Neuropsychiatric Disease and Treatment

Dovepress
Taylor & Francis Group

Open Access Full Text Article

ORIGINAL RESEARCH

Duration Mismatch Negativity in Adults With Autism Spectrum Disorder Versus Healthy Controls

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Objective: The mismatch negativity (MMN) reflects automatic cognitive function in response to auditory stimulation. The MMN to duration deviant (d-MMN) amplitude is known to be lower in children with autism spectrum disorder (ASD) than in healthy controls (HCs). Moreover, the d-MMN is known to be a trait maker of schizophrenia because it is unaffected by the duration of illness. This study aimed to identify robust tools to distinguish adults with ASD from HCs by measuring the d-MMN.

Methods: Fifteen adults with ASD (age range, 20–40 years) and 20 HCs were compared. After excluding patients with a low intelligence quotient, those using central nervous system stimulants, and those with excessive alcohol consumption, we conducted an auditory oddball task to measure the d-MMN.

Results: Compared with HCs, the patients with ASD showed significantly shorter d-MMN latencies for Fz and Cz.

Conclusion: The present findings suggest that the automatic cognitive function indicated by MMN amplitude might be improved by growth. Alternatively, the hypersensitivity indicated by d-MMN latencies suggests that it could persist into adulthood.

Significance: The d-MMN latency was shortened in patients with ASD compared with HCs. We believe that this is the first report to reveal that hypersensitivity in ASD as reflected by a shortened d-MMN latency should be maintained, even in adults.

Keywords: event-related potential, mismatch negativity, autism spectrum disorder, developmental disorder

Introduction

Autism spectrum disorder (ASD) is a neurodevelopmental disorder characterized by impairments in communication and social interaction and restricted and repetitive behaviors.[1] The inability to detect abnormal auditory processing and changes in the environment automatically has also been widely documented in the literature,[1,2] and may be related to clinical symptoms such as inattention, poor language ability, and impaired orientation to social stimuli.[3,4] A previous study estimated that the global prevalence of ASD is 1.5% in developed countries.[5] However, few studies in regard to the epidemiology of ASD in adults have been published, and many adults have never received a formal diagnosis.[6,7] Therefore, adult patients with ASD are often misdiagnosed as having other disorders, such as attention deficit hyperactivity disorder (ADHD), bipolar disorder, depression, and anxiety disorder.[8]

Event-related potentials (ERPs) are brain responses caused by various specific stimuli such as visual, auditory, or motor events imposed on a subject. ERPs are currently being researched as a brain activity index that reflects psychological processes such as cognition, attention, anticipation, memory, identification, and intention. On the other hand, waveforms have large individual differences and depend on psychological sensitivity.[9]

Näätänen suggested that there is no comparable measure in the whole of cognitive neuroscience to the mismatch negativity (MMN), which is considered to be a valid objective measure of the accuracy of central auditory processing in the human brain.[10] The MMN an automatic information-processing mechanism that can function even under inactive

Received: 23 August 2024
Accepted: 21 February 2025
Published: 5 March 2025

conditions, as acknowledged in the MMN, as an indicator of ERPs that reflect automatic auditory discrimination.[11,12] However, there are some deviant target events in MMN measurements, such as duration, pitch frequency, and omission. The MMN can be measured using the oddball task, which consists of a high-frequency standard stimulus and a low-frequency deviant stimulus. The MMN occurs at latencies to the stimulus change in the range of 100–200 ms and is obtained by subtracting the grand average waveform of the standard stimulus from that of the deviant stimulus. MMN paradigms are currently being used to answer a growing range of clinical questions, thereby increasing the understanding of the disease mechanisms underlying major neuropsychiatric, neurological, and neurodevelopmental disorders.[13] The divergence may be related to several factors, including stimulus characteristics and deviant types.[14] The MMN has been proposed as a useful method for the automatic registration of perceptual differences between a current stimulus and previously stored neural representations.[13] The MMN to duration deviant (d-MMN) amplitude is known to be unaffected by the duration of illness, in contrast to the MMN frequency deviant (f-MMN). Consequently, in schizophrenia, the d-MMN appears to be more impaired than that of the f-MMN.[15] Moreover, Shaikh et al[16] suggested that d-MMN deficits are useful to predict the conversion to psychosis from an at-risk mental state. Based on these findings, the d-MMN may be a promising trait maker in schizophrenia.

MMN deficits are robust in patients with ASD, which suggests an altered central ability in auditory discrimination. However, alterations in the MMN with respect to frequency, duration, and phoneme changes have been observed in different profiles.[17] D-MMN amplitudes have been shown to be lower in children with ASD than in healthy controls (HCs).[18–20] By contrast, f-MMN amplitudes have been shown to be increased in children with ASD compared with HCs.[19,21] Interestingly, some studies have reported that f-MMN amplitudes are significantly reduced in children with ASD compared with typically developing children.[21–23] Another study found that prolonged MMN latency to phonetic changes in adults with ASD was associated with the severity of symptoms.[24] Another study demonstrated prolonged MMN latencies to phonetic changes in adults with ASD,[20] and a meta-analysis found that tone f-MMN latencies in child/adolescent patients with autism showed faster MMN latencies, while patients with Asperger syndrome showed delayed MMN latencies compared with HCs.[17] To date, both MMN amplitudes and latencies have been shown to be affected in patients with ASD when speech sounds are used as deviant stimuli. Moreover, patients with ASD, high-functioning ASD, and Asperger syndrome may manifest different impairments in detecting tone-frequency changes.[17]

ASD has genetic heritability and is associated with shared impairments in social and executive functioning.[25] Therefore, we hypothesized that cognitive function-related ERPs could be used to distinguish between patients with ASD and HCs. The d-MMN is said to be a promising trait maker in schizophrenia, and various differences have been identified in previous research on ASD.[16] Therefore, the d-MMN might have potential application as a trait maker in ASD. Given this background, the present study aimed to examine differences in cognitive function in adult developmental disorders by statistically comparing MMN amplitudes and latencies.

Materials and Methods

Participants

The study participants were 15 patients with ASD (male: 8, female: 7) and 20 HCs (male: 11, female: 9). We began recruitment on February 1, 2017, and ended on December 31, 2022. The first subject was in the control group, on March 29, 2017, and the last subject was in the ASD group, on December 22, 2021. With the exception of the HCs, all participants (mean age ± standard deviation [SD], 26±4.6 years; age range, 20–39 years) were recruited from Fukushima Medical University and had been diagnosed with ASD according to the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition, by experienced psychiatrists. Patients with a medical history involving central nervous system stimulants were excluded, as were current smokers (defined as smoking more than six cigarettes per day) and drinkers (defined as drinking 40 g of alcohol per day). All participants were administered the Japanese version of the Wechsler Adult Intelligence Scale-Third Edition (WAIS-III) and the self-administered Japanese version of the autism-spectrum quotient (AQ). Patients with a low intelligence quotient (IQ), defined as <70 according to the tenth revision of the International Classification of Diseases, were excluded.

This study was carried out in accordance with the latest revision of the Declaration of Helsinki. Prior to the study, consent was obtained in writing from each of the participants after they had been informed about the study design and contents both verbally and in writing. This study was approved by the ethics committee of Fukushima Medical University (No. 2693).

MMN Design and Procedure

The measurements were performed in an electronically shielded and sound-attenuated room. During the MMN task, the participants sat in a comfortable chair in a soundproof chamber and watched a movie with subtitles but without any sound. They were instructed to relax, concentrate on the silent movie, and disregard any auditory stimuli. Auditory stimuli with a constant stimulus onset asynchrony of 500 ms were presented to the participants' ears via earphones. Electroencephalograms (EEGs) were recorded from 09:30 to 11:00. The fundamental frequency was 1000 Hz. All stimuli consisted of 75 dB sounds. The standard stimuli (100 ms in duration) were presented at a probability of 80%, and the deviant stimuli (50 ms in duration) at a probability of 20% using a multi-trigger system (MULTI STIM BOX MB-7IP; Medical Try System, Tokyo, Japan). The number of stimulations was set to 4000.

Data Acquisition and Analysis

EEG data were recorded using a Neurofax EEG1218 (NIHON KOHDEN, Tokyo, Japan). A common reference electrode was attached to the tip of the nose. Impedances were kept below 10,000 Ω. The vertical and horizontal electrooculogram (EOG) signals were detected by an electrode placed 1.5 cm above the lateral canthus of the right eye. A ground electrode was attached to the middle of the forehead. The MMN was passband-filtered at 0.5–30 Hz, and notch-filtered at 50 Hz. The EEG and EOG data were elicited using FOCUS software (NIHON KODEN). All EEG epochs (magnitude difference: 100 μV) were excluded from the analysis. Waveform differences were obtained by subtracting the MMN elicited by the standard stimuli from that elicited by the deviant stimuli. The MMN was identified as a positive deflection between 120 and 180 ms, and was obtained by subtracting the results for the nontarget stimuli from those for the target stimuli. M1 and M2 were helpful in separating the MMN.

The peak latency and amplitude for each Fz and Cz component were statistically analyzed. SPSS version 27 J for Windows (IBM, Armonk, NY, USA) and the Mann–Whitney *U*-test were used for the analyses. The effect size was calculated using Z-values.

Results

The present study compared two groups: patients with ASD and HCs. Figure 1 shows the averaged d-MMN waveforms in each group. The thick and thin lines show the Fz and Cz of the d-MMN and the M1 and M2, respectively. Figure 2 shows a comparison of averaged d-MMN waveforms for Fz and Cz between the two groups. The thick and dashed lines indicate the HCs and the patients with ASD, respectively. The horizontal axis shows d-MMN amplitudes ([mean±SD] Fz: HCs, –1.31±0.79 μV; ASD, –1.23±0.90 μV; Cz: HCs, –1.04±0.75 μV; ASD, –0.7±0.73 μV), and the vertical axis shows peak latencies (Fz: HCs, 163±9.22 ms; ASD, 150±9.97 ms; Cz: HCs, 167±10.3 ms; ASD, 152±11.6 ms). The results regarding age, gender, handedness, IQ, and AQ are summarized in Table 1. Table 2 shows the results of a chi-squared test regarding peak amplitudes and latencies between the two groups. Table 3 shows the median, maximum, and minimum values for each group.

No significant differences in the peak d-MMN amplitude for Fz were found between the two groups. Patients with ASD showed a significantly shorter d-MMN latency than did HCs (Fz: Z=–3.10, p=0.001, r=–0.53; Cz: Z=–2.80, p=0.004, r=–0.47).

Because there were significant differences in IQ between the two groups, an additional analysis of covariance with IQ as a covariate was also performed. No significant interactions were found between the independent variables and covariates (Fz latency: p=0.789, Fz amplitude: p=0.490, Cz latency: p=0.293, Cz amplitude: p=0.903). A similar analysis was conducted for age. Similarly, no significant interactions were found (Fz latency: p=0.500, Fz amplitude: p=0.248, Cz latency: p=0.595, Cz amplitude: p=0.647).

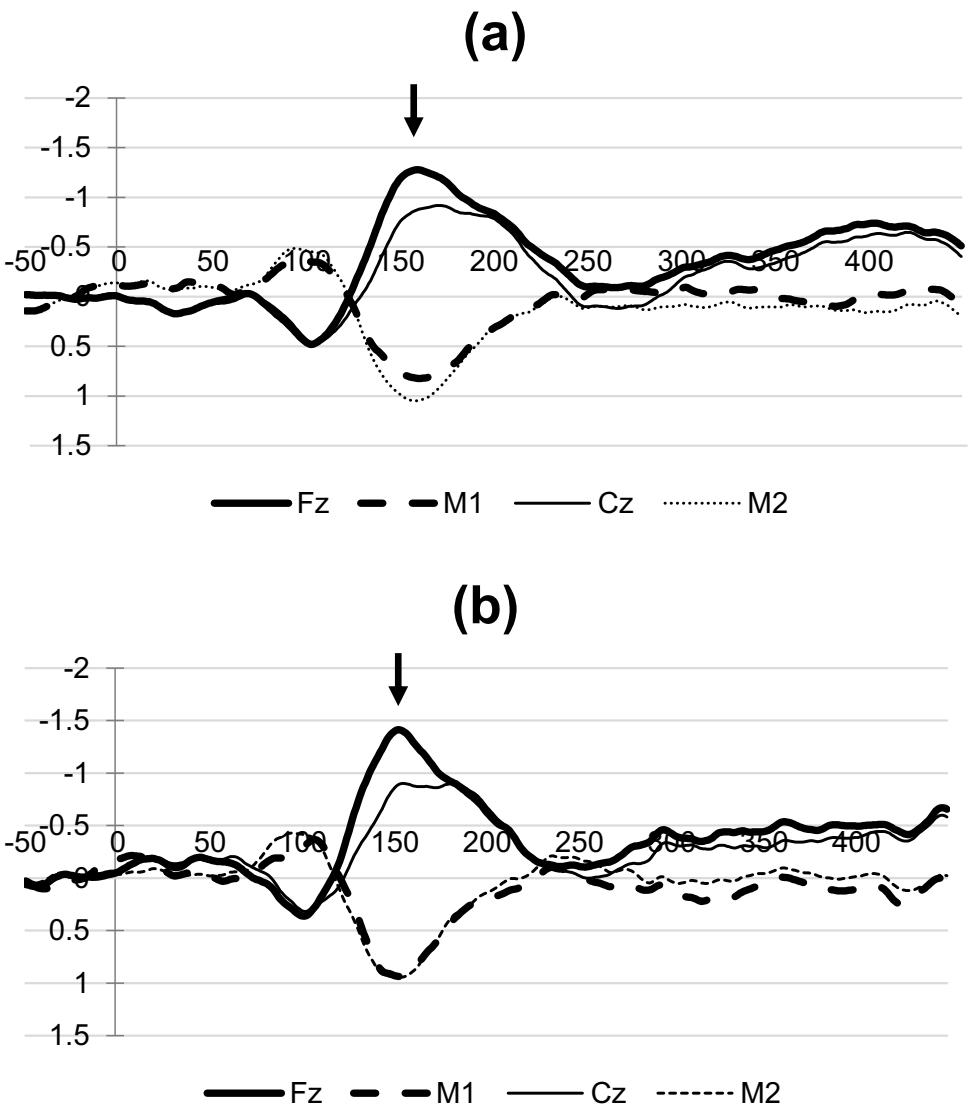

Figure 1 Grand-averaged waveforms for the d-mismatch negativity. (**a**) Autism Spectrum Disorder and (**b**) Healthy controls. Arrows indicate the mismatch negativity. Thick dashed lines show the Fz, thick solid lines the M1, thin dashed lines the Cz, and thin solid lines the M2.

An additional analysis of correlations to self-reported hyperacusis as indicated by the AQ was conducted using Spearman's rank correlation. However, no significant association was found (Fz latency: p=0.047, Fz amplitude: p=0.321, Cz latency: p=0.185, Cz amplitude: p=0.387).

Discussion

In the present study, the d-MMN latency was significantly shorter in patients with ASD than in HCs. Differences based on several deviant types of stimuli have been reported in patients with ASD. Some studies focusing on MMN amplitudes have reported that d-MMN amplitudes are lower in children with ASD than in HCs.[19,20] A meta-analysis found that tone d-MMN amplitudes in child/adolescent patients with ASD decreased compared with HCs. Abdeltawwab et al[22] also reported that the MMN amplitudes in children with ASD were lower than those in healthy children. Another study using speech sound deviants (phoneme changes) found the same results in children.[26] However, other studies have reported that f-MMN amplitudes were increased in children with ASD compared with HCs.[21] The results of the present study also showed that MMN amplitudes tended to be reduced in children with ASD compared with HCs, but this difference was not significant. Aging has been suggested to be associated with declines in the automatic processing of time-dependent

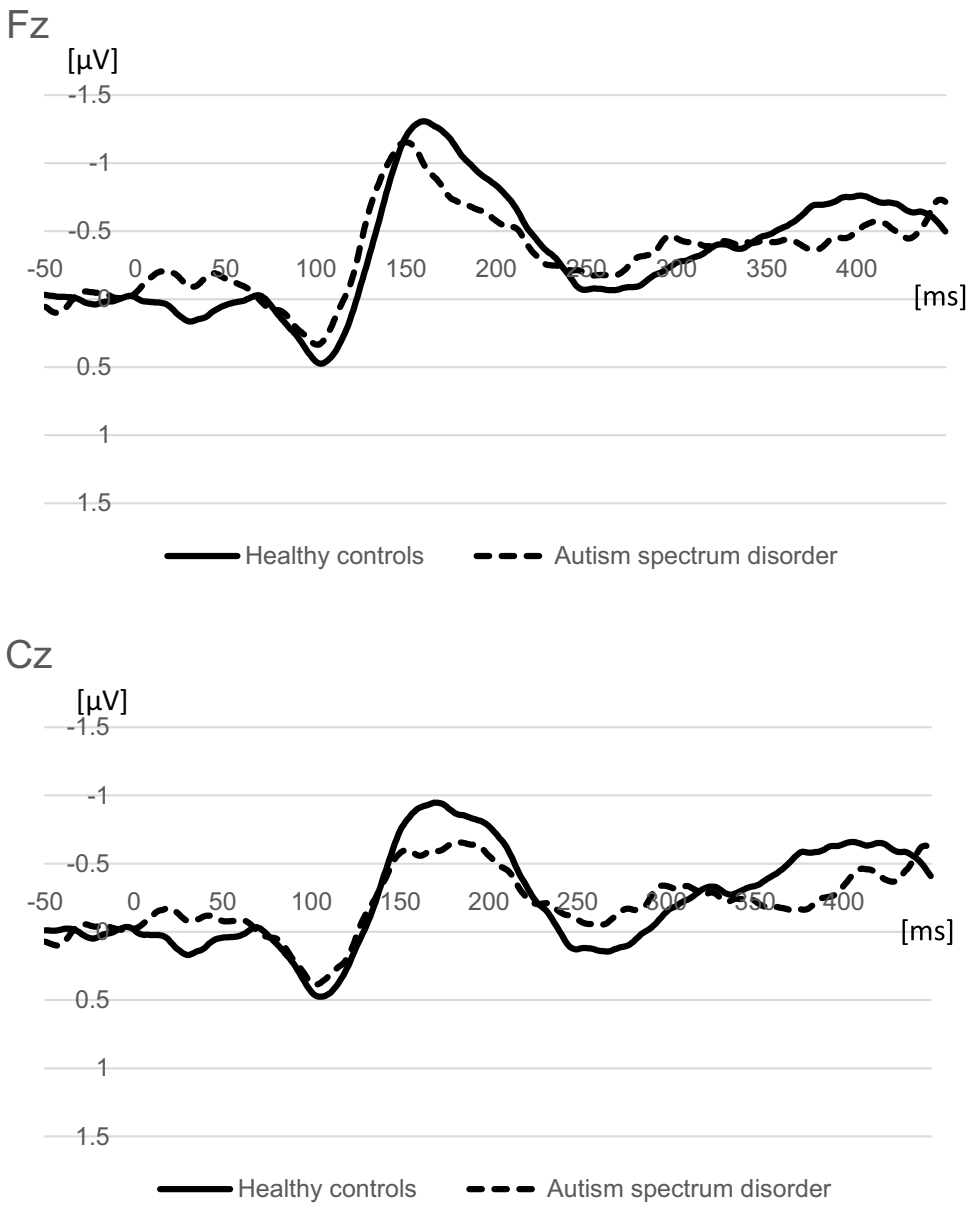

Figure 2 Comparison of averaged mismatch negativity waveforms for Fz and Cz. Thick lines show healthy controls and thin lines autism spectrum disorder.

stimulus features, and the present conclusions are considered to be associated with increases in the susceptibility to task-irrelevant stimuli.[27] The reason why no significant differences were found in the present study could be that because age was adjusted, there were no differences in cognitive function.

This finding may also suggest something completely different. Although individuals with ASD have very different symptoms from one another, the disorder is characterized by core features in two areas—social communication and restricted, repetitive sensory–motor behaviors—irrespective of culture, race, ethnicity, or socioeconomic group.[28] These symptoms result from early altered brain development and neural reorganization.[29,30] However, the diagnosis must be made on the basis of behavior because no reliable biomarkers have been identified. Among young children, those with clear developmental disabilities are likely to be diagnosed.[31] Older children, adolescents, or adults whose families suspect that they might have ASD often already have a history of difficulties.[32] Therefore, relevant psychiatric disorders have to be considered.[6,33,34] In a community sample in a previous study, about one third of adults who were diagnosed with ASD and had average or higher intelligence no longer had obvious ASD features, although many had minor

Table 1 Demographic Data and Intellectual Functioning in Patients With Autism Spectrum Disorder and Healthy Controls

	Healthy Controls Mean (SD)	Autism Spectrum Disorder Mean (SD)	P-value
Age	23.9 (2.27)	29.7 (6.29)	0.02
Gender (male/female)	11/9	9/6	0.521
Handedness (right/left-handed)	19/1	15/0	0.571
FIQ	122 (8.4)	101 (16.7)	<0.01
AQ	11.5 (5.8)	31.5 (6.0)	<0.001

Abbreviations: FIQ, full-scale intelligence quotient; AQ, autism-spectrum quotient.

Table 2 Mean (Standard Deviation) Amplitudes and Latencies to Deviants for Patients With Autism Spectrum Disorder and Healthy Controls

	Healthy Controls	Autism Spectrum Disorder	P-value
Latency			
Fz ms (SD)	163 (9.22)	150 (9.97)	0.001
Cz ms (SD)	167 (10.3)	153 (11.6)	0.004
Amplitude			
Fz μV (SD)	−1.31 (0.79)	−1.23 (0.90)	0.768
Cz μV (SD)	−1.04 (0.75)	−0.7 (0.73)	0.997

Table 3 Median, Maximum, and Minimum Values for Each Group

	Fz					
	Latency			Amplitude		
	ASD	HCs		ASD	HCs	
Median	149	161		−1.36	−1.05	
Max	172	180		0.03	−0.35	
Min	133	149	ms	−3.32	−3.55	μV
	Cz					
	Latency			Amplitude		
	ASD	HCs		ASD	HCs	
Median	151	165		−1.02	−0.95	
Max	175	180		0.53	0.22	
Min	126	145	ms	−2.76	−2.89	μV

Abbreviations: ASD, autism spectrum disorder; HCs, healthy controls.

psychiatric conditions.[35] Adults seeking an initial diagnosis of ASD often have comorbid psychiatric conditions and are not typically intellectually disabled.[36] In this way, the diagnosis differs depending on age. This result suggests that a reduced d-MMN tends to be associated with different characteristics.

Another previous study focusing on MMN latencies demonstrated prolonged MMN latencies to phonetic changes in adults with ASD;[20] however, in the present study, we used the d-MMN latencies that were found to be shortened in the ASD group. A meta-analysis reported that tone f-MMN latencies in child/adolescent patients with ASD showed faster MMN latencies, while patients with Asperger syndrome showed delayed MMN latencies compared with HCs.[17] Thus, preceding studies on

MMN in child/adolescent patients with ASD have reported mixed findings in regard to latencies and amplitudes. At the behavioral level, patients with ASD are hypersensitive to not only simple tones, but also different sensory modalities. Such hypersensitivity has been reported to be associated with the core symptoms of ASD.[14,37] Prolonged MMN latency to phonetic changes in adults with ASD has been shown to be associated with the severity of symptoms.[24] In a meta-analysis, Chen et al[17] also discussed the shortened latency of MMN in relation to hypersensitivity in ASD. The results of the present study indicate that d-MMN latencies in adult patients with ASD are shorter than those in HCs. Similar to previous studies, our results suggest that adult patients with ASD also have hypersensitivity to simple tones and different sensory modalities.[14,37]

Audio stimuli are considered to be affected by growth and development.[38] Therefore, in the present study, we restricted the age range to minimize the effect of age and used robust tools. The characteristics of unconscious auditory stimuli measured by the d-MMN were also characteristic in adults, and the use of the d-MMN showed a clear difference from HCs. In the future, we hope to increase the number of cases.

This study has some limitations. First, as the sample size was small, it is possible that important correlations were not extracted. Second, some of the participants could have had a dual diagnosis with ADHD. Third, the groups were not IQ-matched; however, no significant interactions were found. Fourth, hyperacusis as indicated by the AQ is based solely on self-reporting and is merely a subjective symptom; it was not possible to perform an objective evaluation.

Conclusion

In this study, no significant difference in d-MMN amplitudes was found between the two groups, but d-MMN latencies were shorter in patients with ASD compared with HCs. This result suggests that the automatic cognitive function indicated by MMN amplitudes might be improved by growth. On the other hand, the hypersensitivity indicated by d-MMN latencies suggests that it could persist into adulthood. In addition, the present results were similar to those of shortening MMN latency in children with ASD. This finding suggests that hypersensitivity in ASD as reflected by a shortened d-MMN latency should be maintained, even in adults. As research continues and more cases are accumulated, we may be able to use MMN as a biomarker.

Acknowledgments

This study was supported by Fukushima Medical University and the Medical Affairs Division of Janssen Pharmaceutical K.K. The authors are very grateful to Dr. Hiroshi Ito, Noboru Oriuchi, Hisashi Kubo, Takeyuki Nanbu, Jyunya Matsumoto, Tetsuya Shiga, and Wataru Toda for their helpful comments. The authors also thank all of the patients and healthy controls who participated in this study.

Disclosure

Dr Itaru Miura reports personal fees from Janssen, Eisai, Meiji Seika Pharma, MSD, Otsuka, Sumitomo, Takeda, Tanabe-Mitsubishi, Viatris, Daiichi-Sankyo, and Lundbeck, outside the submitted work. None of the authors have any other potential conflicts of interest to disclose for this work.

References

1. Allen G, Courchesne E. Attention function and dysfunction in autism. *Front Biosci*. 2001;6:D105–D119. doi:10.2741/allen
2. Donkers FCL, Schipul SE, Baranek GT, et al. Attenuated auditory event-related potentials and associations with atypical sensory response patterns in children with autism. *J Autism Dev Disord*. 2015;2:506–523. doi:10.1007/s10803-013-1948-y
3. Kuhl PK, Coffey-Corina S, Padden D, Dawson G. Links between social and linguistic processing of speech in preschool children with autism: behavioral and electrophysiological measures. *Dev Sci*. 2005;1:F1–F12.
4. Roberts TPL, Cannon KM, Tavabi K, et al. Auditory magnetic mismatch field latency: a biomarker for language impairment in autism. *Edgar Biol Psychi*. 2011;70:263–269. doi:10.1016/j.biopsych.2011.01.015
5. Lyall K, Croen L, Daniels J, et al. The changing epidemiology of autism spectrum disorders. *Annu Rev Public Health*. 2017;38:81–102. doi:10.1146/annurev-publhealth-031816-044318
6. Brugha TS, McManus S, Bankart J, et al. Epidemiology of autism spectrum disorders in adults in the community in England. *Arch Gen Psychiatry*. 2011;68:459–465. doi:10.1001/archgenpsychiatry.2011.38
7. Brugha TS. *The Psychiatry of Adult Autism and Asperger Syndrome: A Practical Guide*. Oxford: Oxford University Press; 2018.
8. Kitsune GL, Kuntsi J, Costello H, et al. Delineating ADHD and bipolar disorder: a comparison of clinical profiles in adult women. *J Affect Disord*. 2016;192:125–133. doi:10.1016/j.jad.2015.12.024
9. Dawson GD. A summation technique for the detection of small evoked potentials. *Electroencephalogr Clin Neurophysiol*. 1954;6:65–84. doi:10.1016/0013-4694(54)90007-3

10. Näätänen R. Mismatch negativity (MMN): perspectives for application. *Int J Psychophysiol*. 2000;37:3–10. doi:10.1016/S0167-8760(00)00091-X
11. Näätänen R. *Attention and Brain Function*. Hillsdale, NJ: Erbaum; 1992.
12. Schröger E. On the detection of auditory deviations: a pre-attentive activation model. *Psychophysiology*. 1997;34:245–257. doi:10.1111/j.1469-8986.1997.tb02395.x
13. Näätänen R, Sussman ES, Salisbury D, Shafer VL. MMN as an index of cognitive dysfunction. *Brain Topogr*. 2014;27:4514–4566.
14. Orekhova EV, Stroganova TA. Arousal and attention re-orienting in autism spectrum disorders: evidence from auditory event-related potentials. *Front Hum Neurosci*. 2014;8:34. doi:10.3389/fnhum.2014.00034
15. Daniel U, Sanya K. Mismatch negativity in schizophrenia: a meta-analysis. *Schizophr Res*. 2005;23:1–23.
16. Shaikh M, Valmaggia L, Broome MR, et al. Reduced mismatch negativity predates the onset of psychosis. *Schizophr Res*. 2012;134:42–48. doi:10.1016/j.schres.2011.09.022
17. Chen TC, Hsieh MH, Lin YT, Chan PYS, Cheng CH. MMN to different deviant in autism spectrum disorders: a meta-analysis. *Clin Neurophysiol*. 2020;131:766–777. doi:10.1016/j.clinph.2019.10.031
18. Huang D, Yu L, Wang X, Fan Y, Wang S, Zhang Y. Distinct patterns of discrimination and orienting for temporal processing of speech and nonspeech in Chinese children with autism: an event-related potential study. *Eur J Neurosci*. 2018;47:662–668. doi:10.1111/ejn.13657
19. Lepistö T, Kujala T, Vanhala R, Alku P, Huotilainen M, Näätänen R. The discrimination of and orienting to speech and non-speech sounds in children with autism. *Brain Res*. 2005;1066:147–157. doi:10.1016/j.brainres.2005.10.052
20. Vlaskamp C, Oranje B, Madsen GF, et al. Auditory processing in autism spectrum disorder: mismatch negativity deficits. *Autism Res*. 2017;10:1857–1865. doi:10.1002/aur.1821
21. Ferri R, Elia M, Agarwal N, Lanuzza B, Musumeci SA, Pennisi G. The mismatch negativity and the P3a components of the auditory event-related potentials in autistic low-functioning subjects. *Clin Neurophysiol*. 2003;114:1671–1680. doi:10.1016/S1388-2457(03)00153-6
22. Abdeltawwab MM, Baz H. Automatic pre-attentive auditory responses: MMN to tone burst frequency changes in autistic school-age children. *J Int Adv Otol*. 2015;11:36–41. doi:10.5152/iao.2014.438
23. Dunn MA, Gomes H, Gravel J. Mismatch negativity in children with autism and typical development. *J Autism Dev Disord*. 2008;38:52–71. doi:10.1007/s10803-007-0359-3
24. Kasai K, Hashimoto O, Kawakubo Y, Yumoto M, Kamio S, Itoh K. Delayed automatic detection of change in speech sounds in adults with autism: a magnetoencephalographic study. *Clin Neurophysiol*. 2005;116:1655–1664. doi:10.1016/j.clinph.2005.03.007
25. Antshel KM, Russo N. Autism spectrum disorders and ADHD: overlapping phenomenology, diagnostic issues, and treatment considerations. *Curr Psychiatry*. 2019;21:34. doi:10.1007/s11920-019-1020-5
26. Ludlow A, Mohr B, Whitmore A, Garagnani M, Pulvermüller F, Gutierrez R. Auditory processing and sensory behaviours in children with autism spectrum disorders as revealed by mismatch negativity. *Brain Cogn*. 2014;86:55–63. doi:10.1016/j.bandc.2014.01.016
27. Kisley MA, Davalos DB, Engleman LL, Guinther PM, Davis HP. Age-related change in neural processing of time-dependent stimulus features. *Brain Res Cogn Brain Res*. 2005;25:913–925. doi:10.1016/j.cogbrainres.2005.09.014
28. Khan NZ, Gallo LA, Arghir A, et al. Autism and the grand challenges in global mental health. *Autism Res*. 2012;5:156–159. doi:10.1002/aur.1239
29. Bauman ML, Kemper TL. Neuroanatomic observations of the brain in autism: a review and future directions. *Int J Dev Neurosci*. 2005;23:183–187. doi:10.1016/j.ijdevneu.2004.09.006
30. O'Reilly C, Lewis JD, Elsabbagh M. Is functional brain connectivity atypical in autism? A systematic review of EEG and MEG studies. *PLoS One*. 2017;12:e0175870. doi:10.1371/journal.pone.0175870
31. Developmental Disabilities Monitoring Network Surveillance Year 2010 Principal Investigators; Centers for Disease Control and Prevention (2014). Prevalence of autism spectrum disorder among children aged 8 years – autism and developmental disabilities monitoring network, 11 sites, United States. *MMWR Surveill Summ*. 2010;63: 1–21.
32. Department for Education. Special educational needs in England. (2018).
33. Bishop SL, Seltzer MM. Self-reported autism symptoms in adults with autism spectrum disorders. *J Autism Dev Disord*. 2012;42:2354–2363. doi:10.1007/s10803-012-1483-2
34. Ashwood KL, Gillan N, Horder J, et al. Predicting the diagnosis of autism in adults using the autism-spectrum quotient (AQ) questionnaire. *Psychol Med*. 2016;46:2595–2604. doi:10.1017/S0033291716001082
35. Anderson DK, Liang JW, Lord C. Predicting young adult outcome among more and less cognitively able individuals with autism spectrum disorders. *J Child Psychol Psychiatr*. 2014;55:485–494. doi:10.1111/jcpp.12178
36. Happé FG, Mansour H, Barrett P, Brown T, Abbott P, Charlton RA. Demographic and cognitive profile of individuals seeking a diagnosis of autism spectrum disorder in adulthood. *J Autism Dev Disord*. 2016;46:3469–3480. doi:10.1007/s10803-016-2886-2
37. Schulz SE, Stevenson RA. Sensory hypersensitivity predicts repetitive behaviours in autism and typically-developing children. *Autism*. 2019;23:1028–1041. doi:10.1177/1362361318774559
38. Lai MC, Lombardo MV, Baron-Cohen S. Autism. *Lancet*. 2014;8:896–910. doi:10.1016/S0140-6736(13)61539-1