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Original Article

The effects of positive emotional gesture guidance on speech sound discrimination in Thai children with ASD: A mismatch negativity study

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Abstract

Children with autism spectrum disorders (ASD) experience difficulty with sound discrimination. In such cases, non-verbal communication, such as gestures, is known to improve language performance. The objectives of this study were to compare ‘Thai-words’ speech sound discrimination with positive and neutral emotional stimulus paradigm using the mismatch negativity (MMN) technique, between children with ASD and typically developing children (TDC); and to find the correlation between MMN and clinical severity of ASD. Event-related potentials (ERP) using neutral and positive emotional stimulus paradigm were assessed and the MMN was analyzed. Our results found that children with ASD showed less negative mean amplitude of MMN over Cz electrode compared to the TDC. Moreover, the mean amplitude of MMN in the ASD group was positively correlated with the sensory/cognitive awareness domain of Autism Treatment Evaluation Checklist (ATEC). In conclusion, the MMN can be used as an electrophysiological marker of ASD clinical severity.

Keywords: autism spectrum disorders; mismatch negativity; positive emotion; speech sound discrimination

1. Introduction

Autism spectrum disorder (ASD) is a common neurodevelopmental disorder characterized by atypical social interaction, verbal and nonverbal communication impairment, and abnormal behaviors. As regards language impairment, children with ASD tend to respond less to environmentally deviant stimuli at an early sensory level (Timora & Budd, 2013). Regarding social communication, children with ASD have reduced conversational reciprocity and integrated verbal and nonverbal communication, and atypical scanning pattern during face and emotion perception (Jiang *et al*., 2019). Moreover, children with ASD were found to be slower in processing natural-sounding surface phonological forms in Thai compound (Nattanun, 2019). Neuroimaging of children with ASD has revealed alterations of brain structures and functions in relation to auditory processing (Kujala, Lepistö, & Näätänen, 2013). Interestingly, the defects in auditory processing in ASD were found to be linked to the early stages of sound discrimination (Abdeltawwab & Baz, 2015).

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Event-related potentials (ERP) are commonly used to examine the effects of stimuli on neural activities. For language processing, the mismatch negativity (MMN) or negative deflection of early ERP waveforms, is used in detecting speech sound discrimination. The MMN is considered an automatic auditory-change detection mechanism, which is distributed over the fronto-central scalp regions, usually with a maximum peak response of about 5 μV at 150–250 ms from the onset of the stimulus (Näätänen, Paavilainen, Rinne, & Alho, 2007). The MMN is calculated by subtracting the brain wave response to a “standard” event from the response to a “deviant” event. A “deviant” event is rarely presented as a stream of repeated or familiar events, which would be considered a “standard” event (Nagai *et al*., 2013). Previous studies using MMN on patients with ASD have shown reduced MMN amplitude (Vlaskamp *et al*., 2017), longer MMN latency (O’Connor, 2012) and slower attenuation of the N1 response to infrequent tones (Hudaca *et al*., 2018). However, a study on maternal gestures and language development in infants, who are siblings of children with ASD, have found that mothers of non-diagnosed high-risk siblings tend to gesture more frequently than mothers with low-risk infants. This finding indicates that maternal gestures could lead to more effective communication with their children.

This is a study on the effects of positive emotional gesture guidance on speech sound discrimination measured by MMN, comparing children with ASD to normally developing children. A prior study has shown that simultaneous multi-sensory stimulation can enhance the neural responses (Timora & Budd, 2013) . In addition, the correlation between MMN and clinical severity of ASD was explored. Our hypothesis suggested that emotional guidance could improve speech sound discrimination, measured by MMN, in children with ASD. In addition, the language used in this MMN paradigm is the Thai language, which contains different sound tones. Thus, we investigated the characteristics of MMN responses in this paradigm.

2. Materials and Methods

2.1 Participants

Twenty-six Thai children with age range from 36 to 72 months participated in this study: eleven children with ASD (9 boys and 2 girls; mean age = 47.44 months [SD=9.98]), and 15 typically developing children (TDC; 10 boys and 5 girls; mean age = 45.5 months [SD=8.44]). Children with ASD were recruited from hospitals and the Mahidol University health service institution, in Thailand. The diagnosis of ASD was conducted either by pediatricians or child psychiatrists, in accordance with the DSM-V criteria (American Psychiatric Association, 2013). The exclusion criteria for both groups included history of brain injury, comorbid neurological disorders (e.g., epilepsy), receiving CNS-acting medication (e.g., benzodiazepines, short-acting antihistamine), and children who are unable to cooperate during the experiments. This study was approved by the Ethical Committee of the Mahidol University Central Institutional Review Board (MU CIRB 2018/152.2108).

Before the experiments, parents of all the participants were explained in detail all the steps of the experimental procedures. If the parents and their children consented to participate in this study, they had to sign a Legal Guardian Informed Consent Form. Children were also verbally informed about the agreement.

2.2 Screening process

All participants were assessed for their handedness, enquired about general health information, and underwent specific screening tests, for each group. Their handedness was evaluated using the Edinburgh Handedness Inventory Test (Oldfield, 1971), a self-report for the measurement of a person's hand-use preference. Only right-handed children were recruited. For the general health screening, information regarding developmental milestones, behavioral problems, co-morbid conditions, and current medication use were collected.

For children with ASD, this study used the Autism Treatment Evaluation Checklist (ATEC) in its Thai version, which was developed with back-translation method by Wanaluk, M. (2004) with reliability level 0.84. (Muang monmaneerat, 2004). The ATEC questionnaire was used for the evaluation of the severity level. Only children with ASD in mild (n=1) or moderate levels (n=10), based on the ATEC, were included in this study.

For the TDC group, the Denver II test (Thai version) 3rd edition, a behavioral performance test for screening of developmental milestones, was used (Kotchabhakdi & Lertawasadatrakul, 2008). In addition, parents of the participants were asked to fill a Pervasive Developmental Disorder Screening Questionnaire (PDDSQ) in its short version. This questionnaire showed 75.4% sensitivity and 58% specificity (Ongarjsakulman, 2016), in the screening task for ASD (Chanvit, Ampai, Apirat, & Duanchai, 2002). The Children who received a 'normal development' status from the Denver II test (Thai version) 3rd edition and the "no risk" result from PDDSQ, were recruited into the study. All participants' information is summarized in Table 1.

Table 1. Participant information summary for both groups. The age, ATEC and PDDSQ scores are shown as mean ± SD.

	ASD (n=11)	TDC (n=15)
Gender (Male : Female)	9 : 2	10 : 5
Age (months)	47.44 ± 9.98	45.50 ± 8.44
ATEC score	53.64 ± 8.15	-
PDDSQ score	-	2.00 ± 2.51

2.3 The MMN paradigm

The MMN paradigm was created with the Gentask program of the STIM software version 2.4 (Compumedics Neuroscan, Australia). The MMN stimuli consisted of 2 Thai-word speech sounds and 2 pictures of emotional gestures, shown in Figure 1. The speech sounds were recorded from a female Thai native speaker, [ใช่/Chì/(as "yes" in Thai) and ใช้/Chî/(to "use" in Thai)], and were adapted to 500 ms length with loudness at 90 decibels (Stroganova *et al*., 2013), followed by 1,500 ms before the next trial. The emotional pictures consisted of 2 types of emotions. The neutral emotional gesture guidance was composed of an emotionless face, with arms released in a neutral position, while the positive emotional gesture guidance was composed of a smiling face, with hands in an okay sign stance. All pictures were shots of one single woman, and were adapted to a standard size at 428 pixels width, by 570 pixels height, with 72 pixels/inch resolution. All picture stimuli were shown on a computer screen at a size of 18 cm x 25 cm. The 31 minutes experiment consisted of three blocks, each block with the same paradigm (Figure 2). The MMN paradigm consisted of 200 stimuli, with 160 neutral emotional stimuli as a standard, and 40 positive emotional stimuli as a deviant. The assigned 'neutral stimulus' was a neutral speech sound ใช้/Chî/(to "use" in Thai)], made to emerge together with a picture of a neutral emotional gesture, while the assigned 'positive stimulus' was a positive speech sound [ใช่/Chì/(as "yes" in Thai), made to emerge together with a picture of a positive emotional gesture. Speech sound and the picture of each stimulus were offered for the same time range.

2.4 The ERP recording

The ERP during experiment was recorded using the Neuroscan software version 4.3 (Compumedics Neuroscan,

Figure 1. The components of neutral and positive emotional stimuli for the MMN paradigm

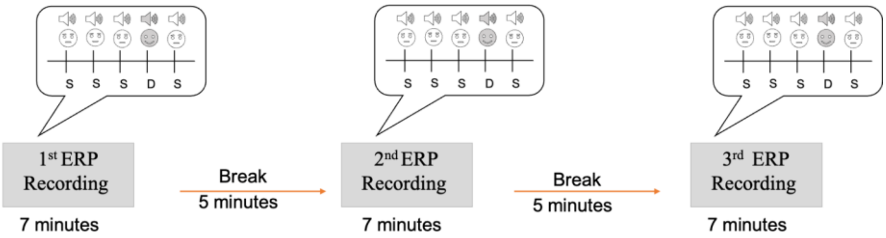

Figure 2. The sequence of ERP recording during positive gestures for children with ASD and typically developing child participants. (S = standard [neutral condition], D = deviant [positive emotional condition])

Australia), with 31 Ag/AgCl electrodes attached on the Electro-Cap, in accordance with the international 10–20 system (Jasper, 1958).

For the process of the EEG cap application, the EEG Quikcell was used before the cap was worn, then the electrolyte solution was filled into every electrode to keep the impedance below 5 KΩ. The pre-recording filter was set at 0.1–60 Hz. The notch was opened at 50 Hz. Analog-to-digital (A/D) rate was set at 500 Hz and the gain was set at 19. The ERP recording was conducted in a quiet room, with comfortable lighting and the temperature set at 25°C. Children in both groups were allowed to sit on the mattress with their parents. During the ERP recordings, pictures were presented on the screen monitor and the speech sounds were presented through headphones. Both the picture and the sound stimuli were generated and controlled by the STIM software (Compumedics Neuroscan, Australia).

2.5 The MMN analysis

This study proposed to compare the effects of neutral and emotional guidance on speech sound discrimination. Thus, the MMN was analyzed based on the differences between the effects of the positive emotional gesture guidance and the neutral emotional gesture guidance. The MMN was analyzed with the BESA Research 7.0 software (BESA Gmbh). The processing of the data started by transforming the continuous EEG data into segmented EEG data, from 200 milliseconds before stimulus onset to 400 milliseconds after stimulus onset; then the data were band-pass filtered (high pass at 0.3 Hz / 12 dB/Octave and low pass at 30 Hz / 24 dB/octave); and artifact rejection was set with the amplitude of EEG data exceeding ± 70 microvolts. The MMN results derived from the averaged ERP when using positive emotion gesture guidance and speech sound were subtracted with the averaged ERP derived when using neutral emotion gesture guidance and speech sound.

For the MMN analysis, the mean amplitude was selected for testing the difference between speech sound discrimination from neutral and positive emotional gesture guidance, for the 2 groups. With all the participants in this study being preschool children, it was quite difficult to identify the peak amplitude and latency of MMN. Thus, the mean amplitude calculated from the averaged amplitude in specific time interval was used instead. The mean amplitude of the whole segment of MMN, the early component of MMN, and the late component of MMN were separately analyzed. The exact time interval for each MMN segment would be set according to the averaged MMN from all participants in this study.

2.6 Statistical analysis

The IBM Statistical Package for Social Science (SPSS), version 23, was selected for the statistical analysis. The Mann-Whitney U test was used to compare the mean amplitude of MMN between children with ASD and the TDC group. Statistical significant was called when the p-value was less than 0.05. Moreover, Spearman's correlation coefficient was used to analyze the correlation between the mean amplitude of MMN and the ATEC scores in children with ASD.

3. Results and Discussion

3.1 The MMN analysis

The mean amplitude of MMN over CZ electrode was used to compare between the 2 groups. The MMN generated in our study showed a longer duration than in previous reports (Figure 3). The mean amplitude of MMN was calculated in 100–400 ms interval (whole segment of MMN), 100–250 ms interval (the early component of MMN that is similar to the standard MMN), and 250–400 ms interval (the late component of MMN) (Table 2).

3.1.1 MMN in 100–400 ms interval

For MMN between 100–400 ms after the onset of the stimulus, the TDC group expressed a typical waveform of

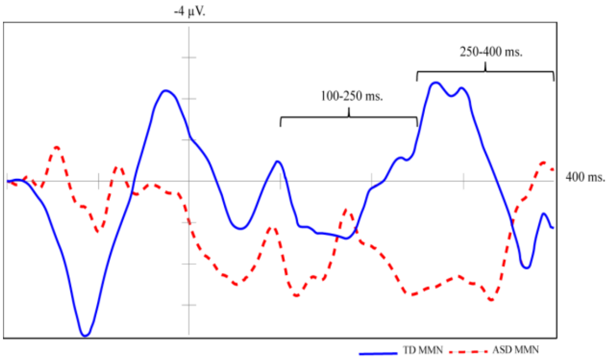

Figure 3. The MMN generated in speech sound discrimination with positive emotional gesture guidance over CZ electrode from the child participants. The MMN from children with ASD is presented with a dashed line, while the MMN from typically developing children is presented with solid line.

MMN compared to the ASD group. Moreover, from the statistical analysis, the ASD group showed lower negative mean amplitude of MMN than the TDC group (2.25 ± 2.88 µV and -1.11 ± 3.20 µV respectively; p = 0.036).

3.1.2 MMN in 100–250 ms interval

The MMN in 100–250 ms interval is typical for the standard MMN paradigm (Näätänen, 1995). Our study found that children with ASD showed lower negative mean amplitude of MMN than the TDC group (1.92 ± 3.67 µV and -0.96 ± 2.74 µV respectively; p = 0.036).

3.1.3 MMN in 251–400 ms interval

The MMN in 251–400 ms interval was additionally analyzed in our study due to the longer MMN duration in TDC. The authors found that children with ASD showed lower negative mean amplitude of MMN than the TDC group (2.57 ± 3.72µV and -1.24 ± 4.38 µV respectively; p = 0.036).

3.2 The correlation analysis

Spearman's correlation between the mean amplitude of MMN over CZ electrode and the severity scores of each ATEC domain were assessed. The correlation analysis found that the mean amplitude of MMN over CZ electrode was positively correlated to the sensory/cognitive awareness domain of ATEC, with the correlation coefficient (r) being 0.741 (Table 3).

3.3 Discussion

The current study was purposed to investigate whether children with ASD were able to discriminate emotional speech sounds when guided by positive emotional gestures, and this was compared with TDC. The speech sounds in this study consisted of 2 meaningful words from the Thai language. The words in Thai language contain five different intonation marks. The different intonations of a Thai word may condone it with different meanings, even when the words have the same consonants and vowels (Kanchanawan, 2015). Thus, the accuracy in the discrimination of the different prosodies is critically important to the Thai language speakers.

For the TDC group, the MMN generated in this paradigm shows an expected pattern of the MMN waveform in relation to the speech sound discrimination processing by the brain. The MMN generated in TDC indicates that the speech sound stimuli of this study are able to stimulate the sound discrimination processing in children; therefore, it can be applied in an investigation of speech sound discrimination in children with ASD. However, the MMN generated in this paradigm showed a longer MMN latency than previous studies. In our study, the main peak of MMN was detected after 250 ms following the onset of the stimulus, while a typical MMN in adults presents a peak within 150–250 ms (Näätänen *et al*., 2007). The explanation is that the MMN generated in children are different from adults due to the immature brain development (Gibb & Anna Kovalchuk,

Table 2. Comparison of the mean amplitude of MMN between children with ASD and TCD

Mean amplitude of MMN	ASD (n=11)	TCD (n=15)	ρ-value
Between 100-400 ms.	2.25 ± 2.88	-1.11 ± 3.20	0.036*
- Between 100-250 ms.	1.92 ± 3.67	-0.96 ± 2.74	0.036*
- Between 251-400 ms.	2.57 ± 3.72	-1.24 ± 4.38	0.036*

*ρ-value<0.05

Table 3. The correlation between the mean amplitude of MMN over CZ electrode with the severity score from ATEC

ATEC severity score	Mean Amplitude of MMN (r)					
	100- 400 ms.	ρ-value	100- 250 ms.	ρ-value	251- 400 ms.	ρ-value
Speech /Language Communication	0.275	0.414	0.023	0.947	0.394	0.231
Sociability	-0.362	0.273	-0.321	0.336	-0.486	0.129
Sensory/Cognitive awareness	0.316	0.344	0.741	0.009*	-0.439	0.176
Health / Physical / Behavior	-0.416	0.204	0.014	0.968	-0.274	0.415
Total score	-0.082	0.811	0.342	0.304	-0.282	0.400

*ρ-value<0.05

2018). A number of MMN studies in children have revealed that children present a later peak amplitude of MMN compared to adults. Moreover, children usually show longer latency in MMN than adults during an evoked auditory potential stimulation. These findings indicate slower neural processing in children, which is explained by the inadequate synaptic connections and incomplete myelination (Deoni, III, Remer, Dirks, & O'Muircheartaigh, 2015). According to the fact that the auditory processing pathway is still under development in children, the MMN of children usually appears between 150 and 300 ms after onset of the stimulus (Ferreira, Bueno, Costa, & Sleifer, 2019). In a study on 3-year-old children, the MMN peak has been observed between 120 and 400 ms post-deviance (Paquette *et al*., 2013). Moreover, a comparison study between children and adults found that the MMN latencies for both speech and non-speech stimuli in younger children are significantly longer than in adults, which is similar to the MMN amplitudes, which are significantly higher in children than in adults (Paquette *et al*., 2013). Another study by Strotseva-Feinschmidt *et al*. (2015) assessed the auditory discrimination of functional words, and made a comparison between 3-year-old children and adults. They found that the children showed MMN peak latency at around 420 ms, compared to 307 ms in adults (Strotseva-Feinschmidt, Cunitz, Friederici, & Gunter, 2015). The second explanation is that, the speech sound stimuli in this study are composed of emotional pronunciations, which emerged together with the emotional gesture guidance. The perception of emotions requires multi-sensory processing (Klucharev & Sams, 2004), including speech prosody, and a facial and body gesture interpretation (Kuusikko *et al*., 2009). Thus, in this case, the sound discrimination process was longer than when using pure sound discrimination. The third explanation is that, the speech sound in this study is associated with meaningful words that the brain interprets as an interference to the complexity of the central auditory processing functions and the speech comprehension processes; therefore, the sound discrimination process in the brain was longer. This reasoning is supported by a previous study conducted by Ahmadi *et al*. (2016), who found that the MMN latency from speech word stimuli in Persian-speaking children was around 380–424 ms after the onset of the stimulus (Ahmadi, Mahmoudian, Ashayeri, Allaeddini, & Farhadi, 2016).

Regarding the MMN responses of children with ASD, it was found that the MMN waveform was not clearly demonstrated. In a statistical comparison, children with ASD showed a lesser mean amplitude of MMN than the TDC group, which indicates an impaired neural processing in speech sound discrimination associated with ASD, even when stimulated with emotional pronunciations and emotional gesture guidance. The impaired MMN response in ASD, despite using a positive emotional gesture guidance with sound stimuli, can be explained by the clinical features of ASD. Children with ASD do not show a preferential response to vocalized sound due to atypical maturation processes in the specialization of temporal regions in voice processing (Bidet-Caulet *et al*., 2017). When considering emotional recognition in children with ASD, especially the ability to recognize the emotional state of others requires the ability to divide the attention and focus of one's gaze onto relevant information (Kujala, Lepistö, Wendt, Näätänen, & Näätänen, 2005). With the classical characteristic of children with ASD being the impairment in skills related to social interactions and a lack of understanding of the emotions and the minds of others, there is a clear indication of an impairment in understanding or being intuitive in the theory of the mind (Kaland, Smith, & Mortensen, 2007). Fan and Cheng (2014), however, found that people with ASD exhibited an MMN response to happy emotional syllables, but had a weaker trend towards an additional posterior temporal source of MMN compared with TDC (Fan & Cheng, 2014). According to the previous evidence and clinical characteristic of ASD, the MMN result suggests that the emotional guidance stimulation for children with ASD should contain highly emotional expressions and distinct presentations, such as animations, especially for meaningful word sound discrimination.

The correlation analysis in this work shows a positive correlation between the mean amplitude of MMN over CZ electrode and the sensory/cognitive awareness domain of ATEC in children with ASD. The lower MMN response (higher positive value) was correlated with more severe ASD symptoms. ATEC consisted of 4 domains including speech/language communication, sociability, sensory/cognitive awareness and health/physical behavior. The sensory/cognitive awareness is the important clinical feature in a preschooler with ASD, because children with ASD usually show hyper- or hypoactivity to sensory input or unusual interest in sensory aspects of the environment (APA, 2013). According to the sensory/cognitive awareness domain of ATEC, the sensory information processing (Kern, Geier, Adams, & Geier, 2010) is similar to the underlying neural mechanism of MMN. The MMN is found to relate with the auditory sensory perception, a kind of sensory information processing. Therefore, this evidence could explain the association between sensory/cognitive awareness domain of ATEC and the amplitude of the MMN in the results.

There were some limitations in this work. First, our participants, especially children with ASD, constituted too small a sample size, which was due to the limited number of children with ASD who were able to pass all the inclusion criteria. Another limitation found in both TDC and children with ASD was the significant occurrence of electrical artifacts during the ERP recordings, resulting from the constant head and body movements. Further study in a larger population including cases with minimal and severe ASD symptoms, as well as a long-term follow-up of MMN in Thai children, are also recommended.

4. Conclusions

This study revealed a longer MMN response when using Thai language with emotional words. Although using a positive emotional gesture guidance with sound stimulus for children with ASD did not restore the MMN response to be similar to the MMN response in TDC, the correlation between MMN amplitude and ATEC score can be applied in clinical practice as an electrophysiological marker of disease severity in cases with ASD, especially in the association between sensory/cognitive symptoms evaluated by ATEC and sensory processing measured by MMN.

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