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Attenuated Auditory Event-Related Potentials and Associations with Atypical Sensory Response Patterns in Children with Autism

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Abstract

Neurobiological underpinnings of unusual sensory features in individuals with autism are unknown. Event-related potentials (ERPs) elicited by task-irrelevant sounds were used to elucidate neural correlates of auditory processing and associations with three common sensory response patterns (hyperresponsiveness; hyporesponsiveness; sensory seeking). Twenty-eight children with autism and 39 typically developing children (4–12 year-olds) completed an auditory oddball paradigm. Results revealed marginally attenuated P1 and N2 to standard tones and attenuated P3a to novel sounds in autism versus controls. Exploratory analyses suggested that within the autism group, attenuated N2 and P3a amplitudes were associated with greater sensory seeking behaviors for specific ranges of P1 responses. Findings suggest that attenuated early sensory as well as later attention-orienting neural responses to stimuli may underlie selective sensory features via complex mechanisms.

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Keywords

Autism spectrum disorder; sensory processing; event-related potentials; P1; N2; P3a

Autism Spectrum Disorder (ASD) is characterized by impairments in communication, abnormal social interaction, and the presence of restricted, repetitive behaviors (DSM-IV-TR; American Psychiatric Association, 2000). Alongside these identifying core features, individuals with ASD often display a range of atypical responses to sensory information (Baranek et al. 2006). Elucidating the neural and behavioral correlates of sensory processing deficits in ASD may inform theories relating to the core characteristics, as well as higher-order cognitive deficits (i.e. Gomot and Wicker 2012; Hill 2004), of the disorder. While a large body of research describes behavioral manifestations of atypical sensory responses in ASD throughout development, few studies have explored neurobiological correlates of these behaviors. Electro- and Magnetoencephalography (EEG and MEG) provide unique tools for exploring the neural basis of sensory processing impairments as they allow for the analysis of distinct temporal components of information processing, and may therefore elucidate the temporal characteristics of atypical sensory processing in individuals with autism. The current study employs EEG to examine aberrations in temporal components of sensory processing in children with ASD and their potential associations with clinical measures of atypical sensory response patterns.

Sensory features in ASD have been documented in infancy (Ben-Sasson et al. 2008), childhood (Leekam et al. 2007; Liss et al. 2006), and adulthood (Crane et al. 2009; Harrison and Hare 2004) with reported prevalence rates ranging from 42% to as much as 100% (Baranek et al. 2006; Dawson and Watling 2000; Kientz and Dunn 1997) with varying levels of severity. While sensory features are not unique to ASD, they appear to be more prevalent in this population than in other developmental disabilities (Baranek et al. 2006; Ben-Sasson et al. 2009; Leekam et al. 2007).

Sensory features in ASD are well documented across all sensory modalities and may aggregate into behavioral sensory response patterns including, but not limited to, sensory hyperresponsiveness, sensory hyporesponsiveness and sensory seeking behaviors (e.g., Baranek et al. 2006; Brock et al. 2012; Dunn 1997; Miller et al. 2007). Sensory hyporesponsiveness is characterized by a lack of, less intense, or delayed response to sensory stimuli (e.g., Baranek et al. 2006; Ben-Sasson et al. 2007; Dunn 1997). For example, a child may show no behavioral orienting to a novel sound, or may have a diminished response to pain. Hyperresponsiveness is characterized by an exaggerated, aversive, or avoidant response to sensory stimuli (e.g., Baranek et al. 2007; Dunn 1997; Mazurek et al. 2013; Reynolds and Lane 2008). For example, a child may show discomfort to grooming activities, or cover ears in response to certain sounds. Sensory seeking behaviors are characterized by a fascination with, or craving of, sensory stimulation which is intense and may be repetitive in nature (e.g., Ausderau et al. under review; Dunn 1997). For example, a child may show a fascination with flickering lights or rubbing textures. Aggregating individual sensory features into behavioral response patterns may help to elucidate

pathogenesis and facilitate understanding of generalized mechanisms supporting multi-modal sensory processes.

Atypical responses to auditory stimuli in infancy are predictive of a later diagnosis of ASD (Baranek 1999; Guiraud et al. 2011; Osterling and Dawson 1994). Early sensory, and especially, auditory experiences are also a prerequisite for the development of speech and language (Jansson-Verkasalo et al. 2010), and any atypical pattern in auditory processing early in life may have detrimental consequences on later language development and hamper effective communication.

Despite the overwhelming evidence for the high prevalence of these unusual sensory features in individuals with ASD, their neurobiological underpinnings have yet to be delineated. One way of investigating the neural signature of auditory information processing is by means of event-related potentials (ERPs). ERPs represent transient changes in the brain's scalp-recorded electrical activity in response to the repetitive presentation of certain stimuli. Because ERPs are non-invasive, have a high temporal resolution, and can be measured without requiring a response, they are particularly well suited to investigating specific stages of (auditory) information processing in very young, nonverbal, and clinical populations. Research investigating auditory information processing in children, adolescents and adults has revealed that ERPs change over the lifespan. These changes can be due to neural maturation, such as white and gray matter volume changes, affecting processing speed and processing efficiency (Albrecht et al. 2000; Caviness et al. 1996; Tonnquist-Uhlen 1996). In typically developing children, the presentation of repeated tones in a sequence elicits a series of "obligatory" midlatency peaks identified as P1 and N1/N2, whereas in adults P1 (a.k.a. P50), N1 and P2 peaks can be discerned. In adults, the P1 peak to simple tone stimuli generally occurs between 40 and 60 ms, the adult N1 peak generally occurs between 90–100 ms, and the adult P2 peak generally occurs between 140–170 ms poststimulus. The N1 and P2 peaks are typically not seen in children under 9 years of age, although the likelihood of observing these components increases with longer (> 1 Hz) inter stimulus intervals, resulting primarily in the domination of these early responses by the N2 peak, which appears to decrease in size from 5–10 years of age and become expressed primarily as an N1 in adults (Ceponiene et al. 1998; Sussman et al. 2008). The N2 peak occurs between 220 and 280 ms. These passive midlatency evoked potentials, elicited in the absence of an overt task, are pre-attentive and reflect the physical properties of a stimulus (Ceponiene et al. 2002; Lepistö et al. 2005), as well as detection, classification, and orientation (see Key et al. 2005, for an overview). When an occasional infrequent deviant sound is interspersed between a series of identical frequently presented "standard" sounds, a measure of sound discrimination can be obtained by subtracting the ERP to the standard sounds from the ERP to the deviant sounds. In adults, this results in a distinctive brain response, the mismatch negativity (MMN), which is hypothesized to reflect a sensory response to the mismatch between the memory trace of the standard and the new incoming stimulus, also known as "preattentive memory" (Näätänen et al. 1978). MMN-like discriminative ERP responses ('mismatch responses'; MMRs) can also be obtained very early in infancy (Cheour 2007). The MMN/MMR is elicited even when the participant is not actively attending to the stream of sounds. In addition, the involuntary capture of attention can be indexed when an unexpected or 'novel' stimulus is introduced into the stream of

standard stimuli. If this stimulus is salient enough, an individual's attention will switch towards the stimulus and a positive deflection, known as the P3a, is elicited roughly 300 ms after onset of the novel stimulus (Comerchero and Polich 1998). Unlike the MMN/MMR, the P3a is attention dependent and reflects higher cognitive processing of stimuli.

Understanding of atypical auditory processing in children with ASD may be important to disentangle different etiologies of autism, target treatments for auditory hypo- and hyperresponsive and sensory seeking behavioral patterns, and potentially improve language learning and communication. Electrophysiological evidence obtained through ERPs indicates that ASD is indeed characterized by abnormal cortical processing of auditory stimuli. However, results have been inconsistent (see Bomba and Pang 2004; Jeste and Nelson 2009; Marco et al. 2011 for reviews). Discrepant findings in the literature are at least partly due to differences in the experimental task protocols, sample characteristics, and small sample sizes. However, few studies have investigated the association between brain electrical responses and clinical measures of sensory features and even fewer have used both observational assessments and parent report to examine responses to sensory stimulation. Gomot et al. (2011) found that children with autism who scored higher on intolerance of change on the Behavior Summarized Evaluations scale (BSE-R) had significantly shorter mismatch negativity latencies and P3a latencies compared to children with autism who scored lower on this scale. Orekhova et al. (2012) in a MEG study showed that atypical P100m lateralization in children with autism was associated with greater severity of sensory abnormalities assessed by the Short Sensory Profile, as well as with auditory hypersensitivity during the first two years of life.

In the current study, we examined responses to sensory stimulation measured by both parent report and observational assessments in a group of children with autism and gender- and age-matched typically developing children, ages 4–12 years. We employed clinical measures of sensory features across three patterns (hyperresponsiveness, hyporesponsiveness, and sensory seeking behaviors), as well as an auditory oddball ERP paradigm for which we focused on the P1, N1/N2, and P3a components elicited by standard (P1, N1/N2), pitch deviant (P1, N1/N2), duration deviant (P1, N1/N2) and novel sounds (P3a) respectively. This particular oddball paradigm allowed us to study the auditory information processing stream across both groups from early detection to later classification and orientation. Given the developmental maturation and potential fusing of the N1 and N2 components during the age window examined in this study, we will refer to this component as the N2 going forward for simplification. Our aims were twofold: 1) to characterize and compare brain responses to different types of auditory stimuli in children with autism and their typically developing peers and 2) to examine the association between auditory brain responses and clinical sensory response patterns, as measured through observational and parental report assessments, in children with autism.

Methods

Participants

The study (N=67) included 28 children with autism and 39 children with typical development (TD), ages 4–12 years. EEG data were collected for an additional 17 children

with autism and 7 typically developing children, but was excluded for the following reasons: eye movement data could not be collected for 16 participants (11 autism and 5 TD) because these children would not tolerate placement of the eye electrodes; 4 participants (2 autism and 2 TD) had bad data due to excessive participant motion; for 3 children with autism the session had to be aborted since they would not tolerate the electrode cap; and for 1 child with autism there was an error with the testing equipment during data collection. Participants in the autism group and the TD group did not differ in chronological age (autism mean: 91.4 months, TD mean: 84.4 months, $p>0.25$). However, the autism group did have significantly lower mental age (autism mean: 73.4 months, TD mean: 97.9 months, $t(64)=2.23$, $p=0.03$) and non-verbal IQ (autism mean: 82.6, TD mean: 108.5; $t(38.5)$[1]$=5.55$, $p<0.0001$). Demographics for both participant groups are reported in Table 1.

Children in the autism group were diagnosed with Autistic Disorder by a licensed psychologist or physician, typically in the context of a multidisciplinary team evaluation. Additionally, all cases met algorithm cut-offs for “Autism” on the Autism Diagnostic Interview-Revised (ADI-R; Lord et al. 1994), and the Autism Diagnostic Observation Schedules-2 (ADOS-2; Gotham, et al. 2007; Lord et al. 2006; Lord et al. 2012), using Modules 1, 2, or 3 as appropriate to the age and verbal ability of the child. Children with typical development had no history of developmental delays or interventions, no symptoms of autism as confirmed by the Childhood Autism Rating Scale (CARS; Schopler et al. 1986), and cognitive and adaptive behavior scores in the average range as confirmed by standardized assessments (see clinical and behavioral measures section below). Exclusion criteria for both groups included a) known genetic conditions (e.g., fragile X syndrome, tuberous sclerosis, Down syndrome), b) seizure disorder with evidence of seizure activity within the past 12 months, c) significant physical impairments/limitations, d) diagnosis of schizophrenia or bipolar disorder and/or any psychiatric condition with hallucinations or delusions, and/or e) currently taking antipsychotic medications (e.g., Risperdal). Participant medications included stimulants (3 participants with autism), antidepressants (2 with autism), and an NMDA receptor antagonist (1 with autism).

Participants were recruited from multiple venues, including a previous large study cohort, a university based autism subject registry, and local community agencies, clinics, schools and parent groups. Project staff contacted interested families via telephone, screened children for eligibility, and scheduled them for onsite developmental and sensory testing, diagnostic confirmation, and an EEG session. Parents completed developmental and sensory questionnaires and interviews about their children. Monetary incentives of $150-$175 were provided for participating families dependent upon the number of assessments completed. Children received a small toy or book and a certificate with a graphical image of their brain waves for completing the study. See Table 1 for a summary of participant and family descriptive and demographic information. The experimental protocol was approved by the university’s Institutional Review Board. All guardians of participants gave written informed consent, and participants gave written assent if applicable.

[1]Degrees of freedom (df) are adjusted due to Satterthwaite’s correction for unequal variances.

Clinical and Behavioral Measures

Prior to EEG, research staff screened children in both groups to confirm normal or corrected to normal vision to acuity of 20/40 using the Cardiff Acuity Test (Adoh et al. 1992) and hearing using otoacoustic emission screening.

Children received a standardized cognitive assessment appropriate to their age and developmental level – either the Mullen Scales of Early Learning (MSEL; Mullen 1995), the Stanford Binet Intelligence Scales, Fifth Edition (SB5; Roid 2003), or the Leiter International Performance Scale - Revised (Roid and Miller 1997). Standardized nonverbal IQ scores were reported descriptively, whereas, mental age (MA) equivalents, a measure of cognitive maturation, were used as a covariate in the analyses to control for the heterogeneity in developmental levels across participants. The Vineland Adaptive Behavior Scales-Survey Edition (VABS; Sparrow et al. 1984), a structured, standardized caregiver interview, was administered to a parent of each participant to describe adaptive functioning levels. Parents also completed a handedness questionnaire to assess children's hand dominance in everyday activities adapted from McManus et al. (1988) and Cornish and McManus (1996). In addition, autism diagnostic instruments (noted in the participants section) were used to rule in/out diagnosis, and to determine severity levels of autistic symptoms. We specifically used the ADOS-2 calibrated severity scores, a standardized metric that can be used across modules (Gothham, et al. 2009), as a covariate in our within-group analyses. Calibrated severity scores on the ADOS-2 can range from 0–10, with scores between 1–3 representing "nonspectrum", 4–5 "ASD" and 6–10 "Autism" classifications. Our autism group had a mean of 8.5 (SD=1.2).

A total of four clinical sensory measures, two observational measures: the Tactile Defensiveness and Discrimination Test-Revised (TDDT-R; Baranek and Berkson 1994), and the Sensory Processing Assessment for Young Children (SPA; Baranek 1999); and two parent questionnaires: the Sensory Experiences Questionnaire (SEQ; Baranek 1999; Baranek et al. 2006), and the Sensory Profile (SP; Dunn 1999) were used to measure the three sensory constructs of interest (hyperresponsiveness, hyporesponsiveness, and sensory seeking patterns).

The TDDT-R is an observational play-based assessment of tactile responsiveness and has been validated with children with autism and developmental disorders (DD) (Baranek et al. 2007; Baranek and Berkson 1994). The SPA is a play-based observational assessment used to identify approach/avoidance behaviors in response to novel sensory toys, orienting/habituating responses to sensory stimuli, as well as stereotyped/seeking behaviors (Baranek et al. 2007; Baranek et al. 2013). The SEQ is a caregiver questionnaire that focuses on frequency of sensory responses across patterns in young children with ASD and other DD (Baranek et al. 2006; Little et al. 2011). The SP (Dunn and Westman 1997; Dunn 1999) is a commonly used parent report measure of frequency of a child's sensory responses across modalities, and has been used previously with clinical populations including children with autism (Kientz and Dunn 1997).

Items from each of the four sensory measures (TDDT-R, SPA, SEQ, and SP) were rigorously evaluated using a combined conceptual and empirical approach to validate the

three sensory dimensional constructs of interest (hyperresponsiveness, hyporesponsiveness, and sensory seeking) in a previous study using confirmatory factor analysis and structural equation modeling (Watson et al. 2011). For this study, we calculated mean summary scores across the items represented by previously validated factors (hyperresponsiveness, hyporesponsiveness, seeking) after reverse scoring the SP, and weighting all items on an equal 5 point scale with concordant valence across assessments. An item score of 1 indicated least severe sensory symptoms and an item score of score of 5 indicated most severe. The TDDT-R contributed 39 items to observed measures [hyporesponsiveness (1) hyperresponsiveness (31) sensory seeking (7)]. The SPA contributed 31 items to observed measures [hyporesponsiveness (7) hyperresponsiveness (17) sensory seeking (7)]. The SEQ contributed 33 items to parent report measures [hyporesponsiveness (6) hyperresponsiveness (14) sensory seeking (13)]. The SP contributed a total of 64 items to parent report measures [hyporesponsiveness (10), hyperresponsiveness (29), sensory seeking (25)]. Item scores were aggregated for the two observational measures (TDDT-R, SPA) and the two parent report measures (SEQ, SP) and a sum calculated across the three constructs, yielding six variables for the final within-group analyses. Table 2 includes the descriptive for the six sensory scores as well as statistical differences between the two groups. Higher scores on the six aggregated indices reflect greater levels of severity across the three sensory response patterns.

Experimental Procedure

To familiarize all children with the experimental procedure, a nonfunctional EEG cap and electrode adhesive pads were mailed to all children to play with at home. Prior to their appointment, children watched a video and/or read a social story depicting the laboratory setting, employees they would encounter during the visit, and the entire experimental procedure. On test day, children were fitted with an Electro Cap (Electro-Cap International, Inc., Eaton, OH) containing 20 tin electrodes, 12 of which (F3, Fz, F4, C3, Cz, C4, P3, Pz, P4, T7, T8) were used for recording electroencephalograms (EEGs). The EEG was acquired with a Neuroscan 4.3 (Neurosoft, Inc., Sterling, VA) system. The right mastoid served as the reference and AFz as the ground. EEG data were amplified, bandpass filtered (0.15Hz–70Hz), and digitized at 500 Hz. Four tin electrodes placed at the outer canthi of both eyes and above and below the right eye measured vertical and horizontal electro-oculogram (VEOG and HEOG). Children were instructed to remain as still and relaxed as possible with their eyes focused on the video screen at all times, and to try not to move, tense their facial muscles, or speak. They then entered a sound-attenuated, dimly lit testing chamber accompanied by a parent or guardian, who either stood behind them or sat down in an adjustable chair holding the child in their arms. The child’s head was positioned roughly at the height of the video screen. During testing, the children watched a self-chosen video with low sound (<60 dB) to enhance auditory inattention while tones were randomly presented through speakers. The speakers were placed to the left and right of the video screen, spaced 60 cm apart, and at approximately 80 cm from the child’s head. Children were instructed to watch the video and to ignore the sounds. All sounds were presented with an average of 80 dB as measured by a digital Sound Level Meter (RadioShack, Cat. No. 33-2055). We used Presentation 13.4 to present the auditory stimuli. Stimuli included standard tones (200 ms duration, 1000 Hz, 88%), pitch deviant tones (200 ms duration, 1100 Hz, 4%), duration

deviant tones (190 ms duration, 1000 Hz, 4%) and novel sounds (200 ms duration, unique environmental sounds such as a dog bark, 4%). Sound stimuli were created with rise and fall times of 5 ms, digitized at a rate of 44.1 kHz and 16 bit resolution. Six semi-randomized sequences of tones were generated, with at least two standard tones following each deviant or novel tone. Each sequence was presented once during the six-run task protocol (five minutes each), yielding a total of 500 tones per run. A stimulus onset asynchrony of 600 ms separated each tone. To familiarize the children with the tones and build up a memory trace for the standard tones, the first run contained no novel sounds and was not recorded. This ensured that the standard tone became a 'frequent familiar' stimulus, the pitch deviant and the duration deviant tones became 'infrequent familiar' stimuli and the novel sounds became 'infrequent unfamiliar' stimuli.

EEG Data Analysis

The EEG data were analyzed with Neuroscan Edit 4.4 and custom Matlab (The MathWorks, Inc., Natick, MA) scripts built on the open source EEGLAB (Delorme and Makeig 2004) and FieldTrip (Oostenveld et al. 2011) toolboxes. After concatenating all runs together, we manually eliminated large artifacts due to subject's motion, gross facial movements, or other irregularities. An eye movement correction algorithm (Semlitsch et al. 1986) corrected for eye movement artifacts. After applying a bandpass zero-phase-shift digital filter (1–15 Hz), continuous EEG data from all channels were subsequently imported into EEGLAB. Continuous data were epoched using a 100 ms prestimulus baseline period and a 500 ms poststimulus period. Individual epochs were passed through an automatic artifact detection algorithm to remove epochs with EEG activity in excess of −90μV or +90μV. Subsequently, epochs containing abnormally distributed data (i.e. joint probability or kurtosis > 5 standard deviations from expected mean values) were rejected. After pre-processing the data, the number of remaining trials for the 4 event types were as follows, standard: 1685.7 (TD) vs. 1563.2 (autism) [$t(37.3^2)=3.24$, $p=0.003$]; pitch deviant: 90.9 (TD) vs. 85.1 (autism) [$t(43.6)=2.97$, $p=0.005$]; duration deviant: 91.3 (TD) vs. 84.0 (autism) [$t(41.0)=3.41$, $p=0.002$]; and novel: 90.6 (TD) vs. 85.4 (autism) [$t(39.1)=2.18$, $p=0.04$] respectively. All participants had at least 55 accepted trials for all 4 conditions. ERPs were obtained by averaging the baseline corrected EEG epochs for each stimulus category and for each participant separately in FieldTrip. The P1, N2 and P3a peaks were identified by an automatic peak detection procedure. First, for the standard, pitch deviant, and duration deviant tones, the P1 and N2 were identified as the most positive and negative, respectively, peak within a specified window (see below) after stimulus onset. Second, their amplitudes were quantified as the mean voltage in a 50 ms window around each subject's individual peak. The P1 peak detection windows for the different event types were 80–150 ms for standard tones, 90–180 ms for pitch deviant tones, and 70–160 ms for duration deviant tones. The N2 windows for the different event types were 150–274 ms for standard tones, 174–274 ms for pitch deviant tones, and 150–274 ms for duration deviant tones. The P3a was identified as the most positive peak between 200 and 400 ms after stimulus onset for the novel sounds only and the amplitude was quantified as the mean voltage in a 50 ms window around each subject's individual peak.

[2]df adjusted due to Satterthwaite's correction for unequal variances.

Analytic Strategy

The first objective of this study was to evaluate between group (autism vs TD) differences in amplitudes of ERP components. Because the morphology of the ERP waveform changes during childhood we examined the group averaged waveforms of children 8 to 12 years and compared them to the group averaged waveform of children aged 4 to 8 years. Since both ERP waveforms showed a similar P1-N2 component structure, ERPs of children aged 4–12 years were averaged together.

We compared group differences in amplitude separately for each ERP component and condition with a 3-way (2 groups (autism, TD) X 3 Anterior-posterior position (frontal (F), central (C), posterior (P)) X 3 Lateral position (left (3), middle (z), right (4))) repeated-measures MANOVA. We also ran analyses with MA entered as a covariate. An identical analysis was performed on the latencies of each peak. All statistical analyses were conducted using SAS (SAS Institute, Inc., Cary, NC).

The second objective of this study was to evaluate associations between ERP components and clinical measures (parent and observed indicators) of sensory response patterns within the autism group only. This was accomplished using a series of ordinary least squares regression models. In an effort to reduce the dimensionality of the data and to reduce the number of accompanying statistical tests a composite measure for each ERP component was created. Hereto, we averaged the responses from central electrodes (C3, Cz, C4) because all ERP components showed largest amplitudes for this position. This resulted in a single value for each ERP component. Preliminary models, which are not presented here, identified up to two cases per outcome that exerted excessive influence (per graphical displays of Cooks D values; see Fox 1991); these cases were excluded from consideration. The initial (“full”) model included the full set of predictors including mental age and ADOS severity as covariates, three ERP composites (P1, N2, P3a) as main effects, and all possible 2-way interactions between ERP composites (i.e., P1 x N2, P1 x P3a, N2 x P3a). The inclusion of interaction terms provided tests of potential conditional associations between ERP components and six indices of sensory response patterns (hyperresponsiveness, hyporesponsiveness, and sensory seeking patterns, each indicated by parent report and observed measures). For each outcome, a second (“trimmed”) model was presented in which any (all) non-significant interaction terms were removed. Following best practice (Aiken and West 1991), ERP composites were mean centered in order to reduce non-essential multicollinearity between main effect and interaction terms, and significant interaction terms were probed by evaluating the simple slopes between a given ERP composite and the sensory outcome at conditional values (i.e., low and high levels, defined as the 25th and 75th percentiles of the observed scores) of the second ERP composite. Both unstandardized (b) and standardized (β) coefficients are tabled, whereas only standardized coefficients are presented in figures (as simple slopes).

Results

Between Group Comparisons of Amplitude and Latency

Group differences in amplitude were analyzed separately for each ERP component for each condition, resulting in 7 separate analyses (Standard P1, Standard N2, Novel P3a, Pitch Deviant P1, Pitch Deviant N2, Duration Deviant P1, and Duration Deviant N2). See figures 1, 2, 3, and 4 for ERP group overlays for the standard, novel, duration deviant, and pitch deviant sounds respectively. Table 3 presents for each group the component amplitudes and latencies at the Cz electrode and the results of the MANOVA analyses. The Group X Anterior position X Lateral position MANOVA analyses revealed group differences for several ERP components:

Standard Tones - Amplitudes

Compared to the TD group, the autism group had marginally smaller amplitudes to standard tones for both the P1: ($F(1,65)=3.2$, $p=0.08$) and the N2: ($F(1,65)=4.0$, $p=0.05$). When MA was included in the model, results were weakened somewhat (P1: ($F(1,63)=2.9$, $p=0.09$); N2: ($F(1,63)=2.6$, $p=0.11$)). Effect sizes were medium (≈ 0.5) for both (Cohen's *d*, P1: 0.43, N2: 0.45). There was not a main effect of MA for either measure ($p>0.3$). There was a main effect of Anterior position for the standard tone P1 ($F(2,126)=14.1$, $p<0.0001$) and the standard tone N2 ($F(2,126)=3.7$, $p=0.03$), such that central electrodes had the highest amplitudes for both groups. For the standard N2, there was also a marginal main effect of Lateral position ($F(2,126)=2.5$, $p=0.09$) and an interaction between Lateral position and MA ($F(2,126) = 3.0$, $p=0.05$). There were no effects of lateral position on the standard P1 ($p>0.5$). No other 2- or 3-way interactions were present for either the standard P1 or N2 ($p>0.1$ for all), reflecting similar effects of electrode location across groups.

Novel Sounds - Amplitudes

Compared to the TD group, the autism group had a significantly smaller P3a amplitude for novel tones ($F(1,64)=5.8$, $p=0.02$). This effect was also present when MA was included in the model ($F(1,62)=6.9$, $p=0.01$) and the effect size was medium (Cohen's $d = 0.62$). There was no main effect of MA ($p=0.2$). There was a main effect of Anterior position ($F(2,124)=16.1$, $p<0.0001$), such that the central electrodes showed highest amplitudes for both groups. There was also a main effect of Lateral position on P3a amplitude ($F(2,124)=437$, $p=0.01$), such that the midline electrodes showed highest amplitudes. Furthermore, there were interactions between Lateral position and MA ($F(2,124)=4.3$, $p=0.02$) and between Anterior position and Lateral position ($F(4,248)=2.6$, $p=0.04$). There were no other 2- or 3-way interactions ($p\geq 0.3$), reflecting similar effects of electrode location across groups.

Deviant Tones - Amplitudes

There were no significant group differences in amplitude for the remaining ERP components: P1 and N2 responses to pitch deviant stimuli ($p=0.9$ for both) and P1 and N2 responses to duration deviant stimuli ($p>0.3$ for both). MA was a marginal predictor of N2 for the pitch deviant tones ($F(1,62)=3.6$, $p=0.06$), but not for the pitch deviant P1 or the

duration deviant P1 or N2 (p>.3 for all). There were no 2- or 3-way interactions between group and electrode position for these 4 ERP components (p>0.05 for all), reflecting similar effects of electrode location across groups. Because there were no significant group effects for the P1 and N2 components for pitch deviant and duration deviant stimuli, they were excluded from all further analyses.

Latencies

We also examined group differences in latency. Separate Group X Anterior position X Lateral position MANOVA analyses were conducted for each ERP component and for each condition. The only significant group difference in latency was found for the pitch deviant P1, such that the autism group had longer latencies than the TD group (F(1,62)=4.18, p=0.05), in addition to a marginal effect of MA (F(1,62)=3.68, p=0.06)[3]. There were no significant group effects for the remaining ERP components and conditions: standard P1, standard N1, novel P3a, pitch deviant N1, duration deviant P1, duration deviant N1 (p>0.15 for all). There was a significant effect of MA only for the standard tone P1 (F(1,62)=15.87, p=0.0002), and a marginally significant effect of MA on pitch deviant N1 (F(1,62)=2.85, p=0.10), but not for the remaining ERP components and conditions (p>.3 for all).

Relating Neural Responses to Sensory Features in Autism: Exploratory Analysis

Given the rarity of having clinical indicators of sensory response patterns (hyperresponsiveness, hyporesponsiveness, sensory seeking behaviors, each indexed by both parent report and observed measures) as well as ERP data in children with autism, we conducted an exploratory set of hypothesis generating analyses, in which ERP amplitudes were used to predict individual differences in sensory features. Given the relatively small sample size, we adopted a liberal alpha level (p<.10) in order to reduce the chance that we might commit a type II error (and potentially miss a clinically meaningful result). Initial bivariate correlations among the predictors and outcomes for regression models indicated that sensory indicators were weakly to moderately correlated with individual ERP composite amplitudes (|rs|=.04 – .30) and failed to reach statistical significance (ps >.10). This suggested that any single ERP component was not an adequate predictor of sensory features. As such, we tested whether multiple ERP components might jointly (additively or multiplicatively) predict sensory features.

Sensory Seeking

The set of ERP composite amplitudes (Standard P1, Standard N2, Novel P3a) and covariates (mental age and ADOS severity) was significantly predictive of greater levels of observed sensory seeking behaviors, (F(8, 17)=7.72, p=.0002), adjusted R^2 =.68. As summarized in Table 4, there was evidence for significant P1 x P3a and P1 x N2, but not N2 x P3a, interaction terms. A trimmed model that excluded the N2 x P3a term continued to explain substantial variation in the outcome, (F(7,17)=9.02, p<.0001), adjusted R^2 =.69. As depicted in Figure 5, the P1 x N2 interaction term indicated that less negative amplitudes of N2 (i.e.,

[3]For the pitch deviant P1, there were no main effects of either Anterior position or Lateral position (p>0.1 for both), however there were significant interactions between Anterior position and both Group (F(2,124)=8.2, p=0.0005) and MA (F(2,124)=4.5, p=0.01), suggesting that group and MA effects varied across anterior positions. No other interactions were significant.

attenuated responses) were associated with higher levels of observed sensory seeking behaviors at lower but not higher amplitudes of P1 (e.g., a 1 standard deviation increase in N2 was associated with a .65 standard deviation increase in seeking behaviors given low levels of P1; see Figure 5). Furthermore, as depicted in Figure 6, the P1 x P3a interaction term indicated that lower amplitudes of P3a were associated with higher levels of observed sensory seeking behaviors at higher but not lower amplitudes of P1. In contrast to observed measures of sensory seeking, there was no evidence that the set of predictors was associated with parent report measures of sensory seeking behaviors, ($F(8,19)=0.90$, $p=.53$), adjusted $R^2=.00$. This continued to be true even after all three non-significant interaction terms were removed, ($F(5,22)= 0.27$, $p=.92$), adjusted $R^2=.00$. Regression coefficients for both models are summarized in Table 4.

Sensory Hyperresponsiveness

There was a trend for the full set of ERP composites and covariates to predict observed sensory hyperresponsiveness, ($F(8,17)=2.22$, $p=.08$), Adjusted $R^2=.28$. As summarized in Table 5, the P1 x N2 interaction term was statistically significant. Re-estimating this model excluding the non-significant P1 x P3a and N2 X P3a terms resulted in comparable model fit, ($F(6,19)=2.60$, $p=.052$), adjusted $R^2 =.28$. Although the magnitude of the association between N2 and observed sensory hyperresponsiveness was conditional on levels of P1 (i.e., increasing levels of N2 were associated with higher and lower levels of hyperresponsiveness at higher and lower levels of P1, respectively), none of the simple slopes were statistically significant. This may be due to the possibility that conditional associations of N2 and sensory hyperresponsiveness were only evident at more extreme levels of P1 than considered here (e.g., 10th and 90th versus the current 25th and 75th percentile scores).

In contrast to observed measures of sensory hyperresponsiveness, there was no evidence that the set of predictors was associated with parent report measures of sensory hyperresponsiveness, ($F(8,18)=1.69$, $p=.17$), adjusted $R^2=.28$. This continued to be true even after all three interaction terms were removed, ($F(5,21)=1.85$, $p=.15$), adjusted $R^2=.14$. Regression coefficients for both models are summarized in Table 5.

Sensory Hyporesponsiveness

The full set of ERP composites and covariates was not significantly associated with observed measures of sensory hyporesponsiveness, ($F(8,17)=2.02$, $p=.11$), adjusted $R^2=.25$. There was a trend for an association once all three interaction terms were removed, ($F(5,20)=2.67$, $p=.053$), adjusted $R^2= .25$. As summarized in Table 6, higher levels of mental age were associated with lower levels of sensory hyporesponsiveness ($\beta=-.55$, $p=.008$); moreover, there was a trend for higher levels of N2 (i.e., attenuated responses) to be associated with higher levels of observed sensory hyporesponsiveness ($\beta=.35$, $p=.07$).

The full set of ERP composites and covariates was not significantly associated with parent reported sensory hyporesponsiveness, ($F(8,18)=1.71$, $p=.16$), adjusted $R^2=.18$; although, the P1 x N2 interaction term was statistically significant ($p=.02$). However, the overall model continued to be non-significant, even after the two non-significant interaction terms were

removed, (F(6,20)=1.83, p=.14), adjusted R^2= .16. Regression coefficients for both models are summarized in Table 6.

Selection Effects

It is important to consider the impact of selection effects on the electrophysiology participant groups. While EEG is relatively non-invasive, it requires the participant to wear a cap with electrodes and gel on their head and to allow the experimenter to touch their head repeatedly. Accordingly, many parents involved in the greater project elected not to attempt an EEG session with their child, while other children were not able to complete an initiated EEG session. It is possible (and likely) that the children who were not able to participate in the EEG study have more severe sensory features than those who were able to participate. In order to investigate this possibility, we performed a post-hoc analysis comparing a sample of the children with autism who participated in the EEG study (N=38) to a sample of the children with autism who elected not to participate or withdrew during the session (N=52). We found evidence that, in fact, the successful EEG participants were higher functioning, as measured by IQ (t(86)= −3.31, p=0.001) and mental age (t(86) =−6.14, p<0.0001). They also had lower severity scores on observed sensory hyperresponsiveness (t(83)=3.24, p=0.002), observed hyporesponsiveness (t(83)=3.43, p=0.001), and observed sensory seeking behaviors (t(83)=2.65, p=0.01). This evidence suggests that the participants in this EEG study represent a subset of the autism population with more mild sensory features and higher levels of cognitive functioning.

Discussion

Relative to typically developing children, the children with autism showed attenuated neural responses to auditory tones, and these responses were related to selective aspects of behavioral sensory features in this population. The children with autism showed marginally reduced early sensory responses (as measured by the P1 and N2 ERP components) during passive exposure to standard, repeated tones. The children with autism also showed reduced attentional responses (as measured by the P3a ERP component) during exposure to infrequent, novel, naturalistic sounds.

Potential Neural Mechanisms Underlying Group Differences in Auditory Processing

Since the P1 and N2 are early sensory ERP components our findings may be suggestive of a disruption (or perhaps maturational delay) in low level sensory processing. Some studies have shown reductions of early sensory ERP components in children with ASD (e.g. Bruneau et al. 1999) where as others (particularly with high functioning adolescent and adult samples) have not (e.g. Kemner et al. 1995; Lincoln et al. 1995). The simplistic nature of “standard” auditory stimuli suggests that deficits in the P1 and N2 responses may be generalizable to a wide category of sound events and support a neural basis of atypical sensory encoding in autism.

Despite the fact that the P1 and N1/N2 are often thought of as ‘obligatory’ ERP components that are primarily determined by bottom-up influences, there is some evidence to suggest that at least the N1/N2 can be modulated by top down inhibitory processes (Sable et al.

2004; Whitehouse and Bishop 2008). Therefore, the marginally attenuated N2 response in the autism group potentially reflects disruptions in both low level stimulus driven as well as higher level top down stages of auditory information processing. It is also important to note that the standard tone was presented well over 1500 times. Therefore, it is possible that the results reported here may be influenced by different habituation rates to these stimuli in children with autism compared to typically developing children. Further analyses are needed to test this hypothesis.

The children with autism also showed significantly attenuated P3a responses to the infrequently presented, novel, naturalistic sounds. The P3a is a later ERP component (occurring ~300ms after stimulus presentation), is attention dependent, and hence reflects higher order cognitive processing of stimuli. Therefore, the attenuated P3a response suggests that attentional orienting or perhaps salience evaluation in children with autism is compromised. This finding of impaired orienting has been frequently reported in the EEG literature (Ceponiene et al. 2003; Dawson et al. 1998; Kemner et al. 1995; Lincoln et al. 1993). Taken together, this set of findings suggest that children with autism have disrupted neural responses to auditory stimuli in both bottom up early sensory processes, as well as later top down attentional processes, both of which are hypothesized to result in less responsiveness to external auditory stimuli.

Contrary to our expectations, this study failed to present significant group differences in ERP amplitudes to small pitch deviant and duration deviant tones. However, for both the pitch deviant tones as well as for the duration deviant tones the P1 and N2 responses were slightly attenuated in the autism group, a direction consistent with the findings for the standard tones. Yet, ERP latency of the P1 peak to pitch deviant sounds was found to be slightly later in the autism group. Several other studies have also observed delayed early auditory responses in ASD especially regarding the N1/M100 peak (i.e. Bruneau, et al. 1999; Sokhadze et al. 2009; Gage et al. 2003; Roberts et al. 2010). These findings are taken to indicate disrupted encoding of simple sensory information. The null findings regarding amplitude might be due to the small differences between the standard and deviant stimuli that were used in our study (1000 Hz vs. 1100 Hz for pitch deviant; and 200 ms vs. 190 ms for duration deviant) and/or the relatively small number of deviant stimuli, resulting in less reliable ERPs.

Early sensory processing differences (e.g., attenuation of P1/N2 to standard tones) may also impact later processing components (discrimination, attention allocation, etc.), and/or multisensory integration. It is possible that if P1/N2 responses are dysfunctional, greater attentional resources or greater alerting mechanisms are needed to compensate for such deficits; however, if concomitant deficits exist in P3a, there are fewer resources to use as a compensatory mechanism and this may have implications for outcomes.

Although the conditional associations between ERP responses and clinical measures of sensory functioning within the autism group were not as easily understood as simple bivariate associations would have been, the pattern of results underscores the importance of considering multiple aspects of ERP responses together. Three sets of findings are noteworthy: First, given attenuated P1 responses to standard tones, attenuated N2 responses

were associated with more severe sensory seeking behaviors observed in children with autism. Therefore, individual differences in N2 response to standard tones are only positively related to more severe sensory seeking behaviors for children with autism who concurrently show attenuated P1 responses to standard tones. Second, given larger P1 responses to standard tones, larger P3a responses to novel tones are associated with less severe sensory seeking behaviors observed in children with autism. Hence, individual differences in P3a responses to novel tones are only negatively related to sensory seeking behaviors for children with larger P1 responses to standard tones. Third, clinical measures of sensory hyperresponsiveness in children with autism also trended toward a relation to an interaction of P1 and N2 responses to standard tones. Given *larger* P1 responses, more attenuated N2 responses were related to more severe sensory hyperresponsiveness. However, given *attenuated* P1 responses, more attenuated N2 responses were related to less severe hyperresponsiveness. These results illustrate the complex association between ERP responses to auditory tones and sensory characteristics of children with autism.

Implications of Aberrant Neural Sensory Processing for Behavioral Sensory Features in Children with Autism

To our knowledge, this is the first study to examine the association of neural ERP components to clinical indices of three separate sensory response patterns, as assessed by both parent report and clinical observations, commonly observed in children with autism. These findings begin to unravel the complex and conditional associations among specific auditory ERP components (P1/N2 and P3a) and severity of behavioral sensory features (even after controlling for mental age and autism severity). The combination of weak N2 responses following weak P1 responses was particularly predictive of more atypical sensory seeking behaviors. This modulation of the N2 amplitude-sensory seeking relation by P1amplitude reflects the complex dynamics of these distinct neural processes.

Because the N1/N2 ERP component is believed to be affected by higher order top down processes to some degree, the relation found here between N2 responses and behavioral characteristics suggests that top down attentional control in children with autism has some effect on their behavioral characteristics related to observed sensory seeking behaviors. Further evidence for this was found in an interaction between P1 responses to standard tones, P3a responses to novel tones, and observed sensory seeking behaviors. Specifically, given increased amplitude levels of P1, the P3a response predicted sensory seeking behaviors, such that lower amplitude levels of P3a predicted more severe sensory seeking behaviors. Again, this provides evidence of a relation between disruptions in neural responses to sensory processing and more severe behavioral characteristics. The P3a ERP component reflects attentional orienting processes, providing additional evidence that disrupted neural attentional processes are related to sensory processing characteristics of individuals with autism.

There are multiple possible mechanisms that could lead from disrupted neural attentional processes to atypical sensory seeking behaviors. Disrupted attentional mechanisms may diminish orienting responses to novel stimuli, and therefore some children with autism may appear preoccupied with intense and repetitive sensory activities because they are unable to

disengage and refocus on other environmental events. Alternatively, disrupted attentional mechanisms may lead to hyper-engagement on existing stimuli or sensory-driven activities due to disruptions in reward pathways. The present study provides evidence of an association between attentional processes and specific sensory features in autism, but more research is needed to distinguish these two (or potentially other) mechanisms underlying these associations. Examination of attentional orienting in the context of overt attention switching tasks in individuals with autism may be able to further illuminate these mechanisms.

The significant P1/N2 interaction predicting observed hyperresponsive behaviors in the autism group was complex and difficult to interpret given that none of the individual slopes were statistically significantly different. Given our limited sample size, we cannot disambiguate whether these are meaningful effects or artifacts from a small number of cases. Further research with larger participant groups may be able to better characterize this association.

Limitations

It is likely that atypical ERP responses found here may be attenuated relative to the general autism population given that individuals were less likely to enroll and/or tolerate the EEG procedures. Thus, children with more severe clinical sensory features may have even stronger neurophysiological disruptions in auditory processing than reported here, and has implications for future research as well as intervention planning. Due to the fact that we used a passive task paradigm and children's attention was directed elsewhere we can't rule out the possibility that our ERP results might be explained (partly) by the fact that children with autism were more 'tuned in' to their movie resulting in reduced ERP component amplitudes compared to the TD group. We were not able to show group differences in ERP responses to pitch deviant and duration deviant tones. It is possible that the small number of pitch deviant and duration deviant stimuli and/or the small differences used between the standard and deviant stimuli did not provide enough sensitivity to capture this effect. Although there were some trends in the predicted directions, we did not find associations between attenuated ERP components and clinical measures of sensory hyporesponsiveness. Although a sampling bias may have been responsible, it is also possible that our clinical measures were not sufficiently sensitive to capture the full range of hyporesponsive features, particularly at the most severe extreme. Moreover, since the clinical measures and EEG could not be conducted on the same day, it is possible that the time gap between study tasks further attenuated potentially significant associations between behavior and neurophysiology. However, we note that there was a moderate correlation (r=0.53) between observed hyporesponsiveness and observed sensory seeking behaviors, thus, it is plausible that the sensory seeking measure indirectly taps some aspects of hyporesponsiveness (e.g., children are under-aroused or overfocused and thus less likely to respond to external stimuli) and is more sensitive to the effects of disrupted neural processing evident in the EEG study. Several studies have theorized about the association between these two clinical response patterns (e.g., Dunn 1997; Ausderau et al. in revision) and how they are especially detrimental to social-communication outcomes such as joint attention and language levels (Watson et al. 2011; Baranek et al. 2013).

We note that whereas significant associations between the observed sensory response measures and the ERP measures were found, such associations were non-existent for the parent report measures. Observed measures and ERP measures are both based on direct observations of responses to sensory stimuli whereas parent report measures are not. Parent report measures may also be confounded by parents' knowledge of symptoms associated with autism and/or parents may be less aware of (or avoid mentioning) unusual behaviors before an official diagnosis has been established (Stone and Hogan 1993). Observed measures might therefore be more sensitive than parent report measures and hence show stronger association with ERP measures. Future studies could include modality-specific clinical measures (e.g., subset of items tapping predominantly auditory features), rather than multimodal sensory features; however, most real-world experiences involve multimodal processing. Another limitation was the lack of a second control group of children with other developmental disabilities to determine the extent to which significant findings are specific to children with autism and not general to intellectual disabilities or clinical populations. This is important as we showed that adding mental age, a measure of cognitive maturation, as a covariate can weaken (as in the case of P1/N2 amplitudes) or strengthen (as in the P3a amplitude) group difference findings. In the future, adding another comparison group, one with known intellectual deficits, would allow additionally controlling for intellectual disability status which is not possible with a typically-developing control group. Investigating children with lower cognitive abilities is difficult but very much needed since most EEG studies focus on older and high functioning cases, and thus results from these studies cannot be generalized to the broader and vastly heterogeneous population of children with autism.

Conclusion

This study provides evidence of sensory processing dysfunctions at the neural level in children with autism compared with typically developing children, ages 4–12 years. While sensory features have been well characterized in autism, this is one of the few studies to report on potential neural bases of some of these clinical behaviors. Specifically, these findings demonstrated marginally attenuated early sensory (P1 and N2) responses to repeated, familiar tones, as well as attenuated attentional responses (P3a) to novel sounds reflecting poor orienting to external stimuli. This study suggests that both low level stimulus driven processes and top down attentional processes are disrupted in children with autism in the temporal stream of sensory processing and furthermore, that these neural disruptions conditionally predict increased levels of clinically observed sensory seeking behaviors via complex mechanisms. With future work, these findings may be able to inform interventions for atypical sensory processing behaviors in children with autism.

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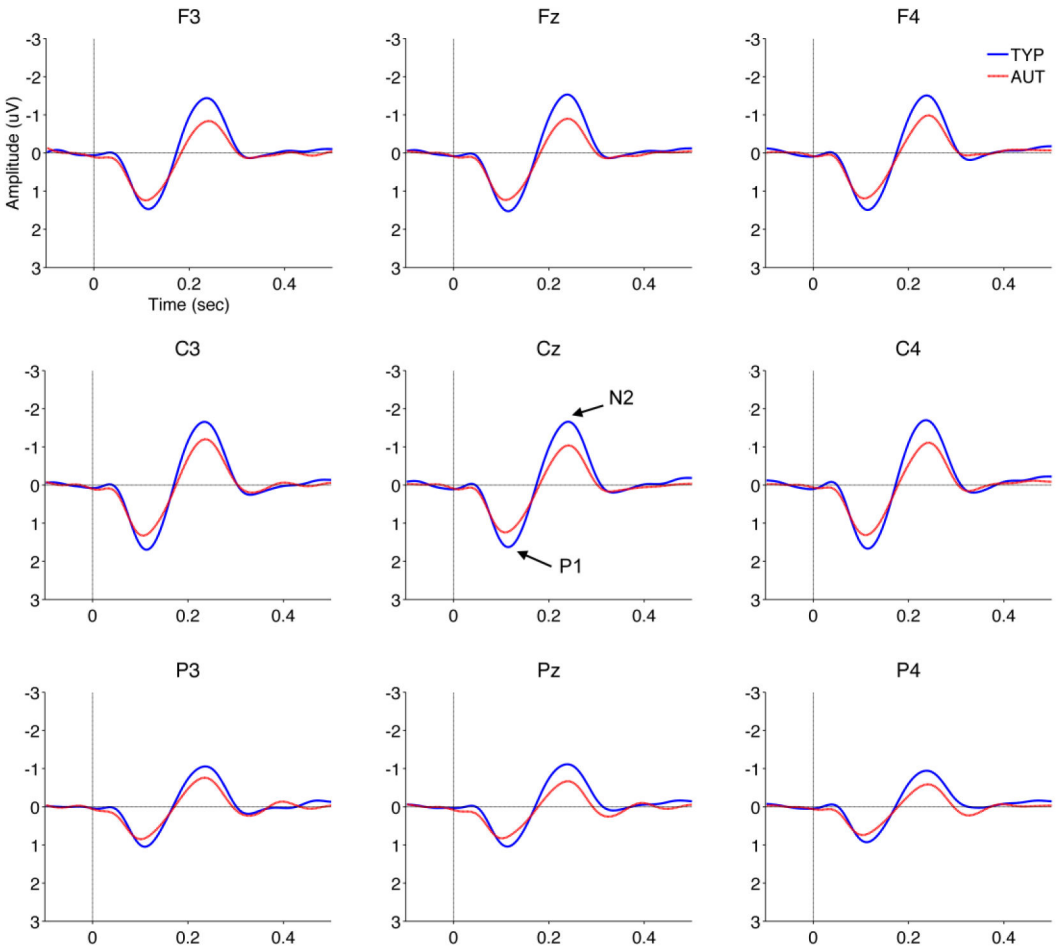

Figure 1.

Group averaged ERPs to standard stimuli. Time is in seconds. Time = 0 indicates stimulus onset. TYP = typically developing group. AUT = group with autism

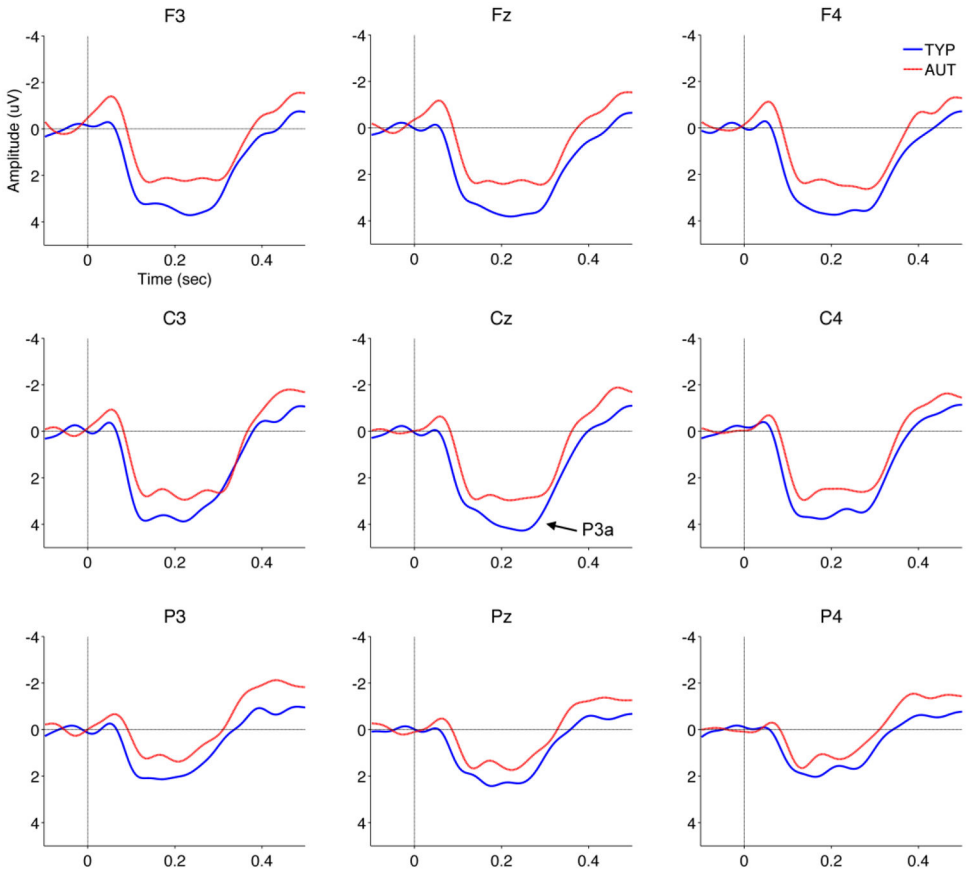

Figure 2.

Group averaged ERPs to novel stimuli. Time is in seconds. Time = 0 indicates stimulus onset. TYP = typically developing group. AUT = group with autism

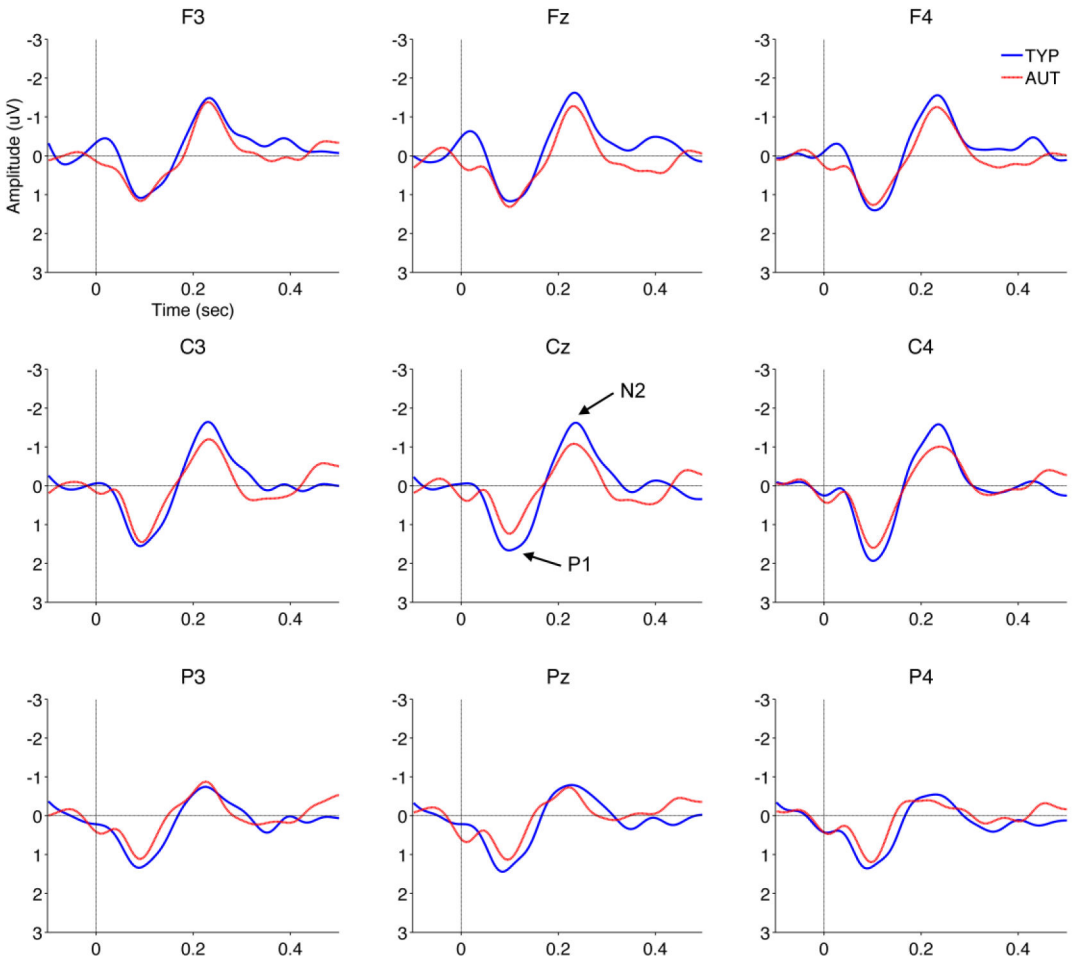

Figure 3.

Group averaged ERPs to pitch deviant stimuli. Time is in seconds. Time = 0 indicates stimulus onset. TYP = typically developing group. AUT = group with autism

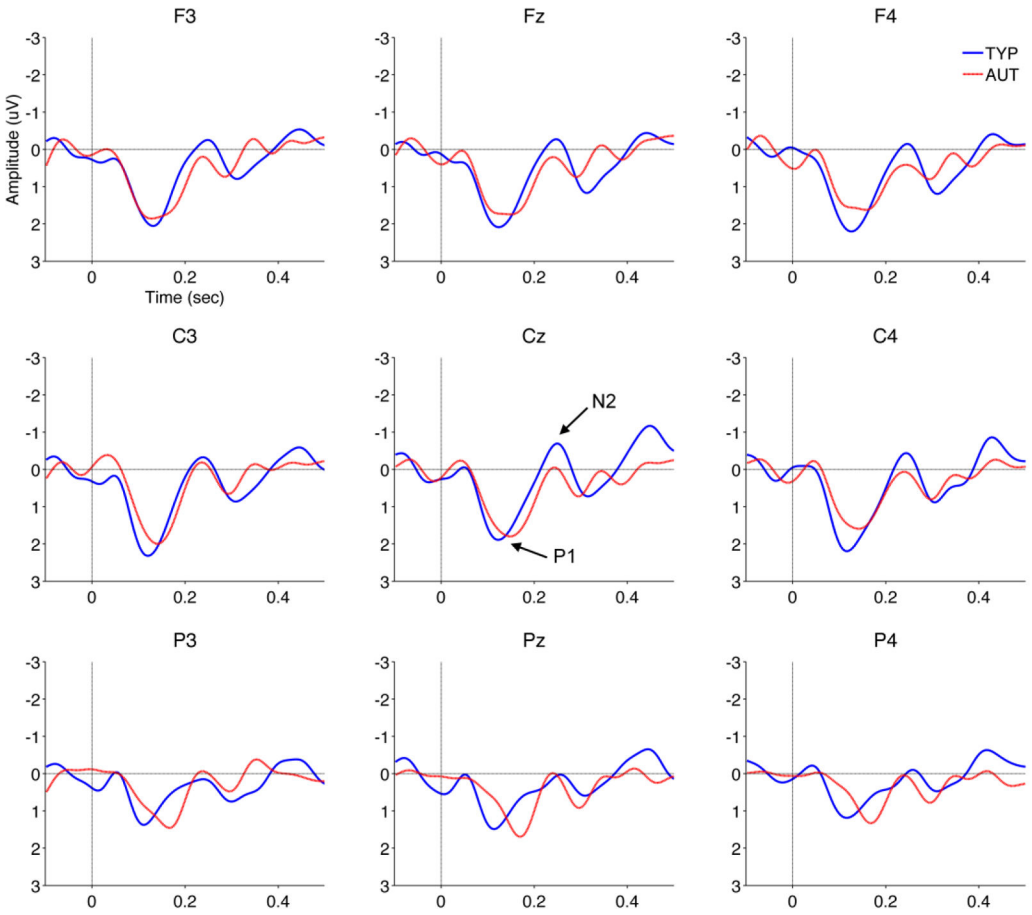

Figure 4.

Group averaged ERPs to duration deviant stimuli. Time is in seconds. Time = 0 indicates stimulus onset. TYP = typically developing group. AUT = group with autism

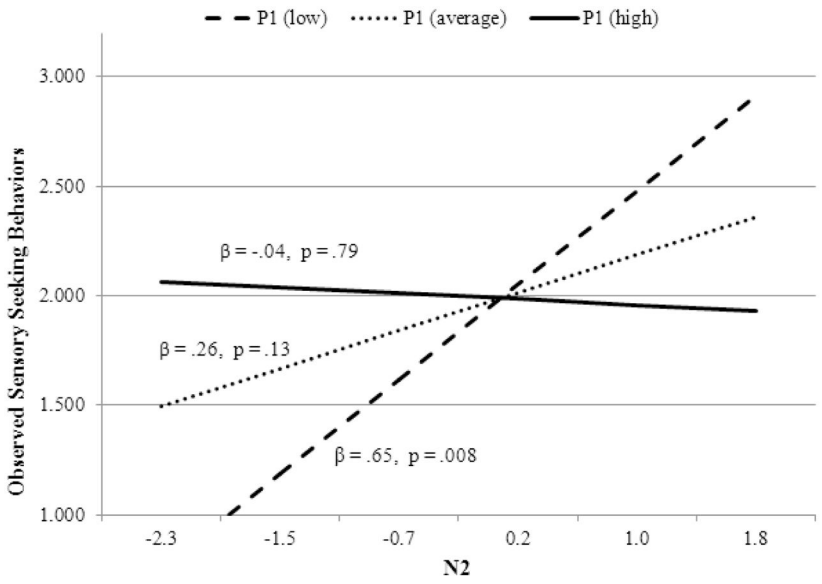

Figure 5.

ERP interactions between P1 and N2 amplitude in the prediction of observed sensory seeking behaviors. Low and high levels were defined as the 25th and 75th percentiles of the observed sensory seeking scores.

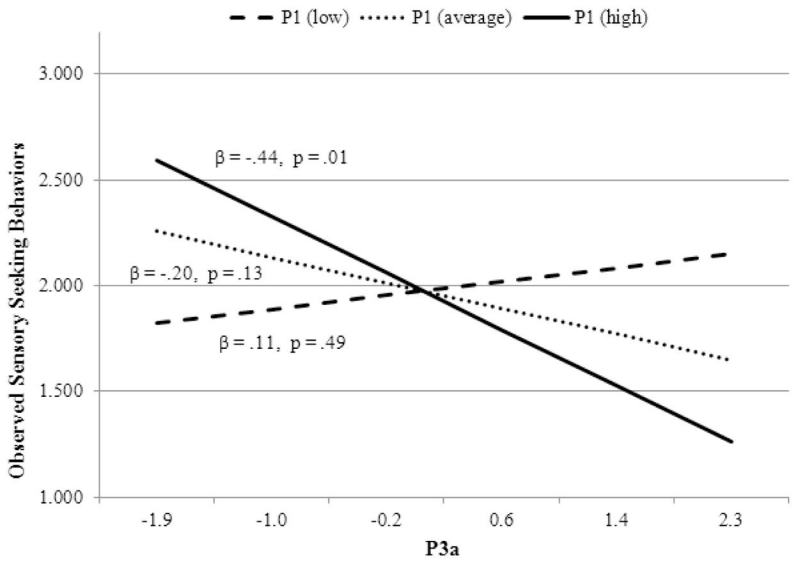

Figure 6.

ERP interactions between P1 and P3a amplitude in the prediction of observed sensory seeking behaviors. Low and high levels were defined as the 25th and 75th percentiles of the observed sensory seeking scores.

Table 1

Demographics for participants with autism and typically developing participants

	Autism N (%)	**TD N (%)**
Total Participants	28 (100)	39 (100)
Gender (Male)	22 (79.0)	31 (79.5)
Maternal Education		
High School or GED	4 (14.3)	1 (2.6)
Associates Degree or higher	23 (82.1)	36 (92.3)
Unknown	1 (3.6)	2 (5.1)
Annual Household Income		
Less than $59,999	7 (24.0)	13 (33.3)
$60,000 to $99,999	11 (39.3)	13 (33.4)
$100,000 or more	9 (32.1)	11 (28.2)
Unknown	1 (3.6)	2 (5.2)
Race		
White	25 (85.7)	29 (74.4)
African-American, Asian, or Multiple Races	4 (14.3)	10 (25.6)
Hispanic or Latino Origin	3 (10.7)	6 (15.4)
Handedness		
Left	4 (14.3)	1 (2.6)
Right	20 (69.0)	34 (87.2)
Mixed or Unknown	4 (14.2)	4 (10.3)
	M (SD)	M (SD)
ADOS Severity Score	8.5 (1.2)	NA
Chronological Age (months)	91.4 (26.6)	84.4 (24.5)
Mental Age (months)	73.4 (42.2)	97.9 (45.6)
Nonverbal IQ	82.6 (22.4)	108.5 (12.1)

Table 2

Comparison of Groups on Parent Report and Observed Sensory Measures.

	Typical (N = 39)	Autism (N = 28)	Comparison	
	M (SD)	M (SD)	t (df)	Prob
Observed Sensory Seeking	1.4 (0.3)	2.1 (0.7)	−5.1 (65)	<.0001
Observed Hyporesponsive	1.5 (0.5)	2.1 (0.7)	−3.8 (65)	0.0003
Observed Hyperresponsive	1.2 (0.2)	1.4 (0.4)	−3.1 (65)	0.0033
Parent Report Sensory Seeking	1.5 (0.3)	2.3 (0.4)	−10.1 (65)	<.0001
Parent Report Hyporesponsive	1.5 (0.3)	2.2 (0.6)	−6.7 (65)	<.0001
Parent Report Hyperresponsive	1.5 (0.3)	2.3 (0.5)	−8.8 (65)	<.0001

Note: M = mean; SD = standard deviation; df = degrees of freedom; Prob = probability

Table 3

Event-Related Potential Component Peak Amplitude and Latency Means at Cz for each Group and Results of Statistical Analysis

ERP Component					Group Effect in Group X Anterior Position X Lateral Position MANOVA co-varying for MA					
	Autism (n=28)		TD (n=39)		Amplitude			Latency		
Standard	Amplitud e, μV	Latency, ms	Amplitud e, μV	Latency, ms	F Value	*p* Value	Effect Size, Cohen's *d*	F Value	*p* Value	Effect Size, Cohen's *d*
P1	1.3 ± 0.7	112 ± 17.7	1.6 ± 0.7	114 ± 17.7	2.9	0.09	0.43	2.1	0.15	0.11
N2	−1.1 ± 0.9	241 ± 13.9	−1.6 ± 1.3	238 ± 16.9	2.6	0.11	0.45	0.4	0.56	0.19
Novel										
P3a	3.8 ± 2.1	249 ± 46.2	5.1 ± 2.1	245 ± 38.0	6.9	0.01	0.62	0.7	0.40	0.09
Pitch Deviant										
P1	2.5 ± 2.2	144 ± 29.9	2.4 ± 1.9	126 ± 28.8	0.0	0.91	0.05	4.2	0.05	0.61
N2	−7 ± 1.7	231 ± 30.9	−1.0 ± 2.1	237 ± 30.1	0.0	0.89	0.16	0.1	0.77	0.20
Duration Deviant										
P1	1.7 ± 1.4	107 ± 29.4	2.1 ± 1.6	112 ± 28.4	0.2	0.63	0.27	0.0	0.85	0.17
N2	−1.7 ± 2.1	217 ± 40.5	−2.1 ± 1.8	229 ± 29.7	0.8	0.37	0.15	1.7	0.19	0.34

Data are given as mean ± SD.

Cohen's d effect sizes are defined as "small, d = .2," "medium, d = .5," and "large, d = .8".

Table 4

Associations between ERP composites and sensory seeking behaviors

	Observed Sensory Seeking				Parent Report Sensory Seeking			
	Full		Trim		Full		Trim	
	b (se)	B	b (se)	β	b (se)	β	b (se)	β
Intercept	2.24 (.69)	0	2.40 (.65)	0	2.11 (.56)	0	1.84 (.50)	0
Mental Age	−0.02 (.00)	-0.71^{***}	−0.02 (.00)	-0.73^{***}	−0.00 (.00)	−0.13	−0.00 (.00)	−0.14
ADOS Severity	0.15 (.08)	0.25	0.12 (.07)	0.21	0.03 (.07)	0.11	0.06 (.06)	0.22
P1	0.08 (.13)	0.10	0.02 (.10)	0.02	−0.09 (.11)	−0.24	−0.03 (.08)	−0.09
N2	0.18 (.14)	0.22	0.21 (.13)	0.26	−0.15 (.09)	−0.40	−0.15 (.09)	−0.40
P3a	−0.19 (.11)	−0.26	−0.15 (.09)	−0.20	0.04 (.10)	0.11	0.07 (.08)	0.18
P1 x P3a	−0.42 (.13)	-0.50^{**}	−0.39 (.13)	-0.48^{*}	−0.22 (.11)	-0.56^{+}	−0.21 (.10)	-0.52^{+}
N2 x P3a	0.13 (.19)	0.13	--	--	−0.03 (.15)	−0.08	--	--
P1 x N2	−0.52 (.13)	-0.79^{***}	−0.55 (.12)	$-.84^{***}$	−0.07 (.06)	−0.29	--	--
F (ndf, ddf)	7.72^{***} (8, 17)		9.02^{***} (7, 18)		0.90 (8, 19)		0.98 (6, 21)	
Adjusted R^2	.68		.69		.00		.00	

Note: ndf = numerator degrees of freedom; ddf = denominator degrees of freedom;

$^{+}p < .10$,

$^{*}p < .05$,

$^{**}p < .01$,

$^{***}p < .001$;

b = unstandardized coefficient; se = standard error; β = standardized coefficient

Table 5

Associations between ERP composites and hyperresponsiveness

	Observed				Parent Report			
	Full		Trim		Full		Trim	
	b (se)	β	b (se)	β	b (se)	β	b (se)	β
Intercept	1.62 (.44)	0.00	1.52 (.43)	0.00	4.39 (.77)	0	3.81 (.66)	0
Mental Age	−0.00 (.00)	−0.28	−0.00 (.00)	−0.27	0.00 (.00)	0.01	0.00 (.00)	−0.03
ADOS Severity	−0.01 (.05)	−0.05	−0.00 (.05)	−0.01	−0.23 (.09)	−0.59*	−0.17 (.08)	−0.43*
P1	0.03 (.13)	0.08	0.04 (.10)	0.09	−0.05 (.13)	−0.11	−0.15 (.09)	−0.32
N2	0.00 (.09)	0.01	0.03 (.07)	0.08	0.21 (.14)	0.42	0.07 (.10)	0.14
P3a	0.07 (.09)	0.20	0.04 (.07)	0.11	0.00 (.11)	0.01	0.10 (.09)	0.21
P1 x P3a	−0.09 (.14)	−0.18	--	--	0.08 (.14)	0.16	--	--
N2 x P3a	−0.15 (.13)	−0.33	--	--	0.23 (.18)	0.41	--	--
P1 x N2	0.27 (0.09)	0.94**	0.20 (0.07)	0.70*	−0.08 (.07)	−0.25	--	--
F (ndf, ddf)	2.22+ (8, 17)		2.58+ (6, 19)		1.69 (8, 18)		1.85	
Adjusted R^2	.28		.28		.18		.14	

Note: ndf = numerator degrees of freedom; ddf = denominator degrees of freedom;

+ $p < .10$,

* $p < .05$,

** $p < .01$,

*** $p < .001$;

b = unstandardized coefficient; se = standard error; β = standardized coefficient

Table 6

Associations between ERP Composites and hyporesponsiveness

	Observed				Parent Report			
	Full		Trim		Full		Trim	
	b (se)	β	b (se)	β	b (se)	β	b (se)	β
Intercept	3.49 (1.02)	0	3.83 (.96)	0	2.23 (.78)	0	2.52 (.75)	0
Mental Age	−0.01 (.01)	−0.48*	−0.02 (.01)	−0.55**	0.00 (.00)	0.37+	0.00 (.00)	0.36+
ADOS Severity	−0.06 (.12)	−0.10	−0.08 (.11)	−0.15	−0.03 (.10)	−0.08	−0.07 (.09)	−0.16
P1	−0.24 (.26)	−0.31	−0.14 (.15)	−0.18	−0.26 (.21)	−0.41	−0.30 (.17)	−0.49+
N2	*0.36 (.17)*	*0.48**	0.26 (.14)	0.35+	−0.11 (.14)	−0.19	−0.16 (.11)	−0.27
P3a	−0.15 (.17)	−0.21	−0.10 (.14)	−0.14	−0.13 (.14)	−0.22	−0.06 (.12)	−0.10
P1 x P3a	0.27 (.29)	0.25	--	--	0.08 (.24)	0.09	--	--
N2 x P3a	0.33 (.26)	0.33	--	--	0.31 (.21)	0.39	--	--
P1 x N2	−0.22 (.18)	−0.39	--	--	−0.37 (.15)	−0.84*	−0.29 (.12)	−0.66*
F (ndf, ddf)	2.0 (8, 17)		2.7+ (5, 20)		1.71 (8, 18)		1.83 (6, 20)	
Adjusted R^2	.25		.25		.18		.16	

Note: ndf = numerator degrees of freedom; ddf = denominator degrees of freedom;

+ $p < .10$,

* $p < .05$,

** $p < .01$,

*** $p < .001$;

b = unstandardized coefficient; se = standard error; β = standardized coefficient