



Original Article

Otoacoustic Emissions in Young Children with Autism

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OBJECTIVE: The aim of this study is to investigate otoacoustic emissions (OAEs) in young children with autism compared with those in an age-matched control group.

MATERIALS and METHODS: Thirty-eight children with autism aged 3-6 years and 27 typically developing (normally developing) control subjects participated in this study. All the participants had normal hearing and middle-ear function. Auditory brainstem responses were used to determine the hearing status in the autism group. Transient-evoked otoacoustic emissions (TEOAEs) and distortion-product otoacoustic emissions (DPOAEs) were measured in the two groups.

RESULTS: The TEOAE response level was higher in the autism group. Analysis of the DPOAE response showed that the mean emission levels at 1.5, 2, 3, and 6 kHz and signal/noise ratios at 2, 4, 6, and 8 kHz were higher in the autism group ($p < 0.05$). The greatest between-group differences were observed in the DPOAE signal levels at 2, 3, and 6 kHz ($p = 0.000$). No statistically significant difference was found between the noise levels in the autism and control groups ($p > 0.05$).

CONCLUSION: The emission responses in the autism group were higher than those in the control group. The increase in DPOAEs at high frequencies may be related to the higher outer cell activation in the autism group. Further studies with larger sample sizes comprising younger children are needed to confirm the result and investigate the possible association between the increased OAEs and auditory sensitivity reported in autism.

KEYWORDS: Autism, hearing (peripheral hearing system), otoacoustic emissions, sound sensitivity (auditory sensitivity)

INTRODUCTION

Autism is a neurodevelopmental disorder characterized by severe impairments in social interaction and communication and a restricted and repetitive behavior^[1]. Children with autism are generally indifferent to their environment, initiating interactions and responding to interaction attempts^[2]. Problems related to language development are regarded as one of the main indicators of autism at an early age. In children with autism, language does not emerge at the normal developmental stage and follows an atypical course^[3]. The aforementioned traits may result in children with autism initially being perceived to have hearing impairment. Children who are eventually diagnosed with autism are often initially suspected to have hearing impairment by their parents^[4]. Therefore, examining the hearing status of children with suspected autism is extremely important and a usual part of the prediagnosis process. In addition to delayed development of spoken language, auditory abnormalities and unusual responses to auditory stimuli have been reported in autism^[5-7]. Indeed, the existence of unusual sensorial responses is considered a trait that accompanies autism^[2, 8]. For example, children with autism may show hyposensitivity or hypersensitivity to touch or textures, lights, and sounds^[7-10].

The existence of hypersensitivity and abnormal responses to noises are based on parental reports, with 32%-81% of parents of children with autism reporting that their children display hypersensitive reactions to sounds^[10-12]. In addition, some individuals with autism have been reported to show enhanced frequency discrimination skills^[13]. Various reactions, such as covering of ears with hands, crying, increased muscle tone, and disruptive and aggressive behaviors, are accepted as indicators of intolerance to auditory stimuli in individuals with autism^[9, 14].

Studies have investigated whether auditory intolerance in autism stems from peripheral auditory mechanisms but have not found any conclusive evidence that confirms the existence of a physiological entity explaining this intolerance^[6, 12, 15]. These studies, which includ-

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ed behavioral, audiometry, and computer-assisted threshold assessments of acoustic reflexes and otoacoustic emissions (OAEs), found no difference between the peripheral function of children with autism and that of typically developing children that could be associated with auditory sensitivity [6, 12, 15]. Several studies [16, 17] have reported that the auditory sensitivity of individuals with autism might be associated with a reduction in the function of the medial olivocochlear (MOC) system or an unusual MOC system asymmetry and suggested that this asymmetry indirectly reflects more central auditory processing alterations [16, 17]. However, MOC functions were found to be normal in Asperger syndrome, which is part of the autistic spectrum and shows auditory sensitivity reactions similar to those observed in autism [18].

Because it is difficult to employ standard behavioral audiometric procedures in the assessment of children with autism, OAE measurements are used. The information obtained from OAE measurements can shed light on whether the sensitivity of children with autism to auditory stimuli is associated with the outer hair cell activation. Transient-evoked otoacoustic emissions (TEOAEs) and distortion-product otoacoustic emissions (DPOAEs) are used to determine the response of the outer hair cells to acoustic stimuli [19]. The measurement of OAEs in individuals with autism has several advantages, such as yielding objective results on cochlear mechanisms. Also, OAEs are simple to measure, and the measurements do not greatly depend on the cooperation of the patient. According to the literature, such objective methods provide a practical way of detecting auditory problems in non-cooperative children [4, 20]. Studies on the OAEs of children with and without autism revealed different results, with some showing no differences between groups and others showing a difference in the emission responses of children with autism [6, 12, 21]. No studies on OAE values have obtained findings that could explain the unusual auditory responses of children with autism [6, 7, 12, 17, 18, 21]. However, studies have reported that reactions to auditory stimuli are more frequent and stronger during early childhood and that the frequency and strength decrease in later years [22, 23]. Given that the reasons underlying the unusual auditory reactions of children with autism are not fully understood and that these traits are observed more frequently during early childhood, studies on small children with autism may help to shed light on the reasons underlying these unusual auditory responses.

This study is based on the idea that studies comprising more number of children belonging to a specific age group will contribute to the understanding of the auditory responses of individuals with autism. To clarify this issue, this study investigated whether the TEOAEs and DPOAEs of children with autism aged 3-6 years differed from those of an age-matched typically developing control group.

MATERIALS and METHODS

The transient evoked otoacoustic emission and distortion product otoacoustic emission responses of 38 children with autism were investigated and compared with those of 27 typically developing control subjects. The study was conducted in Otolaryngology Department at Trakya University School of Medicine, Edirne, Turkey.

Participants

The study was designed and performed according to the Declaration of Helsinki. After obtaining the approval of the local ethical committee and informed consents, children aged 3-6 years were in-

cluded in the study. The study sample comprised children diagnosed with autism according to DSM (Diagnostic and Statistical Manual of Mental Disorders) IV [24] and DSM-5 criteria [2] (4 children) and an age-matched control group of typically developing children with normal bilateral hearing. All the cases had presented to our clinic with suspected autism between 2007 and 2015 for an auditory assessment. Information on the auditory status of the children and OAE results were obtained from the patients' case files. The inclusion criteria for the study were as follows:

- Age, 3-6 years
- A diagnosis of autism by a specialist team, including a child psychiatrist
- Normal middle-ear function (type A tympanogram)
- Normal bilateral hearing
- DPOAE test results for all frequencies (1000 Hz, 1500 Hz, 2000 Hz, 3000 Hz, 4000 Hz, 6000 Hz, and 8000 Hz) in addition to TEOAE results and auditory brainstem responses (ABR)

Because conventional behavioral techniques cannot be reliably used to test children with autism, ABR and TEOAE results were employed to determine their hearing status [25]. Normal hearing was said to be present in the autism group when an ABR wave V was obtained bilaterally with a 20 dB nHL stimulus and TEOAEs were positive, with a reproducibility score of 50% or greater [26].

The control group included typically developing children who had normal hearing according to behavioral audiometry and TEOAE results. Because all the children in the control group could cooperate with behavioral audiometric testing, ABRs were not an inclusion criterion to detect normal hearing in this group.

Sixty-five children satisfying the inclusion criteria were finally included in the study. The study group comprised 11 (29%) girls and 27 (71%) boys, with an average age of 3 years and 3 months \pm 6 months. The control group comprised 9 (33%) girls and 18 (67%) boys, with an average age of 3 years and 6 months \pm 9 months.

Measurements

Behavioral audiometry

Hearing threshold assessment and low-frequency audiometry (AC40 Clinical Audiometer, Interacoustics, Denmark) were performed in a sound-isolated chamber. In the low-frequency audiometry, TDH-39 (Telephonics, USA) earphones were worn. Hearing thresholds were determined by air conduction at frequencies ranging from 0.5 to 4 kHz. Only the children in the control group underwent behavioral audiometric measurements. There were no behavioral audiometric test results in the files of children with autism because children in this group could not be evaluated in this aspect owing to their lack of cooperation during testing.

Tympanometric examination

Middle-ear pathologies and stapes reflexes were assessed by an impedance audiometer (AZ-7, Interacoustics, Denmark) and a recording device (XYT Recorder AG-3, Denmark). The pressure range of the measurement was set at +200 daPa to -400 daPa. Type "A" tympanograms (peak pressure: between +100 daPa and -100 daPa) were accepted as normal.

TEOAE Measurement

The TEOAE tests were performed in a soundproof room using a Capella-Madsen pediatric OAE probe assembly (GN Otometrics A/S Taastrup, Denmark) fitted to the ear canal. Responses to clicks were windowed at 3-20 ms after the stimulus onset and averaged following 2080 repeated responses. The stimulus used was a non-linear, 40 μ s click. The clicks were presented at a sound pressure level (SPL) of 80 dB.

DPOAE Measurements

The DPOAE tests were performed in a soundproof room using a Capella-Madsen pediatric OAE probe assembly (GN Otometrics A/S Taastrup, Denmark) fitted to the ear canal. The acoustic stimuli were two continuous pure tones at the so-called primary frequencies of f1 and f2. The primary L1 and L2 levels were separately adjusted, and the frequency ratio of f2/f1 was fixed at 1.22. The levels of the stimuli were fixed at L1=65 and L2=55 dB SPL. The DPOAE measurement was evaluated when the generation of the 2f1-f2 DPOAE occurred by primaries with geometric mean frequencies of 0.75-8 kHz. The testing time was 60 s. The detection of the DPOAEs was based on the amplitudes being at least 3 dB above the average level of the noise floor sampled at several frequencies surrounding the emission frequency^[27]. The frequency-specific signal/noise ratios (SNRs) in both ears of the children were evaluated.

ABR Measurement

Auditory brainstem responses (ABRs) were obtained from surface electrodes at the two mastoids (A1 and A2, international 10-20 system) referenced to Cz. The electrode impedances were <5 kOhms. Click stimuli (duration: 0.1 ms; frequency bandwidth: 1-4 kHz) were delivered through an audiological earphone (TDH-39 Telephonics, USA), and ABRs were recorded using a Medelec Synergy (Oxford Instruments, UK) device. The repetition rate was 10/s. An average of 2000 sweeps (alternating click) was recorded, and automatic artefacts were rejected. The stimulus intensity was initially 80 dB nHL, followed by 10-dB decrements until waveforms were no longer present, thus determining the threshold of the ABR. The ABR threshold was defined as the lowest dB nHL level that produced a reliable peak V in the ABR waveforms. The ABR measurements were obtained only for the autism group because behavioral audiometry could not be performed in this group.

The ABR and OAE tests in the autism group were performed under sedation with hydroxyzine HC1 (Atarax® UCB, İstanbul, Turkey, 1 mg/kg per oral), whereas the OAE tests in the control group were performed when the subjects were either naturally asleep or awake.

Statistical Analysis

Statistical analysis was performed using Statistical Package for Social Sciences, version 17.0 (SPSS Inc.; Chicago, IL, USA). The variables were compared using Student's t-test or Mann-Whitney U test depending on their distribution of normality, as determined using Shapiro-Wilk test. The level of significance was set at $p < 0.05$. The data obtained from the two groups were compared both separately for the right and left ears and for both ears together. Mann-Whitney U test was used for comparing the following data sets that did not show an equal distribution: left ear DP level, 1 kHz, 6 kHz, and 8 kHz; SNR, 1.5 kHz, 2 kHz, 3 kHz, and 4 kHz; right ear DP level, 6 kHz and 8 kHz; and SNR, 1.5 kHz, 2 kHz, 3 kHz, and 6 kHz. An independent samples t-test was used for comparing the other data.

Table 1. TEOAE test results of children with and without autism

TEOAE	Right ear		Left ear	
	Autism group	Control group	Autism group	Control group
Frequency (Hz)				
Response Level	23.62±5.29*	20.66±5.41	22.62±5.94	20.87±6.34
SNR	13.56±5.05	12.76±5.93	12.76±5.93	12.76±5.93

TEOAE: transient-evoked otoacoustic emission; SNR: signal/noise ratio
* $p < 0.05$

Table 2. Mean values of DPOAE responses in children with and without autism

DPOAE	Right ear		Left ear	
	Autism group	Control group	Autism group	Control group
Frequency (Hz)				
DP Level (dB SPL)				
1000	8.30±8.48	8.07±8.34	8.91±7.75	7.93±6.00
1500	11.51±8.91	8.83±8.75	14.03±6.22*	10.87±5.71
2000	13.40±5.63*	7.04±5.90	12.47±5.85*	7.71±5.62
3000	12.01±5.30*	7.84±7.68	12.95±4.70*	7.89±6.27
4000	14.22±5.12	12.12±7.91	14.54±6.00	12.18±5.66
6000	18.00±8.01	14.56±9.93	20.59±5.62**	12.64±10.95
8000	20.03±8.86	17.86±9.99	20.70±9.29	15.10±12.42
DP-SNR (dB SPL)				
1000	6.43±6.29	5.86±7.98	7.33±5.38	6.23±7.41
1500	10.34±6.50	8.90±7.15	11.84±5.88	10.07±6.04
2000	12.39±5.07	10.87±5.01	13.07±5.77	10.35±3.94**
3000	15.12±6.20	15.31±7.44	17.49±6.20	12.96±5.45**
4000	19.59±6.99*	15.01±6.36	17.93±6.41	16.87±7.03
6000	22.00±9.23	20.57±8.43	22.89±7.43	17.77±9.10**
8000	19.59±9.17	17.20±10.06	20.92±8.60	16.00±10.80**

p values shown by * in Table 2 have been obtained through t-test and p values shown by ** have been obtained through Mann-Whitney U test
DPOAE and DP: distortion-product otoacoustic emission; SNR: signal/noise ratio;
dB SPL: decibel sound pressure level

RESULTS

The mean response levels and SNRs obtained from the TEOAE and DPOAE measurements of the left and right ears are presented in Tables 1 and 2.

There was no significant difference in the TEOAE SNRs of the autism and control groups ($p > 0.05$). With regard to the TEOAE measurements, the only between-group difference was that the response level of the right ear in the autism group was significantly greater than that of the control group ($p = 0.03$, Table 1).

The DPOAE levels at 2 kHz and 3 kHz frequencies in the left ear and 1.5 kHz, 2 kHz, 3 kHz, and 6 kHz frequencies in the right ear were higher in the autism group compared with those in the control group ($p < 0.05$, Table 2). According to the SNR averages, there was a significant between-group difference in the left ear at a frequency of 4 kHz and in the right ear at frequencies of 2 kHz, 3 kHz, 6 kHz, and 8 kHz ($p < 0.05$, Table 2). The DPOAE responses were higher at high frequencies.

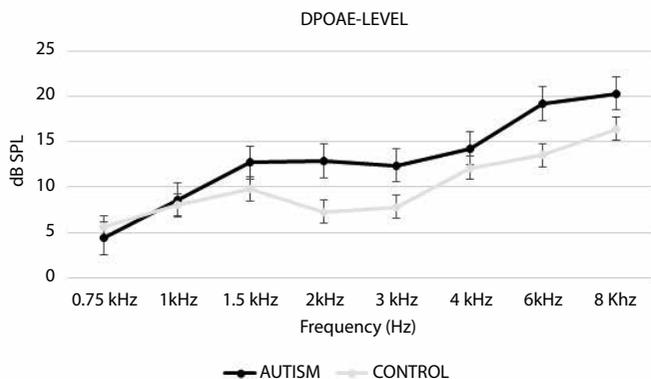


Figure 1. DPOAE levels of children with and without autism for both ears together. DPOAE: distortion-product otoacoustic emission

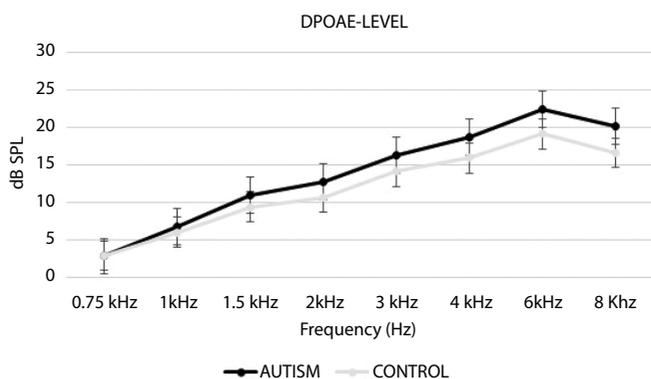


Figure 2. DPOAE SNRs of children with and without autism for both ears together. DPOAE: distortion-product otoacoustic emission; SNR: signal/noise ratio

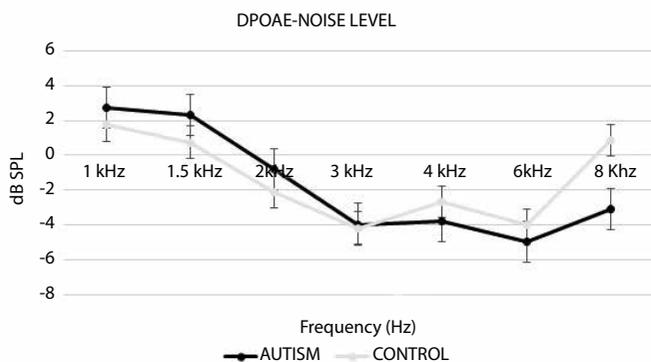


Figure 3. DPOAE noise levels in autism and control groups. DPOAE: distortion-product otoacoustic emission

When data from both ears were analyzed together (76 ears in the autism group and 54 ears in the control group), the TEOAE response level was significantly higher in the study group. The analysis of the DPOAE test results for both ears together showed that the means of emission levels at 1.5 kHz, 2 kHz, 3 kHz, and 6 kHz (Figure 1) and SNRs at 2 kHz, 4 kHz, 6 kHz, and 8 kHz were higher in the autism group ($p < 0.05$, Figure 2). The greatest between-group differences in the DPOAE levels were observed at 2 kHz, 3 kHz, and 6 kHz ($p = 0.000$). There was no statistically significant difference between the noise levels in the autism and control groups ($p > 0.05$; Figure 3).

DISCUSSION

The findings show that OAEs in young children with autism were larger than those in the typically developing control subjects. The DPOAE levels and SNRs at several frequencies in addition to the overall values for the TEOAE levels were higher in the autism group compared with those in the control group. Studies of the auditory characteristics of children with autism showed that the OAE responses in children with autism were either equivalent to those in typically developing children [6, 12] or lower [20, 21]. In a study on children with normal hearing, the TEOAE SNRs and DPOAE levels were similar in children with autism and typically developing control subjects [6]. In a study by Danesh and Kaf [21], the overall SNRs of DPOAEs were lower in the autism group compared with those in the control group (21.5 dB and 26 dB, respectively). Other studies found no difference between the DPOAE levels of children with and without autism [6, 12], although the values in those studies were lower than those in the study by Danesh and Kaf [21] and the present study. The conflicting results of the present study compared with those of the studies reported in the literature may be explained by the ages of the children and the use of sedation in the autism group because of poor cooperation.

Unlike the aforementioned studies, in all the autism cases included in the present study, OAE measurements had been obtained under sedation to ensure that the children remained still during the tests. In the previous studies, the children sat quietly during OAE measurements without requiring sedation [6, 12, 17, 21]. Some studies achieved this by excluding children with poor cooperation [21] or by selecting cases that were at the high end of the spectrum [6]. It was stated that sedation had no significant influence on OAEs [28, 29]. To confirm whether wakefulness or sedation might affect the OAE responses by causing a difference in noise levels during measurements, we compared noise levels and found no statistically significant between-group differences.

In the current study, the higher OAE responses in the autism group might stem from the inclusion of young children. The mean age of the children in this study ($3.3 \text{ years} \pm 6 \text{ months}$) was younger than that of the children in previous investigations because the data were imported from the cases during the diagnostic process. The mean ages of the children in the other studies were 9.5 years [6], 5.7 years [12], 10.6 years [17], and 8.9 years [21]. Studies that included typically developing cases found that TEOAE amplitudes were higher in the first year of life [30, 31]. Studies also showed that the DPOAE responses of children aged 1-3 years were higher than those of teenagers and that amplitudes fell much more rapidly in the first 6 years of life than in the subsequent years [32-34]. A study of the TEOAE responses of children with and without autism aged 4-10 years and 11-18 years found smaller TEOAE amplitudes in children with autism than those in the control subjects after the age of 10 years [17]. Although that study found no significant difference in the TEOAE responses, the responses of young children with autism were higher than those of young control subjects. Another study reported that sound intolerance in children with autism during early childhood began to decline with maturity [22]. The aforementioned findings suggest that outer hair cell activation might be higher in children with autism, particularly at an early age, and that this might make them more sensitive to auditory stimuli. To shed light on the effect of age, a previous study investigated

the DPOAE responses of children with autism aged 6-14 by dividing them into subgroups based on those older and younger than 9 years of age ^[21]. That study found decreased SNRs in the younger autism group when compared with those in the younger and older control subjects. Although these two studies achieved different findings in terms of age (one study found a decrease in TEOAE amplitude with age ^[17], whereas the other found lower DPOAEs ^[21] in younger children with autism), in both studies, the children in the younger group were much older than those in the present study, which makes it difficult to compare the results.

Autism is a very complex disorder. Studies have suggested that the unusual auditory reactions of individuals with autism might be related to neuro-anatomic differences, cross-modal interactions between the auditory and somatosensory systems, and auditory processing dysfunction ^[18, 21]. Although larger emissions in young children with autism point to a potential role of overactive outer hair cells, because this study has limitations, it cannot be concluded that these cells are responsible for auditory sensitivity in children with autism, especially at an early age.

This study has a number of limitations. First, there were no data in the patients' files on the presence or absence of unusual auditory responses; therefore, it was not possible to evaluate the groups on this aspect. Second, the study included only the emission responses of younger children and did not compare them with those of older children. Third, the children in the study group were not subdivided into groups and then analyzed according to the severity of their autism. Sedation is considered to have a negligible effect on OAE responses ^[28, 29], and we found no between-group difference in the noise levels. However, this sedation-related disparity between test-taking conditions of the groups can be considered to be a limitation of the current study.

CONCLUSION

The OAE responses of children with autism during the early childhood period were higher than those of the age-matched typically developing control subjects. Given the young age of the children in the present study compared to that of those in previous studies, we speculate that the auditory responses might be explained by overactive outer hair cells, particularly in the early childhood. However, it is not possible to draw any conclusion on this issue at present. Furthermore, this study cannot answer whether there is a particular age when the high emission responses of children with autism begin to decrease rapidly and reach a level same as or lower than that of the age-matched typically developing control subjects. The findings of the current study reveal the need for further research that involves children of various ages with autism with or without unusual auditory responses.

Ethics Committee Approval: Ethics committee approval was received for this study from the ethics committee of Trakya University School of Medicine Ethic Committee of Noninvasive Clinical 33 Researches (App No:TÜTF-BAEK 2015/120).

Informed Consent: Verbal informed consent was obtained from the patient's parents.

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