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Original Article

Contralateral Suppression of Spontaneous Otoacoustic Emissions in Individuals With Auditory Neuropathy Spectrum Disorder

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BACKGROUND: The current study attempted to assess efferent auditory system functioning in individuals with auditory neuropathy spectrum disorder (ANSD) using a new approach, contralateral suppression of SOAE, which has not yet been extensively researched.

METHODS: Spontaneous otoacoustic emissions (SOAEs) were recorded in a total of 62 ears, divided into 2 groups. Group I comprised of 31 ears with normal hearing (NH), while group II consisted of 31 ears with ANSD. All the participants considered for the study were in the age range of 18-45 years. Synchronized SOAE were recorded using the ILO V6 OAE instrument with and without noise (broadband noise, 50 dB SPL) in the contralateral ear. The frequency and amplitude shifts secondary to the introduction of contralateral noise were analyzed.

RESULTS: The results of the study showed a statistically significant high-frequency shift of SOAE with contralateral noise for the NH and ANSD groups. In addition, the NH group also exhibited a statistically significant reduction in SOAE amplitude in contralateral noise conditions. Such a reduction in SOAE amplitude was not observed in individuals with ANSD.

CONCLUSION: The absence of suppression of SOAE amplitude suggests efferent damage in individuals with ANSD. The shift in SOAE frequency toward higher frequency in the ANSD group, which is similar to NH group, is suggestive of differential allotment of medial olivocochlear (MOC) mechanism in individuals with ANSD, which codes for contralateral frequency changes and not for amplitude changes.

KEYWORDS: Contralateral suppression, amplitude shift, frequency shift, efferent auditory function, auditory neuropathy spectrum disorder

INTRODUCTION

Auditory neuropathy spectrum disorder (ANSD) is a type of retrocochlear pathology characterized by the normal functioning of outer hair cells, evidenced by intact cochlear microphonic (CM) potentials and otoacoustic emissions (OAEs) with absent or severely desynchronized auditory brainstem responses (ABRs).[1] For individuals with ANSD, hearing sensitivity usually varies from normal to profound hearing impairment. The exact site of lesion of ANSD is usually unknown, but the possibilities could be the abnormalities at the synapse of the inner hair cells and auditory nerve and or the auditory nerve itself,[2-4] but with intact functioning of outer hair cells. In humans, the usage of OAEs provides indirect non-invasive measurements of outer hair cell function. On the other hand, the use of ABR in the audiological test battery determines the functional capabilities of the afferent auditory nerve and brainstem. However, the inclusion of both of these tests does not facilitate understanding of efferent auditory functioning, which is also reported to be affected in ANSD patients.[5,6] This inference on efferent auditory nerve activity mediated by medial olivocochlear (MOC) can be duly made by the inclusion of contralateral suppression of OAEs.[6]

Audiologists employ techniques such as transient evoked OAEs (TEOAEs), distortion product OAEs (DPOAEs), and stimulus frequency OAEs (SFOAEs) to acoustically stimulate MOC efferents and make clinical judgments on MOC functioning.[7-9] Although acoustic stimulation in all these techniques can be derived using ipsilateral, contralateral, and bilateral (with respect to the ear being monitored for OAE presence) acoustic stimulations, the use of contralateral stimulation is preferred over the other 2 methods

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as it prevents two-tone suppression effects (i.e., contamination of OAEs recorded due to overlay of tone and response in the same ear which is being monitored). However, all the 3 techniques (TEOAEs, DPOAEs, and SFOAEs) are underpinned by the application of an emission-evoking stimulus, which by itself can elicit an efferent activity and interact with the otoacoustic emission.[9] However, the inclusion of spontaneous otoacoustic emissions (SOAEs), a type of OAE recorded without the use of an external stimulus, can be an effective technique in containing these limitations and can, therefore, be an effective tool for examining efferent auditory functions.[10]

Probst, Lonsbury–Martin, and Martin[11] defined SOAEs as acoustic energy recorded in the ear canal with characteristic frequency components (very narrow bands of energy), which are well above the noise floor. The presence of SOAE is confirmed by the appearance of spikes, typically reaching amplitudes of 10 or 15 dB, at 1 or more frequencies.[12] Hood et al.[5] assessed the contralateral suppression of transient evoked otoacoustic emissions (TEOAE) and found that individuals with ANSD lacked efferent suppression. The poor efferent responses could be probably due to the compromised afferent input to the olivocochlear pathway.[5] Similar inferences were also reported by Abdala et al.[6] who showed a lack of contralateral suppression of DPOAEs in ANSD using suppression tuning curves compared to NH adults.

Studies on SOAEs in individuals with ANSD are scant. From the available reports, Avilala, Mohan, and Barman[13] studied the prevalence of SOAE and reported that individuals with ANSD had higher prevalence than observed for NH adults. Individuals with ANSD had multiple numbers of SOAE that were mostly located in the lower frequency region (<1500 Hz) compared to the NH group. They suggested that the increase in the number of SOAEs could be a result of efferent damage in individuals with ANSD.[13] However, to the current knowledge of the researchers, there are no studies accounting for the magnitude and extent of contralateral suppression of SOAEs in individuals with ANSD. Hence, the current study aimed to assess the efferent auditory system functioning in individuals with ANSD using contralateral suppression of SOAE.

MATERIALS AND METHODS

Participants

A total of 62 ears were considered prospectively for the study. All the participants in the study were in the age range of 18-45 years. Group I comprised 31 ears with normal hearing (NH) sensitivity ($N = 31$, mean age: 25.6 $\pm$ 4.7y), whereas group II consisted of 31 ears with ANSD ($N = 31$; mean age: 25.93 $\pm$ 7.38y). The criteria adopted to diagnose ANSD were those recommended by Starr, Sininger, and Praat.[14] They are, preserved cochlear amplification, reflected by the presence of TEOAE and/or the presence of CM; altered auditory nerve responses as indicated by absent or severely abnormal ABRs; and normal otological and tympanometric findings with absent acoustic reflexes. Another group of 31 ears with a healthy auditory system served as the control group. This was ensured through a detailed case history, pure-tone audiometry, speech audiometry, immittance, and TEOAEs. None of the participants had any history of middle ear infections, ear pain, and Eustachian tube dysfunction at the time of testing.

Informed Consent and Ethical Guidelines

In the present study, all the testing procedures were carried out on humans, using non-invasive techniques and adhering to the guidelines of the Ethics Approval Committee of the institute. All the procedures were explained to the participants, and informed consent was taken from all the participants of the study. The authors declare no conflicts of interest.

Test Environment and Instrumentation

All the tests were carried out in an acoustically and electrically shielded room where the ambient noise levels were within the permissible limits as per ANSI standards (ANSI S3.1-1991, R2018). A calibrated 2-channel diagnostic audiometer according to the American National Standards Institute/Acoustical Society of America (S3.20, 2010), Grason-Stadler Incorporation Audio Star Pro (Grason-Stadler, Inc, 10395 West 70th St. Eden Prairie, MN 55344) with TDH 39 (Telephonics, Farmingdale, NY, United States) supra-aural headphones and Radioear B-71 (RadioEar, Audiometer Allé 1, 5500, Middelfart, Denmark) bone vibrator was used for pure-tone and speech audiometry. GSI tympstar (Grason-Stadler, Inc, 10395 West 70th St. Eden Prairie, MN 55344) was used for the assessment of middle ear status and ILO-V6 (Otodynamics Ltd, 36-38, Beaconsfield Road, Hatfield, Herts, AL-10 United Kingdom) otoacoustic emission equipment was used for obtaining TEOAE and SOAE. Auditory brainstem response was recorded using Bio-logic Navigator Pro evoked potential system (Natus Medical Inc, 50 Commerce Dr #180 Schaumburg, IL, 60173) with ER-3A (Etymotic Research, Inc. 61 Martin Lane, Elk Grove Village, IL 60007, USA) insert earphones.

PROCEDURE

Audiological Evaluation

The routine audiological evaluation was carried out on all the participants, which included the estimation of pure-tone air and bone conduction thresholds. Immittance evaluation was carried out using a 226 Hz probe tone and acoustic reflexes were obtained at 500 Hz, 1000 Hz, 2000 Hz, and 4000 Hz for both the ipsilateral and the contralateral ear. After ensuring routine PTA and immittance evaluation, TEOAEs and ABR were evaluated for determining the candidacy of the ANSD group. For TEOAEs, an adequate probe fit was ensured, and TEOAEs were measured using nonlinear clicks presented at 80 dB SPL. Click-evoked ABR was recorded using 100 ms click stimuli.

SOAE Measurements

SOAE were recorded from each ear of all the participants. The stimulus level in the external ear canal was auto-adjusted to 80 dB SPL. The time analysis for SOAE was 20 ms, and the power spectrum was generated by ILO V6 software. Synchronized SOAE were recorded with and without broadband noise (in the contralateral ear) at 50 dB SPL, presented through the insert earphone through the audiometer.

SOAE Analyses

The presence of SOAE was determined if the emissions recorded were greater than 3 dB SPL above the noise floor. For each of the participants, the SOAEs recorded in conditions with and without noise were analyzed using 2 conventional parameters: amplitude and frequency. The absolute changes in frequency and amplitude of SOAEs with and without noise were compared in each of the groups. In addition, the relative changes in amplitude and frequency (integer fraction obtained as a numeric difference in absolute SOAE amplitude/frequency recorded in conditions with and without contralateral noise) were calculated in both the groups. The relative (difference)

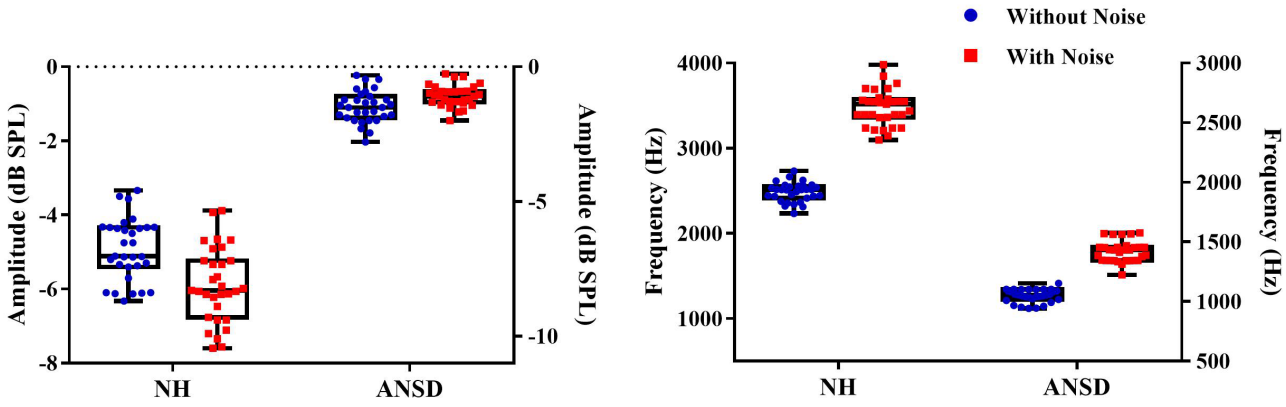

Figure 1. Absolute SOAE amplitude and frequency with and without noise in both the groups (NH and ANSD).

measure thus obtained was quantified as the SOAE amplitude shift for amplitude parameter and frequency shift for frequency parameter. The degree of frequency and amplitude-shift was also compared between the groups.

Statistical Analyses

The data were tabulated in the Statistical Package for the Social Sciences 22.0 (IBM Corp.; Armonk, NY, USA) and subjected to the statistical analyses. Test of normality was performed using the Shapiro–Wilks test, following which a mixed measure ANOVA (groups as the across-subject factor, and with and without contralateral noise conditions as the within-subject factor) was carried out to find the main effect of variables involved in the study. The follow-up analyses were conducted using paired t-tests comparing SOAEs evoked for 2 conditions (with and without contralateral noise) for each group separately. These analyses were conducted for both the frequency and amplitude shifts. The SOAE frequency and amplitude shifts (difference in SOAE amplitude and frequency between 2 noise conditions) of the 2 groups were analyzed using an independent *t*-test. Whenever significant differences were seen, the effect size was calculated using partial η^2 for ANOVA and Cohen's *d* for independent *t*-tests.

RESULTS

The focus of the current study was to analyze the effect of contralateral noise on the frequency and amplitude of SOAE. The data obtained were subjected to the Shapiro–Wilk test for normality. The results revealed normality in the distribution of data ($P > .05$), and therefore parametric tests were administered. Figure 1 represents the box plot of descriptive statistics (mean and standard deviation) for SOAE amplitude (left panels) and frequency (right panels).

As seen in Figure 1, there was a reduction in the mean SOAE amplitude with noise in the NH group. A minor reduction in SOAE amplitude with noise was also seen in individuals with ANSD. In contrast, the figure shows that there was an upward shift in the frequency of SOAE with contralateral noise in both groups. This suggests differential efferent auditory system damage in individuals with ANSD.

These group differences were further complemented by mixed ANOVA results for both SOAE amplitude and frequency. For the SOAE amplitude, significant main effects of both groups [$F_{1,60} = 1537.00$, $P < .001$, partial $\eta^2 = 0.96$] and noise conditions [$F_{1,60} = 257.42$ $P < .001$, partial $\eta^2 = 0.81$] were seen. Additionally, interaction between group and noise condition [$F_{1,60} = 257.32$, $P < .001$, partial $\eta^2 = 0.81$] was also observed. On other hand, the mixed ANOVA results for SOAE frequency revealed significant main effect of group [$F_{1,60} = 2116.52$, $P < .001$, partial $\eta^2 = 0.81$] and condition [$F_{1,60} = 274.04$, $P < .001$, partial $\eta^2 = 0.81$], but no interaction effects [$F_{1,60} = 0.33$, $P > .05$). Follow-up paired *t*-tests revealed statistically significant high-frequency changes in SOAE recorded in conditions with contralateral noise, compared to those recorded without noise. This finding was observed in both the participant groups [NH – t (30) = 12.21, $P < .001$, Cohens $d = 1.08$; ANSD – t (30) = 11.32, $P < .001$, Cohens $d = 1.87$], indicative of similar effects of noise on SOAE frequency in both groups. Contrary to the results of SOAE frequency changes, paired t-tests for SOAE amplitude showed significant noise effect only for the NH group [t (30) = 16.09, $P < .001$, Cohens $d = 2.85$) and not for the ANSD group [t (30) = 0.20, $P > .05$].

On statistical confirmation of group differences, independent t-tests were done separately for frequency and amplitude shifts (difference in frequency and amplitude with and without noise). The results of the t-tests revealed significant differences in contralateral suppression of SOAE amplitude [t (60) = 23.01, $P < .001$, Cohens $d = 0.92$] between groups, as shown in Figure 2. The results supplement the above findings that there was no suppression of amplitude with noise in individuals with ANSD. On the other hand, an independent *t*-test for contralateral shift in SOAE frequency showed no statistically significant differences between the groups [t (60) = 0.57, $P > .05$], as shown in Figure 3, indicative of similar frequency shifts between groups.

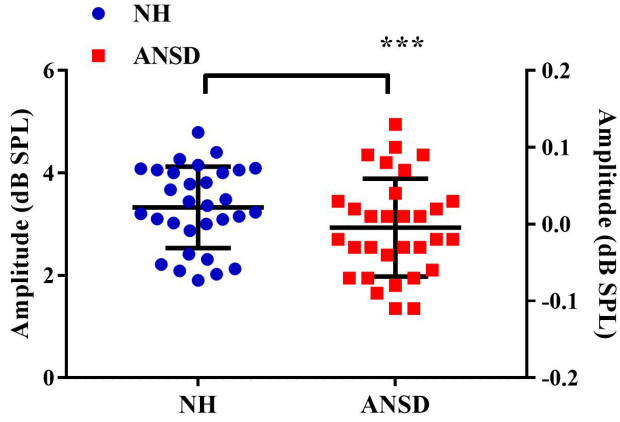

Figure 2. Contralateral suppression of SOAE amplitude in both the groups (NH and ANSD).

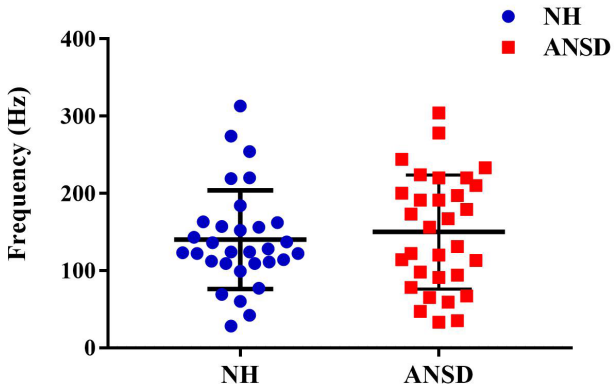

Figure 3. Contralateral shift in SOAE frequency in both the groups (NH and ANSD).

DISCUSSION

The aim of the present study was to assess the efferent auditory system functioning in individuals with ANSD using contralateral suppression of SOAE. The results showed that the SOAE amplitude reduced with contralateral acoustic stimulation in individuals with NH. The reduction in OAE amplitude with contralateral noise is also reported for other OAE types, such as DPOAE,[15] stimulus frequency otoacoustic emissions (SFOAE),[9] and TEOAE[8] in individuals with NH. Murugasu and Russell[16] explained that the change in amplitude due to the contralateral acoustic stimulation was mediated via the MOC, which attenuates the gain of the cochlear amplifier. This reduction in gain is directly related to the basilar membrane vibration due to the MOC activation. The study results also reveal that there was no reduction in the amplitude of SOAE with contralateral noise in individuals with ANSD. This indicates efferent auditory system damage in individuals with ANSD. The results of the study are in consonance with other studies on contralateral suppression of TEOAE and DPOAE.[5,6] They suggest that a poor afferent input to the medial olivocochlear bundle could affect the efferent auditory response in individuals with ANSD.[5] Thus, it could be afferent damage of ANSD, which could be resulting in reduced activation of MOC.

Interestingly, the present study also highlights a similar high-frequency shift in both ANSD and NH groups. This finding is indicative of possible involvement of different MOC regulating mechanisms, which likely manifests as deficits in the amplitude tuning and not the frequency tuning properties of efferent nerves in individuals with ANSD. The mechanism underlying the shift in SOAE frequency has not been vastly discussed in the literature. However, we draw support from the Mott et al.[17] model to explain the differential MOC activation in individuals with ANSD. According to the model, the contralateral noise alters the membrane conductance of the OHC, which in turn changes the feedback force provided by the OHC on basilar membrane mechanics. The product of these 2 physiological processes in OHCs can reflect changes in the intrinsic tuning of the SOAE generator. The Mott et al.[18] model clearly suggest the OHC serves merely as the power source of the SOAE generator. The high-frequency shift indicates the change in tuning properties but not in the location of the emission generator, suggestive of the existence of the role of different mechanisms for frequency shifts in SOAE due to contralateral noise. This mechanism could be preserved in individuals with ANSD because of the normal functioning of the OHC.

In addition to this, Shera[18] proposed another model on the generation of SOAE, which attempted to explain the shift in frequency with the contralateral noise. The model reported that the SOAE is generated based on cochlear standing waves. SOAE is generated by the multiple reflections of the cochlear generation site and middle ear boundary by phase accumulation. Thus, the tuning frequency of the SOAE is determined by the phase accumulated by the traveling wave of the cochlea. It is reported in the literature that activation of MOC can produce a phase lead in the basilar membrane vibration due to the MOC activity.[17,19] This phase can shift the generation site of the SOAE to a more basal end, leading to an increase in the SOAE frequency with contralateral noise. The results of the study indicate that the MOC activity leading to a phase shift on the basilar membrane is intact in individuals with ANSD. Thus, the results of the study indicate different effects of MOC on the amplitude and frequency of SOAE in the presence of contralateral noise. The unique findings from the study help us to delineate further differential physiological processes operating on efferent auditory systems in individuals with ANSD.

CONCLUSION

The present study attempted to determine the effect of contralateral noise on amplitude and frequency of SOAE shifts in individuals with NH and ANSD. The results of the present study showed that the reduction in amplitude of SOAE with noise was seen only for individuals with NH, while no such SOAE amplitude shifts were noticed in individuals with ANSD, suggestive of abnormal afferent input to the MOC in individuals with ANSD. It was also found that there was a significant shift in frequency in the presence of contralateral acoustic stimulation for both groups. This result suggests that the phase shift on the basilar membrane due to MOC activity is not affected in individuals with ANSD.

Ethics Committee Approval: Ethical committee approval was received from the Ethics Committee of All India Institute of Speech and Hearing, (Approval No: AIISH/ERB/2019/23).

Informed Consent: Written informed consent was obtained from all participants who participated in this study.

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Conflict of Interest: The authors have no conflict of interest to declare.

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