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Auditory Magnetic Mismatch Field Latency: A Biomarker for Language Impairment in Autism

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Abstract

Background—Auditory processing abnormalities are frequently observed in Autism Spectrum Disorders (ASD), and these abnormalities may have sequelae in terms of clinical language impairment (LI). The present study assessed associations between language impairment and the amplitude and latency of the superior temporal gyrus magnetic mismatch field (MMF) in response to changes in an auditory stream of tones or vowels.

Methods—51 children with ASD and 27 neurotypical controls, all aged 6–15 years, underwent neuropsychological evaluation, including tests of language function, as well as magnetoencephalographic (MEG) recording during presentation of tones and vowels. The MMF was identified in the difference waveform obtained from subtraction of responses to standard stimuli from deviant stimuli.

Results—MMF latency was significantly prolonged ($p < 0.001$) in children with ASD compared to neurotypical controls. Furthermore, this delay was most pronounced (~ 50 ms) in children with concomitant LI, with significant differences in latency between children with ASD with LI and those without ($p < 0.01$). Receiver operator characteristic analysis indicated a sensitivity of 82.4% and specificity of 71.2% for diagnosing LI based on MMF latency.

Conclusion—Neural correlates of auditory change detection (the MMF) are significantly delayed in children with ASD, and especially those with concomitant LI suggesting both a neurobiological basis for LI as well as a clinical biomarker for LI in ASD.

Descriptors

autism spectrum disorders; mismatch negativity; language impairment; magnetoencephalography; biomarker; electrophysiology

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Introduction

Autism spectrum disorders (ASD) are characterized by disabilities in social interactions, communication, and stereotypical behaviors, with prevalence ~1% in children in the USA[1]. Language abilities in ASD are highly variable, with difficulties ranging from mild to severe impairments in pragmatics and/or social communication [2], with a subset of ASD individuals having language problems characteristic of those observed in developmental language impairment (LI) disorders. Mounting electrophysiological evidence suggests that deficits in discriminating rapid changes in sound may be associated with impaired speech processing in children suffering from developmental language disorders [3-5]. Furthermore, electrophysiological evidence also indicates that a fundamental feature of ASD is abnormal cortical processing of auditory stimuli [6-10]. Therefore electrophysiological examination of speech sounds in individuals with autism may help to identify the neural correlates of auditory deficits contributing to co-morbid LI.

Given that language impairment in ASD may be associated with dysfunction in basic auditory sound processing, an assessment of mechanisms, such as sound discrimination, early in the auditory pathway could be used to address: (i) whether autistic children with and without LI exhibit a more pronounced deficit in speech sound processing and (ii) whether the severity of the neuronal deficit correlates with the degree of LI. In the present study, magnetoencephalography (MEG) was used to record the auditory mismatch response in order to probe speech sound discrimination in children on the autism spectrum with and without concomitant LI. MEG is a non-invasive neuroimaging technique that provides measures of cortical neural activity on a millisecond timescale and with relatively good spatial resolution [11]. Due to the nature of the responses generated by auditory neurons in the supratemporal plane, MEG is well suited for studying basic auditory activity, as cortical generators of evoked auditory responses are favourably positioned to produce strong currents for MEG recordings [12].

The mismatch negativity (MMN)[13] and its magnetic analog, the mismatch field (MMF), is of particular interest in assessing auditory discrimination. The MMN/MMF is a neurophysiological index of auditory change detection that can be elicited in absence of focused attention [14]. The response is typically elicited using an auditory odd-ball paradigm, where listeners are presented a series of stimuli, some frequently (standards) and others infrequently presented (deviants). Relative to the response evoked by standard stimuli, 100-300 ms after stimulus onset deviant stimuli evoke a more pronounced response. In healthy populations, the time course of the MMN/MMF response is considered an indicator of change detection and has been used to probe speech-discrimination [15-19]. Atypical MMN responses have been reported, albeit inconsistently, in populations suffering from developmental language disorders [3]. Thus, the MMN is considered a promising tool for investigating central auditory dysfunction.

Studies in children and adults on the autism spectrum show varied MMN/MMF findings. In Asperger's Syndrome, reduced MMN amplitude and delayed latency was found during speech prosody discrimination in children and adults [20,21]. In children with autism, Lepisto et al. documented differential MMN amplitude in response to temporal cues in speech. The authors suggested that in autistic subjects hypersensitivity to pitch changes adversely affects the ability to discriminate speech sounds, which requires abstracting invariant cue features from varying auditory input [22,23]. Findings on MMN latency in autism are mixed, with some reports suggesting an intact MMN response in ASD. In high-functioning autistic children, Čepionienė et al. reported no difference in MMN latency when varying the complexity of tonal and vowel stimuli [24]. Kemner *et al.* [25] also reported an absence of abnormalities in speech-sound-elicited MMN in children with autism. However,

evidence for an abnormal MMN response in ASD was demonstrated by Jansson-Verkasalo and colleagues who found bilaterally delayed MMN following tones in ASD as well as a right-hemisphere delay following consonant changes in syllabic stimuli [26]. Oram-Cardy [27] reported delayed MMF responses in autism with LI. These delays were not specific to speech, being equivalent for vowel contrasts and acoustically matched tone contrasts. Differences in methods and population characteristics as well as small sample size likely contribute to discrepant findings in the literature; it remains to be determined whether MMN/MMF time course is predictive of LI in autism.

In the present study, the MMF to tone and speech sounds was examined in a large cohort of children with ASD with language impairment (ASD/+LI), children with ASD without language impairment (ASD/-LI), and in age-matched typically developing (TD) controls. MEG measurements probed superior temporal gyrus (STG) auditory MMF brain functioning in two conditions. First, standard and deviant stimuli were sinusoidal tones with carrier frequencies identical to the first formant of the vowel stimuli used in the second condition (300Hz and 700Hz). English vowel-like sounds /u/ and /a/ were presented in the second condition. It was hypothesized that delays in MMF latency in children with ASD/+LI would be observed, indicating an impairment in acoustic/vowel change detection at an early perceptual level.

Methods

Participants

Subjects with ASD were recruited from the Regional Autism Center of The Children's Hospital of Philadelphia (CHOP), the Neuropsychiatry program of the Department of Psychiatry of the University of Pennsylvania School of Medicine, and from local and regional parent support groups such as ASCEND (Asperger Syndrome Information Alliance for Greater Philadelphia), Autism Society of America and Autism Speaks. All children screened for inclusion in the ASD sample had a prior ASD diagnosis made by an expert clinician, typically a developmental pediatrician in the Regional Autism Center. The original diagnosis was made after extensive clinical interview, documentation of DSM-IV criteria for ASD, and use of various ASD diagnostic tools, such as the Childhood Autism Rating Scale and the Autism Diagnostic Observation Schedule. TD subjects were recruited through newspaper advertisements and from pediatric practices of the CHOP primary care network.

Research participants made two visits. During the first visit, clinical and diagnostic testing was performed to confirm referral diagnosis, to administer neuropsychological tests, and to ensure that TD children met inclusion criteria. Assessments were performed by licensed child psychologists with expertise in autism. Given the extensive clinical evaluations upon which original diagnosis was made, an abbreviated diagnostic battery was used to confirm diagnosis. Specifically, the ASD diagnosis was confirmed with gold standard diagnostic tools, including direct observation with the *Autism Diagnostic Observation Schedule* [28] and parent report on the *Social Communication Questionnaire* [29]. Dimensional symptom severity ratings were also obtained by parent report on the *Social Responsiveness Scale* [30]. Asperger's Disorder symptomatology was measured with the *Krug Asperger's Disorder Index* [31]. For final inclusion in the ASD group (including children with diagnosis of Asperger's Syndrome), children were required to exceed established cut-offs on both the ADOS and SCQ. An SCQ cut-off score of 12 in conjunction with an ADOS Autism-Spectrum cut-off score (of 7) was adopted to maximize the likelihood of correctly classifying children as ASD. In prior studies, combining the ADOS with an SCQ cut-off score of 12 resulted in specificity that is comparable to that of the combination of the ADOS and ADI-R (0.86), although sensitivity is modestly low (0.76). To confirm presence of LI, all subjects were evaluated with the *Clinical Evaluation of Language Fundamentals – 4th*

edition [32]. The ASD group with language impairment (ASD/+LI) was comprised of subjects with a *CELF-4* Core Language score below the 16th percentile. The ASD group without LI (ASD/-LI) performed at or above the 16th percentile on the *CELF-4*. To rule out global cognitive delay, all subjects were required to score at or above the 5th percentile (SS> 75) on the Perceptual Reasoning Index (PRI) of the *Wechsler Intelligence Scale for Children-IV* [33].

Inclusion criteria for the TD children included scoring below the cut-off for ASD on all domains of the ADOS and on parent questionnaires, and performance above the 16th percentile on the *CELF-4*. In addition to the above inclusion criteria, subjects were native English speakers and had no known genetic syndromes, neurological (e.g., cerebral palsy) or sensory impairments. The study was approved by the CHOP Institutional Review Board and all participants' legal guardian(s) gave informed written consent. Where competent to do so, children over 7 years gave verbal assent.

78 participants between the ages of 6-15 years were recruited (51 ASD, 49M, 2F; 27 TD, 12M, 15F). Within the ASD group, 33 were classified as ASD/-LI and 18 as ASD/+LI. ASD and TD groups did not differ in age (9.4 ± 2.1 vs. 10.1 ± 2.4 years, mean $\pm$ SD, $p=0.19$). Demographics are shown in Table 1.

Auditory Stimuli—Task Procedures

Tone stimuli consisted of 300 and 700Hz sinusoidal tones 300ms in duration (digitized at 44.1kHz, with a 40ms rise time). The carrier frequencies of tone stimuli were chosen to correspond with the first formant frequencies of the vowel stimuli. The vowels /a/ and /u/ were synthesized as described in [34], 300ms in duration (digitized at 44.1kHz, and with a 50ms rise time). For each condition (tone, vowel) the stimuli were pseudorandomly arranged in separate classic odd-ball sequences [35]. A total of 760 stimuli were presented in each sequence, with deviant stimuli occurring randomly with probability of 15%. Stimuli were separated by stimulus onset asynchrony of 700 ms, with the condition that two deviants never occurred in succession. So that the standard and deviant stimuli were physically identical, subjects were administered two tasks per condition (i.e., tone or vowel conditions), with the status of each stimulus inverted across tasks (i.e., either standard or deviant). Thus, for each subject, 4 separate oddball sequences were presented, resulting in approximately 9 minutes of data acquisition per recording. The order of oddball blocks was fixed across subjects: tone tasks followed by vowel tasks.

Auditory stimuli were presented using Eprime v1.1 experimental software (Psychology Software Tools Inc., Pittsburgh, PA). Auditory stimuli were delivered via a sound pressure transducer and sound conduction tubing to the subject's peripheral auditory canal via eartip inserts (ER3A, Etymotic Research, Illinois, USA). Prior to the MEG exam, each participant's hearing threshold was determined; auditory stimuli were presented binaurally 45 dB above sensation level.

MEG Recordings

Recordings were performed at the Lurie Family Foundations' MEG Imaging Center in a magnetically shielded room using a whole-cortex 275-channel MEG system (VSM MedTech Inc., Coquitlam, BC). At the start of the session, three head-position indicator coils were attached to the scalp. These coils provided specification of the position and orientation of the MEG sensors relative to the head. Because it was necessary for the participant's head to remain in the same place in the MEG helmet across the recording session, foam wedges were inserted between the side of the participant's head and the inside of the helmet to minimize head motion. To reduce subject fatigue and encourage an awake

state during acquisition, subjects viewed a silent movie projected on to a screen positioned at a comfortable viewing distance.

To identify eye-blink activity, the electro-oculogram (EOG; bipolar oblique, upper right and lower left sites) was collected. Electrodes were also attached to the left and right clavicle for electrocardiogram (ECG) recording. After a band-pass filter (0.03 - 150Hz), EOG, ECG, and MEG signals were digitized at 1200Hz with 3rd order gradiometer noise reduction for MEG data.

MEG Data Analysis

Analyses were completed blind to diagnosis. For each condition, trials were defined by epochs of 130ms pre-stimulus to 470ms post-stimulus. To correct for blink artifacts, a typical eye-blink was manually identified in the raw data (including EOG) for each participant. The pattern search function in BESA 5.2 (MEGIS Software GmbH, Gräfelting, Germany) was used to scan the raw data to identify other blinks and compute an average eye-blink topography across MEG sensors. An eye-blink was modeled by its first PCA component topography, typically accounting for >99% of the variance. In addition to eye-blink activity, average heartbeat topography was also computed and modeled by the first two PCA components, typically accounting for >85% of the variance. Additional artifact removal from MEG data included signals exceeding amplitude (>1200fT/cm) and magnetic gradient (>800fT/cm/sample) criteria. Non-contaminated epochs were averaged according to stimulus type and band-pass filtered between 1Hz (6dB/octave, forward) and 40 Hz (48dB/octave, zero-phase).

All 275 channels of MEG sensor data were transferred into brain source space where waveforms modeled source activities. A standard source model was applied to each subject that included left and right STG dipole sources (placed at Heschl's gyrus, $x=\pm 37.27$, $y=-19.71$, $z=17.35$ in MNI space), and seven fixed regional sources that model extraneous brain activity [36-38]. A previous study has shown that the use of a standard source model provides MMF results closely comparable with results obtained via single subject dipole fitting [38], and in the present study the use of such an observer-independent method for MEG analysis was preferred in order to reduce the chance of bias and so that in each subject the same source model could be applied across the four different odd-ball tasks. The eye-blink and heartbeat source vectors were also included in each participant's source model to remove eye-blink and heartbeat activity [39,40]. The final model served as a spatial filter for the projection of raw MEG sensor data into source space [41,42].

To measure MMF STG amplitude and latency, bilateral STG source waveforms were exported from BESA 5.2 and read into MatLab software (Mathworks, Natick, MA). For each condition, the MMF was obtained by subtracting the left and right STG response to the standard version of the stimulus from the deviant version of the same stimulus (e.g. deviant / a/ minus standard /a/). This resulted in four MMF waveforms for each hemisphere, with each difference waveform corresponding to one of the four stimuli (300Hz, 700Hz, /u/, /a/). MMF latency and amplitude were defined as the maximal deflection in the difference waveform, occurring approximately 150–350 ms post stimulus onset. For each subject, MMF activity was accepted on the condition that (i) the mismatch response occurred after a detectable 50 ms evoked response (M50) to the deviant stimuli, and (ii) the mismatch response was present in at least one odd-ball sequence. MMF scoring was performed by a reader blind to subject diagnosis.

Group Comparisons

Linear mixed modeling assessed the effect of Group (TD, ASD/-LI, ASD/+LI), Hemisphere (Left/Right), Frequency (Low/High) and Stimulus (Tone/Vowel), with MMF latency and amplitude as dependent variables. Mixed modeling offers several advantages over a general linear approach to modeling unbalanced data [43,44]. In particular, given repeated measures, mixed modeling is better suited for correlated data and unequal variance arising from repeated measurements from individual subjects. Given associations between age and auditory measures [45,46], age was included as a covariate. Similarly, a measure of non-verbal IQ, the PRI of the WISC-IV was included as a potential co-variate. Bonferroni correction was applied to account for multiple comparisons. Finally, receiver operator characteristic analysis tested the sensitivity and specificity of delayed MMF latency as a predictor of clinical LI.

Results

Table 2 shows the mean and range of accepted deviant and standard trials for each group. In general, ASD subjects had slightly noisier data, resulting in fewer accepted epochs in the ASD than TD group for both standard and deviant stimuli. Although the TD group had more accepted trials than the ASD group, examination of Table 2 shows that the difference between groups was small and, as such, it is unlikely that the MMF findings are due to group differences in trial numbers (i.e., the number of accepted trials between groups is not sufficient to result in significant between-group signal-to-noise ratios).

Of the accepted trials the MMF was computed as the difference between each stimulus presented as a standard and as a deviant. In the tone condition, a viable MMF was scored 44% and 61% of the time in the ASD/-LI and ASD/+LI groups, and 65% of the time in the TD group. For vowels, the MMF was accepted 61% and 75% of the time in ASD/-LI and ASD/+LI groups, and 71% of the time in the TD group.

The age-covaryed Group X Hemisphere X Frequency X Stimulus linear mixed model showed a significant main effect of Group on MMF latency, $F_{(2,301)}$, $p < 0.001$. Simple-effects analyses revealed MMF latency differences between all groups: TD versus ASD/-LI ($p < 0.001$), TD versus ASD/+LI ($p < 0.001$), and ASD/-LI versus ASD/+LI ($p < 0.01$). Examining effect sizes, Cohen's d for each pairwise comparison were: ASD/-LI vs TD=1.89; ASD/+LI vs TD=3.11; ASD/+LI vs ASD/-LI=1.37. Figure 1 shows the grand average of tone MMF waveforms for the three groups (collapsing across hemisphere and frequency).

Figure 2 shows MMF latencies for each group, collapsing across Hemisphere, Stimulus, and Frequency (the group age-corrected means were: ASD/+LI 228.73 ± 5.82 ms; ASD/-LI: 208.68 ± 3.26 ms; TD: 177.27 ± 2.72 ms). No other MMF latency main effects or interactions were observed. Re-running linear mixed model analyses with perceptual reasoning index (PRI) as a covariate (reflecting non-verbal IQ), the simple effects group findings remained unchanged with significant ($p < 0.001$) differences between all pairwise TD, ASD/-LI and ASD/+LI contrasts.

Given the unequal ratio of males to females between groups, additional linear mixed model analysis of MMF latency was conducted for the TD group. In particular, to assess an effect of gender on MMF latency in the TD group, a Type III fixed-effects model was fitted to the data for within-subject factors GENDER, HEMISPHERE, and FREQUENCY, with AGE as a covariate. GENDER did not account for changes in latency measurements, $F_{(1,111)} = 1.29$, $p = .26$. In addition, GENDER did not interact with other factors to modulate mismatch latency, p 's $> .39$.

Although indicated by the lack of any Group interaction terms, lower-level analyses confirmed that the main effect of Group on MMF latency was observed when examining both the high (700Hz and /a/) and the low (300Hz and /u/) frequency stimuli. In addition, the main effect of Group on MMF latency was also observed when examining both tone (300Hz, 700Hz) and vowel stimuli (/u/, /a/). Comparing tone and vowel stimuli, there was a slight (<10ms) MMF latency prolongation for vowel as compared to tone stimuli; this small latency difference is likely due to vowel stimuli onset characteristics (vowel onsets ramped 10ms slower than pure tones).

No main effects or interactions were observed for MMF amplitude. Across Hemisphere, Frequency, and Stimulus, the mean MMF amplitudes in each group were: TD = 16.99 ± 1.02 nAm; ASD/-LI = 16.36 ± 1.05 nAm; ASD/+LI = 18.44 ± 2.14 nAm.

Finally, as shown in Figure 3, receiver operator characteristic (ROC) analysis of the mean MMF latency as a predictor of LI found significant area under the curve, AUC = 0.86, $p < 0.001$, with a sensitivity of 82.4% and a specificity of 71.2%.

Discussion

As hypothesized, the main finding was a delayed MMF latency in children with autism, particularly pronounced in the ASD/+LI group. In light of the Group MMF latency effect, and absence of Group by Hemisphere, Frequency, or Stimulus interactions, the findings demonstrate that a delayed MMF latency in ASD is robust. Thus, it appears that the time course of the auditory mismatch response is a neural index of language impairment in ASD, a finding confirmed by ROC analysis. The present observation of delayed MMF response in children with autism replicates previous preliminary findings [47]. A limitation of the present study is that it remains unclear whether the delayed MMF is a signature of language impairment *per se*, or only of language impairment in the context of ASD, or indeed is also associated partially with ASD. Future studies involving children with varied language abilities in the context of other clinical diagnoses will hopefully shed light on this issue.

Speech processing depends on encoding rapid transients in the stream of acoustic signal. For example, syllable identification is determined by rapid shifts in the distribution of spectral energy (formant transitions) between phonemic segments. During the automatic neuronal process of discriminating these transitions, a delay in auditory change-detection on the order of 50 ms, as observed in this study, could profoundly compromise downstream comprehension mechanisms. In children with ASD, ongoing monitoring and comprehension appear to be delayed, and important contextual cues in the speech signal could abnormally recruit pre-attentive resources, such as mismatch detection [14]. A growing body of evidence from clinical populations indicates an association between behavioral discrimination of speech sounds and MMN time-course (for a review see [5] and [48]). For example, in individuals with Asperger's syndrome, inaccurate prosodic discrimination was associated with diminished and prolonged MMN activity. Also, MMN activity was localized to different neural generators between autistic and control subjects, indicative of a different neurobiological basis of early prosodic speech processing in autism [21].

Some of the inconsistencies across mismatch autism studies are likely associated with methodological variation, low measurement reliability, and low statistical power [3]. In contrast to findings reported by Čeponienė et al. [49,51] and Gomot et al. [50], the large sample size in the present study (N=78) partially accommodates and mitigates the intrinsic heterogeneity that is well-known in studies of ASD and also provides sufficient power to observe medium to large effects. Other study differences, however, may also account for differences between this and previous studies. Using EEG, Gomot et al. [50] demonstrated

MMN latency shortening in a small population of autistic children following frequency changes in tone stimuli. The opposite direction of the latency effect observed in Gomot et al. than our study may relate to use of MMN vs. MMF, to differences in the autistic population (~50% of children in Gomot et al. had mental retardation), or more likely, to sample size (only 10 subjects with ASD in Gomot et al., had data amenable to CSD analyses investigating the temporal lobe responses). With regard to the Čeponienė et al. [51] findings of typical MMN activity following speech-sound differences in nine high-functioning autistic children compared to controls, the discrepancy between our findings and Čeponienė likely arise from differences in (a) sample size and sampling within the autistic population, (b) stimulation parameters, or (c) a combination of both. It should also be noted that the speech condition in the Čeponienė study employed a single synthetic standard vowel stimulus paired with the same stimulus rendered deviant by manipulating its formant frequencies. Linguistically, this approach is quite different from the method employed here, where two phonetically different vowel stimuli probed mismatch discrimination. As such, direct comparison of our MMN results with the Čeponienė findings is somewhat difficult. Of interest, however, is that Čeponienė et. al. [51] did observe that high-functioning children with autism orient differently to acoustic change in their speech stimuli - reflected by the P3a evoked potential which indexes involuntary attentional switching [24]. We would suggest that such differences in downstream recruitment of attentional resources may be adversely affected by the prolongation of neural change detection mechanisms occurring earlier in the auditory system.

We have previously reported a delay in the earlier M100 component in children with ASD compared to age-matched controls (with a mean value of 11ms) [52]. Of note the present findings of more pronounced delays in the MMF (especially in the subpopulation with LI) do not merely propagate earlier delays, but reflect latency delay exacerbation. Separately analyzing all present findings with the relative MMF to M100 shift (i.e., MMF latency minus M100 latency) as the dependent variable (as proposed by Oram Cardy [47]), a main effect of Group and no interactions was again observed; specifically, compared to controls, latency prolongation was observed in the group with ASD without language impairment, and the MMF was even more delayed in the ASD with language impairment group.

To conclude, neural correlates of auditory change detection as indexed by the magnetic mismatch field response are significantly delayed in children with ASD, and especially those with concomitant LI. The increase in the degree of prolongation from TD to ASD without LI to ASD with clinical LI suggests both a neurobiological basis for LI as well as a potential clinical indicator of LI in ASD. Furthermore, the main effect of diagnostic group on latency persisted when covarying non-verbal IQ, suggesting this effect is not accounted for by general cognitive ability. That said, the finding of only ~60-70% success rate in determining a MMF response may preclude its use as a screening technique. Nonetheless, results of this and other recent studies (e.g., [52]) point to the increasing importance of electrophysiological measures of brain function to better understand autism spectrum disorders.

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Figure 1.

Grand-averaged source difference waveforms for 300 and 700 Hz tone stimuli collapsed across hemispheres and frequencies. Mismatch activity was present in both hemispheres 170 to 300 ms following stimulus onset and clearly shows prolongation in ASD subgroups.

Figure 2.

Age-corrected mean MMF latencies (with standard error bars) for each group. Latency is prolonged in ASD/-LI and in ASD/+LI compared with typically developing peers (TD: 177.27 ± 2.72 ms; ASD/-LI: 208.68 ± 3.26 ms; ASD/+LI: 228.73 ± 5.82 ms, all contrasts significant after Bonferroni correction, $p < 0.05$).

Figure 3. Receiver operator characteristic (ROC) analysis of the mean MMF latency as a predictor of LI found significant area under the curve, $AUC = 0.86$, $p < 0.001$, with a sensitivity of 82.4% and a specificity of 71.2%.

Subject Demographics. Characteristics of study sample including neuropsychological tests administered prior to MEG recordings. Battery of tests included: CELF4 (*Clinical Evaluation of Language Fundamentals – 4th edition*), WISC (*Wechsler Intelligence Scale for Children–IV*), ADOS (*Autism Diagnostic Observation Schedule*), SCQ (*Social Communication Questionnaire*), and SRS (*Social Responsiveness Scale*). Values are reported as Mean ± standard error of the mean.

Table 1

	Age	Sex (M/F)	WISC_IQ	CELF4	ADOS	SCQ	SRS
ASD/+LI	8.47 ± 0.36	17/1	89.55 ± 3.33	68.16 ± 3.24	14.66 ± 0.99	20.33 ± 1.66	74.94 ± 2.41
ASD/-LI	9.846 ± 0.39	32/1	109.78 ± 2.55	99.85 ± 1.78	11.72 ± 0.67	21.28 ± 0.76	78.3 ± 1.91
TD	10.065 ± 0.47	12/15	109.25 ± 2.83	108.93 ± 2.05	1.96 ± 0.33	3.77 ± 0.87	45.65 ± 1.69

Table 2

Means and ranges of accepted trial data for each stimulus.

	Standards				Deviants			
	300	700	/u/	/a/	300	700	/u/	/a/
ASD/+LI	491, 440-534	500, 449-545	505, 470-535	503, 427-534	93, 78-105	93, 79-100	94, 84-105	93, 83-103
ASD/-LI	516, 456-542	509, 444-546	512, 445-547	510, 436-538	94, 73-103	96, 85-104	97, 87-107	96, 80-107
TD	529, 470-547	527, 482-544	526, 467-549	525, 429-548	98, 85-106	99, 87-108	99, 84-108	98, 85-106