



Auditory brainstem response to speech in children with high functional autism spectrum disorder

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Abstract

Auditory brainstem response (ABR) provides useful information about the auditory brainstem pathway. However, there is little known about the subcortical speech processing in individuals with autism spectrum disorder (ASD). The aim of the present study was to investigate the subcortical speech processing in children with high functioning ASD. Twenty-eight children with ASD, with a mean age of 14.36 ± 1.86 , and 28 typically developing (TD) children, with a mean age of 14.99 ± 1.92 , were selected from Rofeydeh Rehabilitation Hospital (Tehran, Iran), and speech ABR (sABR) with a 40 ms synthetic /da/ syllable stimulus was recorded. There was no significant difference between the two groups in terms of age and IQ. Latencies of all waves in sABR and duration of V-A complex were significantly longer in children with ASD than in TD children. It was concluded that patients with ASD have deficits in the temporal neural encoding of speech at the brainstem level. Further studies are needed to generalize this result.

Keywords Auditory brainstem response (ABR) · Autism spectrum disorder (ASD)

Introduction

Autism spectrum disorder (ASD) is a group of neurodevelopmental behavioral disorders, with a larger prevalence among males. In 2014, the prevalence of this disorder was reported one in every 88 children in the USA [1]. Based on DSM-V criteria, children with ASD are generally categorized into three groups. The first group requires support, and without support, they have deficits in social communication, initiating social interactions, and planning and organizing, independently. The second group requires substantial support, they have deficits in establishing verbal and non-verbal social communication and are weak in the initiation of social interactions. Additionally, repetitive behaviors are seen frequently in this group. The third group needs substantial support, and has

severe deficits in verbal and non-verbal social communication and has very limited ability in initiation of social interactions. Behaviors of this group are severely limited and repetitive [2].

Common factors for diagnosis of ASD include (1) linguistic and social communication deficits; (2) repetitive and stereotypic patterns of movement and behavior; and (3) deficits in routine functions; and these symptoms are generally seen in the early stages of growth [3–5]. The language deficits in autistic individuals include perceptual, productive, and physiological dysfunctions [6–8]. One of the main causes of these deficits in these patients is auditory processing dysfunction, which can lead to deficits in speech recognition [4]. Studies have shown that most of the language processing is carried out in the cerebral cortex [9]; however, recent studies have highlighted the importance of subcortical areas in this process [10]. Brainstem has been shown to play a central role in the synchronization of neuronal responses, and its deficits are associated with changes in absolute latency, inter peak latency, and amplitude of waves in auditory brainstem response (ABR) to speech stimuli [11, 12].

Brainstem response to the speech, as a more complex auditory stimulus, is a very ideal way for assessment of the subcortical auditory processing [13]. There is a good harmony between the auditory stimulus wave and the response wave of the brainstem which shows the spectral and temporal characteristics of the stimulus [13]. Brainstem response to the speech

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syllables /da/, which is known as speech auditory brainstem response (sABR), consists of two general parts, the “source class” and the “filter class.” The source class includes D, E, and F waves which represent vibrations of vocal fold (transient response), and the distances between them are directly related to the F0 wavelength of speech (sustained response). The filter class includes V, A, C, and O waves (transient response); so that the V and A waves show the onset of auditory processing in the brainstem, the C wave shows the response to the onset of the vowel, and the O wave shows the end of the sound [14].

Despite the numerous studies that have been performed on the processing of simple auditory signals at the brainstem level in children with ASD, there are few studies on the brainstem response to the complex auditory signals, like speech, in these patients. In a study in 2008, Russo et al. investigated the brainstem-evoked response to speech in children with ASD and reported pitch cues processing deficiency [15]. In another study in 2009, the brainstem speech processing was assessed in silent and noisy conditions. Their results indicated that there was a deficit in speech encoding in silence and noise in the ASD group [16]. Many studies have also shown that sABR is a non-invasive and useful electrophysiological test to investigate the auditory brainstem response to complex stimuli such as speech, in a wide range of learning and developmental disorders [13, 17, 18].

So, given the importance of auditory processing in children with ASD, as well as considering the applicability of sABR-based assessments in evaluating auditory processing of speech stimuli subcortically, the present study focused specifically on children with high functioning ASD and investigated their auditory brainstem response to /da/ synthetic syllable, in comparison with TD children. The results of this study can highlight the importance of brain-based functional biomarkers in clinical diagnosis of auditory processing deficits.

Methodology

Participants

Twenty-eight males with ASD (28 males, mean age of 14.36 ± 1.86 years) and 28 TD children (28 males, mean age of 14.99 ± 1.92 years) were selected in Rofeydeh Rehabilitation Hospital (Tehran, Iran), using convenient sampling from available subjects. Children with ASD were diagnosed according to the DSM-V criteria and based on a psychologist's or psychiatrist's evaluation. All participants were investigated in terms of speech comprehension, auditory reflexes, and IQ. All children were right-handed and monolingual Persian speakers. This study was conducted according to the rules of the Ethics Committee of the University of Social Welfare and Rehabilitation Sciences.

Stimulus and recording parameters

The sABR test was conducted for all subjects and the results were analyzed by Bio-logic Navigator Pro system. Silver chloride electrodes were placed on the right mastoid, forehead, and at Cz areas, acted as the reference, ground, and active electrodes, respectively. Contact impedances were less than $5 \text{ k}\Omega$ and inter-electrode impedance difference was less than $1.5 \text{ k}\Omega$. Stimuli were presented through unshielded insert earphones (ER-3A, Etymotic Research, Elk Grove Village, IL). The synthesized syllables /da/ with a 40-ms duration (Auditory Neuroscience Lab of the Northwestern University) was used in this study. The stimuli were introduced using the Biologic AEP standard software (version 7) with intermittent polarity, and in order to minimize the artifact, responses were collected from the right ear using two blocks of 3000 artifact-free sweeps (a total of 6000 sweeps) at a rate of 10.9 s. In each recording period, if false responses were more than 10% of the total number of sweeps, the record was repeated to obtain a cleaner response. In addition, in the recording process, a 100–2000-Hz band-pass filter with 1024 digital sampling points and 85-ms epoch (including 15 ms of pre-stimulation time) was used. Stimulus intensity level of the 80-dB SPL stimulant was measured and calibrated using a 2 cm^3 DB-0138 coupler, the Bruel & Kjaer Type 2203 sound meter and a 1-in. microphone. Patients were in a comfortable and closed-eye position during the electrophysiological test, and no cognitive stimulus was introduced during the test. After the data collection, the peaks and potentials were determined and their latencies and amplitudes were calculated. Finally, all data were analyzed using the MATLAB software version R2014a.

Data processing

All sABR waves were identified and marked manually by two skilled audiologists. In the analysis of the sABR waves, seven waves were identified and marked, including two onset waves A and V, a consonant-vowel transition wave C, an offset wave O, and three FFRs waves or sustained frequency following response waves (FFR) D, E, and F. The wave V was similar to the V_n wave in cABR. The biggest peak was at about 6 ms, just before the negative slope, and the trough after negative slope, was marked as the wave A. according to the normal values reported in previous studies, the waves C, D, E, F, and O were labeled in the deepest trough at their latent time. The normal values were 18, 22, 10, 10, and 48 ms, for the waves C, D, E, F, and O, respectively [19]. If there were two points with equal amplitudes within the trough, the point with shorter latency was marked, and if a point had a plateau, its center was labeled. In the cases where there was a controversy between the two experts, the range smaller than the baseline activity at the pre-stimulation time (0.04–0.4 ms) was also considered unreliable and was excluded from

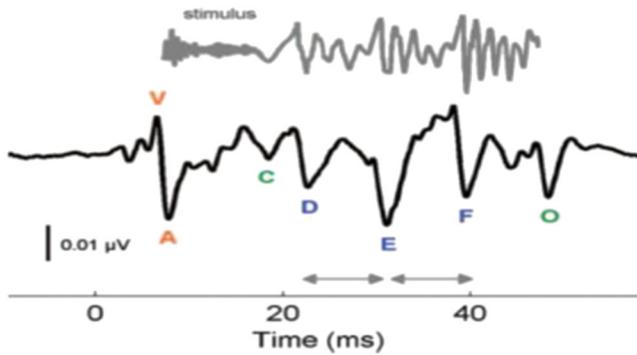


Fig. 1 Transient and sustained characteristics of brainstem response to the syllables /da/

the analysis. In addition, the neural response to the onset of stimulation was measured by calculating V-A inter-peak latency, V-A peak to trough amplitude, and slope of the V-A complex. The value of RMS was calculated to investigate the signal energy for the whole signal and the silence period before determining averages. The SNR was obtained as the ratio of RMS to the whole sABR (0–190 ms) and RMS on the pre-averaging silence (40–0 ms) [20].

Data analysis

The normal distribution of data was investigated by the Kolmogorov-Smirnov test. In order to compare the amplitude and latency, RMS amplitude, duration, amplitude and slope of the V-A competency between the ASD and TD children, the ANOVA test was used.

Results

All subjects had a normal auditory threshold (equal to or better than 25 dB in both ears at 250 to 8000 Hz octave frequencies

(ANSI 2004) and had no history of neurological disorders. All subjects had an IQ greater than 85 based on Wechsler’s standard. Tympanogram and auditory reflex of the middle ear was in the normal range for all participants (ear canal volume equal to 0.9–0.2 cm³, static compliance equal to 0.3–1.5/1 mmHO, and sound pressure levele -50 to +50 dapa). In all the mentioned evaluations, there were no significant differences between the two groups. The brainstem response to the syllables /da/ included seven response peaks (V-O) (Fig. 1).

The C and O waves in some children were not identified in both groups. The C wave was observed in 76% of subjects in ASD group and 80% of subjects in TD group and the O wave was detected in 86% of ASD and TD group. The rest of the sABR waves were well identified. The latency of all the sABR waves and the V-A latency were longer in the ASD group than the control group. SNR was significantly shorter in the ASD group than in the TD group. The mean and standard deviation of the sABR latency and the V-A duration and SNR are shown and compared in Table 1. No significant difference was observed between the mean amplitudes of the two groups.

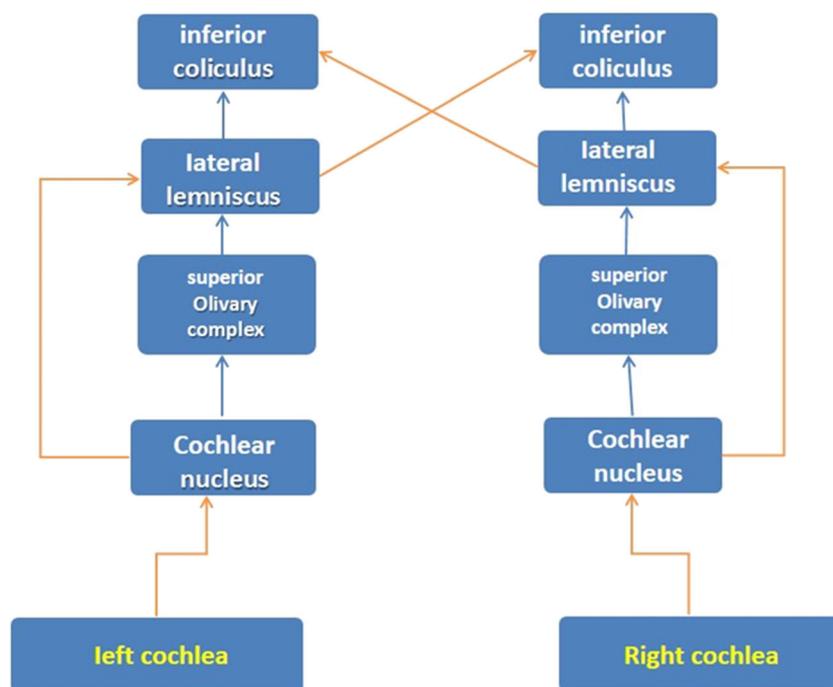
Discussion

In this study, brainstem response to the auditory /da/ stimulus was investigated. To assess the brainstem response to the speech stimuli in ASD subjects, the sABR test was used with the syllables /da/. The latency of all sABR waves in the ASD group showed a significant delay, in comparison with the TD group. Previous studies have reported only an increase in the initial latencies (V, A) and the D and F waves in ASD subjects [16]. Based on the findings of this study and previous ones, in the filter class part of the sABR response, the onset waves (V and A) and the offset wave (O) have longer latencies in ASD cases, which may indicate a weakened synchronization of neural response to find the beginning (onset) and the ending

Table 1 The mean values of sABR measures for children with ASD and TD children

Latencies (ms)	TD children			Children with ASD			P
	Mean	SD	N	Mean	SD	N	
V	6.32	.19	30	6.89	.50	28	<0.001
A	7.18	.15	30	7.82	.46	28	<0.001
C	18.03	.33	24	20.01	.56	21	<0.001
D	22.10	.12	30	24.60	.98	27	<0.001
E	30.74	.10	30	33.35	1.35	28	<0.001
F	39.12	.09	30	41.12	.96	28	<0.001
O	47.68	.45	26	49.58	.85	24	<0.001
Other sABR measures							
V-A duration	.77	.15	30	.93	.22	28	<0.001
RMS amplitude (μV)	.16	.25	30	.08	.02	28	<0.001
SNR	2.75	.35	30	1.92	.41	28	<0.001

Fig. 2 Schematic diagram of the auditory system. Blue arrows correspond to the ipsilateral pathway; red arrows correspond to the contralateral projections. The frequency following response (FFR) reflects ensemble phase-locked responses from a number of subcortical auditory structures, including the cochlear nucleus, superior olivary complex, lateral lemniscus, and the inferior colliculus



(offset) of speech stimulus. In the source class part of the sABR response, the longer latencies of the transient FFR components, including D, E, and F waves, may indicate a delay in the ASD group to comprehend transient elements of FFR, which may lead to a weaker discrimination of consonants in this group. The V-A complex in the sABR represents the synchronization of the neuronal response to the onset of the stimulus [10, 14].

In this study, V-A complex analysis showed a shorter duration and amplitude and a slope with a shallower depth in ASD group compared to the control group. However, only the V-A duration was significantly different between ASD and TD children. These findings might indicate a weaker neuronal synchronization and a weaker representation of the beginning of speech stimulus in children with ASD. The SNR was obtained from the mean amplitude of the response divided by the mean amplitude of the pre-stimulus activity [21]. This value was significantly lower in the ASD group than the control group. Based on the SNR and also the RMS values calculated in the two groups, this difference seems to be due to the higher amplitude of pre-stimulation activity or internal physiological noise during the recording of the response in children with ASD. In spectral analysis of the sABR waves, no significant difference was observed between the two groups in the frequency range F0, F1, and HF, which is consistent with previous studies [22].

Although the origin of response to complex stimuli such as speech has been less studied, initial responses may be the result of a massive synchronization in many types of brainstem cells (in CN and IC) [23]. The FFR is processed within the same brainstem nuclei as initial waves, but through

a distinct network probably involving different synaptic interactions [24, 25]. Two distinct pathways from the cochlear nucleus to the inferior colliculus (IC) have been implicated in the generation of the FFR: a direct pathway to the contralateral IC via the lateral lemniscus (LL), and an ipsilateral pathway via superior olivary complex (SOC) and the lateral lemniscus (LL) [26] (Fig. 2). Considering the findings of this study and the origin of the sABR waves, it can be said that patients with autism have a disturbance in these brain pathways.

In this study, the sABR was recorded in silence to investigate the impacts of ASD on subcortical speech processing. The recording of sABR in the presence of noise, or the use of psychoacoustic tests or speech recognition tests in the presence of noise and comparing behavioral and electrophysiological findings, provides further information in this regard. On the other hand, auditory performance assessment using the evoked response of the brainstem to speech in the ASD population provides objective, non-invasive, and passive information; therefore, this is a safe way to investigate this group of patients. Moreover, the children with an abnormal brainstem response to the speech are the best candidates for auditory rehabilitation [27–29]. Therefore, brainstem response can have a place in diagnosis and assessment of the effectiveness of auditory rehabilitation programs in this group of patients.

Conclusions

In this study, the latency in the temporal encoding of both the source and the filter parts of the sABR response was different

in ASD subjects compared to the TD group. Based on these findings, in ASD subjects, synchronization of neural activity is impaired, which indicates a dysfunction in the processing of speech stimulus at the brainstem level. Since temporal auditory processing in brainstem plays a central role in speech comprehension, ASD may be some kinds of speech processing disorder, especially impaired speech perception in the presence of noise.

Compliance with ethical standards

Ethics approval and consent to participate All stages of this study were conducted with the informed consent of the participants and under the rules of the ethics committee of the University of Social Welfare and Rehabilitation Sciences.

Conflict of interest The authors declare that they have no conflict of interest.

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