RESEARCH ARTICLE

Atypical Perception of Sounds in Minimally and Low Verbal Children and Adolescents With Autism as Revealed by Behavioral and Neural Measures

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The common display of atypical behavioral responses to sounds by individuals with autism (ASD) suggests that they process sounds differently. Within ASD, individuals who are minimally or low verbal (ASD-MLV) are suspected to have greater auditory processing impairments. However, it is unknown whether atypical auditory behaviors are related to receptive language and/or neural processing of sounds in ASD-MLV. In Experiment 1, we compared the percentage of time 47 ASD-MLV and 36 verbally fluent (ASD-V) participants, aged 5–21, displayed atypical auditory or visual sensory behaviors during the administration of the Autism Diagnostic Observation Schedule (ADOS). In Experiment 2, we tested whether atypical auditory behaviors were more frequent in ASD-MLV participants with receptive language deficits. In Experiment 3, we tested whether atypical auditory behaviors correlated with neural indices of sensitivity to perceptual sound differences as measured by the amplitude of neural responses to nonspeech intensity deviants. We found that ASD-MLV participants engaged in atypical auditory behaviors more often than ASD-V participants; in contrast, the incidence of atypical visual behaviors did not differ between the groups. Lower receptive language skills in the ASD-MLV group were predicted by greater incidence of atypical auditory behaviors. Exploratory analyses revealed a significant negative correlation between the amount of atypical auditory behaviors and the amplitude of neural response to deviants. Future work is needed to elucidate whether the relationship between atypical auditory behaviors and receptive language impairments in ASD-MLV individuals results from disruptions in the brain mechanisms involved in auditory processing. ***Autism Res*** *2020, 00: 1–12*. © 2020 International Society for Autism Research and Wiley Periodicals LLC.

Lay Summary: Minimally and low verbal children and adolescents with autism (ASD-MLV) displayed more atypical auditory behaviors (e.g., ear covering and humming) than verbally fluent participants with ASD. In ASD-MLV participants, time spent exhibiting such behaviors was associated with receptive vocabulary deficits and weaker neural responses to changes in sound loudness. Findings suggest that individuals with ASD with both severe expressive and receptive language impairments process sounds differently.

Keywords: autism; auditory processing; language; minimally verbal; mismatch; sensory behaviors

Introduction

Atypical reactions to sensory inputs are a core feature of autism (ASD) that emerge early in life [Ben-Sasson et al., 2009; McCormick, Hepburn, Young, & Rogers, 2016; Rogers, Hepburn, & Wehner, 2003]. Sound sensitivity, in particular, is frequently observed [O'Connor, 2012]. Many children with ASD adopt habits such as covering their ears, requesting headphones, or humming in settings that are loud or include multiple speakers [Frith & Baron-Cohen, 1987; O'Neill & Jones, 1997; Pfeiffer et al., 2017]; these actions can be described as "atypical auditory behaviors." Atypical behaviors across sensory modalities have generally been classified based on presumed function, also referred to as "sensory response patterns," such as for seeking or avoiding stimuli [Baranek, David, Poe, Stone, & Watson, 2006]. However, the existence of these behaviors within a particular sensory modality like audition may be more broadly indicative of disruptions to cortical systems responsible for sensory processing within that modality, regardless of the sensory response pattern.

While most research on this topic has focused on verbally fluent individuals with ASD (ASD-V), atypical auditory behaviors might be particularly pronounced in the subgroup of individuals with ASD who have very limited expressive language, referred to as minimally or low verbal (ASD-MLV). Prior reports have distinguished these two groups based on the module they were administered

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during the Autism Diagnostic Observation Schedule (ADOS)—a common semistructured diagnostic assessment of ASD [Bal, Katz, Bishop, & Krasileva, 2016]. Those classified as ASD-V produce multiclause, fluent speech and are administered the ADOS module 3 or 4, while those classified as ASD-MLV produce single word or simple phrase speech and are administered the ADOS module 1 or 2 [Klein-Tasman, Risi, & Lord, 2007]. Parent reports have shown that ASD-MLV individuals exhibit more severe atypical sensory behaviors than ASD-V peers [Patten, Ausderau, Watson, & Baranek, 2013] and exhibit more atypical behaviors associated with auditory stimuli than with stimuli in other modalities, with the possible exception of visual stimuli [Harrop, Tu, Landa, Kasier, & Kasari, 2018].

The classification of ASD-MLV is based on *expressive* language deficits, but it is *receptive* language that depends directly upon auditory processing. Therefore, atypical auditory sensitivity may be more closely associated with receptive language [Groen, Zwiers, van der Gaag, & Buitelaar, 2008; Siegal & Blades, 2003]. While, by definition, ASD-MLV individuals all demonstrate poor expressive language, their receptive language skills can vary [Rapin, Dunn, Allen, Stevens, & Fein, 2009]. An intuitive but underexplored hypothesis is that atypical auditory behaviors are more prevalent and severe in those with poorer receptive language.

Research on children points to a general association between sensory sensitivity to environmental inputs and combined expressive-receptive language skills [Tomchek, Little, & Dunn, 2015; Watson, Patten, Baranek, Poe, & Boyd, 2011]. This association with language has been identified particularly for combined auditory and visual sensitivity (which have often been grouped together in the literature as one sensory response pattern) [Tomchek et al., 2015; Tomchek & Dunn, 2007]. Complicating matters, there is mixed evidence regarding whether atypical sensory behaviors are more pronounced in those with lower nonverbal intellectual quotients (IQ) or mental age [Baranek, Boyd, Poe, David, & Watson, 2007; Bishop, Richler, & Lord, 2006; Leekam, Nieto, Libby, Wing, & Gould, 2007; Sanz-Cervera, Pastor-Cerezuela, Fernández-Andrés, & Tárraga-Mínguez, 2015; Shattuck et al., 2007]. However, these earlier studies have not differentiated intellectual impairments from language status. Given that many ASD-MLV individuals have low nonverbal IQs, research is needed to explain how atypical auditory behaviors vary with expressive and receptive language abilities after accounting for differences in nonverbal intelligence.

Atypical sensory behaviors may be directly related to the atypical perception of acoustic stimulus properties [Donkers et al., 2015]. Acoustic sensitivity itself can be quantified using psychoacoustic measures of perceptual thresholds for detecting sound differences. Prior research on ASD-V individuals found that participants who performed more poorly on a loudness discrimination task also exhibited more atypical auditory behaviors, particularly behaviors categorized as hypersensitive or aversive [Jones et al., 2009]. Similarly, better performance on intensity discrimination tasks has been associated with fewer restricted interests, both sensory and topic-specific [Kargas, López, Reddy, & Morris, 2015]. When direct reporting of one's own perceptions is not feasible, as is the case for ASD-MLV participants, perception of auditory stimulus properties can be quantified with neuroimaging techniques like EEG and MEG through the measurement of the mismatch neural response (MMN). The MMN is an indirect index of sensitivity to perceptual sound differences that can be measured in active as well as passive paradigms [Näätänen, Simpson, & Loveless, 1982]. The MMN is elicited by deviant sounds that are perceptually distinct from expected sounds (or "standards"). Because it can be measured passively, the MMN can be used to assess auditory processing in ASD-MLV participants [Matsuzaki et al., 2019; Schwartz, Shinn-Cunningham, & Tager-Flusberg, 2018; Schwartz, Wang, Shinn-Cunningham, & Tager-Flusberg, 2020]. In general, researchers have considered the delay and decrease in amplitude of response to deviant sounds that are perceptually distinct in neurotypical listeners to be a sign of auditory processing deficits [Bishop, 2007; Näätänen et al., 2012]. In ASD-V individuals, the amplitude of neural response to speech deviants (as measured by MMNs to phonemic changes) has been shown to be negatively correlated with heightened sensitivity and perceived discomfort to auditory inputs as measured by self-report [Ludlow et al., 2014]. For those who cannot self-report, there is evidence to suggest that a relationship between the strength of neural response to deviant sounds and sensory sensitivities may be better captured from directly observed behavior than through parent report [Donkers et al., 2015]. Overall, these studies provide a strong foundation for investigating the relationship between atypical auditory behaviors and neural indices of sound perception in ASD-MLV, which has yet to be explored.

To better understand atypical auditory behaviors in ASD-MLV individuals, we conducted three experiments. In our first experiment, we sought to expand prior work by quantifying the percentage of time that ASD-MLV and ASD-V children and adolescents spent exhibiting atypical auditory behaviors. To test this, we retrospectively coded atypical auditory behaviors from video recordings of the ADOS. Atypical visual behaviors were also measured in an effort to isolate whether any observed findings were auditory-specific or more dependent on domain-general systems of sensory processing. Subsequent experiments focused exclusively on ASD-MLV participants. Our second experiment investigated the extent to which individual differences in receptive language were related to atypical auditory and visual behaviors. Our third experiment measured the relationship between atypical auditory behaviors and sound perception of distinct acoustic features. We initially quantified sound perception using the MMN to nonspeech intensity deviants; after observing that the standards elicited weak and noisy responses in our paradigm, we then conducted an exploratory, post hoc analysis based on the magnitude of the responses elicited by the deviants alone.

Study Procedures

Study procedures across all three experiments were approved by the Institutional Review Board at Boston University. Procedures for Experiment 1 were additionally approved by the Institutional Review Board at the Massachusetts Institute of Technology. Participants completed a battery of cognitive, behavioral, and experimental assessments that took place over the course of one to four lab visits. Standardized assessment administration procedures were modified to ensure that participants understood testing prompts and cooperated with testing (for details, see Tager-Flusberg et al., 2017].

Experiment 1

The objective of our first experiment was to quantify the percentage of time that ASD-MLV and ASD-V children and adolescents spent exhibiting atypical auditory behaviors during the ADOS and, furthermore, to determine the specificity of those behaviors to the auditory domain by comparing them with the time spent exhibiting atypical visual behaviors.

Participants

Participants included 83 children and adolescents with ASD who ranged in age from 5 to 21 years (Table 1). Participants in this study were selected from two larger research programs focused on phenotyping ASD-V and ASD-MLV individuals [Lu et al., 2016; Tager-Flusberg et al., 2017]. All participants met criteria for ASD as defined by the Autism Diagnostic Observation Schedule (ADOS), a semi-structured interactive interview designed to measure autism severity through a series of social prompts [Lord et al., 2012]. Participants who did not use multiclause functional speech or complex sentences, but rather single words and simple phrase speech, were classified as ASD-MLV (N = 47) and were administered the ADOS Module 1 or 2. ASD-MLV participants aged 5 to 12 (n = 24) were assessed with the ADOS-2 [Lord et al., 2012], while participants aged 12 to 21 (n = 23) were assessed with the Adapted ADOS—an ADOS version designed to provide more age-appropriate materials for minimally and low verbal adolescents and adults [Bal et al., 2020]. The remainder of participants used multiclause functional and complex speech and were classified as ASD-V (N = 36). ASD-V participants aged 5 to

Table 1. Demographic Information for Participants in Experiments 1 and 2

	Group	ASD-MLV	ASD-V	Sig. (p)	η^2
Participants	N	47	36		
Age (years)	Mean (SD)	11.56 (4.54)	12.32 (4.40)	0.50	0.78
M:F	Ratio	37:10	7:29	0.84	
Race				0.07	
	Asian	6	0		
	Black/African American	1	0		
	Two or More Races	3	8		
	Native Hawaiian or Other Pacific Islander	1	0		
	White	34	26		
	Prefer not to respond	2	2		
Ethnicity				0.82	
	Hispanic	4	4		
	Non-Hispanic	39	30		
	Prefer not to respond	4	2		
ADOS CSS	Mean (SD)	7.55 (1.28)	7.66 (1.71)	0.75	
ADOS SA CSS	Mean (SD)	7.02 (1.45)	7.17 (2.05)	0.70	
ADOS RRB CSS	Mean (SD)	8.45 (1.41)	7.89 (1.88)	0.13	
Nonverbal IQ	Mean (SD)	69.79 (19.46)	108.25 (21.21)	<0.001	0.48
Verbal IQ	Mean (SD)	38.40 (21.01)	99.06 (24.16)	<0.001	0.65

Note. Nonverbal IQ (NVIQ) was derived from the Leiter-3 (for ASD-MLV) and the WASI-2 or KBIT-2 (for ASD-V). Effect measured by η^2. The significance cutoff was $p < 0.05$. Verbal IQ is provided to better describe the sample and was not used in any analysis. Verbal IQ was derived from either PPVT-4 (receptive language only) or CELF-4 (core language) standard scores. Language scores from five ASD-MLV participants were not able to be calculated because participants did not reach a basal score. ADOS Calibrated Severity Scores (ADOS CSS) are also provided for the sole purpose of describing the sample; these values were computed based on the tables set forth by Hus and colleagues [Hus, Gotham, & Lord, 2014; Hus & Lord, 2014].

12 (n = 18) and 12 to 21 (n = 18) were assessed with the ADOS-2 Module 3 or 4 [Lord et al., 2012].

Nonverbal Intelligence Measures

For ASD-MLV participants, nonverbal intelligence quotients (IQ) were measured with the Leiter International Performance Scale–Third Edition [Leiter-3; Roid, Miller, Pomplun, & Koch, 2013]. This measure is designed to require no expressive language, but testing procedures were modified to also help limit the amount of receptive language that was required to comprehend testing instructions. For ASD-V children, nonverbal IQ was measured with the Matrices subtest from the Kaufman Brief Intelligence Test–Second Edition [KBIT-2; Kaufman, 2004] and, for ASD-V adolescents, was measured with Performance IQ from the Wechsler Abbreviated Scale of Intelligence, Second Edition [WASI-2; Wechsler, 2011].

Atypical Sensory Behavior Measures

Observational measures of atypical auditory and visual behaviors were coded from video recordings of each participant's ADOS assessment. Researchers coded the onset and offset of atypical behaviors based on their assignment to atypical sensory behavior categories (Table 2). Behavior categories were further classified based on sensory domain (auditory or visual) and sensory response patterns ((a) seeking and/or intensifying inputs or (b) manipulating, filtering, and/or avoiding environmental inputs). Definitions for this coding scheme were developed based on commonly described patterns of atypical sensory behaviors in the Sensory Profile [Dunn, 1999], Sensory Experiences Questionnaire [Baranek et al., 2006], the Sensory Processing Scale Assessment [Schoen, Miller, & Sullivan, 2014], and the Repetitive Behaviors Scales—Revised [Lam & Aman, 2007]. Outcome measures were based on the percentage of time spent engaged in atypical behaviors in each sensory domain, relative to the total time of the ADOS. Coding was implemented using The Observer software system [Noldus, 1991]. Twenty-one percent of participant videos were independently coded by a second observer to ensure inter-rater coding reliability (κ = 0.81 [0.80–0.83], ρ = 0.99, p < 0.01). There was no significant difference between inter-rater reliability for atypical auditory (M = 0.74, SD = 0.21) and visual (M = 0.83, SD = 0.17) behaviors (t[10] = 1.58, p = 0.15).

Statistical Analyses

We compared the percentage of time ASD-V and ASD-MLV participants spent engaged in atypical auditory and visual behaviors while controlling for significant group differences in nonverbal IQ. Based on Shapiro-Wilks tests for normality, it was evident that both the percentage of atypical auditory behaviors and percentage of atypical visual behaviors significantly deviated from normal distributions (p < 0.001). Therefore, Quade's rank analysis of covariance was used for comparisons in lieu of an ANCOVA [Quade, 1967]. Effect sizes were calculated using η^2.

Table 2. Operational Definitions of Atypical Auditory and Visual Behaviors

Domain	Sensory response pattern	Atypical sensory behaviors
Auditory	Seeking and/or intensifying	1. Puts object close to ear. 2. Uses object to make noise repetitively. 3. Vocalizes by humming or producing high-pitched squeals without the clear intent to communicate. Does not including singing or self-talk.
	Manipulating, filtering, and/or avoiding	1. Cups or folds ears with palms. 2. Covers ears with palms or inserts fingers into ears. 3. Appears distressed facially by the current or expected presentation of a sound or requests that a sound be stopped.
Visual	Seeking and/or intensifying	1. Moves object close to eye. 2. Repetitively moves finger or object in front of eyes. 3. Stares intently at object or oneself (for instance, close-up in the mirror).
	Manipulating, filtering, and/or avoiding	1. Moves head down to another level to examine an object from a different perspective or puts hands on either side of eyes. 2. Covers eyes with hands or object. 3. Turns lights off or requests lights be turned off.

Note. Behaviors were assigned to one of twelve atypical sensory behavior categories. Behaviors were either associated with the auditory domain or the visual domain and were further categorized by presumed sensory response pattern ((1) seeking and/or intensifying or (2) manipulating, filtering, and/or avoiding).

Results

Differences between ASD-MLV and ASD-V groups were most pronounced for the amount of time spent engaged in atypical auditory behaviors during the ADOS (Fig. 1). ASD-MLV participants spent proportionately more time engaged in atypical auditory behaviors than ASD-V participants (F[1,81] = 8.27, p < 0.01, η^2 = 0.09). In contrast, there was no significant difference between the groups in terms of the amount of time participants spent engaged in atypical visual behaviors (F[1,81] = 2.95, p = 0.09, η^2 = 0.04).

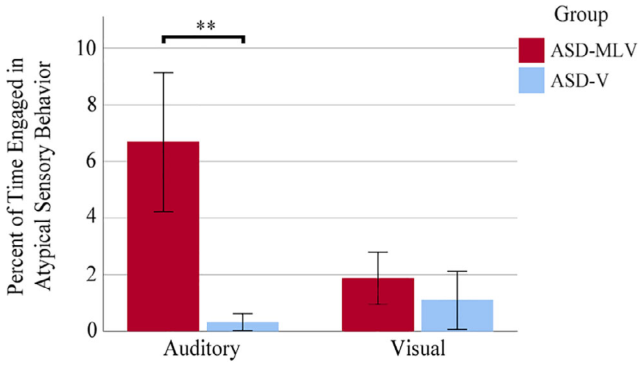

Figure 1. Experiment 1: Classification of ASD-MLV (N = 47) and ASD-V (N = 36) groups by atypical sensory behaviors exhibited during the ADOS. Error bars are based on 95% confidence intervals. ASD-MLV participants spent proportionately more time engaged in atypical auditory behaviors than ASD-V participants ($F[1,81] = 8.27$, $p < 0.01$, $\eta^2 = 0.09$).

Experiment 2

The objective of our second experiment was to test the extent to which atypical auditory and visual behaviors were associated with ASD-MLV participants' receptive language abilities.

Participants

Given the fact that most ASD-V participants did not demonstrate atypical auditory behaviors and consistent with our primary focus on ASD-MLV, only ASD-MLV participants from the sample in Experiment 1 were included in Experiment 2 (N = 47).

Receptive Language Measure

Receptive language was assessed with the Peabody Picture Vocabulary Test–Fourth Edition [PPVT-4; Dunn & Dunn, 2007]. To better capture individual differences, we based our analyses on raw scores rather than standardized scores (since many participants scored at the floor of 20). We excluded data from five ASD-MLV individuals for whom we were unable to obtain basal scores (below a raw score of 3).

Statistical Analyses

A hierarchical linear regression model was constructed to determine the degree to which receptive language abilities were accounted for by differences in the time spent engaged in atypical auditory and visual behaviors, after accounting for effects of age and nonverbal IQ. Specifically, we conducted a linear regression model with age and nonverbal IQ entered first as dependent variables to predict receptive language abilities. After accounting for age and nonverbal IQ, atypical auditory and visual behaviors were entered in a second block as dependent variables in a stepwise linear regression model. Again, the percentage of atypical auditory behaviors and percentage of atypical visual behaviors significantly deviated from normal distributions, as measured by Shapiro-Wilks tests of normality ($p < 0.001$). Therefore, models were computed based on rank sum-based values for these two metrics. Unranked values were used for receptive language, age, and nonverbal IQ, which were normally distributed ($p > 0.05$). All model metrics were computed based on maximal models containing all described predictors. Significance tests were two-sided and conducted at the 5% significance level.

Results

The results from these analyses are summarized in Table 3. Our model revealed that control variables, age ($\beta = 0.70$, $SE = 0.12$) and nonverbal IQ ($\beta = 0.85$, $SE = 0.12$), accounted for a significant proportion of the variance in receptive language abilities (Model 1; $F[2,40] = 32.10$, $p < 0.001$, adjusted $R^2 = 0.60$). The inclusion of ranked atypical auditory behaviors significantly increased the accuracy of the model (Model 2; $\beta = -0.25$, $SE = 0.01$, $F[3,39] = 25.91$, $p < 0.001$, $\Delta F = 6.19$, $p < 0.05$, adjusted $R^2 = 0.65$, Fig. 2), while the inclusion of ranked atypical visual behaviors did not (Model 3; $\beta = -0.18$, $SE = 0.01$, $F[4,38] = 21.50$, $p > 0.05$, $\Delta F = 0.07$, $p > 0.05$, adjusted $R^2 = 0.67$).

Experiment 3

The objective of our third experiment was to test whether there was an association between the frequency in which ASD-MLV participants displayed atypical auditory behaviors and the amplitude of their neural mismatch responses to deviant sounds during a passive auditory perceptual organization task.

Participants

We limited the third experiment to ASD-MLV adolescents, ages 12 and above, because the morphology of auditory-evoked potential signals changes between 8 and 12 [Luck & Kappenman, 2011] and thus makes it difficult to use the same measure of response for both children and adolescents. In contrast, amplitude and latency of MMNs appear be relatively stable during adolescence and young adulthood [Mahajan & Mcarthur, 2015]. Participants were not included if they had less than 100 usable EEG trials in response to the deviant stimulus. Of the data collected from 23 ASD-MLV adolescents, data from 18 participants were available for analyses (Table 4).

Table 3. Experiment 2: Hierarchical Linear Regression Model Predictors of Receptive Language

	Model 1			Model 2			Model 3		
Variable	*B*	*SE B*	*β*	*B*	*SE B*	*β*	*B*	*SE B*	*β*
(Constant)	−123.83	22.29		−77.24	28.67		−62.91	28.88	
Age	5.54	0.90	0.70**	4.65	0.93	0.59**	4.26	0.93	0.54**
NVIQ	1.57	0.21	0.85**	1.37	0.21	0.75**	1.37	0.21	0.75**
Auditory				−0.42	0.17	−0.25*	−0.38	0.17	−0.23*
Visual							−0.26	0.14	−0.18
Adj. R^2		0.60			0.65			0.67	
F		32.10			25.91			21.50	
ΔF		<<0.001			<0.05			0.07	

Note. Reports are based on ASD-MLV children and adolescents with an above-basal receptive language score ($N = 42$).
*$p < 0.05$.
**$p < 0.001$.

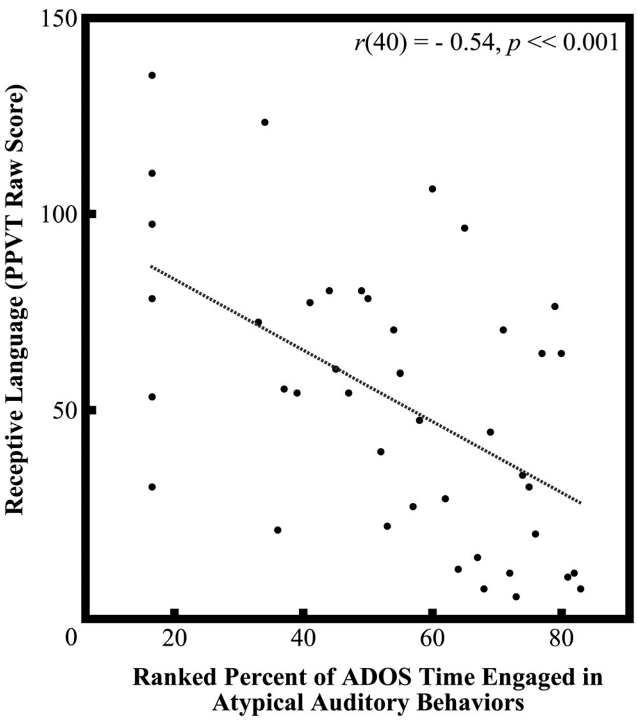

Figure 2. Experiment 2: Depiction of the negative relationship between receptive language abilities and time spent engaged in atypical auditory behaviors during the ADOS, based on 47 ASD-MLV children and adolescents.

Neural Mismatch Measure

Prior to data collection, participants were acclimated to the EEG setup [cf. Tager-Flusberg et al., 2017]. EEG data were collected using a 128-channel HydroCel Geodesic Sensor Net (Electrical Geodesics Inc., Eugene, OR). Participants watched a silent movie with subtitles while they heard a stream of tones that were designed to follow a classic one-stream, oddball mismatch response paradigm with intensity deviants. Sounds were presented through two speakers, placed ±45 degrees in front of the listener. Both standards and deviants were complex tones composed of the first 10 harmonic frequencies of a 110 Hz fundamental. Deviant/standard presentation was counterbalanced. In one block, intensity deviants were presented at 45 dB SPL, 15 dB more intense than 30 dB SPL standard tones; in the other block, the standards were 45 dB SPL, 15 dB more intense than the 30 dB SPL deviant tones. The interstimulus interval was 250 ms with a 0 to 40 ms jitter. Deviants were always proceeded by at least three standards and made up 17% of the trials. Participants were presented with a total of 1000 trials (170 deviants, 830 standards). Additional data were taken to note when participants engaged in behaviors like humming or vocalizations during the EEG; however, it was decided that EEG data collected during these behaviors should not be excluded, since it may be a more wholistic representation of how these individuals process and filter sounds in their daily lives.

EEG data were referenced online to vertex (Cz), online digitally filtered with a 0.1 Hz highpass filter, and digitized at 1000 Hz. After acquisition, data were offline filtered at 1–35 Hz. As is commonly done to quantify the MMN [Näätänen, Paavilainen, Rinne, & Alho, 2007], data from the midline frontal channel (Fz, EGI electrode 12)

Table 4. Demographic Information for Participants in Experiment 3

Participants	*N*	18
Age (years)	Mean (SD)	15.81 (2.01)
M:F	Ratio	11:7
ADOS CSS	Mean (SD)	7.33 (1.57)
ADOS SA CSS	Mean (SD)	6.89 (1.64)
ADOS RRB CSS	Mean (SD)	8.06 (1.55)
Nonverbal IQ	Mean (SD)	62.89 (21.10)
Verbal IQ	Mean (SD)	32.06 (17.90)

Note. Participants comprised a subset of ASD-MLV participants between the ages of 12 and 21 with usable EEG data.

were selected and re-referenced to the average of the left and right mastoids (LM/RM, EGI electrodes 57 and 100). Event-related potentials in response to the 45 dB SPL tones were segmented into 700 ms epochs with a 100 ms prestimulus baseline. Trials were rejected if the amplitude of the trial exceeded 100 μV, peak-to-peak, along either mastoid or the midline frontal channel. Trials were baseline corrected with respect to the mean of the whole trial. The range of deviant trials accepted and analyzed was 109–170. Standard trials were randomly selected to match the number of deviant trials selected for each participant.

Strength of neural response was operationalized as the difference in amplitude between the first major positive and negative peaks of the waveforms being analyzed. Mean latency of these peaks was identified on the group average and a 30 ms window around those mean latency peaks was used to quantify the first positive peak and first negative peak amplitudes for each participant. We first considered for the MMN (the difference waveform between the standard and the deviant), which had mean positive and negative peak amplitudes centered around 100 and 180 ms, respectively. Because the neural responses elicited by standard tones was relatively small, with a poor signal-to-noise ratio, we conducted an additional exploratory analysis of the magnitude of the positive and negative peak amplitudes evoked by the deviant (which correspond to the traditional P1 and N1 peaks to salient sensory events); the deviant tone responses had mean P1 and N1 amplitudes centered around 117 and 181 ms, respectively.

Statistical Analyses

Correlations were measured between atypical auditory and visual behaviors with neural response amplitudes. Pearson's correlations were performed on ranked values for nonparametric data (atypical auditory behaviors and atypical visual behaviors) and unranked values for parametric data (amplitude of neural responses). Significance tests were two-sided and set at the 5% significance level. False discovery rate (FDR) corrections were used to control for multiple comparisons.

Results

Amplitude of the MMN neural response did not significantly correlate with time spent engaged in atypical auditory behaviors ($r[16] = -0.42$, $p = 0.16$). However, the amplitude of the neural to deviant tones was significantly correlated with the percentage of time during the ADOS that participants spent engaged in atypical auditory behaviors ($r[16] = -0.58$, $p < 0.05$; Fig. 3). Time spent engaged in atypical visual behaviors did not significantly correlate with amplitude of the MMN ($r[16] = -0.17$, $p = 0.50$) or amplitude of the neural response to deviant tones ($r[16] = -0.17$, $p = 0.50$).

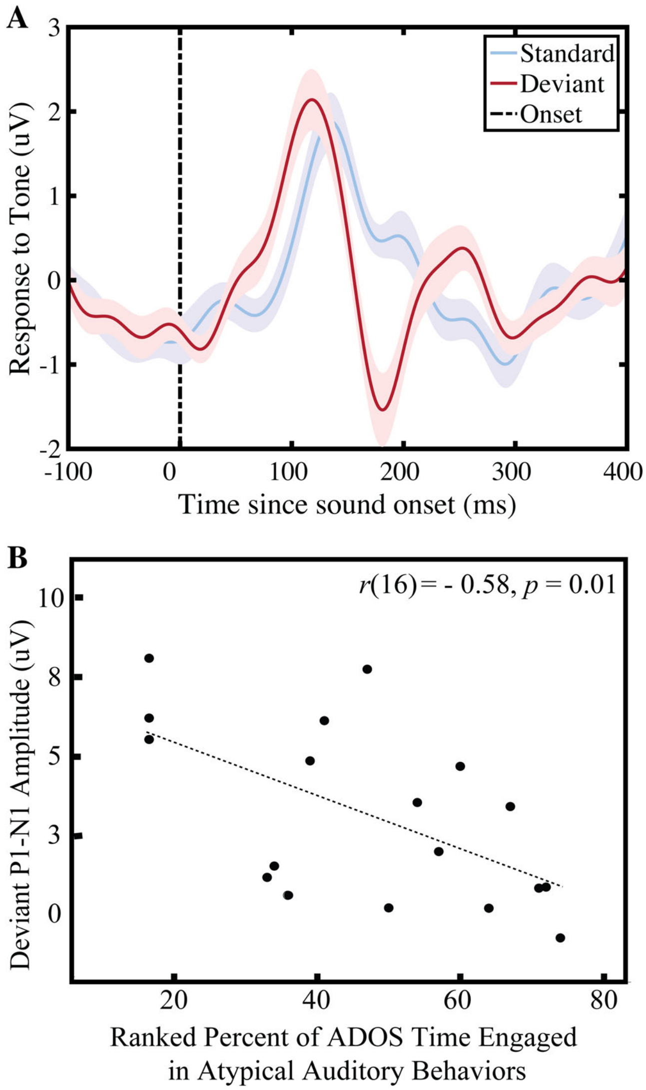

Figure 3. Experiment 3: Results based on adolescents in the ASD-MLV group ($N = 18$). **(A)** ERP in response to deviant and standard complex tones. Shaded confidence regions denote standard error of the mean. **(B)** Scatterplot correlation between neural amplitude response to deviant tones (μV) and ranked percent of time engaged in atypical auditory behaviors.

General Discussion

ASD-MLV children and adolescents were found to engage in significantly more atypical auditory behaviors than ASD-V controls, while in contrast, both groups engaged in similar amounts of atypical visual behaviors. Within the ASD-MLV group, receptive language abilities were predicted by the proportion of time spent engaged in atypical auditory behaviors, beyond what was already accounted for by nonverbal IQ and age. This finding was specific to atypical auditory behaviors and did not extend to both auditory and visual sensory behaviors. Among ASD-MLV adolescents, we found preliminary evidence that neural responses indexing sensitivity to sound stimulus properties are weaker in participants who exhibit higher rates of atypical auditory behaviors.

Results from Experiment 1 support and refine previous reports showing that atypical sensory behaviors are more frequent in ASD-MLV than ASD-V individuals [Patten et al., 2013]. While prior work on young children has not found a distinction between the incidence of atypical auditory and visual behaviors between the two groups, our results on a larger age range of children and adolescents showed that ASD-MLV participants displayed more auditory, but not visual, atypical behaviors relative to ASD-V peers. Importantly, group-level differences in the display of atypical auditory behaviors were evident even after accounting for group-level differences in nonverbal IQ. Our findings may be impacted by the age range investigated, since atypical sensory behaviors, and ASD symptomology more generally, decrease with age, particularly after middle childhood [Ben-Sasson et al., 2009; Kern et al., 2006; Shattuck et al., 2007]. However, improvements in symptomology might be more common in ASD-V individuals, as it has been shown that individuals with ASD but without intellectual disabilities improve significantly more than those with ASD with such disabilities [Shattuck et al., 2007]. Another possibility is that ASD-MLV children enter adolescence with elevated auditory-related symptoms relative to ASD-V peers, and even if those symptoms decrease in frequency and severity with age, they might nonetheless continue to remain higher.

Results from Experiment 2 demonstrated that these atypical auditory behaviors were not uniformly displayed by all participants who were ASD-MLV but rather were more common in those with severe receptive language deficits. Findings lend support to the hypothesis that the brain systems responsible for auditory information processing are more closely linked to receptive than expressive language [Groen et al., 2008; Siegal & Blades, 2003]. Notably, the time spent engaged in atypical auditory behaviors was a significant predictor of receptive language abilities beyond what was accounted for by nonverbal IQ; this mitigates the concern that the observed relationship might be due to a relationship between nonverbal IQ and atypical sensory behaviors [Bishop et al., 2006; Leekam et al., 2007] or nonverbal IQ and language [Mayes & Calhoun, 2003].

In Experiment 3, we found a negative correlation between the amount of time ASD-MLV participants spent engaged in atypical auditory behaviors during the ADOS and the strength of the neural response to deviant sounds—a measure that served to capture the degree to which individuals were sensitive to stimulus properties of nonspeech sound inputs. Findings were not robust when we used a more classically defined measure of mismatch response (the MMN), which appeared to be due in part to noisy estimates of the responses to standard stimuli. In the experiment, we used a relatively rapid stimulus presentation rate, which lead to noisy estimates of the relatively small standard event-related potentials (ERP). We reasoned that for our paradigm, the magnitude of the ERP elicited by the deviant stimuli, which was much larger than the responses to standards, might thus be a more reliable estimate of sensitivity to deviant sounds than the traditional MMN. As noted above, we did find a negative correlation between the deviant response and atypical auditory behaviors; however, this analysis was exploratory and needs further confirmation. Results in our ASD-MLV sample measuring deviant response, while preliminary, expand on prior studies on ASD-V participants that have found an inverse relationship between amplitude of mismatch response to acoustic feature changes and degree of auditory sensory sensitivities [Ludlow et al., 2014]. In our experiment, amplitude of neural response indirectly captured sensitivity to perceptual sound differences in nonspeech sound intensity. Such findings align with prior work showing that the ability to actively discriminate nonspeech sounds based on intensity is negatively correlated with heightened atypical auditory behaviors [Jones et al., 2009].

Preliminary evidence of a relationship between atypical auditory behaviors and atypical processing of acoustic inputs raises the possibility that atypical sensory behaviors serve as external compensatory mechanisms to deal with faulty central auditory processing systems that are typically responsible for organizing sound mixtures and filtering extraneous inputs. For instance, the ability to separate sounds as coming from distinct sources and use that information to suppress irrelevant auditory information is necessary when it comes to effectively filtering incoming sounds [Shinn-Cunningham, 2008]. Without such mechanisms in place, environmental noise could easily become overwhelming, and external behaviors like ear covering and humming might be useful ways to modulate that noise [Alcántara, Weisblatt, Moore, & Bolton, 2004; Lepistö et al., 2009; Russo, Zecker, Trommer, Chen, & Kraus, 2009].

The results from this study's three experiments lead us to hypothesize that internal central auditory processing systems are particularly perturbed in ASD-MLV with major receptive language impairments and atypical auditory behaviors. In particular, we hypothesize that certain individuals with heightened occurrence of atypical auditory behaviors may be unable to distinguish important from unimportant sounds; as a result, they might inadvertently focus on unimportant aspects of sounds and not effectively disengage from those sounds when more important sounds are presented. This irregular perceptual organization of sounds may in turn negatively impact how speech is processed; for instance, speech processing relies on the ability to attend to meaningful linguistic units like phonetic structure and prosody [Kujala et al., 2007]. Because language acquisition typically occurs before the age of 5, the current research could not make a direct comparison between the presence of atypical auditory behaviors and success of language acquisition. However, future studies might address this gap by collecting measures of auditory filtering in young children and testing whether they are predictive of future language ability.

Limitations and Future Directions

In interpreting our results, several additional limitations and future directions should be considered. The first is the sample size of ASD-MLV adolescents in our analysis of brain-behavior correlates and the failure to find a relationship between behaviors and the traditional MMN, presumably due to a weak and therefore noisy neural response to standard stimuli. As in many neuroimaging studies on ASD-MLV individuals, it was hard to acquire neuroimaging data and acquire quality data from a large sample [Nordahl et al., 2016; Plesa Skwerer, Jordan, Brukilacchio, & Tager-Flusberg, 2016; Tager-Flusberg et al., 2017]. Replication of our results, especially with larger samples, is necessary to make stronger conclusions about the relationship between systems underlying atypical auditory behaviors and atypical neural responses to sounds.

Second, while we sought to quantify common manifestations of atypical sensory behaviors, we acknowledge that certain behaviors might not be fully captured during an assessment like the ADOS. For instance, we did not measure responsiveness to sounds that are known to elicit atypical auditory behaviors, such as fire trucks or vacuum cleaners. Hypo-responsiveness to sounds also could not be reliably coded. Furthermore, certain ASD-V individuals, especially as they age and become more cognizant of social norms, may externally camouflage their sensitivities during neurophysiological testing like the ADOS but still report them as internally present [Hull et al., 2017]. In addition, ADOS examiners often interrupt certain repetitive behaviors involving sensory stimuli (e.g., nonfunctional play with a bubble fan) to prompt other diverse behaviors. For these reasons, behaviors coded in the ADOS may not fully capture a given participant's atypical sensory behaviors. Nonetheless, this type of assessment still provides important information that is worth considering about how atypical sensory behaviors manifest and impact people with ASD in common play and work settings. Other measures designed to elicit atypical sensory behaviors, like those demonstrated in the Sensory Assessment for Neurodevelopmental Disorders [Siper, Kolevzon, Wang, Buxbaum, & Tavassoli, 2017] or Sensory Processing Assessment for Young Children [Patten et al., 2013], may be more sensitive in capturing a comprehensive picture of sensory response phenotype in certain ASD individuals.

Another limitation of this research is that we did not produce separate analyses based on the different sensory response pattern (e.g., seeking versus avoiding). While some research has shown trends related to these sensory response patterns [Baranek et al., 2007; Schauder & Bennetto, 2016], our central hypothesis focused on whether the presence of overt atypical behaviors in the auditory domain, regardless of how they functioned, related to language abilities and the neural mechanisms responsible for sound processing. In many ways, we suspect that behaviors, regardless of functionality, indicate cortical disruptions that impact processing of sensory inputs within that sensory modality. Research has demonstrated that, paradoxically, many people with autism show both sensory seeking and sensory avoidance, even within the same sensory modalities [Schauder & Bennetto, 2016], which may suggest an overlap in their function and underlying etiology. Future research might seek to explore distinctions between seeking and avoiding sensitivities in ASD-MLV samples, with the caveat that it might be difficult to assign functionality to behaviors exhibited by those who cannot describe the purpose of their actions.

Finally, the investigation of atypical auditory behaviors is warranted from a clinical perspective in order to understand the extent to which these behaviors are helpful or harmful. Atypical auditory behaviors may help filter sounds that are distracting or overwhelming, but they may also inadvertently block out important sounds and consequently interfere with a person's ability to hear important sounds.

Conclusions

Our findings demonstrate that while atypical reactivity to sensory input is a core characteristic of ASD, the systems underlying the perception of auditory inputs might be particularly disrupted in those within the ASD-MLV subgroup who also have severe receptive language impairments. In addition, this research is the first to show evidence of a relationship between heightened occurrence of atypical auditory behaviors and atypical neural indices of sound perception in ASD-MLV individuals. Further research is needed to elucidate how external behaviors might function to regulate auditory inputs that have not been adequately organized by internal brain mechanisms.

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