ASPI | Afarand Scholarly Publishing Institute; Turkey
ISSN: 7687-2645. Journal of Clinical Care and Skills. 2023;4(1):15-20. 10.58209/jccs.4.1.15

Auditory Processing Skills in Brainstem Level of Autistic Children; a Systematic Review

ARTICLE INFO

Article Type
Systematic Review

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How to cite this article
Ramezani M, Lotfi Y, Hajjari S N. Auditory Processing Skills in Brainstem Level of Autistic Children; a Systematic Review. Journal of Clinical Care and Skills. 2023;4(1): 15-20.

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Article History
Received: November 16, 2022
Accepted: February 22, 2023
ePublished: April 18, 2023

ABSTRACT

Aims Autism is a pervasive developmental disorder. Deficit in sensory functions is one of the characteristics of people with autism, and usually these people show abnormality in processing and correct interpretation of auditory information. Also people with Autism show problems in communicating with others. This review article deals with the accurate understanding of Auditory processing skills of autistic children compared to normal children is done to clarify the auditory processing disorder in this group.
Information & Methods This systematic review was conducted in articles published from 2002 to 2022 in the field of electrophysiological evaluations of auditory brainstem in autism spectrum disorder by searching Scopus, PubMed, Google Scholar, and Science Direct databases.
Findings Disorders were observed in the brainstem electrophysiological responses of patients with ASD compared to the normal group. The results of studies of auditory brainstem evoked responses with click stimuli showed an increase in wave V latency and I-V interpeak latency in ASD subjects compared to normal groups. Studies of brainstem evoked responses with speech stimuli also showed a decrease in amplitude and an increase in latency.
Conclusion Auditory processing disorders in verbal and non-verbal stimuli in people with autism spectrum have been reported. Most studies show disorders in speech stimuli, which play a very important role in communicating.

Keywords Autism; Auditory Brainstem Responses; Speech Auditory Brainstem Responses

CITATION LINKS

[1] Autism diagnostic interview-revised: A revised version of a diagnostic interview for caregivers of individuals with possible pervasive developmental ... [2] Sensory abnormalities in children with autism spectrum ... [3] Sensory processing in autism: A review of neurophysiologic ... [4] Cortical auditory processing of simple stimuli is altered in autism: A meta-analysis of auditory evoked ... [5] Atypical longitudinal development of speech-evoked auditory brainstem response in preschool children with autism spectrum ... [6] Abnormal auditory brainstem response in the pons region in youth with ... [7] Autism spectrum disorders and the amplitude of auditory brainstem response ... [8] Auditory neuropathy: Physiologic and pathologic evidence calls for more diagnostic ... [9] Subclinical dysfunction of cochlea and cochlear efferents in migraine: An otoacoustic emission ... [10] Study of auditory evoked potentials in ... [11] Continued development of auditory ability in autism spectrum disorder children: A clinical study on click-evoked auditory brainstem ... [12] Auditory processing in autism spectrum disorder: A ... [13] Prolonged auditory brainstem responses in infants with ... [14] Evidence for atypical auditory brainstem responses in young children with suspected autism spectrum ... [15] Electrophysiologic assessment of central auditory processing by auditory brainstem responses in children with autism spectrum ... [16] Characteristics of auditory brainstem response latencies in children with autism spectrum ... [17] Auditory brainstem response in infants and children with autism spectrum disorder: A meta-analysis of ... [18] Brainstem transcription of speech is disrupted in children with autism spectrum ... [19] Prolonged auditory brainstem response in universal hearing screening of newborns with autism spectrum ... [20] Click-evoked auditory brainstem responses and autism spectrum disorder: A meta-analytic ... [21] The effect of rate stress on the auditory brainstem response in autism: A preliminary ... [22] Binaural interaction component of the auditory brainstem response in children with autism spectrum ... [23] Auditory brainstem response to complex sounds: A ... [24] Brainstem origins for cortical 'what'and 'where'pathways in the auditory ... [25] Abnormal auditory forward masking pattern in the brainstem response of individuals with Asperger ... [26] Deficient brainstem encoding of pitch in children with autism spectrum ... [27] Auditory brainstem response to speech in children with high functional autism spectrum ... [28] Evidence for atypical auditory brainstem responses in young children with suspected autism spectrum ... [29] Auditory brainstem response in children with autism spectrum disorder: a case-control ... [30] Brainstem auditory evoked potentials in children with autism spectrum ...

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Introduction

Autism spectrum disorder (ASD) is a spectrum of early-onset neurodevelopmental disorders characterized by limitations in language, communicative-social functions, and repetitive stereotyped behaviors. ASD is a heterogeneous group of disorders, with a prevalence of about 14.7 per 1000 8-year-old children, which affects boys more than girls [1]. The etiology and underlying pathogenic mechanisms of the diseases are unknown, but complex environmental factors along with genetics play an important role in the development of this disorder. Having siblings with ASD, old parents, and genetic disorders, such as fragile X syndrome, Down syndrome, and tuberous sclerosis can cause ASD [2].

The ability to communicate with others is a sensory processing process, which ASD patients often have problems with. Language delay and abnormal responses to sensory information appear to be more common in ASD patients than in other developmental disorders [3-12]. Sensory dysfunction may be associated with auditory, visual, vestibular, or tactile processing disorders [13-18]. Chen et al. evaluated the pattern of auditory information processing at the brainstem level in preschool children with ASD using brainstem responses evoked by speech stimuli. They observed that auditory processing in children with ASD at the same age was immature and abnormal. Incorrect speech processing at the level of the brainstem and cortex may significantly contribute to the language disorder of children with ASD in preschool age [19-24].

Atypical auditory processing for speech and non-speech stimuli has been reported in ASD patients. We aimed to provide a clear insight into the auditory processing disorder at the brainstem level by reviewing the studies on auditory brainstem electrophysiological evaluation in ASD patients.

Information and Methods

In this systematic review, studies on brainstem electrophysiological evaluations in ASD patients from 2002 to 2022 were searched by "Autism", "Auditory Brainstem Responses", and "Speech" keywords in Scopus, PubMed, Google Scholar, and ScienceDirect databases.

The title and then the abstract of the articles were first evaluated. The English articles with available full-text on electrophysiological studies on hearing with speech and click stimuli, assessing patients with autism without other disabilities and hearing loss, and those comparing two autism and norm groups were entered the study. Studies on psychological aspects, accompanying imaging assessments, and those on autistic individuals with mental problems were excluded. At the end, 20 articles were selected.

Findings

The summary of the selected articles was presented in Table 1.

Table 1. Results of studies on auditory brainstem electrophysiological evaluation in ASD patients

Author/Year	Title	Variable	Results
Marco *et al.* [3]/2011	Study of auditory evoked potentials in autism.	ABR	In 16 children with autism, absolute latencies of wave III and V and IPL I-III and I-V were increased.
Chen *et al.* [5]/2019	Atypical longitudinal development of speech-evoked auditory brainstem response in preschool children with autism spectrum disorders.	sABR	ABR and sABR were assessed from 15 ASD children at a time interval of one year and it was observed that with increasing age lat and Amp (amplitude) in the ASD group is changing and approaching the normal range.
Claesdotter-Knutsson *et al.* [6]/2019	Abnormal auditory brainstem response in the pons region in youth with autism	ABR	Assessing the BS response using complex stimuli in 39 ASD children, the amplitude of wave III in AfraASD was smaller than that of normal subjects.
Santos *et al.* [7]/2017	Autism spectrum disorders and the amplitude of auditory brainstem response wave I	ABR	An increase in the amplitude of the B wave compared to the V wave was seen in children, which could be due to the disorder in the maturation of the auditory system in this group.
Magliaro *et al.* [10]/2010	Study of auditory evoked potentials in autism	ABR	16 children with autism were compared with the normal group and different results were found with the control group.
Li *et al.* [11]/ 2020	Continued development of auditory ability in autism spectrum disorder children: A clinical study on click-evoked auditory brainstem response	ABR	In 20 autistic children, ABR was compared in two stages with an interval of one year between two normal and autism groups. The results showed a decrease in absolute latencies and IPLs in the autism group.
Miron *et al.* [13]/2016	Prolonged Auditory Brainstem Responses in Infants with Autism	ABR	70 children with autism were studied in terms of ABR. In the group of infants with ASD, absolute and interpeak latencies were longer compared to the normal group
Kwon *et al.* [15]/2007	Electrophysiologic Assessment of Central Auditory Processing by Auditory Brainstem Responses in Children with Autism Spectrum Disorders	ABR	71 ASD children showed increased latency of wave V and increased IPL I_V by ABR evaluation.
Dabbous [16]/2012	Characteristics of auditory brainstem response latencies in children with autism spectrum disorders	ABR	Comparing ABR in 25 autistic children with the control group, 44% of wave III showed more latency time.
Miron *et al.* [17]/2018	Auditory brainstem response in infants and children with autism spectrum disorder: A meta-analysis of wave V	ABR	The latency time of wave V was compared in people with ASD over 18 years old and under 18 years old. It was found that the latency time decreases more with increasing age in ASD than in the normal group.

Continue of Table 1 from the last page

Russo *et al.* [18]/2009	Brainstem transcription of speech is disrupted in children with autism spectrum disorders	ABR	45 ASD children were subjected to ABR and sABR evaluation, ABR lat was within the normal range, but sABR evaluation showed a clear difference in the onset and FFR of the response.
Miron *et al.* [19]/2021	Prolonged Auditory Brainstem Response in Universal Hearing Screening of Newborns with Autism Spectrum Disorder	ABR	ABR321 examination of children with ASD at the intensity level of 35dB, and it was observed that the V-negative wave was longer than the control group.
Fujikawa-Brooks *et al.* [21]/2010	The effect of rate stress on the auditory brainstem response in autism: a preliminary report.	ABR	Evaluation of ABR response with different presentation rates and investigation of the effect of the rate change on ABR responses in 20 children with autism, which showed that in high latency rate, V wave in autistic children is more than normal children.
ElMoazen *et al.* [22]/2020	Binaural interaction component of the auditory brainstem response in children with autism spectrum disorder	ABR	Comparison of single-ear and two-ear responses in 20 ASD children and the norm group. The amplitudes in the two-phone responses in the ASD group were smaller than those in the normal group.
Källstrand *et al.* [25]/2010	The abnormal auditory forward masking pattern in the brainstem response of individuals with Asperger syndrome	ABR	16 ABRs were taken from ASD children with forward noise and while presenting the noise, the amplitude of wave III was significantly smaller than that of normal subjects.
Russo *et al.* [26]/2008	Deficient brainstem encoding of pitch in children with autism spectrum disorders.	sABR	The use of speech syllables with ascending and descending pitch and its comparison in the ASD and normal groups of the impairment in understanding pitch in the speech was seen in the ASD group compared to the normal group. But there was no difference in ABR between the two groups.
Ramezani *et al.* [27]/2019	Auditory brainstem response to speech in children with a high functioning autism spectrum disorder.	sABR	28 evaluations of sABR in ASD children and it was observed that the latencies of all waves and duration of V-A complex increased in the ASD group compared to the normal group.
Roth *et al.* [28]/2012	Evidence for atypical auditory brainstem responses in young children with suspected autism spectrum disorders	ABR	In 26 children with autism, absolute latencies and IPLs were increased compared to the normal group
Othman *et al.* [29]/2022	Auditory Brainstem Response in Children with Autism Spectrum Disorder	ABR	In 21 children with autism, an increase in the latency of the A, C, and O sABR waves were seen.
Kamita *et al.* [30]/2020	Brainstem auditory evoked potentials in children with autism spectrum disorder	ABR, sABR	For people with autism spectrum disorder, the intervals between peak III---V were higher for brainstem auditory evoked potentials with speech stimuli, the latencies of waves A, C, D, E, F, and O were shorter in subjects with ASD.

Discussion

Auditory Brainstem Responses (ABRs)

The brainstem is a structure with neurons characterized by high neural synchronization. In the clinical setting, injuries affecting the brainstem are manifested as an effect on the latency time or inter-peak latencies (IPLs) of ABR with an accuracy of tens of milliseconds and this accuracy in differentiating abnormal cases from the norm is the main reason for the widespread use of ABRs with click and tone burst auditory stimuli for brainstem investigation. Each response peak is the simultaneous activity of auditory system neurons in response to an external acoustic stimulus [8].

Impaired reception and integration of sensory information, especially auditory data, is one of the main characteristics of ASD children. The brainstem plays a key role in receiving and integrating auditory and sensory data [9]. Most studies on the processing of ABR in individuals with ASD have used click stimuli and have shown an increase in V wave latency and I-V interpeak latency in ASD individuals compared to the normal group [10-16]. However, in a meta-analysis, Mirron *et al.* compared the latency time of wave V in people with ASD over 18 years old and under 18 years old. They found that the prolongation of the absolute latency time of wave V in the ASD group compared to the norm group had a clear negative correlation with age and a reduction in latency time is associated with increasing age in ASD compared to the normal group [17]. These results were observed in the studies by Li *et al.* and Kuntsson *et al.* [6, 11, 17], indicating that with increasing age and maturation of the nervous system, the latency time of the waves approaches the normal range. In a few studies, there was no difference in the lat and amplitude of ABR waves in the ASD group [18], which is due to assessing older people, which is in line with the results of other studies reporting that with increasing age and maturation of the nervous system, the results approach the normal range. Miron *et al.* observed an increase in V-negative in children with ASD, which indicates that children exhibit ASD-related neurophysiological changes at birth [19].

Knutssona *et al.* compared ABRs in two ASD and normal groups by comparing backward and forward noise presentation to investigate changes in ABRs in ASD and observed an increase in the wave III amplitude in ASD patients compared to the control group. Because the origin of wave III is from the pons, it seems that more neural firing occurs in this region in response to acoustic stimuli in the ASD group than in the normal group. Also, the pons is involved in the processing of other sensory information, such as taste, pain, touch, and facial feeling, and more nerve firing in this area can explain the hypersensitivity of children with ASD to pain and touch [6]. These results were also observed in the meta-analysis by Talge *et al.* [20]. The simplest interpretation of the increase in neural firing in the pons can be an increase in sensitivity to sound in the ASD group.

Fujikawa *et al.* used fast and slow presentation rates

and indicated that the latency time of wave V in the ASD group was longer than the control group for the fast presentation rate [21]. This difference was not seen in the slow presentation rate and it indicates that it is not always sensitive enough to detect brainstem disorder in people with ASD and the fast presentation rate provides more information related to the integrity of the brainstem in this group. Therefore, increasing the stimulus rate can increase the sensitivity of ABR as a marker for identifying hearing dysfunction in this group. Elmoazen *et al.* compared the difference in the ABR-BIC interaction in 20 ASD children and 20 normal children. The ABR-BIC amplitude in the ASD group significantly reduced compared to the normal group because the ABR-BIC shows binaural interaction and is a valid and proven response that reflects binaural processing. This finding indicates two-ear processing disorder in children with ASD and can represent the reduction or absence of two-ear interactions in this group, making listening environments with high background noise difficult [22].

Considering that the ABR test is a common and available clinical test, the increase in the latency of wave V and the amplitude of wave III, especially at a high stimulation rate, can be used as an indicator for the prognosis of this disorder in children.

Speech auditory brainstem responses (sABR)

In addition to transient responses, persistent responses are also produced in the brainstem in response to speech stimuli. During the last two decades, more complex stimuli, such as speech sounds or music, which challenge the brainstem more, have been more used. One of these complex stimuli is the speech syllables /da/, which has been used in various studies. The sABR response is divided into two main parts: onset response and frequency following response (FFR) [23, 24]. When using the speech syllables /da/, the initial part represents the beginning of the consonant and contains non-periodic information. The initial waves are similar to the ABR waves in response to the click stimulus (I and III peak and Complex V-A). The FFR is a reflection of the phase lock to the fundamental frequency of the stimulus and is created in response to the periodic information in the vowel. Therefore, the time intervals between the peaks D, E, and F in the FFR related to the stimulus basic frequency F0, while the peaks between the FFR waves D, E, and F represent the phase locking at the frequencies of the first formant (F1) [23].

A few studies have not been done using this test in this group. The presence of speech perception disorders in ASD people is partly due to a disorder in the sABR. However, how speech sounds are processed in children with ASD remains largely unknown. Nonetheless, even in click stimulus studies where noise is used as an agent to challenge the nervous system, a decrease in amplitude and an increase in latency are observed [25].

Studies of ABRs in ASD have shown that these children have atypical responses compared to the normal group. Russo *et al.* used speech syllables (falling and rising). In this study, in order to check modulation tracking, frequency error (accuracy of encoding modulation during the stimulation) and modulation power (response frequency evaluation, which shows the strength of neural phase locking to the stimulus base frequency) were used. The modulation tracking was reduced in ASD people compared to the normal group, and wave analysis showed that these people show impairment in modulation coding in speech [26]. Ramezani *et al.* using 28 ASD children assessed the processing of subcortical brain responses using brainstem potentials with speech stimuli and found that the latency time of the V-A complex was significantly different between the two control and ASD groups. These results indicated weaker neural synchrony and poorer perception of speech stimulus onset in ASD children. The delay in the temporal coding of the sABR in ASD subjects compared to the control group indicates that the synchrony in neural firing is affected, which reflects the dysfunction in processing the temporal features of the speech stimulus at the level of the brainstem. As temporal auditory processing plays an important role in speech understanding, this disorder can be a reason for speech understanding disorders, especially understanding speech in noise in this group [27].

Chen evaluated the developmental pattern of auditory information processing at the brainstem level in 15 children with ASD versus 20 typically developing children using the sABR. The results showed that auditory processing at the subcortical level is well developed in normal children, but it is immature and abnormal in children with ASD of the same age [5]. This impairment in sABR can be the reason and justification for speech perception disorders in this group. According to the results of this review, ABR evaluation is a suitable, available and quick tool and marker for ASD diagnosis at a young age, by which fast-tracking is possible in this group.

One of the limitations of the present study is the heterogeneity in the studied groups in terms of the number, the performed test, and even the selection of people with ASD. More detailed studies are needed in ASD patients and different types of auditory stimuli in the developmental stages of people with ASD to gain better knowledge about the auditory processing of this group and to be sure that these electrophysiological tests can serve as biomarkers in the diagnosis of the ASD population.

Conclusion

There is an impairment in ABRs with click stimulus and complex speech stimulus in children with ASD, and this group has difficulty at the brainstem level due to the disruption in the pathways and

connections in the brainstem in receiving environmental auditory information and integrating information from the two ears. Abnormal auditory processing can be observed in the lower parts of the auditory system in ASD patients, and the complexity of these disorders is evident from receiving to processing complex information. However, most studies using speech or complex stimuli that challenge the nervous system more tend to show functional impairment. Impaired speech stimulus processing and speech understanding in these people can be considered a result of auditory temporal processing impairment at the level of the brainstem and indicates the important role of temporal processing in speech understanding.

Acknowledgments: None declared by the authors.
Ethical Permissions: None declared by the authors.
Conflicts of Interests: None declared by the authors.
Authors' Contribution: Ramezani M (First Author), Main Researcher/Methodologist/Introduction Writer/Discussion Writer (70%); Lotfi Y (Second Author), Assistant Researcher/Data Analyst/Discussion Writer (20%); Hajri SN (Third Author), Assistant Researcher/Discussion Writer (10%)
Funding/Support: This article is taken from the PhD thesis in audiology by the 1st author guided by the 2nd author at the University of Rehabilitation Sciences and Social Health.

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