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# AUDITORY BRAINSTEM NEURAL VARIABILITY, AUTISTIC TRAITS, AND SENSORY SENSITIVITIES IN SCHOOL-AGED CHILDREN

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## Abstract

***Purpose:*** Understanding the contributions of neural variability, measured by trial-to-trial fluctuations in an evoked neural response, to behavior has been particularly interesting to researchers since recent findings suggest that decreased cortical neural stability correlates with heightened autistic traits. This correlation has led some researchers to hypothesize a causal link between increased neural variability and heightened autistic traits and sensory sensitivities. Notably, these cortical findings are in response to multisensory stimuli, including auditory stimuli. In the brainstem, elevated neural variability evoked from monaurally presented auditory stimuli is associated with poorer syntactic performance, and some, albeit not all, studies have found group differences when comparing neural variability between autistic and nonautistic individuals. Yet, the potential relationship between neural variability in the brainstem and autistic traits and sensory sensitivities remains unexplored. The current study sought to elucidate (1) whether the neural variability observed in auditory brainstem responses (ABRs) elicited by click and synthetic 40ms /da/ stimuli differed depending on when analyzed post-stimulus onset and by stimulus type, (2) if neural variability was significantly related to sensory sensitivities evaluated through the parent-report Sensory Profile (SP) survey (3) and whether neural variability predicted the spectrum of parent-reported autistic traits, quantified using the Autism Quotient (AQ) and the Social Responsiveness Scale, Second Edition (SRS-2) among a combined group of nonautistic and autistic school-age children.

***Methods:*** Forty-four children, including 18 autistic and 26 nonautistic peers aged 6-16.9 years, participated. Before electrophysiological recording, participants underwent a routine hearing evaluation and an IQ assessment using the Wechsler Abbreviated Scale of Intelligence, Second Edition (WASI-II). Parent(s)/caregivers completed the SP, AQ, and SRS-2. The ABRs were

evoked by binaural presentation of clicks and a 40 ms synthetic /da/ stimulus and recorded ipsilaterally using a two-channel montage via scalp electrodes. Two waveforms, each comprised of 3000 sweeps, were correlated together for the entire click response (1-8 ms) and the various response components of the sABR: the complete response (0-55 ms), the onset (5-10 ms), the frequency-following (22-40 ms), and the offset (45-50 ms) responses. A repeated measures of analysis of variance was conducted to determine if the degree of neural variability differed by response components. Multiple linear regression models were constructed and tested to determine if neural variability was a significant predictor of sensory sensitivities or autistic traits.

***Results:*** Significant differences in neural variability were found among the response components analyzed. Neural variability in the onset sABR and click ABR were not significantly different, aligning with existing literature suggesting the two response components are analogous. No meaningful predictive relationships emerged between neural variability and sensory sensitivities. In contrast, neural variability of the sABR offset response and entire click ABR predicted autistic traits after controlling for verbal IQ. Specifically, increased neural variability was associated with heightened total scores on AQ and SRS-2.

***Conclusions:*** The study challenges current methods by highlighting the relevance of analyzing different response components within the sABR, instead of only the FFR, and advocates for a paradigm shift from case-control studies toward individualized predictive modeling studies, especially in heterogeneous conditions like autism. Although neural variability within the auditory brainstem pathway did not predict sensory sensitivities, it emerged as a predictor of autistic traits. By further understanding neural variability's complex relationship with behavioral traits, researchers may be able to facilitate a more comprehensive understanding of individual differences in auditory processing and autistic traits.

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by

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## 1.0 Introduction

Determining the extent to which evoked neural variability affects behavior is an important endeavor that may lead to targeted therapeutic interventions. In the presence of eliciting sensory stimuli, neural variability refers to trial-by-trial fluctuations in neural responses across repetitions to the same sensory input. Greater degrees of neural variability signify an unstable neural response, resulting in a neural system that is less efficient and has 'noisier' neural processing. Researchers have developed the Neural Noise Theory, which proposes that unstable neural responses have an integral role in shaping an individual's interactions with their environment (e.g., Dinstein et al., 2015; Haigh, 2018). Given the significant role of the cortex in influencing behavioral manifestations, most research has concentrated on recording, quantifying, and comprehending cortical neural variability. Some of the findings at the cortical level suggest that heightened levels of neural variability (corresponding to reduced neural stability) are associated with behavioral outcomes, such as diminished attention (Lutz et al., 2009), increased autistic traits (Hecker et al., 2022; Heller Murray et al., 2022; Park et al., 2017; Vilidaite et al., 2017), and heightened sensitivity to loudness (Dwyer et al., 2022). Neural variability may also have a potential link with cognition and reaction times (e.g., Milne, 2011). However, it is essential to recognize that brainstem neural variability may also play a pivotal role in influencing behavior.

Neural variability within the brainstem auditory pathway can be assessed using a gross, electrophysiological potential known as the auditory brainstem response (ABR). ABR captures synchronized neural activity along the auditory brainstem pathway in response to an evoking auditory stimulus by short-duration stimuli, such as a click (click ABR) or consonant-vowel clusters (e.g., /da/). The ABR comprises canonical 'waves' that are measured in the time period

after the evoking stimulus. Neural variability can be measured via the ABR by examining the trial-to-trial changes in wave amplitudes and latencies, calculated by computing the linear relationship (Pearson correlation) between two ABR waveforms. Increased ABR neural variability in school-aged children has been related to the conditions of dyslexia (Hornickel & Kraus, 2013) and autism (e.g., Otto-Meyer et al., 2018; Rosenblum et al., 1980) and poorer syntactic performance (Tecoulesco et al., 2020).

The limited studies that compare the degree of neural variability between groups of autistic[1] and nonautistic individuals have yielded conflicting results. Some studies have reported significantly increased neural variability in click ABR and speech-evoked ABR (sABR) in groups of autistic individuals compared to nonautistic individuals (Otto-Meyer et al., 2018; Patel et al., 2022; Rosenblum et al., 1980), while another found no difference between the two groups (Tecoulesco et al., 2020). Notably, as Otto-Meyer et al. (2018) demonstrated, there is an overlap in the degree of neural variability between autistic and nonautistic participants even when a significant difference between groups is present.

Autism spectrum disorder is a highly complex neurodevelopmental condition characterized by varying degrees of impairments in social communication, social reciprocity, and the presence of restricted interests and repetitive behaviors (American Psychiatric Association, 2013a; CDC, 2022). Additionally, the diagnosis of autism includes disturbances in sensory function, termed sensory sensitivities in the current paper, as a fundamental diagnostic feature of autism. These sensitivities are estimated to affect approximately 90% of autistic individuals and span all sensory modalities, including taste, touch, vision, smell, and, significantly for this study,

[1] The preferred terms of most people diagnosed with autism are ‘autistic person’ and ‘person on the autism spectrum’ (Bury et al., 2023; Kenny et al., 2016). With respect to these preferences, these terms will be used to refer to individuals on the spectrum.

audition (Robertson & Baron-Cohen, 2017; Tomchek & Dunn, 2007). It is crucial to acknowledge that autism is a heterogeneous condition, with autistic traits[2] and sensory sensitivities varying significantly amongst autistic individuals as well as within the general population. It is plausible that the wide range of autistic traits and sensory sensitivities that span both autistic and nonautistic individuals may be linked to the variance in neural variability and the overlap in neural variability between groups of autistic individuals and nonautistic individuals.

The Neural Noise Theory posits that unstable neural responses have the potential to drive observable atypical behaviors in individuals because neural variability creates an inconsistent perception of the environment (Dinstein et al., 2015; Haigh, 2018; Park et al., 2017; Vilidaite et al., 2017). Based on this theory, cortical measures of neural variability have been proposed as proxies for behavioral characteristics in autism (Dinstein et al., 2012, 2015; Haigh, 2018). The current study seeks to expand whether support for the Neural Noise Theory extends to the auditory brainstem. In addition to studying neural variability in the brainstem, instead of employing traditional case-control paradigms that often overlook the heterogeneity amongst individuals, the current study investigates relationships between neural variability and sensory sensitivities and autistic traits across a range of school-aged children, both with and without autism.

The current study addresses three distinct aims. The first aim tests whether the degree of neural variability differs depending on the evoking stimuli and the time frame over which the response is measured. The ABR can be evoked using various types of stimuli, and it is essential

[2] In the current paper, autistic traits is a broad term that is being used to describe autistic characteristics measured by the Autism Quotient total score and SRS-2 total score.

to determine if the choice of stimulus influences the degree of neural variability. Furthermore, within the sABR, in relation to stimulus onset, the timing of which the response is analyzed represents a specific neural response to a particular aspect of the stimuli (/d/ vs./a/; onset, frequency following response, and offset), referred to here as response components. Therefore, it is also essential to establish whether the different response components have differing degrees of neural variability. Secondly, this study examines whether neural variability can predict sensory sensitivities, as assessed by the Sensory Profile. Considering the diverse range of sensory sensitivities in response to various sensory stimuli, it is crucial to investigate the potential relationship between auditory-evoked neural variability in the brainstem and sensory sensitivities. Determining whether neural variability is a more robust predictor of a measure that combines sensitivities across multiple sensory modalities or within a single modality is essential. Finally, the study's last aim is to explore whether neural variability can predict autistic traits, as measured by the Autism Quotient and the Social Responsiveness Scale (Second edition). Therefore, the overarching research question driving this study is: To what extent is subcortical neural variability, measured via ABR, predictive of the heterogeneity of parent-reported sensory overresponsivity and autistic traits in school-aged children with and without autism, and does this relationship differ depending on the ABR evoking stimuli? If the degree of neural variability is predictive of sensory overresponsivity or autistic traits, then the current study will have found support for the Neural Noise Theory in the brainstem.

## 2.0 Review of Literature

### 2.1 Neural Variability

Neural variability, defined here as neural intra-individual variability, can be separated into two categories: ongoing neural variability and stimulus-evoked neural variability. Ongoing

neural variability refers to the spontaneous fluctuations in neural activity in the absence of stimuli. Stimulus-evoked neural variability represents the trial-by-trial variability in stimulus-evoked neural response amplitude or timing (Arazi et al., 2017). The underlying assumption behind functional magnetic resonance imaging (fMRI) and event-related potentials (ERP) is that repetitive stimuli are uniformly processed in the body, evoking consistent response amplitudes and timings. As such, variability across repetitions is typically disregarded. However, recent scientific research has implicated that evoked neural variability itself is crucial to explore (e.g., Haigh, 2018; Hecker et al., 2022; Heller Murray et al., 2022; Holtzer et al., 2020; Lutz et al., 2009; Millar et al., 2021; Simmons et al., 2009). Consequently, the current investigation focuses explicitly on stimulus-evoked neural variability, and therefore, all subsequent references to "neural variability" pertain to stimulus-evoked neural variability.

When discussing neural variability, two crucial aspects require consideration. First, neural variability can be assessed independently for different parts of the stimulus, such as variability measured in response to early versus late parts of the stimulus. For that reason, when studying neural variability, it is essential to consider the period following stimulus onset in which neural variability is being assessed. Second, the degree of variability may be the same across the entire brain but not always: variability can be localized to a specific brain area (Dinstein et al., 2015). Consequently, one should not assume that an increase or decrease in neural variability in one part of the brain reflects neural variability of the brain as a whole. This thinking can also be extended to subcortical processing; for example, the degree of auditory brainstem neural variability may differ along the brainstem.

#### 2.1.1 Neural Noise Theory is based on an increase in neural variability.

The Neural Noise Theory posits that an increase in trial-by-trial variability diminishes the overall stability in the processing of external stimuli (Dinstein et al., 2015; Haigh, 2018; Park et

al., 2017; Simmons et al., 2009; Vilidaite et al., 2017). Increased neural variability results in less efficient and noisier neural processing, reducing the ability to distinguish the signal from noise and the ability to predict external events. Noisy neural processing, in turn, impairs an individual's capacity to interact with their environment, leading to atypical sensory sensitivities (Haigh, 2018) or behaviors (Dinstein et al., 2015; Park et al., 2017; Vilidaite et al., 2017). As Dinstein et al. (2015) clearly outlined, a heightened level of unstable neural responses can create an unpredictable environment for someone. Because of this, they exhibit behaviors reflective of this unpredictability. These behaviors can be accentuated in social situations because human communication is highly variable; thus, an individual may retract from social interactions and engage in repetitive behaviors that are likely to generate predictable responses.

Reliable sensory information plays a pivotal role in facilitating the development and retention of cognitive functions (Krizman et al., 2014; Skoe et al., 2013). While some degree of variability in the neural system may be advantageous for predicting regularities within an environment (Waschke et al., 2021), excessive variability may contribute to feelings of sensory overload (Haigh et al., 2022a). Therefore, further investigation is warranted to fully understand the functional implications of neural variability, specifically within the auditory brainstem, for which little has been investigated.

#### 2.1.2 Support for Neural Noise Theory in the cortex.

Neural variability can be assessed at the cortical level using various measurement techniques, including fMRI, magnetoencephalography (MEG), and electroencephalogram (EEG). Each measurement technique of neural variability has its advantages and disadvantages. For instance, fMRIs can measure the standard deviation of blood oxygen level-dependent (BOLD) signals following a task or stimulus presentation in specific areas of the brain but are poor in elucidating the timing of responses relative to the stimuli (Månsson et al., 2022). In

contrast, EEG recordings have a superior temporal measure of neural variability via the consistency of oscillatory neural responses following stimulation but are poorer at place specificity (Lutz et al., 2009).

Although the technologies mentioned above provide different measures of neural variability, all have shown evidence of increased neural variability and have been found in multiple areas of the cortex[3]. Some findings have suggested a link between increased neural variability in anterior brain regions and decreased attention (Lutz et al., 2009). Increased neural variability in the cortex is correlated with reduced cognitive function in aging populations (e.g., Dykiert et al., 2012; Holtzer et al., 2020). Compelling evidence supporting the Neural Noise Theory has emerged when neural variability is analyzed across broad networks of brain areas, including the sensorimotor area, auditory cortex, and cerebellum. Specifically, increased neural variability has been associated with reduced attentional control (Millar et al., 2021), heightened autistic traits (Hecker et al., 2022; Heller Murray et al., 2022; Park et al., 2017; Vilidaite et al., 2017) and heightened sensitivity to loudness (Dwyer et al., 2022).

Elevated levels of neural variability have been observed in cortical regions involved in sensory processing amongst individuals with Attention Deficit Hyperreactivity Disorder (ADHD; Saville et al., 2015) and schizophrenia (Haigh et al., 2022b) when compared to neurotypical counterparts. Additionally, greater degrees of neural variability have been documented in the motor and sensory areas of the cortex amongst autistic individuals compared to nonautistic counterparts (e.g., Dinstein et al., 2012; Haigh, 2018; Haigh et al., 2022a; Haigh et

[3] Neural variability can vary depending on the specific brain region under analysis (Dinstein et al., 2015). Consequently, the specified brain area is noted when discussing the cortical findings for increased neural variability. Contradictory findings may emerge in the literature when examining different brain regions.

al., 2022b; Milne, 2011; Park et al., 2017; Vilidaite et al., 2017:see Appendix A for more information).

### 2.2 Subcortical Processing is Critical for Subsequent Cortical Processing

The effective utilization of incoming sensory information in higher cortical areas hinges on the reliability of the output from the brainstem (Deneve & Pouget, 2004; Faisal et al., 2008). Sensory input undergoes complex processing in the brainstem before reaching the respective cortical areas. Furthermore, the brainstem is multifaceted and is involved in many functions that encompass sleep regulation, startle responses, sensory gating, and sensory processing (e.g., Seif et al., 2021).

It is imperative to know if the neural responses within the brainstem effectively relay stable signals to the cortex and if the sensory processing that occurs within the brainstem is affected by variable neural responses. If incoming information is processed in an unstable, inefficient manner at the brainstem level, then this could have negative implications for how the information is communicated to the cortex. In short, the Neural Noise Theory suggests that increased unstable neural responses in the cortex lead to atypical behavioral manifestations, such as greater autistic traits (Hecker et al., 2022; Heller Murray et al., 2022; Park et al., 2017; Vilidaite et al., 2017). However, it is unknown if the behavioral consequences of increased neural variability are due to the noisier processing taking place within the cortex or if increased neural variability in the brainstem also impacts behavior. Therefore, it is critical to understand if the stability of neural processing in the brainstem is linked to behavioral manifestations.

## 2.3 Brainstem Measures of Neural Variability

When assessing response variability in the brainstem, auditory evoked potentials (AEP) can be measured and offer several advantages. AEPs generated early in response to stimulation provide insights into neural activity in the brainstem. One well-known AEP for assessing auditory processing along the brainstem is the ABR. Compared to fMRI, ABRs offer clinical feasibility, efficiency, fine temporal resolution, and straightforward interpretability.

An ABR captures the precise timing of auditory stimulus processing evoked by short-duration stimuli along the auditory brainstem pathway. An ABR can be evoked with different types of stimuli, such as a transient stimulus (i.e., click, tone burst, or chirp stimuli) or more acoustically complex stimuli, such as a synthetic speech cluster (i.e., /da/ or /ya/).

### 2.3.1 Click-evoked auditory brainstem potential.

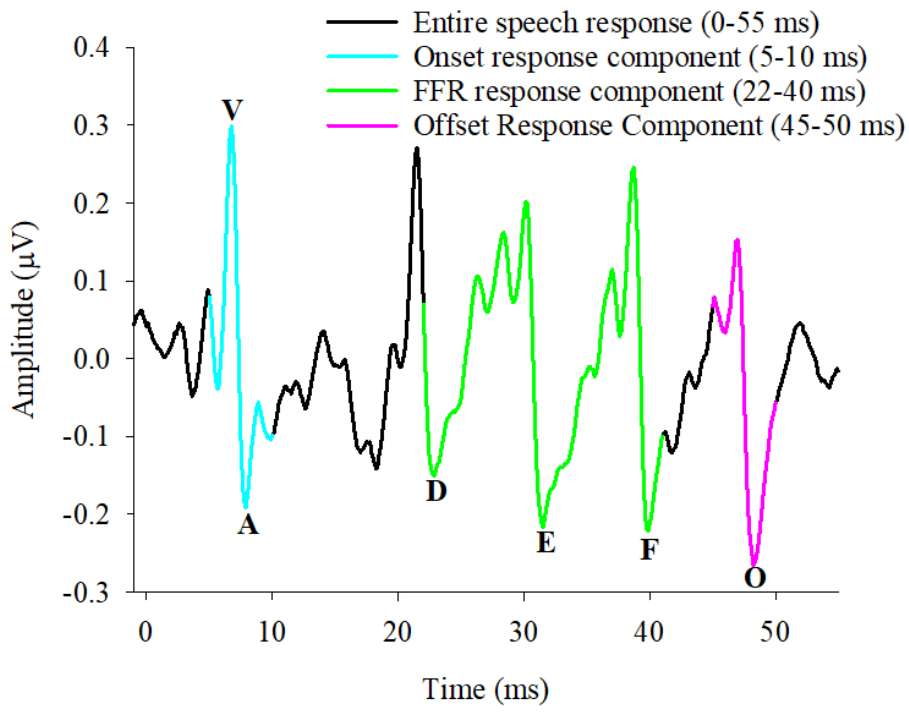
A click-evoked ABR (click ABR) is an objective far-field measure of neural conduction time through the brainstem that is time-locked to a repetitive transient click stimulus. An ABR elicited by a click consists of five main waveforms primarily reflecting neural synchrony in the auditory nerve (waves I and II), the cochlear nucleus and superior olivary complex (Wave III), the lateral lemniscus (wave IV), and the lateral lemniscus and inferior colliculus (wave V). The interpeak latency (IPL), measured between peaks I-III, III-V, and I-V, provides a measure of neural conduction time over the lower, upper, and entire brainstem, respectively (Hood, 1998). Factors such as larger neural axons, reduced myelination, decreased synaptic efficacy, and increased inhibitory inputs, either individually or in combination, can extend neural conduction time (e.g., Eggermont, 1988; Talge et al., 2021). For these reasons, the timing of brainstem potentials, which is in the order of milliseconds, can detect subtle timing abnormalities suggestive of pathologies.

### 2.3.2 Speech-evoked auditory brainstem potential.

An ABR can also be evoked using complex stimuli such as speech tokens (e.g., /da/). Although a 40 ms /da/ stimulus is short compared to natural speech, it is acoustically complex (Kraus & Nicol, 2005). Therefore, an ABR evoked by a speech token can provide insight into the brainstem's ability to encode speech-like features. The sABR comprises seven waves (V, A, C, D, E, F, and O). Figure 1 depicts an sABR waveform with the waves labeled and the various response components partitioned, which include the complete response (0-55 ms), the onset (5-10 ms), the FFR portion (22-40 ms), and the offset (45- 50 ms). Waves V and A, primarily generated by the lateral lemniscus and inferior colliculus, reflect the neural response to sound onset resulting from the initial friction in the production of the stop consonant /d/. Wave C, not always present, signifies the transition from consonant to vowel or voicing onset (Russo et al., 2004). Wave O marks the transition from

**Figure 1**

*Response Components*




*Note.* Figure 1 illustrates a sABR waveform with the different response components highlighted. The entire speech response, which is represented by the solid black line is from 0-55 ms. The onset response component is the blue solid line from 5-10 ms. The FFR response component is from 22-40 ms, represented in the figure above by the green solid line and the last response component, the offset response, is highlighted in pink and spans from 45-50 ms.

stimulus offset to sound absence. These waves represent the transient segments of the stimuli, with their timing influenced by the acoustic filter characteristics, which include the speech articulators in natural speech (Kraus & Nicol, 2005). Waves D, E, and F, correspond to the sustained portion of the response and are associated with the acoustic source of the stimuli: vocal fold vibration. This sustained part of the response, known as the frequency following response (FFR), reflects the neural phase locking to the fundamental frequency ($F_0$) and its harmonics in the eliciting stimuli (Nada et al., 2016; Russo et al., 2004). Although there is some debate regarding the neural generators of the FFR, evidence suggests it arises mainly from the inferior colliculus (e.g.,Bidelman, 2018). Temporally, the intervals between these peaks correspond to the wavelength of $F_0$ (Kraus & Nicol, 2005). In the frequency domain, the FFR can be analyzed to quantify the neural response to $F_0$, first harmonic ($F_1$), and subsequent higher harmonics (HH) (Skoe & Kraus, 2010). In summary, an sABR provides a precise assessment of the brainstem's processing of acoustic features of speech in both the time and frequency domains.

#### 2.3.3 Clinical analysis of auditory brainstem responses.

In clinical practice, ABR traces with low noise levels can be analyzed in a dichotic manner; either response is present or absent. If present, the peaks, Wave I, III, and V, are identified and analyzed in terms of absolute latency, which is the timing of these peaks relative to the onset of the stimulus and the IPL, to determine the neural conduction time along the brainstem. An sABR is not recorded and analyzed in clinical settings and is typically only utilized in research.

## 2.4 Neural Variability in the Auditory Brainstem Response

While not a standard clinical practice, analyzing the ABR response stability makes it possible to assess the extent of neural variability in processing auditory stimuli in the brainstem.

This variability can be quantified by examining the linear relationship (Pearson Correlation) between two ABR waveforms, typically sub-averages derived from a predetermined number of sweeps, in response to the same stimuli. This analysis yields an R-value, with an R-value closer to 1 indicating a higher correlation between traces, suggesting reduced variability and greater neural stability (Hornickel & Kraus, 2013).

### 2.4.1 Support for Neural Noise Theory in the auditory brainstem response.

Despite the crucial role of the brainstem in sensory processing, particularly sound sensitivities (Pillion et al., 2018), relatively few studies have explored neural variability at this level using ABR. To date, ABR studies examining neural variability have revealed associations between increased neural variability and aging in adulthood (Skoe et al., 2015), as well as syntactic language performance (Tecoulesco et al., 2020). ABR neural variability studies have typically employed a case-control paradigm, comparing the degree of ABR neural variability in clinical and subclinical populations.

This line of research has demonstrated that individuals with dyslexia exhibit higher levels of neural variability than those without dyslexia (Hornickel & Kraus, 2013). Similarly, a few studies have reported greater neural variability in groups of autistic individuals than in nonautistic individuals (Otto-Meyer et al., 2018; Patel et al., 2022; Rosenblum et al., 1980). However, it is worth noting that conflicting results exist, with one study finding no significant difference in the degree of neural variability between groups of autistic and nonautistic individuals (Tecoulesco et al., 2020). This limited number of studies and the inconsistencies among group comparison studies (autistic versus control group) underscore the need for a deeper understanding of neural variability in the brainstem. Further research in this area is warranted to shed light on the intricate relationship between brainstem neural variability and behavioral

characteristics, similar to the research that has been conducted on cortical neural variability (e.g., Hecker et al., 2022; Park et al., 2017; Vilidaite et al., 2017).

### 2.5 Autism Spectrum Disorder

Incorporating autistic participants into studies exploring ABR neural variability offers a unique opportunity to understand if brainstem neural variability impacts behavior. Autism is a complex neurodevelopmental condition characterized by varying degrees of impairments in social communication and social reciprocity, alongside the presence of restricted interests and repetitive behaviors (APA, 2013; CDC, 2020). Impairments in social communication include poor eye contact, lack of coordinated eye gaze, limited pragmatics (such as “turn-taking”), lack of facial expression, etc. Restricted interests and repetitive behaviors include sensory sensitivities, hand flapping, delayed echolalia, repetitive asking of questions, repeated lining up of toys, etc. (APA, 2013).

The Autism Diagnostic Observation Schedule, Second Edition (ADOS-2), is one of the "gold standard" assessment tools used for diagnosing autism (Gotham et al., 2008). It involves a module-based, semi-structured play assessment where a trained clinician administers a protocol of social interactions and scores behavioral items related to autistic traits, including restricted repetitive behaviors and social communication. Assessment of autistic traits and sensory sensitivities in autistic children primarily relies on parent/teacher-report surveys or observations by trained clinicians.

### 2.6 Sensory Sensitivities

Sensory sensitivities are included as part of the core diagnostic criteria for autism in the Diagnostic and Statistical Manual of Mental Disorders, fifth edition (DSM-5; APA, 2013). This

update marked disturbances in sensory function, referred to here as sensory sensitivities, as a fundamental diagnostic feature of autism. As a result, researchers have begun to focus on sensory sensitivities as they relate to autism. Sensory information is the building block for higher-order social and cognitive functions; therefore, it can be argued, as some researchers do, that the sensory features of autism are not only an additional trait associated with the heterogenous condition but rather a critical cornerstone for characterizing and understanding autism (Baum et al., 2015).

### 2.6.1 Sensory features of autism.

Despite being officially recognized in the diagnostic criteria only since the publication of the DSM-5 in 2013, sensory sensitivities have been documented in descriptions of autistic individuals since 1943 (Kanner, 1943). An estimated 90% of autistic individuals experience sensory sensitivities, which can span all sensory modalities, including taste, touch, vision, smell, and, significantly for this study, audition (Robertson & Baron-Cohen, 2017; Tomchek & Dunn, 2007). Examples of behaviors that represent various sensory sensitivities include being preoccupied with textures, oblivious to [bad] odors, prolonged concentration or fixation on objects or pictures, distress in response to getting wet, lack of response to pain (e.g., such as no response to being stung by a bee), etc.(Talay-Ongan & Wood, 2000).

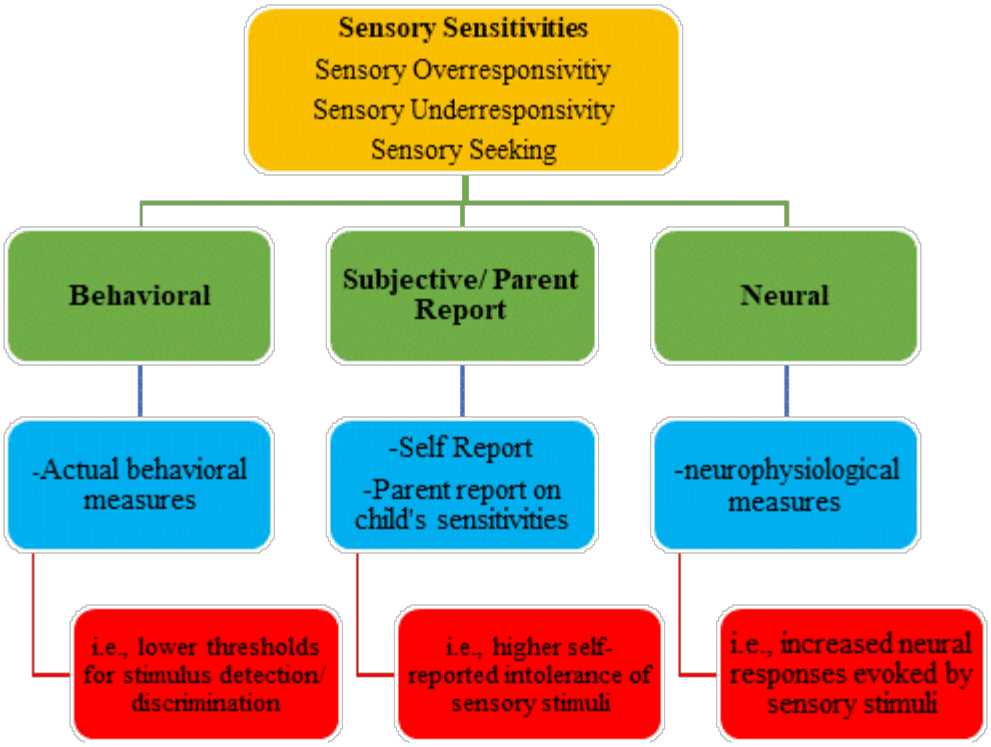
These sensory sensitivities can be present as early as six months of age in infants later diagnosed with autism (Robertson & Baron-Cohen, 2017). Sensory sensitivities are, therefore, evident in early development before communication milestones are met. Sensory sensitivities also predict an individual's social-communication deficits (Turner-Brown et al., 2013) and repetitive behaviors in childhood (Baron-Cohen et al., 2009). Therefore, a better understanding of the neural underpinnings of sensory sensitivities is necessary.

### 2.6.2 Measuring sensory sensitivities.

It is essential to recognize that various methods are employed to measure sensory sensitivities, as depicted in Figure 2. These methods include behavioral, neurological, subjective, and, most pertinent to this study, parent-report measures. Distinguishing between the perceptual, behavioral, and neural measures is critical because these types of sensitivity measures are

**Figure 2**

*Measures of Sensory Sensitivities*




*Note.* Sensory sensitivities are described in terms of how they are measured. The top row (yellow) states three types of sensory sensitivities in terms of behavior modulation categorization. The middle top row (green) describes the three ways that sensory sensitivities are measured (behavioral, subjective, neural) followed by two bottom rows that describe examples of each measurement.

typically unrelated to each other (e.g., Donkers et al., 2015; Dunlop et al., 2016; Dwyer et al., 2020; Kuiper et al., 2019; Tharpe et al., 2006) and without the proper distinction research can become misleading. For example, a study that measured all three, behavioral auditory thresholds,

auditory ERPs, and parent-reported sensory experiences, found that the three measures were largely unrelated (Dwyer et al., 2020). In the current paper, the sensory sensitivities measured are parent-report sensory sensitivities.

Sensory sensitivities can also be further categorized. For example, they can be described in terms of behavioral "response patterns": hyperreactivity (excessive or defensive reactions to stimuli typically considered innocuous by others), hyporeactivity (diminished or absent responses to sensory stimuli most people would respond to), and sensory seeking (an unusual craving or fixation on sensory stimuli; APA, 2013). Another categorization is based on sensory modulation behaviors, which include sensory overresponsivity, sensory underresponsivity, and sensory seeking (Miller et al., 2007; Patten et al., 2013). Sensory overresponsivity involves exaggerated, rapid-onset, or prolonged reactions to sensory stimuli, often resulting in negative emotional responses or avoidance of specific sensory inputs. Individuals with sensory overresponsivity tend to react faster, with more intensity or extended durations, compared to those with typical sensory responsiveness. However, expression can vary based on personal and contextual factors (Miller et al., 2007). Sensory underresponsivity refers to a slow response or a lack of awareness regarding sensory stimuli. Individuals with sensory underresponsivity may appear not to detect incoming sensory information, such as pain or extreme temperatures (hot or cold). Sensory seeking entails a heightened interest in sensory input, with individuals craving an unusual amount of sensory stimulation (Miller et al., 2007).

#### 2.6.3 The heterogeneity of sensory sensitivities amongst autistic individuals.

The study of sensory sensitivities in autism is further complicated by the considerable variation in the degree and type of sensory-related behaviors observed amongst autistic individuals. Much like other autistic traits encompassing language, cognition, and social communication, sensory behaviors associated with autism can vary both between individuals and

within the same individual. For instance, an autistic individual may exhibit overresponsivity to auditory stimuli and underresponsivity to external tactile stimuli (Ausderau et al., 2014; Iarocci & McDonald, 2006; Lane et al., 2010). Due to the diverse nature of sensory sensitivities observed among autistic individuals, concentrating on a specific sensory pattern when investigating underlying neural processing could enhance understanding of the specific neural basis for particular sensitivities. This study will measure multimodality and auditory-only sensory overresponsivity to explore this idea.

#### 2.6.4 Auditory-related sensory sensitivities.

Autism is associated with a wide range of both advantageous and adverse auditory-related sensory sensitivities. Autistic individuals do not typically exhibit lower or higher absolute auditory thresholds (hearing thresholds; Bonnel et al., 2003; Khalfa et al., 2004; Kuiper et al., 2019). However, a frequently observed characteristic associated with autism is an atypical response to auditory stimuli (e.g., Applebaum et al., 1979; Bonnel et al., 2003; Gomes et al., 2008; Jones et al., 2009; Kern et al., 2006; O'Connor, 2012; Osterling & Dawson, 1994; Rosenhall et al., 1999). An example of an advantageous auditory sensitivity in autism is superior pitch perception and better performance in identifying musical notes compared to nonautistic individuals (Applebaum et al., 1979; Bonnel et al., 2003). Early retrospective studies first identified what could be considered adverse or atypical responses to auditory stimuli. For example, home videos of children later diagnosed with autism depicted them failing to orientate toward their name being called (Osterling & Dawson, 1994). One of the most commonly reported auditory-related sensitivities associated with autism is an increased prevalence of decreased sound tolerance disorders (DSTD) which include hyperacusis, misophonia, and phonophobia (e.g., Danesh et al., 2021; Demopoulos & Lewine, 2016; Gomes et al., 2008; Khalfa et al., 2004; O'Connor, 2012; Rimland & Edelson, 1995; Rosenhall et al., 1999).

Hyperacusis is reported in a high percentage of autistic people. Studies in the general population estimate hyperacusis prevalence from 3.2% (Aazh & Moore, 2017) to 17.1% (Khalfa et al., 2002). The prevalence of hyperacusis in autistic individuals ranges from 37% (Demopoulos & Lewine, 2016) to 69% (Danesh et al., 2015). The severity of DSTD impact on an individual can range from bothersome to debilitating (Danesh et al., 2021), which makes the high prevalence of hyperacusis in autistic people a significant problem. DSTDS are considered sensory overresponsivity behaviors and are associated with significant functional impairments, deficits in social and adaptive skills, and anxiety (Ben-Sasson et al., 2008; Liss et al., 2006; Pfeiffer et al., 2005).

#### 2.6.5 Subjective measurement of sensitivities.

A standard tool for assessing sensory sensitivities in autistic school-aged children is the Sensory Profile Caregiver Questionnaire (SP). The SP is a 125-item caregiver-report questionnaire that requires parents to rate the degree to which their child tends to display specific responses to various sensory experiences on a 5-point Likert scale. These sensory experiences encompass sensory processing, modulation, behavior, and emotional response across various sensory modalities (e.g., visual, tactile, auditory). Initially developed in 1999, the SP underwent revision in 2006 to align with the evolving understanding of sensory processing (Ohl et al., 2012). The SP is widely employed by researchers studying autism. A meta-analysis conducted in 2008 revealed that 79% of studies measuring hyperreactivity, hyporeactivity, and sensory-seeking traits in autistic individuals utilized some version of the SP (Ben-Sasson et al., 2009). In addition to being a standard assessment tool of sensory behaviors heavily used in autism literature, the SP has a moderate to high internal consistency (Dunn, 2014).

Parent responses are scored and categorized into one of four quadrants: Seeking, Registration, Avoidance, and Sensitivity. Seeking/Seeker is the degree to which a child pursues

sensory input. Avoiding/avoider is the degree to which a child is bothered by sensory input. Sensitivity/sensory is the degree to which a child detects sensory input. Registration is the degree to which a child misses sensory input.

### 2.6.6 The Heterogeneity of Sensory Sensitivities Across the General Population

The SP can serve as a tool for measuring sensitivities in the general population and among individuals with other disabilities. It is important to note that sensory sensitivities exhibit heterogeneity both within the general population and among individuals with disabilities (Grapel et al., 2015; Little et al., 2017).

Parent responses to the SP questionnaire are scored, and the results are compared to those from the general population, represented by a normal bell curve, indicating how an individual's sensitivities compare to the general population's in each of the four quadrants. When a score deviates by more than one standard deviation from the mean, the child is categorized as either "more" or "less" than the general population in that quadrant, depending on the direction of the deviation from the mean. If their score is one standard deviation above the mean, their sensitivities are considered "more than others." Two standard deviations above the mean are classified as "much more than others." The use of the normal bell curve to classify degree of sensory sensitivities exemplifies how sensitivities vary widely within the general population, with autistic individuals typically falling into the "much more than others" category.

### 2.6.7 Measuring sensory overresponsivity.

While the SP assessment measures sensory sensitivities, it does not explicitly measure sensory overresponsivity. Previous research, however, has established a composite measure of Sensory Overresponsivity (SOR) derived from a subset of items on the SP (Green et al., 2015; McKernan et al., 2020). The SOR is a multimodal construct measure of subjective sensory overresponsivity consisting of 14 items (see Appendix B) from the SP, including items related to

auditory filtering, visual/auditory sensitivity, and tactile sensitivity (Green et al., 2015; McKernan et al., 2020). Among these 14 items, six directly address auditory filtering (i.e., focusing on distraction and inattention caused by auditory stimuli), and two assess sensitivity to auditory stimuli.

Despite being composed of only 8 out of 14 items that pertain to sensory behaviors related to auditory stimuli, higher SOR scores are positively correlated with higher amplitudes of auditory-evoked measures of habituation measured through mismatch negativity (MMN; Cary et al., 2023). Because the SOR is a multimodal construct, it has also been shown to predict the difference between adaptation and no adaptation in a tactile habituation experiment in autistic individuals (McKernan et al., 2020). These findings suggest that the SOR serves as a measure of sensory overresponsivity that can be correlated with the neural processing of stimuli across various sensory modalities, including auditory. However, the question remains whether using a single-modality measure and neural processing evoked by a stimulus in the same sensory modality would yield a stronger relationship. In other words, a parent-report sensory overresponsivity measure focusing solely on auditory sensory sensations, such as DSTD, may be more closely linked to the neural processing of auditory stimuli.

#### 2.6.8 Measurements of sensory overresponsivity in the auditory domain.

There is currently no standardized assessment protocol for hyperacusis or DSTDs (Bigras et al., 2022), which are considered to be sensory overresponsivity behaviors. Audiologists typically base their diagnosis on a combination of behavioral and subjective criteria, such as the patient's reason for consultation, case history reports, loudness discomfort levels (LDL), and questionnaires. In a recent scoping review of articles on AEPs and hyperacusis, questionnaires emerged as the preferred method for assessing hyperacusis in these research studies (Bigras et al., 2022). Therefore, because questionnaires are more reliable (Dang et al., 2020) and perhaps

the more ethical option to measure sensory overresponsivity in children, the current study will rely on the parent-report measure, the SP, for an auditory-only measure of overresponsivity. For more detailed information regarding why an objective measure of auditory overresponsivity is not feasible, please see Appendix C.

Although the SP is not used solely for assessing DSTD, it has been used in AEP and hyperacusis studies to quantify the degree of sensory sensitivities (e.g., De Meo-Monteil et al., 2019; Dwyer et al., 2022; Matsuzaki et al., 2012, 2014, 2017; Ruiz-Martínez et al., 2020). Recently, a multi-site integrative data analysis aimed to assess the validity of multimodal constructs (scores representing behaviors across sensory modalities) and determine the added benefits of single-sensory modality measures of hyperreactivity, hyporeactivity, and sensory seeking. For instance, behaviors categorized as seeking or hyperreactivity in response to a specific sensory stimulus (e.g., auditory stimuli) were designated as auditory-hyper or auditory-seeking (Williams et al., 2023). While the study validated multimodal constructs (such as the SOR) for hyperreactivity, it also found that single-modality measures of hyperreactivity (e.g., auditory-hyperreactivity) explained a slight majority (54%) of the shared variance within multimodality measures. Modality-specific sensory constructs were considered to have added extra value over multimodality measures, indicating that they could explain additional individual differences in sensory reactivity to a greater degree than multimodality measures (Williams et al., 2023). The study suggests that single-modality measures may be useful when assessing individual sensitivity differences in a specific sensory modal.

For this reason, the auditory-only measure of overresponsivity, termed Auditory HYPER in Williams et al. (2023), has been modified and utilized in the current study, referred to here as AUD-SOR. The Auditory HYPER comprises five items from the SP and two from the Sensory

Experiences Questionnaire (SEQ). The two SEQ items are repetitive to the items from the SP. The AUD-SOR comprises the same five items from the SP (see Appendix D) included in the composition of the Auditory HYPER.

In Williams et al. (2023), the Auditory HYPER was not related to cognitive IQ, adaptive functioning, or participant age, suggesting that it accurately measures subjective hyperreactivity rather than influenced by other individual factors. Additionally, the measure was found to have added value in explaining individual differences in auditory sensitivities compared to a multi-modality measure.

## 2.7 Autistic Traits

As mentioned earlier, autism encompasses a constellation of characteristics that include impairments in social interaction, social responsiveness, communication, and restricted and repetitive behaviors, as well as limitations in imagination and attentional control. ‘Autistic traits’ is a general term that describes autistic characteristics extending to the general population. Of important note, the term does not adequately describe all autistic characteristics, and it is well established that many positive and neutral autistic characteristics are typically not included under the term autistic traits.

Similar to sensory sensitivities, these traits can be assessed using parent-report surveys. Two well-established and extensively researched parent-report surveys for assessing autistic traits are the Autism Quotient (AQ) and the Social Responsiveness Scale, Second Edition (SRS-2).

### 2.7.1 Autism Quotient (AQ).

The AQ is a 50-item questionnaire designed to evaluate traits associated with Autism Spectrum Disorder (ASD) across five distinct domains: social skills, attention switching,

attention to detail, communication, and imagination (Baron-Cohen et al., 2001). Parents (or participants older than 16) rate items (e.g., "I notice patterns in things all the time") on a 4-point scale ranging from "definitely agree" to "definitely disagree." Total AQ scores vary from 0 to 50, with higher scores indicating a greater degree of autistic traits. A score of 32 or higher is highly predictive of autism (Baron-Cohen et al., 2001). AQ scores also exhibit a normal distribution within the general population (Baron-Cohen et al., 2001; Ruzich et al., 2015; Whitehouse et al., 2011).

### 2.7.2 Social Responsiveness Scale, Second Edition (SRS-2).

The SRS-2 is a 65-item rating scale designed to measure social behaviors associated with autism (Bruni, 2014). Parents are asked to rate various statements on a 4-point Likert-type scale, ranging from "not true =1" to "almost always true =4". The survey can be divided into subscales covering social awareness, social cognition, social communication, social motivation, restricted interests, and repetitive behaviors. The overall total score represents the most reliable measure for social deficits linked to autism (Bruni, 2014).

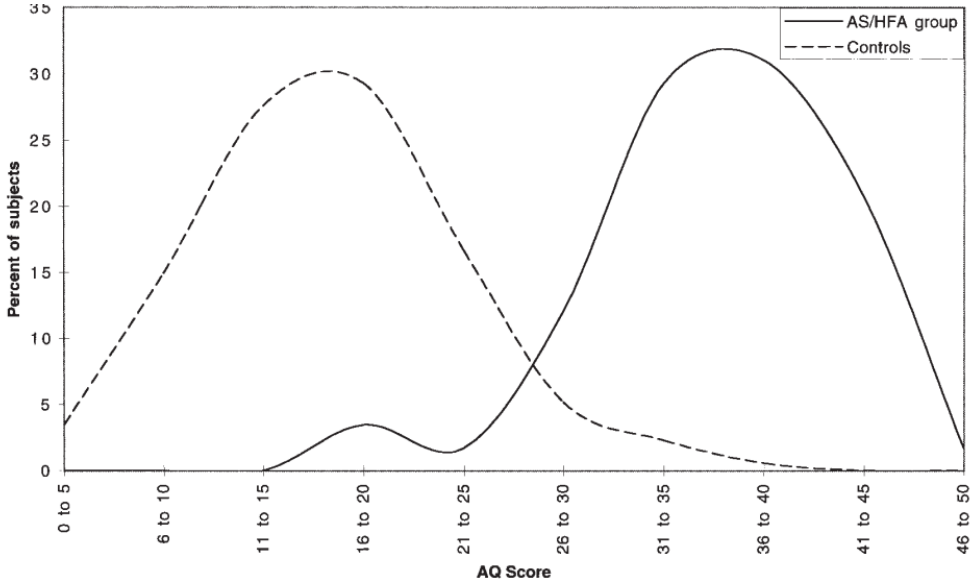
Scores from the SRS-2 are reported as T-scores (M=50, SD=10). A score of 76 or higher is considered severe, indicating clinically significant deficits in social functioning. Scores ranging from 66-75 are categorized as moderate, 60-65 indicate mild to moderate deficiencies, and scores below 59 suggest the absence of social difficulties during interactions with others, which is not indicative of a potential autism diagnosis (Bruni, 2014). Importantly, these scores also exhibit a normal distribution throughout the general population (Constantino & Todd, 2003).

### 2.7.3 Autistic traits across the general population.

Autistic traits vary among the general population as well as across autistic people. To illustrate that autistic traits follow a normal distribution within the general population, Figure 3 (adapted from Baron-Cohen et al., 2001, Figure 1) provides a graphical representation. This distribution is derived from a study conducted by Baron-Cohen et al. (2001) examining the distribution of autistic traits amongst the general population. The percentage of subjects is depicted on the y-axis, while the range of AQ scores is presented on the x-axis. The dashed line corresponds to a histogram curve for participants in the study without a diagnosis of autism (n=174). The solid black line represents the distribution of scores for autistic participants (n=58 high-functioning autistic individuals). While the two groups are distinct, there is overlap, with the greatest overlap observed in scores ranging from 20 to 31. Notably, the graph demonstrates a broad continuum of behaviors when collapsed across both groups.

**Figure 3**

*Autistic Traits in the General Population*




*Note.* Figure 3 is adapted from Baron-Cohen et al. (2001) Figure 1. This Figure displays histograms for AQ scores across autistic individuals (sold line: n=58 high functioning autistic adults Male and Females) and across a subclinical population (dotted line: n=174 nonautistic adult males and females). This graph displays the overlapping of traits between these two populations, illustrating a complete spectrum of traits.

## 2.8 Autistic vs. Control Group Differences in ABR Neural Variability

Numerous studies have yielded conflicting findings of differences in the absolute and interpeak latencies of ABRs between groups of autistic individuals and neurotypical counterparts (e.g., Miron et al., 2018; Rosenhall et al., 2003; Tanguay et al., 1982). Although latency differences between autistic vs. nonautistic groups is not the focus of the current study, a literature review with this information can be found in Appendix E.

The neural variability of brainstem responses in autistic children was first explored in 1980 using click-evoked ABRs. It was discovered that the variability in autistic children's (n=6) responses was greater than in those without autism (n=6; Rosenblum et al., 1980). In this study, as well as all subsequently discussed brainstem neural variability studies, the degree of neural variability was calculated by taking the linear relationship (Pearson Correlation) between two subaverage ABRs. This study also analyzed variability within various response time windows. They found that the greatest variability in the click ABR occurred at an average of 4.10 ms in the autistic group. In comparison, the control group showed the highest variability at an average of 5.34 ms. These results not only highlighted differences in the degree of neural variability between autistic and nonautistic children but also that the timing of when the response was most unstable differed between groups.

In a retrospective analysis, Otto-Meyer et al. (2018) observed that autistic school-aged children (mean age = 10.71, SD = 2.07, range of 7-13 years) displayed greater variability in their ABRs evoked by click stimuli, synthetic speech tokens /da/, rising /ya/, and falling /ya/ compared to nonautistic children. The analysis involved measures from 24 children, with 12 in each group. The authors found a large variance of neural variability and an overlap in the degree of neural variability within and across both groups. The authors noted that the range of neural

variability resembled the possible heterogeneity of autistic traits and auditory processing difficulties among their participants, although these relationships were not explored. Importantly, these findings suggest a link between neural variability and autistic traits.

More recently, neural variability in the sABR was examined in autistic school-aged children and their parents in comparison to nonautistic children and their parents. Autistic children exhibited significantly greater neural variability than control children, indicated by lower response consistency. Similarly, parents of autistic children displayed marginally greater response variability compared to that of control parents ($F = 3.45$, $p = 0.07$, $d = 0.43$; Patel et al., 2022). Providing further support for a connection between brainstem neural variability and atypical behaviors associated with autism, Patel et al. (2022) found that neural variability correlated with increased pragmatic language violations ($r = -0.53$, $p < 0.001$) and impairments in nonverbal communication, including atypical eye contact and gestures, as well as an increase in suprasegmental difficulties, such as intonation modulation and speech rate, across all children, regardless of group. However, it's essential to note that all relationships tested did not survive a Bonferroni correction for multiple comparisons. An association between increased pragmatic language violations and response variability was also observed in the combined parent group, but an increase in suprasegmental difficulties drove the relationship. Additionally, the authors found an association between receptive prosody skills and neural variability in both children and parent groups.

In contrast to the studies mentioned above, Tecoulesco et al. (2020) did not find significant group differences in the degree of neural variability between autistic children ($n = 13$) and a control group ($n = 12$) in the FFR portion of the sABR. However, these researchers did identify a significant relationship between syntactic performance, measured by the Clinical

Evaluation of Language Fundamentals (CELF) Formulated Sentences, and neural variability ($p < 0.01$). Specifically, increased neural variability was significantly associated with greater syntactic errors, and individuals with more stable responses performed better on the CELF Formulated Sentence task. Additionally, the authors found that phonemic discrimination mediated the relationship between syntactic performance and neural variability. It is worth noting that the aforementioned sABR studies only analyzed the response variability of the FFR portion of the sABR (19.5-44.2 ms).

### 2.9 Limitation of Only Analyzing The FFR Portion

While the variability of the sABR has been analyzed in neurotypical children throughout the entire response (Hornickel et al., 2012), it has not been thoroughly investigated in autistic children. Furthermore, the degree of neural variability has not been compared across different latency components or to the variability of the click-evoked ABR. As previously mentioned, neural variability can be deconstructed based on when it occurs following stimulation; therefore, distinguishing the degree of neural variability between response components is possible (Dinstein et al., 2015). In the context of the sABR, the various response components (i.e., onset, FFR, and offset) represent neural activity time-locked to different parts of the stimulus and are believed to originate from different brainstem nuclei (e.g., Kraus & Nicol, 2005; Russo et al., 2004; Skoe & Kraus, 2010). Consequently, understanding how neural variability differs among response components can provide insights into how neural variability varies within the brainstem (e.g., inferior colliculus vs. lateral lemniscus) and whether the brainstem is more proficient at encoding one aspect of the stimulus (e.g., the onset versus fundamental frequency) compared to another.

## 2.10 Significant Overlap of Brainstem Neural Variability Between Groups

While three out of four studies that analyzed group differences in neural variability of ABRs between autistic and nonautistic individuals reported significant differences, there was considerable overlap between groups. Considering the Neural Noise Theory, a plausible explanation for the overlap in neural variability between groups, is the range of behavioral characteristics, such as autistic traits and sensory sensitivities, seen across individuals with and without autism.

As a reminder, autistic traits and sensory sensitivities vary considerably within the general population. It is possible that increased neural variability is not pathogenic to autism, but rather, the autistic traits or sensitivities are a consequence of increased neural variability. Therefore, similar to autistic traits and sensory sensitivities, there may be a greater degree of increased neural variability in autistic individuals, but an overlap in the degree of neural variability between autistic and nonautistic individuals also exists. Instead of conducting case-control studies to ascertain whether autistic individuals have higher levels of neural variability, it is beneficial to explore the relationship between autistic traits/sensory sensitives and neural variability. This exploration could provide a better understanding of the neural basis of sensory sensitivities and autistic traits.

## 2.11 Summary

Research has identified a significant relationship between neural variability recorded through gross electrophysiological measures in the cortex and behavioral outcomes (e.g., Dinstein et al., 2012; Millar et al., 2021; Milne, 2011), thereby providing support for the Neural Noise Theory (Haigh, 2018). This theory posits that increased neural variability, indicating decreased neural stability and less efficient neural processing, results in a noisier neural system

and leads to atypical behaviors. Although support for this theory is found at the cortical level, limited investigation indicates that the Neural Noise Theory can be extended to subcortical brainstem levels.

The brainstem serves as a critical processing site for incoming sensory information before cortical processing, making it crucial to determine whether unstable neural responses at this level of processing also support the Neural Noise Theory. The auditory brainstem response is a gross, far-field electrophysiological measure that represents the neural processing of auditory stimuli through the auditory brainstem pathway. The ABR can be elicited by simple transient stimuli, such as a click, and more complex stimuli, like synthetic /da/. Analyzing the linear relationship between two ABR subaverages can be done to assess brainstem neural variability, which has been done in a limited number of studies (e.g., Otto-Meyer et al., 2018; Rosenblum et al., 1980).

Most studies investigating neural variability of the brainstem have adopted case-control paradigms, comparing measures between clinical and subclinical groups. For example, research has identified increased neural variability of the ABR in groups of autistic individuals compared to nonautistic individuals (e.g., Otto-Meyer et al., 2018; Rosenblum et al., 1980). Nevertheless, these studies reveal an overlap in the amount of neural variability between these groups (Otto-Meyer et al., 2018), and other researchers find no differences in neural variability between groups of autistic and nonautistic individuals (Tecoulesco et al., 2020).

The Neural Noise Theory suggests that unstable neural responses contribute to atypical behavioral responses. The case-control approach researchers have used in the past masks individual variations in neural variability by focusing on group averages. Consequently, individual differences in neural variability could hold significance for understanding variations in behavior. Moreover, previous studies focused only on a limited segment of ABR, the FFR of

the sABR, potentially overlooking valuable insights that could arise from a comprehensive analysis of the entire sABR waveform. By narrowly focusing on the FFR, these studies missed the opportunity to examine how various stimulus characteristics are more/less susceptible to being processed unstably, which could provide a more nuanced understanding of the underlying mechanisms of stimulus processing.

Autism is a highly heterogeneous condition, with both autistic traits and sensory sensitivities varying significantly within the autistic population and the general population. Consequently, across individuals with and without autism, there exists a broad range of traits, some of them considered autistic and sensory sensitivities. This range offers an opportunity to study individual differences in neural variability in relation to meaningful individual differences in autistic traits and sensory sensitivities.

The substantial overlap in the degree of ABR neural variability between autistic and nonautistic individuals reported in the literature may be related to a possible overlap in sensory sensitivities or autistic traits between groups. According to the Neural Noise Theory, variable neural responses have the potential to drive observable atypical behaviors by creating an unstable perceptual environment (Haigh, 2018). In cortical research, measures of neural variability have been proposed as proxies for behavioral characteristics in autism (Dinstein et al., 2012, 2015; Haigh, 2018). In light of these considerations, the current study aims to investigate whether support for the Neural Noise Theory can be found by examining neural variability in the auditory brainstem. Notably, instead of relying on traditional case-control paradigms that often overlook the diversity among individuals, this study focuses on exploring relationships between neural variability and both sensory sensitivities and autistic traits across a range of school-aged children, both with and without autism.

## 2.12 Specific Aims

The *long-term goal* of my research is to understand the neurological mechanisms underlying sensory sensitivities and autistic traits. The current study serves as a critical step towards achieving this goal by framing questions based on the Neural Noise Theory. Specifically, this study addressed the following research question: To what extent is subcortical neural variability, measured via ABR, predictive of parent-report sensory overresponsivity and autistic traits in school-aged children with and without autism, and does the relationship differ depending on the ABR-evoking stimuli and response component, or the sensory modality(s) for which sensitivity is measured? To answer this question, the current study had the following three specific aims:

**Specific Aim #1** investigated the influence of evoking stimuli on neural variability. ABRs were recorded using speech and click stimuli to achieve specific aim #1. Neural variability was calculated for each ABR and specific temporal segments of the sABR post-stimulus onset, referred to as response components, including the full speech response, onset, frequency-following response, and offset. The degree of neural variability for each response component was statistically compared using repeated measures analysis of variance (RMANOVA).

The rationale for this aim stemmed from the recognition that neural variability is influenced by both the timing of analysis (responses evoked by early versus later parts of the stimulus) and the site of response generation (Dinstein et al., 2015). Therefore, it was crucial to explore these factors specifically in the speech-evoked responses rather than solely analyzing the FFR portion, as observed in previous literature.

The hypothesis guiding this aim was grounded in the fundamental differences between speech and click stimuli. The click stimulus is a transient stimulus marked by rapid onset and offset, which was contrasted with the more complex speech stimuli, characterized by sustained

and transient components. It was hypothesized that the degree of neural variability in the entire sABR and click ABR would significantly differ. Specifically, the neural variability evoked by the simplistic, transient click stimulus was anticipated to be markedly higher than that elicited by the entire speech stimulus due to the brevity of the stimulus. However, it was further hypothesized that the neural variability in the click ABR would not significantly differ from the onset response component of the sABR because they are analogous (Kraus & Nicol, 2005; Song et al., 2006). Within the sABR, it was anticipated that the different response components, corresponding to various aspects of the speech stimulus, would exhibit varying degrees of neural variability. This expectation was rooted in the understanding that different characteristics of the speech stimuli evoke unique neural responses (e.g ., Kraus & Nicol, 2005; Russo et al., 2004). Therefore, it was hypothesized that the neural variability in the temporal segments of the sABR (full response, onset, FFR, and offset) would be distinct from one another.

Achieving this specific aim addresses the critical question of how different auditory stimuli (speech versus non-speech sounds) and the response components analyzed impact brainstem neural variability. Understanding these influences is essential for selecting appropriate stimuli and response components to analyze in future research endeavors.

**Specific Aim #2** explored the relationship between neural variability in the brainstem and parent-reported sensory overresponsivity across sensory modalities (SOR) compared to an auditory-only sensory overresponsivity (AUD-SOR) measure. To achieve this aim, the neural variability of click ABR and sABRs was measured. Parental responses from the SP survey were used to derive a SOR and AUD-SOR score for each participant. To ensure a comprehensive range of sensory sensitivities and a range of the degree of neural variability, participants included autistic children and nonautistic children. Correlations between neural variability and both SOR

and AUD-SOR were examined. Significant correlations were further analyzed using linear regression models to assess the predictive power of neural variability for overresponsivity measures.

The justification for specific aim #2 is rooted in the Neural Noise Theory; specifically, the interpretation by Haigh et al. (2018) posits that unstable neural responses lead to atypical behavioral reactions to sensory stimulation. Therefore, the first hypothesis (hypothesis #1) proposed that neural variability will significantly predict parent-reported sensory overresponsivity, encompassing multimodal (SOR) and auditory-only (AUD-SOR) domains. Furthermore, the second hypothesis (hypothesis #2) suggested that neural variability evoked by auditory stimulation would be a stronger predictor of AUD-SOR compared to a broader, multimodality measure of overresponsivity, SOR.

This aim sought to unravel the relationship between sensory overresponsivity and neural variability at the level of the brainstem, offering crucial insights into the neural basis of sensory sensitivities, potentially providing support for the Neural Noise Theory in the brainstem across the combined autistic and subclinical population. It was also crucial to determine whether neural variability is more closely linked to a single or multimodal parent-reported measure of sensory overresponsivity. This could provide insights into how neural variability should be assessed in its potential role in predicting sensory sensitivities: whether neural variability should be used to predict sensitivities within the specific context of evoking stimuli type (i.e., auditory-evoked neural variability predicting auditory sensory sensitivities) or if neural variability evoked by any type of sensory stimuli could be utilized to predict multimodal sensory sensitivities (i.e., auditory-evoked neural variability predicting multimodality sensory sensitivities). The findings could also inform future research practices by potentially suggesting a focused approach when

investigating sensory processing and measuring sensory sensitivities within distinct domains rather than utilizing multimodal measures.

**Specific Aim #3** analyzed the relationship between neural variability in the brainstem and parent-reported autistic traits assessed through the AQ and SRS-2 surveys. Similar to Specific Aim#2, the neural variability of click and sABR was measured to achieve this aim. Both autistic and nonautistic children's parents completed the AQ and SRS-2 surveys, ensuring the analysis encompassed a full range of autistic traits. Correlations between neural variability and autistic traits were examined. Significant correlations underwent further analysis using linear regression models.

The rationale for this investigation stems from the Neural Noise Theory, which suggests that increased cortical neural variability induces atypical behavioral characteristics, such as those associated with autism (Dinstein et al., 2012, 2015; Haigh, 2018). Supported by recent research linking decreased neural stability in the cortex with heightened autistic traits (Hecker et al., 2022; Heller Murray et al., 2022; Park et al., 2017; Vilidaite et al., 2017), this aim examines whether this link can also be made with brainstem neural variability because the brainstem is where significant processing of incoming stimuli occurs before reaching the cortex. Considering literature indicating greater brainstem neural variability in individuals with autism compared to those without, albeit with substantial overlap between groups (Otto-Meyer et al., 2018), this study investigates the relationship between brainstem neural variability and autistic traits. It was hypothesized that decreased neural stability would predict greater autistic traits, as measured by the AQ and SRS-2 surveys.

Understanding if unstable neural responses in the brainstem support the Neural Noise Theory is crucial. This insight could advocate for further investigations using brainstem neural

variability as an objective proxy measure for autistic traits. Such an approach is faster, easier, and more cost-efficient than analyzing cortical neural variability. Additionally, it underscores the importance of individual differences in neural variability and emphasizes brainstem processing's substantial contribution to individual traits.

## 3.0 Design and Methodology

Participants were recruited through the Center for Autism Research and Electrophysiology (C.A.R.E) Laboratory under the direction of Dr. Natalie Russo as part of a collaborative research project with the Pediatric Audiology Laboratory directed by Dr. Beth Prieve. This collaborative project was funded by a Collaboration for Unprecedented Success and Excellence (CUSE) grant from Syracuse University. I was involved in all auditory data collection for the collaborative research project, for which the goal was to characterize subcortical to cortical processing of speech and tonal sounds in autistic children compared to their age-IQ-matched peers. The project presented here is a secondary analysis of the data whose conception, analysis, and interpretation were my own. The methodological approach utilized in the current study was to record auditory brainstem responses evoked by a click and a 40 ms /da/ stimulus from verbal, native English-speaking school-aged children (6-17 years old) diagnosed with and without autism. Methodologically, each enrolled and consented participant was expected to undergo IQ testing, and their parent(s) was encouraged to complete the SP, AQ, and SRS-2 to quantify the participant's sensory sensitivities and autistic traits. Statistical analyses include descriptive statistics, a repeated measure of analysis of variance (RMANOVA), Pearson correlations, and linear regression models with a covariate.

### 3.1 Participants

A total of 44 school-aged children aged 6-16.9 years, consisting of 18 autistic children

and 26 neurotypical peers, were enrolled in the study. Table 1 displays participant demographic information, including race, education level, gender, and highest completed parental education. A total sample size of 31 participants was necessary based on *a priori* power analysis. However, as discussed in the results section, not all participants were able to complete all aspects of the study; therefore, the number of participants who completed each data set is reported.

**Table 1**

*Participant Demographics*

| **Biological Sex** | **N** | |
|---|---|---|
| Male | 21 | |
| Female | 23 | |
| **Education Level (grade)** | | |
| Kindergarten | 2 | |
| 1st grade | 4 | |
| 2nd grade | 9 | |
| 3rd grade | 2 | |
| 4th grade | 6 | |
| 5th grade | 3 | |
| 6th grade | 4 | |
| 7th grade | 3 | |
| 8th grade | 2 | |
| 9th grade | 2 | |
| unknown | 7 | |
| **Race** | | |
| White, not Hispanic or Latino | 33 | |
| White, Black, not Hispanic or Latino | 1 | |
| Native American and White, not Hispanic or Latino | 1 | |
| Unknown | 9 | |
| **Parental Education** | Mother's | Father's |
| Highschool | 2 | 7 |
| Some College | 2 | 3 |
| Associate's | 3 | 2 |
| Bachelor's | 7 | 6 |
| Graduate School | 3 | 5 |
| Master's | 7 | 2 |
| Doctorate's | 8 | 7 |
| Unknown | 12 | 12 |

*Note.* Table 1 displays the demographics of the participants included in the current study. Education level refers to the grade level the child was in or had just completed when they participated in the study. Parental education refers to the reported degree or highest level of education completed. Some college means that the parent reported they attended college but did not report completing a degree.

Autism diagnoses were confirmed by trained student clinicians at the C.A.R.E lab based on clinical judgment adhering to DSM-5 criteria, ADOS-2, and the Autism Diagnostic Interview-Revised (ADI-R). Participants were excluded from the study if they had a reported medical history positive for epilepsy, neurological, genetic, psychiatric, or learning disorders or a hearing loss defined by a behavioral threshold greater than or equal to 25 dB HL at two or more octave frequencies between 250-8000 Hz, or an elevated threshold (≥25 dB HL) at one frequency and an abnormal tympanogram (peak-compensated static admittance magnitude <0.2 or >1.4 mmho and middle-ear pressure <-150 or >+25 daPa). For inclusion in the study, participants had to be between the ages of 6 and 17 years old, verbal English speakers, and have a full-scale IQ above 80. Participants' parents or guardians provided written informed consent, and all participants assented before enrolling in the study. Participants were compensated for their time ($10 per hour).

### 3.2 IQ Measure

Participants underwent an IQ assessment by a trained psychology graduate member of the C.A.R.E. lab using the Wechsler Abbreviated Scale of Intelligence, Second Edition (WASI-II). The WASI-II is an abbreviated measure of verbal, non-verbal, and general cognitive intelligence for individuals aged 6 to 90 years (Irby & Floyd, 2013). The WASI-II yields the following measures: full-scale IQ (FSIQ), verbal comprehension IQ (VCI), and Perceptual Reasoning Index (PRI). The VCI assesses verbal intelligence and language communication, while the PRI assesses visuospatial skills and is less influenced by verbal communication. All scores are standardized (M=100, SD=15). The FSIQ, VCI, and PRI were independently correlated with neural variability of the ABRs, as well as measures of sensory sensitivities and autistic traits, to determine if any significant confounding relationships with IQ needed to be considered in the

statistical analysis.

## 3.3 Survey Measures

The participant's parent(s)/caregiver completed a series of surveys during experimental testing. These surveys included the SP, AQ, and SRS-2. Parents could complete these surveys in any order they prefer. Following completion of the surveys, parent(s)/caregivers were instructed to leave the surveys with a lab member. Surveys were returned to the C.A.R.E. lab for scoring.

### 3.3.1 The sensory profile.

Two versions of the SP Caregiver Questionnaire were used in the current study. Parents of thirty-six participants were asked to complete the SP, and two parents completed the revised version, the Sensory Profile-2 Caregiver Questionnaire (SP-2). The two versions of the SP differ in the number of items (SP-2 consists of 83 items, and SP consists of 125 items) but assess the same behaviors.

In completing the questionnaire, parents were requested to assess the degree to which their child exhibited the behavior described in each item on a five-point Likert scale, ranging from "almost never" to "almost always" or "does not apply." All items were scored by graduate students at the C.A.R.E. Lab and provided to me. Items of the SP were reversed scored to be consistent with the Likert scale described above.

The SP has acceptable psychometric properties. The test-retest reliability of the SP is good, with interclassed correlation coefficients ranging from .80-.90 across quadrants (Registration, Seeking, Sensitivity, and Avoiding). The SP has moderate to high internal consistency across quadrants with Cronbach’s alpha coefficients that range from 0.89-0.95 (Ohl et al., 2012). The SP's convergent validity is good; compared to the Home and Main Classroom Forms of the Sensory Processing measure, the correlation is 0.86 (Brown et al., 2010).

The 14 SOR items (Appendix B), including items from tactile sensitivities, auditory filtering, and visual/auditory sensitivities, were totaled for each participant. The items included in the SOR were based on McKernan et al. (2020), who selected the items based on an overresponsivity measure by Green et al. (2015), who measured sensory overresponsivity using the Short Sensory Profile and the Sensory Over-Responsivity Scales. Cronbach's alpha for the SOR in the current study is 0.923, indicating excellent internal consistency.

The AUD-SOR score was calculated using the items listed in Appendix C, which included items from the auditory sensitivity and auditory filtering categories. The items selected for AUD-SOR were based on Williams et al. (2023) Auditory HYPER measure, which included five experts in selecting items and used *a priori* criteria for reliability and validity for retaining items in the measure. Auditory HYPER was found to have a high reliability (coefficient omega of 0.91). The Auditory HYPER is correlated with the Repetitive Behavior Scale-Revised, Repetitive Sensory Motor, total psychopathology, and ADHD symptoms, but not cognition (Williams et al., 2023). The Cronbach's alpha for the AUD-SOR in the present study is 0.903, indicating excellent internal consistency.

The SOR and AUD-SOR were utilized in the current study as measures of sensory sensitivity. As discussed in the introduction, sensory sensitivities exhibit significant variation in degree and type, such as overresponsivity, underresponsivity, and seeking, both between and within individuals (Ausderau et al., 2014; Larocci & McDonald, 2006; Lane et al., 2010). Therefore, focusing on a specific sensory modulation behavior was essential to enable a more nuanced interpretation of underlying neural processing since the comparison was also made between a multimodal and single-modality measure.

Overresponsivity was chosen as the target sensory modulation behavior for two primary

reasons. Firstly, these behaviors align closely with descriptions of behaviors outlined in the Neural Noise Theory, encompassing avoidance and negative emotional responses (Dinstein et al., 2015). Secondly, auditory processing was of particular interest in the current study because neural variability was being evoked with auditory stimuli and assessed in the auditory brainstem pathway. DSTDs are frequently reported among autistic individuals (e.g., Danesh et al., 2021; Demopoulos & Lewine, 2016; Gomes et al., 2008; Khalfa et al., 2004; O'Connor, 2012; Rimland & Edelson, 1995; Rosenhall et al., 1999) and exist in nonautistic individuals (e.g., Aazh & Moore, 2017; Khalfa et al., 2002). All DSTDs fall within the sensory modulation category of sensory overresponsivity. Hence, it was logical to use measures of sensory overresponsivity to assess sensory sensitivities in the current study.

### 3.3.2 Autism quotient.

The reference standard for quantifying the level of autism trait severity is the ADOS-2 or the Autism Diagnostic Interview-revised (ADI-R); however, because participants in the current study included those with and without autism, not all participants have an overall autism severity score from one of these instruments. Therefore, the present study used the overall total score from the AQ and the total SRS-2 score as measures of autistic traits.

The AQ is a 50-item survey designed to assess traits associated with autism and is widely used in clinical and research settings. Highlighting its common use in research settings, the AQ has been used over 2,300 times as of 2019 (English et al., 2020). The AQ produces five different subscales: social skills, attention switching, attention to detail, communication, and imagination, as well as an overall total score (Baron-Cohen et al., 2001).

Although there is debate in the literature regarding the use of the total AQ score because only moderate correlations exist between the subscales (e.g., English et al., 2020), and therefore, the overall total AQ score is not as homogenous as it was initially believed to be (Baron-Cohen

et al., 2001), the present study elected to use the AQ total because the total score encompasses both autistic traits associated with social skills and restricted repetitive behaviors. It is important to include both of these autistic traits because, as Dinstein et al. (2015) suggest, an increase in neural variability contributes to difficulty predicting what will occur in the external environment. Therefore, individuals with increased neural variability may exhibit difficulties in predicting their environment, which leads them to have atypical social responses to human communication, which is highly variability from person to person. This, in turn, increases the probability that individuals will engage in repetitive behaviors, which are predictable behaviors. It was of interest in the current study to see if neural variability was predictive of overall autistic traits that encompass the areas of both social interactions and restricted and repetitive behaviors, as opposed to selecting a specific subscale from the AQ.

Parents completed one of two forms depending on the participant's age: the parent-report Child AQ for ages 4-11 or the Adolescent AQ for ages 12-15. Participants 16 and older (n=4; 2 autistic participants and 2 control group participants) were asked to complete the self-report Adult AQ before or after the experimental task. Each form addresses the same content, but the items on each form are adapted for different developmental levels.

The items (e.g., "I notice patterns in things all the time") are rated on a 4-point scale from "definitely agree" to "definitely disagree." Each item is then converted into a dichotomous response (agree/disagree), which aligns with a binary code (0/1). When the AQ is scored in this binary manner, the total AQ scores range from 0 to 50, with a higher score indicating a higher degree of autistic traits. A score of 32 or higher is highly predictive of autism. The sensitivity and specificity of the AQ, using a cut-off value of 32, are 0.79 and 0.98, respectively (Baron-Cohen et al., 2001). There is also evidence of good convergent validity of the AQ (Woodbury-

Smith et al., 2005). The AQ total has good internal validity with a Cronbach's alpha of 0.74 and strong test-retest reliability of 0.82 (Pearson's correlation coefficient; Stevenson & Hart, 2017). A systematic review found that nonautistic adults have an average score of 16.94 (Ruzich et al., 2015). As previously discussed, because the AQ total score is normally distributed throughout the general population, this is an appropriate measure to evaluate autistic traits in the present study, which included autistic and nonautistic individuals.

#### 3.3.3 Social responsiveness scale, second edition.

The SRS-2 is a 65-item rating scale that measures deficits in social behavior associated with autism (Bruni, 2014). Parents in this study completed the School Aged form used for participants aged 4-18 years. To complete the survey, parents were asked to rate various statements on a 4-point Likert-type scale that ranged from "not true =1" to "almost always true =4". Although this survey is frequently described as a measure of social communication, the survey can be broken down into the subscales of social awareness, social cognition, social communication, social motivation, and restricted interest and repetitive behaviors. The overall total score is the most reliable measure for social deficits related to autism (Bruni, 2014) and is the measure from the survey used for analysis in the current study. The rationale for using the total score from the SRS-2 is the same as it is for using the AQ total score.

The scores from the SRS-2 are reported as T-scores (M=50, SD=10). A score of 76 or higher is considered severe, suggesting that an individual has clinically significant deficits in social functioning. In contrast, scores between 66-75 are considered moderate, 60-65 are considered mild to moderate deficiencies, and scores below 59 suggest that an individual probably does not have significant social difficulties while interacting with others and is not indicative of a possible ASD diagnosis (Bruni, 2014). Similarly to the AQ, the SRS-2 is normally distributed throughout the general population (Constantino & Todd, 2003).

The SRS, from which the SRS-2 is derived, has good psychometric properties. The test-retest reliability of the SRS ranges from 0.72-0.97 (intraclass correlation) and the internal consistency of the measure ranges from 0.91-0.97 (Conbach's alpha). The specificity and sensitivity of the SRS total score of 85, when differentiating between autistic and nonautistic individuals, is 0.81 and 0.73, respectively. The SRS has moderate to good convergent validity. When compared to the ADI-R domains of social interaction, communication, and stereotyped behavior, the convergent validity was r=0.46, 0.40, and 0.38, respectively (Bölte et al., 2008).

Although the AQ and SRS-2 surveys are similar, there are important differences. The AQ measures attention for details and imagination and the SRS-2 does not. The SRS-2 measures social motivation, while the AQ does not. However, there is good convergent validity between the two surveys supported by the significant correlation between ratings of the SRS and AQ (r=0.64, p=0.00; Armstrong & Iarocci, 2013). Compared to the AQ, the SRS-2 is a poorer predictor of autism (Bezemer et al., 2021).

Both the SRS-2 and AQ were used as parent report measures to quantify autistic traits in the participants in the current study to serve as a robustness check. Because the two measures are similar, with slight differences, they were expected to be highly correlated with one another and have similar predictive models. If the same neural variability response components were predictive of both autistic trait measures, it would add credibility to the findings. Specifically, that neural variability predicts autistic traits regardless of the survey used to quantify autistic traits.

### 3.4 Audiometry

Due to hearing loss's impact on ABR (e.g., Jalaeia, 2019; Koravand et al., 2017; Nada et al., 2016), a routine hearing evaluation was conducted on each participant before the

electrophysiological recording. This evaluation took place in the Pediatric Audiology Laboratory. It included air-conduction behavioral thresholds at octave frequencies ranging from 250 to 8000 Hz (including inter-octaves 3000 and 6000 Hz), distortion product otoacoustic emissions (DPOAEs) from 1.5 to 8 kHz ($f_2$: $f_1$ = 1.22; $L_1$:$L_2$ = 10 dB; $L_2$ = 55 dB SPL), 83 dB SPL click-evoked transient otoacoustic emissions (TEOAEs), and wideband acoustic immittance (WAI). Conditioned play audiometry was employed to elicit threshold responses if a participant was unable to complete standard behavioral audiometric testing. If behavioral thresholds were elevated (≥25 dB HL) at any frequency tested, tympanometry was performed on the participant to assess the middle ear's status. A tympanogram was considered abnormal if the peak-compensated static admittance magnitude was <0.2 or >1.4 mmho and middle-ear pressure fell between -150 and +25 daPa.

### 3.5 Electrophysiology

Following the peripheral hearing assessment, participants were seated comfortably in a reclined chair housed in a double-walled, sound-treated booth. The participants had the choice to either watch a movie of their choice in silence or sleep during ABR acquisition.

#### 3.5.1 ABR Methods

The Intelligent Hearing System, SmartEP, was used for stimulus presentation and recording. The click ABR was evoked using a 100μs broadband click presented at 70 dB nHL (98 dB pSPL) at a rate of 27.7/sec using condensation polarity. The sABR was evoked by a 40 ms synthetic /da/ with alternating polarity at a rate of 11.1/sec. The /da/ stimuli were presented at 63 dB nHL (80 dB SPL). All stimuli were presented binaurally and monaurally to each ear through insert ER-3A earphones. Stimuli were calibrated in an HA-1 coupler coupled to a sound level meter following standard procedures for calibrating insert earphones.

A two-channel montage, right and left channels, was used to record a click and an sABR from four scalp electrodes: right and left mastoids (inverting), forehead (noninverting), and low forehead (ground). The four areas were prepped with an alcohol pad and Nuprep gel. Tab electrodes were placed on the washed areas. Electrode impedances were < 3 kohms and within 1 kohm of each other.

Responses recorded over the right channel were the ipsilateral recordings from right ear stimulation; similarly, the responses recorded over the left channel were the ipsilateral recordings from the left ear stimulation. Both ears were stimulated synchronously during binaural stimulation, and right and left ipsilateral responses were recorded simultaneously. Responses were amplified with a gain of 100,000 and bandpass filtered from 100-3000 Hz[4]. Trials exceeding ±35 $\mu$V were rejected from the running average and were not included in the final analysis. At least two averages containing 1500 low-noise runs were collected over a 60 ms and a 25 ms window to speech and click stimuli, respectively, for each channel.

As stated previously, the speech stimulus was presented using alternating polarity, meaning that every other stimulus presentation was flipped 180 degrees with respect to the preceding stimulus, referred to as condensation and rarefaction presentation. Responses for right and left channels evoked by rarefaction stimuli were stored in their respective buffers (for example, buffer 'A'). Responses evoked by condensation stimuli for each channel were stored in a second buffer (for example, buffer 'B'). The responses in the two buffers for each channel were averaged together to produce one trace consisting of 1500 sweeps in each channel. Two traces consisting of 1500 sweeps were averaged together in each channel, resulting in a waveform

[4] Responses were recorded on two different computers utilizing the same equipment and set-up except for online vs offline filtering of the sABR. Nine of the usable sABR data were bandpass filtered offline and 28 were bandpass filtered online. An independent t-test (unequal variance) indicated that there was no difference in online vs offline filtering on the degree of neural variability (p=0.608).

containing 3000 sweeps. The resulting waveform consisted of 1500 responses evoked by condensation and rarefaction stimuli in each channel.

### 3.5.2 Offline Analysis

For the sABR, the spectral content of the FFR portion was analyzed in MATLAB by Dr. Spencer Smith, Ph.D. A Fast Fourier Transformation of the response and noise was calculated from the averaged time domain response for each participant's waveform. The purpose of calculating the FFR for each participant was to evaluate if the response was above the noise floor, as has been done previously (e.g., Madrid et al., 2021; Picton et al., 2003). If the response was not above the noise floor, then the sABR waveform was not included in the final analysis.

The root-mean-square (RMS) of the interval prior to stimulus presentation was calculated to control for individual differences in prestimulus noise. For the click ABR, the prestimulus interval was 0.8 ms and for the sABR, it was 5 ms. The length of the prestimulus interval was calculated by taking 10% of the length over which the response was analyzed (8 ms and 55 ms, for click and speech ABR, respectively; Hall, 2007). The prestimulus noise was correlated with all variables to determine if it should be entered into the statistical models as a covariant. A similar method has previously been employed to account for individual prestimulus noise differences in a neural variability study, and no effect of prestimulus noise on group differences was found (Anderson et al., 2012).

As stated above, ABRs were recorded to monaural (right or left ear) and binaural (right and left ears simultaneously) stimulation. The analysis used responses evoked during binaural stimulation to replicate a more natural listening environment. Because 3000 sweeps were recorded over right and left channels (two recordings consisting of 1500 sweeps per channel), the total number of sweeps included in the neural variability calculation was 6000.

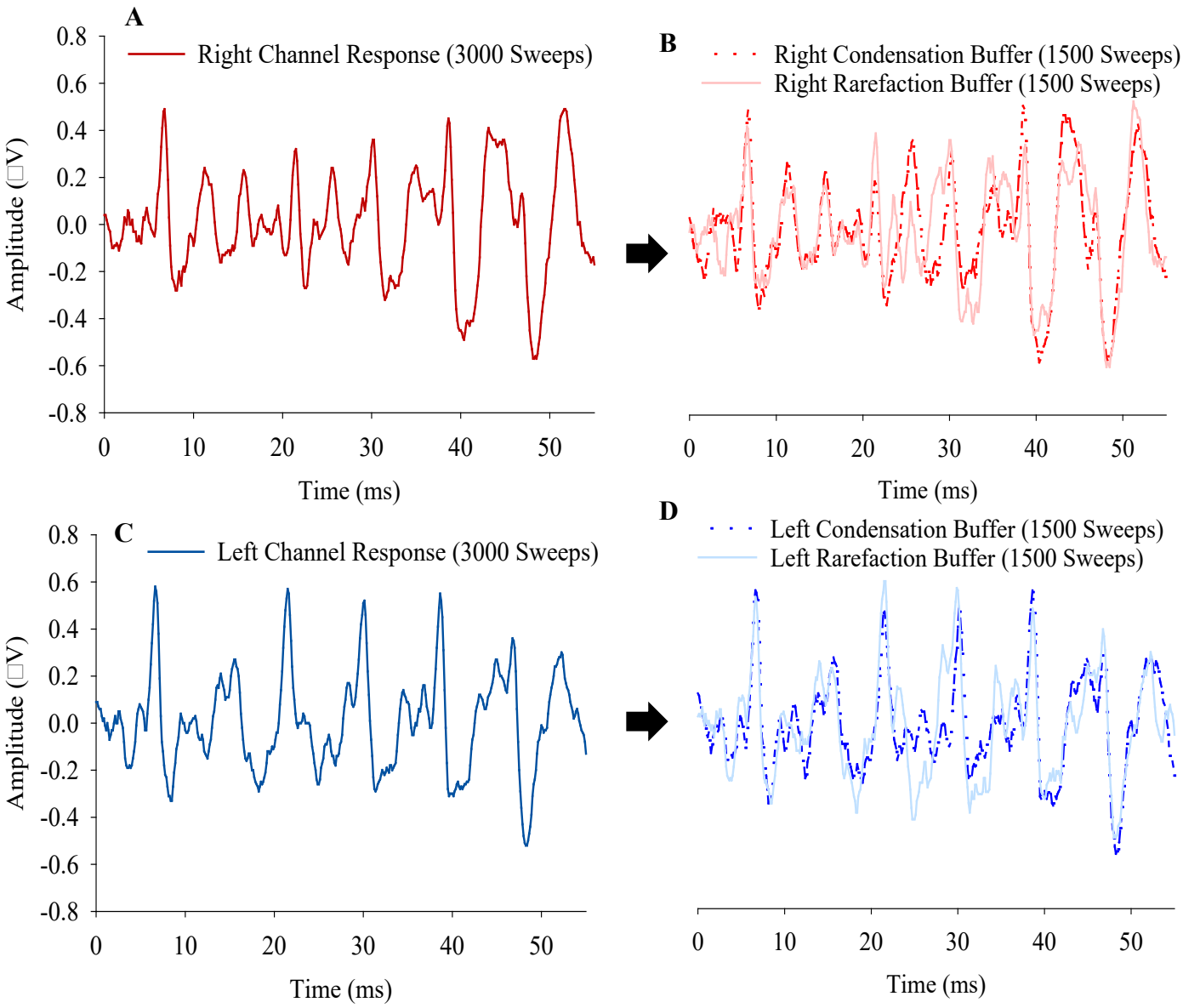
### 3.5.3 Calculating neural variability

Figures 4, 5, and 7 display the three steps to calculating neural variability. A visual explanation for the choice of averaging responses evoked by condensation and rarefaction stimuli is illustrated in Figure 6.

The first step in calculating neural variability is depicted in Figure 4. The right and left channel sABR, each composed of 3000 sweeps, are illustrated in panels A and C, respectively. Panels B and D illustrate that the sABR is evoked by 1500 condensation (dashed line) and rarefaction stimuli (solid line). Step 2 is shown in Figure 5. To eliminate the possible effects of stimulus polarity and right versus left channel recordings on the ABR, the rarefaction and condensation buffers (each comprising 1500 sweeps) from opposite channels (right and left) were averaged together, resulting in two distinct waveforms, referred to as Average response 1 and 2.

**Figure 4**

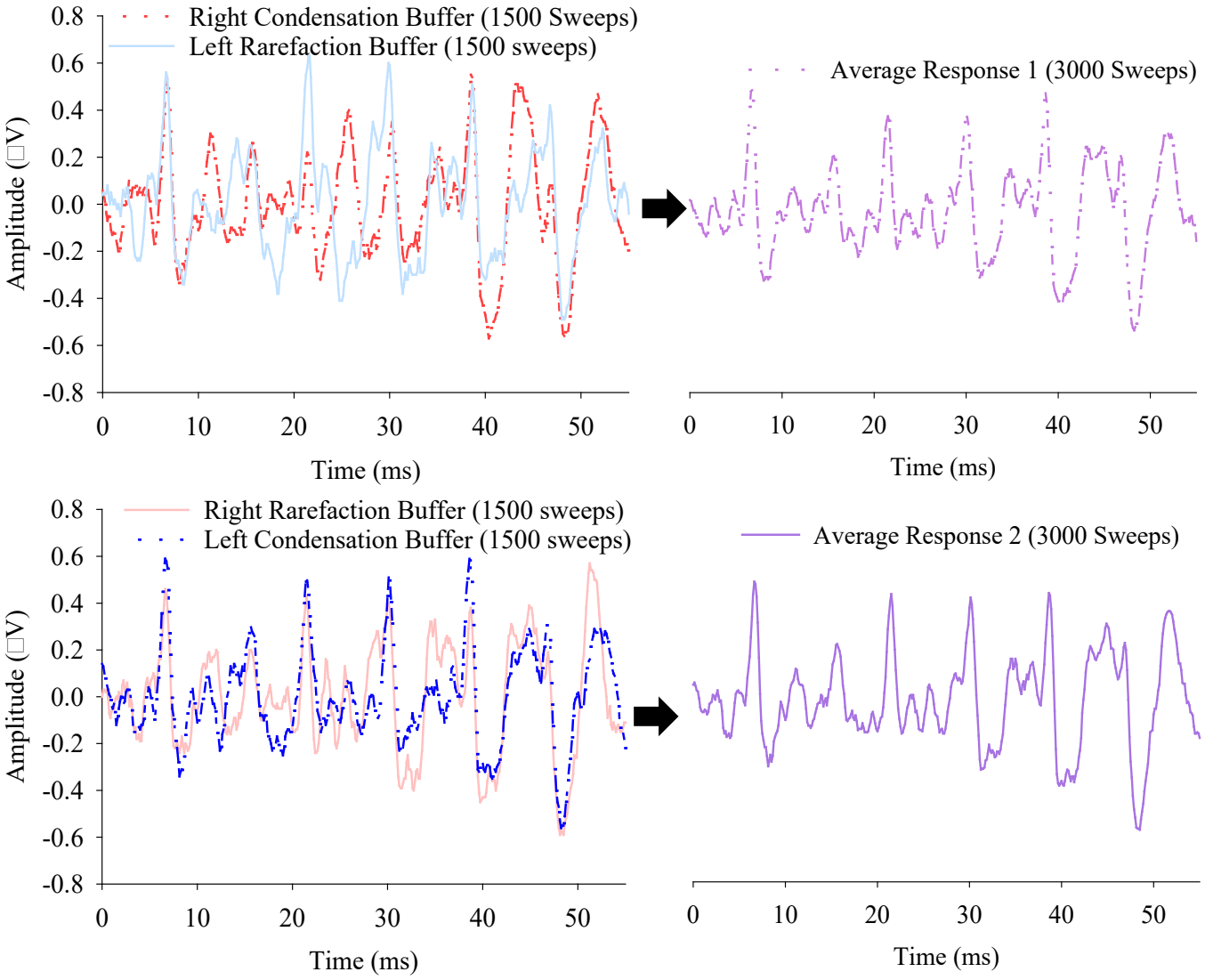
*Steps to Calculating Neural Variability- Step 1*




*Note.* Figure 4 displays the first step involved in calculating neural variability, which was to segregate the average waveforms from the right and left channels from the condensation and rarefaction buffers.

**Figure 5**

*Steps to Calculating Neural Variability- Step 2*

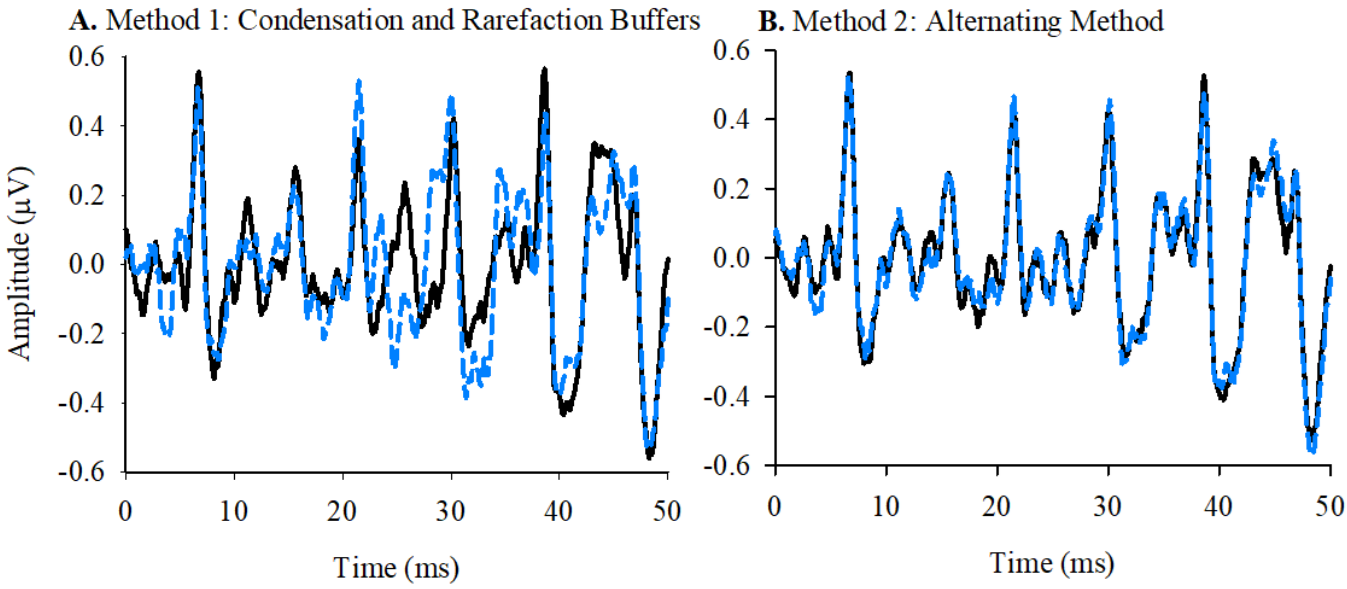



*Note.* Figure 5 illustrates the second step in calculating neural variability. As shown above, the rarefaction and condensation buffers (each comprising of 1500 sweeps) from opposite channels were averaged to create two distinct waveforms, labeled as Average response 1 and 2. Each average waveform contains 3000 sweeps and integrates responses recorded from right and left channels.

Figure 6 illustrates the importance of creating two averages containing responses evoked by alternating stimuli rather than one average containing responses evoked by only condensation stimuli and another evoked by rarefaction stimuli. Panel A represents two waveforms composed of 3000 sweeps recorded from a single participant: one averaged from responses evoked by rarefaction stimuli and the other from condensation stimuli. Figure 6b represents the same data from that single participant, but responses evoked by condensation and refraction stimuli are averaged together to create two waveforms composed of 3000 sweeps, referred to as the alternating method. As evident in panel 6b, the alternating method produced waveforms that were similar to each other. The peaks and valleys of the waveforms illustrated in 6A have slightly different latencies and amplitudes, most likely due to the timing differences in neural

**Figure 6**

*Averaging Methods*



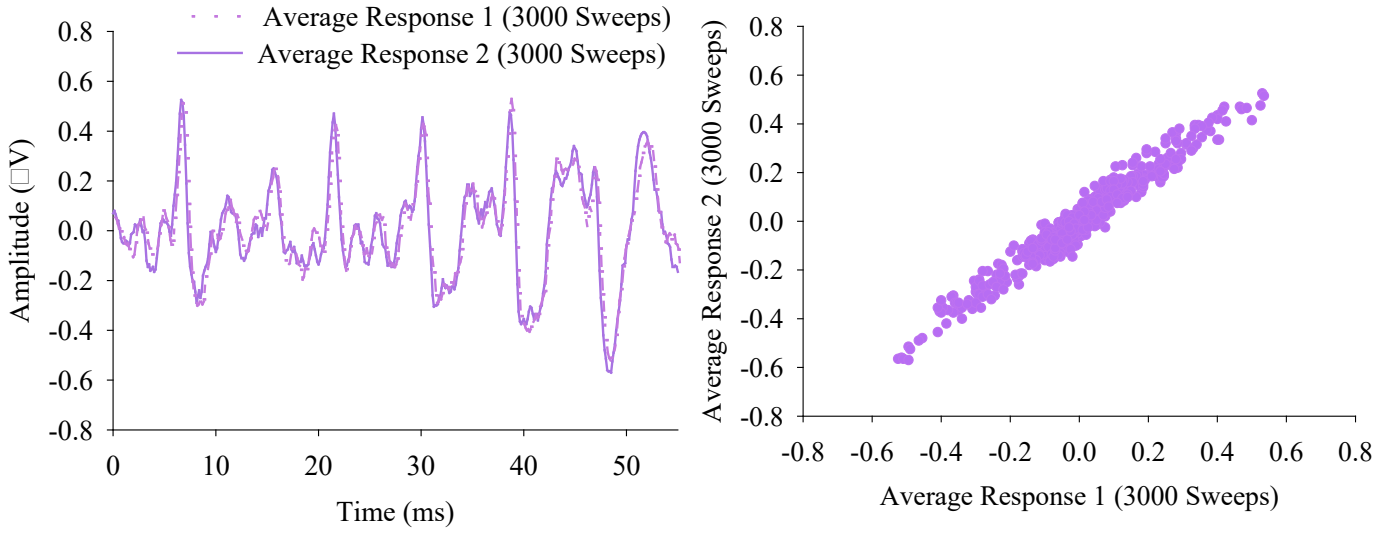

*Note*. Figure 6 depicts data recorded from one participant but averaged together in two different methods. Panel **A** displays two waveforms: an average condensation waveform (3000 sweeps) recorded to condensation polarity (black solid line) and an average rarefaction waveform (3000 sweeps; blue broken line). Panel B displays the alternating waveforms, in which the responses evoked by condensation and rarefaction sweeps are averaged together.

firings evoked by condensation and rarefaction stimuli. Therefore, the alternating method was used to calculate neural variability for all participants. Although the click ABRs were only evoked by condensation polarity, the same averaging method, shown in step two, Figure 5, was also employed for the click analysis.

Figure 7 illustrates step 3, in which neural variability was calculated using Pearson Correlation, which examined the linear relationship between averaged response 1 and 2 as depicted in Figure 5. Because the averaged response waveforms are composed of responses from right and left channels and averaged across the first and second traces collected, the correlation genuinely represents neural variability free from the effects of condensation/rarefaction stimulation, recording channel, or data collection order (first vs second trace composed of 1500 averages). The correlation for the click ABR was calculated for the response segment between 1 and 8 ms, which is when the waveforms typically occur post-stimulus. For the sABR, the

**Figure 7**

*Steps to Calculating Neural Variability- Step 3*




*Note.* Figure 7 illustrates the 3rd step in the computation of neural variability, which is to compute the Pearson Correlation coefficient between response 1 and response 2. This statistical measure is used as a proxy for neural variability.

correlation analysis was conducted for four separate time segments, displayed in Figure 1: the complete response (0-55 ms), the onset (5-10 ms), the FFR portion (22-40 ms), and the offset (45- 50 ms). The Pearson Correlation analysis provides an r value. An r value of 1 indicates a perfect correlation between average responses 1 and 2, while a correlation of 0 indicates no correlation between the waveforms. The r values were Fisher-transformed to z values (Zr) to guarantee normal distribution for the subsequent statistical analyses.

### 3.6 Statistical Analyses

All statistical analyses were performed using IBM SPSS software (version 17). The descriptive statistics, including the mean, median, range, and standard deviation for the binaural neural variability of the click ABR, the sABR (for each response component: entire response, onset, offset, and FFR portion), the RMS of the pre-stimulus noise, and the sensory sensitivity and autistic trait measures were calculated.

A two-way repeated measure of ANOVA (RMANOVA) between right and left responses evoked by monaural stimulation was conducted to determine if the degree of neural variability differed between right and left ear stimulation. This analysis was necessary to ensure it was appropriate to calculate neural variability from binaural stimulation, which required averaging responses collected from the left and right channels together. Although the analyses focused on the data recorded from binaural stimulation, for the comparison to previously published data, right ear neural variability data can be found in Appendix F.

One-sample nonparametric Kolmogorov Smirnov and Shapiro-Wilk tests were conducted for each variable to assess whether the data was normally distributed. The Kolmogorov Smirnov test was corrected using the Lilliefor's method. If the data was found not normally distributed using the Lilliefor's method, a less strict criterion was used, which uses an asymptotic

significance and the individual variables' mean and standard deviation. Although this method is a less strict way of assessing the normality of the data, visual assessment of quantile-quantile (Q-Q) plots supplemented these tests to ensure the data was suitable for parametric statistics.

To address statistical hypotheses for SA#1 **(**$H_a: onset_{z_r} \neq offset_{z_r} \neq FFR_{z_r} \neq sABR_{z_r} \neq click_{z_r}$ $and H_a: click_{z_r} > sABR_{z_r}$) which states that neural variability is significantly different between response components and that the click ABR is significantly more stable than the entire sABR, a repeated measures of ANOVA (RMANOVA) of the various latency components of the sABR (onset, offset, FFR, sABR as a whole) and the entire click ABR was conducted. The RMANOVA had five levels of the independent variable, referred to as response components: total sABR response, the onset, the offset, the FFR portion, and the complete click ABR response. The dependent variable is the $Z_r$. The results of the RMANOVA were interpreted to determine if the null hypothesis **(**$H_0: onset_{z_r} = offset_{z_r} = FFR_{z_r} = sABR_{z_r} = click_{z_r}$) can be rejected at alpha <0.05. If the assumption of sphericity is violated, then the Greenhouse-Geisser correction was used. Post-hoc testing was then conducted to determine if the null hypothesis ($H_0: click_{z_r} = sABR_{z_r}$) could be rejected and to determine which response components were statistically different from one another.

To address specific aims #2 and #3, all data was checked to ensure it met the assumptions of a linear regression model. Scatter plots and Pearson correlations analyses were conducted to check for linear relationships between all response components $Z_r$ and AUD- SOR, SOR, AQ, and SRS-2. To determine if age, IQ, or prestimulus noise should be entered into the model as covariates, Pearson correlation analyses were also conducted to determine if significant relationships existed between age, IQ, or prestimulus noise and response component $Z_r$ or autistic traits and sensory sensitivities. The variance inflation factor (VIF) values were checked

to ensure that there was no multicollinearity between independent variables in the regression models. The models' residuals were checked to ensure they were normally distributed through the Kolmogorov-Smirnov test and assessed for homoscedasticity and outliers via scatter plots.

To address specific aim #2, that neural variability, $Z_r$, is a significant predictor of AUD-SOR and SOR while controlling for confounding variables, the data was fit by the following models using ordinary least squares:

$$\text{Model 1: AUD-SOR} = \beta_0 + \beta_{Z_r} + \beta_{CFV}$$

$$\text{Model 2: SOR} = \beta_0 + \beta_{Z_r} + \beta_{CFV}$$

The dependent variable is AUD-SOR and SOR for models 1 and 2, respectively. The regression coefficient of the independent variable, $Z_r$ of the response component, is represented by the $\beta_{Z_r}$ in both models. A model was only constructed for response components that were determined to be significantly correlated with AUD-SOR or SOR. The need for a covariate, whose regression coefficient is represented by $\beta_{CFV}$, is determined based on the above analysis that assessed the correlation between age, IQ, or prestimulus noise and response component $Z_r$ or autistic traits and sensory sensitivities. $\beta_0$ is the y-intercept.

Ordinary least squares was used to estimate the model coefficients. The model's statistics and overall model fit were assessed for statistical significance at an alpha level of 0.05 to test the hypothesis ($H_a: F < 0.05$). An ANOVA provides an overall significance value for the entire model used to test if the model is a significant predictor of AUD-SOR or SOR based on the *F* test.

If neural variability was determined to be a significant predictor of both AUD-SOR and SOR, a second statistical analysis would have been conducted to determine which variable (AUD-SOR or SOR) neural variability was a stronger predictor of ($H_a$: $\beta_{Z_{r\,model\,1}} >$

$\beta_{Z_{r\,model\,2}}$ ). To make this comparison, an F-statistic was going to be computed by using the following formula:

$$F = \frac{SS_{model\,1}}{SS_{model\,2}}$$

$SS_{model\,1}$ was the residual sum of squares for the first model predicting AUD-SOR and $SS_{model\,2}$ was the residual sum of squares for the second model predicting SOR. An F-statistic could have been determined using the degrees of freedom with a corresponding p-value. In this test, the null hypothesis was that model 2 is statistically better than model 1 ($H_0$: $\beta_{Z_{r\,model\,1}} < \beta_{Z_{r\,model\,2}}$ ). The null hypothesis would have been accepted if the p-value was less than an alpha level of 0.05. For a p-value >0.05, then the null hypothesis would have been rejected, and the alternative hypothesis would have been accepted, stating that model 1 is statistically better. However, as further discussed in the results, no significant models predicted AUD-SOR or SOR. Therefore, this analysis was not performed.

To address specific aim #3, that neural variability, $Z_r$ , is a significant predictor of AQ and SRS-2 while controlling any confounding variables, the data was fit by the following models using ordinary least squares:

$$\text{Model 3: AQ} = \beta_0 + \beta_{Z_r} + \beta_{VCI}$$

$$\text{Model 4: SRS-2} = \beta_0 + \beta_{Z_r} + \beta_{VCI}$$

The dependent variables are AQ and SRS-2 for models 3 and 4, respectively. The regression coefficient of the independent variable, the Fisher transformed Z-value of response reproducibility, is represented by the $\beta_{Z_r}$ in both models. One model was created for each response component that revealed a significant correlation between AQ and SRS-2: the click response neural variability ($\beta_{Z_{click}}$ ) and the offset response $\beta_{Z_{offset}}$ ) neural variability.

The covariance term, whose regression coefficient is represented by $\beta_{VCI}$ , is the verbal IQ. There was no significant relationship (at alpha <0.05) between $Z_{click}$ / $Z_{offset}$ or autistic trait measures and prestimulus noise or participant age from the correlation analysis; therefore, these variables were not entered into the model as additional covariance terms. However, VCI was significantly correlated with both AQ and SRS-2. The $\beta_0$ is the y-intercept.

After ordinary least squares was used to estimate the model coefficients, the model's statistics and overall model fit were assessed for statistical significance at an alpha level of 0.05 to test the hypothesis. The analysis of variance (ANOVA) provided an overall significance value for the entire model used to test if the model is a significant predictor of AQ or SRS-2 based on the *F* test.

The p-value for each model's $\beta_{Z_r}$ coefficient was evaluated to determine if neural variability was significant in predicting the AQ/ SRS-2 measure and test the null hypothesis ( $H_0$: $\beta_{Z_r} = 0$). The standard error of the estimate and the $R^2$ and adjusted $R^2$ value were also reported in the assessment of overall model strength when controlling for prestimulus noise.

### 3.6.1 Exploratory statistical analysis.

In an exploratory analysis, which was not the main focus of this study, analyses were conducted to determine if group differences existed between the degree of neural variability by response component and if there were different relationships between variability and autistic traits and sensory sensitivities by group. These analyses were performed as exploratory analyses because the power was limited due to the small sample size in the autistic group.

## 4.0 Results

Although 44 participants enrolled in the study, a full data set was not usable or collected from each participant due to various factors, including time constraints, patient fatigue, equipment, and recording complications, such as large amounts of artifacts and audiometric

**Table 2**

*Descriptive Statistics*

| | N | Min | Max | Mean | Std. Error of mean | Std. Deviation |
|---|---|---|---|---|---|---|
| SRS-2 | 37 | 38.00 | 90.00 | 59.11 | 2.55 | 15.52 |
| AQ | 43 | .00 | 46.00 | 21.56 | 1.91 | 12.53 |
| FSIQ | 41 | 83.00 | 143.00 | 110.41 | 2.02 | 12.95 |
| PRI | 41 | 88.00 | 160.00 | 109.51 | 2.19 | 13.99 |
| VCI | 41 | 73.00 | 134.00 | 109.24 | 2.24 | 14.35 |
| AUD-SOR | 38 | .00 | 18.00 | 5.92 | .86 | 5.28 |
| SOR | 38 | .00 | 40.00 | 16.50 | 1.90 | 11.70 |
| Neural Variability (Pearson's R) | | | | | | |
| Full Speech | 34 | .60 | .98 | .85 | .02 | .09 |
| Onset | 34 | .18 | .99 | .88 | .03 | .16 |
| FFR | 34 | .62 | .98 | .87 | .02 | .10 |
| Offset | 34 | .33 | .98 | .83 | .02 | .14 |
| Click | 41 | .59 | .99 | .93 | .01 | .08 |
| Neural Variability (Fisher's Z) | | | | | | |
| Full Speech | 34 | .70 | 2.23 | 1.37 | .06 | .36 |
| Onset | 34 | .19 | 2.83 | 1.68 | .10 | .58 |
| FFR | 34 | .73 | 2.28 | 1.48 | .07 | .43 |
| Offset | 34 | .35 | 2.44 | 1.34 | .08 | .44 |
| Click | 41 | .67 | 2.80 | 1.89 | .07 | .45 |
| Speech RMS | 34 | .02 | .23 | .07 | .01 | .04 |
| Click RMS | 41 | .01 | .33 | .09 | .01 | .05 |

*Note.* Table 2 provides the n size for each variable measured, as well as the following descriptive statistics: the minimum and maximum, mean, standard error of the mean and standard deviation. SRS-2 = Social responsiveness scale-2 total score; AQ = Autism Quotient total score; FSIQ = Full-scale IQ; PRI =Perceptual Reasoning Index; VCI = Verbal Comprehension Index; AUD-SOR= Auditory-sensory overresponsivity; SOR = Sensory overresponsivity; Full speech =neural variability of the entire sABR; click = neural variability of entire click ABR; Speech-RMS = prestimulus noise of the sABR; Click RMS = prestimulus noise of click ABR.

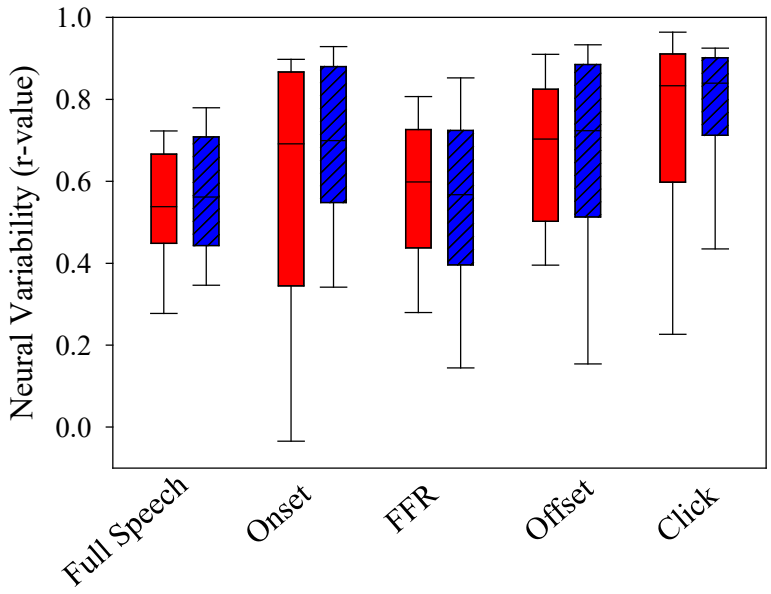
results. Table 2 displays descriptive statistics (the minimum and maximum, mean, standard error of the mean and standard deviation) and the number of participants for all data collected. The descriptive statistics of the neural variability ABR are displayed in two ways. First, the descriptive statistics are provided for the Pearson Correlation values (Pearson's R), and then the Fisher transformed Z- values (Fisher's Z) are displayed. Two participants did not have usable electrophysiological data because either one or both ears indicated abnormal peripheral hearing. Electrophysiology data was incomplete for three participants, and binaural sABRs in five participants had excessive noise (did not pass the F-test). Twenty-six participants had a complete data set (electrophysiological data, full audiometric test battery, all IQ measures, and surveys completed). Forty-one participants had usable click-ABRs and 34 had usable sABRs. Appendix G provides the average audiometric thresholds, otoacoustic emission levels, and right ear absolute and interpeak ABR latencies for the participants who had useable click-ABR and sABRs.

All the data in Table 2 passed the Kolmogorov-Smirnov and Shapiro-Wilk tests for normality except for speech prestimulus RMS and click Z. However, these data did pass the Kolmogorov-Smirnov test for normality when Lilliefor's criterion was not used (speech prestimulus RMS, $p=0.189$; click Z, $p=0.30$). Click-prestimulus RMS, AUD-SOR, and PRI did not pass the Shapiro-Wilk test for normality but did pass the Kolmogorov-Smirnov test. Additionally, a visual assessment of the Q-Q plots (see Appendix H, Figures H1-H5) was conducted to ensure that these data were normally distributed to meet assumptions for parametric statistics.

Figure 8 displays box-and-whisker plots for the degree of neural variability in each of the different ABR response components evoked by right (red solid boxes) and left (blue striped

**Figure 8**

*Box and Whisker Plot of Right and Left Neural Variability*




*Note.* Figure 8 displays a box and whiskers plot of the right (solid red boxes) vs left (striped blue boxes) neural variability. As indicated by the RMANOVA, there was no significant difference between responses.

boxes) ear stimulation. The box and whiskers represent the 5$^{th}$-95$^{th}$ percentile of data and the solid line across each box plot depicts the median value. A two-way repeated-measures ANOVA was performed to evaluate the effect of ear and response component on the degree of neural variability. Mauchly's test of Sphericity indicated that the assumption of sphericity for response component had been violated, $X^2$ (9) = 83.67, p= 0.000, and therefore degrees of freedom were corrected using Greenhouse-Geisser estimates of Sphericity ($\varepsilon$ = 0.599). The effect of the response component on the degree of neural variability was significant (F (2.395,76.636)= 11.710, p<0.0005), indicating that the degree of neural variability was dependent on the response component analyzed. There was no significant effect of ear (F(1,128)=0.118, p=0.734) or ear-by-response component interaction (p=0.704), supporting the use of binaural stimulation and combining recordings from the right and left ears for studying neural variability. A three-factor

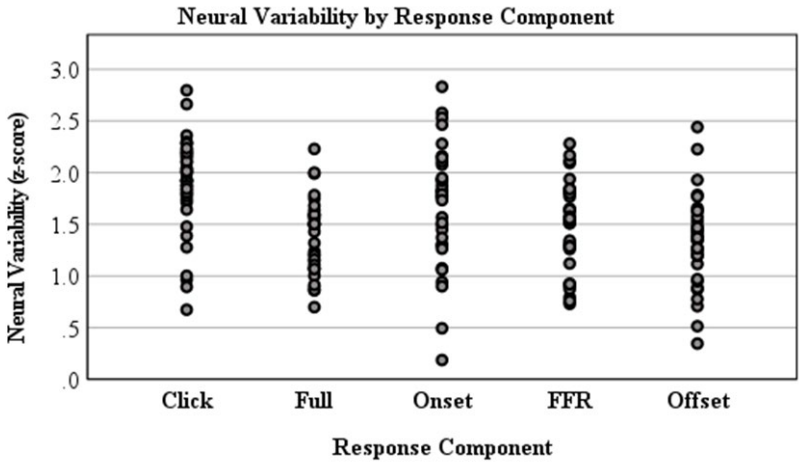
RMANOVA was also conducted with a between-participant factor of "group" (autistic vs. nonautistic participants) to see if evoked neural variability differed by ear of stimulation, response component and group. These findings were insignificant, indicating no effect of group ($F(1,1) = 0.321$, $p = 0.575$).

### 4.1 Specific Aim #1: There are Significant Differences in the Degree of Neural Variability by Response Component

Figure 9 depicts a dot plot illustrating the binaural neural variability in each response component. A repeated-measures ANOVA was performed to evaluate whether response components differed in the degree of neural variability. Mauchly's test of Sphericity indicated that the assumption of sphericity had been violated, $X^2$ (9) = 65.123, p= <.0005, and therefore degrees of freedom were corrected using Greenhouse-Geisser estimates of Sphericity ($\varepsilon = 0.653$). The effect of the response component on the degree of variability was significant alpha level 0.05, ($F(2.61, 86.15) = 17.82$, $p<0.0005$, partial $\eta 2=0.351$), indicating that the degree of neural variability was dependent on the response component analyzed. Post-hoc pairwise comparisons with a Bonferroni adjustment for multiple comparisons indicated that the click response was significantly more stable than all speech response components (full speech,

**Figure 9**

*Dot Plot of Binaural Neural Variability*




*Note.* Figure 9 displays a dot plot of binaural evoked neural variability (Fisher's z-value) for each response component (x-axis). All response components are significantly different from one another except for the following pairs: onset and click, offset and full, offset and FFR, and FFR and onset.

$p<0.0005$; FFR, $p<0.0005$; and offset, $p<0.0005$) except for the sABR onset. The degree of neural variability between the click and onset components was not significantly different ($p=0.403$). For speech components, there was no significant difference between the full speech and offset response ($p=1.00$) and between the FFR and onset response ($p=0.152$) and FFR and offset response ($p=0.249$), which had equal degrees of neural variability. The onset response was significantly higher (more stable) than the offset response ($p=0.018$) and the full response ($p=0.001$). The full response was significantly less stable than the FFR response ($p=0.011$).

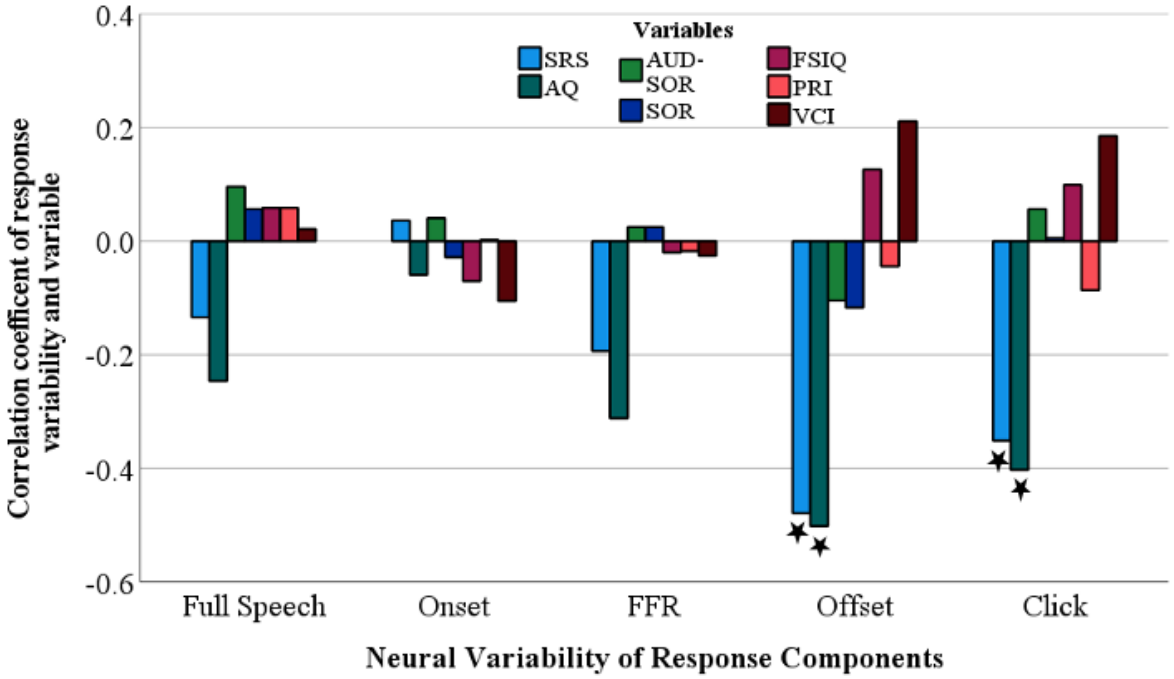
### 4.2 Specific aim #2: Neural variability is Not a Predictor of AUD-SOR or SOR

No participant demographic variables (age, r=-0.162; FSIQ, r=-0.80; VCI, r=-0.129; PRI, r=0.43) were significantly correlated with AUD-SOR or with SOR (age, r=-0.223; FSIQ, r=-0.158; VCI, r=-0.206; PRI=0.003) at an alpha level of 0.05. Therefore, it was concluded that these variables did not have to be entered as covariables in the regression analysis because they did not influence AUD-SOR or SOR. Similarly, there were no significant correlations between participant age and IQ and binaural evoked-neural variability. There were also no significant correlations between prestimulus noise and the neural variability of any response component or AUD-SOR/SOR measures.

Preliminary Pearson Correlations between response components and participant measures: IQ, AUD-SOR, SOR, SRS-2, and AQ are displayed in Figure 10. In Figure 10, the y-axis is the Pearson Correlation R-value and the x-axis shows the various response components, $Z_r$. Each bar represents a different participant measure (i.e., PRI, VCI, SOR, etc.), and the bar's direction indicates if the correlation is positive or negative. Table 3 displays all correlation values for each response component. Scatter plots depicting all response component correlations with AUD-SOR, SOR, AQ and SRS-2 are found in Appendix I. This preliminary analysis revealed no significant correlations between neural variability response components and AUD-SOR or SOR. Because there is no relationship between AUD-SOR/SOR and any $Z_r$, there would

**Figure 10**

*Pearson's Correlations between Participant Measures*




*Note.* Figure 10 displays the correlation coefficient of each response component for the various participant measures. Social Responsiveness Scale (SRS): blue; Autism Quotient (AQ): dark green; Auditory sensory overresponsivity (AUD-SOR): green; Sensory Overresponsivity (SOR): dark blue; Full-scale IQ (FSIQ): maroon; Perceptual Reasoning index (PRI): light pink; Verbal Compressive index (VCI): brown. Significant correlations are indicated by a star.

not be a significant predictive model of AUD-SOR or SOR incorporating any response components as a predictor variable.

**Table 3**

*Binaural Neural Variability Correlations*

| | | Full Speech | Onset | FFR | Offset | Speech RMS | Click | Click RMS |
|---|---|---|---|---|---|---|---|---|
| Age | Pearson r | .070 | .180 | .119 | .116 | -.440 | -.197 | -.500 |
| | Sig. (2-tailed) | .695 | .309 | .503 | .512 | **.009*** | .217 | **.001*** |
| | N | 34 | 34 | 34 | 34 | 34 | 41 | 41 |
| SRS | Pearson r | -.134 | .036 | -.194 | -.479 | -.216 | -.351 | .025 |
| | Sig. (2-tailed) | .481 | .849 | .305 | **.007*** | .252 | **.042*** | .889 |
| | N | 30 | 30 | 30 | 30 | 30 | 34 | 34 |
| AQ | Pearson r | -.246 | -.059 | -.312 | -.501 | -.139 | -.402 | -.040 |
| | Sig. (2-tailed) | .167 | .744 | .078 | **.003*** | .441 | **.010*** | .806 |
| | N | 33 | 33 | 33 | 33 | 33 | 40 | 40 |
| FSIQ | Pearson r | .059 | -.070 | -.020 | .126 | .159 | .099 | -.121 |
| | Sig. (2-tailed) | .750 | .703 | .914 | .492 | .385 | .554 | .470 |
| | N | 32 | 32 | 32 | 32 | 32 | 38 | 38 |
| PRI | Pearson r | .059 | .002 | -.017 | -.044 | -.008 | -.086 | -.044 |
| | Sig. (2-tailed) | .749 | .990 | .924 | .809 | .966 | .606 | .793 |
| | N | 32 | 32 | 32 | 32 | 32 | 38 | 38 |
| VCI | Pearson r | .021 | -.105 | -.026 | .211 | .242 | .185 | -.150 |
| | Sig. (2-tailed) | .908 | .566 | .888 | .246 | .182 | .266 | .370 |
| | N | 32 | 32 | 32 | 32 | 32 | 38 | 38 |
| AUD-SOR | Pearson r | .096 | .041 | .025 | -.105 | .205 | .056 | .035 |
| | Sig. (2-tailed) | .614 | .831 | .897 | .583 | .278 | .744 | .838 |
| | N | 30 | 30 | 30 | 30 | 30 | 36 | 36 |
| SOR | Pearson r | .057 | -.028 | .025 | -.117 | .202 | .005 | .127 |
| | Sig. (2-tailed) | .767 | .883 | .897 | .538 | .285 | .975 | .459 |
| | N | 30 | 30 | 30 | 30 | 30 | 36 | 36 |

*Note.* Table 3 provides the correlation and significant values between the various response components and participant variables. Correlations that are significant ($p<0.05$) are indicated by an * and bolded. SRS-2 = Social responsiveness scale-2 total score; AQ = Autism Quotient total score; FSIQ = Full-scale IQ; PRI =Perceptual Reasoning Index; VCI = Verbal Comprehension Index; AUD-SOR= Auditory-sensory overresponsivity; SOR = Sensory overresponsivity; Full speech =neural variability of the entire sABR; click = neural variability of entire click ABR; Speech-RMS = prestimulus noise of the sABR; Click RMS = prestimulus noise of click ABR.

No significant linear regression models predicted AUD-SOR or SOR. Therefore, it can be concluded that a binaural evoked neural variability measured in the brainstem in school-aged participants does not predict hypersensitivity in the auditory domain or across modalities. Because neural variability was not a predictor of sensory sensitives across modalities or in the auditory-only modality, no further analysis was necessary to answer the second hypothesis of specific aim #2.

### 4.3 Specific aim #3: The Neural Variability of the Offset of sABR and Click ABR are Significant Predictors of AQ and SRS-2

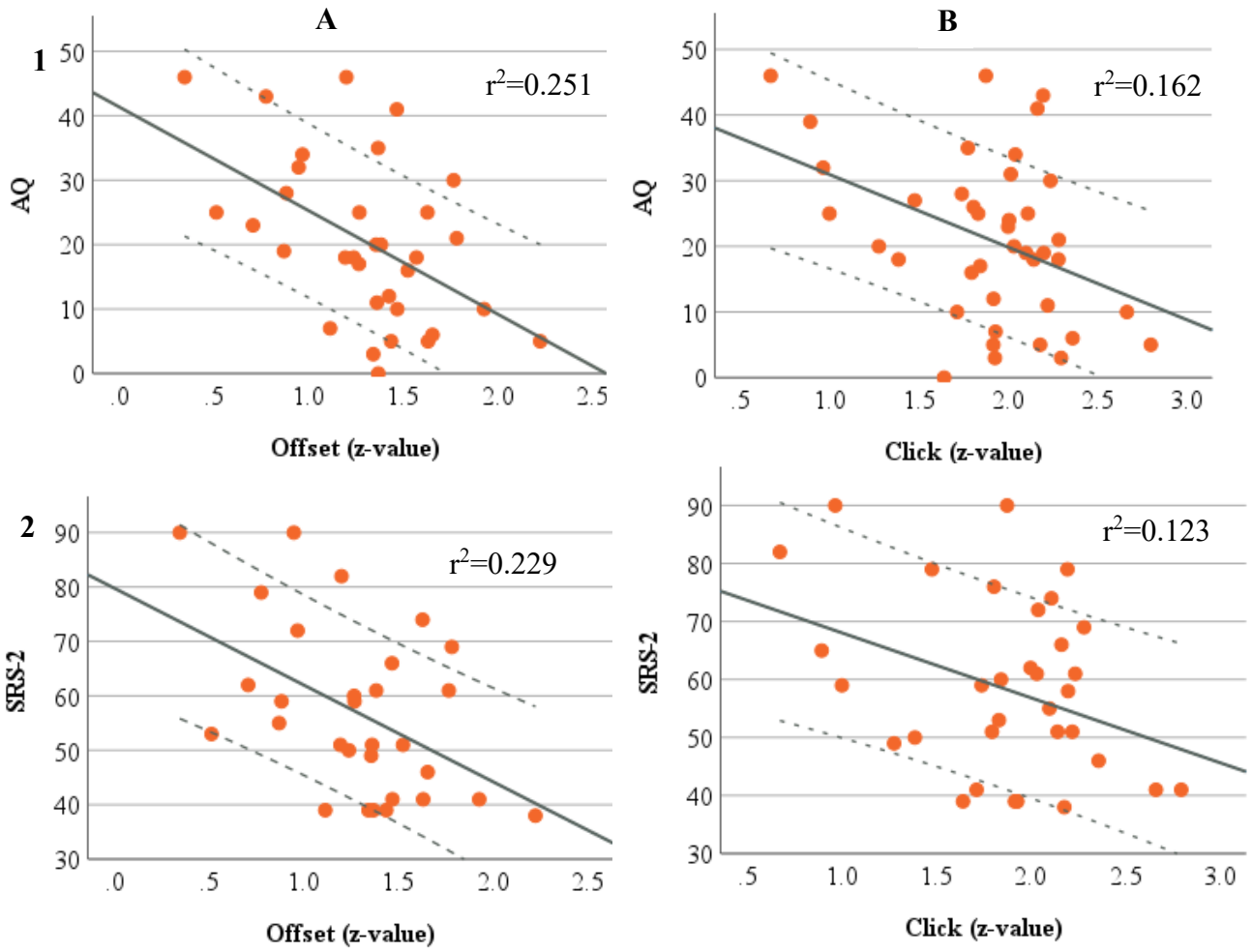
The preliminary analysis revealed that SRS-2 and AQ correlate with the neural variability of the click ABR and the offset response component of sABR. These four relationships between neural variability (click or offset response) and SRS-2 or AQ are depicted in Figure 11. Because these variables were significant correlators with AQ and SRS-2, the offset response component of the sABR and click response neural variability were the independent variables in the regression models.

Importantly, participant age was not significantly correlated with SRS-2 or AQ (SRS-2, $r=0.045$, $p=.792$; AQ, $r=.183$, $p=0.239$). AQ was significantly correlated with VCI ($r=-0.342$, $p=0.031$) but not FSIQ or PRI (FSIQ, $r = -0.185$, $p= 0.253$; PRI $r=0.145$, $p=0.373$). Therefore, VCI was entered into the model as a covariate to control for participant verbal comprehension in the prediction of AQ. Similarly, the SRS-2 was significantly correlated with VCI ($r=-0.486$, $p=0.003$) and FSIQ ($r=-0.389$, $p=0.21$). PRI was not significantly correlated with SRS-2 ($r=-0.057$, $p=0.745$). Because FSIQ is composed of both VCI and PRI and only the VCI was

significantly related to SRS-2, the VCI measure and not the FSIQ measure was used in the linear regression models predicting SRS-2.

**Figure 11**

*Pearson's Correlations with AQ, SRS-2, offset and click neural variability*




*Note.* Figure11 significant correlations between offset (column A) and onset (column B) neural variability and Autism Quotient scores (row 1) and Social Responsiveness Scale-2 scores (row 2). The dashed lines indicate the 75$^{th}$ percentile.

The measures of prestimulus noise (speech prestimulus RMS and click prestimulus RMS) were not significantly correlated with any response component or autistic trait measures (SRS-2 and AQ scores). Therefore, prestimulus noise was not included as a covariate in any model.

An important note is that the current study's SRS-2 and AQ scores were highly correlated ($r=0.88$, $p<0.0001$). Therefore, it was expected that the models of neural variability predicting the two measures of autistic traits were similar, serving as a robustness check.

### 4.3.1 Neural variability predicting AQ.

The first multiple regression was conducted to see if the neural variability of the offset response component of the sABR ($Z_{offset}$) and the covariates VCI predicted AQ scores in school-aged children. The data (dependent variable =AQ, predictor variable = offset response variability [$Z_{offset}$], covariable = VCI) met the assumption of non-zero variances (AQ variance = 156.97; Offset response variability, variance = 0.193; VCI, variance = 206.04). A multicollinearity test indicated that the data met the assumption of collinearity (tolerance = 0.955, VIF = 1.047). The residuals passed the Shapiro-Wilks test of normality ($W= 0.958$, $p=0.257$; the Q-Q plot and the scatterplot of residuals are illustrated in Figures H6 and H7, respectively, in Appendix H). The following model was tested:

$$\textbf{Model 5: AQ} = 62.245 + (-12.822 * Z_{offset}) + (-0.216 * VCI)$$

It was found that when controlling for VCI, offset neural variability explained a significant amount of the variance in AQ ($F (2, 29) = 6.501$, $p=0.005$, $R^2 = 0.310$, $R^2_{Adjusted} = 0.262$). Specifically, offset neural variability explained 20.2 % of the variance in AQ. The analysis indicates that the neural variability of the offset component negatively predicted the AQ after controlling for VCI ($\beta = -12.822$, $t (31) = -2.845$, $p= 0.008$); however, VCI did not significantly contribute to the model ($\beta = -0.216$, $t (31) = -1.564$, $p =0.129$). Table 4 displays the ANOVA table for model 5.

**Table 4**

*ANOVA for Model 5*

| Model | | Sum of Squares | df | Mean Square | F | Sig. |
|---|---|---|---|---|---|---|
| #5 | Regression | 1506.248 | 2 | 753.124 | 6.501 | .005 |
| | Residual | 3359.722 | 29 | 115.852 | | |
| | Total | 4865.970 | 31 | | | |

*Note.* Table 4 provides the Sum of Squares, degrees of freedom (df), Mean Square, F value, and significant value for model 5. The dependent variable for model five is AQ and the predictor variable is the neural variability of the offset component of the sABR with the covariate, VCI.

The second model evaluated the amount of variance in the AQ scores predicted by the neural variability of the click response ($Z_{click}$) after controlling for VCI. Once again, the data (dependent variable =AQ, predictor variable = click response variability [$Z_{click}$], covariable = VCI) met the assumption of non-zero variances ($Z_{click}$ variance = 0.20). A multicollinearity test indicated that the data met the assumption of collinearity (tolerance = 0.966, VIF = 1.035). The residuals passed the Shapiro-Wilks test of normality (W= 0.959, p=0.193; Q-Q plot and scatterplot of residuals are illustrated in Figures H8 and H9, respectively, in Appendix H). The following model was tested:

$$\textbf{Model 6: AQ} = 66.574 + (-9.843 * Z_{click}) + (-0.242 * \text{VCI})$$

It was found that when controlling for VCI, click neural variability explained a significant amount of the variance in AQ (F (2, 35) = 5.40, p=0.009, $R^2$ = 0.236, $R^2_{Adjusted}$ = 0.192). Specifically, click neural variability explained 12.3 % of the variance in AQ. The analysis indicated that the neural variability of the click response negatively predicted the AQ after controlling for VCI (β = -9.843, t (37) = -2.335, p= 0.025). VCI did not significantly contribute to the model (β = -0.242, t (37) = -1.841, p =0.074). Table 5 displays the ANOVA table for model 6.

**Table 5**

*ANOVA for Model 6*

| Model | | Sum of Squares | df | Mean Square | F | Sig. |
|---|---|---|---|---|---|---|
| #6 | Regression | 1369.562 | 2 | 684.781 | 5.400 | .009 |
| | Residual | 4438.208 | 35 | 126.806 | | |
| | Total | 5807.771 | 37 | | | |

*Note.* Table 5 provides the Sum of Squares, degrees of freedom (df), Mean Square, F value, and significant value for model 6. The dependent variable for model 6 is AQ and the predictor variable is the click neural variability with the covariate, VCI.

### 4.3.2 Neural variability predicting SRS-2.

Similar to the AQ models, the first multiple regression analysis found that the neural variability of the offset response component of the sABR ($Z_{offset}$) and the covariate VCI predict SRS-2 scores in school-aged children.

The data (dependent variable =SRS-2, predictor variable = offset response variability [$Z_{offset}$], covariable = VCI) met the assumption of non-zero variances (SRS-2 variance = 240.77). A multicollinearity test indicated that the data met the assumption of collinearity (tolerance = 0.955, VIF = 1.047). The residuals did not pass the Shapiro-Wilks test of normality (W= 0.930, p=0.03); however, as illustrated in Appendix H Figures H10 and H11, the residuals appeared to follow a normal distribution in the Q-Q and scatterplot, respectively). The following model was tested:

$$\textbf{Model 7: SRS-2= 125.285}+(\textbf{-13.917*}Z_{offset}) + (\textbf{-0.435*VCI})$$

From this model, it was determined that offset neural variability, after controlling for VCI, explained a significant amount of the variance in SRS-2 ($F(2,27) = 8.422$, $p = 0.001$, $R^2 = 0.384$, $R^2_{Adjusted} = 0.339$). The analysis shows that offset neural variability negatively predicted the SRS-2 after controlling for VCI ($\beta = -13.917$, $t(29) = -2.548$, $p = 0.017$). VCI also

significantly contributed to the variance of SRS (β = -0.435, t(29) = -2.548, p =0.015). Specifically, the neural variability of the offset response explained 15.5% of the variance in SRS-2 scores, while VCI explained 16.2% of the variance. Table 6 displays the ANOVA table for model 7.

**Table 6**

*ANOVA for Model 7*

| Model | | Sum of Squares | df | Mean Square | F | Sig. |
|---|---|---|---|---|---|---|
| #7 | Regression | 2682.398 | 2 | 1341.199 | 8.422 | .001 |
| | Residual | 4299.809 | 27 | 159.252 | | |
| | Total | 6982.207 | 29 | | | |

*Note.* Table 6 provides the Sum of Squares, degrees of freedom (df), Mean Square, F value, and significant value for model 7. The dependent variable for model 7 is SRS-2 and the predictor variable is the neural variability of the offset component of the sABR with the covariate, VCI.

For the second model predicting SRS-2 (dependent variable =SRS-2, predictor variable = click response variability [$Z_{click}$], covariable = VCI), the data met the assumption of non-zero variances and passed a test of multicollinearity (tolerance = 0.966, VIF = 1.035). The residuals passed the Shapiro-Wilks test of normality (W= 0.938, p=0.067). The Q-Q plot and scatterplot of residuals also agree with these results and are displayed in Appendix H (figures H12 and H13). The following model was tested:

$$\textbf{Model 8: SRS-2} = 79.26 + (-11.20 * Z_{click})$$

A test of model 8 indicated that the neural variability of the click ABR was a significant predictor of SRS-2 scores when controlling for VCI (F (2,31) = 6.860, p=0.003, $R^2 = 0.307$, $R^2_{Adjusted} = 0.262$). Importantly, however, the analysis indicated that click neural variability was not a significant predictor of SRS-2 (β = -9.392, t(33) = -1.777, p= 0.085) and accounted for only 7.2% of the variance in SRS-2 after controlling for VCI. VCI significantly contributed to the

variance of SRS and was a significant predictor (β = -0.471, t(33) = -2.865, p =0.007). VCI accounted for 19% of the variance in SRS-2. Table 6 displays the ANOVA Table for model 7.

**Table 7**

*ANOVA for Model 8*

| Model | | Sum of Squares | df | Mean Square | F | Sig. |
|---|---|---|---|---|---|---|
| #8 | Regression | 2437.581 | 2 | 1218.790 | 6.860 | .003 |
| | Residual | 5507.689 | 31 | 177.667 | | |
| | Total | 7945.270 | 33 | | | |

*Note.* Table 7 provides the Sum of Squares, degrees of freedom (df), Mean Square, F value, and significant value for model 8. The dependent variable for model 8 is SRS-2 and the predictor variable is the neural variability of the click ABR with the covariate, VCI.

## 4.4 Exploratory Group Analysis

**Table 8**

*Descriptive Statistics by Group (autistic vs. control group)*

| | Group | N | Mean | Std. Deviation | Std. Error Mean | t | Sig (2. tailed) |
|---|---|---|---|---|---|---|---|
| Age | ASD | 18 | 12.64 | 2.66 | .63 | -0.04 | 0.965 |
| | CG | 26 | 12.67 | 2.89 | .57 | | |
| SRS | ASD | 16 | 73.13 | 10.29 | 2.57 | 7.87 | 0.000* |
| | CG | 21 | 48.43 | 8.77 | 1.91 | | |
| AQ | ASD | 18 | 32.72 | 8.44 | 1.99 | 7.61 | 0.000* |
| | CG | 25 | 13.52 | 7.96 | 1.59 | | |
| FSIQ | ASD | 18 | 104.50 | 14.29 | 3.37 | -2.80 | 0.008 |
| | CG | 23 | 115.04 | 9.79 | 2.04 | | |
| PRI | ASD | 18 | 109.06 | 17.59 | 4.15 | -0.18 | 0.856 |
| | CG | 23 | 109.87 | 10.80 | 2.25 | | |
| VCI | ASD | 18 | 100.44 | 14.75 | 3.48 | -3.90 | 0.001* |
| | CG | 23 | 116.13 | 9.68 | 2.02 | | |
| AUD-SOR | ASD | 16 | 9.44 | 5.24 | 1.31 | 3.99 | 0.001* |
| | CG | 22 | 3.36 | 3.63 | .77 | | |
| SOR | ASD | 16 | 25.44 | 9.03 | 2.26 | 5.27 | 0.000* |
| | CG | 22 | 10.00 | 8.83 | 1.88 | | |

*Note.* Table 8 provides the descriptive statistics and t-test results of the participant measures by group. The significance value is adjusted for multiple comparisons (Bonferroni; alpha level= 0.006). **indicates a significant difference.* ASD= autistic participants, CG=nonautistic participants.

The descriptive statistics for age, AUD-SOR, SOR, the SRS-2, AQ, and all IQ measures (FSIQ, PRI, and VCI) for the autistic and control group, as well as the results of the independent sample t-tests are displayed in Table 8. The t-test results indicated that SRS-2, AQ, VCI, SOR, and AUD-SOR significantly differed between groups when the participants were categorized by autism diagnosis (autistic vs. nonautistic-control group). Descriptive statistics, including the minimum, maximum, mean, standard deviation, and standard error of the mean for the neural variability in each response component for each group, are found in Table 9.

**Table 9**

*Degree of Neural Variability in Each Response Component by Group*

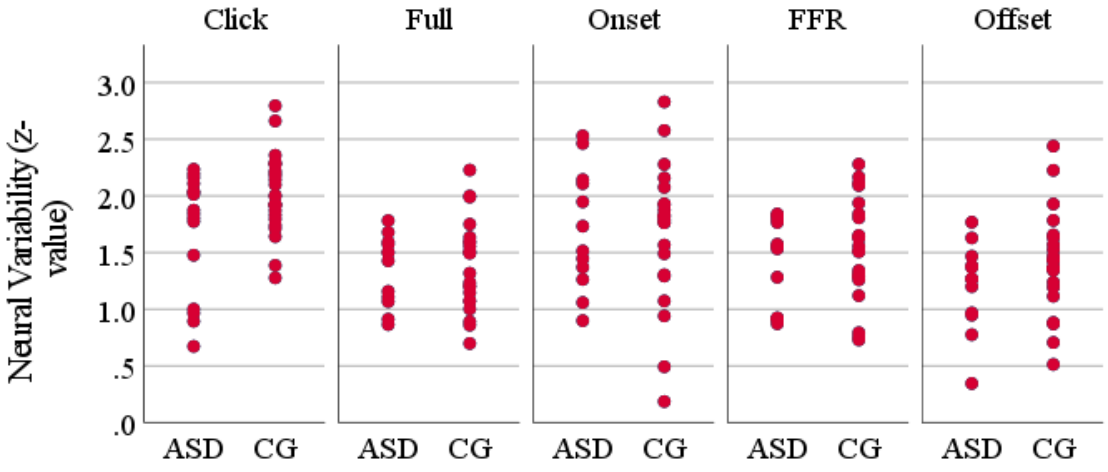
| | Group | Mean | Std. Deviation | Std. Error Mean |
|---|---|---|---|---|
| Neural Variability (Fisher's z) | | | | |
| Full Speech | ASD | 1.35 | .31 | .09 |
| | CG | 1.39 | .40 | .08 |
| Onset | ASD | 1.71 | .53 | .15 |
| | CG | 1.67 | .62 | .13 |
| FFR | ASD | 1.40 | .40 | .11 |
| | CG | 1.53 | .45 | .10 |
| Offset | ASD | 1.20 | .39 | .11 |
| | CG | 1.41 | .45 | .10 |
| Click | ASD | 1.69 | .52 | .13 |
| | CG | 2.02 | .35 | .07 |
| Prestimulus Speech RMS | ASD | .07 | .02 | .01 |
| | CG | .07 | .05 | .01 |
| Prestimulus Click | ASD | .10 | .07 | .02 |
| | CG | .09 | .04 | .01 |

*Note.* Table 9 provides the degree of neural variability in each response component by group, autistic vs. control. Full speech =neural variability of the entire sABR; click = neural variability of entire click ABR; Speech-RMS = prestimulus noise of the sABR; Click RMS = prestimulus noise of click ABR.

Figure 12 displays neural variability in each response component by group. A repeated-measures ANOVA was performed to evaluate the within-effect of response component on the degree of neural variability and between-effect of participant group. Mauchly's test of Sphericity indicated that the assumption of sphericity had been violated, $X^2(9) = 65.565$, $p<0.0005$, and therefore degrees of freedom were corrected using Greenhouse-Geisser estimates of Sphericity ($\varepsilon = 0.655$). As discussed in Specific Aim#1 results, the effect of the response component on degree of variability was significant ($F(2.62, 83.83)= 15.926$, $p<0.0005$, partial $\eta^2=0.332$), indicating that the degree of neural variability was dependent on the response component analyzed. However, there was no effect of group ($F(1,32) =0.921$, $p=0.344$, partial $\eta^2=0.028$) or significant group by response component interaction ($F(2.62, 83.83) = 1.029$, $p=0.377$, partial $\eta^2=0.031$).

**Figure 12**

*Response Component Neural variability by group*




*Note.* Figure 12 displays dot plot for each response component by group, autistic (ASD) and control (CG)

Pearson correlations analyses were conducted for each group between all response components and SOR, AUD-SOR, FSIQ, VCI, PRI, SRS-2, and AQ. These correlations are

found in Tables 10 and 11 for the nonautistic and autistic participants, respectively. Figure 12 illustrates the linear relationship between offset neural variability and AQ and SRS-2. Intriguingly, these relationships were different for each group. In the autistic group, the offset was significantly correlated with SRS-2 but not AQ. In the nonautistic control group, the offset was significantly correlated with AQ but not SRS-2.

**Table 10**

*Control Group Correlation Analysis*

| | | Full Speech | Onset | FFR | Offset | Speech RMS | Click | Click RMS |
|---|---|---|---|---|---|---|---|---|
| Age | Pearson r | .118 | .167 | .141 | .132 | -.442 | -.289 | -.476 |
| | Sig. (2-tailed) | .602 | .458 | .531 | .559 | **.039** | .162 | **.016** |
| | N | 22 | 22 | 22 | 22 | 22 | 25 | 25 |
| SRS | Pearson r | -.236 | -.135 | -.215 | -.410 | -.108 | -.032 | .084 |
| | Sig. (2-tailed) | .331 | .582 | .376 | .081 | .658 | .894 | .725 |
| | N | 19 | 19 | 19 | 19 | 19 | 20 | 20 |
| AQ | Pearson r | -.541 | -.313 | -.555 | -.603 | -.134 | -.376 | -.017 |
| | Sig. (2-tailed) | **.014** | .179 | **.011** | **.005** | .573 | .077 | .939 |
| | N | 20 | 20 | 20 | 20 | 20 | 23 | 23 |
| FSIQ | Pearson r | .048 | -.060 | -.150 | -.052 | .236 | .014 | .375 |
| | Sig. (2-tailed) | .840 | .801 | .529 | .829 | .316 | .949 | .086 |
| | N | 20 | 20 | 20 | 20 | 20 | 22 | 22 |
| PRI | Pearson r | .019 | -.037 | -.154 | -.082 | .039 | .115 | .366 |
| | Sig. (2-tailed) | .937 | .877 | .516 | .730 | .870 | .611 | .094 |
| | N | 20 | 20 | 20 | 20 | 20 | 22 | 22 |
| VCI | Pearson r | .068 | -.054 | -.101 | .009 | .386 | -.077 | .261 |
| | Sig. (2-tailed) | .776 | .820 | .671 | .970 | .093 | .733 | .240 |
| | N | 20 | 20 | 20 | 20 | 20 | 22 | 22 |
| AUD-SOR | Pearson r | .127 | -.085 | .282 | -.063 | .259 | .101 | -.119 |
| | Sig. (2-tailed) | .604 | .730 | .242 | .798 | .284 | .662 | .608 |
| | N | 19 | 19 | 19 | 19 | 19 | 21 | 21 |
| SOR | Pearson r | .029 | -.160 | .218 | -.095 | .224 | .012 | -.019 |
| | Sig. (2-tailed) | .907 | .512 | .369 | .697 | .357 | .960 | .935 |
| | N | 19 | 19 | 19 | 19 | 19 | 21 | 21 |

*Note.* Table 10 provides the correlations between the neural variability of the various response components and participant variables found among the nonautistic participants.

**Table 11**

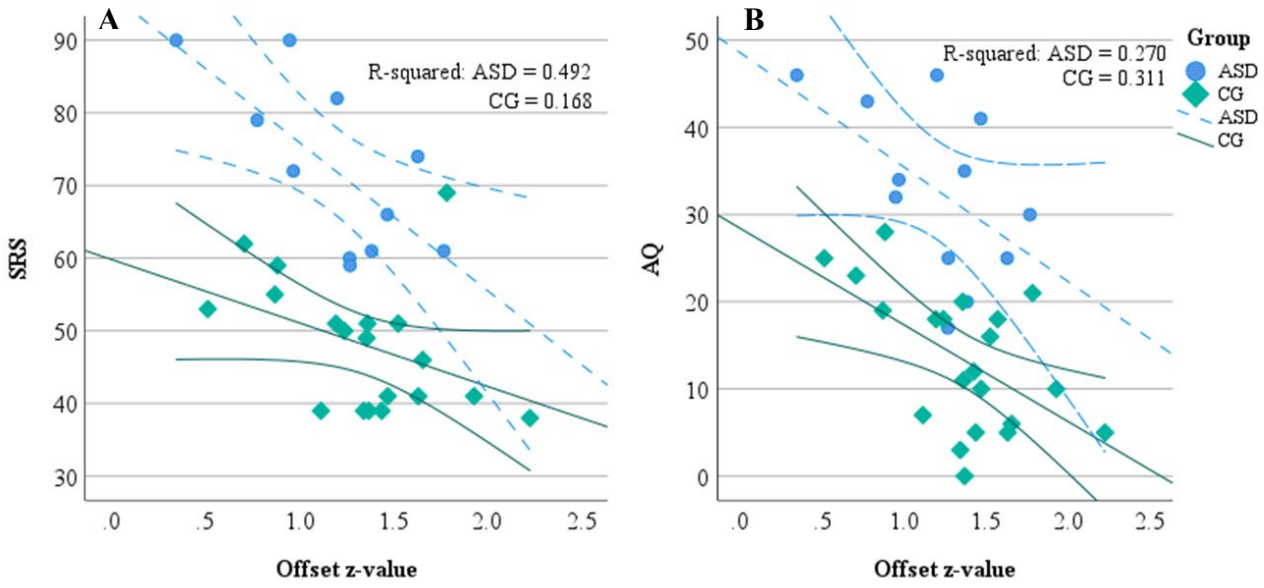
*Autistic Group Correlation Analysis*

| | | Full Speech | Onset | FFR | Offset | Speech RMS | Click | Click RMS |
|---|---|---|---|---|---|---|---|---|
| Age | Pearson r | -.090 | .223 | .044 | .054 | -.482 | -.198 | -.578 |
| | Sig. (2-tailed) | .780 | .486 | .892 | .866 | .113 | .462 | **.019** |
| | N | 12 | 12 | 12 | 12 | 12 | 16 | 16 |
| SRS | Pearson r | -.203 | -.018 | -.200 | -.701 | -.382 | -.211 | -.023 |
| | Sig. (2-tailed) | .550 | .959 | .556 | **.016** | .246 | .469 | .937 |
| | N | 11 | 11 | 11 | 11 | 11 | 14 | 14 |
| AQ | Pearson r | -.322 | -.148 | -.379 | -.520 | -.216 | -.173 | -.270 |
| | Sig. (2-tailed) | .307 | .647 | .224 | .083 | .499 | .522 | .313 |
| | N | 12 | 12 | 12 | 12 | 12 | 16 | 16 |
| FSIQ | Pearson r | .013 | -.086 | -.007 | .159 | -.044 | -.057 | -.335 |
| | Sig. (2-tailed) | .967 | .790 | .983 | .622 | .893 | .833 | .205 |
| | N | 12 | 12 | 12 | 12 | 12 | 16 | 16 |
| PRI | Pearson r | .150 | .040 | .182 | .081 | -.049 | -.194 | -.246 |
| | Sig. (2-tailed) | .642 | .901 | .571 | .801 | .879 | .472 | .358 |
| | N | 12 | 12 | 12 | 12 | 12 | 16 | 16 |
| VCI | Pearson r | -.180 | -.207 | -.236 | .144 | -.054 | .054 | -.297 |
| | Sig. (2-tailed) | .575 | .519 | .459 | .655 | .867 | .842 | .264 |
| | N | 12 | 12 | 12 | 12 | 12 | 16 | 16 |
| AUD-SOR | Pearson r | .077 | -.052 | -.209 | .232 | .356 | .401 | -.010 |
| | Sig. (2-tailed) | .822 | .880 | .537 | .493 | .282 | .139 | .971 |
| | N | 11 | 11 | 11 | 11 | 11 | 15 | 15 |
| SOR | Pearson r | .116 | -.184 | -.186 | .328 | .430 | .498 | .129 |
| | Sig. (2-tailed) | .733 | .588 | .584 | .326 | .187 | .059 | .646 |
| | N | 11 | 11 | 11 | 11 | 11 | 15 | 15 |

*Note.* Table 11 provides the correlations between the neural variability of the various response components and participant variables found among the autistic participants.

**Figure 13**

*Correlation between Offset Response Component and Autistic Traits by Group*




*Note.* Figure 13 displays the correlations between SRS-2 and offset neural variability (panel A) and AQ and offset neural variability (panel B). The correlations are displayed separately for each group.

## 5.0 Discussion

This study comprehensively analyzed ABR neural variability measured in 41 school-aged children. The findings revealed significant variations in neural variability based on the response component analyzed. While the results showed no significant predictive relationships between neural variability and sensory sensitivities, neural variability of the sABR offset response and entire click ABR predicted greater autistic traits after controlling for VCI. Specifically, the results showed that increased variability is associated with heightened total scores on AQ and SRS-2 in school-aged children with and without autism.

### 5.1 Calculating Neural Variability from ABR

Previous research that calculated neural variability of the ABR has provided limited information on the methodology for calculating neural variability aside from stating "by correlating the two subaverage waveforms, with *r* values closer to 1 representing more

morphologically coherent subaverages" (Hornickel & Kraus, 2013). Therefore, to ensure that the neural variability calculation made in the current study reliably reflects evoked neural variability of each participant, added methodological information and a lengthy discussion regarding the calculation steps are provided. Three factors were heavily considered in the calculation of neural variability in the present study: (1) the stimulus polarity, (2) avoiding a measure that reflects test-retest reproducibility, and (3) the effects of the recording channel (right versus left channel).

The stimulus polarity alternated between condensation and rarefaction stimuli presentation. The responses evoked by the alternating polarity stimuli were each stored in its own buffer: one for condensation responses and the other for rarefaction responses. Importantly, these response waveforms exhibit slight timing differences (Hall, 2007). Therefore, correlating condensation and rarefaction buffers to calculate neural variability would not reflect neural variability; instead, it would primarily capture the effects of stimulus polarity (as shown in Figure 6). Similarly, correlating the responses from the first set of recordings with the second would result in a "neural variability" measure representing test-retest reproducibility rather than trial-by-trial variations in neural fluctuations. Finally, a distinctive consideration in the current study when calculating neural variability was recording responses over two different channels and testing whether neural variability was different for right and left ear stimulation.

To eliminate these possible effects on the calculation of neural variability, the opposite channel (right vs. left) condensation and rarefaction buffers, composed of sweeps from the first and second trials, were averaged together. This approach enabled a linear relationship (Pearson Correlation) to be calculated between these waveforms, resulting in a correlation value that genuinely represented neural variability, free from the effects of stimulation, hemisphere, or response reproducibility.

Another potential confounder of neural variability is participant noise, which can be measured in a number of ways (Hall, 2007). For the current study, two ways were utilized: prestimulus noise and the number of artifacts during recording. However, the analysis revealed that neither the number of artifacts during recording nor prestimulus noise correlated significantly with the neural variability calculation in the current study or autistic traits and sensory sensitivity measures.

### 5.2 Differences Between Response Components

A key finding in the current study was the significant difference in degree of neural variability based on the analyzed response component. As anticipated, the stability of the click response significantly differed from that of all speech components except for the onset response component. This observation is significant as it affirms that neural variability is related to the location within the auditory brainstem pathway where the response is generated or to the characteristics of evoking stimuli. The onset component of the speech stimuli and the click response are thought to originate from the same neural nuclei and are analogous (e.g., Song et al., 2006). The onset response to speech ABR primarily reflects the gross neural response to the brief onset burst of sound, akin to brief transient click stimuli. Consequently, it is logical that the degree of neural variability in these two response components aligns closely.

Another noteworthy finding from the analysis of neural variability across different response components is the significant variability observed between the individual speech response components. Previous research has often focused solely on analyzing the neural variability of the FFR response component, neglecting the other portions of the sABR. Given the observed differences in neural variability based on the response component, in conjunction with

the results from the models in the current study, it is evident that previous research might have overlooked valuable findings by restricting the analysis to a single component of the sABR.

While the FFR component of the response is typically evaluated because it provides a measure of how well the neural system phase-locks to the fundamental frequency ($F_0$) of the vowel and its harmonics, when analyzed in the time domain, these factors do not significantly influence the degree of neural variability. Examining the degree of phase-locking provides a measure of speech-ABR encoding in terms of both timing and latency in reference to the evoking stimuli. Calculating neural variability is rooted in estimating the linear relationship between two subaverage response waveforms, providing insights into the trial-to-trial changes in neural fluctuations, irrespective of their relation to the fundamental frequency. Consequently, the FFR should not be the only component analyzed, and the current study further underscores the value of examining other response components, specifically the offset response component.

### 5.3 Predicting Sensory Sensitivities

The current study aimed to see if sensory sensitivities could be predicted by evoked neural variability. The current study found that sensory sensitivities, as measured by the SOR and AUD-SOR, did not significantly correlate with any response components. Consequently, the response component could not serve as a predictor of sensory sensitivities, and therefore, a predictive model was not constructed. The primary conclusion is that brainstem neural variability, elicited binaurally by click and speech stimuli, does not predict parent-reported sensory overresponsivities, either when assessed across sensory modalities or within an auditory-only modality. There are three potential caveats to consider when interpreting these results. Firstly, the lack of correlation between neural variability and sensory sensitivities might stem from the objective nature of the neural variability measure contrasted with the parent-reported

measures. It is plausible that an objective behavioral measure of sensory sensitivities would exhibit a relationship with neural variability; however, the absence of an appropriate measure of hypersensitivities in school-aged children with autism complicates such an investigation. It should be noted that research has suggested measuring the medial olivocochlear reflex through otoacoustic emission suppression as a potential method for objectively measuring hyperacusis in autistic children (Wilson et al., 2017). Future studies may consider correlating neural variability with a physiological measure of hyperacusis to evaluate the relationship between auditory sensitivities and neural variability. Secondly, it is possible that neural variability does not predict hypersensitivity but rather seeking or hyposensitivity. To explore this possibility, a subsequent analysis involving measures of hyposensitivity and seeking derived from the SP was conducted. This analysis also did not reveal significant relationships with any response component (see Appendix J for these findings).

The final caveat distinguishing this study from prior research is that the neural variability was assessed through right and left channels with ears stimulated binaurally. Monaural stimulation might yield different relationships between neural variability and sensory sensitivity. However, the correlation analysis involving right ear neural variability and sensory sensitivities does not suggest such a difference (see Appendix F). Additionally, it is possible that because the binaural analysis included a total of 6000 sweeps, averaging such a large number of sweeps together smoothed out small amounts of intraindividual noise. This over-averaging could have diminished the range of variability measured across participants and consequently eliminated potential correlations with sensory sensitivities. Future research should consider investigating how the number of sweeps included in the calculation of neural variability influences the

measure and possibly use a lower number of sweeps in their calculation to explore how it relates to sensory sensitivities.

### 5.4 Predicting Autistic Traits

An innovative aspect of the current study was the exploration of brainstem neural variability as a predictor of autistic traits. Autistic traits were measured using parent-reported surveys, specifically the SRS-2 and AQ. As outlined in the introduction, the AQ total score comprises items related to restricted repetitive behaviors and social communication, including imagination, attention, and attention switching (Baron-Cohen et al., 2001). The SRS-2 primarily focuses on a child's social interaction and communication abilities but also contains a restricted repetitive behavior component (Bruni, 2014). The analysis revealed that the offset response and the entire click response were the only two response components significantly correlated with either measure of autistic traits. Therefore, these two measures were incorporated into linear regression models with the covariate VCI, which was also correlated with SRS and AQ.

The models, including the offset response's neural variability and VCI as a covariate, significantly predicted SRS-2 and AQ scores. Specifically, the models that included the neural variability of the offset response component explained 31.0% (26.2% adjusted) of the variance in AQ scores and 38.4% (33.9% adjusted) of the variance in SRS-2 scores. In contrast, the click neural variability and VCI accounted for 23.6% (19.2% adjusted) of the variance in AQ scores and 30.7% (26.2% adjusted) in SRS-2 scores. However, click neural variability was not a significant predictor in the model predicting SRS-2. Two things were evident from these results: first, the models that included the click neural variability as a predictor were weaker than the offset neural variability models, and second, VCI had a greater influence on the models predicting SRS-2.

The offset neural variability emerged as the stronger predictor of autistic traits overall. The offset response in sABR signifies sound termination (Skoe & Kraus, 2010). These responses are generally less salient than sound onsets (Phillips et al., 2002) and may be associated with specific offset pathways throughout the auditory pathway, distinct from onset response pathways (Kopp-Scheinpflug et al., 2018). These offset pathways may be particularly relevant to auditory processing deficits associated with disease and aging (for review, see Kopp-Scheinpflug et al., 2018).

Offset responses play a crucial role in the temporal processing of sounds (Anderson et al., 2013; Rocha-Muniz et al., 2014; Sayegh et al., 2011) and neural offset recordings contribute to various perceptual tasks, including perceptual grouping (Bregman, 1994), duration discrimination (Li et al., 2021), gap detection (Kopp-Scheinpflug et al., 2018; Solyga & Barkat, 2021), and consonant discrimination (Lisker et al., 1977). Many of these tasks are known to be impaired in individuals with autism (e.g., Bhatara et al., 2013; Foss-Feig et al., 2017, 2018). Therefore, the findings in the current study highlight the significance of the offset response component in auditory processing, specifically related to autism and autistic traits.

Further research is needed to elucidate the precise mechanisms through which unstable offset neural responses may contribute to these perceptual challenges. A potential explanation may be because offset responses are generated in the superior olivary complex within the auditory brainstem pathway (Kopp-Scheinpflug et al., 2018), which is known to exhibit anatomical differences in autistic individuals (Kulesza et al., 2011; Kulesza & Mangunay, 2008; Lukose et al., 2011). As a result, further investigation is warranted to explore the relationship between unstable offset responses, autistic traits, and perceptual challenges involving the processing of offset responses.

VCI was more influential in the models that predicted SRS-2 scores. This finding suggests that although the AQ and SRS-2 surveys are similar, they have subtle differences. Because the SRS-2 is composed mainly of measures related to communication, whereas the AQ is composed of multiple measures unrelated to communication, there was a greater influence of VCI on the SRS-2 score.

### 5.5 Exploratory Group Analysis

Although the primary focus of the current study did not center on comparative group analysis, an exploratory, mixed repeated measures ANOVA was used to assess whether neural variability, when evoked binaurally, differed between autistic and nonautistic children. The analysis indicated that while neural variability varied by response component, the two groups did not exhibit significant differences. These findings contrast with some prior studies that reported less stable responses in autistic children when evoked via the right ear compared to nonautistic children (Otto-Meyer et al., 2018; Patel et al., 2022). The results of the exploratory analysis in the current study align more closely with Tecoulesco et al. (2020), who reported no difference in neural variability in the FFR portion of the speech ABR between autistic and nonautistic children. The present findings suggest that examining relationships allows for exploring heterogeneity not captured by conventional group comparisons. The significant models found by combining autistic and nonautistic participants emphasize that individual differences in neural variability relate to meaningful differences in autistic traits. Specifically, decreased stability is related to greater autistic traits. This individual variation, which is often overlooked in group comparisons, can provide valuable insights into how neural processing contributes to the range of autistic traits.

The results of the current study also highlight the potential reasons for conflicting findings in studies comparing groups of autistic and nonautistic individuals, specifically in auditory brainstem studies. Autistic traits can vary significantly both within autistic individuals and across the general population. When comparing groups, the extent to which these traits overlap might explain the absence of significant differences in some cases. This study demonstrated that autistic traits are linked to neural variability. Consequently, if groups overlap in autistic traits, there might also be a corresponding overlap in the measure being studied, such as neural variability, which can lead to the lack of significant differences between groups in that particular measure.

Notably, the exploratory group analysis revealed different correlation strengths between neural variability (offset response) and autistic traits (SRS-2 and AQ) depending on whether the relationships were analyzed across groups or within individual groups. Both relationships were strong and significant in combined group analysis, while within-group analysis exhibited varying correlation strengths.

Specifically, in nonautistic individuals, greater neural variability was related to greater autistic traits measured by the AQ (Pearson R of -.6); however, it should be noted that this relationship does not survive a Bonferroni correction of multiple comparisons. Conversely, within the autistic group, greater neural variability in the offset response was associated with more severe social communication deficits, quantified by the SRS-2 (Pearson R of -.7); once again, this relationship did not survive Bonferroni correction.

The results from individual groups imply that nonautistic individuals with higher variability (less stable responses) exhibit a greater degree of autistic traits, primarily measured by the AQ rather than the SRS-2. This observation may be attributed to recent findings suggesting

that the AQ is a superior predictor of autism compared to the SRS-2 (Bezemer et al., 2021). Therefore, decreased neural stability may be more "autistic" and individuals with less stable responses possess more autistic qualities than those with more stable responses. In the autistic group, greater degrees of variability (indicating less stability in neural responses) are associated with heightened autistic traits measured by the SRS-2. This association may be influenced by the fact that the SRS-2 scores have a greater range of variability within the autistic group compared to the AQ (SRS-2 standard deviation = 10.3, variance = 106.0; AQ standard deviation = 8.4, variance = 71.3), allowing for more significant correlations between values. It is also plausible that within the autistic group, the degree of neural variability is more closely related to social communication skills than other autistic traits. As previously stated, the SRS-2 survey focuses on questions about social communication and pragmatic language abilities. Conversely, the AQ encompasses a broader range of questions, including items related to attention to detail and imagination.

Interpreting these findings collectively, one might conclude that individuals with greater neural variability (less stability) in their sABR offset response tend to exhibit more autistic traits. However, upon closer examination of the relationship between the offset response and autistic traits within the autistic group, it becomes evident that autistic individuals who have more pronounced social communication deficits have the most unstable offset responses. It is essential, however, to acknowledge that the size of the autistic group in these correlations was small (n=11); consequently, these findings remain exploratory and warrant replication in a larger sample of subjects to draw definitive conclusions.

## 6.0 Limitations

The present study has limitations that may have impact the findings and generalizability of the outcomes. First, sensory sensitivities were measured via a parent-report survey (SP) rather than through behavioral measures. While using the SP is common within the literature, the absence of significant findings between SOR/AUD-SOR and neural variability might be attributed to the chosen measurement method. Consequently, the results may not be extendable to behavioral assessments of sensory sensitivities, where a significant relationship might have emerged.

Furthermore, the scores range for participants on the SOR was relatively constrained (0-40), and a more expansive range (e.g., 0-70) among a different set of participants could have yielded more informative results. Another noteworthy limitation is the limited variation in items assessing auditory overresponsivity using the SP. Only two out of five items directly inquired about hypersensitivity, potentially overlooking children who may exhibit hypersensitivity without the combination of overt behavioral responses of responding negatively to unexpected or loud noises (item#34) and holding their hands over their ears to protect from sound (item#35). Increasing the number of items focusing on hypersensitivity or auditory DSTDs could have provided a more comprehensive score of AUD-SOR.

A substantial constraint in the study is the restricted diversity among participants, which limits the generalizability of the results. Most participants were Caucasian and had at least one parent with some education beyond high school. Therefore, this sample was not representative of the broader population. Additionally, all participants were required to have a full-scale IQ greater than 80, which limits the inclusion of autistic individuals with below-average IQ. Autistic individuals are highly heterogenous in their IQ. Although the results are conflicting regarding the exact IQ percentages for autistic individuals (Wolff et al., 2022), it is understood that there is a

large percentage of autistic individuals with a below-average IQ. The relationship between neural stability and IQ may be nuanced and warrant exploration in future studies. Although full-scale IQ did not exhibit a significant correlation with any response components, as evident in Figure 10, a potential positive relationship may emerge between FSIQ and the click and offset if a greater range of IQ existed among the participants included. Future research should include participants with a full-scale IQ below 80 to enhance the generalizability of findings, as the current results can only be generalized to individuals with an IQ above 80.

## 7.0 Conclusion

This study explored neural variability within the auditory brainstem pathway via ABR, which shed light on the intricate relationship between stimulus characteristics, response components, sensory sensitives, and autistic traits. Notably, this research introduced innovative methodology by measuring neural variability from binaural stimulation. A key finding was the significant variation in neural variability based on when the response was analyzed within the sABR post-stimulus onset. The difference in neural variability between the response components challenges the traditional method, which focuses on analyzing the FFR component of the sABR alone. The comparison between the degree of neural variability in the onset sABR and click ABR, which demonstrated no significant difference, supports the established literature that neural variability is linked to either characteristics of the stimuli or the neural source of generation.

Contrary to expectations, brainstem neural variability, elicited by both click and speech stimuli, did not predict parent-reported overresponsivities, either in a multimodal or auditory-only domain. In contrast, examining the link between neural variability and autistic traits yielded intriguing results. The entire click response and, notably, the offset response component emerged

as predictors of autistic traits, with the latter exhibiting stronger predictability. Specifically, less stable neural responses indicate heightened autistic traits, measured by the SRS-2 and AQ. These findings underscore the significance of auditory processing in shaping autistic traits and hint at a nuanced relationship between decreased neural stability in response to sound cessation and increased autistic traits.

While the current study illustrated the link between neural stability in auditory processing in the brainstem and autistic traits, especially concerning individual differences, the results necessitate further exploration within a larger cohort better representative of the general and autistic population. Overall, this research not only emphasizes the importance of comprehensively examining neural variability in the auditory brainstem (including onset/offset responses and not only the FFR component, as is the focus of most current research) but also advocates for a paradigm shift from traditional case-control group analyses to individualized predictive modeling studies that account for individual differences, particularly in heterogenous conditions like autism.

# Appendix A

## Cortical Measure of Neural Variability in Autism

An increase in neural variability, or greater intra-individual variability, has been documented in autistic people at the level of the cortex through measures of fMRI, magnetoencephalography (MEG) and electroencephalogram (EEG). Dinstein et al.(2012) found higher trial-by-trial variation in blood-oxygen-level dependent (BOLD) responses and lower signal-to-noise ratios in cortical areas in response to visual, auditory, and somatosensory stimuli in adults with autism compared to matched controls, even though the amplitude of responses were indistinguishable from the two groups. Importantly, there was no significant difference between groups (autism and CG) in ongoing neural variability suggesting that increased neural variability in the autism group was specifically associated with sensory processing. These findings have been replicated, confirming a presence of increased intra-individual variability measured via BOLD signals in response to sensory stimuli in people with autism (Haigh et al., 2015). Another fMRI study that examined trial-by-trial variability in BOLD signals following a speech production task, found that responses were significantly more variable in autistic people than those without autism. This study also found that the degree of variability was significantly related to ADOS calibrated severity scores, such that a greater degree of variability is associated with higher autism severity ratings (Murray et al., 2022). These studies support that there is a relationship between neural variability at the level of the cortex and autism symptomology.

Electroencephalogram measures in adolescents with autism also show increased variability in response to visual stimuli. One of the first studies to evaluate EEG intra-individual variability assessed the P1 from a visual evoked potential (VEP) in autistic adolescents (Milne, 2011). Specifically, the researchers assessed the variability of the median absolute deviation of

P1 amplitude and latency by calculating the inter-trial phase coherence in the frequency domain. The authors found that the group of autistic teens had greater P1 amplitude and latency variability and a lower inter-trial phase coherence compared to the group of nonautistic teens. Further, the individuals in the study had to press a button in reaction to an odd visual stimulus (i.e., image of zebra). The authors quantified the amount of time it took for the participants to react to the image and correlated it to the measure of neural variability. Although there was no significant difference in reaction time between the groups, there was a significant relationship between reaction time variability and peak amplitude variability of P1 ($r_S(22) = 0.479$, $p = 0.024$), suggesting that neural variability is related to behavioral measures.

Neural variability has also been found in response to auditory stimuli. Lower inter-trial coherence was found in a MEG study of the superior temporal gyrus in response to 500 and 1000 Hz tones in a group of autistic children (n=52) compared to a group of nonautistic children (n=63) (Edgar et al., 2015). Greater neural variability has also been noted in auditory evoked mismatch negativity in autistic adults (n=24) compared to nonautistic adults (n=28). Although, the authors found no significant correlations between ADOS calibrated severity scores or IQ with trial-by-trial variability, they suggest a possible relationship between neural variability and sensory sensitivities (Haigh et al., 2022a). Similarly, in another study, Haigh et al. (2022b), found greater degrees of variability in an MMN auditory-evoked task in autistic adults and adults with schizophrenia compared to a CG. The authors suggest that variability in processing simple stimuli combined with hyperactive neural responses evoke overwhelming feelings in individuals leading to atypical subjective sensory sensitivities (Haigh et al., 2022a).

To date, only one study has specifically looked at neural variability in the cortex in relation to Decreased Sound Tolerance Disorders (DSTDs). This study found that increased

levels of neural variability in the cortex measured by inter-trial phase coherence elicited by 50 dB HL stimuli was associated with an increased estimate of loudness discomfort level (LDL). Although these researchers did not find greater neural variability between groups of autistic and nonautistic individuals, they found that increased neural variability was positively correlated with a measure of estimated LDLs ($p=0.027$). This supports the idea that greater neural variability is related to auditory-sensory sensitivities (Dwyer et al., 2022). In summary, these cortical studies suggest that increased neural variability is a key feature of sensory processing in autism that may have behavioral consequences.

It is important to note that some studies found no differences in the degree of neural variability between groups of autistic and nonautistic individuals (Butler et al., 2017; Dwyer et al., 2022). The lack of support for increased neural variability in groups of autistic individuals emphasizes the importance of conducting statistical analysis that adequately assess the heterogeneity that exists among people with autism. In case-controlled, group-difference statistical designs, the participants are often matched on age, gender and sometimes IQ, but the heterogeneity of autistic characteristics is overlooked.

# Appendix B

**Items from the SP used to calculate Sensory Overresponsivity (SOR)[5]**

Tactile Sensitivity Items:

1. [item #1] Express distress during grooming
2. [item #4] Reacts emotionally or aggressively to touch
3. [item #7] Rubs or scratches out a spot that has been touched

Auditory Filtering Items:

4. [item #22] Is distracted or has trouble functioning if there is a lot of noise around
5. [item #23] Appears to not hear what you say
6. [item #24] Can't work with background noise
7. [item #25] Has trouble completing tasks when the radio is on
8. [item #26] Doesn't response when name is called but you know the child's hearing is OK
9. [item #27] has difficult paying attention

Visual/auditory sensitivity

10. [item #34] Response negatively to unexpected or loud noises
11. [item #35] Holds hands over ears to protect from sound
12. [item #36] Is bothered by bright lights after others have adapted to the light
13. [item #37] Watches everyone when they move around the room
14. [item #38] Covers eyes or squints to protect eyes from light

[5] This measure was created by Green et al., 2015 and are listed in table 2 in McKernan et al., 2020.

# Appendix C

**Loudness discomfort levels are not a viable option to measure sensory overresponsivitiy**

There is a lack of standardized assessment guidelines for hyperacusis or DSTDs (Bigras et al., 2022). Audiologists base their diagnosis of DSTDs on a combination of parent-report history and behavioral measures such as: patient's reason for consultation, case history report, loudness discomfort levels (LDL), and questionnaires. Loudness discomfort levels are a behavioral response in which a patient/participant will indicate that a sound is at a level that is loud to them and causes discomfort. One study reported that patients with hyperacusis, have a LDL ≤77 dB HL averaged across pure tone frequencies of 0.25, 0.5, 1, 2, 4, and 8 kHz (Aazh & Moore, 2017). However, use of LDLs as a measurement to indicate hyperacusis is problematic. In a study of 381 participants, LDLs to pure tones were highly variable, and it was concluded that they are neither specific or sensitive for diagnosing hyperacusis (Sheldrake et al., 2015). Similarly, another study with 62 participants found inconsistent patterns in the relationships between LDLs and questionnaire measures of hyperacusis (Jüris et al., 2013). This may be why in a recent scoping review of articles on auditory evoked potentials (AEP) and hyperacusis, Bigras et al. (2022) found that only four out of 35 articles reviewed used LDLs to assess hyperacusis in their participants, and the most popular method in research studies was questionnaires. Particularly, it was noted that in studies that assessed hyperacusis and AEPs in autistic individuals, a version of the SP was used.

The preferred method for assessment of hyperacusis in autistic children is behavioral observation, case history, and subjective measures, such as the SP. Measurements of LDLs are unreliable for various reasons, such as differences in how individuals interpret verbal directions, ability to communicate uncomfortable levels, and overall variability in behavior responses

(Danesh et al., 2021). Morally, asking participants, specifically children, who have auditory sensory sensitivities, such as hyperacusis, is questionable. It would be uncomfortable for the participant to tolerate even short bursts of tones at high intensity levels. Additionally, instructing a young child to sit still in anticipation of hearing loud tones may cause the patient to experience anxiety and anxiousness that could otherwise be avoided by the use of questionnaires.

# Appendix D

## Items from the SP used to calculate an auditory-only measure of sensory overresponsivity (AUD-SOR)

Auditory Filtering Items:

1. [item #22] Is distracted or has trouble functioning if there is a lot of noise around
2. [item #24] Can't work with background noise
3. [item #25] Has trouble completing tasks when the radio is on

Visual/auditory sensitivity

4. [item #34] Response negatively to unexpected or loud noises
5. [item #35] Holds hands over ears to protect from sound

# Appendix E

## Click ABR Latencies in Group Comparisons (Autistic versus Control Groups)

The click ABR has been of particular interest in investigating auditory processing in autistic individuals. Some research suggests that when group comparisons are made between autistic people and those without autism, the autistic groups have prolonged click-evoked ABRs compared to CGs (Azouz et al., 2014; Delgado et al., 2023; Fujikawa-Brooks et al., 2010; Gillberg et al., 1983; Kwon et al., 2007; Maziade et al., 2000; McClelland et al., 1992; Miron et al., 2016, 2021; Rosenhall et al., 2003b; Skoff et al., 1980; Tanguay et al., 1982; Tas et al., 2007; Taylor et al., 1982; Thivierge et al., 1990; Wong & Wong, 1991). However, not all studies find group differences in click evoked ABR latencies between groups of individuals with and without autism (e.g., Courchesne et al., 1985; Dabbous, 2012; Rumsey et al., 1984; Russo et al., 2009). One possible reason for conflicting results may be due to an increase in response variability of the click ABR recorded from autistic people. Increased variability of the neural response could lead to changes in ABR waveform morphology, such as broader peaks, which could influence the latency of the response. Therefore, it is possible that poorer morphology of the ABR in autistic groups contributes to the contrasting findings among studies. Supporting this idea is that the standard deviations of ABR peak latencies in groups of autistic individuals are larger than the standard deviations of the CG (Delgado et al., 2023; Miron et al., 2021; Ramezani et al., 2019). These findings could be linked to neural variability and support that there is a relationship between auditory brainstem processing and heterogenous factors associated with autism (such as sensory sensitivity and autistic traits).

**Speech ABR Latencies in Group Comparisons (Autistic versus Control Groups)**

The complexity of a speech token may tax the auditory system more than a click stimulus, resulting in a higher probability of detecting subtle timing differences. That being noted, there have only been a few studies that analyze sABR latencies between groups of autistic and nonautistic people, and results vary among studies. Russo et al. (2009) examined sABR in 21 autistic children and 18 children without a diagnosis of autism  aged 7-13 years. Responses were evoked in quiet and noise conditions. They found many significant differences in the sABR between the groups, including significantly prolonged absolute latencies of waves V, A, D, and F and a prolonged VA interpeak interval in the quiet condition for the group of autistic children. Ramezani et al. (2019) concluded similar findings: that all latencies of the sABR, including the interpeak latency of VA, was prolonged in a group of autistic children compared to a CG. Another study found only significant prolongations of waves C, D, F, and O in autistic children compared to children without autism (Shennawy et al., 2014). In contrast, Kamieta et al. (2020) found a significant difference in only the mean absolute sABR wave V (p-value = 0.011) between 15 school-aged autistic children (7-12 years old) and 15 children without autism matched by age and gender; however, their findings indicated that the absolute latency was significantly shorter in the group of autistic children compared to those without autism.

Chen et al. (2019) examined the development of sABR wave amplitudes and latencies in preschoolers on the spectrum (n=15) compared to preschoolers without autism at two different time points with a starting age of 4.86± 1.48 and 4.57± 0.53 years for the autism and control group, respectively. The researchers found that wave V and A latencies were significantly prolonged in the autistic preschoolers at time 1 compared to the CG (wave V: $p$=0.028; Wave A: $p$=0.023). At time 2, which was an average of 10.78 and 9.68 months after time 1 for the autistic

and control group respectively, they found that wave E was significantly smaller in amplitude and wave F latency was significantly prolonged in the autism group compared to the control group (wave E: p=0.022; wave F: p=0.044). Overall, their study suggested that in preschoolers on the spectrum, the sABR is still developing and is significantly different than that for preschoolers without a diagnosis of autism.

Most of the studies suggest that groups of autistic individuals have prolonged sABR latencies compared to CG. The findings among studies, however, were mixed in regard to which waveforms were prolonged in the autistic group. The results may have differed among studies due to the heterogeneity among their autistic participants, such as autism severity, sensory sensitivities, and language abilities. As previously discussed, some studies have explored the relationship between ABR latencies with language abilities and autism severity, but no studies have looked at the relationship between auditory processing in the brainstem and sensory sensitivities. One study separated the autistic participants into two groups based on autism severity rating: mild-to-moderate and severe. The study found that the latency of Wave D in the group of children with mild-to-moderate autism severity rating had prolonged latencies compared to the children with severe autism severity rating (Othman et al., 2022). The results from this study suggest that there is a relationship between autism severity and sABR latency. Although the findings suggested a more complex relationship than anticipated. Jones et al. (2020) studied sABR and click-evoked ABR latencies in autistic toddlers aged 2-4 years old (*M*= 2.941 years) and age- and gender-matched toddlers without autism. The researchers used the ADOS-2 to measure the severity of autism. Language abilities were measured via Preschool Language Scales – Fifth Edition and the words produced measured by the MacArthur-Bates Communicative Development Inventories. The researchers correlated the severity ratings of

autism and words produced with click-evoked and sABR absolute and interpeak latencies and the sABR FFR amplitudes and FFR response consistency. Although they found significant differences in latencies (wave I-V, III-V and O) between the group of children with autism and that of the CG, they found no significant correlations between any electrophysiological measures and autism severity or language ability measures. These two studies considered the heterogeneity of autism, but focused on language aspects of the disorder and failed to consider how the heterogeneity of sensory processing, critical for higher order processing, and autistic traits may be related to the ABR.

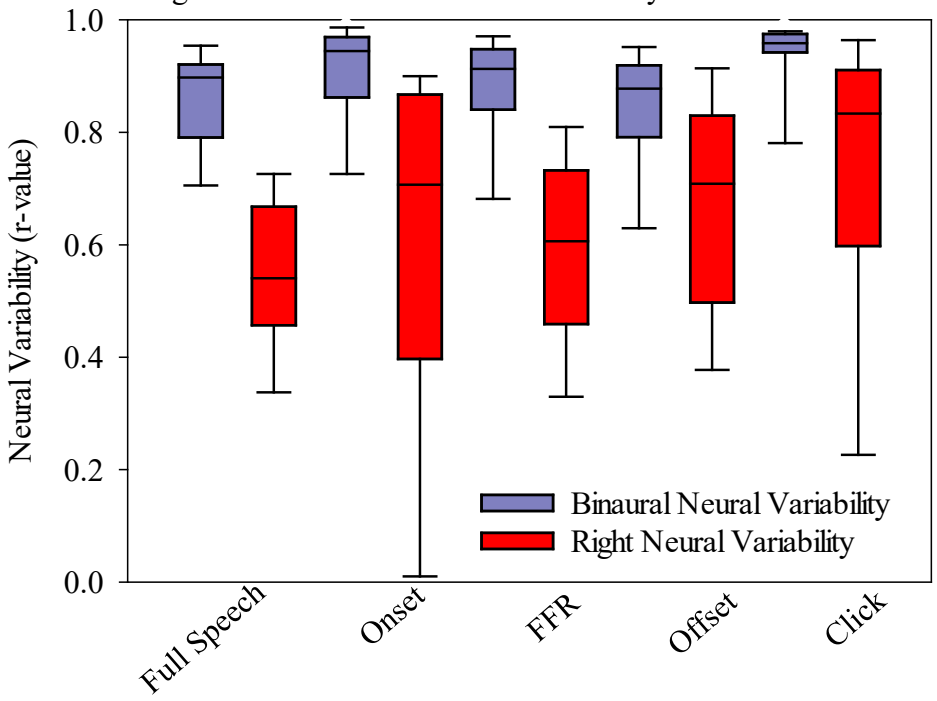
# Appendix F

## Comparison between right and binaural neural variability

Figure F1 displays a box and whiskers graph of the neural variability values for the binaural evoked neural variability and right evoked neural variability. Results of an independent samples t-test revealed that all binaural response components had significantly greater degrees of neural variability (more stable) compared to the right ear neural variability.

**Figure F1**

Right versus Binaural Neural Variability




## Right-ear evoked neural variability

Descriptive statistics, including the minimum, maximum, mean, and standard deviation of the neural variability evoked by the right ear for all components of the speech ABR (full, onset, FFR, and offset) as well as the entire click response are found in Table F1 for all participants.

**Table F2**

*Right Ear Neural Variability*

| | N | Minimum | Maximum | Mean | Std. Deviation |
|---|---|---|---|---|---|
| Full | 36 | .13 | 1.13 | .63 | .22 |
| Onset | 36 | -.20 | 1.86 | .83 | .53 |
| FFR | 36 | -.01 | 1.25 | .70 | .30 |
| Offset | 36 | -.09 | 2.00 | .92 | .45 |
| Click | 44 | -.32 | 2.19 | 1.09 | .62 |

A paired sample t-test was conducted to determine if there was any significant difference between autistic participants and nonautistic participants in the degree of neural variability of each response component. Results indicated that there was no significant difference in the degree of neural variability between groups. Table F2 provides the descriptive statistic for degree of right sABR and click neural variability for each group.

**Table F2**

*Autistic vs. Nonautistic Statistics for Right Ear Neural Variability*

| | Group | N | Mean | Std. Deviation | Std. Error Mean |
|---|---|---|---|---|---|
| Full | CG | 25 | .60 | .21 | .04 |
| | ASD | 11 | .69 | .24 | .07 |
| Onset | CG | 25 | .74 | .48 | .10 |
| | ASD | 11 | 1.05 | .59 | .18 |
| FFR | CG | 25 | .67 | .29 | .06 |
| | ASD | 11 | .77 | .33 | .10 |
| Offset | CG | 25 | .93 | .52 | .10 |
| | ASD | 11 | .89 | .27 | .08 |
| Click | CG | 26 | 1.16 | .59 | .12 |
| | AS | 18 | 1.00 | .66 | .15 |

Pearson Correlation analysis was conducted between all response components and parent-reported survey measures, shown in Table F3. AUD-SOR and right onset neural variability were positively correlated with one another (p=0.02), however, this correlation would not survive Bonferroni's correction factor.

**Table F3**

*Correlations between Right Neural Variability and Parent-report Measures*

| | | Full | Onset | FFR | Offset | Click |
|---|---|---|---|---|---|---|
| AUD-SOR | Pearson Correlation | .23 | .40 | .17 | .17 | .16 |
| | Sig. (2-tailed) | .21 | .02 | .35 | .37 | .33 |
| | N | 31 | 31 | 31 | 31 | 38 |
| SOR | Pearson Correlation | .23 | .35 | .23 | .12 | .14 |
| | Sig. (2-tailed) | .22 | .05 | .22 | .54 | .40 |
| | N | 31 | 31 | 31 | 31 | 38 |
| SRS-2 | Pearson Correlation | .01* | .05 | .01 | -.09 | .03 |
| | Sig. (2-tailed) | .94 | .78 | .94 | .65 | .84 |
| | N | 31 | 31 | 31 | 31 | 37 |
| AQ | Pearson Correlation | .09 | .15 | .15 | -.05 | .01 |
| | Sig. (2-tailed) | .60 | .40 | .39 | .78 | .97 |
| | N | 35 | 35 | 35 | 35 | 43 |

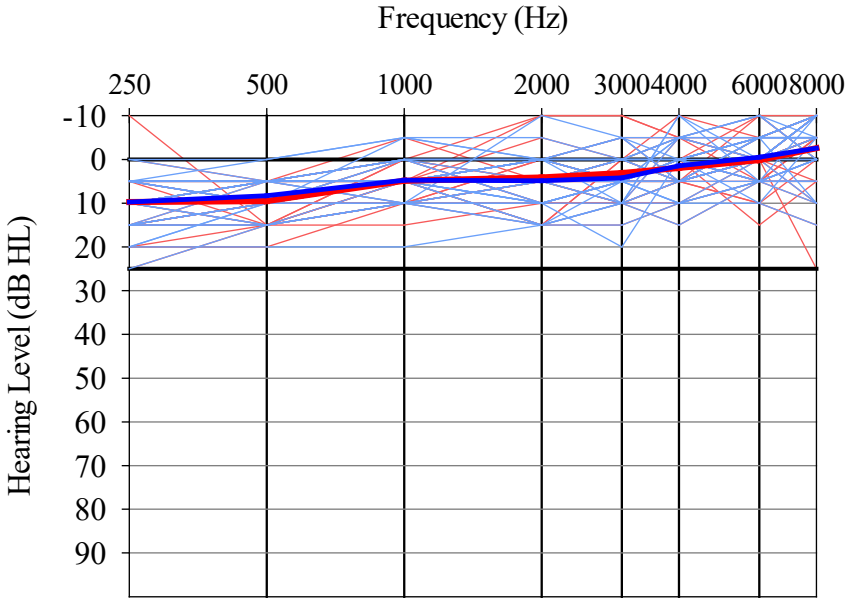
# Appendix G

## The audiometric behavioral thresholds, the transient evoked otoacoustic (TEOAE) levels, and monaural ipsilateral right sABR and click ABR latencies

### Behavioral Audiometric Thresholds

**Figure G3**

*Audiometric Behavioral Thresholds*




*Note*. Figure G1 displays the audiometric thresholds for the 41 participants enrolled in the current study. Individual left and right thresholds are indicated by light blue and red solid lines, respectively. The bolded solid red and blue lines represent the average right and left thresholds, respectively.

**Table G4**

*Hearing Thresholds*

| | Right Ear | | | | Left Ear | | | |
|---|---|---|---|---|---|---|---|---|
| Frequency | Min | Max | Mean | Std. Deviation | Min | Max | Mean | Std. Deviation |
| 250Hz | -10 | 25 | 9.8 | 6.2 | 0 | 25 | 9.8 | 5.7 |
| 500Hz | 0 | 20 | 9.5 | 4.4 | 0 | 20 | 8.3 | 4.3 |
| 1000Hz | -5 | 15 | 4.9 | 4.1 | -5 | 20 | 4.8 | 4.7 |
| 2000Hz | -10 | 15 | 4.1 | 5.8 | -10 | 15 | 4.9 | 6.0 |
| 3000Hz | -10 | 15 | 3.1 | 5.4 | -5 | 20 | 4.2 | 5.4 |
| 4000Hz | -10 | 15 | 2.0 | 5.0 | -10 | 15 | 1.5 | 5.7 |
| 6000Hz | -10 | 15 | 0.1 | 5.4 | -10 | 10 | -0.5 | 5.2 |
| 8000Hz | -10 | 25 | -2.6 | 8.0 | -10 | 15 | -2.6 | 6.9 |

*Note*. Table G1 displays the minimum, maximum, mean, and standard deviation for the behavioral audiometric thresholds of the 41 participants enrolled in the current study for the left and right ear. There were no significant differences in thresholds between ears at any frequency ($p>0.05$)

When participant thresholds were compared via independent sample t-test between autistic individuals and nonautistic individuals there was a significant difference in thresholds at 2 kHz in both ears and at 4 kHz in the left ears between groups. Specifically, the autistic participants had significantly lower (better) behavioral thresholds compared to the nonautistic participants. Table G2 displays the mean and standard deviation, as well as standard error of the mean, for the thresholds that were significantly different between ears. Importantly, these differences did not withstand Bonferroni correction.

**Table G2**

*Group Differences in Behavioral Thresholds*

| | | N | Mean | Std. Deviation | Std. Error Mean | t-value | p-value |
|---|---|---|---|---|---|---|---|
| Right 2kHz | CG | 25 | 5.60 | 5.65 | 1.12 | 2.09 | 0.043 |
| | ASD | 16 | 1.88 | 5.44 | 1.36 | | |
| Left 2kHz | CG | 25 | 6.80 | 4.97 | .99 | 2.79 | 0.008 |
| | ASD | 16 | 1.88 | 6.29 | 1.57 | | |
| Left 4kHz | CG | 25 | 3.00 | 5.59 | 1.12 | 2.25 | 0.03 |
| | ASD | 16 | -0.94 | 5.23 | 1.31 | | |

*Note*. Table G2 displays thresholds that were significantly different between groups. CG = control participants; ASD = autistic participants.

**Transient-evoked Otoacoustic Emissions (TEOAE) level**

**Table G3**

*TEOAE levels and Paired Sample Statistics*

| | | Mean | Std. Deviation | Std. Error Mean | t | Sig. (2-tailed) |
|---|---|---|---|---|---|---|
| 1k Hz | Right | -.77 | 5.25 | .84 | 2.25 | 0.03 |
| | Left | -2.71 | 5.54 | .89 | | |
| 1.5k Hz | Right | .69 | 5.54 | .89 | 1.29 | 0.21 |
| | Left | -.43 | 5.57 | .89 | | |
| 2k Hz | Right | -1.54 | 5.82 | .93 | 3.14 | 0.00 |
| | Left | -5.09 | 6.68 | 1.07 | | |
| 3k Hz | Right | -2.17 | 6.75 | 1.08 | 1.29 | 0.20 |
| | Left | -3.25 | 6.45 | 1.03 | | |
| 4k Hz | Right | -1.48 | 7.60 | 1.22 | 0.84 | 0.40 |
| | Left | -2.13 | 6.45 | 1.03 | | |

*Note*. Table G3 displays the mean, standard deviation, and standard error of the mean for the right and left TEOAE level for 39 participants. The t and significance value are reported from a paired sample t-test comparing left and right TEOAE level.

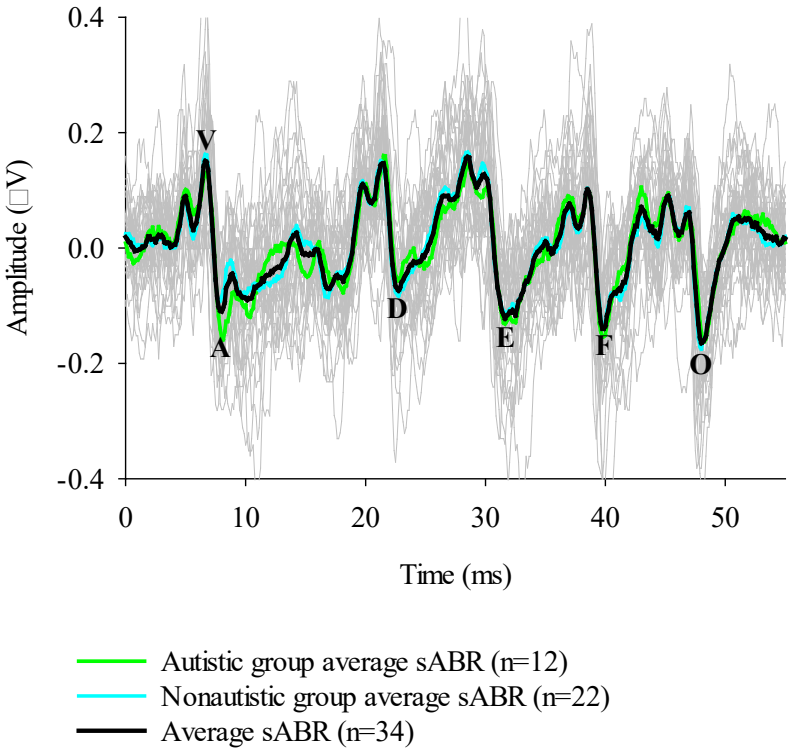
The results of the paired sample t-test indicated that the right TEOAE level was significantly higher compared to the left TEOAE level at 1 and 2 kHz. Independent sample t-test revealed that there were no significant differences in TEOAE levels between the groups of autistic and nonautistic participants.

**Right sABR and click ABR data**

The Right ipsilateral sABR and click ABR, evoked from monaural stimulation is reported for comparison to previously published data.

**Figure G2**

*Average Speech- ABR*




*Note.* The thin grey lines display all individual traces. The average of all participants, autistic group, and nonautistic group sABR are depicted by the black solid line, green and blue solid lines, respectively.

**Table G4**

*Speech-ABR absolute and Interpeak Latencies*

| | Minimum | Maximum | Mean | Std. Deviation |
|---|---|---|---|---|
| Wave V | 6.25 | 7.25 | 6.8007 | .27853 |
| Wave A | 7.25 | 8.75 | 7.9404 | .36910 |
| Wave D | 22.25 | 25.13 | 22.9147 | .77734 |
| Wave E | 30.50 | 34.00 | 31.6918 | .74732 |
| Wave F | 39.13 | 42.00 | 39.9423 | .66513 |
| Wave O | 47.38 | 48.88 | 48.0468 | .32157 |
| A-O interpeak | 39.25 | 40.63 | 40.0905 | .29949 |
| V-A_interpeak | .75 | 2.25 | 1.1379 | .33557 |

*Note.* Table G4 provides the minimum, maximum, average absolute and interpeak latencies for the speech ABR. N=34.

Independent sample t-tests revealed that there was a significant difference between the group of autistic participants and nonautistic participant in the absolute latency of A and O. Table G5 provides the mean, standard deviation, standard error of the mean, as well as the paired sample statistics, of absolute and interpeak sABR latencies by group.

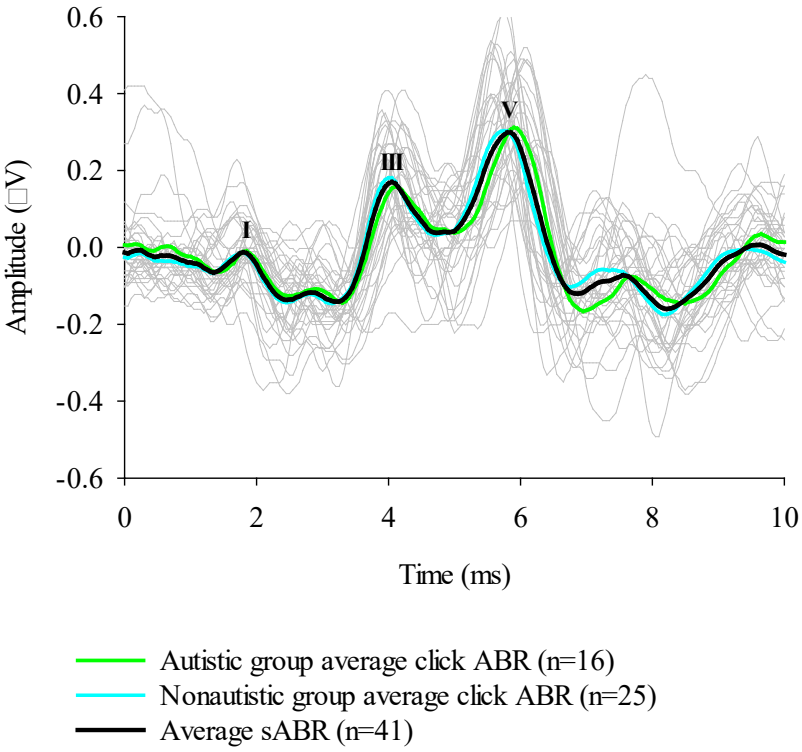
**Table G5**

*Absolute and Interpeak sABR Latencies, by Group and Paired Sample statistics*

| | Group | N | Mean | Std. Deviation | Std. Error Mean | t | Sig. (2-tailed) |
|---|---|---|---|---|---|---|---|
| Wave V | CG | 22 | 6.78 | .27 | .06 | -0.71 | 0.49 |
| | ASD | 12 | 6.85 | .29 | .08 | | |
| Wave A | CG | 22 | 7.82 | .35 | .07 | -2.81 | 0.01 |
| | ASD | 12 | 8.16 | .31 | .09 | | |
| Wave D | CG | 22 | 22.67 | .39 | .08 | -2.16 | 0.05 |
| | ASD | 12 | 23.37 | 1.08 | .31 | | |
| Wave E | CG | 22 | 31.53 | .68 | .14 | -1.74 | 0.09 |
| | ASD | 12 | 31.98 | .81 | .23 | | |
| Wave F | CG | 22 | 39.85 | .61 | .13 | -1.06 | 0.30 |
| | ASD | 12 | 40.11 | .75 | .22 | | |
| Wave O | CG | 22 | 47.97 | .37 | .08 | -2.31 | 0.03 |
| | ASD | 12 | 48.18 | .15 | .04 | | |
| A-O interpeak | CG | 22 | 40.13 | .25 | .05 | 1.00 | 0.32 |
| | ASD | 12 | 40.02 | .38 | .11 | | |
| V-A interpeak | CG | 22 | 1.04 | .22 | .05 | -1.98 | 0.07 |
| | ASD | 12 | 1.31 | .44 | .13 | | |

**Figure G3**

*Average Click- ABR*




*Note.* The thin grey lines display all individual traces. The average of all participants, autistic group, and nonautistic group click ABR are depicted by the black solid line, green and blue solid lines, respectively.

**Table G6**

*Click ABR absolute and Interpeak Latencies*

| | N | Minimum | Maximum | Mean | Std. Deviation |
|---|---|---|---|---|---|
| Wave I | 39 | 1.30 | 2.40 | 1.8651 | .19058 |
| Wave III | 41 | 3.10 | 4.60 | 4.0820 | .26736 |
| Wave V | 41 | 5.40 | 6.45 | 5.9095 | .24364 |
| I-III | 39 | 1.15 | 2.80 | 2.2026 | .29823 |
| III-V | 41 | 1.30 | 2.80 | 1.8276 | .26305 |
| I-V | 39 | 3.45 | 4.65 | 4.0372 | .28602 |

*Note.* Table G6 provides the minimum, maximum, average absolute and interpeak latencies for the click ABR. An independent sample t-test revealed that there was no significant difference between the group of autistic participants and nonautistic participant in the absolute or interpeak latencies of the click ABR.

## Appendix H

**Normality of plots of data that did not initially pass the Kolmogorov Smirnov test or Shapiro-Wilk test.**

**Figure H1**

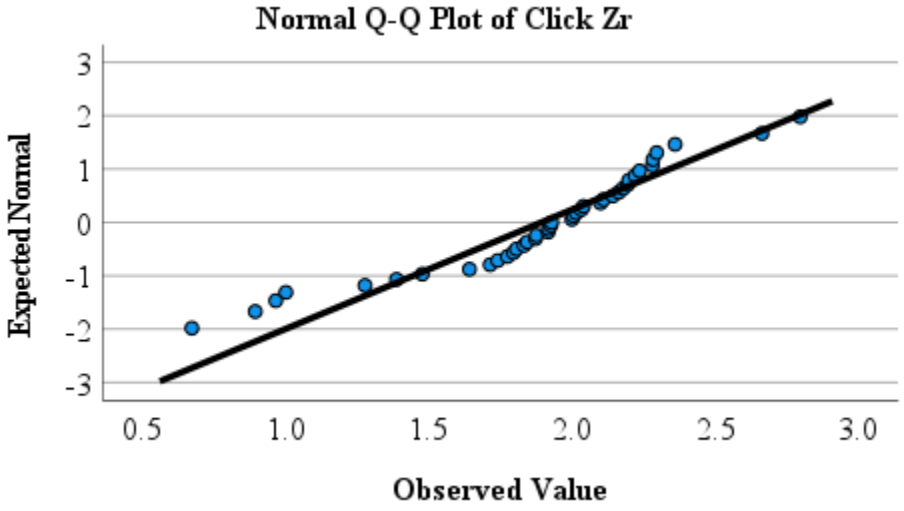



**Figure H2**

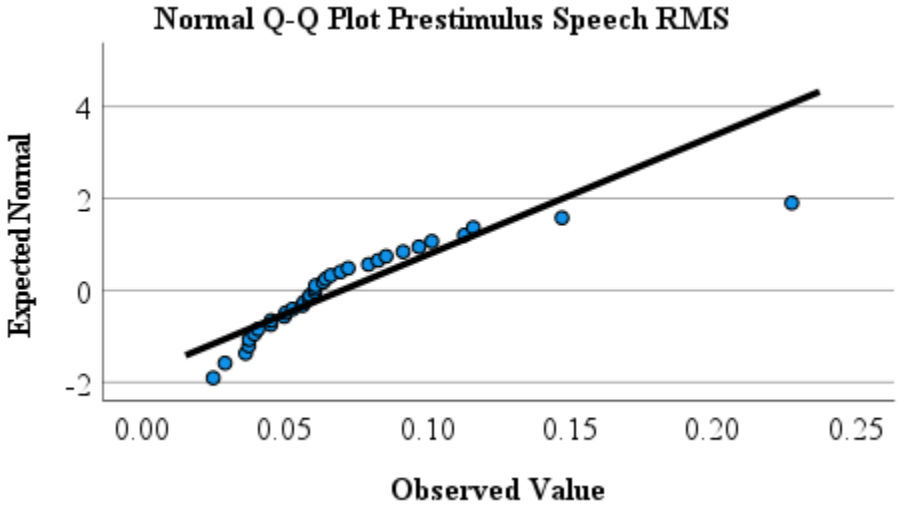


**Figure H3**

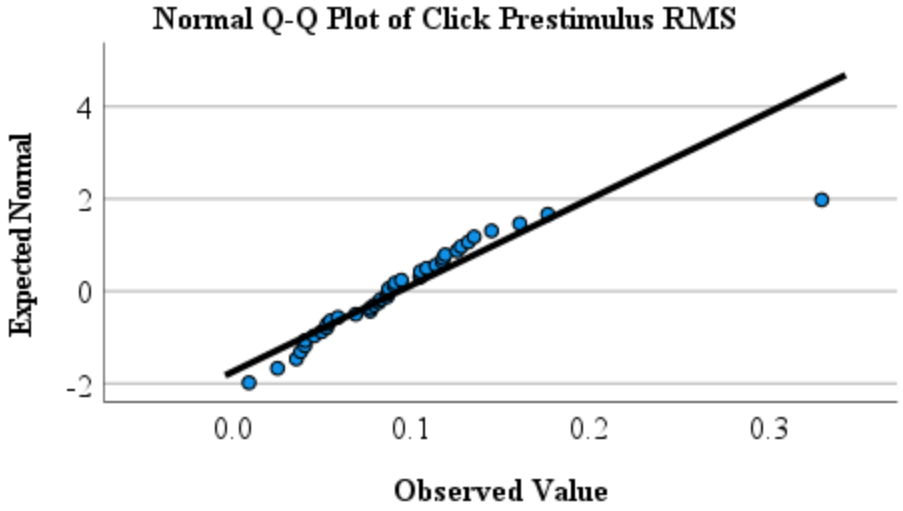



**Figure H4**

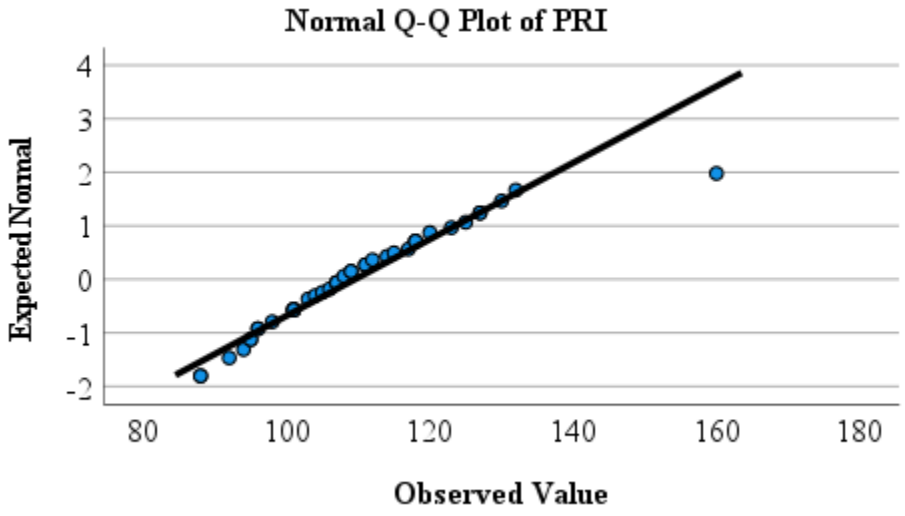
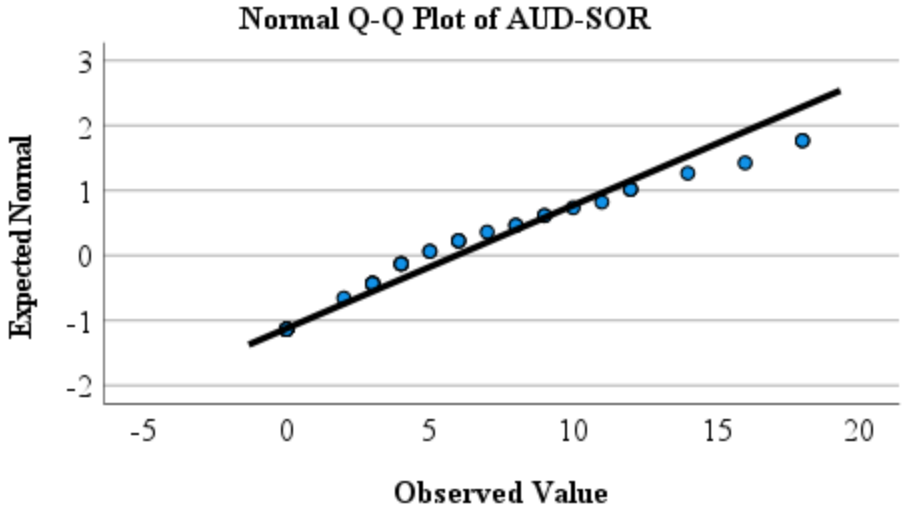


**Figure H5**




**Normality (Q-Q) and scatter plots for the residuals from the models.**

**Figure H6 –** Model #5

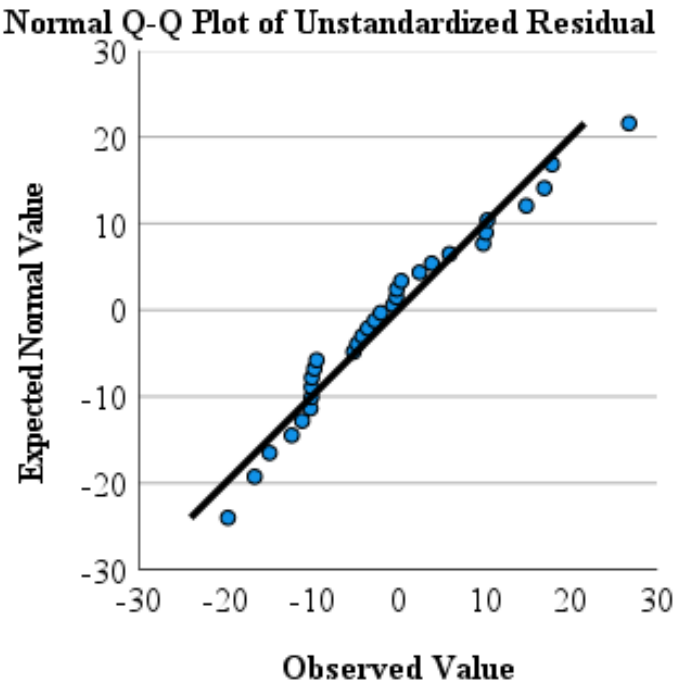


**Figure H7**

Model #5 Residual Scatter Plot

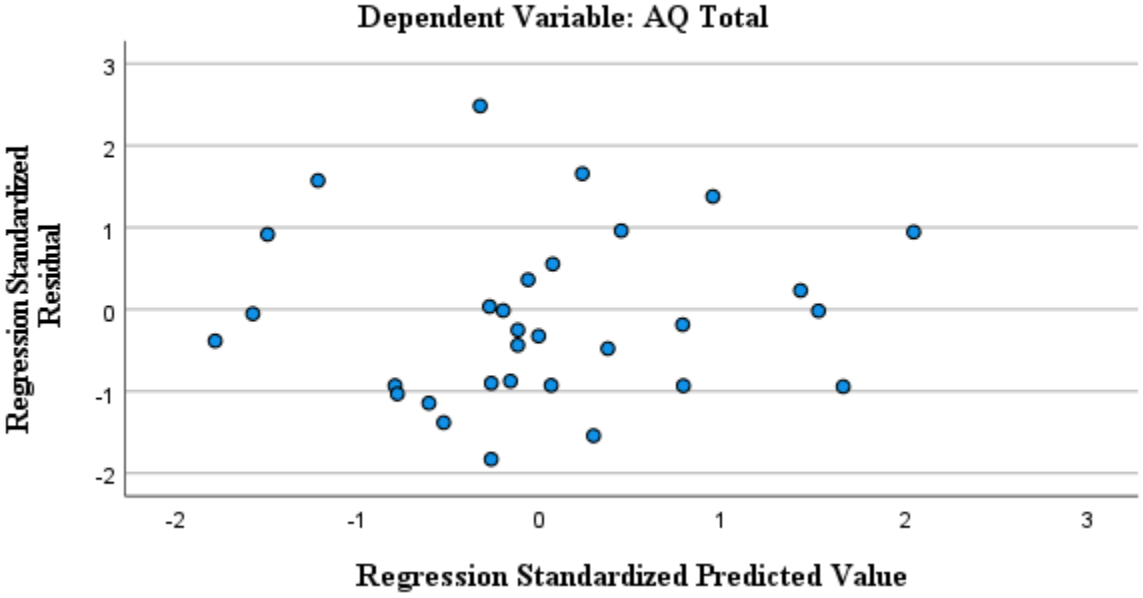



**Figure H8 –** Model #6

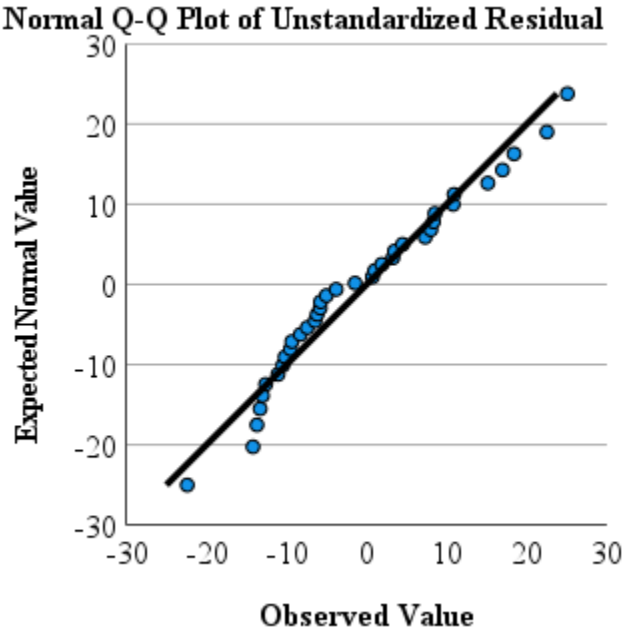


**Figure H9**

Model #6 Residual Scatter Plot

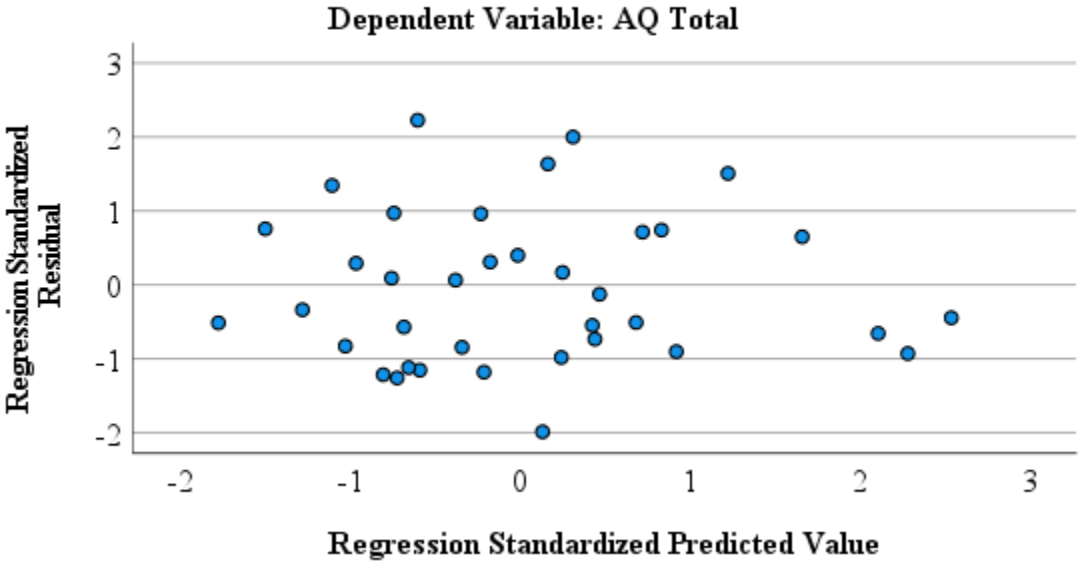



**Figure H10 –** Model #7

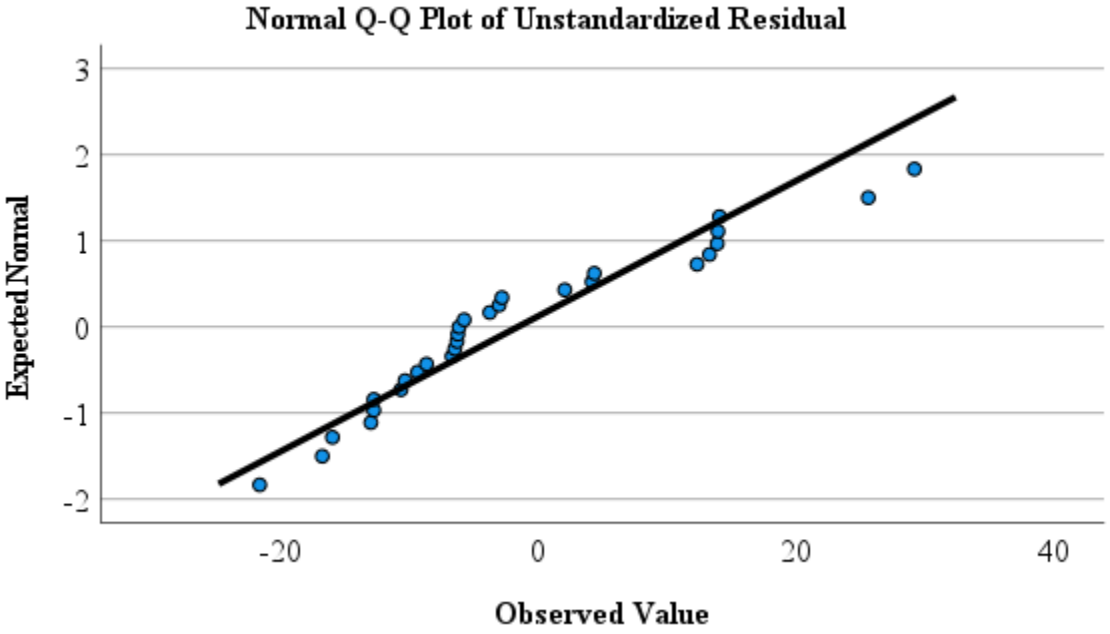


**Figure H11**

Model #7 Residual Scatter Plot

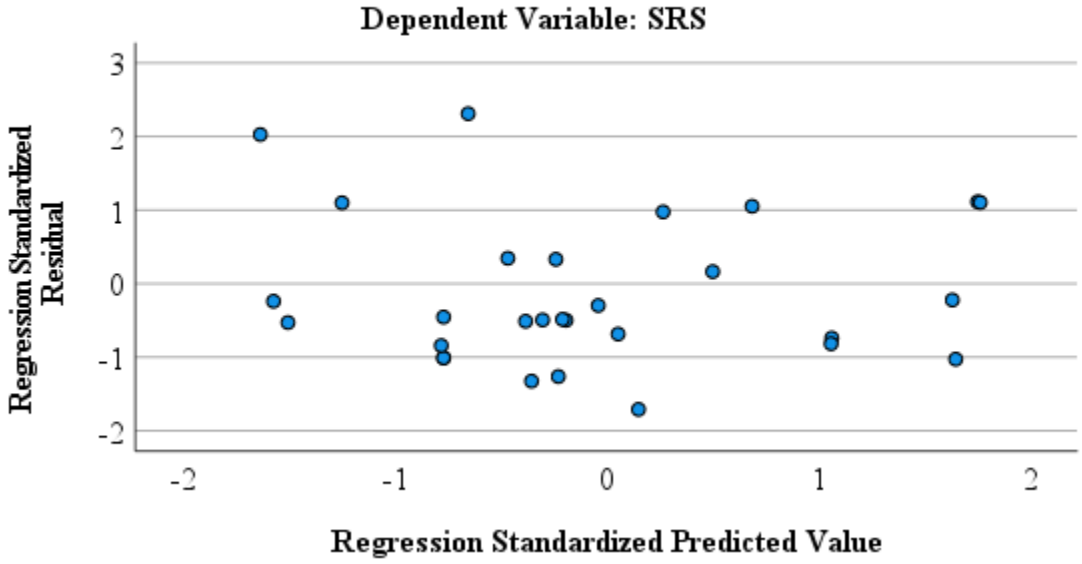



**Figure H12 –** Model #8

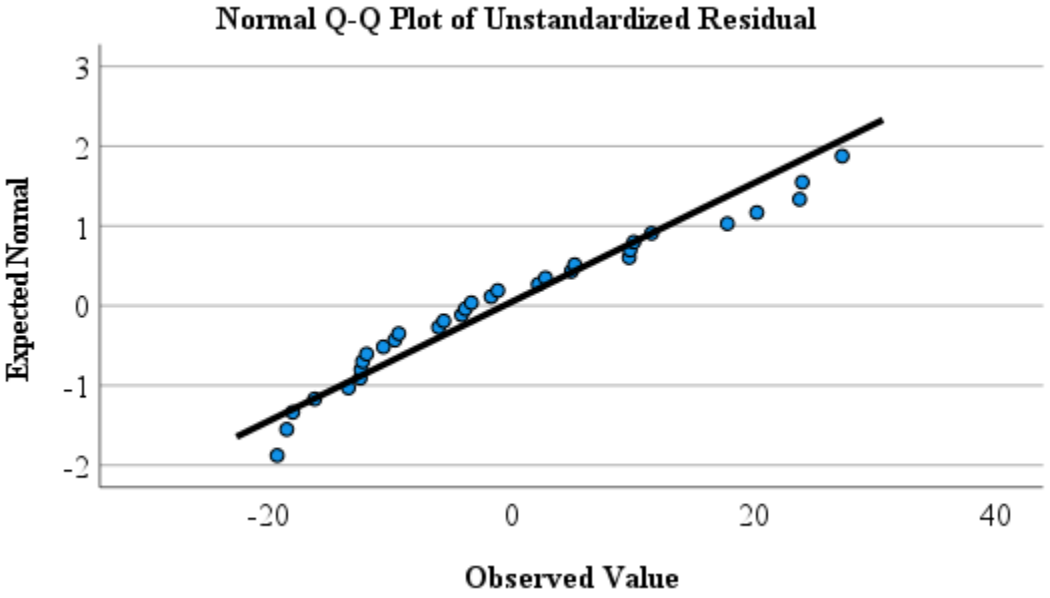
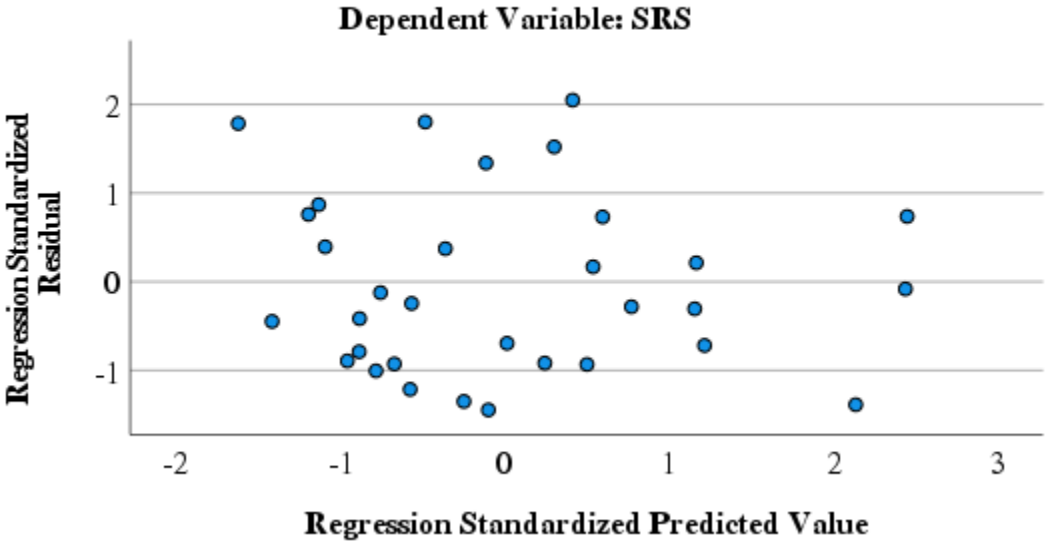


**Figure H13**

Model #8 Residual Scatter Plot



# Appendix I

Scatter Plotts of  the correlation of AQ, SRS-2, SOR, and AUD-SOR and each of the response components are shown below.

Click correlations

**Figure I1.**

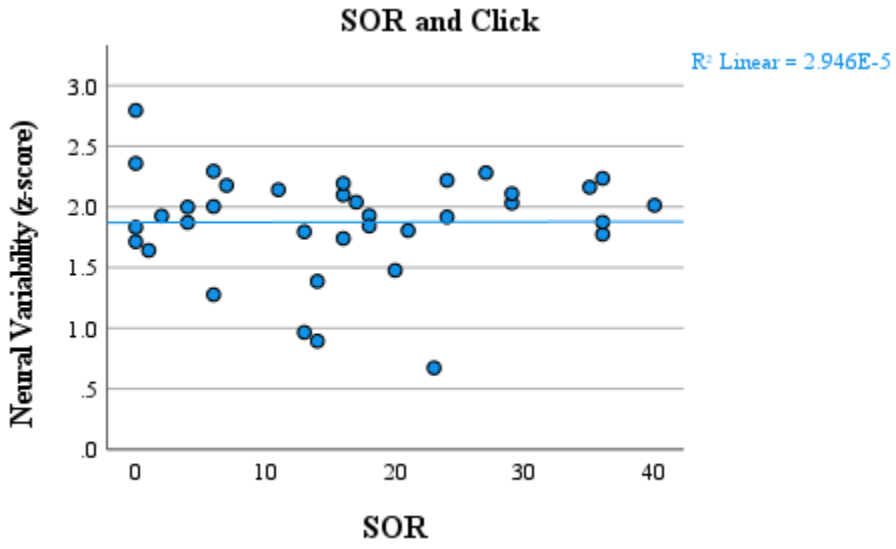



**Figure I2.**

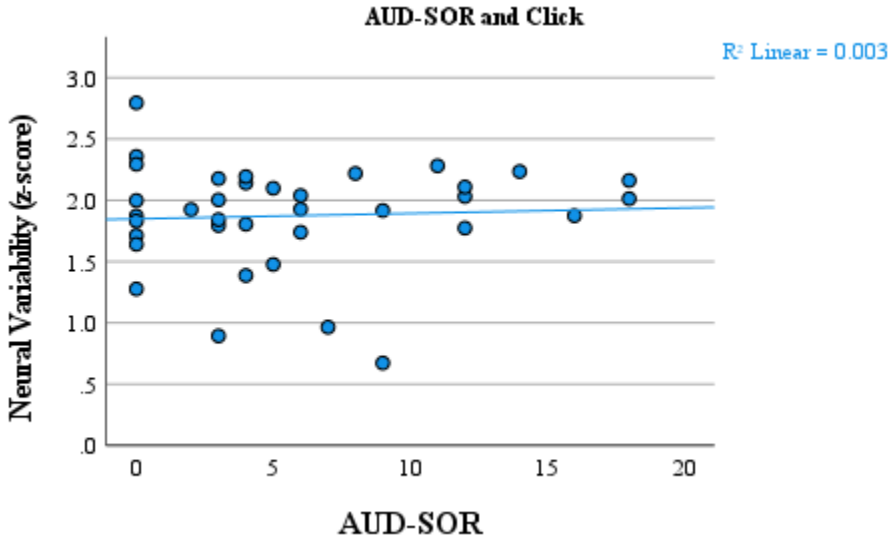


**Figure I3.**

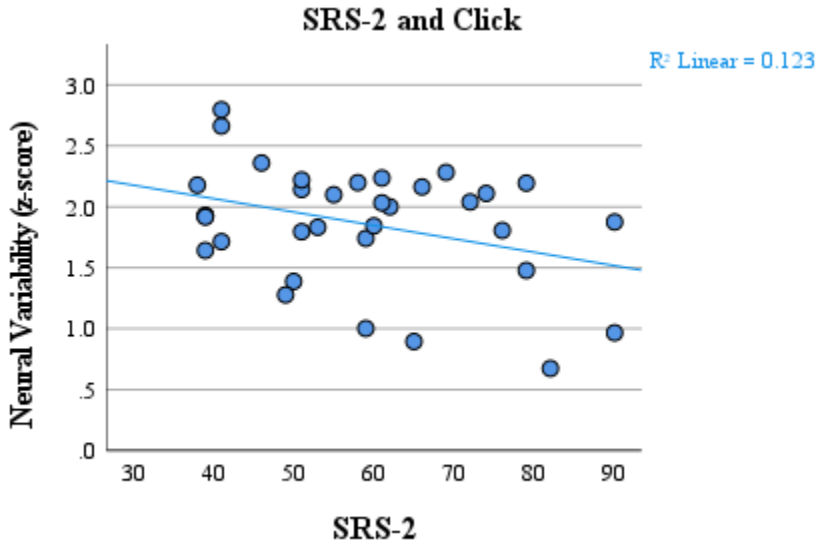
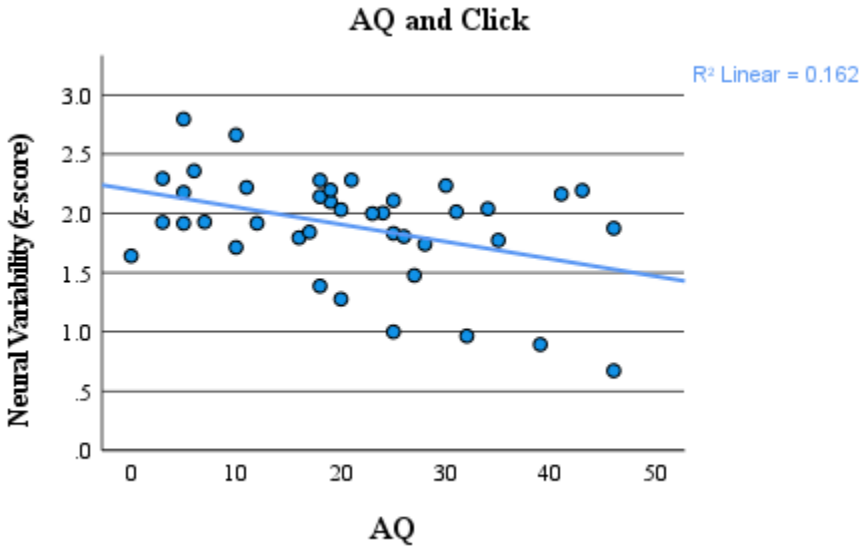



**Figure I4.**



Total speech response correlations

**Figure I5.**

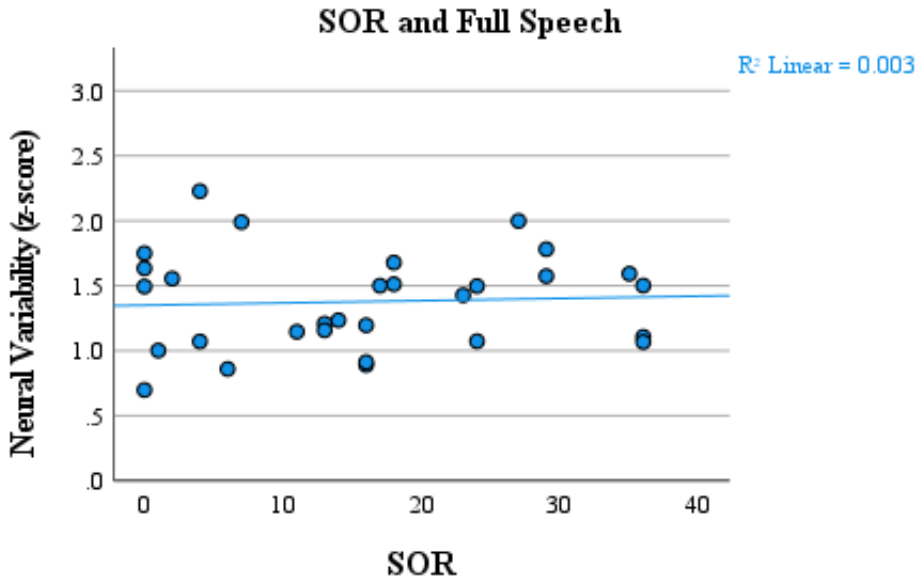



**Figure I6.**

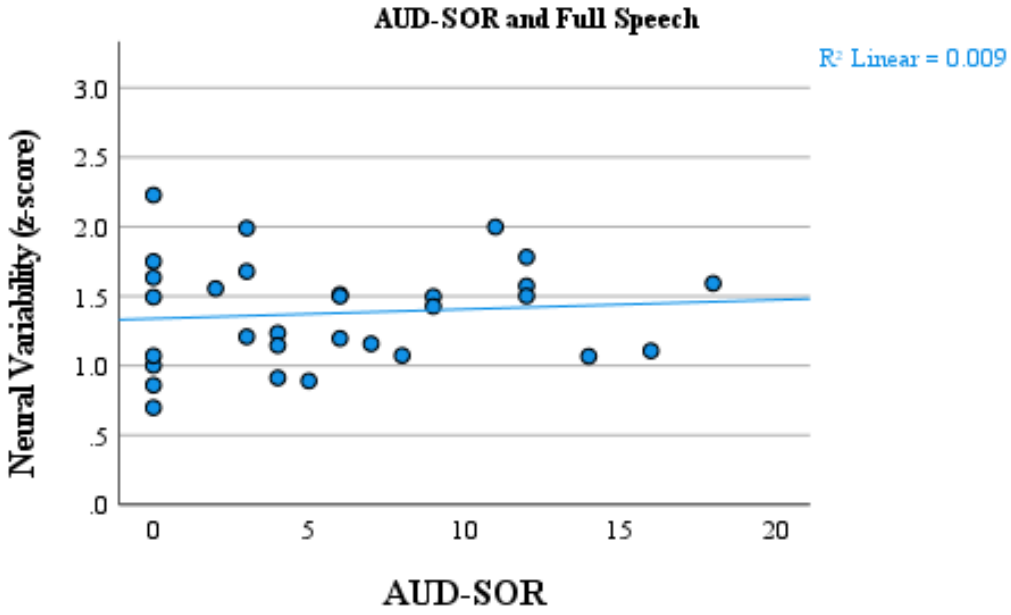


**Figure I7.**

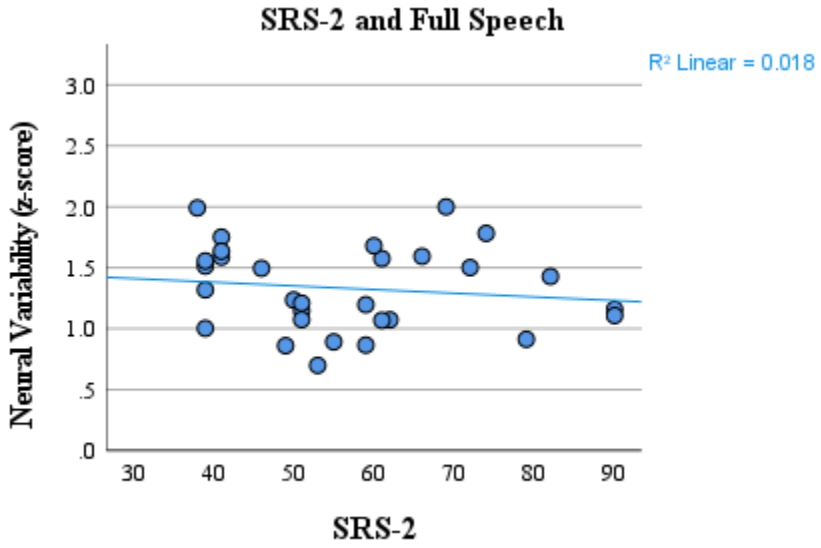
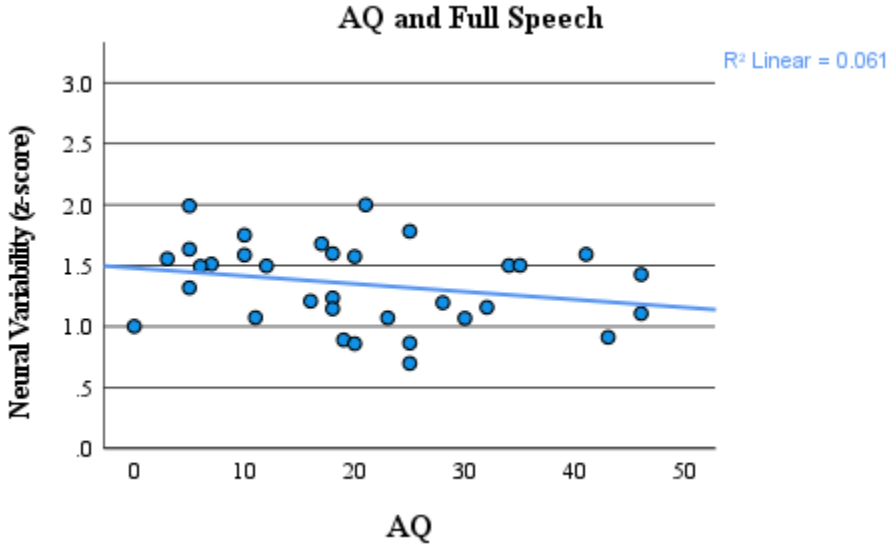



**Figure I8.**



Onset response correlations

**Figure I9.**


**Figure I10.**

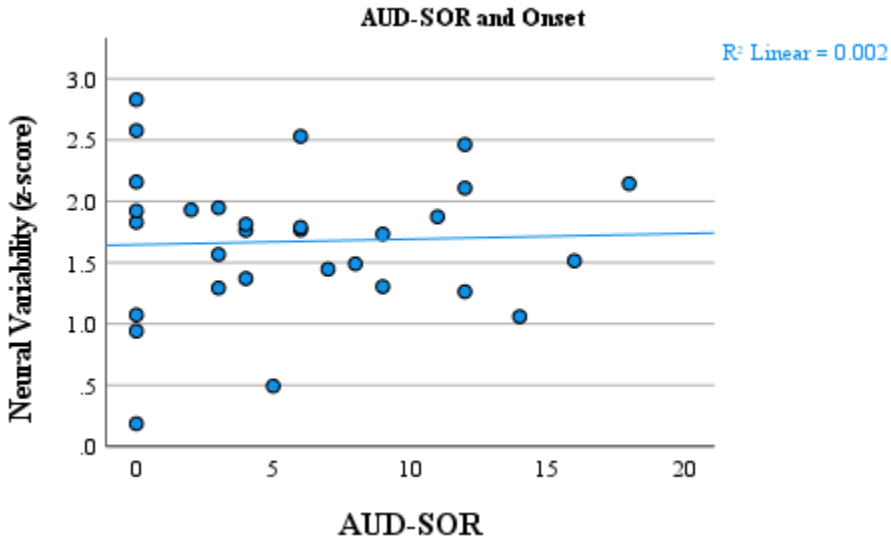


**Figure I11.**

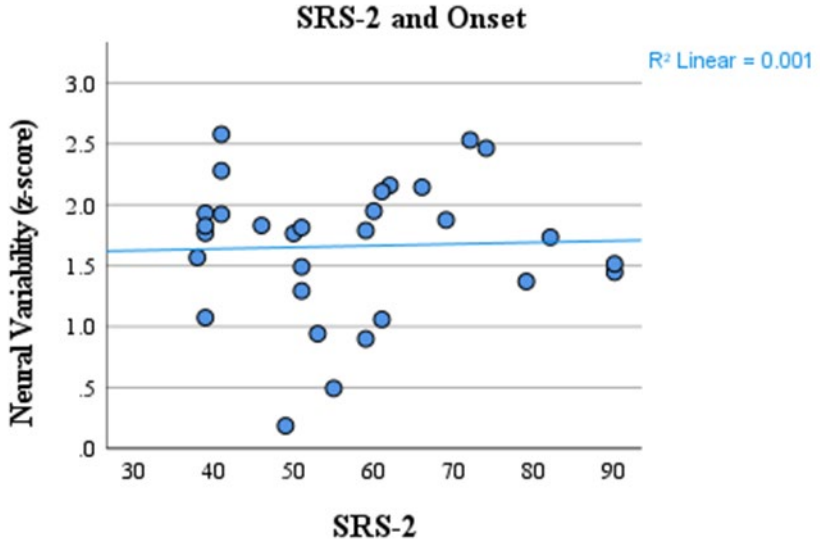
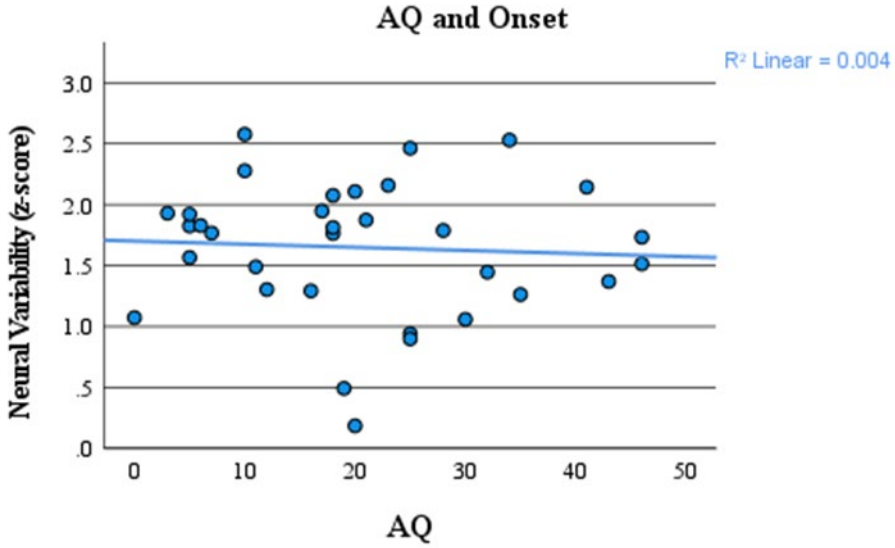



**Figure I12.**



Frequency following response correlations

**Figure I13.**

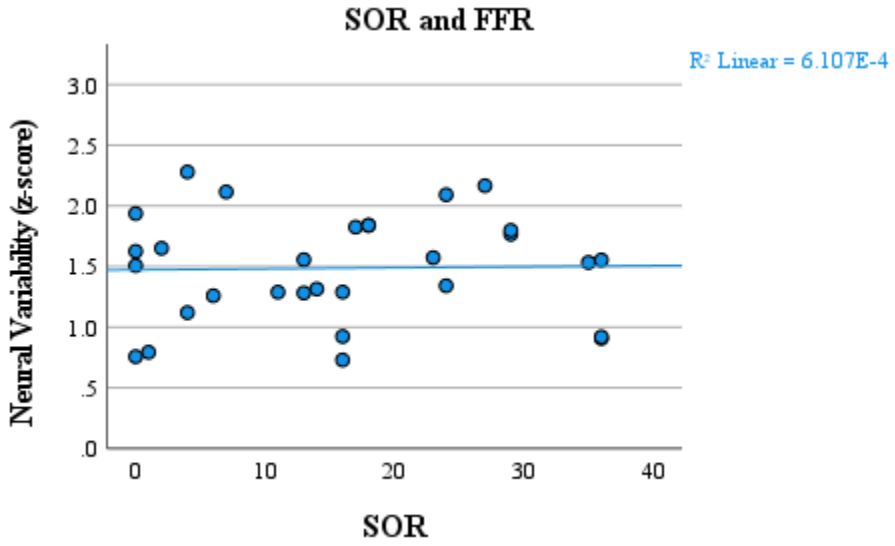



**Figure I14.**

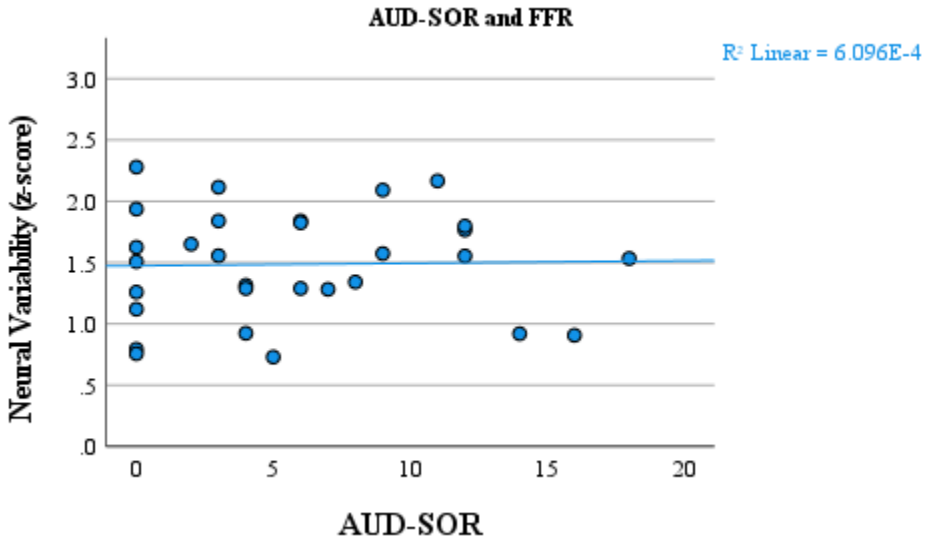


**Figure I15.**

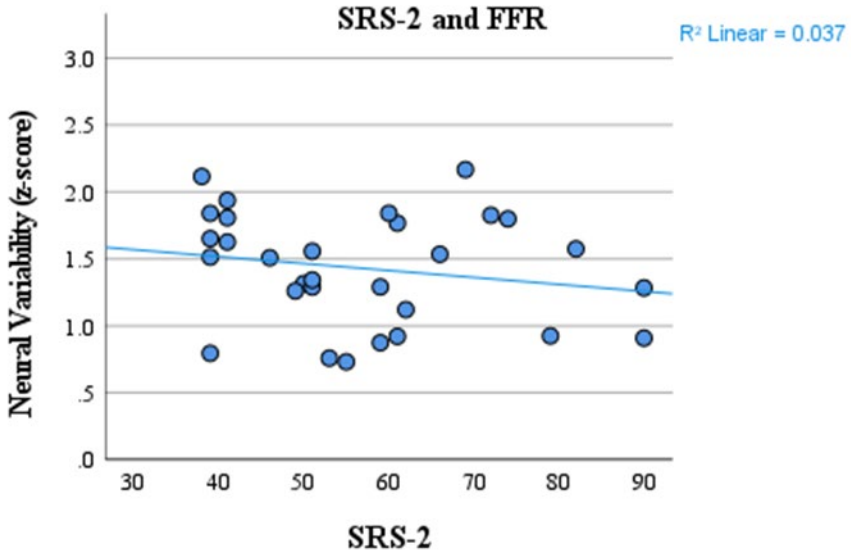
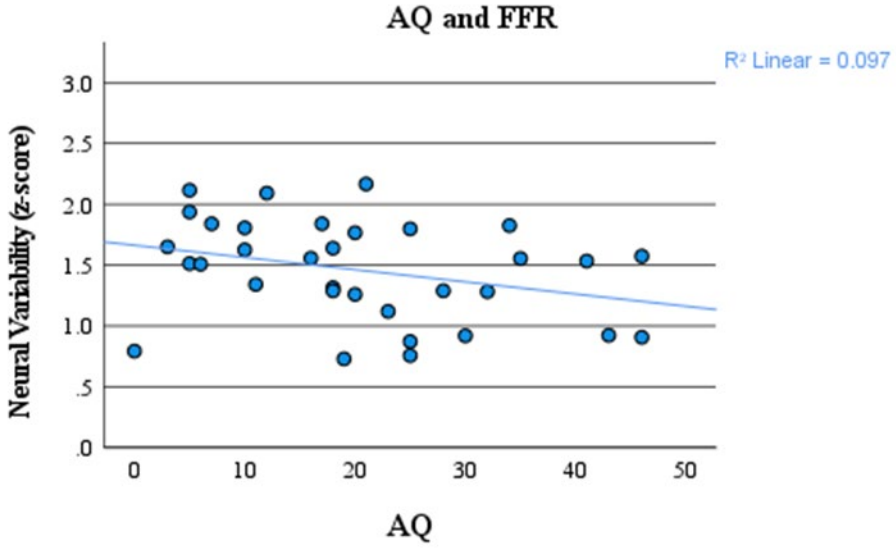



**Figure I16.**



Offset response correlations

**Figure I17.**

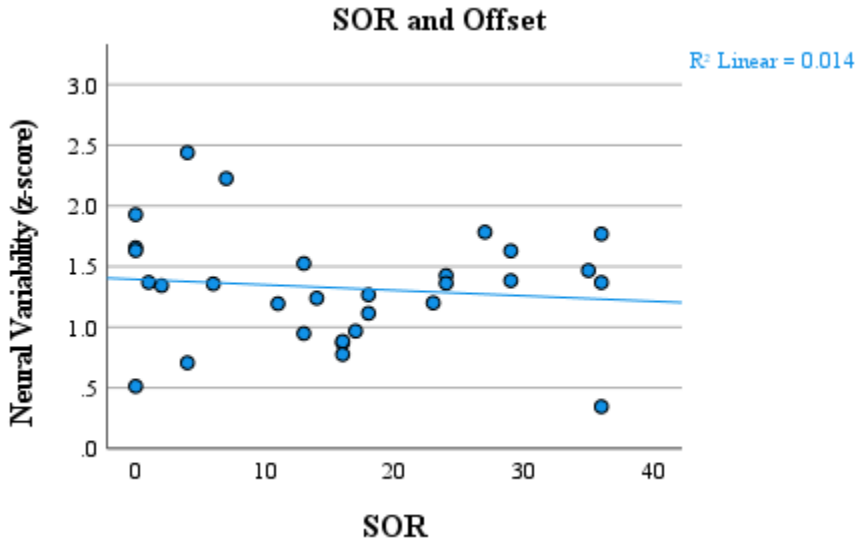



**Figure I18.**

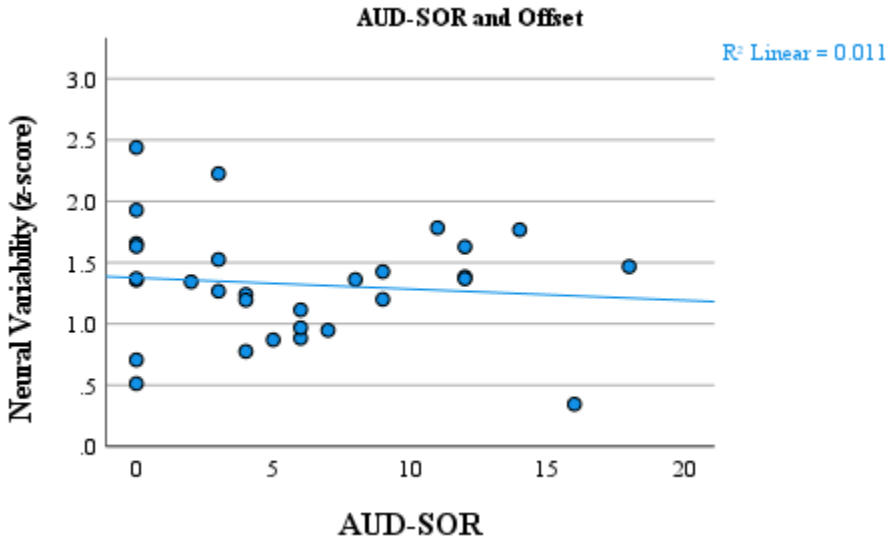


**Figure I19.**

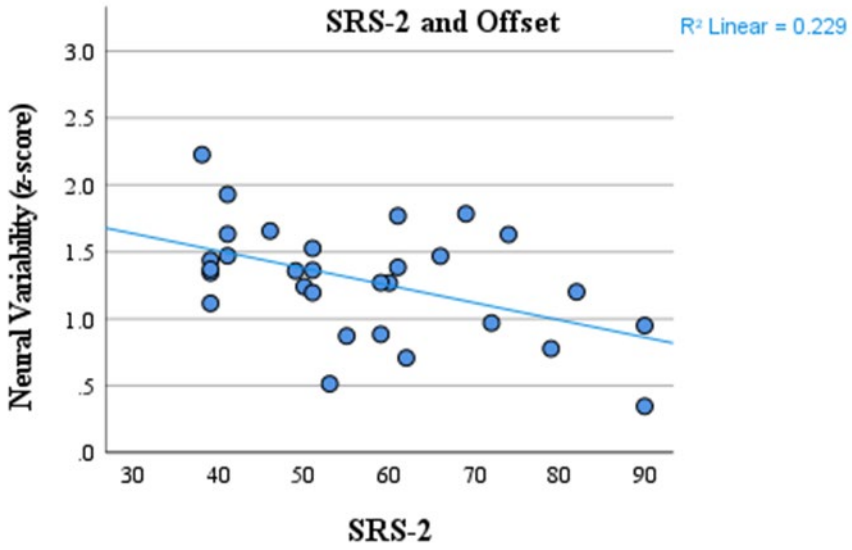
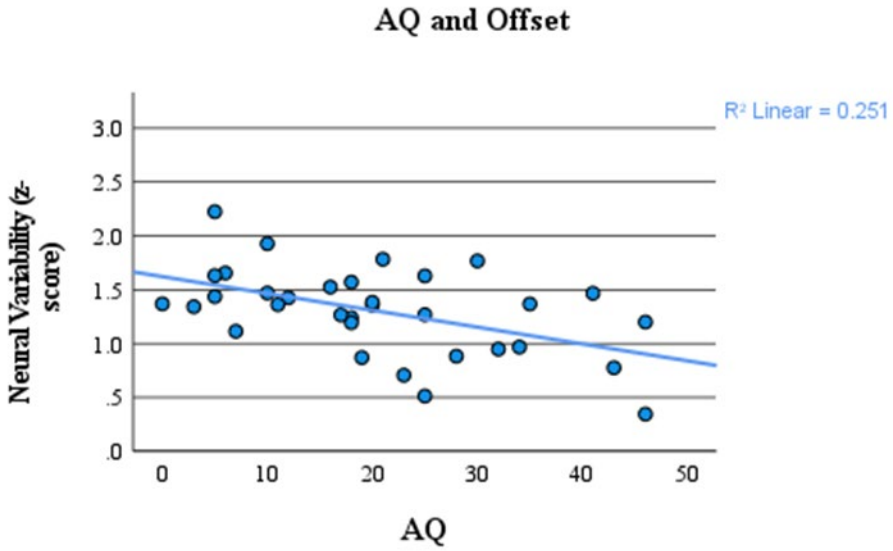



**Figure I20.**



## Appendix J

**Neural Variability correlations with multimodality Hypo and Seeking measures of sensory sensitivities.**

Measures of hypo and seeking, across all sensory modalities, were derived from the SP and correlated with the neural variability of various response components. As indicated in the table below, there were no significant correlations with either of these measures of sensory sensitivity.

**Table I1**

*Neural Variability correlations with Hypo and Seeking*

| | Hypo | | Seeking | |
|---|---|---|---|---|
| | Pearson Correlation | Sig. (2-tailed) | Pearson Correlation | Sig. (2-tailed) |
| Full sABR | .02 | .91 | -.04 | .83 |
| Onset | -.05 | .79 | -.09 | .64 |
| FFR | -.01 | .95 | -.04 | .83 |
| Offset | -.23 | .22 | -.23 | .21 |
| Click | -.11 | .54 | -.04 | .81 |

*Note.* Table I1 provides the Pearson Correlation values between Hypo and Seeking scores derived from the SP and the neural variability of the various response components. The n size for the speech response components and click was 34 and 36, respectively.

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# Devon Pacheco Major, AuD

## EDUCATION

**Syracuse University** *Anticipated completion:*
Doctorate of Philosophy *December 2023*
*Dissertation*: Auditory Brainstem Neural Variability and Sensory Sensitivities in School-Aged Children
PhD Advisor: Beth Prieve, PhD

**Syracuse University**
Doctorate of Audiology August 2021
GPA 3.96

**Syracuse University**
Bachelor of Science, Communication Sciences and Disorders May 2016
Bachelor of Science, Neuroscience May 2016

## AUDITORY RESEARCH EXPERIENCE

**Pediatric Audiology Laboratory**, *Syracuse University* 2017 - Present
Director, Beth Prieve, PhD

Predictive Validity of Auditory Responses, Bayley III and MBCDI at 5-6 Years of Age in Preterm Infants – coinvestigators: Dr. Natalie Russo and Dr. Stephanie McMillen

- Trained and mentored junior lab members in audiological data collection
- Analyzed data for junior AuD lab members presenting at the American Auditory Society Annual Scientific and Technology Conference

Sensation, Perception and Cognition in Typical and Atypical Development – coinvestigator: Dr. Natalie Russo

- Lead graduate student in Pediatric Audiology Laboratory on project
- Assisted in development and assemblance of test battery implemented in research
- Coordinated with the Center for Autism Research and Electrophysiology Laboratory on exchange of data collected between the two laboratories, including: IQ measures, parent-report surveys, autism diagnoses, and cortical recordings
- Collected all audiological data including transient evoked otoacoustic emissions, distortion-product otoacoustic emissions, wideband immittance, click-evoked auditory brainstem response, speech-evoked auditory brainstem response and behavioral thresholds from participants with and without Autism Spectrum Disorder aged 6-17 years old.

Characteristics of Joint Reflection and Distortion Type Otoacoustic Emission Profiles in Normal Hearing Adults

- First year research project, a requirement of the PhD program
- Assisted in grant writing, development, and organization of the study
- Wrote Institutional Review Board protocol for the study
- Recruited, consented, and collected all data from participants
- Collaborated with bioengineering PhD candidate for modeling of data
- Analyzed and interpreted data and published findings

Equipment Comparison of Wideband Absorbance Measures Recorded in Preterm Infants Across for Ages

- Quantitatively evaluated changes in wideband absorbance measures in infants born preterm across different test ages, between two pieces of equipment, and presence of middle ear dysfunction

**Eaton-Peabody Laboratories,** *Massachusetts Eye and Ear* Spring 2021
Assisted Dr. Stéphane Maison in data analysis and interpretation

## PUBLICATIONS

Cary, E., **Pacheco, D.,** Kaplan-Kahn, E., McKernan, E., Matsuba, E., Prieve, B., & Russo, N. (2023). Brain Signatures of Early and Late Neural Measures of Auditory Habituation and Discrimination in Autism and Their Relationship to Autistic Traits and Sensory Overresponsivity. *Journal of Autism and Developmental Disorders*.

Matsuba, E. S. M., Prieve, B. A., Cary, E., **Pacheco, D.,** Madrid, A., McKernan, E., Kaplan-Kahn, E., & Russo, N. (2022). A Preliminary Study Characterizing Subcortical and Cortical Auditory Processing and Their Relation to Autistic Traits and Sensory Features. *Journal of Autism and Developmental Disorders*.

**Pacheco, D.**, Rajagopal, N., Prieve, B. A., & Nangia, S. (2022). Joint Profile Characteristics of Long-Latency Transient Evoked and Distortion Otoacoustic Emissions. *American Journal of Audiology*, *31*(3), 684–697.

*In Preparation*

**Pacheco, D**., Prieve, B., Hood, L., & Arduini, S., (In preparation). Comparison of Titan and Mimosa systems in Evaluation of Wideband Absorbance Measures in Premature Neonates over four test ages.

**Pacheco, D.,** Cary, E., Madrid, A., Prieve, B., Russo, N., (In preparation). Click- and speech-evoked auditory brainstem response latencies are symmetrical in children diagnosed with Autism Spectrum Disorder

## PRESENTATIONS

*Invited Speaker*

**Pacheco, D.**, (2022). *Relationship between Auditory Brainstem Response and Autistic Traits in School-age Children with and without Autism.* Neuroscience Research Day, Syracuse University, Syracuse, New York.

*Poster Presentations*

**Pacheco, D.**, Madrid, A., Cary, E., Matsuba, E., Russo, N., Prieve, B. (2023). *Auditory Brainstem Responses are Symmetrical in Children with Autism*. Poster Presentation at the American Auditory Society, Phoenix, AZ. **Awarded Mentored Student Travel Award**

Ingram, K., **Pacheco, D.**, Mulvihill, G., Prieve, B. (2023). *Wideband Acoustic Immittance in Children Born Preterm*. Poster Presentation at the American Auditory Society, Phoenix, AZ.

Mulvihill, G., **Pacheco, D.,** Ingram, K., Prieve, B. (2023). *Transient-Evoked Otoacoustic Emissions in Children Born Preterm*. Poster Presentation at the American Auditory Society, Phoenix, AZ. **Awarded Mentored Student Travel Award**

Matsuba, E., Prieve, B., Cary, E., **Pacheco, D.,** Madrid, A., McKernan, E., Kaplan-Kahn, E., Russo, N. (2022). *Speech from the brainstem to the cortex to behaviour: Characterizing subcortical and cortical auditory processing and their relation to autistic traits and sensory features.* Poster Presentation at the International Society for Autism Research, Austin, TX.

Cary, E. L., Kaplan-Kahn, E., Masters, E., Matsuba, E., MacKenzie, C., Rodrigues, A., Prieve, B., **Pacheco, D.**, Madrid, A., & Russo, N. (2021). *Relating ASD Traits and Sensory Overresponsivity to Early Electrophysiological Indices of Auditory Processing in Children with and without ASD*. Poster Presentation at the International Society for Autism Research, Boston, MA.

**Pacheco, D.,** Prieve, B., & Rajagopa, N. (2019). *Characteristics of Transient Evoked Otoacoustic Emissions with Different Time Windows.* Poster Presentation at the American Auditory Society, Phoenix, AZ. **Awarded Mentored Student Travel Award**

Walker, K., Prieve, B., Hood, L., & **Pacheco, D.** (2018). *Absorbance Levels in Preterm Infants Based on OAE Outcomes*. Poster Presentation at Association for Research in Otolaryngology, San Diego, CA.

## GRANT WRITING EXPERIENCE

NIDCD Research Dissertation Fellowship for AuD Audiologist (F32) December 2021
PAR-21-093 Role: Primary Investigator
Title: *"Severity of autism traits and language as predictors of auditory brainstem response latency in preschoolers with Autism Spectrum Disorder"*

The goal of the study was to investigate whether ABR latencies in autistic children are predicted by the spectrum of language abilities and autism traits, with the goal of better understanding auditory processing in autistic children. The grant was scored but not funded.

## HONORS AND AWARDS

| | |
|---|---|
| 2023 Mentored Student Travel Award, American Auditory Society | 2023 |
| Research Excellence Doctoral Funding Fellowship, Syracuse University | 2022-2023 |
| Outstanding Teaching Assistant, Syracuse University | 2022 |
| Graduate Assistantship, Syracuse University College of Arts and Sciences | 2019-2020/ 2021-2022 |
| Audiology/Hearing Science Research Travel Award, ASHA Convention | 2019 |
| Graduate Fellowship, Syracuse University College of Arts and Sciences | 2017-2019 |
| 2019 Mentored Student Travel Award, American Auditory Society | 2019 |
| Graduate Assistantship, Syracuse University College of Arts and Sciences | 2016-2017 |

## TEACHING EXPERIENCE

| | |
|---|---|
| Instructor of Record: Anatomy and Physiology of the Speech and Hearing Mechanisms [CSD 315] | Fall 2023 |
| Instructor of Record: Introduction to Communication Sciences and Disorders [CSD212] | Fall 2021 |
| Teaching Assistant for Advance Clinical Audiology I [CSD 661] | Fall 2019 |
| Guest Lecturer for Auditory Anatomy and Physiology [CSD 658]: Lecture on Basilar Membrane Mechanics | Spring 2019 |
| Teaching Assistant for Fundamentals of Hearing Science [CSD 325] | Spring 2017 |
| Teaching Assistant for Introduction to Communication Sciences and Disorders [CSD 212] and Phonetics [CSD 316] | Fall 2016 |

## CLINICAL PRACTICUM EXPERIENCE

| | |
|---|---|
| **Massachusetts Eye and Ear,** *Boston MA* | Summer 2020 – Summer 2021 |
| **Pediatric Audiology Laboratory**, *Syracuse University* | Spring 2019 – Spring 2020 |
| **Communication Disorder Unit**, *Upstate University Hospital* | Fall 2018 |
| **Syracuse Veteran's Hospital**, *Syracuse NY* | Summer 2018 |
| **Watertown Audiology at Fayetteville**, *Fayetteville NY* | Spring 2018 |
| **Onondaga –Cortland –Madison BOCES**, *Solvay NY School District* | Fall 2017 |
| **Gebbie Speech and Hearing Clinic,** Syracuse *University* | Fall 2016 – Summer 2017 |