizes the history of language used to refer to autism and autistic people. Third, it summarizes the current language the autistic community prefers as collected from surveys to autistic people. The

paper then discusses some of the current controversies surrounding language in autism research with concrete suggestions for how researchers should approach it.

Relevance: As autism researchers, it is important to be sensitive and aware of the community's preferences. Thus, this article is an important reference point in choosing linguistic practices to frame our research within.

Unique Features: Compiled autistic adult's perspectives and preferences about ableist language. Table 1 includes a list of ableist terms and the suggested alternatives. Very concise and easy to refer to.

Research methodology: Perspective Article

The strengths, weaknesses or biases in the material: An important strength of this article is how it drew on autistic scholars and surveys of autistic individuals to assert the community's preferences.

Cohen, I. L., Gardner, J. M., Karmel, B. Z., Phan, H. T., Kittler, P., Gomez, T. R., Gonzalez, M. G., Lennon, E. M., Parab, S., & Barone, A. (2013). Neonatal brainstem function and month arousal-modulated attention are jointly associated with autism. *Autism Research: Official Journal of the International Society for Autism Research, 6*(1), 11–22. https://doi.org/10.1002/aur.1259

Purpose: To assess correlation between four-month-olds with a preference for high rates of stimulation and atypical ABRs with later diagnosis of ASD.

Summary: Researchers measured ABRs and AMAs in 4-month-olds and then followed up with autism testing in the children when they were on average 3.5 years old with the PDDBI and Griffiths Mental Development Scales which was administered at 28, 34, and 42 months old. Researchers findings suggest that initially abnormal ABRs and

increased fixation on higher rates of stimulation at four months in NICU graduates could be a marker of later ASD diagnosis. 93% percent of ASD cases were in the Abnormal ABR group versus 56% of non-ASD cases.

Its relevance to the topic: Further evidence suggesting atypical brainstem development in children with autism, identifiable as early as 4-months-old.

Any special or unique features about the material: Table 1 and Table 2 have a great summary of relevant study information on demographics and atypical ABR results.

Research methodology: Longitudinal study or neonatal ABRs and 4-month-old Arousal Modulated Attention and later ASD behaviors.

The strengths, weaknesses or biases in the material: The sample is relatively small, and it could be that atypical ABR results are associated with other NICU confounding factors rather than ASD, or both.

Crane, L., Goddard, L., & Pring, L. (2009). Sensory processing in adults with autism spectrum disorders. *Autism: The International Journal of Research & Practice*, *13*(3), 215–228. <https://doi.org/10.1177/1362361309103794>

Purpose: This study was designed to assess the extent of sensory processing differences in autistic adults. While there is a great body of literature on sensory processing in autistic children, there is less research across the lifespan and this article begins to address how sensory processing differences impact autistic individuals in adulthood.

Summary: In this study, autistic adults took a sensory processing self-reporting assessment. 94.4% demonstrated extreme levels of sensory processing in at least one of the assessment areas. They then discuss how sensory processing may impact autistic

adults into adulthood and how that can influence treatment and diagnosis of ASD in adulthood.

Relevance: This underscores the importance of developing greater understanding of sensory processing in autistic individuals because of the ramifications across the lifespan.

Unique features: This paper has very concise definitions of sensory terms such as low registration, sensory seeking, sensory sensitivity, and sensation avoiding.

Research methodology: 36 adults participated in this study (18 adults with ASD, 18 comparison participants). Three measures were administered: Wechsler Abbreviated Scale of Intelligence (WASI: Wechsler, 1999a), Autism-Spectrum Quotient (AQ: Baron-Cohen et al., 2001), and Adult/Adolescent Sensory Profile (AASP: Brown and Dunn, 2002). T-tests were performed and it was found that the autistic adults scored higher in low registration, sensation avoidance and sensory sensitivity.

The strengths, weaknesses or biases in the material: They used a questionnaire to measure sensory processing, making results reliant on self-reporting or awareness of sensory processing difficulties.

Demopoulos, C., & Lewine, J. D. (2016). Audiometric profiles in autism spectrum disorders: Does subclinical hearing loss impact communication? *Autism Research: Official Journal of the International Society for Autism Research*, *9*(1), 107–120. https://doi.org/10.1002/aur.1495

Purpose: To compare audiological functioning in people with ASD in comparison to the general population and then to see if hearing impairment significantly impacted their communication abilities.

Summary: 60 participants with ASD and 16 typically developing peers between 5-18 were assessed in both communication abilities and audiology. In both areas, testing was fairly comprehensive. Results demonstrated that 55% of those in the ASD group had atypical test results in at least one audiological test in comparison to their typically developing peers in which 14.9% had atypical results for an audiological test. This also should be compared to the general population which is estimated to have 6% of individuals testing abnormally in audiological tests.

Its relevance to the topic: Discussing the importance of hearing in communication, as well as the prevalence of hearing impairment or atypical hearing in people with ASD.

Any special or unique features about the material: They were able to assess hearing using a variety of audiological tests including: pure tone audiometry, uncomfortable loudness level, tympanometry, acoustic reflexes, distortion product otoacoustic emissions, and auditory brainstem response

Research methodology: 60 ASD participants and 16 typically developing participants in an analytic observational study. Both sets or participants were thoroughly assessed with communication assessments and audiometric measures.

The strengths, weaknesses or biases in the material: The study relocated to a different location partway through. Therefore, they had to collect data with different equipment and did not have access to all of their previous equipment, meaning there is some missing data for uncomfortable loudness level and DPOAE.

ElMoazen, D., Sobhy, O., Abdou, R., & AbdelMotaleb, H. (2020). Binaural interaction component of the auditory brainstem response in children with autism spectrum disorder. *International Journal of Pediatric Otorhinolaryngology*, *131*, Article 109850. https://doi.org/10.1016/j.ijporl.2019.109850

Purpose: To assess the differences in binaural interaction component of the auditory brainstem (ABR-BIC) between children with ASD and typical peers.

Summary: Researchers collected data from a group of 20 children with ASD and a control of 20 typically developing peers over 10 months in 2018. ABR data was collected using a stimulus of 65 dB HL in both ears independently and at the same time. Binaural waveforms were then compared to the predicted binaural waveform. It was found that there was significant delay of the latency of wave V in the ASD group, with no significant difference between the left and right ear. ABR-BIC amplitudes in the ASD group were smaller than the control group, which could suggest reduced binaural interaction and was correlated with more severe language and social deficits.

Relevance: Demonstrates low amplitude ABR-BIC in children with ASD compared to typically developing peers and links low amplitude ABR-BIC with severity of language and social deficits.

Unique Features: Evaluates binaural ABR interaction at 65 db HL

Research methodology: Click evoked ABR were measured in left monaural, right monoaural, and binaural stimulation at 65 dBnHL in all participants. The ABR-BIC was calculated to evaluate the difference between binaurally evoked ABR and predicted binaural waveform by algebraically summing the left and right monaurally evoked ABRs. This difference in amplitude is what causes ABR-BIC happens at IV-VI waves.

The strengths, weaknesses or biases in the material: Each participant's communication was assessed using the Test of Acquired Communication Skills (TACS) which is designed for children with ASD or other conditions relating to language delay. It has high sensitivity and specificity. All children were assessed in the same setting to reduce confounds.

Engel-Yeger, B., & Dunn, W. (2011). The relationship between sensory processing difficulties and anxiety level of healthy adults. *British Journal of Occupational Therapy, 74(*5), 210- 216.<http://dx.doi.org.erl.lib.byu.edu/10.4276/030802211X13046730116407>

Purpose: To study the relationship between sensory processing and anxiety.

Summary: 135 healthy adults took Adolescent/Adult Sensory Profile to assess sensory processing. They then took the Spielberger's State-Trait Anxiety Inventory to assess anxiety. Individuals with sensory hypersensitivity and individuals with low registration also presented with higher traits of anxiety and state anxiety. Interestingly, men with low registration had more anxiety than women. Sensation avoiding was an important factor in predicting state of anxiety.

Relevance: Our study is about auditory processing and its therapeutic implications. This study touches on important aspects of how sensory processing impacts an individual's quality of life.

Unique Features: The study examined the relationship between sensory processing and anxiety in neurotypical adults.

Research methodology: Causal-Comparative Research Study

The strengths, weaknesses or biases in the material: Same size of 135 adults.

Geurts, H. M., Grasman, R. P., Verté, S., Oosterlaan, J., Roeyers, H., van Kammen, S. M., & Sergeant, J. A. (2008). Intra-individual variability in ADHD, autism spectrum disorders and Tourette's syndrome. *Neuropsychologia*, *46*(13), 3030–3041.

<https://doi.org/10.1016/j.neuropsychologia.2008.06.013>

Purpose: To study response variability in varied disorders including attention deficit hyperactivity disorders (ADHD), high functioning autism (HFA), autistic children with ADHD (ASD +ADHD), children with Tourette's syndrome (TS), and compare these results with typically developing peers (TD).

Summary: There were 334 child participants in this study in the various groups (ADHD, HFA, ASD + ADHD, TS, and TD). Data was collected from the Change Task on three different occasions. Data was analyzed using ex-Gaussian modeling, intraindividual variability analysis, and spectral analysis. Researchers found variability in response in both the ADHD group and the ASD group.

Relevance: We are using intra-individual variability in our study, so relying on other literature in the field using this as a measure is a helpful reference.

Unique Features: Compared results in intra-individual variability between ADHD, Tourettes, and Autism.

Research methodology: Statistical measures: ex-Gaussian modeling, intraindividual variability analysis, and spectral analysis.

The strengths, weaknesses or biases in the material: Decent sample sizes, smallest group had 21 participants and largest had 53 participants.

Källstrand, J., Olsson, O., Nehlstedt, S. F., Sköld, M. L., & Nielzén, S. (2010). Abnormal auditory forward masking pattern in the brainstem response of individuals with Asperger syndrome. *Neuropsychiatric Disease and Treatment*, *6*(1), 289–296. https://doi.org/10.2147/ndt.s10593

Purpose: To investigate the auditory brainstem response in people with AS (Asperger's syndrome) to forward masking

Summary: Researchers measured the ABRs of 16 AS subjects, 16 healthy individuals, 16, schizophrenic patients, and 16 attention deficit hyperactivity disorder patients. AS group had unusually low activity in the early part of their ABRs, especially wave III amplitudes were lower in the AS group than in all the control groups in response to forward masking. A square-shaped click pulse was used as stimulus. Forward masking increased the latencies wave III and wave V in all groups. There were differences in the ABR waveform between AS patients and controls with a high level of statistical significance.

Relevance: Discusses the role of the auditory brainstem and ABRs in ASD.

Unique Features: I found the description of the ABR in the introduction comprehensive and easy to understand. I especially liked that it listed the anatomical landmarks associated with each peak.

Research methodology: 16 AS subjects, 16 healthy individuals, 16, schizophrenic patients, and 16 attention deficit hyperactivity disorder patients, tests were performed in a quiet, dark room

The strengths, weaknesses or biases in the material: Relatively small sample sizes. Marco, E. J., Hinkley, L. B., Hill, S. S., & Nagarajan, S. S. (2011). Sensory processing in autism: A review of neurophysiologic findings. *Pediatric Research*, *69*(5 Pt 2), 48R–54R. <https://doi.org/10.1203/PDR.0b013e3182130c54>

Purpose: To review neurophysiologic research about sensory processing in autism.

Summary: This article summarize research on sensory processing both across all modalities and individual senses in autism research. It draws upon various imaging techniques such as EEG, MEG, and fMRI. It then describes both low-level and high-level sensory integration and the impact of attention across sensory processing. Finally, they discuss selective attention and how autistic children may struggle in this area, thus struggling with sensory overload.

Relevance: Important review of sensory information on autism and the neurobiological causes. The auditory section is especially relevant to our study.

Unique Features: Extensive summary of research on auditory processing in autism, very helpful.

Research methodology: Literature review

The strengths, weaknesses or biases in the material: It is a review article, not a research study and has very thorough information on other current studies.

Miron, O., Delgado, R. E., Delgado, C. F., Simpson, E. A., Yu, K. ‐. H., Gutierrez, A., Zeng, G., Gerstenberger, J. N., & Kohane, I. S. (2020). Prolonged auditory brainstem response in universal hearing screening of newborns with autism spectrum disorder. *Autism Research, 14*(1), 46-52. https://doi.org/10.1002/aur.2422

Purpose: To determine if healthy newborns who later develop ASD have ABR anomalies. Summary: Researchers did a retrospective study of data from 139,154 newborns Universal Newborn Hearing Screening and compared ABR results in infants who were later diagnosed with ASD to infants who were not later diagnosed with autism. They found that newborns later diagnosed with ASD had prolonged ABR phase and Vnegative latency compared with the non-ASD newborns. ASD newborns also

demonstrated greater variance in their latencies compared to previous studies, possibly because of the low intensity of the ABR stimulus. They tested ABR using 35 dB nHL, which is a much lower intensity than what is used in most ASD studies. The typical intensity is 85 dB nHL. Because of the low intensity, and lower signal-to-noise ratio, it was difficult to previscely label wave V-positive. For this reason, researchers focused on wave V-negative which was easy to detect, and ABR phase. These results suggest that newborns who later develop ASD show neurophysiological variation at birth.

Relevance: This study demonstrated a correlation between prolonged ABR response and variance in V-negative latencies and later autism diagnosis, suggesting that newborn hearing screenings could be used to predict future autism risk.

Unique Features: This is a retrograde study, similar design to ours, just with a different age group.

Research methodology: Retrospective case-control design study with 321 newborns who were later diagnosed with ASD and a control group of 138,844 newborns who did not receive a diagnosis of

The strengths, weaknesses or biases in the material: No apparent significant weaknesses.

Miron, O., Roth, D. A., Gabis, L. V., Henkin, Y., Shefer, S., Dinstein, I., & Geva, R. (2015). Prolonged auditory brainstem responses in infants with autism. *Autism Research*, *9*(6), 689-695. https://doi-org.erl.lib.byu.edu/10.1002/aur.1561 Purpose: To identify early physiological differences in infants and young children who will later be diagnosed with ASD by focusing on irregular ABRs.

Summary: Researchers used ABR data from 70 children's who were later diagnosed with ASD to measure how predictive abnormally prolonged ABRs can be of a later ASD diagnosis. They found that prolonged ABR wave V latency was could accurately identify children who would later receive an ASD diagnosis with 70% accuracy and the controls with an 80% accuracy.

Relevance: Similar to our research, demonstrates the possibility of the ABR being used in wide scale screening for ASD risk.

Unique Features: Table 1 has a chart comparing the ABR results of the ASD group to control group.

Research methodology: Researchers assessed ABR results for 118 children who were later diagnosed with autism. 48 were excluded from the study because of elevated ABR thresholds, genetic aberrations, or old testing age, so 70 children in the sample were actually used for the study, all who were later diagnosed with ASD. 30 of the children's ABRs were tested between the ages of 0-3 months and 40 of the children's ABRs were tested between 1.5-3.5 years old.

The strengths, weaknesses or biases in the material: Possible sampling bias because participants were selected on the basis of risk for hearing impairment and or neurodevelopmental delay, making it difficult to generalize findings to other groups.

Nash-Kille, A., & Sharma, A. (2014). Inter-trial coherence as a marker of cortical phase synchrony in children with sensorineural hearing loss and auditory neuropathy spectrum disorder fitted with hearing aids and cochlear implants. *Clinical Neurophysiology: Official Journal of the International Federation of Clinical Neurophysiology*, *125*(7), 1459–1470. https://doi.org/10.1016/j.clinph.2013.11.017

Purpose: Researchers wanted to measure cortical phase synchrony in children with normally hearing (NH), sensorineural hearing loss (SNHL) and auditory neuropathy spectrum disorder (ANSD) to learn about the lack of neural synchrony in ANSD.

Summary: They measured cortical phase synchrony to speech by using inter-trial coherence in children with SNHL and ANSD compared to NH. They found that children with ANSD had decreased phase synchrony in comparison to NH. Children with ANSD generally have lower phase coherence compared with children with SNHL.

Relevance: Discusses brainstem dys-synchrony, which we want to measure using the data from ABRs.

Unique Features: Figure 1 and 2 do a great job illustrating the results of ITC in a clear and concise way.

Research methodology: Researchers measured time-frequency analyses on the cortical auditory evoked responses from 41 NH, 91 SNSD, and 50 SNHL and compared results. Data was collected over 15 years from synthesized speech stimulus of /ba/ at a level that was comfortable for each participant (typically 85 dB SPL/75 dB HL).

The strengths, weaknesses or biases in the material: Data was collected over a long period of time.

Ramezani, M., Lotfi, Y., Moossavi, A., & Bakhshi, E. (2019). Auditory brainstem response to speech in children with high functional autism spectrum disorder. *Neurological Sciences: Official Journal of the Italian Neurological Society and of the Italian Society of Clinical Neurophysiology*, *40*(1), 121–125. <https://doi.org/10.1007/s10072-018-3594-9> Purpose: This study investigates subcortical speech processing in children with high functioning ASD.

Summary: The latencies of waves from speech ABR are longer in children with ASD than in TD patients. The study concluded that it is possible that children with ASD might have deficits in the temporal neural coding of speech at the level of the brainstem. Findings imply that synchronization of neural activity is impaired, which further denotes difficulties in processing speech stimulus in the level of the brainstem. Discussed how ASD may be related to difficulty processing speech, especially processing speech in noise.

Relevance: Data on speech ABR latencies in children with high-functioning autism.

Unique Features: Speech ABR at 80 db SPL

Research methodology: 28 children with ASD and 28 TD children were selected from Rofeydeh Rehabilitation Hospital. All participants had an IQ of 85 or higher and tympanogram and auditory reflex were within normal limits. They all did a speech ABR with 40 ms synthetic /da/ syllable stimulus at 80-dB SPL. Participants were in a comfortable close-eyed position during data collection. Data was analyzed using MATLAB software version R2014a.

The strengths, weaknesses or biases in the material: No apparent great strengths of weaknesses in material.

Roth, D. A., Muchnik, C., Shabtai, E., Hildesheimer, M., & Henkin, Y. (2012). Evidence for atypical auditory brainstem responses in young children with suspected autism spectrum disorders. *Developmental Medicine and Child Neurology, 54*(1), 23- 29. <https://doi.org/10.1111/j.1469-8749.2011.04149.x>

Purpose: This study attempted to characterize the ABRs of young children with suspected ASD and compare them to the ABRs of children with language delay as well as comparing them to established clinical norms.

Summary: This is the first study to compare the ABRs of children with suspected ASD and age-matched children with language delay. It was found that the language delayed children have more delayed ABRs than the clinical norms, but that the children with suspected ASD had even more delayed ABRs. That both the suspected ASD group and the language delayed group had delayed ABRs indicates that auditory processing may be at the core of both of these issues.

Relevance: Compares the click ABRs of children with suspected ASD, language delayed, and clinical norms.

Unique Features: Table 1 has absolute and interpeak latency times in ASD, language delay, and clinical norms

Research methodology: The click ABRs of 26 children with suspected ASD and 26 age and sex matched children with language delay were analyzed. Click ABRs were elicited at 85 dB nHL with a presentation rate of 39.1/second. Responses were filtered with a bandwidth of 100 to 3000Hz. They measured the absolute latencies of waves I, III, and V, and interpeak latencies I to III, I to V, and III to V

The strengths, weaknesses, or biases in the material: The autism group and language delay group results were compared to clinical norms for the same facility the study's data was collected at. Since the same equipment was used and medical personal collecting the data, this is a good way to rule out confounds for differences in equipment, procedure etc., even though there wasn't a typically developing group in the study. It would be good to know how many children made of the clinical norms however.

Rubenstein, J. L., & Merzenich, M. M. (2003). Model of autism: Increased ratio of excitation/inhibition in key neural systems. *Genes, Brain, and Behavior*, *2*(5), 255–267. <https://doi.org/10.1034/j.1601-183X.2003.00037.x>

Purpose: This article discusses the theory that autism is caused by an imbalance in the ratio of excitation/inhibition in sensory, mnemonic, social, and emotional systems.

Summary: This article summarizes previous research indicating that there is a genetic factor in autism inheritance, but that it is not yet linked to a specific gene, instead stipulating that there are several genes that contribute to the probability of having autism and that no one gene is the predominant cause of autism. They then hypothesis that some forms of autism are formed by high levels of excitation in neural circuits and low levels of inhibition in the pathways that control language and social behaviors, and discuss how this theory would influence therapy. They then stipulate that if this is the case, intensive perceptual and movement therapies could improve the signal-to-noise ratio caused by the imbalance of excitation/inhibition pathways, and that this could decrease the probability of young, at-risk children from developing autism.

Relevance: Lays out a theory of ASD that we could gather information about during our research study.

Unique Features: Discusses theory of the cause of ASD.

Research methodology: Review article, not based on original research but discussing previously established research and drawing conclusions.

The strengths, weaknesses or biases in the material: No apparent great strengths or weaknesses.

Sharma, M., Bist, S. S., & Kumar, S. (2016). Age-related maturation of wave v latency of auditory brainstem response in children. *Journal of Audiology & Otology*, *20*(2), 97-101. https://doi.org/10.7874/jao.2016.20.2.97

Purpose: Measure ABR in children between the ages of birth and 12 years old.

Summary: Researchers measured wave V latency in ABR in 80 children ages birth to 12 years old. Click ABR was used to measure latency of wave V. Wave V is generated in the inferior colliculus. Wave V latencies decrease rapidly in the first three years of life as the auditory brainstem develops. At three years old, this rate slows, but latencies continue to decrease steadily until 12 years old. Wave V latencies reach adult values sometime between 6 and 12 years of age.

Relevance: Very useful to our study because it has mean latency and standard deviation for children between the ages of 0 and 12.

Unique Features: Table 1 has summaries of previous studies findings regarding to ABR latency peaks by age. Table 3 has a chart of mean latency in wave V and standard deviation from ages 0 months to 144 months.

Research methodology: Researchers measured acoustic click ABR at 30 dBnHL in 80 children between the ages of 0 and 12 years old.

The strengths, weaknesses or biases in the material: This study had 80 participants divided into fairly small groups to control for age, however, that is very necessary because the ABR changes drastically as a child ages. It would be useful to have larger sample sizes, but the small groups make sense in context of the study.

Sohal, V. S., Rubenstein, J. L. R., (2019). Excitation-inhibition balance as a framework for investigating mechanisms in neuropsychiatric disorders. *Molecular Psychiatry*, *24*(9), 1248–1257. https://doi.org/10.1038/s41380-019-0426-0

Purpose: T[o clarify and update Rubenstein and Merzenic](https://doi.org/10.1038/s41380-019-0426-0)h's theory that ASD is caused by an imbalance in the excitatory-inhibitory circuits in light of greater understanding of neuronal circuits.

Summary: E-I balance (excitation-inhibition) refers to the "stable global level of activity within a particular circuit." A change in the E-I balance means that the state is altered or disturbed. E-I balance is very complex and can impact important structures in the brain such as the cortex and the hippocampus. This article expands upon the theory that autism is caused by E-I imbalance by observing ASD gene mutations in mice.

Relevance: Further discusses the E-I balance framework in context of autism research.

Unique Features: Figure 1 has an excellent visual to explain E-I balance.

Research methodology: Perspective article

The strengths, weaknesses, or biases in the material: As this is a perspective article there is no methods section. The reasoning throughout the article is clear, consistent, and easy to follow.

Suarez, M. A. (2012). Sensory processing in children with autism spectrum disorders and impact on functioning. *Pediatric Clinics of North America, 59*(1), 203–214.

https://doi.org/10.1016/j.pcl.2011.10.012

Purpose: To discuss how sensory processing impacts autistic children and their participation in activities.

Summary: This paper defines sensory processing and related terms and explains the prevalence for these difficulties in autism. Suarez then discusses the physiologic evidence for sensory processing or modulation disorders. She then discusses the functional impact of sensory processing disorders for autistic children in various domains such as: social functioning and feeding and eating.

Relevance: This paper discuses sensory processing in autistic children and how it impacts functioning. Our research is about the impact of auditory processing and how it impacts autistic children, making this paper very relevant.

Unique Features: The definitions are well worded and Figure 1 has a great chart of the divisions of sensory processing disorder.

Research methodology: Descriptive, not experimental research design

The strengths, weaknesses, or biases in the material: No great apparent strengths or weaknesses in material.

Thye, M. D., Bednarz, H. M., Herringshaw, A. J., Sartin, E. B., & Kana, R. K. (2018). The impact of atypical sensory processing on social impairments in autism spectrum disorder. *Developmental Cognitive Neuroscience*, *29*, 151–167.

<https://doi.org/10.1016/j.dcn.2017.04.010>

Purpose: This paper's goal is to discuss the connection between sensory processing in autism and how it impacts social functioning.

Summary: This paper breaks down each sense (vision, hearing, etc.) into subsets and discusses the different ramifications of atypical sensory processing in autism. Most

applicable to our study is their discussion of auditory processing, in particular speech perception and prosody. They also discuss theoretical autism models that incorporate sensory processing and social results. Finally, they summarize relevant information on the neurobiological underpinnings of sensory processing in autism.

Relevance: This paper is relevant to our study because it discusses the real-world impacts sensory processing difficulties have on autistic individuals, thereby establishing the importance of understanding sensory processing and how to prepare the clinical environment to be a supportive setting.

Unique Features: Each sense (vision, hearing, olfaction, etc.) is discussed individually with examples of atypical processing in autism.

Research methodology: Mostly literature review, not an experimental research design.

The strengths, weaknesses or biases in the material: Draws perspectives from current research. The paper is clear and concise.

Tharpe, A. M., Bess, F. H., Sladen, D. P., Schissel, H., Couch, S., & Schery, T. (2006). Auditory characteristics of children with autism. *Ear and Hearing*, *27*(4), 430–441. <https://doi.org/10.1097/01.aud.0000224981.60575.d8>

Purpose: Describe the auditory characteristics in autistic children compared to typically developing children and assess the test-retest reliability of behavioral auditory tests in this population.

Summary: 22 autistic children and 22 typically developing children underwent audiological testing with auditory brainstem response, distortion product otoacoustic emissions, and acoustic reflexes. Additionally, participants used a behavioral measure of
visual reinforced audiometry, tangible reinforcement operant conditioning audiometry, and conditioned play audiometry. Results found that autistic children had similar scores to typically developing children on physiologic measures, but scored outside of normal limits on behavioral measures. Additionally, test results in the autistic group were less consistent and had lower test-retest reliability on behavioral measures.

Relevance: Our study is on auditory processing in children so these descriptions of auditory characteristics in autistic children is relevant and helpful.

Unique Features: This is one of the studies that showed typical ABR references which is an interesting counterpoint to the body of literature that shows atypical ABR results in autism.

Research methodology: 22 autistic children and 22 typically developing peers audiometric profiles compared.

The strengths, weaknesses or biases in the material: Each participant underwent several audiological tests, which provides a robust audiological profile for both the typically developing group and the autistic group.