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Original Article

Left-hemispheric atypicalities in the primary auditory cortex are associated with language comprehension and social skills in children with Autism Spectrum Disorder

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Low-level auditory processing difficulties have been previously reported in children with Autism Spectrum Disorder (ASD), and some studies showed the relationship between these difficulties in the primary auditory cortex and language impairment in ASD. However, there is still a limited number of studies that comprehensively assess (i) amplitudes, latencies, and sensory gating effects in all early components of auditory processing (M50–M100–M200 complex) at the source level in magnetoencephalography with their relation to structural anatomy (gray matter volume, thickness, gyrification) (ii) and the association between brain metrics and clinical phenotype in the same group of children. To address this question, we used a standard paired-clicks paradigm in magnetoencephalography and brain morphometry analysis in children with and without ASD ($N_{ASD} = 20$, $N_{TD} = 20$). First, the results revealed a reduction of M200 and altered M200 sensory gating effect in the left auditory cortex in children with ASD. Second, these alterations were related to lower language comprehension skills and higher autistic symptom severity. Finally, altered MEG responses were associated with gray matter thickness reduction as well as abnormal gyrification in the primary auditory cortex in ASD. The study revealed low-level functional and structural atypicalities in children with ASD and their relation to clinical phenotype.

Keywords: Autism Spectrum Disorder; auditory event-related fields; language comprehension; magnetoencephalography; brain morphometry.

Introduction

Autism Spectrum Disorder (ASD) is a highly heterogeneous neurodevelopmental condition that is characterized by deficits in social interaction and communication, the presence of stereotyped/repetitive behavior, and restricted interests or atypical response to sensor information (American Psychiatric Association 2013). Usually, ASD is accompanied by co-occurring conditions (Leader et al. 2020), among which language impairment (Kjelgaard and Tager-Flusberg 2001), intellectual disability (Polyak et al. 2015), and attention deficit (Matson et al. 2013) are the most frequently reported. Some studies have revealed that atypical low-level sensory processing in the neural networks accounted for the altered development of high-level cognitive functions in ASD (Robertson and Baron-Cohen 2017). Therefore, addressing low-level neural processing in the primary auditory cortex is essential in ASD as it can be related to language difficulties in this population.

Previous studies using auditory event-related potentials/fields (ERPs/ERFs) measured with electro-/magnetoencephalography (EEG/MEG) have identified a complex of components (P50–N100–P200 in EEG and the MEG's M50–M100–M200 equivalent) that are associated with early stimulus feature extraction and integration with the topology in the primary auditory cortex and its vicinity (eg Näätänen and Picton 1987; Woods 1995; Näätänen and Winkler 1999; Bomba and Pang 2004; Key et al. 2005; Alain and Winkler 2012). The main functional features of these components reflect the extent of the involvement of neural resources in the sound processing (amplitude), the speed of stimulus "detection"/classification (latency), and filtering the redundant sensory information (sensory gating), see Luck (2014). Thus, addressing these basic EEG/MEG-derived parameters will allow us to identify which specific step(s) or mechanism(s) of the sound processing is(are) altered in ASD. A number of previous studies have focused on these brain measures in response to

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low-level sound perception in individuals with ASD (eg Edgar et al. 2014, 2015a; Port et al. 2015, 2016; Roberts et al. 2019; Jorgensen et al. 2021).

Comparisons in the amplitudes of all these components between individuals with ASD and typically developing (TD) controls have shown inconsistent results (eg Bomba and Pang 2004; Jeste and Nelson 2009; Haesen et al. 2011; Marco et al. 2011; Donkers et al. 2015, 2019; Kikuchi et al. 2016; Hudac et al. 2018; Green et al. 2020). Latencies of these responses have been reported to be delayed in ASD in multiple studies (eg Demopoulos et al. 2015; Yu et al. 2018; Roberts et al. 2019; Matsuzaki et al. 2020); however, some studies revealed the opposite effect with the evidence of shorter latencies in ASD (eg Martineau et al. 1984; Ferri et al. 2003). The sensory gating effect registered with the paired-clicks paradigm reflects the inhibitory effect of the first stimulus (S1) to the response of a shortly followed identical second stimulus (S2); it is calculated as an S2/S1 ratio and has been shown to be altered in ASD in a number of studies, and the severity of autistic traits and nonverbal intelligence quotient (IQ) were the main contributors to these alterations (eg Orekhova et al. 2008; Chien et al. 2019). Finally, a recent comprehensive meta-analysis (Williams et al. 2021), addressing all these brain responses to basic auditory stimuli in ASD, revealed delayed P50/M50 and M100 latencies as well as altered sensory gating, pointing to different abnormalities at early stages of sound processing in the primary auditory cortex.

The previous studies have also identified that the alterations in these low-level auditory processing are associated with language impairment in ASD (eg Roberts et al. 2011, 2019; Berman et al. 2016; Matsuzaki et al. 2019). For example, Roberts et al. (2011), using the mismatch field paradigm in MEG (MMF), have shown that a delayed latency of this response was related to the language abilities of children with ASD. In a group of minimally verbal autistic individuals, the delayed latencies of M50 and M100 components in comparison to verbal individuals with ASD has been revealed (Roberts et al. 2019). Other low-level auditory abnormalities (such as a neural response to amplitude-modulated tones and sweeps) have also been reported to be related to language difficulties in ASD (Arutiunian et al. 2023a; Roberts et al. 2021).

A very limited number of multimodal studies have examined the relationship between functional (MEG/EEG) and structural brain characteristics in the primary auditory cortex in the same group of children with ASD (eg Berman et al. 2016; Roberts et al. 2020). These studies have identified, for example, that fractional anisotropy (FA) of the arcuate fasciculus (one of the main language-related pathways that is also involved in the auditory processing, see, Ivanova et al. 2021) contributes to latency delays of both early and the late auditory components.

The main goal of the present research is to comprehensively address both functional and structural brain characteristics in the primary auditory cortex of children with ASD in relation to clinical phenotype, including language skills. First, using the paired-clicks paradigm in MEG, we aim to identify the sources of M50–M100–M200 auditory complex and to provide between-group comparisons (ASD vs. TD) in the amplitudes, latencies, and sensory gating effects for all these components. Based on the previous studies, we predict to identify the delayed M50 and M100 latencies, reduction in the amplitude of the late M200 component, and altered sensory gating in the ASD group. Second, we aim to address the relevance of the altered neural responses for the clinical phenotype in ASD. Given the previous reports on the low-level auditory contributions to language functioning, we expect that these alterations will be associated with language skills of children with ASD revealed in behavioral assessment. Finally, we aim to calculate morphometric (both volume- and surface-based) characteristics for the cortical sources of the detected MEG auditory atypicalities and to assess whether structural brain measures are related to functional abnormalities in ASD.

Materials and methods

Participants

The data were collected from 20 children with ASD (5 girls, age range 8.02 to 14.01 years, $M_{age} = 10.03$, $SD = 1.7$) and 20 age-matched TD controls (9 girls, age range 7.02 to 12.03 years, $M_{age} = 9.11$, $SD = 1.3$), see Table 1 (this is the same sample of participants as in Arutiunian et al. 2023a, 2024). All ASD participants had a confirmed clinical diagnosis of ASD based on the criteria of the International Classification of Diseases–10 (World Health Organization 2016), and 18 out of 20 children were also assessed by a licensed psychiatrist with Autism Diagnosis Observation Schedule–Second Edition, ADOS-2 (Lord et al. 2012). The exclusion criteria were comorbid neurological disorders (eg epilepsy) and the presence of a known chromosomal syndrome (eg Rett syndrome, Fragile X syndrome). TD participants did not have a previous history of psychiatric and/or neurodevelopmental problems. Both groups of children had normal hearing and normal or corrected-to-normal vision.

Recruitment

Children with ASD were recruited though the clinical and educational center affiliated with the Moscow State University of Psychology and Education (Federal Resource Center for Organization of Comprehensive Support to Children with Autism Spectrum Disorders), and TD children were recruited through advertising in social media.

Ethics approval disclosure

The study was approved by the ethics committees of Moscow State University of Psychology and Education and the HSE University (Institutional Review Board HSE) and was conducted according to the Declaration of Helsinki (approval date: 2019 November 25, there is no specific ID). A written consent form was signed by all parents, and verbal assent was obtained from each child and a parent. Participants were informed that they could withdraw from the study at any time during the experiment.

Behavioral assessment

- The severity of autistic traits was measured with the Autism Spectrum Quotient: Children's Version, AQ (Auyeung et al. 2008) in both groups of children. The standard scores for five AQ "scales" associated with autism and broader phenotype were estimated for each child (AQ social skills, AQ attention switching, AQ attention to details, AQ communication, and AQ imagination).
- Language production and language comprehension abilities were screened with the Russian Child Language Assessment Battery (Arutiunian et al. 2022) in both groups of participants. Language production score (LPS) and language comprehension score (LCS) were calculated for each child.
- The nonverbal IQ was evaluated with the Kaufman Assessment Battery for Children K-ABC II (Kaufman and Kaufman 2004) or the Wechsler Intelligence Scale for Children–Third Edition (Wechsler 1991) in the ASD group; and Raven's Colored Progressive Matrices (Raven 2000) in the TD group.

Table 1. The demographic information for ASD and TD groups of children, M ± SD (range).

Characteristics	Group		t	P
	ASD ($n = 20$, 5 girls)	TD ($N = 20$, 9 girls)		
Age in years	10.03 ± 1.7 (8.02 to 14.01)	09.11 ± 1.3 (7.02 to 12.03)	0.70	0.48
Language production (LPS)	0.76 ± 0.24 (0.12 to 0.95)	0.96 ± 0.02 (0.93 to 0.99)	−3.66	0.001**
Language comprehension (LCS)	0.73 ± 0.24 (0.24 to 0.94)	0.95 ± 0.03 (0.88 to 1.00)	−4.07	<0.001***
AQ social skills	15.9 ± 6.0 (4 to 25)	7.6 ± 3.0 (3 to 12)	5.50	<0.001***
AQ attention switching	16.2 ± 4.0 (11 to 23)	12.3 ± 3.0 (6 to 20)	3.39	0.001**
AQ attention to details	14.9 ± 4.9 (4 to 23)	12.8 ± 4.9 (3 to 23)	1.37	0.17
AQ communication	21.1 ± 4.2 (9 to 29)	8.6 ± 4.7 (1 to 18)	8.94	<0.001***
AQ imagination	15.4 ± 6.4 (2 to 27)	8.9 ± 3.1 (4 to 14)	4.07	<0.001***
Nonverbal IQ	85.4 ± 17.9 (41 to 118)	31.8 ± 2.7 (23 to 36)	ND	ND
ADOS, raw score				
Module 1 ($N_{children} = 1$)	12	NA	ND	ND
Module 2 ($N_{children} = 5$)	16.2 ± 4.96 (8 to 20)	NA	ND	ND
Module 3 ($N_{children} = 12$)	10.5 ± 1.98 (8 to 14)	NA	ND	ND
ADOS, severity score (CSS)			ND	ND
Module 1 ($N_{children} = 1$)	6	NA	ND	ND
Module 2 ($N_{children} = 5$)	6.8 ± 1.6 (4 to 8)	NA	ND	ND
Module 3 ($N_{children} = 12$)	6.5 ± 1.0 (5 to 8)	NA	ND	ND

Note: We run *t*-tests to compare the characteristics of ASD and TD groups of children. The significance is labeled with $^{*}P < 0.05$, $^{**}P < 0.01$, $^{***}P < 0.001$. Nonverbal IQ of children was screened with different assessment tools; therefore, a direct between-group comparison was not provided. NA, not available. ND, no data.

Stimuli and procedure

The auditory stimuli were pure tone clicks with 5 ms duration (sampling rate was 44,100 Hz). We used a classical paired-clicks paradigm so that the stimuli were presented in pairs (S1 and S2) with 500 ms interval between S1 and S2 and 10 s interpair interval (S2 and S1). Overall, 100 pairs of clicks were presented binaural during three ∼6 min blocks via the PsychoPy software (Peirce 2007). Stimuli were delivered via plastic ear tubes with foam tips inserted into the ear canals, and the intensity level was set at 83.7 dB sound pressure level. During the experimental blocks, children were asked to look at the fixation cross on the screen in front of them.

Structural magnetic resonance imaging

T1-weighted structural magnetic resonance imaging (MRI) was acquired with a 1.5T Siemens Avanto scanner using the following parameters: repetition time = 1,900 ms, echo time = 3.37 ms, flip angle = 15°, matrix size = 256 × 256 × 176, and voxel size = 1.0 × 1.0 × 1.0 mm^3. Cortical reconstructions and parcellations were generated with the FreeSurfer software (Dale et al. 1999). The surface was down-sampled to 15,000 vertices for each participant in the Brainstorm toolbox (Tadel et al. 2011). Coregistration between MRI and MEG data was performed with the Brainstorm toolbox based on the six reference points (left and right pre-auricular points, nasion, anterior and posterior commissure, and interhemispheric point) and the digitized head points ($N = \sim 150$ for each child).

For all TD children, we were able to obtain the T1 MRIs, whereas, in 5 ASD children, MRIs were not available due to behavioral issues and intolerance to the MRI procedure. For these children, we used a template anatomy ("MRI: ICBM152") and applied a warping algorithm implemented in Brainstorm to build pseudo-individual brains based on the real head shape of each child.

MEG data collection and preprocessing

The MEG acquisition procedure is identical as in Arutiunian et al. (2023a, 2024). MEG data were collected in a magnetically shielded room in a sitting position with a whole-head 306-channel MEG (Vectorview, Elekta Neuromag). The position of children's head within the MEG helmet was monitored every 4 ms during the experiment via four head position indicator (HPI) coils digitized together with fiducial points using the 3D digitizer "Fastrak" (Polhemus). A temporal signal space separation (Taulu and Simola 2006) and movement compensation procedures were applied via the MaxFilter software (Elekta Neuromag) to remove external interference signals generated outside the brain and to compensate for head movements. We recorded an electrooculogram (EOG) with four electrodes placed above and below the left eye and at the left and right outer canthi to detect eye blinks and horizontal eye movements. Also, an electrocardiography (ECG) was monitored with ECG electrodes to detect cardiac activity. These biological artifacts (eye movements and heartbeats) were cleaned with the EEGLAB's (Delorme and Makeig 2004) independent component analysis (ICA) implemented in Brainstorm.

MEG was recorded at 1,000 Hz sampling rate and filtered offline with a band-pass filter of 0.1 to 25 Hz for the ERF analysis. We chose such a restricted band-pass filter because of two main reasons. First, the auditory components that we are focusing on (M50–M100–M200) are within this frequency band; second, such a band-pass filter helps to reduce muscle noise presented in some ASD participants (see also Sysoeva et al. 2020).

The cleaned MEG data were cut in 400 ms epochs, ranging from −100 to 300 ms, and DC offset correction from −100 to −2 ms was applied. Then epochs were inspected visually and those affected by the muscular or technical artifacts were manually rejected. The number of artifact-free epochs did not differ between groups of children in S1 and S2: S1, $M_{ASD} = 95.05$, range 65 to 100; $M_{TD} = 92.25$, range 64 to 100; $t(37.98) = -0.06$, $P = 0.95$; S2, $M_{ASD} = 94.70$, range 65 to 100; $M_{TD} = 95.15$, range 62 to 100; $t(37.95) = -0.13$, $P = 0.90$. Also, there were no difference in the number of artifact-free epochs between S1 and S2 in ASD and TD groups of children: ASD group, $t(37.99) = 0.10$, $P = 0.92$; TD group, $t(37.96) = 0.03$, $P = 0.98$.

MEG source localization

We used only gradiometers for the source analysis. The individual head models were built with the "overlapping spheres" method

(Huang et al. 1999), and the inverse problem was solved with the depth-weighted linear L2-minimum norm estimate method (Lin et al. 2006), with the dipole orientation constrained to be normal to the cortical surface. To calculate a noise covariance, MEG data were recorded in the absence of a subject (empty room) after each participant's recording session and then were processed using the same parameters as the experimental MEG data. In order to provide the comparison between subjects, the individual MNEs were projected to the "MRI: ICBM152" template brain.

According to the previous findings (eg Roberts et al. 2010, 2019; Edgar et al. 2015b), cortical generators of the basic auditory components (M50–M100–M200) are spread over the "core auditory area" in both hemispheres, so, we have selected the following regions of interest (ROIs) to estimate the sources of each component: transverse temporal gyrus, transverse temporal sulcus, planum temporale of the superior temporal gyrus, lateral superior temporal gyrus, superior temporal sulcus, planum polar of the superior temporal gyrus, and inferior part of the circular sulcus of the insula in the left and right auditory cortices, based on the Destrieux parcellation cortical atlas (Destrieux et al. 2010). First, the signal was averaged over epochs, the individual time course was calculated for each of 15,000 vertices, and a special smoothing function based on the Gaussian smoothing (full width at half maximum, FWHM = 3 mm) was applied. Second, the cortical map was normalized with a z-score, using the prestimulus baseline of −100 to −2 ms. For each child, z-score-normalized absolute values were averaged in three time intervals for each auditory component (between 40 and 90 ms for M50; 90 and 190 ms for M100; 200 and 300 ms for M200). Third, as different components can have different cortical generators within the "core/primary auditory area," for each time window, we estimated the region with the highest z-score value. Amplitudes and latencies of the auditory components were extracted from defined ROIs in both hemispheres for further statistical analysis. Sensory gating effects were calculated as the S2/S1 ratio for each component for each child.

Volume-based and surface-based morphometric analyses

The processing of the MRI data was performed with Computational Anatomy Toolbox, CAT12 (http://www.neuro.uni-jena.de/cat/), and Statistical Parametric Mapping, SPM (https://www.fil.ion.ucl.ac.uk/spm/software/spm12/), on MATLAB R2017a, using the identical pipeline from Arutiunian et al. (2023b): (i) T1-weighted MRIs were aligned with the anterior commissure–posterior commissure (AC-PC) plane; (ii) T1-images were segmented into native-space gray matter (GM), white matter (WM), and cerebrospinal fluid (CSF) images (the results of the segmentation of each MRI were visually inspected for quality); (iii) the alignment of brain images from the native space to the Montreal Neurological Institute standard space MNI-152 template; and (iv) standard smoothing procedure with 8 mm FWHM Gaussian kernel (for volume files), 15 mm FWHM Gaussian kernel (for thickness files), and 20 mm FWHM Gaussian kernel (for the gyrification). The volumetric analysis was based on the neuromorphometric atlas (http://www.neuromorphometrics.com), whereas cortical statistics were based on the Desikan–Killiany anatomical atlas (Desikan et al. 2006). GM volume, GM thickness, and gyrification index (GI) were calculated for each child. GM volume and GM thickness are one of the most frequently reported morphometric variables that are related to alterations in the auditory processing in ASD (see, for example, Hyde et al. 2010), whereas GI was less often included in the studies. At the same time, the GI represents an essential surface-based parameter that measures the quantity of the amount of cortex buried within the sulcal folds in comparison to the amount of cortex on the outer of the visible cortex so that the cortex with the extensive folding has a large GI, and this parameter has been reported to be associated with language skills in children with ASD (Arutiunian et al. 2023b). The three variables were calculated for each ROI identified in the MEG source analysis.

Statistical analysis

All models were estimated in R (R Core Team 2019) with the *lme4* (Bates et al. 2015) package. The data were plotted with *ggplot2* (Wickham 2016), and the figures for neural responses were created using Brainstorm (Tadel et al. 2011). The structure of the models will be specified in Results.

Data availability

The datasets of the current study are available from the corresponding author upon reasonable request. Codes for statistical analysis and visualization are presented in Supplementary Material.

Results

Sample characteristics

As expected, although children with and without ASD did not differ in age, the ASD group had a higher presence of autistic symptoms according to four out of five AQ "scales" in comparison to TD group. As for language abilities, ASD participants had lower LPS and LCS (see Table 1).

MEG raw data visualization

Figure 1 represents the grand-averaged raw sensor-level data for both groups of children. It showed the pattern of identifiable M50, M100, and M200 in ASD and TD groups as well as the power distribution at these timepoints in the sensors over the temporal regions.

Between-group comparisons of the amplitude and latency of the MEG auditory responses

The results of the source estimation demonstrated that the neural generators of M50, M100, and M200 components are located in the primary auditory cortex or in the vicinity of this region (with the highest response values in the Broadman areas 41 and 42) in both hemispheres (Fig. 2).

Table 2 summarizes the mean amplitudes and latencies for each component in both groups of children in the left and right hemispheres. To provide between-group comparison in the amplitudes and latencies of the auditory responses, we fitted linear mixed-effects models for each component separately (three models with amplitudes and three models with latencies as dependent variables), including the main effects of hemisphere (left vs. right), group (ASD vs. TD), stimulus (S1 vs. S2), and hemisphere × group × stimulus interaction as fixed effects and participants as a random intercept (predictors are significant at the $\alpha \leq 0.02$, according to Bonferroni correction).

M50 component

For the amplitude of M50, the results showed only a significant main effect of stimulus, indicating that the amplitude of M50 was lower for the S2, $\beta = -1.73$, SE = 0.53, $t = -3.24$, $P = 0.001$. No significant effects were observed for the latency of M50. The

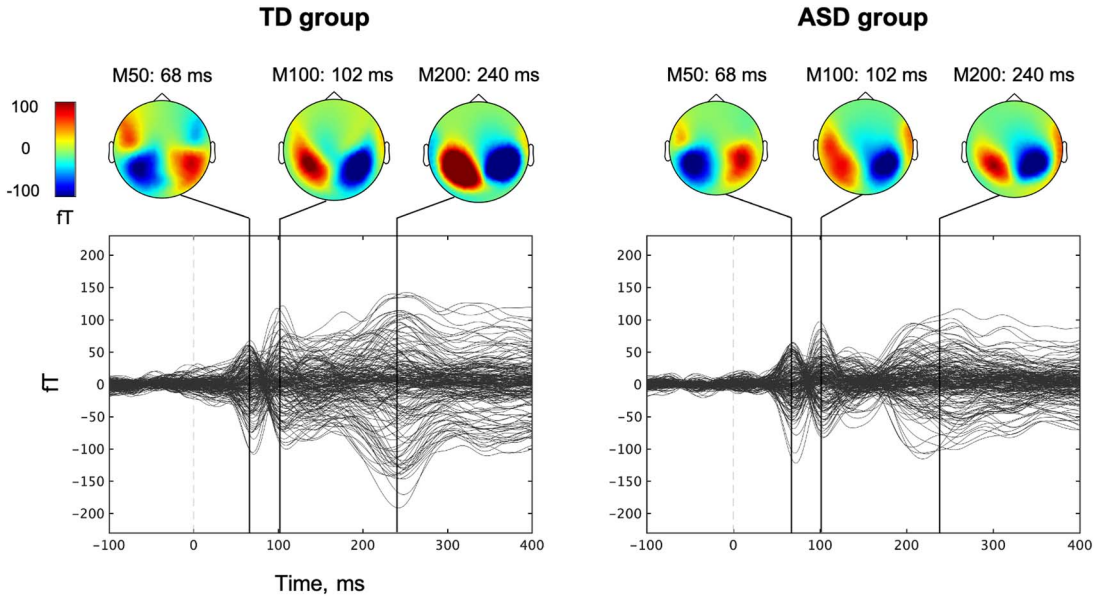

Fig. 1. The grand-averaged sensor-level "butterfly" plots of 204 gradiometers for ASD and TD groups of children. The black lines correspond to the MEG auditory components (M50, M100, and M200); top panels show the power distribution across the sensors at these timepoints.

full models' outcomes are presented in Supplementary Tables 1 and 2.

M100 component

For the amplitude of M100, as for M50, there was a significant main effect of stimulus so that the amplitude of M100 was lower for the S2, $\beta = -2.43$, SE = 0.44, $t = -5.52$, $P < 0.0001$; no effects were detected for the latency of M100. See Supplementary Tables 3 and 4 with full models' outcomes.

M200 component

For the amplitude of M200, we found a significant main effect of group, $\beta = 2.48$, SE = 0.65, $t = 3.80$, $P = 0.0003$, stimulus, $\beta = -1.32$, SE = 0.49, $t = -2.68$, $P = 0.008$, and group × stimulus interaction, $\beta = -1.85$, SE = 0.69, $t = -2.67$, $P = 0.008$. The follow-up model with nested contrasts showed that the amplitude of S1 M200 was reduced in the left auditory ROI in children with ASD in comparison to TD controls, $\beta = 3.31$, SE = 1.01, $t = 3.28$, $P = 0.001$; similarly to M50 and M100, the main effect of stimulus indicated lower amplitude for S2. For the latency of M200, the results revealed a main effect of stimulus, $\beta = -15.85$, SE = 5.88, $t = -2.65$, $P = 0.008$ so that the S2 had shorter latency than S1. The main effect of group was nonsignificant after correction for multiple comparisons, $\beta = -12.95$, SE = 6.10, $t = -2.12$, $P = 0.03$. See Supplementary Tables 5 and 6 with full models' outcomes.

Summarizing, between-group difference in the auditory responses was observed only for the amplitude of the late S1 M200 component in the left hemisphere of children with ASD with the evidence of reduced response.

Sensory gating effects

In order to compare sensory gating effects between groups, we calculated the S2/S1 ratio for each component for each child. The models included the main effect of hemisphere, the effect of group nested in each hemisphere and participants as a random intercept (the predictors are significant at the $\alpha \leq 0.02$, according to Bonferroni correction). The results for M50 and M100 showed neither significant main nor nested effects: M50, hemisphere, $\beta = -0.05$, SE = 0.08, $t = -0.58$, $P = 0.56$, hemisphere (left)/group (TD), $\beta = -0.15$, SE = 0.18, $t = -0.80$, $P = 0.43$, hemisphere (right)/group (TD), $\beta = -0.19$, SE = 0.18, $t = -1.03$, $P = 0.30$; M100, hemisphere, $\beta = -0.02$, SE = 0.05, $t = -0.35$, $P = 0.73$, hemisphere (left)/group (TD), $\beta = -0.09$, SE = 0.12, $t = -0.74$, $P = 0.46$, hemisphere (right)/group (TD), $\beta = -0.02$, SE = 0.12, $t = -0.16$, $P = 0.88$. By contrast, for M200, there was a significant main effect of hemisphere, $\beta = 0.24$, SE = 0.10, $t = 2.46$, $P = 0.018$, and a significant nested effect in the left hemisphere, $\beta = -0.58$, SE = 0.20, $t = -2.82$, $P = 0.006$ (Fig. 3A). According to the results, children with ASD had an altered sensory gating effect for the late M200 component in the left auditory ROI. The nested effect for the right hemisphere was nonsignificant: hemisphere (right)/group (TD), $\beta = -0.02$, SE = 0.21, $t = -0.09$, $P = 0.92$.

Relation of MEG auditory responses to phenotype in children with ASD

To analyze how atypical brain responses (amplitude of S1 M200 and M200 sensory gating in the left auditory ROI) were related to phenotype, we fitted two linear models with nine predictors: language skills (LPS and LCS), severity of autistic traits based on the five AQ "scales" (social skills, attention switching, attention to details, communication, and imagination), nonverbal IQ, and age (to account a variability in age). The effects were significant at the $\alpha \leq 0.025$, according to Bonferroni correction.

The first model with the amplitude of S1 M200 as a dependent variable revealed two statistically significant associations: a reduction of M200 amplitude was related to lower language comprehension skills and higher autistic traits on the "social skills" scale: LCS, $\beta = 10.64$, SE = 4.06, $t = 2.62$, $P = 0.025$; AQ social skills, $\beta = -0.32$, SE = 0.10, $t = -2.93$, $P = 0.014$ (Fig. 3B). The second model with M200 sensory gating effect as a dependent variable showed one statistically significant effect: more altered sensory gating was linked to higher autistic traits on the AQ "social skills" scale, $\beta = 0.20$, SE = 0.06, $t = 3.39$, $P = 0.007$ (Fig. 3B). Other predictors in both models were not significant after correction for multiple comparisons.

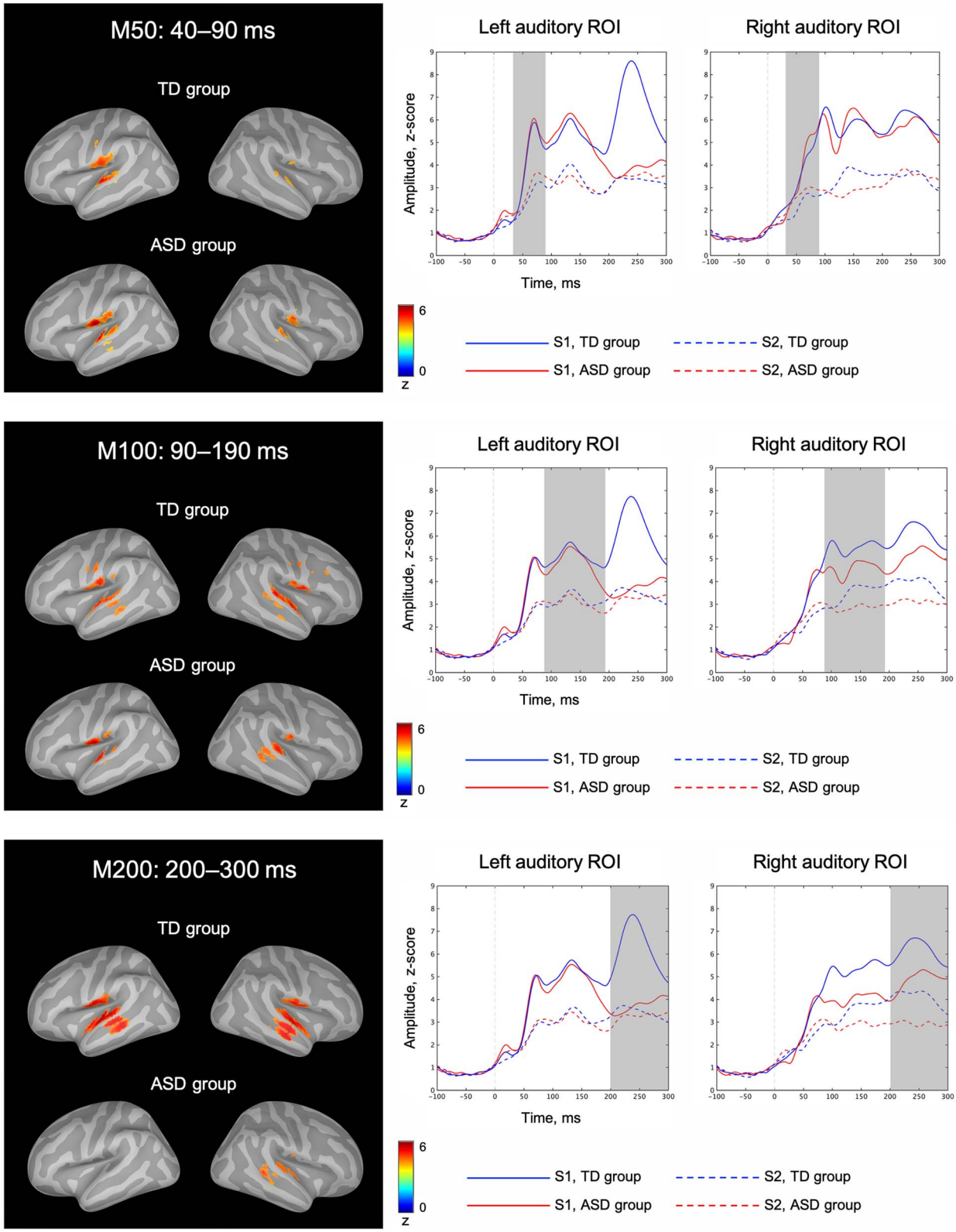

Fig. 2. Source localization of auditory components (M50, M100, and M200) in children with and without ASD in the left and right hemispheres: The left panel represents a z-score distribution of neural activity across the cortex averaged in the specific time intervals for the first (S1) click for each component (the amplitude threshold is set at 70% of the highest values); the right panel represents a timecourse of event-related field responses in the left and right auditory ROIs for the first (S1) and second (S2) clicks (gray bars correspond to the time windows).

Table 2. Amplitude and latency of auditory event-related fields in children with and without ASD, M ± SD.

Neural response	Group	
	ASD	TD
Amplitude, z-score		
Left auditory cortex		
M50 S1	5.45 ± 4.01	4.82 ± 3.52
M50 S2	3.40 ± 2.00	2.70 ± 1.70
M50 ratio	0.86 ± 0.74	0.71 ± 0.55
M100 S1	6.40 ± 2.66	6.41 ± 2.58
M100 S2	3.66 ± 1.70	3.62 ± 1.50
M100 ratio	0.69 ± 0.58	0.60 ± 0.23
M200 S1	4.42 ± 2.01	7.74 ± 4.44
M200 S2	3.99 ± 1.71	4.01 ± 1.37
M200 ratio	1.20 ± 1.53	0.62 ± 0.29
Right auditory cortex		
M50 S1	4.25 ± 4.70	3.87 ± 2.01
M50 S2	2.85 ± 1.32	2.63 ± 1.61
M50 ratio	0.96 ± 0.51	0.77 ± 0.48
M100 S1	5.34 ± 3.07	6.31 ± 2.83
M100 S2	3.22 ± 1.41	4.01 ± 1.47
M100 ratio	0.73 ± 0.35	0.71 ± 0.31
M200 S1	5.73 ± 1.99	7.38 ± 3.64
M200 S2	3.53 ± 1.52	4.76 ± 2.35
M200 ratio	0.72 ± 0.47	0.70 ± 0.26
Latency, ms		
Left auditory cortex		
M50 S1	69.30 ± 9.74	67.20 ± 8.04
M50 S2	68.00 ± 13.03	67.20 ± 13.55
M100 S1	137.1 ± 25.51	144.9 ± 21.19
M100 S2	134.3 ± 22.75	127.8 ± 18.64
M200 S1	256.1 ± 28.72	240.0 ± 14.65
M200 S2	247.6 ± 32.67	237.6 ± 25.84
Right auditory cortex		
M50 S1	66.4 ± 11.17	66.1 ± 12.30
M50 S2	63.9 ± 11.83	68.0 ± 11.68
M100 S1	129.4 ± 27.11	119.1 ± 25.89
M100 S2	143.0 ± 30.05	144.1 ± 26.51
M200 S1	257.9 ± 24.51	248.1 ± 23.26
M200 S2	234.7 ± 32.55	238.3 ± 27.75

Summarizing, altered brain responses to basic auditory stimuli in the left primary auditory cortex of children with ASD had a clinical/behavioral relevance.

Relation of MEG auditory responses to morphometric (MRI) characteristics in children with ASD

In order to reveal whether the left-hemispheric atypicality in the amplitude of M200 as well as in M200 sensory gating in children with ASD are related to structural brain characteristics, we fitted six linear models with MEG auditory responses as dependent variables and morphometric parameters (GM volume, GM thickness, and GI abstracted from the same region as M200) as predictors. The effects were significant at the $\alpha \leq 0.0085$ based on Bonferroni correction.

The results showed that the altered MEG responses in the primary auditory cortex were associated with structural cortical parameters: reduction of the M200 amplitude was related to a higher GI (and, thus, more altered cortical folding, see Kohli et al. 2019; Libero et al. 2019; Wallace et al. 2013); M200 sensory gating abnormality was related to higher GI and reduced GM thickness (Table 3, Fig. 3C). Between-group comparisons in GM thickness and GI of this cortical region confirmed atypically lower GM thickness in children with ASD, $\beta = 0.41$, SE = 0.16, $t = 2.58$, FDR-corrected $P = 0.02$, and a borderline effect with higher GI in ASD after correction for multiple comparisons, $\beta = -1.55$, SE = 0.84, $t = -1.84$, FDR-corrected $P = 0.07$ (Fig. 3D).

Discussion

The present study aimed to investigate the basic MEG auditory components (M50–M100–M200) in response to pure tone clicks at the source level and sensory gating effects in children with ASD, their relation to clinical phenotype and structural brain characteristics (GM volume, GM thickness, and GI). In general, we identified a reduction of M200 amplitude and altered M200 sensory gating effect in the left hemisphere in the ASD group; these alterations were associated (i) with lower language comprehension skills and higher presence of autistic traits in the social domain and (ii) a higher GI and reduced GM thickness.

The MEG source estimation has identified that the neural generators of the basic auditory components are located in the primary auditory cortex or in the vicinity of this region (with the highest response values in the Broadman areas 41 and 42) in both hemispheres in both groups, which is in line with the previous studies (eg Ponton et al. 2002; Edgar et al. 2015a; Roberts et al. 2019). Between-group comparisons in amplitudes, latencies, and sensory gating effects did not reveal any differences in M50 and M100 components, suggesting that the early stages of sound processing are intact in the ASD group. We hypothesized the delayed M50 and M100 latencies in children with ASD according to both existing studies as well as the recent comprehensive meta-analysis (eg Gage et al. 2003; Roberts et al. 2019; Williams et al. 2021), however, we did not observe these effects in our sample of participants. There can be multiple potential explanations for the absence of the effects, including, but not limited to, methodological differences between studies, such as the complexity of the auditory stimuli or MEG source estimation methods, as well as the highly heterogeneous nature of the ASD population, specifically, their language skills (eg Roberts et al. 2019; Jorgensen et al. 2021).

In comparison to early auditory components (M50 and M100), we identified a reduction of M200 amplitude as well as an altered M200 sensory gating effect in the left hemisphere in children with ASD, which is in line with the previous limited findings on atypicalities in the late auditory evoked potentials (eg Donkers et al. 2015; Yu et al. 2018). M200 occurs between the 200 and 300 ms time window after auditory stimulus onset, although it is still associated with the basic low-level processes but can also be related to high-order stimulus processing (involving attention) in comparison to M50 and M100 (Crowley and Colrain 2004; Wang et al. 2014). Interestingly, the alterations in both M200 amplitude and M200 sensory gating in children with ASD were observed specifically in the left hemisphere. Some authors have proposed that the abnormal M200 in individuals with ASD can have different etiology in different hemispheres mostly due to the maturational delay (see Edgar et al. 2015a). It is known that the left auditory cortex matures later than the right auditory cortex due to the demands of an increased number of connections that need to be coordinated with other regions involved in language processing (Poulsen et al. 2009; Edgar et al. 2016). Therefore, an atypical left-hemispheric M200 in children with ASD can be related to language skills, which are dominantly a

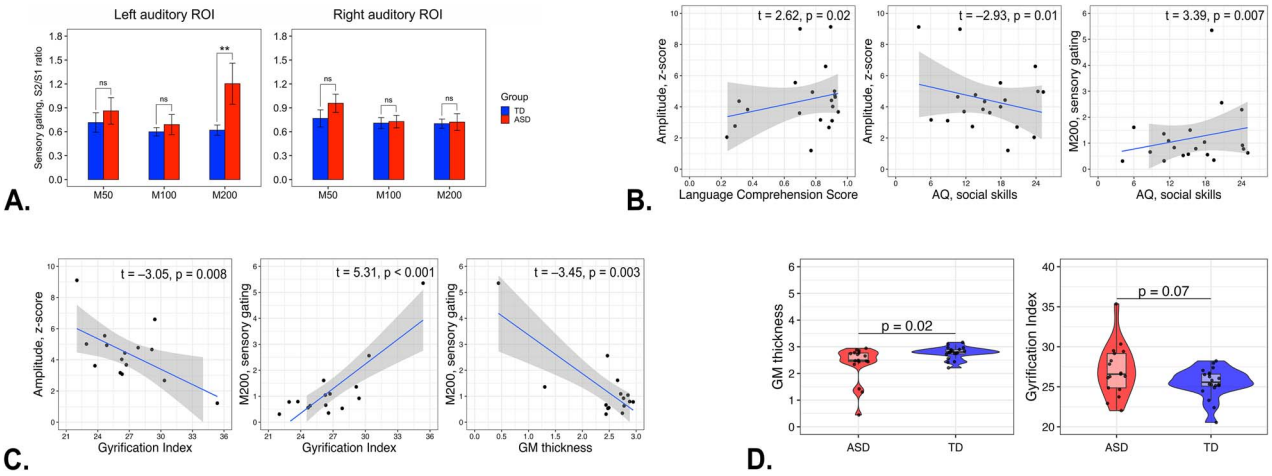

Fig. 3. Comparisons in functional and structural brain characteristics, their relation to each other and behavior in children with ASD: A) between-group differences for sensory gating effects for each auditory component (M50, M100, and M200): $*P < 0.05$, $**P < 0.01$, $***P < 0.001$, ns, nonsignificant; B) relations of the brain responses (amplitude of S1 M200 and M200 sensory gating in the left auditory cortex) to behavioral measures in children with ASD; C) associations between MEG auditory responses and morphometric characteristics; and D) between-group comparisons in morphometric parameters (GM thickness, GI).

Table 3. The relationships between MEG auditory responses and morphometric parameters (gray matter (GM) volume; GM thickness, gyrification index, GI) in children with ASD in the left primary auditory cortex.

Regressions	Estimate	SE	t	P
M200 amplitude ~				
GM volume	0.78	2.43	0.32	0.75
GM thickness	0.96	0.65	1.49	0.16
GI	−0.35	0.11	−3.05	**0.0080**
M200 sensory gating ~				
GM volume	−0.58	1.65	−0.36	0.73
GM thickness	−1.21	0.35	−3.45	**0.0036**
GI	0.31	0.06	5.31	**<0.0001**

The significance is set to $\alpha \leq 0.0085$, according to Bonferroni correction, and highlighted in bold (reported *P*-values are uncorrected).

"left-hemispheric" function (eg Hickok and Poeppel 2007; Ivanova et al. 2016).

Indeed, we found that the reduction of M200 amplitude in the language-dominant left auditory cortex was associated with lower language comprehension skills revealed in behavioral assessment in the ASD group. This is in line with the previous studies that have identified altered low-level auditory processing in the "core auditory area" and its relation to language impairment in ASD (eg Arutiunian et al. 2023a; Berman et al. 2016; Matsuzaki et al. 2019; Roberts et al. 2011, 2019, 2021). For example, delayed latencies of both M50/M100 and MMF have been identified to be related to language skills in ASD, including those individuals who are minimally verbal (Roberts et al. 2011, 2019). The reduced amplitude of another low-level neural response, i.e. auditory response to amplitude-modulated tones and sweeps, Auditory Steady-State Response has also been reported to be associated with lower language skills in children and youth with ASD (Arutiunian et al. 2023a; Roberts et al. 2021). In addition, we revealed that the left-hemispheric alterations in both M200 amplitude and M200 sensory gating were related to the greater severity of autistic traits in social domain, which is in agreement with some previous studies showing that temporal regions are usually related to social perception and communication in ASD (eg Bedford et al. 2020; Boddaert et al. 2004; Meresse et al. 2005; Parks et al. 2009).

We also identified that the functional alterations in M200 were related to anatomical brain characteristics in children with ASD. Specifically, reduced M200 amplitude was associated with increased gyrification (or GI), whereas altered M200 sensory gating was associated with an increased GI and reduced GM thickness in the primary auditory cortex. An atypically increased GI (which reflects the extensive cortical folding) and reduced GM thickness have been previously reported not only in individuals with ASD (Courchesne et al. 2011; Baribeau and Anagnostou 2013; Wallace et al. 2013; Libero et al. 2014, 2019; Kohli et al. 2019), but also in other disorders, such as schizophrenia (Edgar et al. 2012). Complementing the previous findings, we revealed that these anatomical characteristics of the primary auditory cortex in ASD contributed to MEG neural responses to basic auditory stimuli.

To conclude, in the present study, using a standard paired-clicks paradigm in MEG and anatomical brain characteristics abstracted from structural MRI, we revealed the left-hemispheric alterations in the functioning of the late neuromagnetic M200 component (reduced amplitude and abnormal sensory gating) in primary-school-aged children with ASD. Moreover, we showed that these abnormalities were associated with language comprehension and the severity of autistic traits in the social domain. Finally, we identified the relationships between the altered MEG responses and anatomical characteristics in the

primary auditory cortex in the ASD group. It is important to note, however, that the abnormal M200 sensory gating effect and its relation to clinical phenotype and to anatomical characteristics in the ASD group were most likely driven by the reduction and between-group differences in the M200 S1 amplitude. Therefore, perhaps, our autistic sample had difficulties in encoding auditory stimuli rather than auditory gating deficit.

The study has some limitations that should be highlighted here. First of all, although we comprehensively addressed MEG low-level auditory processing alterations in relation to structural brain characteristics and clinical phenotype in children with ASD, the sample size is not large enough. There is still a need to replicate and extend our findings in larger samples to reveal a potential to generalize the results. Second, sex distribution in the ASD group is not equal (25% girls); at the same time, some studies have identified that male and female ASD individuals can have different profiles with respect to brain functioning and language abilities (eg Neuhaus et al. 2021, 2022). Thus, future studies would benefit from including the same numbers of autistic males and females to replicate the effects identified in the present study. Third, the study did not provide any behavioral measures of sensory sensitivity to assess auditory hyper/hypo-reactivity and to analyze the relationships between these measures and auditory cortical responses. Fourth, we did not account for individual differences in hearing thresholds and loudness perception that can play a role in the strengths of auditory responses.

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Author contributions

Vardan Arutiunian (Conceptualization, Methodology, Investigation, Data curation, Formal analysis, Writing—original draft, Writing—review & editing, Project administration), Irina Buyanova (Investigation), Alina Minnigulova (Data curation, Formal analysis), Elizaveta Davydova (Investigation), Darya Pereverzeva (Investigation), Alexander Sorokin (Investigation), Svetlana Tyushkevich (Investigation), Uliana Mamokhina (Investigation), Kamilla Danilina (Investigation), and Olga Dragoy (Writing—Review & Editing, Resources). All authors read and approved the final manuscript.

Supplementary material

Supplementary material is available at *Cerebral Cortex* online.

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References

Alain C, Winkler I. 2012. Recording event-related brain potentials: Application to study auditory perception. In: *The human auditory cortex* Poeppel D, Overath T, Popper AN, Fay RR (eds), Vol. 43. Springer, New York, pp. 69–96. https://doi.org/10.1007/978-1-4614-2314-0_4.

American Psychiatric Association. 2013. *Diagnostic and statistical manual of mental disorders: DSM-5*, 5th edn. American Psychiatric Publication, Washington (DC); London. https://doi.org/10.1176/appi.books.9780890425596.

Arutiunian V et al. 2022. Language abilities of Russian primary-school-aged children with autism spectrum disorder: evidence from comprehensive assessment. *J Autism Dev Disord*. 52:584–599. https://doi.org/10.1007/s10803-021-04967-0.

Arutiunian V et al. 2023a. Neuromagnetic 40 Hz auditory steady-state response in the left auditory cortex is related to language comprehension in children with autism spectrum disorder. *Prog Neuro-Psychopharmacol Biol Psychiatry*. 122:110690. https://doi.org/10.1016/j.pnpbp.2022.110690.

Arutiunian V et al. 2023b. Structural brain abnormalities and their association with language impairment in school-aged children with autism spectrum disorder. *Sci Rep*. 13:1172. https://doi.org/10.1038/s41598-023-28463-w.

Arutiunian V et al. 2024. Abnormalities in both stimulus-induced and baseline MEG alpha oscillations in the auditory cortex of children with autism spectrum disorder. *Brain Struct Funct*. 229:1225–1242. https://doi.org/10.1007/s00429-024-02802-7.

Auyeung B, Baron-Cohen S, Wheelwright S, Allison C. 2008. The autism spectrum quotient: Children's version (AQ-Child). *J Autism Dev Disord*. 38:1230–1240. https://doi.org/10.1007/s10803-007-0504-z.

Baribeau DA, Anagnostou E. 2013. A comparison of neuroimaging findings in childhood onset schizophrenia and autism spectrum disorder: a review of the literature. *Front Psych*. 4:175. https://doi.org/10.3389/fpsyt.2013.00175.

Bates D, Mächler M, Bolker BM, Walker SC. 2015. Fitting linear mixed-effects models using lme4. *J Stat Softw*. 67:1–48. https://doi.org/10.18637/jss.v067.i01.

Bedford SA et al. 2020. Large-scale analyses of the relationship between sex, age and intelligence quotient heterogeneity and cortical morphometry in autism spectrum disorder. *Mol Psychiatry*. 25:614–628. https://doi.org/10.1038/s41380-019-0420-6.

Berman JI et al. 2016. Multimodal diffusion-MRI and MEG assessment of auditory and language system development in autism spectrum disorder. *Front Neurosci*. 10:30. https://doi.org/10.3389/fnana.2016.00030.

Boddaert N et al. 2004. Superior temporal sulcus anatomical abnormalities in childhood autism: a voxel-based morphometry MRI study. *NeuroImage*. 23:364–369. https://doi.org/10.1016/j.neuroimage.2004.06.016.

Bomba MD, Pang EW. 2004. Cortical auditory evoked potentials in autism: a review. *Int J Psychophysiol*. 53:161–169. https://doi.org/10.1016/j.ijpsycho.2004.04.001.

Chien Y-L, Hsieh MH, Gau SS-F. 2019. P50–N100–P200 sensory gating deficits in adolescents and young adults with autism spectrum disorders. *Prog Neuro-Psychopharmacol Biol Psychiatry*. 95:109683. https://doi.org/10.1016/j.pnpbp.2019.109683.

Courchesne E, Campbell K, Solso S. 2011. Brain growth across the life span in autism: age-specific changes in anatomical pathology. *Brain Res*. 1380:138–145. https://doi.org/10.1016/j.brainres.2010.09.101.

Crowley KE, Colrain IM. 2004. A review of the evidence of P2 being an independent component process: age, sleep and modality. *Clin Neurophysiol*. 115:732–744. https://doi.org/10.1016/j.clinph.2003.11.021.

Dale AM, Fischl B, Sereno MI. 1999. Cortical surface-based analysis: I. Segmentation and surface reconstruction. *NeuroImage*. 9:179–194. https://doi.org/10.1006/nimg.1998.0395.

Delorme A, Makeig S. 2004. EEGLAB: an open source toolbox for analysis of single-trial EEG dynamics including independent component analysis. *J Neurosci Methods*. 134:9–21. https://doi.org/10.1016/j.jneumeth.2003.10.009.

Demopoulos C et al. 2015. Deficits in auditory processing contribute to impairments in vocal affect recognition in autism spectrum disorders: a MEG study. *Neuropsychology*. 29:895–908. https://doi.org/10.1037/neu0000209.

Desikan RS et al. 2006. An automated labeling system for subdividing the human cerebral cortex on MRI scans into gyral based regions of interest. *NeuroImage*. 31:968–980. https://doi.org/10.1016/j.neuroimage.2006.01.021.

Destrieux C, Fischl B, Dale A, Halgren E. 2010. Automatic parcellation of human cortical gyri and sulci using standard anatomical nomenclature. *NeuroImage*. 53:1–15. https://doi.org/10.1016/j.neuroimage.2010.06.010.

Donkers FCL et al. 2015. Attenuated auditory event-related potentials and associations with atypical sensory response patterns in children with autism. *J Autism Dev Disord*. 45:506–523. https://doi.org/10.1007/s10803-013-1948-y.

Donkers FCL, Carlson M, Schipul SE, Belger A, Baranek GT. 2019. Auditory event-related potentials and associations with sensory patterns in children with autism spectrum disorder, developmental delay, and typical development. *Autism*. 24:1093–1110. https://doi.org/10.1177/1362361319893196.

Edgar JC et al. 2012. Temporal and frontal cortical thickness associations with M100 auditory activity and attention in healthy controls and individuals with schizophrenia. *Schizophr Res*. 140:250–257. https://doi.org/10.1016/j.schres.2012.06.009.

Edgar JC et al. 2014. Missing and delayed auditory responses in young and older children with autism spectrum disorder. *Front Hum Neurosci*. 8:417. https://doi.org/10.3389/fnhum.2014.00417.

Edgar JC et al. 2015a. Auditory encoding abnormalities in children with autism spectrum disorder suggest delayed development of auditory cortex. *Mol Autism*. 6:69. https://doi.org/10.1186/s13229-015-0065-5.

Edgar JC et al. 2015b. Neuromagnetic oscillations predict evoked-response latency delays and core language deficits in autism Spectrum disorders. *J Autism Dev Disord*. 45:395–405. https://doi.org/10.1007/s10803-013-1904-x.

Edgar JC et al. 2016. Translating adult electrophysiology findings to younger patient populations: difficulty measuring 40-Hz auditory steady-state response in typically developing children and children with autism spectrum disorder. *Dev Neurosci*. 38:1–14. https://doi.org/10.1159/000441943 2016.

Ferri R et al. 2003. The mismatch negativity and the P3a components of the auditory event-related potentials in autistic low-functioning subjects. *Clin Neurophysiol*. 114:1671–1680. https://doi.org/10.1016/S1388-2457(03)00153-6.

Gage NM, Siegel B, Callen M, Roberts TPL. 2003. Cortical sound processing in children with autism disorder: an MEG investigation. *Neuroreport*. 14:2047–2051. https://doi.org/10.1097/00001756-200311140-00008.

Green HL, Edgar JC, Matsuzaki J, Roberts TPL. 2020. Magnetoencephalography research in pediatric autism spectrum disorder. *Neuroimaging Clin N Am*. 30:193–203. https://doi.org/10.1016/j.nic.2020.01.001.

Haesen B, Boets B, Wagemans J. 2011. A review of behavioural and electrophysiological studies on auditory processing and speech perception in autism spectrum disorders. *Res Autism Spectr Disord*. 5:701–714. https://doi.org/10.1016/j.rasd.2010.11.006.

Hickok G, Poeppel D. 2007. The cortical organization of speech processing. *Nat Rev Neurosci*. 8:393–402. https://doi.org/10.1038/nrn2113.

Huang MX, Mosher JC, Leahy RM. 1999. A sensor-weighted overlapping-sphere head model and exhaustive head model comparison for MEG. *Phys Med Biol*. 44:423–440. https://doi.org/10.1088/0031-9155/44/2/010.

Hudac CM et al. 2018. Early enhanced processing and delayed habituation to deviance sounds in autism spectrum disorder. *Brain Cogn*. 123:110–119. https://doi.org/10.1016/j.bandc.2018.03.004.

Hyde KL, Samson F, Evan AC, Mottron L. 2010. Neuroanatomical differences in brain areas implicated in perceptual and other core features of autism revealed by cortical thickness analysis and voxel-based morphometry. *Hum Brain Mapp*. 31:556–566. https://doi.org/10.1002/hbm.20887.

Ivanova MV et al. 2016. Diffusion-tensor imaging of major white matter tracts and their role in language processing in aphasia. *Cortex*. 85:165–181. https://doi.org/10.1016/j.cortex.2016.04.019.

Ivanova MV, Zhong A, Turken A, Baldo JV, Dronkers NF. 2021. Functional contribution of the arcuate fasciculus to language processing. *Front Hum Neurosci*. 15:672665. https://doi.org/10.3389/fnhum.2021.672665.

Jeste SS, Nelson CA. 2009. Event related potentials in the understanding of autism spectrum disorders: an analytical review. *J Autism Dev Disord*. 39:495–510. https://doi.org/10.1007/s10803-008-0652-9.

Jorgensen AR, Whitehouse AJO, Fox AM, Maybery MT. 2021. Delayed cortical processing of auditory stimuli in children with autism spectrum disorder: a meta-analysis of electrophysiological studies. *Brain Cogn*. 150:105709. https://doi.org/10.1016/j.bandc.2021.105709.

Kaufman AS, Kaufman NL. 2004. *Kaufman assessment battery for children*. 2nd ed. Circle Pines, MN: American Guidance Service.

Key APF, Dove GO, Maguire MJ. 2005. Linking brainwaves to the brain: an ERP primer. *Dev Neuropsychol*. 27:183–215. https://doi.org/10.1207/s15326942dn2702_1.

Kikuchi M, Yoshimura Y, Mutou K, Minabe Y. 2016. Magnetoencephalography in the study of children with autism spectrum disorder. *Psychiatry Clin Neurosci*. 70:74–88. https://doi.org/10.1111/pcn.12338.

Kjelgaard MM, Tager-Flusberg H. 2001. An investigation of language impairment in autism: implications for genetic subgroups. *Lang Cogn Process*. 16:287–308. https://doi.org/10.1080/01690960042000058.

Kohli JS et al. 2019. Local cortical Gyrification is increased in children with autism spectrum disorders, but decreases rapidly in adolescents. *Cereb Cortex*. 29:2412–2423. https://doi.org/10.1093/cercor/bhy111.

Leader G, Tuohy E, Chen JL, Mannion A, Gilroy SP. 2020. Feeding problems, gastrointestinal symptoms, challenging behavior and sensory issues in children and adolescents with autism spectrum disorder. *J Autism Dev Disord*. 50:1401–1410. https://doi.org/10.1007/s10803-019-04357-7.

Libero LE, DeRamus TP, Deshpande HD, Kana RK. 2014. Surface-based morphometry of the cortical architecture of autism spectrum disorders: volume, thickness, area, and gyrification. *Neuropsychologia*. 62:1–10. https://doi.org/10.1016/j.neuropsychologia.2014.07.001.

Libero LE, Schaer M, Li DD, Amaral DG, Nordahl CW. 2019. A longitudinal study of local Gyrification index in young boys with

autism spectrum disorder. *Cereb Cortex*. 29:2575–2587. https://doi.org/10.1093/cercor/bhy126.

Lin Fa-H et al. 2006. Assessing and improving the spatial accuracy in MEG source localization by depth-weighted minimum-norm estimates. *NeuroImage*. 31:160–171. https://doi.org/10.1016/j.neuroimage.2005.11.054.

Lord C et al. 2012. *Autism diagnostic observation schedule*. 2nd ed. Torrance, CA: Western Psychological Services.

Luck SJ. 2014. *An introduction to even-related potential technique*. 2nd ed. Cambridge, MA: The MIT Press.

Marco EJ, Hinkley LBN, Hill SS, Nagarajan SS. 2011. Sensory processing in autism: a review of neurophysiologic findings. *Pediatr Res*. 69:48R–54R. https://doi.org/10.1203/PDR.0b013e3182130c54.

Martineau J, Garreau B, Barthelemy C, Lelord G. 1984. Evoked potentials and P300 during sensory conditioning in autistic children. *Ann N Y Acad Sci*. 425:362–369. https://doi.org/10.1111/j.1749-6632.1984.tb23557.x.

Matson JL, Rieske RD, Williams LW. 2013. The relationship between autism spectrum disorders and attention-deficit/hyperactivity disorder: an overview. *Res Dev Disabil*. 34:2475–2484. https://doi.org/10.1016/j.ridd.2013.05.021.

Matsuzaki J et al. 2019. Abnormal auditory mismatch fields are associated with communication impairment in both verbal and minimally verbal / nonverbal children who have autism spectrum disorder. *Autism Res*. 12:1225–1235. https://doi.org/10.1002/aur.2136.

Matsuzaki J et al. 2020. Delayed auditory evoked responses in autism spectrum disorder across the life span. *Dev Neurosci*. 41, 41: 223–233. https://doi.org/10.1159/000504960.

Meresse IG et al. 2005. Autism severity and temporal lobe functional abnormalities. *Ann Neurol*. 58:466–469. https://doi.org/10.1002/ana.20597.

Näätänen R, Picton T. 1987. The N1 wave of the human electric and magnetic response to sound: a review and an analysis of the component structure. *Psychophysiology*. 24:375–425. https://doi.org/10.1111/j.1469-8986.1987.tb00311.x.

Näätänen R, Winkler I. 1999. The concept of auditory stimulus representation in cognitive neuroscience. *Psychol Bull*. 125:826–859. https://doi.org/10.1037/0033-2909.125.6.826.

Neuhaus E et al. 2021. Resting state EEG in youth with ASD: age, sex, and relation to phenotype. *J Neurodev Disord*. 13:33. https://doi.org/10.1186/s11689-021-09390-1.

Neuhaus E et al. 2022. Language and aggressive Behaviors in male and female youth with autism Spectrum disorder. *J Autism Dev Disord*. 52:454–462. https://doi.org/10.1007/s10803-020-04773-0.

Orekhova EV et al. 2008. Sensory gating in young children with autism: relation to age, IQ, and EEG gamma oscillations. *Neurosci Lett*. 434:218–223. https://doi.org/10.1016/j.neulet.2008.01.066.

Parks LK et al. 2009. Neural correlates of communication skills and symptom severity in autism: a voxel-based morphometry study. *Res Autism Spectr Disord*. 3:444–454. https://doi.org/10.1016/j.rasd.2008.09.004.

Peirce JW. 2007. PsychoPy – psychophysics software in python. *J Neurosci Methods*. 162:8–13. https://doi.org/10.1016/j.jneumeth.2006.11.017.

Polyak A, Kubina RM, Girirajan S. 2015. Comorbidity of intellectual disability confounds ascertainment of autism: implications for genetic diagnosis. *Neuropsychiatr Genet*. 168:600–608. https://doi.org/10.1002/ajmg.b.32338.

Ponton C, Eggermont JJ, Khosla D, Kwong B, Don M. 2002. Maturation of human central auditory system activity: separating auditory evoked potentials by dipole source modeling. *Clin Neurophysiol*. 113:407–420. https://doi.org/10.1016/S1388-2457(01)00733-7.

Port RG et al. 2015. Prospective MEG biomarkers in ASD: pre-clinical evidence and clinical promise of electrophysiological signatures. *Yale J Biol Med*. 88:26–36.

Port RG et al. 2016. Maturation of auditory neural processes in autism spectrum disorder – a longitudinal MEG study. *NeuroImage Clin*. 11:566–577. https://doi.org/10.1016/j.nicl.2016.03.021.

Poulsen C, Picton TW, Paus T. 2009. Age-related changes in transient and oscillatory brain responses in auditory stimulation during early adolescence. *Dev Sci*. 12:220–235. https://doi.org/10.1111/j.1467-7687.2008.00760.x.

R Core Team. 2019. *R: a language and environment for statistical computing*. Vienna: R Foundation for Statistical Computing. https://www.R-project.org/.

Raven J. 2000. The Raven's progressive matrices: change and stability over culture and time. *Cogn Psychol*. 41:1–48. https://doi.org/10.1006/cogp.1999.0735.

Roberts TPL et al. 2010. MEG detection of delayed auditory evoked responses in autism spectrum disorders: toward an imaging biomarker for autism. *Autism Res*. 3:8–18. https://doi.org/10.1002/aur.111.

Roberts TPL et al. 2011. Auditory magnetic mismatch field latency: a biomarker for language impairment in autism. *Biol Psychiatry*. 70: 263–269. https://doi.org/10.1016/j.biopsych.2011.01.015.

Roberts TPL et al. 2019. Delayed M50/M100 evoked response component latency in minimally verbal/nonverbal children who have autism spectrum disorder. *Mol Autism*. 10:34. https://doi.org/10.1186/s13229-019-0283-3.

Roberts TPL et al. 2020. A multimodal study of the contributions of conduction velocity to the auditory evoked Neuromagnetic response: anomalies in autism Spectrum disorder. *Autism Res*. 13: 1730–1745. https://doi.org/10.1002/aur.2369.

Roberts TPL et al. 2021. Magnetoencephalography studies of the envelope following response during amplitude-modulated sweeps: diminished phase synchrony in autism Spectrum disorder. *Front Hum Neurosci*. 15:787229. https://doi.org/10.3389/fnhum.2021.787229.

Robertson CE, Baron-Cohen S. 2017. Sensory perception in autism. *Nat Rev Neurosci*. 18:671–684. https://doi.org/10.1038/nrn.2017.112.

Sysoeva OV, Molholm S, Djukic A, Frey H-P, Foxe JJ. 2020. Atypical processing of tones and phonemes in Rett syndrome as biomarkers of disease progression. *Transl Psychiatry*. 10:188. https://doi.org/10.1038/s41398-020-00877-4.

Tadel F, Baillet S, Mosher JC, Pantazis D, Leahy RM. 2011. Brainstorm: a user-friendly application for MEG / EEG analysis. *Comput Intell Neurosci*. 2011:1–13. https://doi.org/10.1155/2011/879716.

Taulu S, Simola J. 2006. Spatiotemporal signal space separation method for rejecting nearby interference in MEG measurements. *Phys Med Biol*. 51:1759–1768. https://doi.org/10.1088/0031-9155/51/7/008.

Wallace GL et al. 2013. Increased gyrification, but comparable surface area in adolescents with autism spectrum disorders. *Brain*. 136:1956–1967. https://doi.org/10.1093/brain/awt106.

Wang Y et al. 2014. Overlapping auditory M100 and M200 abnormalities in schizophrenia and bipolar disorder: a MEG study. *Schizophr Res*. 160:201–207. https://doi.org/10.1016/j.schres.2014.10.042.

Wechsler D. 1991. *The Wechsler intelligence scale for children*. 3rd ed. San Antonio, TX: The Psychological Corporation.

Wickham H. 2016. *Ggplot 2: elegant graphics for data analysis*. Springer-Verlag, New York. https://doi.org/10.1007/978-3-319-24277-4.

Williams ZJ, Abdelmessih PG, Key AP, Woynaroski TG. 2021. Cortical auditory processing of simple stimulus is altered in autism: a meta-analysis of auditory evoked responses. *Biol Psychiatry Cogn Neurosci Neuroimaging*. 6:767–781. https://doi.org/10.1016/j.bpsc.2020.09.011.

Woods DL. 1995. The component structure of the N1 wave of the human auditory evoked potential. *Electroencephalogr Clin Neurophysiol Suppl*. 44:102–109.

World Health Organization. 2016. *International statistical classification of diseases and related health problems: ICD-10*. 5th ed. Geneva: WHO Press.

Yu L, Wang S, Huang D, Wu X, Zhang Y. 2018. Role of intertrial phase coherence in atypical auditory evoked potentials to speech and nonspeech stimuli in children with autism. *Clin Neurophysiol*. 129:1374–1382. https://doi.org/10.1016/j.clinph.2018.04.599.

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