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Reduced Sensory Habituation in Autism and Its Correlation with Behavioral Measures

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Abstract

Autism is strongly associated with sensory processing difficulties. We investigate sensory habituation, given its relevance for understanding important phenotypic traits like hyper- and hypo-sensitivities. We collected electroencephalography data from 22 neuro-typical(NT) and 13 autistic(ASD) children during the presentation of visual and auditory sequences of repeated stimuli. Our data show that the ASD children have significantly reduced habituation relative to the NT children for both auditory and visual stimuli. These results point to impaired habituation as a modality-general phenomenon in ASD. Additionally, the rates of habituation are correlated with several clinical scores associated with competence along diverse phenotypic dimensions. These data suggest that the sensory difficulties in autism are likely to be associated with reduced habituation and are related to clinical symptomology.

Keywords Sensory habituation · Autism · Hyper and hypo-sensitivity · Audition · Vision · Electroencephalography

Introduction

Autism is a neurodevelopmental disorder characterized by impaired social communication skills and repetitive behaviors (American Psychiatric Association 2013), estimated to affect over 1% of all children (Christensen et al. 2016). A key correlate of autism is unusual sensory perception. Observations of sensory differences date to the original reports by Kanner (1943). Over 90% of individuals with autism report sensory difficulties in several modalities (Leekam et al. 2007; Marco et al. 2011). The strong association with ASD of hyper- and hypo-sensitivity to sensory stimuli has led to the DSM-5 (American Psychiatric Association 2013) now including them as diagnostic features of ASD.

Despite the prevalence of sensory issues in autism, a mechanistic understanding of their causal basis has been elusive. One possibility is that autism affects basic sensory sensitivities, leading to a perceived enhancement or diminishment of normal intensity stimuli (Heaton et al. 1998; Gomot et al. 2002; Bonnel et al. 2003; Ferri et al. 2003; Khalfa et al. 2004; Ashwin et al. 2009). However, this account has been questioned by several follow-up studies that failed to find significant sensory acuity differences between NT and ASD participant groups in visual, auditory and somatosensory domains (Bölte et al. 2012; DePape et al. 2012; Marco et al. 2011; Dabbous 2012; Cascio et al. 2008; O'Riordan and Passetti 2006).

A more recent alternative account suggests that abnormal sensitivities may arise not because of instantaneous differences in sensory thresholds, but rather because of how stimuli are processed over time. Specifically, it is hypothesized that autism may be associated with a reduction in sensory habituation. On the one hand, this reduction may contribute to an inability to detect novel stimuli in the presence of ongoing ones, leading to a hypo-sensitivity to changes in the sensory environment (Guiraud et al. 2011), while on the other hand, the compromised ability to habituate would reduce stimulus suppression and may lead to hyper-sensitivity due to immersion in unrelentingly salient stimuli (Sinha et al. 2014).

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Habituation is broadly defined as response decrement due to stimulus repetition (Montagu and Coles 1966; Rankin et al. 2009). With behavioral assays, there is evidence to suggest that children with ASD do not show progressive dampening of response to repeated standard tones or clicks (Guiraud et al. 2011; Martineau et al. 1992). Perry et al. found that ASD participants required more trials to reach maximal habituation and suggested that ASD participants have a generalized slowing of habituation to repeated stimuli (Perry et al. 2007). In adults, Lawson et al. presented a 30 dB, 1 KHz continuous tone for 190 s to the right ear and collected periodic subjective ratings of loudness (Lawson et al. 2015). ASD loudness ratings were significantly higher than NTs as the stimulus progressed, consistent with reduced habituation. Barry and James (1988) found that the autistic group differed from the control groups in its failure to show response habituation to simple visual and auditory stimuli. Additionally, slower behavioral habituation to faces has been shown to be positively correlated with higher symptom severity in ASD (Webb et al. 2010).

Reports of behavioral evidence showing reduced habituation in autism, mentioned above, can be strengthened by neural assays that potentially sidestep response subjectivity. Neural habituation would entail reduction in cortical responses over time with successive repetition of a stimulus (Plichta et al. 2014; Thompson and Spencer 1966). Although data on neural habituation in ASD are still fairly sparse, the findings thus far suggest that this is a potentially promising avenue of inquiry. An fMRI study showed reduced neural habituation to repeated exposures to faces in ASD wherein individuals with highest symptom severity demonstrated the least amount of neural habituation to repetition (Kleinhans et al. 2009). In a two-back working memory task flanked by faces with different emotions as task-irrelevant distractors, Tam et al. reported a lack of amygdala habituation in adults with ASD (Tam et al. 2017). In a study of 8-month-olds at low and high likelihood of developing autism (based on older sibling diagnosis) the high-likelihood infants later diagnosed with autism (n = 14) showed reduced repetition suppression when compared to the high-likelihood infants with typical development (n = 44) (Kolesnik et al. 2019). A longitudinal social intervention study showed greater reduction in habituation times in responses to faces and a more typical P400 response to faces and objects in the high-likelihood group of infants whose parents accessed and delivered the promoting-first-relationships (PFR) parent-led intervention than the high-likelihood infants whose parents did not receive training in the intervention, suggesting that the intervention affected neural responses related to habituation (Jones et al. 2017). A recent study of children and young adults showed that those on the autism spectrum displayed atypical responses on multiple auditory paradigms, including less reduction in P3a response to novel sounds over time

and slower N1 attenuation in response to oddball stimuli (Hudac et al. 2018).

Notwithstanding the aforementioned evidence, the relationship between autism features and reduced habituation is not yet firmly established. Several studies have not found differences in habituation rates between ASD and NT participants. For instance, work by Miller et al. (2001), showed a lack of evidence for reduced habituation in autism with an electrodermal activity (EDA) assay. They suggest that differences in habituation could be dependent on factors such as stimulus intensity and modality that are specific to the study. An earlier study by Bernal and Miller (1970) showed hypo-responsiveness in the ASD group as indicated by reduced responses to the initial three visual stimuli in the ASD group, but no other differences in sensory reactivity.

Given these mixed findings regarding sensory habituation in autism, we believe that this domain merits further investigation, ideally employing objective electrophysiological measures and careful control for factors of cognitive ability and stimulus delivery. With this motivation, the current study has three goals. First, we investigate whether neural habituation is reduced in ASD even with simple sensory stimuli that do not have any social connotations. Second, we examine whether changes in habituation are specific to a sensory modality or apply across modalities, suggesting a more general underlying mechanism. Third, to understand the practical implications of any observed habituation reduction, we explore the relationship between neural habituation and clinical characteristics of ASD, as measured by clinical assessments of sensory, cognitive and behavioral performance.

Materials and Methods

Subjects and Stimuli

Twenty-two neurotypical subjects (9 females) ranging from 7.1 to 12.8 years and 13 ASD (2 females) ranging from 7.4 to 12.8 years participated in the experiments. All participants were administered the Weschler Intelligence Scales for Children—Fifth Edition (WISC-V) and scored 85 or greater in the nonverbal index. The average nonverbal index score for the ASD group was 104.42 (with a range of 90–126) compared with the NT average of 116.90 (with a range of 100–135). All ASD participants met criteria for autism or autism spectrum disorder based on administration of the Autism Diagnostic Observation Schedule-2 (ADOS-2), Module 3.

Two 6-min passive observation experiments (one auditory and one visual) were conducted with concurrent EEG recordings for all participants. In each experiment, participants were presented with 300 trials of either auditory

or visual repetitive stimuli. Each auditory stimulus in the sequence was a beep of 250 Hz frequency, 116 ms duration, and 73 dB volume, presented repeatedly with an inter-stimulus interval of 1 s. The visual stimulus was a radial checkerboard on a gray background with 116 ms duration and 1 s inter-stimulus interval. Order of presentation for the auditory and visual experiments was counterbalanced across participants.

This study was approved by Massachusetts Institute of Technology (MIT) Committee on Use of Humans as Experimental Subjects (COUHES) in accordance with all institutional review board requirements. The experimental protocol was explained in detail prior to the start of the study, children and their legal guardians were notified that participation was voluntary, written consent was obtained from the legal guardians, and assent from each participant.

Behavioral Measures

We administered the WISC-V (Wechsler 2014) and the ADOS-2 (Lord et al. 2012) as well as several caregiver-report questionnaires, including the Short Sensory Profile Second Edition (SSP-2) (Dunn 2014), the Child Behavior Checklist (CBCL) Total Syndrome and Total Competence Scores (Achenbach and Rescorla 2004), the Social Communication Questionnaire (SCQ) (Rutter et al. 2003), Current and Lifetime. All assessments and questionnaires were administered for all participants, except the ADOS-2, which was only administered to those children in the study with a previous autism diagnosis, in order to determine eligibility for inclusion in the study. The scores for these standardized measurements are calculated according the scoring manual for each questionnaire. We collected data for all study participants for the CBCL, SSP-2, and SCQ. Please see Table 1 for group averages for each measure.

The SSP-2 is a caregiver report questionnaire that measures children's sensory processing patterns in everyday activities. Higher scores indicate increased frequency of

atypical sensory behavior relative to peers. The CBCL, a component of the Achenbach System of Empirically Based Assessment (ASEBA), is a caregiver-report questionnaire that measures behavioral and emotional problems in children and adolescents ages 6–18 years. The CBCL provides two composite scaled scores, The Total Syndrome and Total Competence Scores, which are norm-referenced and derived from subtests in the Syndrome Scales and the Competence Scales. The Syndrome Scale composite score is comprised of 8 sub scales: anxious/depressed, withdrawn/depressed, somatic complaints, social problems, thought problems, attention problems, rule-breaking behavior, and aggressive behavior, as well as six DSM-oriented scales consistent with DSM-5 categories. Higher scores on the Total Syndrome scaled score indicates greater degree of these features. The Total Competence scaled score, on the other hand, measures activities, social relations, and school performance. Higher scores on the Total Competence scaled score indicates greater frequency of engaging in these categories of activities. The SCQ is a caregiver-report questionnaire that measures communication skills and social functioning in children ages 4 and older, with a mental age of 2 years or greater. In the SCQ-Lifetime, the parent is asked to report whether the behaviors were ever present during the child's life. In the SCQ-Current, the parent is asked to report whether the behaviors were present at any point in the past 3 months. Higher scores indicate more ASD symptomology. We used the above measures from the SCQ, SSP and CBCL to examine associations between habituation measures and autistic symptomatology, sensory profiles and, in aggregate, the syndromic traits linked to autism, respectively.

EEG Recordings and Analysis

We recorded 32 channel electroencephalography (EEG) signals with the BioSemi ActiveTwoTM electrode system, at a 512 Hz sampling rate. The electrodes were mounted in an elastic cap using a subset of the International 10/20 System

Table 1 Group mean and, in parentheses, standard deviations for each of the characterization measures outlined in the correlational analyses

Measure	NT mean (SD)	ASD mean (SD)
WISC-V nonverbal index	116.90 (9.73)	104.42 (12.59)
SSP-2 seeking/seeker quadrant (raw score/35)	9.00 (3.22)	18.25 (6.84)
SSP-2 avoiding/avoider quadrant (raw score/45)	12.10 (4.04)	25.42 (7.95)
SSP-2 sensitivity/sensor quadrant (raw score/50)	13.19 (3.63)	33.08 (10.38)
SSP-2 registration/bystander quadrant (raw score/40)	8.24 (2.21)	24.25 (9.18)
SSP-2 sensory section raw (raw score/70)	18.00 (5.63)	39.83 (13.64)
SSP-2 behavior section (raw score/100)	24.29 (7.33)	59.25 (18.31)
CBCL total competence t-score	55.95 (5.07)	39.50 (9.99)
CBCL total syndrome t-score	41.57 (8.29)	61.42 (11.80)
SCQ Current	3.05 (2.01)	14.00 (8.34)
SCQ lifetime	2.76 (3.00)	23.00 (10.03)

sites as depicted in Fig. 1. We checked that the BioSemi electrode offsets were < 20 mV to ensure quality of the electrode contact, as recommended by BioSemi's user manual. To detect blinks and lateral eye movements for later correction, electro-oculogram (EOG) electrodes were placed at the infraorbital ridge of the left eye and the lateral canthus of the right eye. The data were visually inspected prior to and throughout the recording to ensure quality of the EEG signal. Out of the 22 NT participants we collected data from, one child did not complete the auditory experiment so the data was excluded from the analysis. We excluded 1 ASD and 1 NT participant from visual experiment analysis, as they were unable to complete the full experiment. Participants who were unable to complete the full length of the stimulus protocol were excluded from the analysis since their EEG data did not have adequate trials to complete the analysis and thus compare habituation profiles with other participants. All offline EEG analyses and preprocessing were done using the Signal Processing Toolbox of Matlab. The left and right mastoids were used for offline re-referencing of the EEG signals to the average of the mastoid signals. The EEG data were low- and high-pass filtered to (0.5–45 Hz). Independent component analysis was used to identify and remove ocular artifacts. Trials with muscle artifacts were also rejected prior to averaging. Overall, 23.9% (mean 71.7, standard deviation 11.3) and 25.3% (mean 75.9, standard deviation 9.8) trials were rejected from the NT and ASD group respectively due to artifacts. There were no significant differences (p < 0.05) in the number of trials rejected between the ASD and NT group.
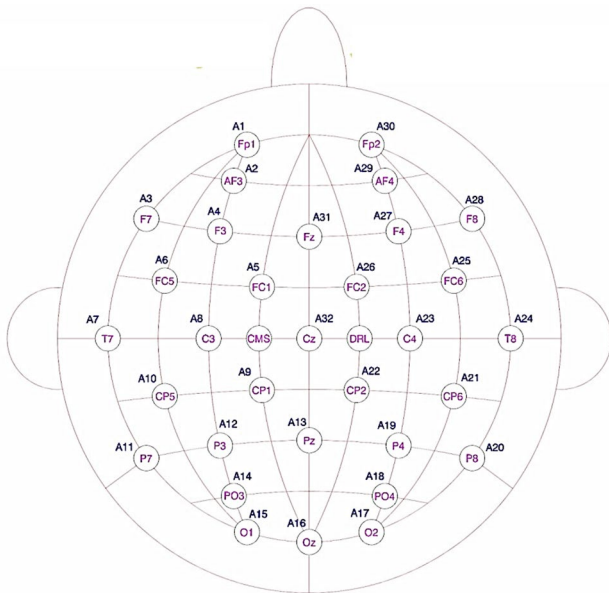
The temporal ERP changes across standard repetition of stimuli were used to operationalize habituation. The EEG recording was epoched between 100 ms pre-stimulus and 900 ms post stimulus and baseline normalized. We calculated ERPs over all 32 channels for each subject in 50 trial segments using a sliding window over all trials. This method provides a measure of ERP over trials as the experiment progresses which can be later modelled to characterize habituation. For EEG signals $x(t, k)$ for time t, trial k where N=total number of trials and w_l=window length 50, we calculated the ERP.

$$\bar{x}(t, w) = \frac{1}{z(w)} \sum_{k=1}^{N} x(t, k).I(k, w)$$

$$z(w) = \sum_{k=1}^{N} I(k, w)$$

$$I(k, w) = 1, \quad if \ w + w_l > k \geq w \quad \forall(w, k)$$
$$0, \quad otherwise$$
$$1 \leq k \leq N$$
$$1 \leq w \leq N - w_l$$

We detected the amplitude of the most prominent peak $p(w)$, of the ERP $\bar{x}(t, w)$ over successive w and approximated the line of best fit on $p(w)$ using the least square method. Slopes (m) of the best fit line for each subject were used to determine the overall change in stimulus-induced activation. This approach quantifies the degree of habituation independent of the initial reaction differences across subjects.

The mean of the standardized auditory and visual habituation measures (slope, m) was used to generate a composite sensory response score (CSR) for the participants. The independent samples t-test was used to compare group differences in the slopes (m) which serve as measures of auditory, visual and CSR habituation.

Brain-Behavior Correlations

Pearson's r correlations were calculated to test for associations between a composite sensory response profile (derived from the average of the ERP slopes for the auditory and visual stimuli) and the behavioral scores on the CBCL competence and syndromic normalized score, the SSP-2 subscores and the SCQ. There were a total of 10 correlations.

Fig. 1 Electrode recording montage

Results

Auditory and Visual Event Related Potentials

Evoked responses for the auditory and visual experiments were computed separately by averaging the electroencephalography (EEG) signals across 50 trial segments using a sliding window approach described in the methods section. The gradual changes in the amplitudes of the positive component of ERPs in response to repetitive tones/visual stimuli during passive listening/watching were used to test for differences in rates of habituation. Figure 2 shows the first and the last auditory and visual ERPs averaged across a window of 50 trials for sample NT and ASD subjects. As expected, the NT participants exhibited marked habituation over the course of the experiment. The positive (P1)

event-related component elicited by the impulses in the initial section of both the auditory and visual stimulus sequence were stronger than those evoked by the later ones. By contrast, the amplitude of evoked responses in ASD participants did not show reduction between the first and the last ERP. In fact, in some cases, as shown in Fig. 2, ASD participants exhibited an *increased* positive component towards the end of the experiments.

The individual subject slopes m, of the best fit line of the ERP amplitude were used to examine group differences in habituation. Figure 3a (left panel) shows sample ERP peaks and the best-fit line from one NT and one ASD participant in response to auditory tones at channel Fp1. The NT participant shows gradual reduction in ERP amplitude over time (negative slope), while the ASD participant shows an increase (positive slope). In order to determine the most pertinent effect of auditory habituation, we conducted
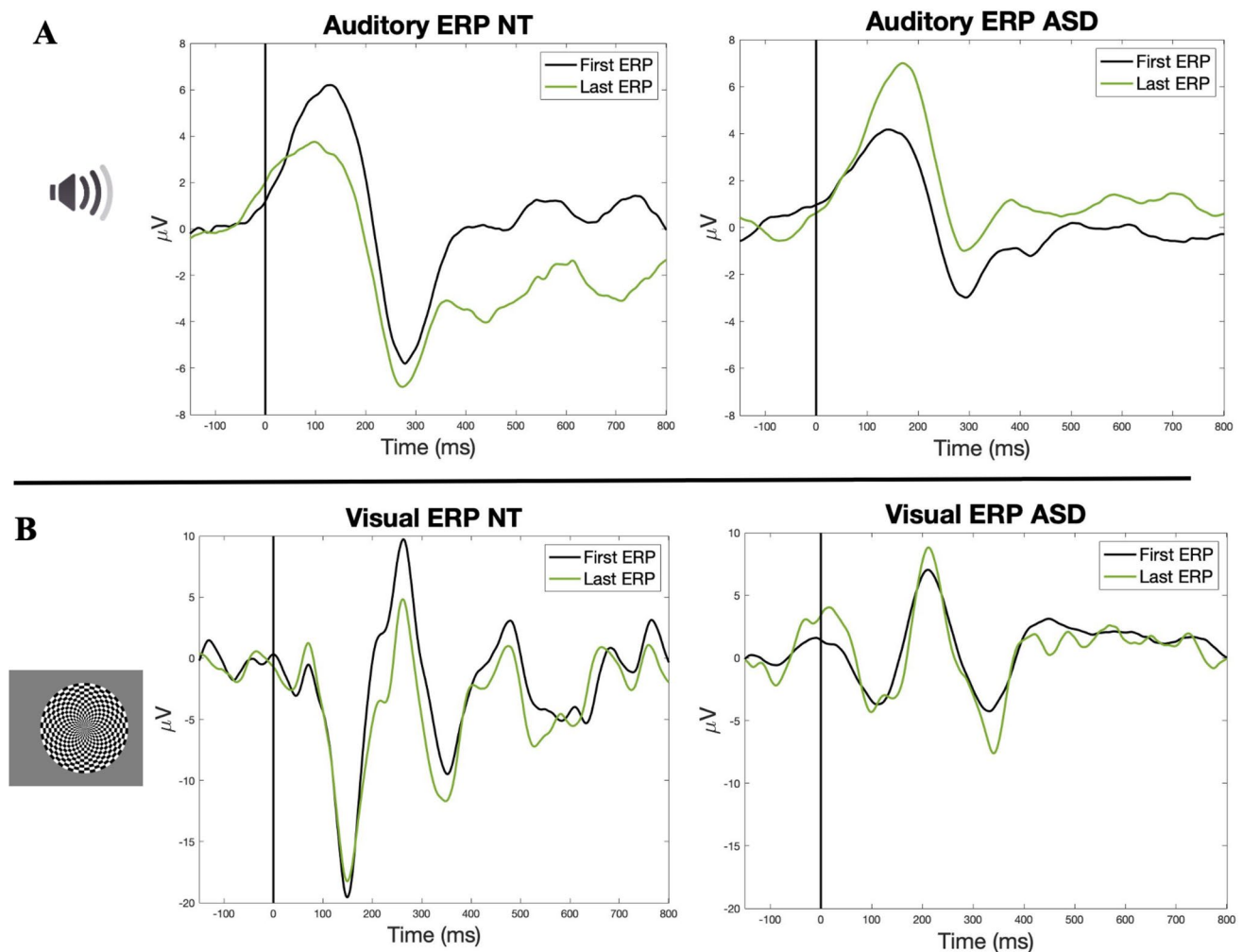

Fig. 2 First and last ERP for the Auditory and Visual experiment for sample NT and ASD participants. **a** ERPs for auditory stimuli at Fp1. **b** ERPs for visual stimuli at C3. In each condition, the black curves show ERP computed for the first 50 repetitions, while the green curves correspond to the last 50 repetitions in a 300 event sequence
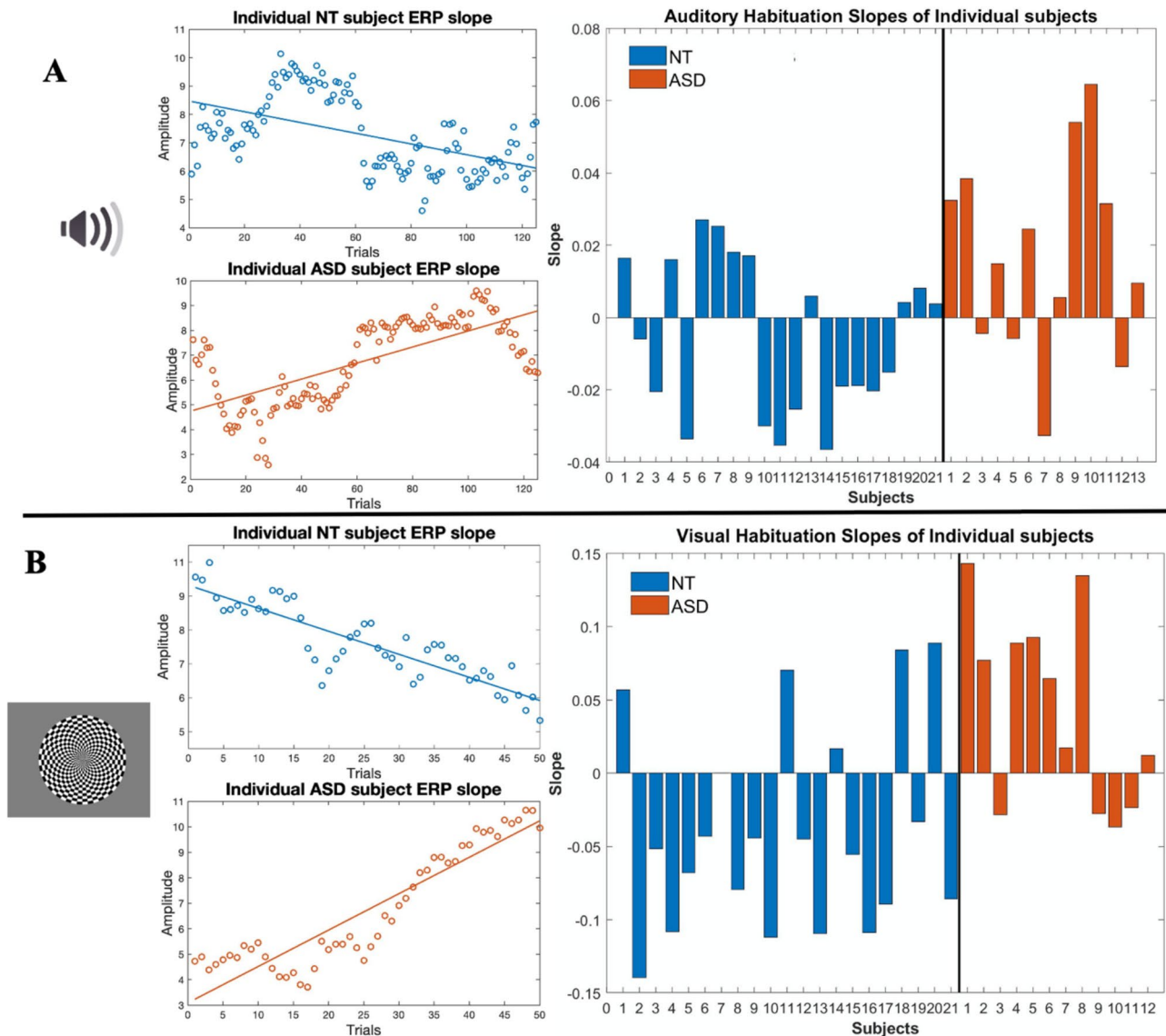
Fig. 3 Left panels: ERP plots for the Auditory **a** response at Fp1 and Visual **b** response at C3 for one NT and one ASD participant. Right panels: Habituation slopes of all ASD and NT participants, the latter exhibiting pronounced habituation in both auditory (Fp1) and visual (C3) experiments, in contrast to those with ASD

significance tests on the individual subject slopes across all electrodes. The bar plot on the right shows the habituation slopes of all ASD (n = 13) and NT (n = 21) participants at Fp1, with the latter exhibiting pronounced habituation, in contrast to those with ASD ($t(32) = -2.67$, p = 0.012, 95% CI [$-0.040, -0.005$]). When compared across all electrode sites, this phenomenon has the greatest difference at channel Fp1 and in the frontal and fronto-central electrodes for auditory stimuli. This is consistent with previous research, which investigated the topography of ERP changes with standard repetition where ERP related repetition effects were only observed over the fronto-central scalp (Haenschel et al. 2005).

For the visual domain, we employed the direct analogue of the auditory analysis described above. We observed that habituation in the visual ERP signals emerged similarly to the results from our auditory paradigm. Figure 3b shows the evoked potential response and slope analysis for the visual experiment at channel C3 (NT, n = 21; ASD, n = 12). We find significant differences ($t(31) = -3.41$, p = 0.002, 95% CI [$-0.13, -0.033$]) in visual habituation profiles between our ASD and NT groups for the visual experiment. ASDs show reduced habituation as indicated by positive or less negative slopes compared to NTs. The greatest difference between habituation in the two groups occur in the central and centro-parietal electrodes in keeping with previous work

in the domain of Brain Computer Interface (BCI) showing robust visual responses over the central region of the scalp (Bleichner et al. 2015). Research in visual habituation in infants indicates information about the stimulus acquired for habituation is processed centrally (Kavšek and Bornstein 2010). Furthermore, early work showed decreased contingent negative variation (CNV) in these regions over the time course of the experiment, due to the effects of habituation (McAdam 1966).

To validate our results further, we ran the significance tests for both auditory and visual habituation using the bootstrapping method with matched participant numbers in each group. Over 5 bootstrap iterations, all cases returned significant results ($p < 0.05$) where the average $p = 0.020$ (s.d 0.0066) for auditory habitation at Fp1and the average $p = 0.012$ (s.d 0.0010) at C3 for visual habituation.

As described in the methods, we computed the individual "composite sensory response" (CSR) score of each participant by averaging their auditory response slope at electrode Fp1 and visual response slope at C3. Figure 4 shows the significant group differences in the CSR scores with $t(30) = -4.10$, $p < 0.001$ 95% CI [-0.080, -0.027]. Since CSR is a slope-derived measure, high CSR scores correspond to lower habituation rates.

Relationships Between CSR Scores and Clinical/Behavioral Measures

The individual CSR scores were used to determine the correlations between the habituation profiles and each of multiple behavioral measures. The WISC nonverbal IQ group difference between ASD and NT had a p value of less than 0.05. Further analysis of correlation between the CSR scores and the WISC nonverbal IQ show the results are not significant. ($p = 0.30$, $r(30) = -0.19$) hence there is no relationship between habituation and IQ. Table 1 shows the means and standard deviations of each measure for each group.

Habituation Rate Versus Autism Symptoms

Correlations between CSR scores and the SCQ current and lifetime scores obtained at the time of the experiment were calculated for the participants. We found that, across all subjects, higher SCQ scores were associated with higher CSR scores (i.e. lower rates of habituation) indicated by $p < 0.001$ (Fig. 5).

Habituation Versus Behavioral Measures

In order to examine the relationships between altered ERP-derived habituation scores and measures of psychological well-being, we calculated correlations between the CSR scores and the CBCL, SSP-2, and SCQ Current and Lifetime scores across all participants. The SSP-2 is used to characterize the severity of sensory processing differences in autism or with other developmental conditions as well as to characterize sensory preferences in children who are typically developing (Tomchek and Dunn 2007).

Child Behavior Checklist (CBCL) CBCL syndromic score represents parent ratings of the child's behavior linked to diagnostic categories from the DSM such as anxiety, depression, and attention problems, wherein a higher score represents a higher presence of these symptoms. There were signifi-

Fig. 4 Composite sensory response scores from NT (n = 20) and ASD (n = 12). These scores merge slope results from auditory and visual habituation studies to derive a composite measure of habituation response. ASD participants generally have higher scores relative to NT participants, indicating reduced habituation in the former group
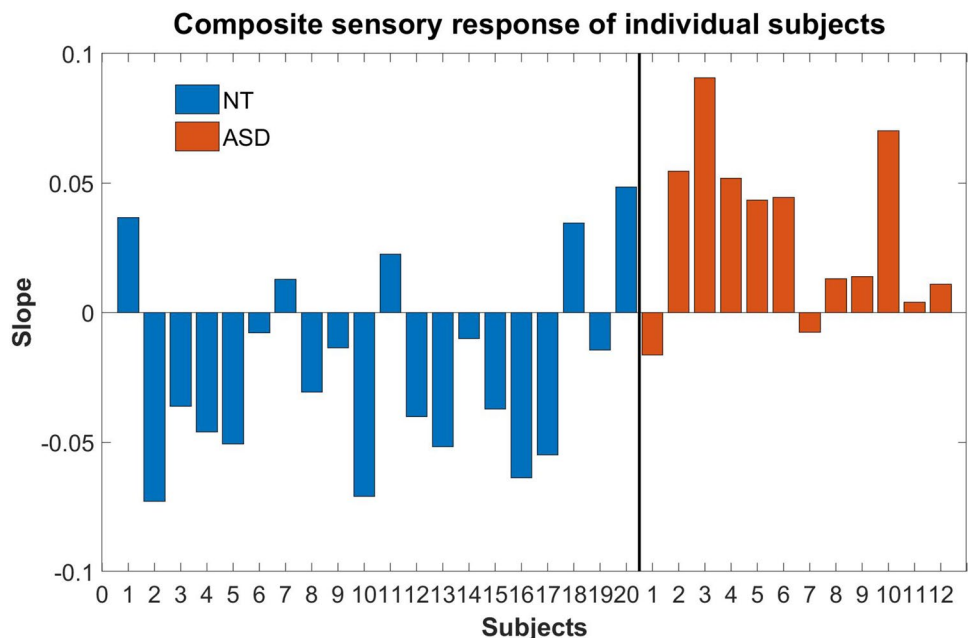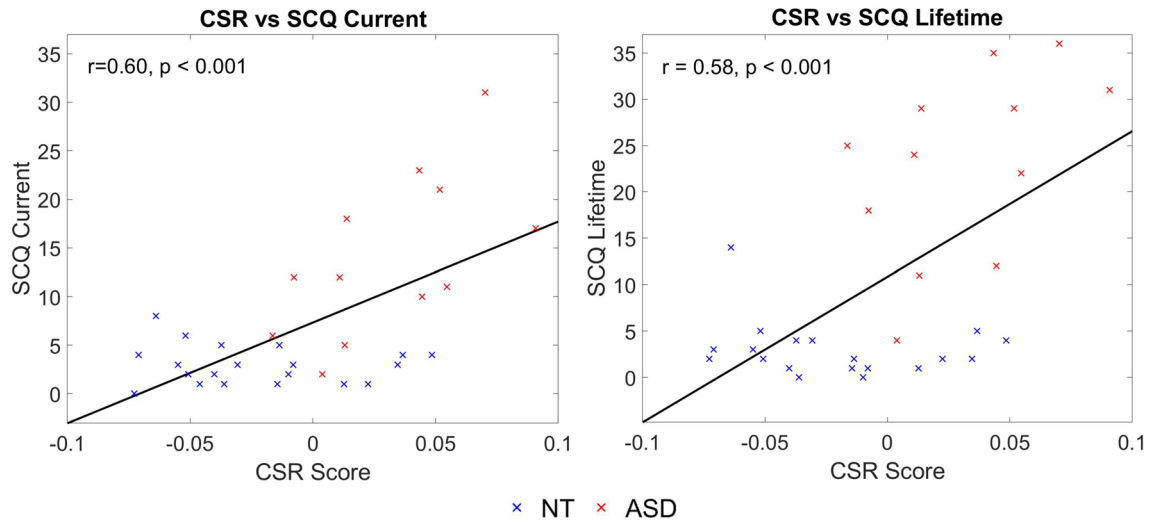
Fig. 5 Relationship between Composite Sensory Response (CSR) scores and ASD symptoms. There is a significant correlation between the extent of reduction in habituation and the current (Pearson's r = 0.60, p < 0.001) and lifetime (Pearson's r = 0.58, p < 0.001) Social and Communication Questionnaire (SCQ) scores in the ASD group
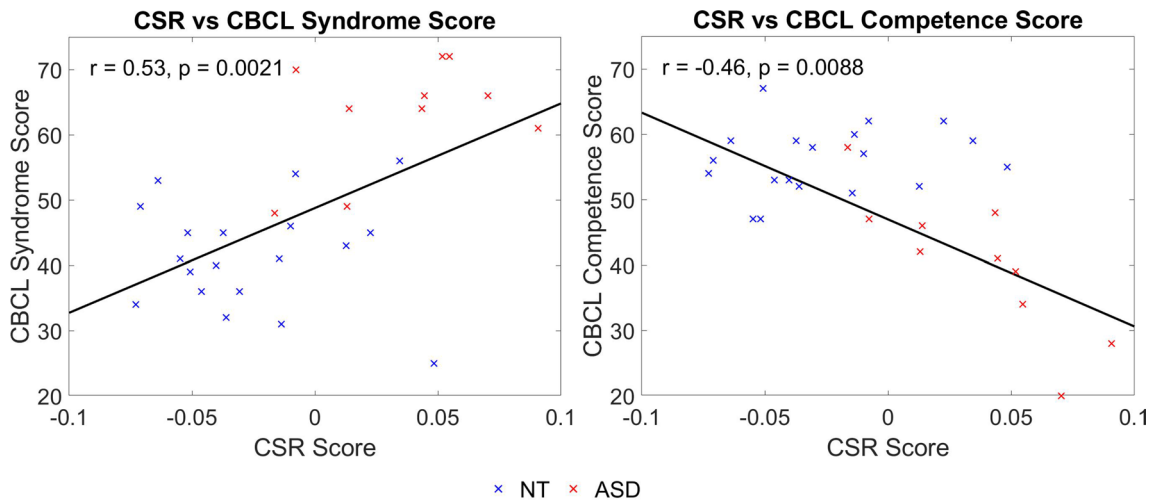

Fig. 6 Relationship between CSR scores and behavioral characteristics. Sensory response is positively correlated with CBCL Syndrome score across all subjects. The CBCL Competence score has a negative relationship with participants' CSR scores

cant correlations between CSR scores and CBCL syndrome scores derived from parent questionnaires at the time of the experiment (Pearson's r (30)=0.53; p=0.002). In contrast there was a negative correlation between CSR scores in all children and the CBCL total competence score as shown in Fig. 6 (Pearson's r (30)=− 0.46; p=0.009). Total competence score represents parent ratings of the child's performance in academic activities, social, and school behavior, wherein a higher score represents a higher degree of competence in these domains.

Short Sensory Profile (SSP-2) Correlations were also used to determine whether there were relationships between

CSR scores derived from composite EEG habituation slope and sensory profiles as measured by the SSP-2 sub-scores. Figure 7 shows strong positive relationships between CSR scores and all SSP-2 sub-scores with p < 0.05 in Pearson's r correlation test. The sensitivity sensor quadrant, registration bystander quadrant, sensory section raw score and behavior section raw score correlations with CSR had p values < 0.001 and r values of 0.64, 0.60, 0.58 and 0.61 respectively. The seeking quadrant (r (30)=0.45, p=0.010) and avoider quadrant (r (30)=0.55, p=0.0012) also showed significant correlation.
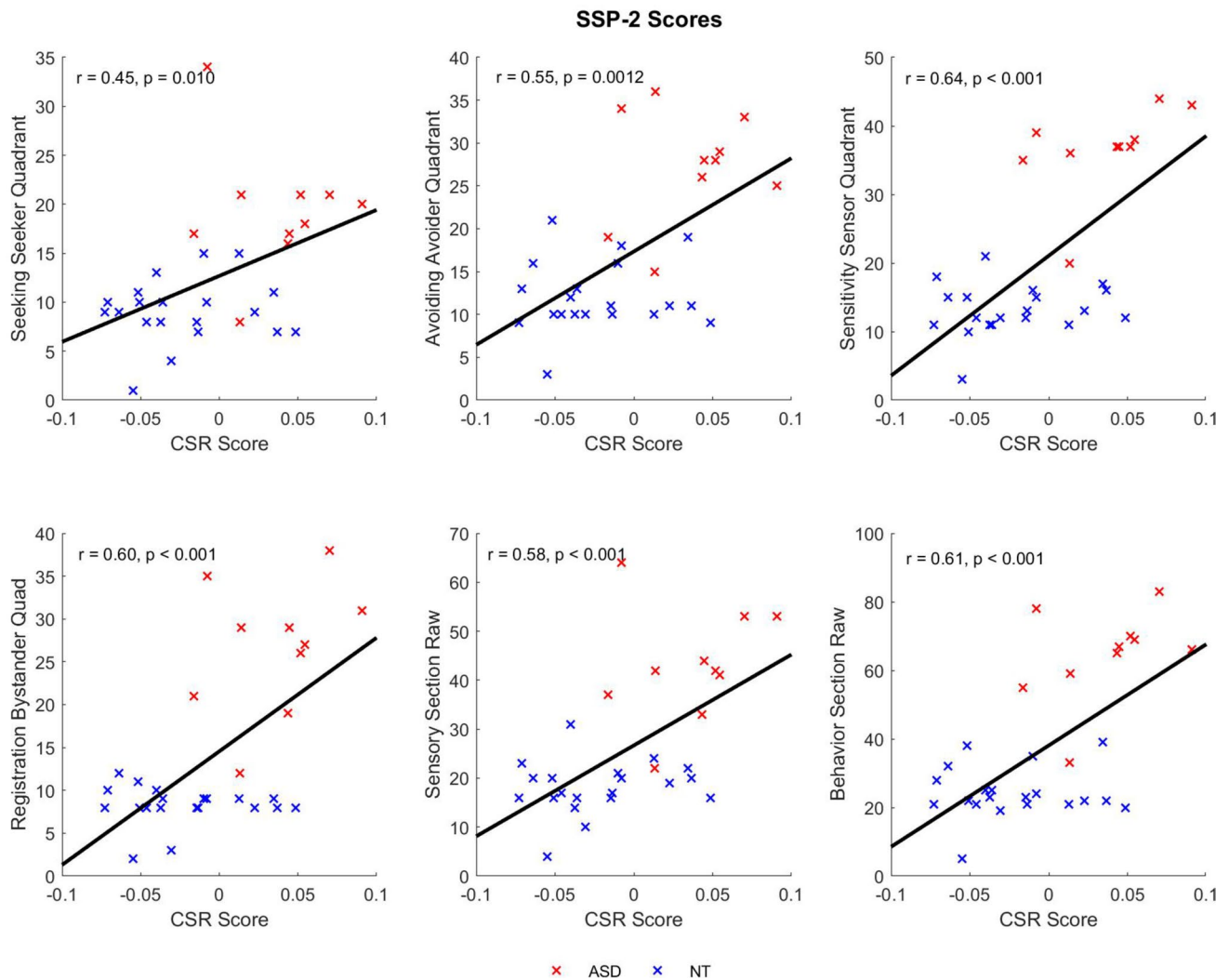
SSP-2 Scores

Fig. 7 Relationship between CSR scores and sensory profile scores. The rate of habituation is strongly correlated with the sensory scores of the SSP across all subjects

Discussion

Data from our experiments have allowed us to address the three goals we stated at the outset: (1) To examine whether with non-social, repeating stimuli there are differences in the neural habituation profiles of ASD and NT children, (2) To determine whether differences in habituation apply across sensory modalities, and (3) To determine whether neural habituation profiles correlate with clinical measures used to characterize phenotypic features of autism. On all of these fronts, our empirical data indicate affirmative answers. To briefly recapitulate, in neurotypical participants, EEG responses to a metronomic sequence of tones and repeated visual stimuli showed expected patterns of habituation, or attenuated neural response over time. By contrast, participants with ASD exhibited significantly reduced habituation. Unlike NTs, the ASD group did not show a decrement in

the P1 positive polarity wave in their ERPs, supporting the inference that these individuals have reduced habituation to repeated stimuli.

The finding of reduced habituation in both the auditory and visual sensory modalities suggests that the phenomenon may be domain general in ASD. This has important implications for the nature of causal mechanisms underlying the observed differences in habituation. It seems plausible, though not certain [for a discussion of sensory subtypes, see work by Lane et al. (2014)], that reductions in habituation may arise from central mechanisms that affect sensory processing across modalities, rather than from modality specific peripheral factors.

Finally, our results show significant correlations between the degree of habituation and parent reports of participants' social communication difficulties, as measured by the SCQ, a tool used to screen for ASD. The extent of neural

habituation also correlated with parents' impressions of the severity of sensory differences, as measured by the SSP-2. The CBCL competence (negatively) and syndrome scales (positively) correlate with the composite sensory response (CSR) scores, indicating that psychological symptomatology and habituation appear to be related as well. Recently, it has been hypothesized that differences in predictive abilities in autism are related to the compendium of features of autism (Sinha et al. 2014). Habituation to a repetitive, invariant stimulus represents a most basic form of prediction. If, as we hypothesize, predictive abilities are dampened for autistic individuals, the ability to ignore irrelevant sensory stimuli would lead to an overwhelming sensory experience. The findings here suggest that reduced habituation, a form of prediction, is associated with autistic symptomology, as measured by the SCQ, SSP-2 and general psychological well-being, as measured by the CBCL.

These relationships between neural habituation and social communication, sensory difficulties and psychological symptomatology imply that that the degree of habituation impairment may be useful as one of several factors informing neuropsychological interventions that may benefit the individual. In neuropsychology, much reliance is now necessarily placed on parental reports to identify and diagnose, which are often problematic with regards to reliability (Mazefsky et al. 2011). The relative ease of collecting sensory response data using a protocol of the kind we have described here makes this assay a potential candidate for inclusion in the early detection battery for ASD. Of course, doing so pre-supposes that the habituation differences we have observed with our cohort of participants will be evident even much earlier in the developmental timeline, prior to the age of formal diagnosis. Despite a number of previous research studies investigating habituation in autism, the field currently largely lacks empirical data regarding how habituation profiles change with age and whether children at elevated likelihood of ASD are systematically different in their profiles relative to those at typical likelihood. This is one of the avenues of research we are pursuing by recording sensory responses to repeating stimuli from infants at low and elevated likelihood of ASD.

It is worth pointing out that the reductions in habituation in ASD we have reported here are consistent with, and may be partially accounted for, by a theory for autism we have recently proposed (Sinha et al. 2014). According to the theory, autism is accompanied by an impairment in temporal prediction. Given that stimulus predictability is a key modulating factor for the extent to which the stimulus elicits habituation (Rankin et al. 2009), an endogenous reduction in predictive abilities would be expected to lead to a corresponding reduction in habituation. The theory has relevance beyond understanding sensory responses; it may also account for autism symptoms manifested in the domains of language, social interactions and motor control. Given its broad relevance, it is important to test the theory's predictions empirically in well-defined domains, as is the case in the present study. However, it needs to be noted that the data we have found so far, while consistent with the theory, need to be strengthened further to more rigorously test the theory. For instance, it will be important to examine how exogenous changes in stimulus predictability (say, by making the sequence more stochastic rather than purely deterministic) affect habituation rates in neurotypical participants. Furthermore, we have not considered potential contributions from attentional or memory consolidation processes that have previously been reported to be able to modulate habituation (Lagemann et al. 2010; Sörqvist et al. 2012), although with more complex stimuli and over longer time-scales than those used in the present study. These factors are especially important for further exploration given the known atypicalities in memory and attention in autism (Ames and Fletcher-Watson 2010; Williams et al. 2006).

While acknowledging the aforementioned limitations of the present study, some arising from constraints on numbers of subjects and circumscribed stimulus conditions, we are encouraged by the systematicity of the data observed. The basic finding of a reduction in habituation accompanying autism is potentially an important explanatory factor for understanding the commonly observed sensory abnormalities in the condition. While on the one hand, reduction in habituation can lead to a sense of immersion in unrelentingly salient stimuli and hence, an aversive response (a 'hypersensitivity'), on the other hand, it might result in abnormally sustained deployment of attention to specific stimuli. For neurotypical individuals, stimuli that initially have positive valence (a pleasing jingle, an interesting video clip) eventually 'lose their charm' as a person habituates to them. However, a reduction in habituation would be expected to lead to a stimulus maintaining its appeal for extended periods of time, and the individual would be seen as having an obsessive interest in the item. Additionally, the focus of attention on one stimulus might render it hard to disengage and attend to another, leading to seeming 'hypo-sensitivity' to the latter. In this way, atypicalities in habituation can be important for understanding multiple, sometimes contradictory, aspects of an individual's response to his/her sensory environment.

In summary, with the broad objective of examining sensory processing in ASD and NT participants, our study specifically highlights differences in habituation across the two groups, and the possible role of reduced habituation to simple sensory stimuli as a potential underlying mechanism for understanding sensory sensitivities in autism. Our data also demonstrate relationships between neural habituation and sensory, cognitive and behavioral traits. We have shown that neural habituation is domain-general, at least across two sensory modalities, and is behaviorally-relevant in autism.

Compliance with Ethical Standards

Conflict of interest The authors declare that they have no conflict of interest.

Consent to Participate Written consent was obtained from the legal guardians, and assent from each participant.

Ethical Approval This study was approved by Massachusetts Institute of Technology (MIT) Committee on Use of Humans as Experimental Subjects (COUHES) in accordance with all institutional review board requirements.

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