Title

Habituation of auditory responses in young autistic and neurotypical children

Journal

Autism Research, 16(10)

ISSN

1939-3792

Authors

Dwyer, Patrick

Williams, Zachary J

Vukusic, Svjetlana

et al.

Publication Date

2023-10-01

DOI

10.1002/aur.3022

Peer reviewed

HHS Public Access

Author manuscript

Autism Res. Author manuscript; available in PMC 2024 October 01.

Published in final edited form as:

Autism Res. 2023 October ; 16(10): 1903–1923. doi:10.1002/aur.3022.

Habituation of Auditory Responses in Young Autistic and Neurotypical Children

Patrick Dwyer[*],
Department of Psychology, UC Davis, Davis, CA, USA

Center for Mind and Brain, UC Davis, Davis, CA, USA

MIND Institute, UC Davis, Davis, CA, USA

Zachary J. Williams,
Medical Scientist Training Program, Vanderbilt University School of Medicine, Nashville, TN, USA

Department of Hearing & Speech Sciences, Vanderbilt University Medical Center, Nashville, TN, USA

Vanderbilt Brain Institute, Vanderbilt University, Nashville, TN, USA

Frist Center for Autism and Innovation, Vanderbilt University, Nashville, TN, USA

Vanderbilt Kennedy Center, Vanderbilt University Medical Center, Nashville, TN, USA

Svjetlana Vukusic,
Center for Mind and Brain, UC Davis, Davis, CA, USA

Department of General Practice, Melbourne Medical School, the University of Melbourne, Melbourne, VIC, Australia

Clifford D. Saron[†],
Center for Mind and Brain, UC Davis, Davis, CA, USA

MIND Institute, UC Davis, Sacramento, CA, USA

Susan M. Rivera[†]
Department of Psychology, UC Davis, Davis, CA, USA

Center for Mind and Brain, UC Davis, Davis, CA, USA

MIND Institute, UC Davis, Sacramento, CA, USA

Abstract

[*]Corresponding author, patricksrdwyer@gmail.com.
[†]Co-senior authors

Author Contributions

SMR and CDS designed the experiment. SV contributed to data preparation and ZJW calculated loudness discomfort scores and assisted with methodology/statistical analyses. PD conducted the statistical analysis and drafted the manuscript. All authors read, critically revised, and approved the final manuscript.

Conflict of Interest

ZJW has received consulting fees from Roche. He is also a Family Partner of the Autism Speaks Autism Care Network site at Vanderbilt University. ZJW and PD are members of the Autistic Researcher Review Board of the Autism Intervention Research Network on Physical Health (AIR-P). The other authors have no relevant conflicts of interest to declare.

Prior studies suggest that habituation of sensory responses is reduced in autism and that diminished habituation could be related to atypical autistic sensory experiences, e.g., by causing brain responses to aversive stimuli to remain strong over time instead of being suppressed. While many prior studies exploring habituation in autism have repeatedly presented identical stimuli, other studies suggest group differences can still be observed in habituation to intermittent stimuli. The present study explored habituation of electrophysiological responses to auditory complex tones of varying intensities (50–80 dB SPL), presented passively in an interleaved manner, in a well-characterized sample of 127 autistic (M_{DQ}=65.41, *SD*=20.54) and 79 typically-developing (M_{DQ}=106.02, *SD*=11.50) children between 2–5 years old. Habituation was quantified as changes in the amplitudes of single-trial responses to tones of each intensity over the course of the experiment. Habituation of the auditory N2 response was substantially reduced in autistic participants as compared to typically-developing controls, although diagnostic groups did not clearly differ in habituation of the P1 response. Interestingly, the P1 habituated less to loud 80 dB sounds than softer sounds, whereas the N2 habituated less to soft 50 dB sounds than louder sounds. No associations were found between electrophysiological habituation and cognitive ability or participants' caregiver-reported sound tolerance (Sensory Profile Hyperacusis Index). The results present study results extend prior research suggesting habituation of certain sensory responses is reduced in autism; however, they also suggest that habituation differences observed using this study's paradigm may not be a primary driver of autistic participants' real-world sound intolerance.

Lay Summary

Young children listened to tones, presented at a mixture of different volumes, while we recorded their brain responses. We studied whether brain responses habituated (got smaller over time) as the tones repeated. There was less habituation of a brain response ~250 ms after high-volume (loud) tones in autistic children than in non-autistic children. Unexpectedly, we did not find relationships between brain response habituation and parents' reported perceptions of their children's loudness discomfort.

Keywords

Autism; habituation; adaptation; electrophysiology; sensory behaviours

Introduction

Sensory Experiences in Autism

The sensory experiences of autistic people[1] are increasingly recognized as an important topic of investigation for researchers, both due to their salience in the lives of many autistic people and due to their potential role in the development of autistic phenotypes. Sensory

[1]Autism identifying language remains a controversial area, including among individuals on the autism spectrum themselves (Bury et al., 2023). In deference to the preferences of many individuals on the autism spectrum (Bury et al., 2023; Kenny et al., 2016), and in light of concern that person-first language may be conducive towards or at least reflective of stigma (Gernsbacher, 2017), we have chosen to use identity-first language (e.g., "autistic person"). We have also chosen, again partly in deference to autistic opinion, but also out of a desire to avoid subjective value judgements in academic terminology, to use neutral descriptive terms such as "autism spectrum development" in preference to value-laden terms like "disorder" or "condition."

reactivity in Autism Spectrum Development (ASD) is even related to, or an aspect of, quality of life (Lin & Huang 2019; McConachie et al. 2019). Furthermore, studies have identified relationships between sensory experiences/behaviours in ASD and participation in everyday activities (Ismael et al., 2018; Little et al., 2015) and sleep quality (Tzischinsky et al., 2018).

Beyond their intrinsic importance, differences in how autistic people attend to and process sensory information early in development might have important consequences for later development. For example, atypical sensory processing might interfere with social and language learning. Distracting sensory inputs can lead autistic people to exhibit atypical brain activity in social tasks (Green et al., 2018), and altered sensory processing predicts later social and language outcomes in ASD (Baranek et al., 2018; Damiano-Goodwin et al., 2018; Kolesnik et al., 2019). Furthermore, one might expect that autistic children's experiences of sensory distress could lead them to develop anxious vigilance and fears surrounding the possibility these uncomfortable stimuli might recur (Verhulst et al., 2022). This supposition is supported by evidence; early sensory over-responsivity in infants and in young autistic children is associated with later anxiety (Green et al., 2012; Narvekar et al., 2022). Other infant studies' findings of behavioural and neurophysiological differences in sensory processing suggest such alterations of developmental trajectories could begin very early in life (Baranek, 1999; Miron et al., 2020).

In the auditory domain specifically, a number of auditory sensory phenotypes can be distinguished, both in autism and the general population (Williams et al., 2021b). These include various forms of sound intolerance, such as misophonia, or strong emotional responses (often anger and/or disgust) to specific trigger sounds; phonophobia, or phobias towards sounds; and hyperacusis, or finding sounds (even those of moderate intensity) to be excessively loud, painful, or overwhelming. Hyperacusis does seem to be common in autism (Danesh et al., 2015; Khalfa et al., 2004; Williams et al., 2021c), although it is arguably unclear whether it can be easily distinguished from "sensory overload" (described in Belek, 2018; Scheydt et al., 2017). For this reason, we will ordinarily use the more general term "sound (in)tolerance."

Habituation

Reductions in habituation or suppression of neural responses to repeated stimuli are a neural-level mechanism that could potentially account for many autistic sensory experiences. It seems reasonable to assume that a lack of neural habituation could exacerbate experiences of distress or overload caused by prolonged or repeated loud sounds or result in poorer filtering of distracting background stimuli.

The idea that habituation is reduced in autism appears consistent with some autistic people's qualitative accounts (Robertson & Simmons 2015), subjective ratings (Lawson et al., 2015), and autonomic arousal to stimuli (Gandhi et al., 2021), as well as with many functional imaging studies using different methods and approaches. These studies include paradigms involving repetition of stimuli within pairs (Orekhova et al., 2008; Stroganova et al., 2013), repetitions of standard stimuli between occasional oddballs (Kolesnik et al., 2019; Ruiz-Martínez et al., 2019), rapid trains of identical stimuli (Font-Alaminos et al., 2020),

and slower delivery of identical stimuli either in blocks (Millin et al., 2018) or over whole experiments (Gandhi et al., 2021; Jamal et al., 2021; Martineau et al., 1992; Matsuzaki et al., 2014). Differences in habituation between typically developing and autistic individuals appear very early in life: studies have found that reduced repetition suppression of responses to auditory (Kolesnik et al., 2019) and tactile (Piccardi et al., 2021) stimuli predicts an eventual autism diagnosis among infants at elevated autism likelihood; as a group, infants at elevated autism likelihood also show reduced habituation to auditory standards (Guiraud et al., 2011).

Interestingly, reductions in habituation in autistic participants are not solely observed in paradigms in which identical stimuli are delivered repetitively. Hudac and colleagues (2018) observed reduced attenuation over trials of P3a responses, or brain responses towards a variety of different novel stimuli (e.g., chimes, cricket chirps, drums, whooshing) occasionally interspersed among standard stimuli; P3a responses may reflect focal attention towards these novel events and representation of them in working memory (Polich, 2011). Habituation of the P3a may therefore reflect participants coming to expect strange, novel stimuli to appear, and devoting gradually less attention to them over time[2]. Thus, Hudac and colleagues' study suggests that ASD–Typical Development (TD) group differences in habituation could manifest in a wide variety of everyday contexts: not only ones in which stimuli are prolonged or repeated without any change in their properties, but also in contexts in which non-identical stimuli are repeated in some way that is still physically or functionally similar or predictable.

One other important question is whether altered habituation in ASD can be directly related to the sensory experiences and behaviours of autistic people, including hyper-responsive patterns such as distractibility towards background stimuli and distress caused by intense stimuli. On this point, there is some positive evidence (Font-Alaminos et al., 2020; Green et al., 2019; Jamal et al., 2021; Lawson et al., 2015; Matsuzaki et al., 2014). However, other studies find no link between habituation and the sensory experiences or behaviours of autistic people (Millin et al., 2018; Ruiz-Martínez et al., 2019).

Explanations for Habituation Differences

A number of different neurobiological and cognitive theories of autism have been postulated that could account for, or be consistent with, reductions in habituation in ASD. The present study is not intended to compare these accounts against one another – and indeed, it is quite possible that more than one could be true in different individuals, or even that different mechanisms on different levels might operate in the same individuals. Indeed, research suggests habituation is often atypical in animal models of genetic variants associated with autism (among other diagnoses and conditions; e.g. McCullaugh et al., 2020), but different genes can affect different aspects of habituation, suggesting multiple mechanisms are involved (McDiarmid et al., 2020).

[2]The P3a was not examined in the present study, as this study was intended to explore differences in neural responses as a function of the intensity of equiprobable stimuli, and the paradigm changes necessary to evoke a P3a response would have interfered with this aim.

One theory proposes that the autistic brain is characterized by an atypical balance of neural excitation and inhibition: specifically, in comparison to TD, reduced inhibition relative to excitation (Rubenstein & Merzenich, 2003; Sohal & Rubenstein, 2019). Within this framework, repeated and/or irrelevant sensory inputs might not be inhibited in autism as they would be in TD, resulting in a more robust neural response to these repeated stimuli (Ethridge et al., 2016; Kolesnik et al., 2019). There is evidence from typically-developing individuals linking inhibitory processing and habituation (Palermo et al., 2011), and recent evidence suggests that arbaclofen, a GABA receptor agonist, appears to enhance repetition suppression in autistic adults (Huang et al., 2023). Moreover, decreased inhibition in the auditory cortex has been shown in animal models to directly lead to loudness hyperacusis, a form of sound intolerance (McGill et al., 2023).

Researchers have also proposed various other frameworks to interpret autism, including a family of theories related to prediction and learning (e.g., Lawson, Rees, & Friston, 2014; Pellicano & Burr, 2012; Qian & Lipkin, 2011; Sinha et al., 2014; Van de Cruys et al., 2014). In most of these accounts, autistic people are postulated to place relatively greater weight on bottom-up information such as momentary sensory inputs, while placing less weight on top-down generalizations and predictions about environments (Angeletos Chrysaitis & Seriès, 2022). Researchers have proposed that such a pattern could be consistent with reductions of habituation: if autistic people are less able learn regularities, or fail to apply such expectations to predict stimuli, the neural response to repeated stimuli might not diminish (Cannon et al., 2021).

However, the suggestion that autistic people in general are unable to effectively predict basic regularities should be regarded with caution. An alternative interpretation may emerge from findings suggesting that autistic people's attention is susceptible to being exogenously captured by stimuli (Keehn et al., 2016; Keehn et al., 2019b). Autistic people are also often slow to disengage attention from stimuli (Keehn et al., 2019a; Sacrey et al., 2014); thus, they might have difficulty disengaging their attention from repeating stimuli. Furthermore, autistic people often experience sensory anxieties (Halim et al., 2018; Kerns et al., 2014; Lau et al., 2020), and anxiety is associated with attentional vigilance towards potentially threatening stimuli (Eysenck et al., 2007). Autism is also associated with symptoms of misophonia (Williams et al., 2021b, 2022), and in misophonic people, attention may be captured by repetitive trigger sounds (da Silva & Sanchez, 2019; Simner et al., 2022). Thus, autistic people might be very well able to effectively predict repetition of stimuli (Cannon et al., 2023; Sharer et al., 2015) – indeed, some might be frustrated due to knowing that an aversive stimulus will soon repeat itself – but due to focusing their attention on the repetitive stimuli, they might continue to show a strong response instead of habituating. This account has intuitive appeal to the autistic first author of this paper and comports with his personal experience. However, there is a lack of rigorous qualitative autism research regarding anticipatory consequences of repeated aversive and non-aversive stimuli. Moreover, whether or not the first author's experience generalizes to other autistic people, it is unclear whether/how reportable, subjective experiences of awareness of stimulus repetition map onto neural-level processes related to prediction.

Ultimately, given the heterogeneity of ASD, as well as the existence of multiple levels of explanation such as the neurobiological and the cognitive, it is unclear whether a single cause can be expected to be responsible for reduced habituation across all autistic individuals.

Auditory Event-Related Potentials in Young Autistic Children

The present study examines habituation in auditory event-related potentials (ERPs) from young autistic children between 2–5 years of age. As they are commonly described in prior research literature (the "canon"), canonical auditory ERPs evident over frontocentral scalp sites in this age range include the P1 response, a large positive voltage deflection occurring approximately ~100–150 ms after stimulus onset, and the frontocentral N2, a negative voltage deflection occurring approximately ~250 ms after stimulus onset (Čeponiene et al., 2003; Ponton et al., 2002; Shafer et al., 2015). These ERP responses have been previously described in the present study sample by Dwyer and colleagues (2021), who found that the N2 response was attenuated at the group average level in ASD, which is consistent with prior research (reviewed by Williams et al., 2021a). More specifically, Dwyer et al. (2021a) found autistic participants exhibited less negative voltages over frontocentral sites in the time window of the N2 in responses to 60 through 80 dB stimuli, though no group difference was observed in responses to the softer 50 dB stimuli. This may reflect the intensity-dependency of the N2 itself, which was elicited by louder stimuli but not by softer stimuli.

Present Study

In the present study, habituation was examined using ERPs in a large sample of young autistic and typically-developing children from the Autism Phenome Project (APP) at the UC Davis MIND Institute (Amaral et al., 2017; Nordahl et al., 2022). Cognitive abilities of autistic participants in the present study ranged widely, with some participants having significant developmental delays while others appeared to be cognitively gifted. Auditory stimuli of four different intensity levels were presented in randomly interspersed manner, allowing for exploration of group differences in habituation over the course of the experiment across these different intensities. While participants listened to these stimuli, they also watched a quiet video chosen specifically to be of interest to them personally, so that habituation to the auditory stimuli in the present study might reflect successful suppression of responses to a less interesting stimulus. After data were collected, an intensive data processing pipeline that included second-order blind source identification (SOBI) independent components analysis (ICA; Belouchrani et al., 1997) was used to eliminate putatively artefactual signal sources. We made the following hypotheses regarding habituation and intra-individual variability in these data:

- First, given prior research, we expected to find reduced habituation in ASD, relative to TD, of the auditory event-related P1 and N2 responses; and
- Second, insofar as reduced habituation might be responsible for sensory experiences of autistic people, we expected that reduced habituation in ASD would be related to caregiver-reports of behaviours consistent with hyperacusis and auditory sensory sensitivity.

We also took advantage of the opportunity to explore associations between habituation and cognitive abilities.

Materials and methods

Participants

APP electrophysiological data have previously been presented in several studies focused on averaged ERPs (De Meo Monteil et al., 2019; Dwyer et al., 2020, 2021a, 2021b) as well as a report about overall inter-trial variability (Dwyer et al., 2022), but systematic habituation of electrophysiological responses from the APP has not previously been described.

As part of the APP, between 2006 and 2011, attempts were made to collect ERP data from 216 autistic and 104 typically-developing children, aged between 2–5 years. These participants' medical histories were screened for suspicion of hearing impairment prior to their participation in the ERP portion of the APP. Autistic participants were required to meet criteria for a pervasive developmental disorder (based on DSM-IV and Collaborative Programs of Excellence in Autism Network criteria) and pass ADOS-G (Lord et al., 2000) cut-off scores as well as cut-offs for either the social or communication subscales of the ADI-R (Lord, Rutter, & Le Couteur, 1994). Further information about the APP and participant recruitment can be found in Libero et al. (2016) and Nordahl et al. (2011). A number of participants were excluded from the present study due to failure to collect ERP data; due to noisy data; due to insufficient acceptable-quality trials (<400); due to excessive poor-quality channels (>6–7); due to neuroanatomical abnormalities revealed by magnetic resonance imaging collected in the APP; or due to abrupt changes in global field power at the single trial level over the course of the experiment, plotted using ERPimage (Delorme et al., 2015), that were assumed to be recording-related rather than neural in origin and thus probable confounds in analyses at the single-trial level. One participant entered the study in the TD group but was diagnosed with autism at a later APP time-point; this participant's data are also excluded. The final sample of children with data included in the present study compromised 79 typically-developing participants (27 female, 52 male) and 127 autistic participants (20 female, 107 male) (Table 1). There were more male-sex participants in the autistic group, χ^2=8.38, p=.004, Cramér's V=.21, 95% CI=[.08, .35]. The study was approved by the UC Davis Institutional Review Board and informed consent was obtained from the parent/guardian of each participant.

Measures

Loudness Discomfort.—Loudness discomfort was measured with the Sensory Profile Hyperacusis Index (SPHI; Dwyer et al., 2022; Williams et al., 2020). This measure is derived from the Short Sensory Profile (SSP; McIntosh et al., 1999), a caregiver-report questionnaire commonly used in investigations of sensory processing in autistic children (Williams et al., 2018; Williams, 2021). Five SSP items reflecting sound intolerance/noise distress and auditory filtering challenges (items 22, 24, 25, 34, and 35) are included in the SPHI, making it well-suited to measure behavioural auditory hyperreactivity that could potentially be linked to altered habituation patterns. A bifactor item response theory model is used to estimate loudness discomfort scores based on the expected a posteriori (Bock

& Mislevy, 1982) estimate of standing on the "general factor" underlying all five items. SPHI scores (on a Z-score scale) range from −1.45 to 2.16, with higher scores reflecting greater loudness discomfort. Usable SPHI data were available from 106 autistic and 64 typically-developing participants.

Because the SPHI includes both noise distress and auditory filtering items, we also conducted additional analyses in the Supplementary Materials separately using SSP Noise Distress and Auditory Distractibility scores (per Williams et al., 2018) in lieu of SPHI estimates, in order to explore whether they might have differential relationships to habituation.

Cognitive Ability.—Cognitive ability (in Table 1) was measured with the Mullen Scales of Early Learning (MSEL; Mullen, 1995). Four MSEL subscales were administered: Visual Reception (VR), Fine Motor (FM), Expressive Language (EL), and Receptive Language (RL). A ratio developmental quotient (DQ) was calculated by dividing mental age by chronological age, then multiplying by 100.

EEG Task

Participants were seated on a caregiver's lap in a dimly lit, audiometrically quiet, shielded chamber and allowed to watch a quiet video of their choice or a video that their caregiver believed would be of interest to them. While they watched this video, Sony MDR-222KD binaural headphones calibrated with a B&K artificial ear (model 4153) and sound meter (model 2229) were used to passively present 50ms (including 5ms rise and decay time) complex tones (sine waves of equal amplitude overlaid at the following 7 frequencies (musical notes): 249 Hz (B3); 616 Hz (D5), 788 Hz (G5), 1042 Hz (C6), 1410 Hz (F6), 1952 Hz (B6), and 2749 Hz (F7)) presented at a randomly variable (uniform) ISI of 1–2s. Tones randomly varied in intensity (50 dB, 60 dB, 70 dB, and 80 dB SPL); tones of the same intensity were never presented twice in succession. Presentation of tones was temporarily paused as required (e.g., when participants appeared to become restless). Approximately ~1100–1200 trials (~275–300 trials/condition) were collected from each participant (Table 1). Data collection often lasted approximately 30–40 minutes, not including capping time, but including pauses in the EEG recordings. Further details regarding the EEG task are available in De Meo-Monteil et al. (2019).

EEG Data Acquisition and Processing

EEG was collected with a 61-channel cap (www.easycap.de) with an equidistant electrode montage differing from the standard 10–20 system, as well as a Compumedics Neuroscan Synamp II amplifier sampling at a rate of 1000 Hz with Cz as a reference. EEG data were then low-cut (i.e., high-pass) filtered offline in BESA 5.2 (www.besa.de) with a cut-off of 0.4 Hz (12dB/octave roll-off). After low-cut filtering, the data were separated into epochs (spanning −200 ms to 900 ms, including 300 ms necessary for subsequent independent components analysis (ICA)), average-referenced, baseline-corrected (using the period from −100 to 0 ms), and manually inspected for noisy channels, which were removed in preparation for later interpolation. The artifact scan tool of BESA 5.2 was then used to screen for and remove epochs with extreme amplitudes; amplitude cut-offs were set

manually based on inspection of single epoch waveforms and of corresponding Raster plots of maximum amplitudes per epoch. In this manual inspection, the cut-off was iteratively moved along the Raster plot of maximum amplitudes until a point was found at which (1) inspecting four trials of those approaching, but below the amplitude cut-off yielded at least three good trials and (2) inspecting four trials of those approaching, but above the cut-off yielded at least three bad trials. The selected amplitude thresholds did not statistically differ between autistic (M=321, SD=95) and comparison (M=317, SD=116) participants, Wilcoxon p=.26, Cliff's δ=.09 [95% CI: −.07, .25]. All epochs were then manually inspected for abrupt voltage changes suggestive of temporary disconnection of electrode channels; epochs with such artefacts were removed.

The remaining epochs were then submitted to a Second-Order Blind source Identification (SOBI; Belouchrani et al., 1997; Tang, Sutherland, & McKinny, 2005) ICA. SOBI employs joint diagonalization of covariance matrices across different time delays, thereby taking into account temporal information from the EEG data, in order to separate the data into maximally uncorrelated "sources" with different spatial topographies and time courses. A semi-automatic artifact removal tool (SMART, Saggar et al., 2012, https://stanford.edu/~saggar/Software.html) was used to characterize the spatial topography, power spectra, autocorrelation, and time series of each SOBI source. These outputs were used to manually judge sources to be either putatively non-neural in origin (e.g., EMG, EOG, and blinks) or putatively neural. SOBI and SMART were applied separately to the first and second half of the data, consistent with recommendations for exploration of effects of ICA on the data (Luck, 2014b).

Data were subsequently reconstructed with putatively non-neural sources removed, and the artifact scan tool of BESA 5.2 was used once again to remove any remaining extreme amplitudes. Averages from each participant were computed and Cartool (Brunet, Murray, & Michel, 2011) was used to screen the data for any channels that appeared to be systematically deviant from adjacent channels in the averaged data. Returning to the trial-by-trial data, these channels, as well as previously removed noisy channels, were interpolated using a spherical spline approach (Perrin et al., 1989) as implemented by Fieldtrip (Oostenveld et al., 2011) and baseline correction (using the 100 ms prior to stimulus onset) was repeated. Finally, separate trial epochs (now spanning 200 ms pre-stimulus onset to 599 ms post-stimulus onset) from each participant were filtered (high-cut, i.e., low-pass: second-order Butterworth with 40 Hz cutoff and 12dB/octave roll/off; notch: 60 Hz Park-McClellan) using ERPLAB (Lopez-Calderon & Luck, 2014).

EEG Habituation Analysis

For the habituation analysis, a slope representing change in voltage amplitude over the course of the experiment was computed separately within each participant and each loudness condition, separately at each channel, and separately at each time-point within epochs (Figure 1). To ensure that outliers did not overly influence slope values, Kendall's τ was used to obtain rank-based slopes representing the ordinal association between voltage amplitude and the ordinal number representing the position of the trial within the

experiment. Owing to the unequal numbers of trials obtained across different participants (see Table 1), the total number of trials used to generate the slope values did vary.

Habituation slopes were analyzed in terms of canonical ERP responses, on the theory that habituation slopes would approximately appear as inverses of these responses: habituation of a positive-going ERP would take the form of a negative slope, while habituation of a negative-going ERP would appear as a positive slope.

Habituation of the P1 and N2 was quantified by taking the mean slope value within a given spatiotemporal window. Spatial windows are given in Figure 2, and these were defined based on observed grand-averaged ERP voltage topographies. Within these spatial windows, the P1 temporal windows were defined in each loudness condition as ±50ms on either side the greatest peak in any channel in the grand-averaged raw ERP voltage data across both diagnostic groups. This yielded the P1 windows of 73–173 ms (50 dB), 61–161 ms (60 dB), 45–145 ms (70 dB), and 43–143 ms (80 dB). Due to the relatively poor definition of the N2 ERP component, especially in softer intensity conditions, we did not attempt to locate peaks; instead, the temporal window was predefined as 201 – 350 ms.

One-Sample T-tests.—To determine whether mean slope values significantly differed from zero (that is, whether habituation was present) in any group or intensity condition, Bayesian one-sample *t*-tests were conducted with default priors (Morey et al., 2021) and are presented in Supplementary Materials.

Group Comparisons.—To compare habituation across groups and conditions, we used Bayesian multilevel models in *brms* (Bürkner, 2017) to examine the fixed effects of diagnostic group, hemisphere, and their interaction on habituation; intercepts were allowed to vary between each individual participant (i.e., we allowed for “random intercepts” of participant). Models used default priors and included 18,000 iterations (9,000 warmup). 95% equal-tailed credible intervals were estimated and reported for inferential purposes. In the models, continuous variables were converted to scaled *z*-scores to ease interpretation; categorical variables were sum-coded factors.

To examine the role of stimulus intensity in habituation, we used varying (“random”) effects. After building the baseline model, which did not include stimulus intensity as a predictor, we fitted a series of more complex models. First, we allowed varying (“random”) intercepts to differ across stimulus intensity conditions. Second, we estimated separate varying (“random”) slope models allowing effects of either diagnostic group or hemisphere to differ across intensities. Finally, we considered a model allowing effects of group, hemisphere, and their interaction to differ across intensities. Model fit was compared using the leave-one-out cross validation (LOO) method, computed via Pareto-smoothed importance sampling (Vehtari et al., 2017). Models were considered superior if improvements in LOO expected log pointwise predictive density ($elpd_{loo}$) exceeded estimates of the standard error of the difference. If the improvement in $elpd_{loo}$ did not exceed the estimate of the standard error of the difference between $elpd_{loo}$ values, the model with fewer parameters (i.e., the more parsimonious model) was retained, as the predictive performance of the two models was considered approximately equivalent.

This multilevel modelling framework also allowed us to include fixed effects of within- and between-subjects covariates. As noted previously, stimulus presentation was sometimes paused due to participants' comfort and behaviour, and the number of such pauses varied considerably across participants (Table 1, Supplementary Figure 1). Moreover, we have previously found that some participants in this dataset, including many autistic children, display positive voltages in the approximate spatiotemporal window of the canonical frontocentral N2 negativity (Dwyer et al., 2021b); habituation of a positive-going response would produce a negative slope, not the positive habituation slope expected for a negative-going N2 response. Due to the possibility that either pauses in stimulus presentation or group differences in averaged ERP voltages might account for differences in habituation, and given the statistical difference in sex between the autistic and comparison groups, we included the number of pauses, observed ERP voltages (mean amplitudes of the EEG response averaged over the same spatiotemporal windows used to measure habituation), and sex as fixed effect covariates in the multilevel models. As with other variables, continuous covariates were entered as *z*-scores, while sex was a sum-coded factor.

Additionally, in Supplementary Materials, participants with unexpected positive or less negative voltages in this period were identified with clustering and removed prior to analyses of N2 habituation. The results of the analyses presented in the main text were replicated.

Correlations.—To determine whether habituation was related to SPHI estimates or to cognitive ability, linear correlations between habituation slopes, as collapsed across hemispheres, were examined within a Bayesian framework using the *correlation* R package (Makowski et al., 2020). For all models, we used the default Bayesian correlation test (Ly et al., 2016) with "medium" priors (*r* scale parameters of 1/3), and Bayes factors (BF_{10}) were calculated to summarize evidence for or against the hypothesis of a significant linear correlation. We conducted these analyses specifically within the autistic group, to prevent any influence of group differences on results. *P*-values from equivalent frequentist tests are also presented.

For reference, linear correlations involving habituation slopes over each hemisphere separately are presented in the Supplementary Materials, along with linear correlations from typically-developing participants.

Results

P1 Habituation

One-Sample T-tests—One-sample *t*-tests found clear evidence of habituation of the P1 response over both hemispheres in the 50 dB and 70 dB conditions in the ASD group (Supplementary Table 1; Figures 3–5, 6A–D). Conversely, there was evidence ($BF_{10} \leq 0.33$) that typically-developing participants' responses to 80 dB sounds did not habituate over either hemisphere (Supplementary Table 1).

Group Comparisons—The model allowing intercepts to vary across stimulus intensities proved to have a better fit, $elpd_{loo} = -2290.1$, $SE = 29.6$, than the baseline model ignoring intensity, $elpd_{loo} = -.2294.6$, $SE = 29.5$; the improvement in model fit, $\Delta elpd_{loo} = 4.5$, was

greater than the estimated standard error of the difference, SE=3.2. However, the models with intensity slopes varying by group, $elpd_{loo}$ =−2290.8, SE=29.6, intensity slopes varying by hemisphere, $elpd_{loo}$ =−2290.9, SE=29.6, and intensity slopes varying by the interaction of hemisphere and group, $elpd_{loo}$ =−2292.6, SE=29.6, offered no further improvement in fit. This suggests that habituation slopes differed across different intensities, but that effects of group and hemisphere did not vary in an intensity-dependent manner.

In the selected model with varying intercepts of intensity, the estimated fixed effect of the ERP voltage covariate, β=−0.07, 95% CrI: [−0.13, −0.02], Pd = 99.74%, appeared to be robust, suggesting that participants with larger P1 amplitudes experienced greater habituation of the P1 (more negative slopes).

There was also some tendency for autistic participants to undergo *more* habituation of the P1 response than typically-developing controls, but the credible interval for this effect crossed zero, β=−0.06, 95% CrI: [−0.13, 0.02], and the probability of direction, Pd = 93.34%, was below 97.50%, suggesting that the data did not provide sufficient evidence to conclude that there are diagnostic group differences in P1 habituation (Figures 3, 4, and 5, 6A–D).

Credible intervals of the effects of hemisphere, β=0.00, 95% CrI: [−0.05, 0.05], Pd = 54.20%, the interaction of group and hemisphere, β=−0.01, 95% CrI: [−0.05, 0.04], Pd = 60.01%, number of pauses, β=0.00, 95% CrI: [−0.05, 0.05], Pd = 88.73%, and sex, β=0.05, 95% CrI: [−0.03, 0.12], Pd = 87.57%, also crossed zero.

To explore the marginal effect of intensity on habituation, we calculated highest-density credible intervals from model posterior predictions using *emmeans* (Lenth et al., 2021). Habituation was reduced (more positive slopes) in the 80 dB condition compared to the 70 dB condition, β=0.20, 95% CrI: [0.06, 0.35], and the 50 dB condition, β=0.14, 95% CrI: [0.00, 0.26]; there was also a strong tendency for habituation to 80 dB sounds to be less than that to 60 dB sounds (i.e., for slopes to be more positive for 80 than 60 dB sounds), but the credible interval crossed zero, β=0.12, 95% CrI: [−0.01, 0.25]. Credible intervals of differences between the 70 dB condition and the 50 dB, β=−0.06, 95% CrI: [−0.19, 0.05], and 60 dB, β=−0.07, 95% CrI: [−0.20, 0.04], conditions also crossed zero, as did the credible interval for differences between 60 dB and 50 dB, β=0.01, 95% CrI: [−0.11, 0.13].

Correlations—In the autistic group, when P1 habituation was collapsed across hemisphere, no substantial evidence (BF_{10} > 3) was found to support the existence of any association between P1 habituation and either SPHI estimates or MSEL DQ, whereas substantial evidence (BF_{10} < 0.33) suggested that there was no association between SPHI estimates and P1 habituation to 70 dB and 80 dB sounds in ASD, and no association between cognitive ability and P1 habituation to 50 and 60 dB sounds in ASD (Table 2). Analyses conducted in the typically-developing group (Supplementary Table 2) and separately in each hemisphere (Supplementary Tables 3–4) also found no evidence of associations, and some evidence of null effects.

N2 Habituation

One-Sample T-tests—One-sample *t*-tests found clear evidence of habituation of the N2 response, but only in the TD group and only in the 70 dB and 80 dB conditions (Supplementary Table 5, Figures 6E–H, 7, 8, 9). In the autistic group, evidence suggested that habituation slopes did not differ from zero over either hemisphere in the 60, 70, and 80 dB conditions, $BF \leq 0.14$.

Group Comparisons—The model allowing intercepts to vary across intensities proved to have a better fit, $elpd_{loo}$ =−2251.5, *SE*=30.6, than the baseline model ignoring intensity, $elpd_{loo}$=−.2259.2, *SE*=30.4; the improvement in model fit, $\Delta elpd_{loo}$=7.7, was greater than the estimated standard error of the difference, *SE*=3.8. However, the models with intensity slopes varying by group, $elpd_{loo}$ =−2251.6, *SE*=30.5, and intensity slopes varying by hemisphere, $elpd_{loo}$ =−2252.1, *SE*=30.7, and intensity slopes varying by the interaction of hemisphere and group, $elpd_{loo}$ =−2252.1, *SE*=30.7, offered no further improvement in fit. This suggests that habituation slopes differed across different intensities, but that effects of group and hemisphere did not vary in an intensity-dependent manner.

In the selected model, wherein intercepts vary across intensities, there was a clear and robust fixed "main" effect of diagnostic group on N2 habituation, β=−0.17, 95% CrI: [−0.25, −0.10], *P*d > 99.99%, which was driven by more positive habituation slopes – i.e., greater habituation of the N2 negativity – in typically-developing comparison participants (Figures 6E–H, 7, 8, 9).

There also appeared to be an effect of the number of pauses in the EEG recordings on N2 habituation, β=0.11, 95% CrI: [0.04, 0.18], *P*d=99.90%; surprisingly, participants whose recordings were paused more often displayed more habituation. However, the credible intervals of the effects of hemisphere, β=−0.02, 95% CrI: [−0.06, 0.02], *P*d=81.09%, the interaction of group and hemisphere, β=−0.00, 95% CrI: [−0.05, 0.04], *P*d=55.73%, ERP voltages, β=−0.03, 95% CrI: [−0.09, 0.02], *P*d=87.57%, and sex, β=−0.05, 95% CrI: [−0.13, 0.03], *P*d=87.72%, all crossed zero.

To follow up on the increase in model fit from allowing intercepts to vary across intensities – suggesting a "main effect" of intensity on N2 habituation – we, as with the P1, examined marginal effects and calculated highest-density credible intervals from model posterior predictions. The N2 exhibited less habituation to 50 dB sounds than 60 dB, β=−0.13, 95% CrI: [−0.25, −0.01], 70 dB, β=−0.21, 95% CrI: [−0.35, −0.08], or 80 dB sounds, β=−0.23, 95% CrI: [−0.37, −0.10]. There was less evidence that N2 habituation differed between the 80 dB condition and either the 70 dB condition, β=0.02, 95% CrI: [−0.10, 0.13], or the 60 dB condition, β=0.10, 95% CrI: [−0.02, 0.22], as well as between the 70 dB condition and the 60 dB condition, β=0.08, 95% CrI: [−0.03, 0.20].

Supplementary Control Analyses—As described in Supplementary Materials, participants were clustered on the basis of their N2 ERP amplitudes (Supplementary Figures 2–3, Supplementary Tables 6–7). N2 habituation was then examined after removing a cluster of participants with apparent positive-going ERP responses, and again after removing all

participants except a subset/cluster with the clearest negative-going N2 ERP responses. ASD-TD group differences in N2 habituation persisted in both cases.

Correlations—There was little evidence of associations between N2 habituation and either SPHI estimates or MSEL DQ. In autistic participants, when N2 habituation was collapsed across hemispheres, no substantial evidence ($BF_{10} > 3$) supported the existence of any association between N2 habituation and either SPHI estimates or MSEL DQ, whereas substantial evidence ($BF_{10} < 0.33$) suggested that there was no association between SPHI estimates and N2 habituation to 80 dB sounds, and no association between cognitive ability and N2 habituation to 50, 60, and 70 dB sounds (Table 3). Analyses conducted in typically-developing participants also found no evidence of associations, and some evidence of null effects (Supplementary Table 8).

When hemispheres were examined separately, evidence supported the existence of a statistical relationship between autistic participants' SPHI estimates and N2 habituation to 60 dB sounds over the right hemisphere (Supplementary Table 9), but this can easily be dismissed as a spurious finding due to the large number of comparisons considered.

Discussion

The present study investigated habituation of electrophysiological responses to auditory stimuli of varying intensities in a large sample of young autistic and typically-developing children. As predicted, habituation of the N2 response to auditory tones was robustly greater in the typically-developing group than in the autistic group, even after controlling for covariates. In those conditions, in the TD group, habituation slopes robustly differed from zero, indicating that N2 amplitudes changed over the course of the experiment. Surprisingly, we observed a tendency for autistic participants to show *elevated* habituation of the P1 response, but the data did not provide sufficient evidence for the credible interval of the effect of group on the P1 to differ from zero. Thus, the first hypothesis of the study – that habituation of the P1 and N2 responses would be reduced in autism – was partially supported. Habituation of the N2 response was reduced in autism, at least in response to higher-intensity stimuli, but the P1 trends were unexpected. However, if the trend towards elevated P1 habituation in autistic participants is not spurious, the possibility that it could reflect increased habituation of a negative-going response that cancels out in ERP averages should be borne in mind: ERPs of opposite polarities ordinarily cancel each other out, leaving only the stronger response (Luck, 2014a), but it is not impossible that response with the strongest contribution to the average ERP might differ from the response that makes the largest contribution to habituation over time.

The second hypothesis of the present study was not supported. We predicted that habituation slopes would be associated with an estimate of everyday sound tolerance derived from the caregiver-report Short Sensory Profile questionnaire, but no such effects were observed. Limitations of caregiver-report measures of the internal sensory experiences of the autistic individuals are discussed by Grandin and Panek (2014, pp. 75–87), who illustrate how an autistic person's external behaviour may not match up with their internal experience by, for example, describing a scenario in which an autistic person was externally unresponsive

to stimuli but feeling overwhelmed internally. Indeed, some autistic communities use the term “shutdown” to refer to extreme internal feelings of overload, which may not be accompanied by outward “meltdown” reactions (Belek, 2018). Interestingly, autistic people self-report more atypical sensory processing than their caregivers’ proxy reports (Keith et al., 2019; Millington et al., 2021), and one study suggests that self-reports, but not caregiver-reports, are related to autonomic arousal during noise exposure (Keith et al., 2019). Thus, it seems possible that caregivers might misunderstand and systematically underestimate autistic people’s atypical and aversive sensory experiences. On the other hand, prior research in the present study sample has found associations between the amplitudes of ERPs, as averaged across trials, and parent-report measures of sensory behaviour (Dwyer et al., 2020); various other studies also find associations between neural responses and parent-report or observational measures of sensory behaviour (e.g., Donkers et al., 2015; Karhson & Golob, 2016; Schwartz et al., 2020), including studies of neural habituation (Hudac et al., 2018). Some studies specifically find relationships between neural habituation and caregiver-reported hyperresponsive sensory patterns (Font-Alaminos et al., 2020; Jamal et al., 2021) or group differences in habituation between those with and without caregiver-reported hyperresponsivity (Green et al., 2019; Matsuzaki et al., 2014). Thus, it may be that neural habituation of the sort measured in the present study, simply has too little influence on day-to-day sensory experience for it to be correlated with a measure of sensory behaviours – but other sensory measures or other habituation paradigms could yield different results.

This raises the question of what habituation is likely to represent in the context of the present study, as compared to other studies. As with the habituation of oddball responses reported by Hudac et al. (2018), habituation in the context of the present study does not strictly reflect suppression of responses to repetition of identical stimuli in pairs, trains, or over whole experiments as in many prior studies observing links to sensory hyper-responsiveness (Font-Alaminos et al., 2020; Jamal et al., 2021; Kisley et al., 2004; Matsuzaki et al., 2014): instead, in the present study, tones of the same intensities were never presented twice in succession. By never presenting strictly identical stimuli in succession, the present study even differs from the paradigms used by Green and colleagues (2019), who examined changes over long periods wherein stimuli changed between blocks, but repeated within blocks, and Lawson and colleagues (2015), who presented a continuous stimulus in one ear while varying stimuli in the other. Thus, “habituation” in the present study, relative to other studies, may be less tightly related to suppression of responses to precisely identical stimuli.

Another key observation that may suggest an explanation of what habituation represents in the present study is that P1 responses, on average, appeared to habituate less to loud 80 dB sounds than sounds of lower intensities, whereas N2 responses, on average, appeared to habituate less (or even dishabituate more) to soft 50 dB sounds than at other intensities. In children from the age range of the present study, the P1 can be influenced by previously-engaged selective attention (Karns et al., 2015; Sanders et al., 2006), but our interleaved stimuli do not allow participants to confidently predict upcoming stimuli or direct their attention accordingly. Subjectively, in this study’s paradigm, we feel a loud 80 dB stimulus can be particularly striking due to its noticeably high intensity, and given the unpredictability of stimulus intensity, it may be difficult for even typically-developing participants to suppress a strong response to such sounds so early in cortical auditory processing. In this

regard, our P1 habituation results might be very different from those yielded by the sensory gating paradigms, with paired identical stimuli delivered at short interstimulus intervals, widespread in the current literature (reviewed by Williams et al., 2021a). However, it is possible that some participants may, over the course of the experiment, learn to more successfully and specifically inhibit their responses to loud sounds by the time window of the N2. Prior research does suggest inhibitory processing plays a key role in habituation (Palermo et al., 2011), so it seems possible that the relative lack of N2 habituation in autistic participants may, in at least some participants, be related to the balance of neural excitation and inhibition, which may be atypical in autistic people (see Sohal & Rubenstein, 2019).

It does seem reasonable to assume that participants would want to inhibit responses to our auditory tones, as participants might want to watch the quiet video that was specifically selected to be of interest to them. While this interpretation must be regarded as speculative, prior research does suggest that even relatively basic EEG refractory effects can be modulated by attention (Stevens et al., 2015), and an extensive literature describes attention differences in young autistic children that could have been relevant to our study; for example, autistic children appear to display slower attention disengagement (Sacrey et al., 2014) and appear to be more influenced by stimulus salience (Amso et al., 2014; Venker et al., 2021).

Moreover, if this is correct, it may suggest one way to understand why habituation differs across groups, but not within groups: in a manner of speaking, the substantial inter-individual variability in habituation slopes (depicted in Figure 3 and Figure 7) could reflect variability of states, not traits: attentional states relatively specific to this experimental paradigm, and/or specific to how the individuals happened to attend to stimuli in their environment during the session in which the EEG was recorded. Autistic people might have tended to differ from typically-developing people in inhibition of responses to distracting sounds and in attention allocation, producing group differences in habituation, but momentary between-participants attention fluctuations might have been random enough to mask relationships to real-world sensory behaviours within the autism group. For example, a participant might have focused attention on the sounds for a few minutes, then disengaged and returned to focusing on the video, but the occurrence and timing of such shifts could be very unpredictable. Other studies, with less of this random variability, might have more easily found relationships between habituation and within-group variability in real-world sensory behaviour.

However, as noted in the introduction, there are other theories that could account for ASD-TD habituation differences. These notably include theories based on predictive coding. It is unclear whether these interpretations can be ruled out on the basis of the present study; indeed, not only is the interpretation outlined above quite speculative, but it seems possible that multiple explanations for habituation differences could hold in different individuals or even in the same individual at different times.

It also seems reasonable to assume that the striking reduction in N2 habituation we observe in these young participants may have implications for subsequent development. For example, to the extent that the reduction in N2 habituation affects conscious awareness

of and attention towards stimuli, a lack of habituation might exacerbate autistic people's tendency to have difficulty disengaging from stimuli (see Sacrey et al., 2014), which could have implications for autistic people's ability to find opportunities to find novel learning opportunities.

Limitations

We believe that the present study has a number of strengths, particularly its large sample, the large number of trials obtained from each participant, and the rigorous data cleaning pipeline used to remove putatively non-neural, recording-related noise. Furthermore, the present study data were collected using a passive paradigm in a multisensory environment (that is, while participants watched a quiet video), which may make the study more naturalistic and relevant to sensory processing in real-world environments. We also believe that we can rule out the possibility that group differences in N2 habituation could be simple consequences of group differences in N2 voltage amplitudes. However, we do want to draw readers' attention to some limitations of our study.

First, this study has primarily focused on differences between *groups* of autistic and typically-developing children. In light of the heterogeneity of the multidimensionally variable constellation of autistic individuals, and the considerable heterogeneity we have observed in ERP responses from participants in this very dataset (Dwyer et al., 2020, 2021b), it is unclear how study findings might map onto particular autistic individuals. Indeed, out of the 216 autistic and 104 typically-developing participants from whom attempts were made to record electrophysiological data, usable data for these analyses were obtained from 127 (59%) and 79 (76%), respectively. The large number of autistic participants from whom usable data were not obtained suggests that the ASD group included in the final analyses is likely not representative of all autistic individuals; it is also notable that late-diagnosed autistic individuals would be excluded from the present study sample of young children. Thus, caution should be exercised in generalizing these results, whether to specific individuals included in this sample, or to other populations that might have been excluded from the present study sample.

Second, auditory detection thresholds were not measured in the present study, due to the difficulty of collecting audiometric data in children from such a young age range. It is thus possible that hearing acuity may have been reduced to some degree in the autistic sample, consistent with prior research (e.g., Demopoulos & Lewine, 2016; Rosenhall et al., 1999, but see also Beers et al., 2014), and it is unclear how this might have affected our habituation results.

Third, the quiet videos were individually chosen to be of specific interest to the participants, and a number of different videos were selected by different participants. While this helps to ensure that the quiet video is an engaging stimulus for each specific individual, it means that the sensory properties of individual videos are not equivalent, and it is unclear how this might have affected habituation of electrophysiological responses to the auditory tones. There is some evidence that media consumption habits differ between autistic and non-autistic people (Chapple et al., 2021; Stiller & Mößle, 2018), including in the age range of participants in the present study (Chonchaiya et al., 2011).

Fourth, we did interrupt stimulus presentation and recordings when required by participant behaviour, introducing considerable between-participants differences in the number of times when the recordings were paused. We covaried for these pauses, so we are confident that they do not account for the group differences we observed in N2 habituation, but they did appear to be systematically related to the magnitude of habituation. If future studies incorporate pauses, they should ideally be systematically manipulated, insofar as the constraints of participants' reactions in the moment permit.

Finally, the SPHI, although validated for use in autism (Williams et al., 2020), relies on a small number of items that might not capture all relevant aspects of sensory experiences. Moreover, these items are based on caregivers' reports about their children's sensory behaviours, and it is possible that some of the children's internal, real-world sensory experiences might not have been readily apparent from their behaviour. Thus, despite the evidence provided by this study's data, it is difficult to be completely rule out the possibility that habituation – even specifically habituation of the form measured in this study – is related to autistic people's real-world sensory experiences.

Summary

The present study found that autistic and typically-developing groups did significantly differ in levels of habituation, even though the auditory stimuli from this study were not repeated identical sounds but were instead tones of varying intensity presented in an intermixed manner. Specifically, habituation of the later N2 response was robustly greater in TD than ASD, while a trend for autistic people to unexpectedly display *greater* habituation of the P1 response did not appear to be statistically robust. Interestingly, N2 responses habituated less in the 50 dB condition than to louder intensities, whereas P1 responses showed the least habituation to 80 dB sounds compared to softer intensities. Unexpectedly, no associations were observed between habituation of electrophysiological responses and parent-reported sound tolerance. This could imply that the habituation effects observed in this study are not characteristic of participants' sensory behaviours and experiences in their everyday lived environments, but instead are at least in part reflective of states that are relatively specific to the momentary context of the experiment.

Future autism habituation research may benefit from manipulating attention, to determine whether attention allocation may be related to reductions in habituation in autism. Such manipulations could include attention tasks (e.g., selective attention paradigms), as well as manipulations explicitly adding or subtracting background sensory stimuli that might influence attention allocation. Studies of habituation in the visual modality might offer some advantages over auditory studies in this regard, as eye-tracking technology could be used to more transparently track the effects of attention manipulations (Falck-Ytter et al., 2013). Studies could also test other putative explanations of habituation differences by incorporating other factors, such as stimulus predictability, into their designs. One challenging but intriguing direction would be to contrast the effects of predictability and control by allowing participants some control over stimuli whilst still preserving timing differences; this could (for example) potentially be addressed by giving participants control over initiation/termination of blocks, but not sequences of stimuli within blocks.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgements

We wish to gratefully acknowledge all of the children and families who generously devoted considerable time and effort to participating in this large study, which included many other components besides ERP data collection. We warmly acknowledge the MIND Institute APP implementation and assessment team for their neuropsychological screening work and for coordinating the logistics of ERP appointments with participants' families. We thank all of the research assistants and junior specialists for their help with EEG data collection and processing (including Sarah Abedi, Margarita Beransky, Costanza Columbi, Sam Cheyette, Sharon Corina, Tucker Fisher, Sevan K. Harootonian, David Horton, Ryan Hubbard, Anne Kalomiris, Sarabeth Maciey, Lindsey Marcelino, Joshua Martin, Saloni Mathur, Thomas McLennan, Tracy Riggins, and Ashley Stark). We also thank Manish Saggar and Iman Mohammadrezazadeh for software development, and Yukari Takarae and Rosanna De Meo-Monteil for scientific support. We thank Dr. Tal Kenet, of the Harvard Medical School Department of Pediatric Neurology, who provided the stimuli used in this study, and we thank Zachary Nicholas Houghton for assistance with the Bayesian multilevel models.

Funding

Funding was received from the MIND Institute, the UC Davis Deans' Distinguished Graduate Fellowship, the NIH (1RO1 MH089626), Robert Shoes Fund, Scott & Jennifer Fearon, NIDCD (F30 DC019510), NIGMS (T32 GM007347), Swiss National Science Foundation (P2LAP3_164911), an Autism Center of Excellence grant awarded by the NICHD (P50 HD093079), a Royal Arch Masons CAPD Fellowship awarded by Autism Speaks.

Data Availability

The data that support the findings of this study are available from the corresponding author upon reasonable request.

References

Amaral DG, Li D, Libero L, Solomon M, Van de Water J, Mastergeorge A, Naigles L, Rogers S, & Nordahl CW (2017). In pursuit of neurophenotypes: The consequences of having autism and a big brain. Autism Research, 10(5), 711–722. 10.1002/aur.1755 [PubMed: 28239961]

Amso D, Haas S, Tenenbaum E, Markant J, & Sheinkopf SJ (2014). Bottom-Up Attention Orienting in Young Children with Autism. Journal of Autism and Developmental Disorders, 44(3), 664–673. 10.1007/s10803-013-1925-5 [PubMed: 23996226]

Angeletos Chrysaitis N, & Seriès P (2022). 10 years of Bayesian theories of autism: A comprehensive review. Neuroscience & Biobehavioral Reviews: 105022. 10.1016/j.neubiorev.2022.105022 [PubMed: 36581168]

Baranek GT (1999). Autism during infancy: A retrospective video analysis of sensory-motor and social behaviors at 9–12 months of age. Journal of Autism and Developmental Disorders, 29(3), 213–224. 10.1023/A:1023080005650 [PubMed: 10425584]

Baranek GT, Woynaroski TG, Nowell S, Turner-Brown L, DuBay M, Crais ER, & Watson LR (2018). Cascading effects of attention disengagement and sensory seeking on social symptoms in a community sample of infants at-risk for a future diagnosis of autism spectrum disorder. Developmental Cognitive Neuroscience, 29, 30–40. 10.1016/j.dcn.2017.08.006 [PubMed: 28869201]

Beers AN, McBoyle M, Kakande E, Dar Santos RC, & Kozak FK (2014). Autism and peripheral hearing loss: A systematic review. International Journal of Pediatric Otorhinolaryngology, 78(1), 96–101. 10.1016/j.ijporl.2013.10.063 [PubMed: 24300947]

Belek B (2018). Articulating sensory sensitivity: From bodies with autism to autistic bodies. Medical Anthropology, 38(1), 30–43. 10.1080/01459740.2018.1460750 [PubMed: 29727204]

Belouchrani A, Abed-Meraim K, Cardoso J-F, & Moulines E (1997). A blind source separation technique using second-order statistics. IEEE Transactions on Signal Processing, 45(2), 434–444. 10.1109/78.554307

Bock RD, & Mislevy RJ (1982). Adaptive EAP estimation of ability in a microcomputer environment. Applied Psychological Measurement, 6(4), 431–444. 10.1177/014662168200600405

Bölte S, Schlitt S, Gapp V, Hainz D, Schirman S, Poustka F, … Walter H (2012). A close eye on the eagle-eyed visual acuity hypothesis of autism. Journal of Autism & Developmental Disorders, 42, 726–733. 10.1007/s10803-011-1300-3 [PubMed: 21660498]

Brunet D, Murray MM, & Michel CM (2011). Spatiotemporal analysis of multichannel EEG: CARTOOL. Computational Intelligence and Neuroscience, 2011: 813870. 10.1155/2011/813870 [PubMed: 21253358]

Bürkner P-C (2017). brms: An R Package for Bayesian Multilevel Models Using Stan. Journal of Statistical Software, 80(1). 10.18637/jss.v080.i01

Bury SM, Jellett R, Spoor JR, & Hedley D (2023). "It defines who I am" or "it's something I have": What language do [autistic] Australian adults [on the autism spectrum] prefer? Journal of Autism and Developmental Disorders, 53, 677–687. 10.1007/s10803-020-04425-3 [PubMed: 32112234]

Cannon J, Eldracher E, Cardinaux A, Irfan F, Bungert L, Li C, O'Brien A, Treves I, Diamond S, & Sinha P (2023). Rhythmic and interval-based temporal orienting in autism. Autism Research. Advance online publication. 10.1002/aur.2892

Cannon J, O'Brien AM, Bungert L, & Sinha P (2021). Prediction in autism spectrum disorder : A systematic review of empirical evidence. Autism Research, 14(4), 604–630. 10.1002/aur.2482 [PubMed: 33570249]

Čeponiene R, Lepistö T, Alku P, Aro H, & Näätänen R (2003). Event-related potential indices of auditory vowel processing in 3-year-old children. Clinical Neurophysiology, 114(4), 652–661. 10.1016/S1388-2457(02)00436-4 [PubMed: 12686274]

Chapple M, Williams S, Billington J, Davis P, & Corcoran R (2021). An analysis of the reading habits of autistic adults compared to neurotypical adults and implications for future interventions. Research in Developmental Disabilities, 115: 104003. 10.1016/j.ridd.2021.104003 [PubMed: 34116300]

Chonchaiya W, Nuntnarumit P, & Pruksananonda C (2011). Comparison of television viewing between children with autism spectrum disorder and controls: TV viewing in autistic children. Acta Paediatrica, 100(7), 1033–1037. 10.1111/j.1651-2227.2011.02166.x [PubMed: 21244489]

Cliff N (1993). Dominance statistics: Ordinal analyses to answer ordinal questions. Quantitative Methods in Psychology, 114(3), 494–509. 10.1037/0033-2909.114.3.494

da Silva FE, & Sanchez TG (2019). Evaluation of selective attention in patients with misophonia. Brazilian Journal of Otorhinolaryngology, 85(3), 303–309. 10.1016/j.bjorl.2018.02.005 [PubMed: 29673780]

Damiano-Goodwin CR, Woynaroski TG, Simon DM, Ibañez LV, Murias M, Kirby A, … Cascio CJ (2018). Developmental sequelae and neurophysiologic substrates of sensory seeking in infant siblings of children with autism spectrum disorder. Developmental Cognitive Neuroscience, 29, 41–53. 10.1016/j.dcn.2017.08.005 [PubMed: 28889988]

Danesh AA, Lang D, Kaf W, Andreassen WD, Scott J, & Eshraghi AA (2015). Tinnitus and hyperacusis in autism spectrum disorders with emphasis on high functioning individuals diagnosed with Asperger's Syndrome. International Journal of Pediatric Otorhinolaryngology, 79(10), 1683–1688. 10.1016/j.ijporl.2015.07.024 [PubMed: 26243502]

De Meo-Monteil R, Nordahl CW, Amaral DG, Rogers SJ, Harootonian SK, Martin J, … Saron CD (2019). Differential altered auditory event-related potential responses in young boys on the autism spectrum with and without disproportionate megalencephaly. Autism Research, 12(8), 1236–1250. 10.1002/aur.2137 [PubMed: 31157516]

Delorme A, Miyakoshi M, Jung T-P, & Makeig S (2015). Grand average ERP-image plotting and statistics: A method for comparing variability in event-related single-trial EEG activities across subjects and conditions. Journal of Neuroscience Methods, 250, 3–6. 10.1016/j.jneumeth.2014.10.003 [PubMed: 25447029]

Demopolous C, & Lewine JD (2016). Audiometric profiles in autism spectrum disorders: Does subclinical hearing loss impact communication? Autism Research, 9(1), 107–120. 10.1002/aur.1495 [PubMed: 25962745]

Donkers FCL, Schipul SE, Baranek GT, Cleary KM, Willoughby MT, Evans AM, Bulluck JC, Lovmo JE, & Belger A (2015). Attenuated auditory event-related potentials and associations with atypical sensory response patterns in children with autism. Journal of Autism and Developmental Disorders, 45(2), 506–523. 10.1007/s10803-013-1948-y [PubMed: 24072639]

Dwyer P, De Meo-Monteil R, Saron CD, & Rivera SM (2021a). Effects of age on loudness-dependent auditory ERPs in young autistic and typically-developing children. Neuropsychologia: 107837. 10.1016/j.neuropsychologia.2021.107837 [PubMed: 33781752]

Dwyer P, Vukusic S, Williams ZJ, Saron CD, & Rivera SM (2022). "Neural Noise" in Auditory Responses in Young Autistic and Neurotypical Children. Journal of Autism and Developmental Disorders. 10.1007/s10803-022-05797-4

Dwyer P, Wang X, De Meo-Monteil R, Hsieh F, Saron CD, & Rivera SM (2020). Defining clusters of young autistic and typically developing children based on loudness-dependent auditory electrophysiological responses. Molecular Autism, 11, 48. 10.1186/s13229-020-00352-3 [PubMed: 32539866]

Dwyer P, Wang X, De Meo-Monteil R, Hsieh F, Saron CD, & Rivera SM (2021b). Using clustering to examine inter-individual variability in topography of auditory event-related potentials in autism and typical development. Brain Topography, 34, 681–697. 10.1007/s10548-021-00863-z [PubMed: 34292447]

Ethridge LE, White SP, Mosconi MW, Wang J, Byerly MJ, & Sweeney JA (2016). Reduced habituation of auditory evoked potentials indicate cortical hyper-excitability in fragile X syndrome. Translational Psychiatry, 6(4). 10.1038/tp.2016.48

Eysenck MW, Derakshan N, Santos R, & Calvo MG (2007). Anxiety and cognitive performance: Attentional control theory. Emotion, 7(2), 336–353. 10.1037/1528-3542.7.2.336 [PubMed: 17516812]

Falck-Ytter T, Bölte S, & Gredebäck G (2013). Eye tracking in early autism research. Journal of Neurodevelopmental Disorders, 5(1), 28. 10.1186/1866-1955-5-28 [PubMed: 24069955]

Font-Alaminos M, Cornella M, Costa-Faidella J, Hervás A, Leung S, Rueda I, & Escera C (2020). Increased subcortical neural responses to repeating auditory stimulation in children with autism spectrum disorder. Biological Psychology, 149: 107807. 10.1016/j.biopsycho.2019.107807 [PubMed: 31693923]

Gernsbacher MA (2017). Editorial Perspective: The use of person-first language in scholarly writing may accentuate stigma. Journal of Child Psychology and Psychiatry and Allied Disciplines, 58(7), 859–861. 10.1111/jcpp.12706 [PubMed: 28621486]

Gotham K, Pickles A, & Lord C (2009). Standardizing ADOS scores for a measure of severity in autism spectrum disorders. Journal of Autism and Developmental Disorders, 39, 693–705. 10.1007/s10803-008-0674-3 [PubMed: 19082876]

Grandin T, & Panek R (2014). The autistic brain: Helping different kinds of minds succeed. Boston, MA, USA: Mariner Books.

Green SA, Ben-Sasson A, Soto TW, & Carter AS (2012). Anxiety and sensory over-responsivity in toddlers with autism spectrum disorders: Bidirectional effects across time. Journal of Autism & Developmental Disorders, 42(6), 1112–1119. 10.1007/s10803-011-1361-3 [PubMed: 21935727]

Green SA, Hernandez LM, Bowman HC, Bookheimer SY, & Dapretto M (2018). Sensory over-responsivity and social cognition in ASD: Effects of aversive sensory stimuli and attentional modulation on neural responses to social cues. Developmental Cognitive Neuroscience, 29, 127–139. 10.1016/j.dcn.2017.02.005 [PubMed: 28284787]

Green SA, Hernandez L, Lawrence KE, Liu J, Tsang T, Yeargin J, … Bookheimer SY (2019). Distinct patterns of neural habituation and generalization in children and adolescents with autism with low and high sensory overresponsivity. American Journal of Psychiatry, 176(12), 1010–1020. 10.1176/appi.ajp.2019.18121333 [PubMed: 31230465]

Guiraud JA, Kushnerenko E, Tomalski P, Davies K, Ribeiro H, & Johnson MH (2011). Differential habituation to repeated sounds in infants at high risk for autism. NeuroReport, 22(16), 845–849. 10.1097/WNR.0b013e32834c0bec [PubMed: 21934535]

Halim AT, Richdale AL, & Uljarević M (2018). Exploring the nature of anxiety in young adults on the autism spectrum: A qualitative study. Research in Autism Spectrum Disorders, 55, 25–37. 10.1016/j.rasd.2018.07.006

Huang Q, Velthuis H, Pereira AC, Ahmad J, Cooke SF, Ellis CL, Ponteduro FM, Puts NAJ, Dimitrov M, Batalle D, Wong NML, Kowalewski L, Ivin G, Daly E, Murphy DGM, & McAlonan GM (2023). GABAergic regulation of auditory repetition suppression in adults with and without Autism Spectrum Disorder [Preprint]. medRxiv. 10.1101/2023.02.15.23285928

Hudac CM, DesChamps TD, Arnett AB, Cairney BE, Ma R, Webb SJ, & Bernier RA (2018). Early enhanced processing and delayed habituation to deviance sounds in autism spectrum disorder. Brain and Cognition, 123, 110–119. 10.1016/j.bandc.2018.03.004 [PubMed: 29550506]

Ismael N, Lawson LM, & Hartwell J (2018). Relationship between sensory processing and participation in daily occupations for children with autism spectrum disorder: A systematic review of studies that used Dunn's sensory processing framework. American Journal of Occupational Therapy, 72(3): 7203205030. 10.5014/ajot.2018.024075

Jamal W, Cardinaux A, Haskins AJ, Kjelgaard M, & Sinha P (2021). Reduced sensory habituation in autism and its correlation with behavioral measures. Journal of Autism and Developmental Disorders, 51, 3153–3164. 10.1007/s10803-020-04780-1 [PubMed: 33179147]

Karhson DS, & Golob EJ (2016). Atypical sensory reactivity influences auditory attentional control in adults with autism spectrum disorders. Autism Research, 9(10), 1079–1092. 10.1002/aur.1593 [PubMed: 26778164]

Karns CM, Isbell E, Giuliano RJ, & Neville HJ (2015). Auditory attention in childhood and adolescence: An event-related potential study of spatial selective attention to one of two simultaneous stories. Developmental Cognitive Neuroscience, 13, 53–67. 10.1016/j.dcn.2015.03.001 [PubMed: 26002721]

Keehn B, Nair A, Lincoln AJ, Townsend J, & Müller RA (2016). Under-reactive but easily distracted: An fMRI investigation of attentional capture in autism spectrum disorder. Developmental Cognitive Neuroscience, 17, 46–56. 10.1016/j.dcn.2015.12.002 [PubMed: 26708773]

Keehn B, Kadlaskar G, McNally Keehn R, & Francis AL (2019a). Auditory attentional disengagement in children with autism spectrum disorder. Journal of Autism and Developmental Disorders, 49, 3999–4008. 10.1007/s10803-019-04111-z [PubMed: 31201579]

Keehn B, Westerfield M, & Townsend J (2019b). Brief report: Cross-modal capture: Preliminary evidence of inefficient filtering in children with autism spectrum disorder. Journal of Autism and Developmental Disorders, 49(1), 385–390. 10.1007/s10803-018-3674-y [PubMed: 30014248]

Keith JM, Jamieson JP, & Bennetto L (2019). The importance of adolescent self-report in autism spectrum disorder: Integration of questionnaire and autonomic measures. Journal of Abnormal Child Psychology, 47, 741–754. 10.1007/s10802-018-0455-1 [PubMed: 30073571]

Kenny L, Hattersley C, Molins B, Buckley C, Povey C, & Pellicano E (2016). Which terms should be used to describe autism? Perspectives from the UK autism community. Autism, 20(4), 442–462. 10.1177/1362361315588200 [PubMed: 26134030]

Kerns CM, Kendall PC, Berry L, Souders MC, Franklin ME, Schultz RT, … Herrington J (2014). Traditional and atypical presentations of anxiety in youth with autism spectrum disorder. Journal of Autism and Developmental Disorders, 44(11), 2851–2861. 10.1007/s10803-014-2141-7 [PubMed: 24902932]

Khalfa S, Bruneau N, Rogé B, Georgieff N, Veuillet E, Adrien J-L, Barthélémy C, & Collet L (2004). Increased perception of loudness in autism. Hearing Research, 198(1–2), 87–92. 10.1016/j.heares.2004.07.006 [PubMed: 15617227]

Kisley MA, Noecker TL, & Guinther PM (2004). Comparison of sensory gating to mismatch negativity and self-reported perceptual phenomena in healthy adults. Psychophysiology, 41(4), 604–612. 10.1111/j.1469-8986.2004.00191.x [PubMed: 15189483]

Kolesnik A, Ali JB, Gliga T, Guiraud J, Charman T, & Jones EJH (2019). Increased cortical reactivity to repeated tones at 8 months in infants with later ASD. Translational Psychiatry, 9: 46. 10.1038/s41398-019-0393-x [PubMed: 30700699]

Lau BY, Leong R, Uljarevic M, Lerh JW, Rodgers J, Hollocks MJ, … Magiati I (2020). Anxiety in young people with autism spectrum disorder: Common and autism-related anxiety experiences and their associations with individual characteristics. Autism, 24(5), 1111–1126. 10.1177/1362361319886246 [PubMed: 31852214]

Lawson RP, Aylward J, Roiser JP, & Rees G (2018). Adaptation of social and non-social cues to direction in adults with autism spectrum disorder and neurotypical adults with autistic traits. Developmental Cognitive Neuroscience, 29, 108–116. 10.1016/j.dcn.2017.05.001 [PubMed: 28602448]

Lenth RV, Bolker B, Buerkner P, Giné-Vázquez I, Herve M, Jung M, Love J, Miguez F, Riebl H, & Singmann H (2021). Package 'emmeans'. https://cran.r-project.org/web/packages/emmeans/emmeans.pdf

Libero LE, Nordahl CW, Li DD, Ferrer E, Rogers SJ, & Amaral DG (2016). Persistence of megalencephaly in a subgroup of young boys with autism spectrum disorder. Autism Research, 9(11), 1169–1182. 10.1002/aur.1643 [PubMed: 27273931]

Lin L-Y, & Huang P-C (2019). Quality of life and its related factors for adults with autism spectrum disorder. Disability and Rehabilitation, 41(8), 896–903. 10.1080/09638288.2017.1414887 [PubMed: 29228834]

Little LM, Ausderau K, Sideris J, & Baranek GT (2015). Activity participation and sensory features among children with autism spectrum disorders. Journal of Autism and Developmental Disorders, 45(9), 2981–2990. 10.1007/s10803-015-2460-3 [PubMed: 25975628]

Lopez-Calderon J, & Luck SJ (2014). ERPLAB: An open-source toolbox for the analysis of event-related potentials. Frontiers in Human Neuroscience, 8: 213. 10.3389/fnhum.2014.00213 [PubMed: 24782741]

Lord C, Risi S, Linda L, Cook EH Jr., Leventhal Bennett, L., DiLavore PC, … Rutter M (2000). The Autism Diagnostic Observation Schedule - Generic: A standard measure of social and communication deficits associated with the spectrum of autism. Journal of Autism and Developmental Disorders, 30(3), 205–223. 10.1023/A:1005592401947 [PubMed: 11055457]

Lord C, Rutter M, & Le Couteur A (1994). Autism Diagnostic Interview-Revised: A revised version of a diagnostic interview for caregivers of individuals with possible pervasive developmental disorders. Journal of Autism and Developmental Disorders, 24(5), 659–685. 10.1007/BF02172145 [PubMed: 7814313]

Luck SJ (2014a). Chapter 2: A closer look at ERPs and ERP components. In Luck SJ, An Introduction to the Event-Related Potential Technique (2nd ed). Cambridge, MA: MIT Press. Retrieved from https://mitpress.mit.edu/books/introduction-event-related-potential-technique-second-edition

Luck SJ (2014b). Chapter 6 supplement: A closer look at ICA-based artifact correction. In Luck SJ, An Introduction to the Event-Related Potential Technique (2nd ed.). Cambridge, MA: MIT Press. Retrieved from https://mitpress.mit.edu/books/introduction-event-related-potential-technique-second-edition

Ly A, Verhagen J, & Wagenmakers E-J (2016). Harold Jeffreys's default Bayes factor hypothesis tests: Explanation, extension, and application in psychology. Journal of Mathematical Psychology, 72, 19–32. 10.1016/j.jmp.2015.06.004

Makowski D, Ben-Shachar M, Patil I, & Lüdecke D (2020). Methods and Algorithms for Correlation Analysis in R. Journal of Open Source Software, 5(51), 2306. 10.21105/joss.02306

Martineau J, Roux S, Garreau B, Adrien JL, & Lelord G (1992). Unimodal and crossmodal reactivity in autism: Presence of auditory evoked responses and effect of the repetition of auditory stimuli. Biological Psychiatry, 31(12), 1190–1203. 10.1016/0006-3223(92)90338-Z [PubMed: 1391280]

Matsuzaki J, Kagitani-Shimono K, Sugata H, Hirata M, Hanaie R, Nagatani F, … Taniike M (2014). Progressively increased M50 responses to repeated sounds in autism spectrum disorder with auditory hypersensitivity: A magnetoencephalographic study. PLoS One, 9(7): e102599. 10.1371/journal.pone.0102599 [PubMed: 25054201]

McConachie H, Wilson C, Mason D, Garland D, Parr JR, Rattazzi A, … Magiati I (2019). What is important in measuring quality of life? Reflections by autistic adults in four countries. Autism in Adulthood. Advance online publication. 10.1089/aut.2019.0008

McCullagh EA, Rotschafer SE, Auerbach BD, Klug A, Kaczmarek LK, Cramer KS, Kulesza RJ, Razak KA, Lovelace JW, Lu Y, Koch U, & Wang Y (2020). Mechanisms underlying auditory processing deficits in Fragile X syndrome. FASEB, 34, 3501–3518. 10.1096/fj.201902435R

McDiarmid TA, Belmadani M, Liang J, Meili F, Mathews EA, Mullen GP, Hendi A, Wong W-R, Rand JB, Mizumoto K, Haas K, Pavlidis P, & Rankin CH (2020). Systematic phenomics analysis of autism-associated genes reveals parallel networks underlying reversible impairments in habituation. Proceedings of the National Academy of Sciences, 117(1), 656–667. 10.1073/pnas.1912049116

McIntosh DN, Miller LJ, & Shyu V (1999). Development and validation of the Short Sensory Profile. In Dunn W (Ed.), Sensory Profile: User's manual (pp. 59–73). Psychological Corporation.

McGill M, Kremer C, Stecyk K, Clayton K, Skerleva D, Hancock K, Kujawa SG, & Polley DB (2023). Cortical contributions to the perception of loudness and hyperacusis [Preprint]. bioRxiv. 10.1101/2023.03.24.534013

Millin R, Kolodny T, Flevaris AV, Kale AM, Schallmo M-P, Gerdts J, … Murray S (2018). Reduced auditory cortical adaptation in autism spectrum disorder. ELife, 7: e36493. 10.7554/eLife.36493 [PubMed: 30362457]

Millington E, Brown L, McMahon H, Robertson AE, & Simmons D (2021). Children's Glasgow Sensory Questionnaire (C-GSQ): Validation of a Simplified and Visually Aided Questionnaire [Preprint]. PsyArXiv. 10.31234/osf.io/f6bg2

Miron O, Delgado RE, Delgado CF, Simpson EA, Yu K-H, Gutierrez A, … Kohane IS (2021). Prolonged auditory brainstem response in universal hearing screening of newborns with autism spectrum disorder. Autism Research, 14(1), 46–52. 10.1002/aur.2422 [PubMed: 33140578]

Morey RD, Rouder JN, Jamil T, Urbankek S, Forner K, & Ly A (2021). Package 'BayesFactor.' R package version 0.9.12–4.3. https://cran.r-project.org/web/packages/BayesFactor/index.html

Vehtari A, Gabry J, Magnusson M, Yao Y, Bürkner P, Paananen T, Gelman A (2023). "loo: Efficient leave-one-out cross-validation and WAIC for Bayesian models." R package version 2.6.0, <https://mc-stan.org/loo/>. - this is the raw Citation("loo") and you may want to reformat some.

Mullen EM (1995). Mullen scales of early learning (AGS ed.). Circle Pines, MN: American Guidance Service.

Murray D, Lesser M, & Lawson W (2005). Attention, monotropism and the diagnostic criteria for autism. Autism, 9(2), 139–156. 10.1177/1362361305051398 [PubMed: 15857859]

Murray F (2018, November 30). Me and monotropism: A unified theory of autism. The Psychologist. Retrieved from https://thepsychologist.bps.org.uk/me-and-monotropism-unified-theory-autism

Narvekar N, Carter Leno V, Pasco G, Johnson MH, Jones EJ, & Charman T (2022). A prospective study of associations between early fearfulness and perceptual sensitivity and later restricted and repetitive behaviours in infants with typical and elevated likelihood of autism. Autism, 26(8), 1947–1958. 10.1177/13623613211068932 [PubMed: 35021899]

Neil L, Olsson NC, & Pellicano E (2016). The relationship between intolerance of uncertainty, sensory sensitivities, and anxiety in autistic and typically developing children. Journal of Autism and Developmental Disorders, 46(6), 1962–1973. 10.1007/s10803-016-2721-9 [PubMed: 26864157]

Nordahl CW, Andrews DS, Dwyer P, Waizbard-Bartov E, Restrepo B, Lee JK, Heath B, Saron C, Rivera SM, Solomon M, Ashwood P, & Amaral DG (2022). The Autism Phenome Project: Toward identifying clinically meaningful subgroups of autism. Frontiers in Neuroscience, 15: 786220. 10.3389/fnins.2021.786220 [PubMed: 35110990]

Nordahl CW, Lange N, Li DD, Barnett LA, Lee A, Buonocore MH, … Amaral DG (2011). Brain enlargement is associated with regression in preschool-age boys with autism spectrum disorders. Proceedings of the National Academy of Sciences, 108(50), 20195–20200. 10.1073/pnas.1107560108

Oostenveld R, Fries P, Maris E, & Schoffelen JM (2011). FieldTrip: Open source software for advanced analysis of MEG, EEG, and invasive electrophysiological data. Computational Intelligence and Neuroscience, 2011: 156869. 10.1155/2011/156869 [PubMed: 21253357]

Orekhova EV, Stroganova TA, Prokofyev AO, Nygren G, Gillberg C, & Elam M (2008). Sensory gating in young children with autism: Relation to age, IQ, and EEG gamma oscillations. Neuroscience Letters, 434(2), 218–223. 10.1016/j.neulet.2008.01.066 [PubMed: 18313850]

Palermo A, Giglia G, Vigneri S, Cosentino G, Fierro B, & Brighina F (2011). Does habituation depend on cortical inhibition? Results of a rTMS study in healthy subjects. Experimental Brain Research, 212(1), 101–107. 10.1007/s00221-011-2701-4 [PubMed: 21537965]

Pellicano E, & Burr D (2012). When the world becomes “too real”: A Bayesian explanation of autistic perception. Trends in Cognitive Sciences, 16(10), 504–510. 10.1016/j.tics.2012.08.009 [PubMed: 22959875]

Perrin F, Pernier J, Bertrand O, & Echallier JF (1989). Spherical splines for scalp potential and current density mapping. Electroencephalography and Clinical Neurophysiology, 72(2), 184–187. 10.1016/0013-4694(89)90180-6 [PubMed: 2464490]

Piccardi ES, Begum Ali J, Jones EJH, Mason L, Charman T, Johnson MH, & Gliga T (2021). Behavioural and neural markers of tactile sensory processing in infants at elevated likelihood of autism spectrum disorder and/or attention deficit hyperactivity disorder. Journal of Neurodevelopmental Disorders, 13(1): 1. 10.1186/s11689-020-09334-1 [PubMed: 33390154]

Polich J (2011). Neuropsychology of P300. In Kappenman ES & Luck SJ (Eds.), The Oxford Handbook of Event-Related Potential Components (pp. 160–188). 10.1093/oxfordhb/9780195374148.013.0089

Ponton C, Eggermont J, Khosla D, Kwong B, & Don M (2002). Maturation of human central auditory system activity: Separating auditory evoked potentials by dipole source modeling. Clinical Neurophysiology, 113, 407–420. 10.1016/S1388-2457(01)00733-7 [PubMed: 11897541]

Qian N, & Lipkin RM (2011). A learning-style theory for understanding autistic behaviors. Frontiers in Human Neuroscience, 5, 77. 10.3389/fnhum.2011.00077 [PubMed: 21886617]

Robertson AE, & Simmons DR (2015). The sensory experiences of adults with autism spectrum disorder: A qualitative analysis. Perception, 44(5), 569–586. 10.1068/p7833 [PubMed: 26422904]

Rosenhall U, Nordin V, Sandström M, Ahlsén G, & Gillberg C (1999). Autism and hearing loss. Journal of Autism and Developmental Disorders, 29(5), 349–357. 10.1023/A:1023022709710

Rubenstein JLR, & Merzenich MM (2003). Model of autism: increased ratio of excitation/inhibition in key neural systems. Brain, 2(5), 255–267. 10.1046/j.1601-183X.2003.00037.x

Ruiz-Martínez FJ, Rodríguez-Martínez EI, Wilson CE, Yau S, Saldaña D, & Gómez CM (2019). Impaired P1 habituation and mismatch negativity in children with autism spectrum disorder. Journal of Autism and Developmental Disorders, 50, 603–616. 10.1007/s10803-019-04299-0

Sacrey L-AR, Armstrong VL, Bryson SE, & Zwaigenbaum L (2014). Impairments to visual disengagement in autism spectrum disorder: A review of experimental studies from infancy to adulthood. Neuroscience and Biobehavioral Reviews, 47, 559–577. 10.1016/j.neubiorev.2014.10.011 [PubMed: 25454358]

Saggar M, King BG, Zanesco AP, MacLean KA, Aichele SR, Jacobs TL, … Saron CD (2012). Intensive training induces longitudinal changes in meditation state-related EEG oscillatory activity. Frontiers in Human Neuroscience, 6, 256. 10.3389/fnhum.2012.00256 [PubMed: 22973218]

Sanders LD, Stevens C, Coch D, & Neville HJ (2006). Selective auditory attention in 3- to 5-year-old children: An event-related potential study. Neuropsychologia, 44(11), 2126–2138. 10.1016/j.neuropsychologia.2005.10.007 [PubMed: 16289144]

Sassenhagen J, & Draschkow D (2019). Cluster-based permutation tests of MEG/EEG data do not establish significance of effect latency or location. Psychophysiology, 56(6): e13335. 10.1111/psyp.13335 [PubMed: 30657176]

Scheydt S, Müller Staub M, Frauenfelder F, Nielsen GH, Behrens J, & Needham I (2017). Sensory overload: A concept analysis. International Journal of Mental Health Nursing, 26, 110–120. 10.1111/inm.12303 [PubMed: 28185369]

Schwartz S, Wang L, Shinn-Cunningham BG, & Tager-Flusberg H (2020). Atypical Perception of Sounds in Minimally and Low Verbal Children and Adolescents With Autism as Revealed by Behavioral and Neural Measures. Autism Research, 13(10), 1718–1729. 10.1002/aur.2363 [PubMed: 32881387]

Shafer VL, Yu YH, & Wagner M (2015). Maturation of cortical auditory evoked potentials (CAEPs) to speech recorded from frontocentral and temporal sites: Three months to eight years of age. International Journal of Psychophysiology, 95(2), 77–93. 10.1016/j.ijpsycho.2014.08.1390 [PubMed: 25219893]

Sharer E, Crocetti D, Muschelli J, Barber AD, Nebel MB, Caffo BS, Pekar JJ, & Mostofsky SH (2015). Neural correlates of visuomotor learning in autism. Journal of Child Neurology, 30(14), 1877–1886. 10.1177/0883073815600869 [PubMed: 26350725]

Simner J, Koursarou S, Rinaldi LJ, & Ward J (2022). Attention, flexibility, and imagery in misophonia: Does attention exacerbate everyday disliking of sound? Journal of Clinical and Experimental Neuropsychology, 43(10), 1006–1017. 10.1080/13803395.2022.2056581

Sinha P, Kjelgaard MM, Gandhi TK, Tsourides K, Cardinaux AL, Pantazis D, … Held RM (2014). Autism as a disorder of prediction. Proceedings of the National Academy of Sciences, 111(42), 15220–15225. 10.1073/pnas.1416797111

Sohal VS, & Rubenstein JLR (2019). Excitation-inhibition balance as a framework for investigating mechanisms in neuropsychiatric disorders. Molecular Psychiatry, 24, 1248–1257. 10.1038/s41380-019-0426-0 [PubMed: 31089192]

Stiller A, & Mößle T (2018). Media Use Among Children and Adolescents with Autism Spectrum Disorder: A Systematic Review. Review Journal of Autism and Developmental Disorders, 5(3), 227–246. 10.1007/s40489-018-0135-7

Stroganova TA, Kozunov VV, Posikera IN, Galuta IA, Gratchev VV, & Orekhova EV (2013). Abnormal pre-attentive arousal in young children with autism spectrum disorder contributes to their atypical auditory behavior: An ERP study. PLoS ONE, 8(7): e69100. 10.1371/journal.pone.0069100 [PubMed: 23935931]

Tang AC, Sutherland MT, & McKinney CJ (2005). Validation of SOBI components from high-density EEG. NeuroImage, 25(2), 539–553. 10.1016/j.neuroimage.2004.11.027 [PubMed: 15784433]

Thatcher RW (2012). Coherence, phase differences, phase shift, and phase lock in EEG/ERP analyses. Developmental Neuropsychology, 37(6), 476–496. 10.1080/87565641.2011.619241 [PubMed: 22889341]

Tzischinsky O, Meiri G, Manelis L, Bar-Sinai A, Flusser H, Michaelovski A, … Dinstein I (2018). Sleep disturbances are associated with specific sensory sensitivities in children with autism. Molecular Autism, 9(1): 22. 10.1186/s13229-018-0206-8 [PubMed: 29610657]

Van de Cruys S, Evers K, Van der Hallen R, Van Eylen L, Boets B, De-Wit L, & Wagemans J (2014). Precise minds in uncertain worlds: Predictive coding in autism. Psychological Review, 121(4), 649–675. 10.1037/a0037665 [PubMed: 25347312]

Vehtari A, Gelman A, & Gabry J (2017). Practical Bayesian model evaluation using leave-one-out cross-validation and WAIC. Statistics and Computing, 27(5), 1413–1432. 10.1007/s11222-016-9696-4

Venker CE, Mathée J, Neumann D, Edwards J, Saffran J, & Weismer SE (2021). Competing perceptual salience in a visual word recognition task differentially affects children with and without autism spectrum disorder. Autism Research, 14(6), 1147–1162. 10.1002/aur.2457 [PubMed: 33372400]

Verhulst I, MacLennan K, Haffey A, & Tavassoli T (2022). The Perceived Causal Relations Between Sensory Reactivity Differences and Anxiety Symptoms in Autistic Adults. Autism in Adulthood, 4(3), 183–192. 10.1089/aut.2022.0018 [PubMed: 36606154]

Williams ZJ (2021). Short Sensory Profile in Autism. In Volkmar FR (Ed.), Encyclopedia of Autism Spectrum Disorders (pp. 4345–4351). Springer. 10.1007/978-3-319-91280-6_102311

Williams ZJ, Abdelmessih PG, Key AP, & Woynaroski TG (2021a). Cortical auditory processing of simple stimuli is altered in autism: A meta-analysis of auditory evoked responses. Biological Psychiatry: Cognitive Neuroscience and Neuroimaging, 6(8), 767–781. 10.1016/j.bpsc.2020.09.011 [PubMed: 33229245]

Williams ZJ, Cascio CJ, & Woynaroski TG (2022). Psychometric validation of a brief self-report measure of misophonia symptoms and functional impairment: The duke-vanderbilt misophonia screening questionnaire. Frontiers in Psychology, 13: 897901. 10.3389/fpsyg.2022.897901 [PubMed: 35936331]

Williams ZJ, Failla MD, Gotham KO, Woynaroski TG, & Cascio C (2018). Psychometric evaluation of the Short Sensory Profile in youth with autism spectrum disorder. Journal of Autism and Developmental Disorders, 48(12), 4231–4249. 10.1007/s10803-018-3678-7 [PubMed: 30019274]

Williams ZJ, Feldman JI, Dunham K, Suzman E, Liu Y, Davis SL, … Woynaroski TG (2020). The measurement and clinical correlates of decreased sound tolerance (hyperacusis) in autism spectrum disorder. Poster presentation accepted by the Gatlinburg Conference; cancelled due to COVID-19.

Williams ZJ, He JL, Cascio CJ, & Woynaroski TG (2021b). A review of decreased sound tolerance in autism: Definitions, phenomenology, and potential mechanisms. Neuroscience and Biobehavioral Reviews, 121, 1–17. 10.1016/j.neubiorev.2020.11.030 [PubMed: 33285160]

Williams ZJ, Suzman E, & Woynaroski TG (2021c). Prevalence of decreased sound tolerance (hyperacusis) in individuals with autism spectrum disorder: A meta-analysis. Ear & Hearing, 42(5), 1137–1150. 10.1097/AUD.0000000000001005 [PubMed: 33577214]

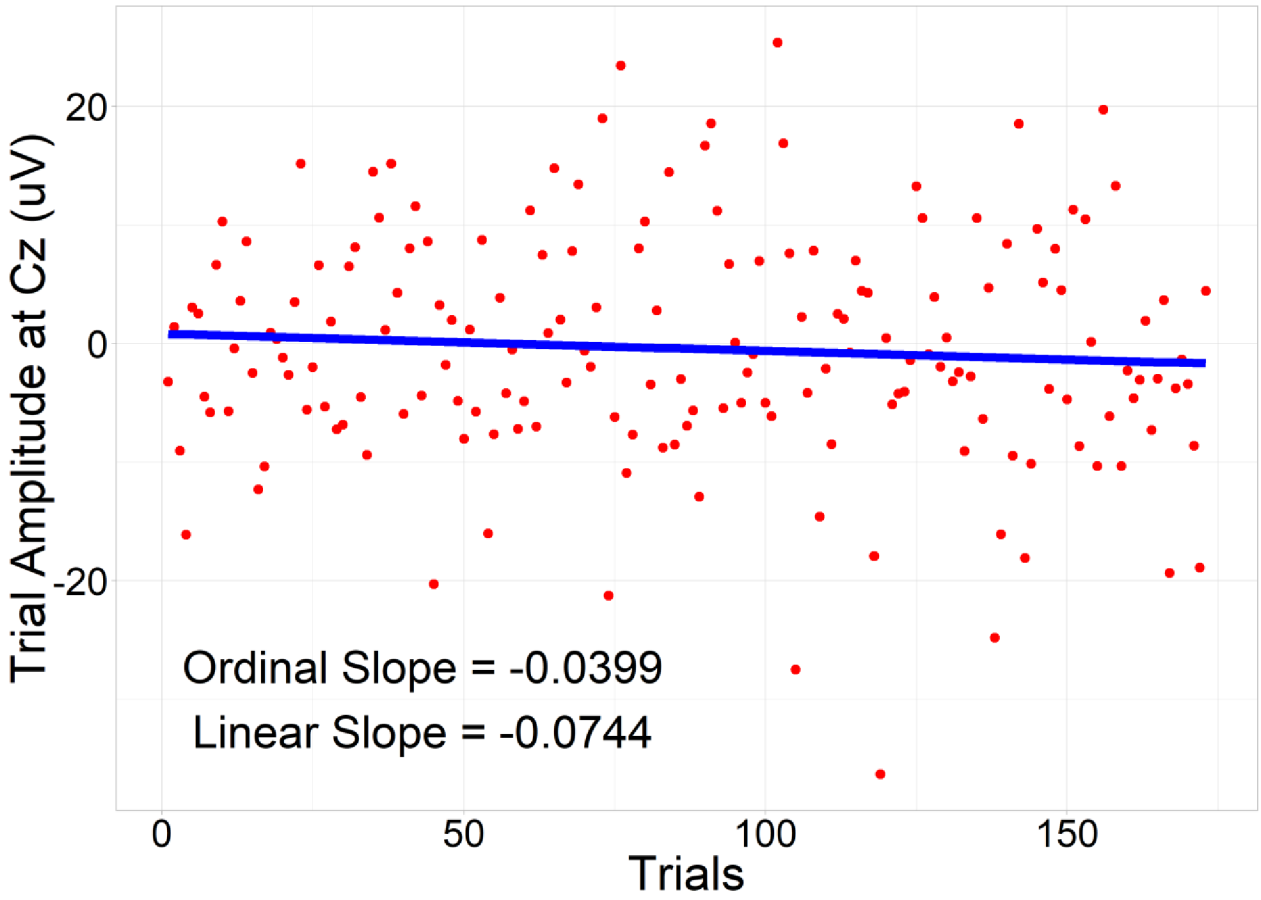

Figure 1.

An example of a slope taken from a single participant. This scatterplot depicts voltage amplitudes from this participant recorded at channel Cz exactly 100 ms after stimulus onset in each trial from the 80 dB condition. The diagonal blue line depicts the linear slope, while the values describe both the linear slope (Pearson's correlation coefficient) and the ordinal slope (Kendall's tau); the ordinal slope was employed in the analysis. Slopes like this were calculated for every participant, condition, channel, and time-point between −100ms and 350 ms post-stimulus onset. With 206 participants, 4 loudness conditions, 61 channels, and 451 time points, a total of 22,669,064 separate slope values like the one depicted in this example plot were generated. Habituation slopes were then averaged over spatiotemporal regions associated with the P1 and N2 components.

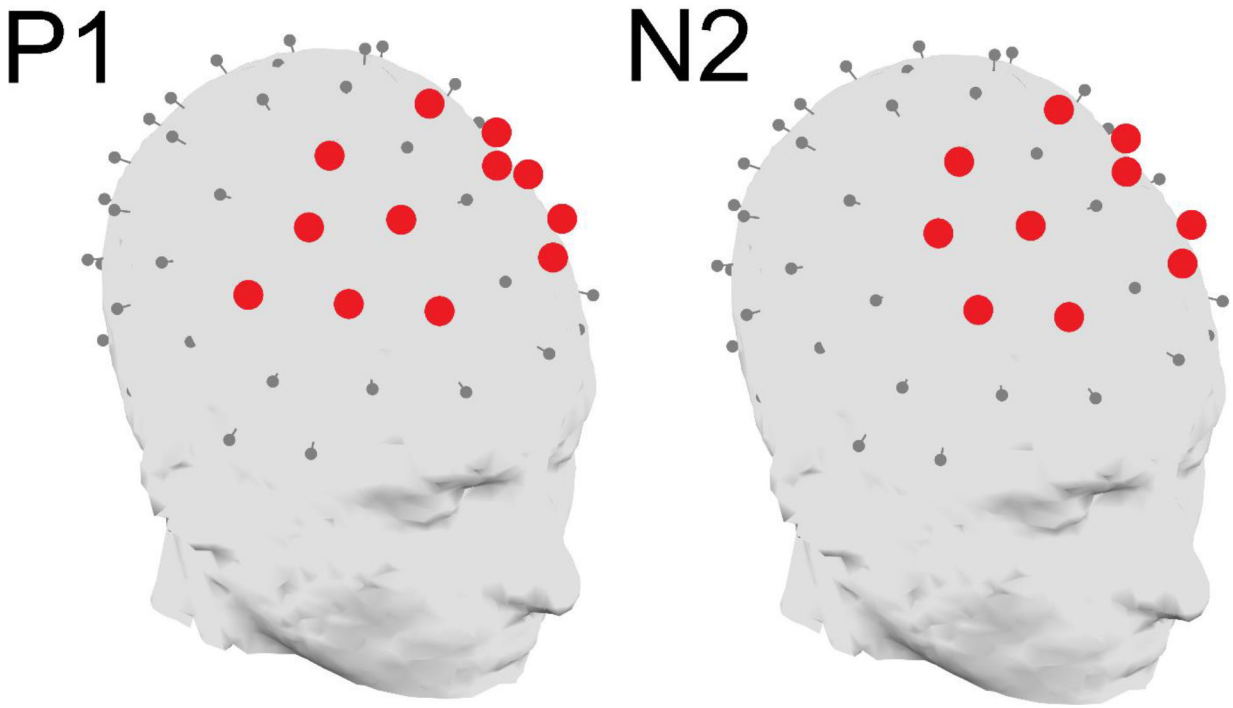

Figure 2.

Regions of interest over left and right hemisphere frontocentral scalp. *Left*. Frontocentral regions of interest for analysis of P1 response (red electrodes). *Right*. Frontocentral regions of interest for analysis of N2 response (red electrodes). The N2 region of interest was defined slightly more narrowly than the P1 region in order to avoid overlap with temporal components such as the TP200 response. Channel positions may appear slightly irregular; this is because channel positions are based on actual electrode positions obtained from a subset of participants using a Polhemus digitizer.

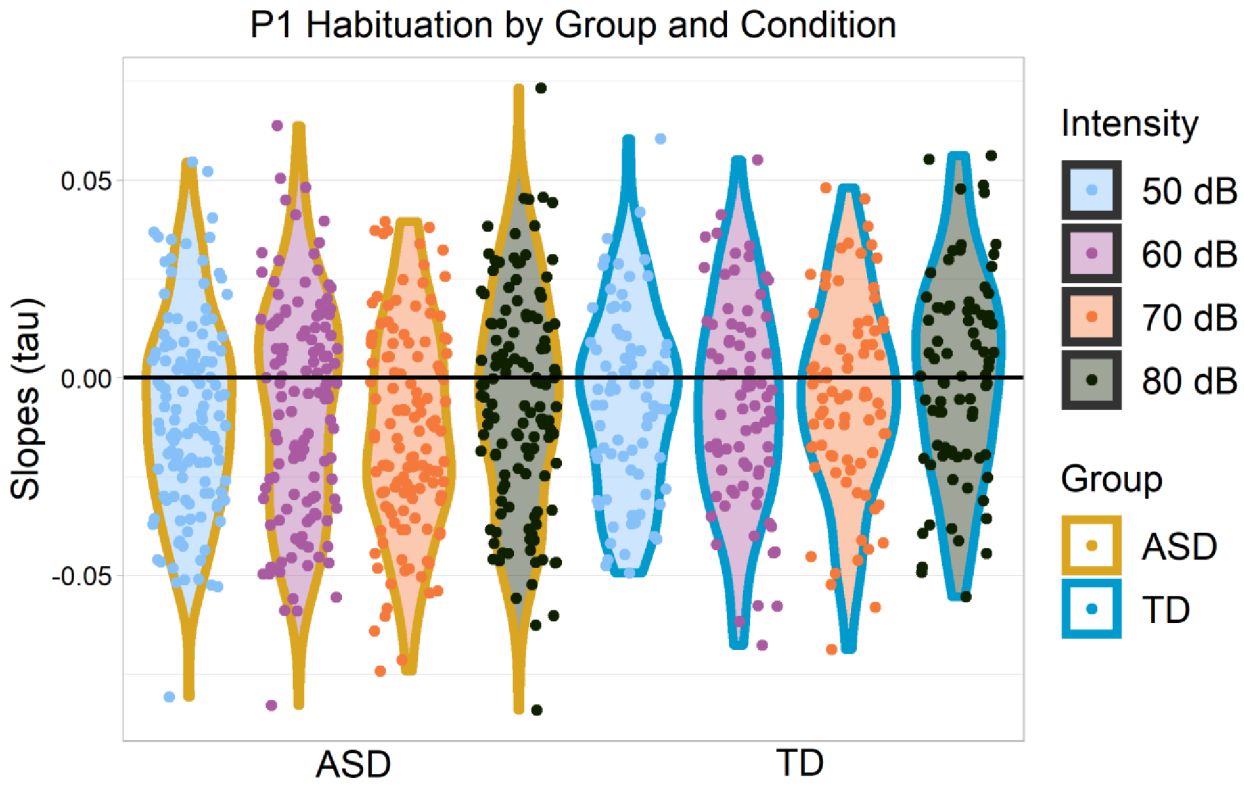

Figure 3.

Violin plots showing distribution of slope data points indexing habituation of the P1 response in each group and intensity condition. Horizontally jittered data points of individual participants are also shown in each condition. Unexpectedly, habituation initially appeared to be greater in ASD than TD in the 70 dB condition (reflected by more negative values in ASD), but this effect disappeared in analyses controlling for potential confounds.

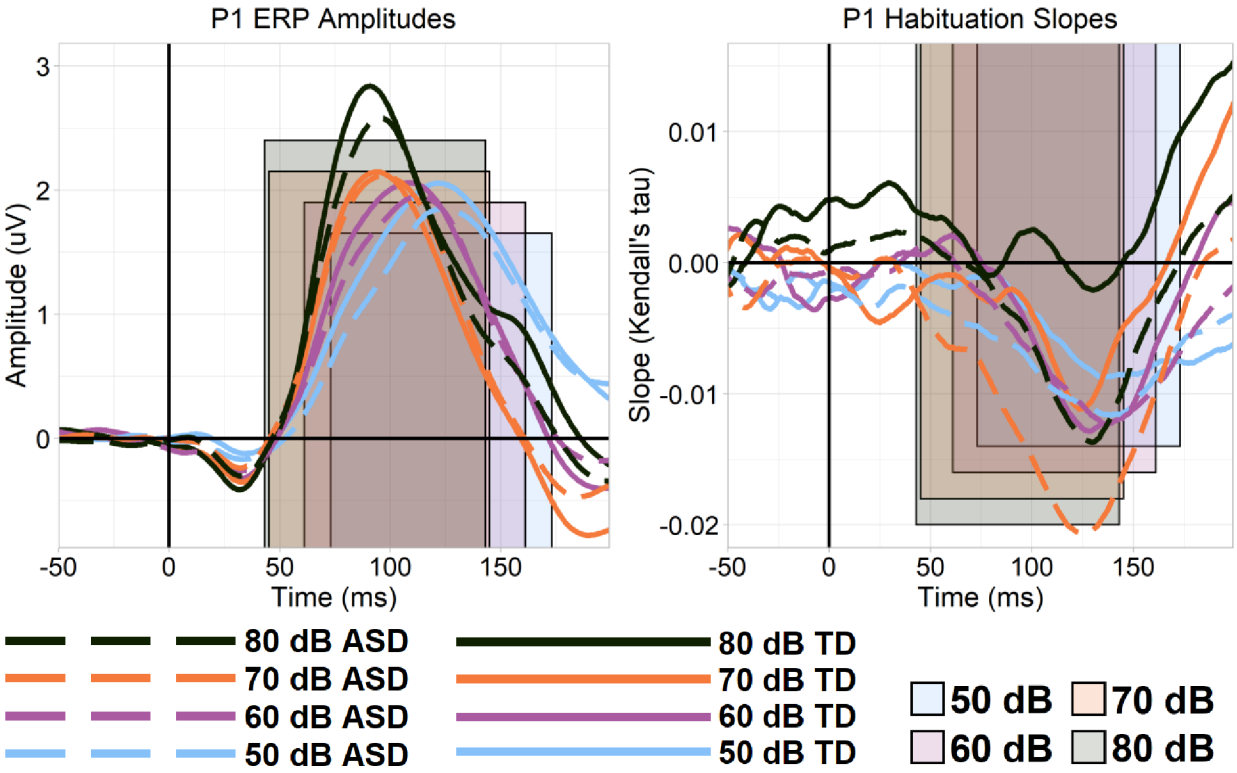

Figure 4.

Waveforms depicting both the averaged ERP voltages observed in each diagnostic group across the whole of the P1 spatiotemporal region (left), as well as habituation slopes indexing change in voltages over the course of the experiment (right). As the P1 ERP (left) is positive-going, habituation is indicated by negative slopes (right). The measurement window is highlighted in grey.

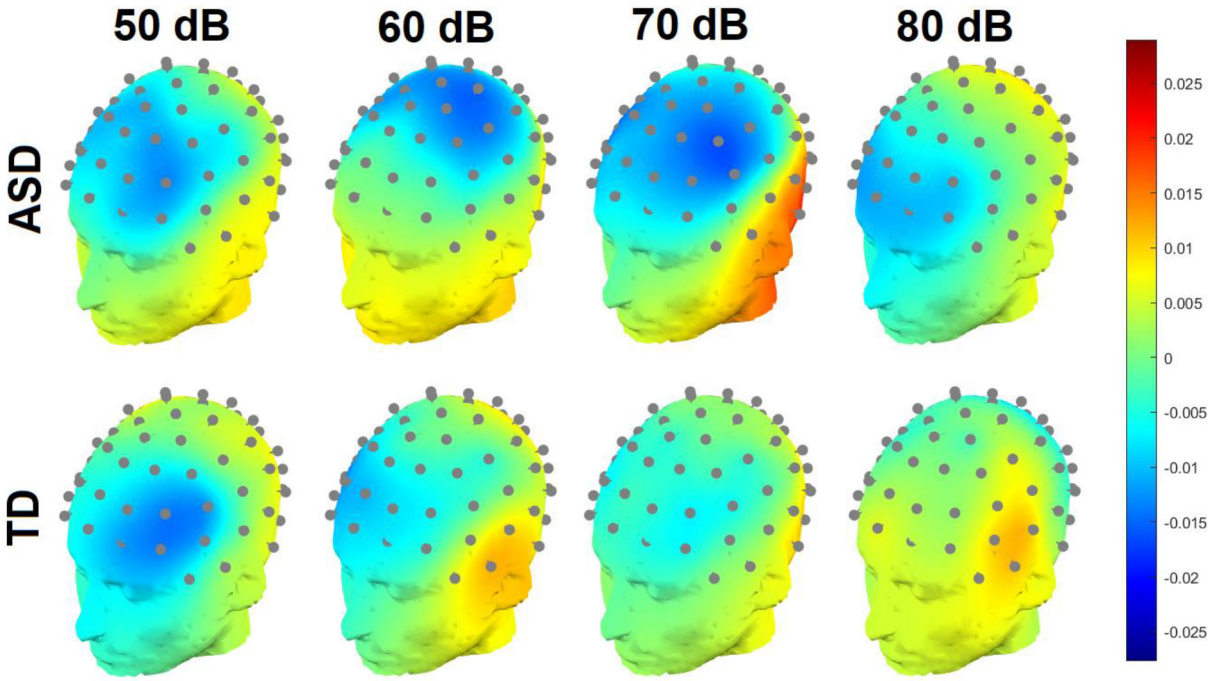

Figure 5.

Topographic plots depicting habituation slopes indexing change in voltages over the course of the experiment averaged over the P1 measurement window, i.e., 73 – 173 ms (50 dB), 61 – 161 ms (60 dB), 45 – 145 ms (70 dB), or 43 – 143 ms (80 dB). In the ASD group, negative slopes – reflecting less positive amplitudes over the course of the experiment, or habituation of the P1 positivity – are clearly apparent in the 50 dB and 70 dB conditions. Trends for habituation slopes to differ from zero in other conditions did not attain statistical significance after correction for multiple comparisons.

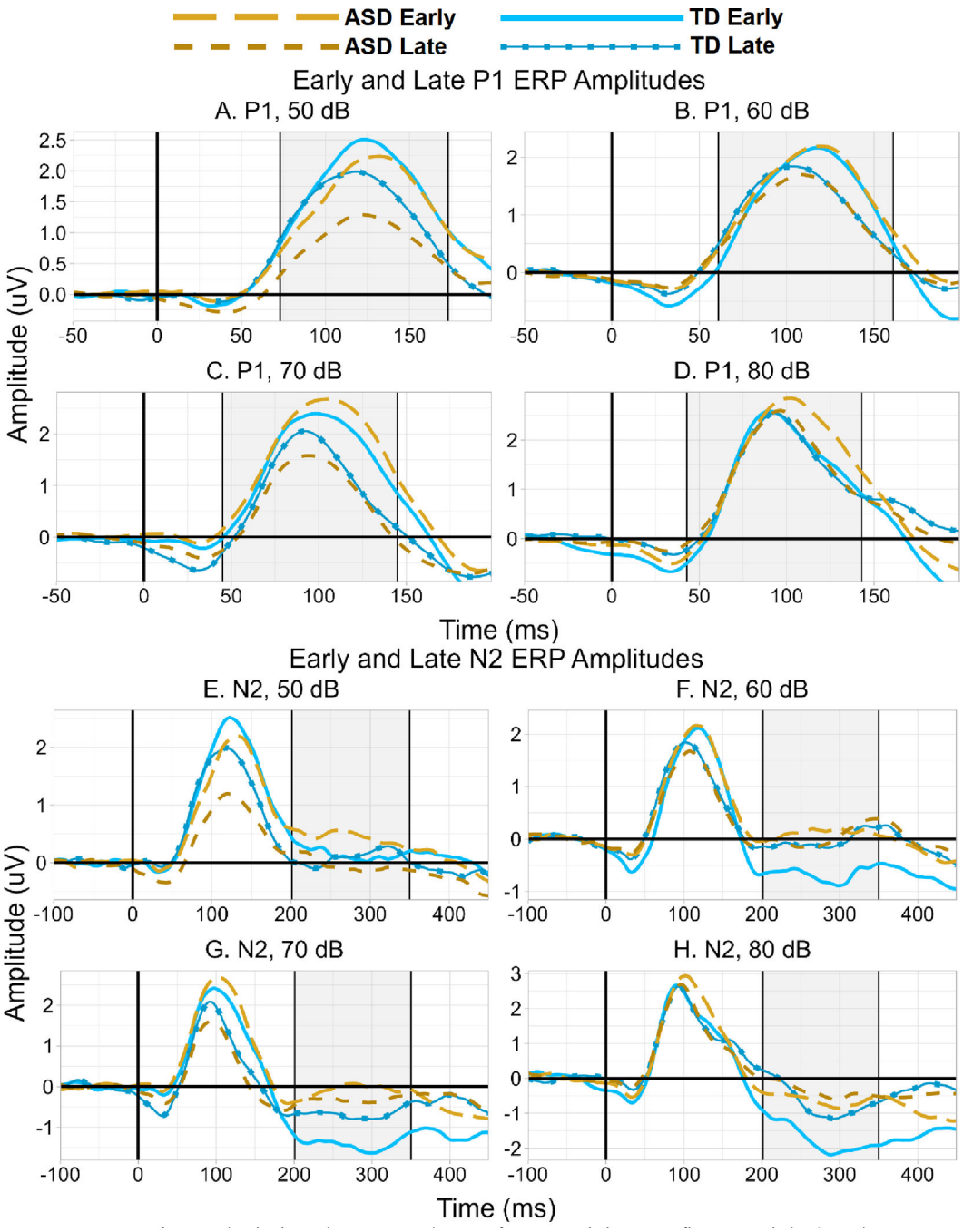

Figure 6.

Waveforms depicting the ERP voltages from participants' first 40 trials ("early amplitudes"), as well as from participants' last 40 trials ("late amplitudes") in each group and condition. P1 and N2 time windows are highlighted in grey. As the P1 ERP (left) is positive-going, its habituation would result in a more positive voltage in the first 40 trials than the final 40 trials. Conversely, as the N2 (right) is a negative-going response, its habituation would result in more negative voltages in the first 40 trials than the last 40. This figure is for visualization

only; binning ERP responses from ranges of trials had no place in our statistical analytic approach.

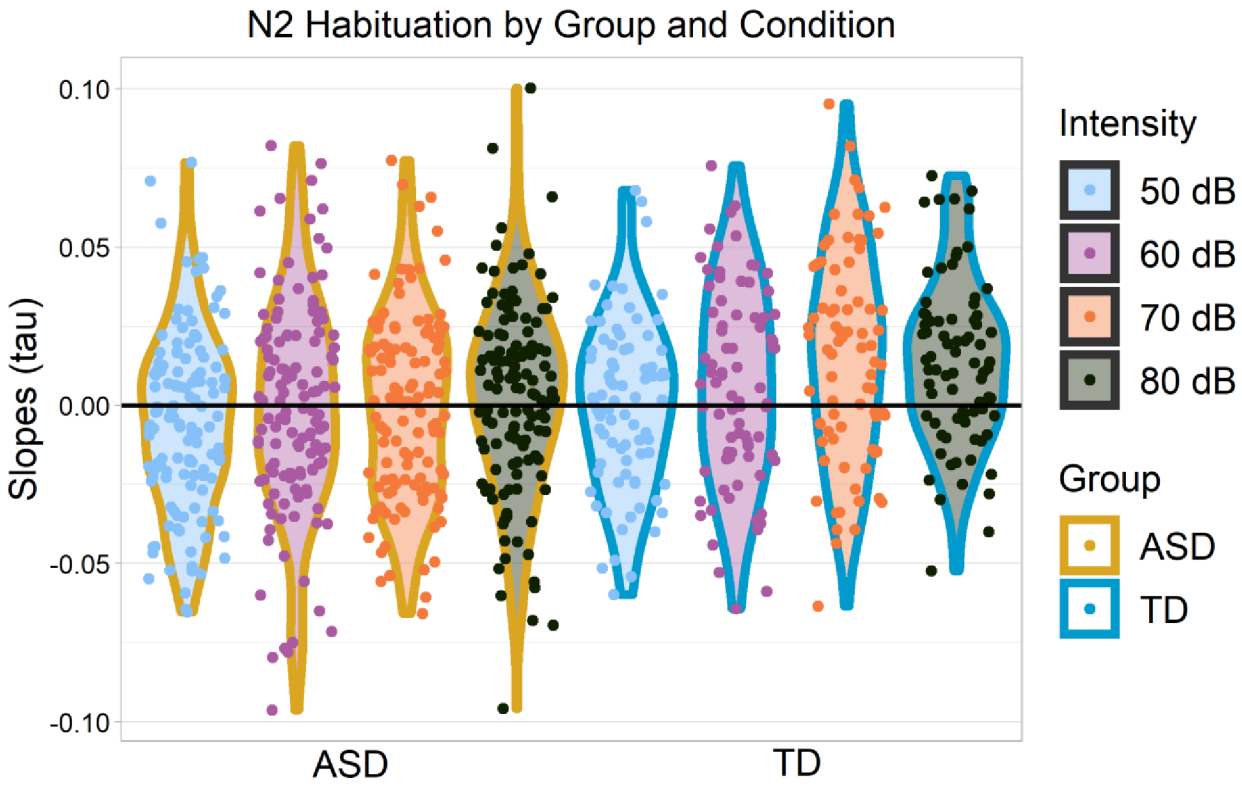

Figure 7.

Violin plots showing distribution of slope data points indexing habituation of the N2 response in each group and intensity condition. Horizontally jittered data points of individual participants are also shown in each condition. Habituation of the N2 response was observed primarily in the 70 and 80 dB conditions, wherein average slopes significantly differed from zero, but only in the TD group.

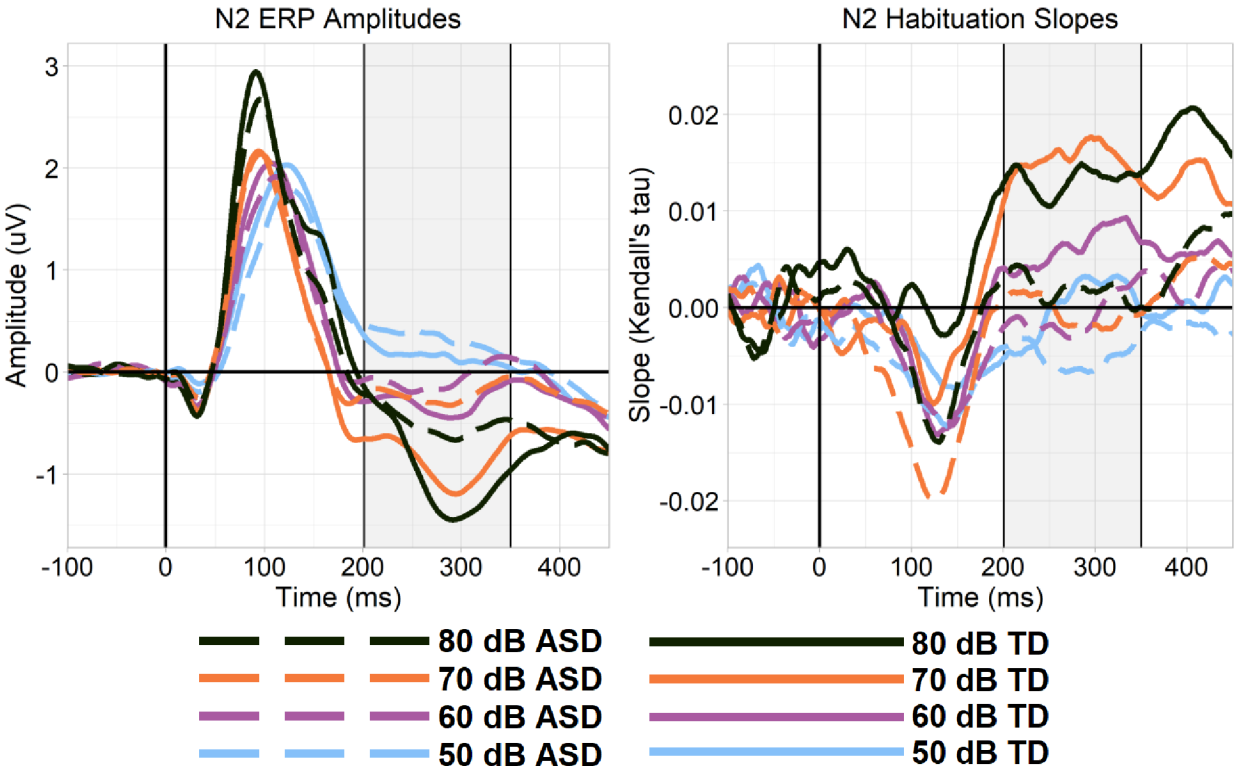

Figure 8.

Waveforms depicting both the averaged ERP voltages observed in each diagnostic group across the whole of the N2 spatiotemporal region (left), as well as habituation slopes indexing change in voltages over the course of the experiment (right). As the N2 ERP (left) is negative-going, habituation is indicated by positive slopes (right). The measurement window is highlighted in grey.

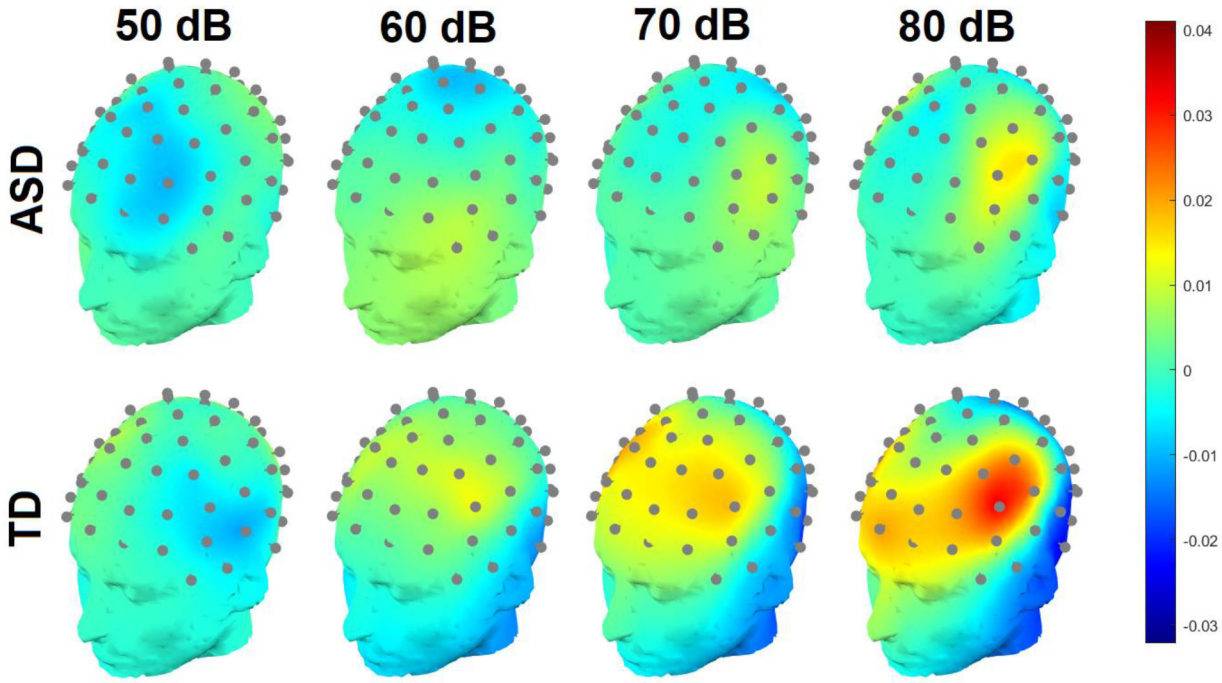

Figure 9.

Topographic plots depicting habituation slopes indexing change in voltages over the course of the experiment averaged over the N2 measurement window (201 – 350 ms). In the 70 and 80 dB conditions, in TD, positive habituation slopes are visible over the N2 measurement region, indicating that N2 amplitudes became less negative or habituated over the course of the experiment. Interestingly, in the 80 dB condition, the habituation was concentrated laterally, at the periphery of the N2 measurement region. This implies that the habituation manifested as an increasingly compact N2 response over the course of the experiment.

Table 1.

Characteristics of typically-developing and autistic participants with usable electrophysiological data. Statistical comparisons employ Wilcoxon rank-sum tests. Cliff's δ (Cliff, 1993) is reported as an effect size.

	TD		ASD		*p*	Cliff's δ [95% CI]
	Mean (SD)	**Range**	**Mean (SD)**	**Range**		
Chronological Age (months)	37.06 (6.48)	25.80 to 56.33	38.49 (5.97)	25.50 to 54.87	.031	−.18 [−.33, −.02]
MSEL Developmental Quotient (DQ)	106.02 (11.50)	79.89 to 128.62	65.41 (20.54)	30.39 to 132.45	< .0001	.89 [.82, .94]
ADOS Calibrated Score (Gotham et al., 2009)	N/A		7.60 (1.65)	4 to 10	N/A	N/A
SPHI	−0.45 (0.68)	−1.45 to 1.11	0.04 (0.83)	−1.45 to 2.16	.0002	−.34 [−.49, −.16]
Total Trials	1166.75 (197.59)	711 to 1530	1142.14 (205.19)	639 to 1643	.55	.05 [−.11, .21]
Usable Trials	935.95 (214.63)	448 to 1410	873.72 (193.33)	509 to 1375	.055	.16 [−.01, .32]
Rejected Trials	230.80 (103.29)	59 to 495	268.43 (101.93)	80 to 667	.01	−.20 [−.36, −.04]
Number of Pauses in EEG Recordings	20.62 (11.33)	1 to 58	31.53 (21.38)	3 to 146	.0002	−.31 [−.44, −.16]

Table 2.

In the autistic group only,

Bayesian linear correlations between slopes reflecting habituation of the P1 response in each intensity condition, collapsed across hemispheres, and SPHI estimates and MSEL DQ. Estimates, credible intervals, and Bayes factoes are presented for Bayesian correlations, along with corrected *p*-values for eight comparisons (Bonferroni-Holm method) based on analogous Pearson's *r* correlations in a frequentist framework.

	50 dB			60 dB			70 dB			80 dB		
	Bayesian ρ [95% CrI]	p_{cor}	BF_{10}	**Bayesian ρ [95% CrI]**	p_{cor}	BF_{10}	**Bayesian ρ [95% CrI]**	p_{cor}	BF_{10}	**Bayesian ρ [95% CrI]**	p_{cor}	BF_{10}
SPHI	−.08 [−.27, .10]	>.99	0.34	.17 [.00, .35]	.45	1.27	.07 [−.11, .26]	>.99	0.32	.00 [−.18, .19]	>.99	0.22
MSEL DQ	−.09 [−.25, .08]	>.99	0.35	−.07 [−.25, .09]	>.99	0.28	−.01 [−.20, .15]	>.99	0.21	.12 [−.06, .28]	>.99	0.50

Table 3.

In the autistic group only,

Bayesian linear correlations between slopes reflecting habituation of the N2 response in each intensity condition, collapsed across hemispheres, and SPHI estimates and MSEL DQ. Estimates, credible intervals, and Bayes factors are presented for Bayesian correlations, along with corrected *p*-values for eight comparisons (Bonferroni-Holm method) based on analogous Pearson's *r* correlations in a frequentist framework.

	50 dB			60 dB			70 dB			80 dB		
	Bayesian ρ [95% CrI]	p_{cor}	BF_{10}	**Bayesian ρ [95% CrI]**	p_{cor}	BF_{10}	**Bayesian ρ [95% CrI]**	p_{cor}	BF_{10}	**Bayesian ρ [95% CrI]**	p_{cor}	BF_{10}
SPHI	.14 [−.04, .32]	.73	0.70	.20 [.03, .38]	.22	2.25	.11 [−.07, .29]	>.99	0.43	−.01 [−.18, .18]	>.99	0.22
MSEL DQ	−.04 [−.20, .13]	>.99	0.23	−.04 [−.22, .12]	>.99	0.23	.05 [−.14, .20]	>.99	0.24	.18 [.01, .34]	.26	1.67