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Auditory System Synchronization and Cochlear Function in Patients with Normal Hearing With Tinnitus: Comparison of Multiple Feature with Longer Duration and Single Feature with Shorter Duration Tinnitus

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Abstract

Objective: To observe cochlear and brainstem function in normal hearing ears with tinnitus using DPOAE and ABR audiometry. **Design:** Case-control study. **Sample size:** Included 60 normal hearing male patients with age less than 45 years; control group consisted of 30 patients without tinnitus and the study group consisted of those with unilateral tinnitus of at least 6 month duration. Pure tone audiometry, tinnitus matching (pitch & loudness), DPOAE (SNR & Amplitude) and ABR results of absolute latency of wave I, III and V, with IPL difference of I-III, III-V & I-V, and ILD-V were investigated. **Results:** SNR and amplitude value of DPOAE were significantly different between tinnitus ears and without tinnitus ears. Abnormal prolonged absolute latencies of peak I, III, V suggesting presence of hearing loss above 8 kHz and significant difference of only IPL III-V in the tinnitus ear suggesting of upper brain steam lesion in tinnitus patients were found. The IPL of III-V and ILD-V findings were significantly different in longer duration with multiple features (more than one type of pitch) than shorter duration with single feature tinnitus. Thus whole brainstem function has significant relationship with the presence of tinnitus, longer duration with multiple nature of tinnitus perception. **Conclusion:** Abnormal OAE and ABR results were present in patients with tinnitus. It was more prominent in patients with longer duration with multiple features of tinnitus perception.

Keywords: tinnitus, auditory brainstem response audiometry, auditory synchronization, otoacoustic emission.

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INTRODUCTION

"Tinnitus is the sensation of sound without external stimulation"[1]. Even if the tinnitus signal itself is very weak, it may be heard in the existence of high levels of environmental sound. It can be persistent and annoying, simply because it is an atypical signal, and unlike perception, enervated by external sounds[2]. The incidence of tinnitus in the general adult population has been estimated to rise from 4% to as high as 32%[3]. Approximations of prevalence of tinnitus vary, but estimates of the American Tinnitus Association (ATA) report that approximately 40 to 50 million individuals in the United States experience tinnitus[4]. Perception of tinnitus has been associated with abnormal synchronization of auditory nerve activity[5], imbalanced activity of type I and type II afferent fibres in the auditory nerve[6], discordant damage to outer hair cells (OHC) and inner hair cells (IHC) systems[3,7] or central abnormalities[7,8]. Individuals with subjective tinnitus have no noticeable signs of disease, and the disease has few detectable physical correlates. Subjective tinnitus can be high frequency sounds similar to the sounds of crickets, and constant or pulsatile.

The precise mechanics of subjective tinnitus are still not clearly understood and many probable causes have been proposed. With subjective tinnitus, the site of generation is important in hypothesizing the potential reason. It could either be, in the ears, or in the head[9]. It has been hypothesized that mild to moderate tinnitus may be generated in the ear, whereas, severe tinnitus may be generated in the central nervous system[10]. Jastreboff considered that tinnitus frequently starts in the cochlea and then the abnormal activity is generated in the central pathways that prolong their symptoms[7]. Therefore, the test of cochlear and brainstem dysfunction has been implicated in tinnitus generation.

DPOAE are believed to be fast, objective, consistent and reproductible measure of the physiological integrity of the OHC of the cochlea. These phenomena can be recorded in almost all normal ears, and are known to be reduced or absent in ears with hearing loss. DPOAE would be convenient for understanding tinnitus by evaluating the cochlea, especially the OHC, since they allow the analysis of a great spectrum of frequencies, providing a detailed analysis of almost all the cochlea[11].

Auditory Brainstem Response (ABR) can be used in evaluating tinnitus patients for a number of reasons, including its objectivity in evaluating the cochlea and the brainstem auditory pathways. It is the test of choice when patients present with symptoms that suggest a cochlear or retrocochler lesion site to facilitate differential diagnosis. Thus ABR may contribute to clarify tinnitus origin and this is very important for managing such patients[12].

The objective of the present study was to evaluate auditory system synchronization using Auditory Brainstem Response audiometry (ABR) and cochlear function using Distortion Product Oto-acoustic emission (DPOAE) in patients with tinnitus within normal hearing sensitivity and to compare them with normal hearing ears without tinnitus. It was also designed to assess whether cochlear and brainstem function has any relation with longer duration and multiple feature (more than one pitch) of tinnitus.

METHODOLOGY

Participants

The control group included 30 normal hearing male participants with age less than 45 years. While the study group consisted of a total of 30 normal male participants with age less than 45 years (to eliminate effect of age) with unilateral tinnitus for at least 6 months duration. They were drawn from the Audiological department of National Institute of Speech and Hearing Disabilities, ERC, Kolkata, West Bengal, India, using purposive sampling method.

Inclusion criteria

The patients had minimum 6- month duration of chronic tinnitus in unilateral ear with bilateral normal peripheral hearing thresholds (< 20 dB) with 100% WRS scores and normal middle ear function with a type tympanogram.

Exclusion criteria

The patients with any history of any otological, psychological or neurological problems were excluded.

Procedure

Written consent was obtained from all the patients after explaining the test procedure. All of them underwent otologic examination followed by basic audiological evaluation-pure tone audiometry, speech audiometry using MAICO MA-53. Immittance audiometry was done using GSI-39 to rule out middle ear pathology. Mid octave frequencies of 3 kHz and 6 kHz were also tested to avoid inclusion of individuals with audiograms that displayed minor dips. Tinnitus matching for intensity and frequency was also conducted. Auditory brainstem response audiometry (ABR) was recorded using two channel Smart-Eps of Intelligent Hearing System (IHS) using the following parameters: 4 electrodes; impedance was < 3 Ω; alternate polarity click stimulus with 19.3 repetition rate per second; number of sweeps was 2000; filter setting (LFF)150 Hz to (HFF) 3 kHz.

Stimuli were delivered through ER-3A-insertphone. The peak was identified at 95 dB nHL by the first researcher and cross check was done by another experimenter to reduce the bias. The absolute latencies of wave I, III and V, interpeak latencies (IPLs) I–III, III–V and I–V as well as the interaural latency difference of wave V (ILD-V) were calculated. DPOAE were measured using the DP-gram procedure, in response to pure tones of levels (L1 = 65 dB, L2 = 55 dB SPL) with 2f1-f2 frequency ratio in the frequency range of 2 kHz to 5 kHz using a Capella Cochlear Emission Analyzer (Madsen, Denmark). DPOAE were tested for the following frequencies: 2, 3, 4 and 5 kHz.

Statistical analysis

To investigate the objectives of the present study, statistical analysis using Statistical Package for the Social Sciences (SPSS) software (version 16.0) was carried out for the obtained data. The t-test and ANOVA were used to compare the DPOAE and ABR results (absolute latencies, IPLs and ILD-V) between both groups.

RESULTS

The mean age for patients with tinnitus was 39.61 years with standard deviation ± 3.56 years and that of patients with non-tinnitus was 37.59 ± 4.14 years. Tinnitus duration on average was 15.06 ± 8.76 months. Tinnitus patients reported their tinnitus as a pure tone in 26.6% (8/30), NBN in 53.3% (16/30) while for 20% (6/30) it was multiple feature (patients perceive tinnitus as a combination of different sounds) with longer duration tinnitus and could not match tinnitus with external stimulus. Eleven (36.7%) cases matched their tinnitus at higher frequencies, between 4 kHz and 8 kHz.

ANOVA test revealed no significant differences (F-test = 4.287 $p = 0.085$, $p < 0.05$) of pure tone threshold between ear with and without tinnitus.

Table 1 showed a significant difference in SNR value of DPOAE at 4 kHz ($t = 0.000$, $p < 0.05$) and 5 kHz ($t = 0.000$, $p < 0.05$) between non-tinnitus ear and tinnitus ear.

Table 2 showed a significant difference in amplitude value of DPOAE at 4 kHz ($t = 0.000$, $p < 0.05$) and 5 kHz ($t = 0.000$, $p < 0.05$) between non-tinnitus ear and tinnitus ear.

Further, ANOVA test was applied for determining amplitude value differences between the non-tinnitus ears and tinnitus ears groups at each frequency. Results indicated that difference was present only at 4 kHz ($p = 0.023$, $p < 0.05$) and 5 kHz ($p = 0.014$, $p < 0.05$), which means that the undetected DPOAE could be influenced by tinnitus.

Table 3 showed a significant difference in SNR value of DPOAE at 4 kHz ($t = 0.004$, $p < 0.05$) and 5 kHz ($t = 0.002$, $p < 0.05$) between longer duration tinnitus ears and shorter duration tinnitus ears. Thus the undetected DPOE could be influenced by longer duration tinnitus.

Table 4 showed a significant difference in SNR value of DPOAE at 4 kHz ($t = 0.003$, $p < 0.05$) and 5 kHz ($t = 0.004$, $p < 0.05$) between multiple feature tinnitus ear and single feature tinnitus ear.

Thus the undetected DPOAE could be influenced by multiple feature with longer duration tinnitus. Therefore, although tinnitus may not have been caused by changes in the outer hair cells (OHC), but it seems be affected by that.

Absolute and interpeak latencies (IPLs) of ABR of wave I, III, V and interaural latency difference of wave V (ILD-V) were calculated and compared at 90 dB nHL between both groups. They were considered prolonged if they increased by more than 2 standard deviation (SD) from absolute latency and IPLs in control group. It was noted that wave I was prolonged in 20% of patients (6/30), wave III was prolonged in 13.3% (4/30) and wave V was prolonged in 17% (5/30). With respect to IPLs, I–III was prolonged in 10% (3/30), III–V was prolonged in 10% (3/30) and I–V was prolonged in 3.3% (1/30). These findings were more prominent in cases with multiple

Table 1. Paired t-test Signal to Noise Ratio (SNR) value of DPOAE at 4 kHz and 5 kHz of tinnitus ear and non-tinnitus ears.

Variables	Sample size	Mean	Std. Dev.	df	t-value	P-value
Test ear SNR value of DPOAE at 4 kHz	30	-4.87	10.89			
Non test ear SNR value of DPOAE at 4 kHz	30	10.21	4.188	29	0.001	<0.05
Test ear SNR value of DPOAE at 5 kHz	30	1.58	6.59			
Non test ear SNR value of DPOAE at 5 kHz	30	9.50	3.05	29	0.001	<0.05

Table 2. Paired t-test amplitude value of DPOAE at 4 kHz and 5 kHz of tinnitus ears and non-tinnitus ears.

Variables	Sample size	Mean	Std Dev.	df	t-value	P-value
Test ear amplitude value of DPOAE at 4 kHz	30	-11.1	12.34			
				29	0.001	< 0.05
Non test ear amplitude value of DPOAE at 4 kHz	30	9.44	4.2			
Test ear amplitude value of DPOAE at 5 kHz	30	-4.76	8.58			
				29	0	< 0.05
Non test ear amplitude value of DPOAE at 5 kHz	30	8.831	4.67			

Table 3. Two-sample t-test with equal variances SNR value at 4 kHz and 5 kHz for longer duration versus shorter duration tinnitus ear.

Variables	Sample size	mean	Std. Dev.	df	t-value	P-value
Test ears SNR value with shorter duration tinnitus at 4 kHz	18	-0.42	11.05			
				28	0.004	< 0.05
Test ears SNR value with longer duration tinnitus at 4 kHz	12	-11.56	6.52			
Test ears SNR value with shorter duration tinnitus at 5 kHz	18	0.31	17.07			
				28	0.002	< 0.05
Test ears SNR value with longer duration tinnitus at 5 kHz	12	3.49	5.54			

Table 4. Two-sample t-test with equal variances SNR value of DPOAE on multiple feature versus single feature tinnitus ear at 4 kHz and 5 kHz.

Variables	Sample size	Mean	Std. Dev.	df	t-value	P-value
Test ear SNR value of DPOAE of single feature tinnitus at 4 kHz	24	-2.14	9.05			
				28	0.004	< 0.05
Test ear SNR value of DPOAE of multiple feature tinnitus at 4 kHz	6	-15.15	6.05			
Test ear SNR value of DPOAE of single feature tinnitus at 4 kHz	24	-1.45	5.58			
				28	0.004	< 0.05
Test ear SNR value of DPOAE of multiple feature tinnitus at 4 kHz	6	6.36	3.42			

Table 5. Paired t-test absolute latency of peak-I, III and V of tinnitus ear and non-tinnitus ear.

Variables	Sample size	Mean ms	Std. Dev.	df	t-value	P-value
Test ear absolute latency of peak I	30	1.82	0.51			
Non test ear absolute latency of peak I	30	1.36	0.11	29	0.001 (HS)	< 0.05
Test ear absolute latency of peak III	30	3.76	0.78			
Non test ear absolute latency of peak III	30	3.42	0.27	29	0.033 (S)	< 0.05
Test ear absolute latency of peak V	30	5.87	1.23			
Non test ear absolute latency of peak V	30	5.25	0.28	29	0.014 (S)	< 0.05

Table 6. Paired t-test IPL of peak I-III, III-V and I-V of tinnitus ear and non-tinnitus ear.

Variables	Sample size	Mean ms	Std. Dev.	df	t-value	P-value
Test ear IPL difference of peak I-III	30	1.97	0.46		0.41	
Non test ear IPL difference of peak I-III	30	2.05	0.27	29	(NS)	< 0.05
Test ear IPL difference of peak III-V	30	2.10	0.56		0.025	
Non test ear IPL difference of peak III-V	30	1.83	0.28	29	(S)	< 0.05
Test ear IPL difference of peak I-V	30	4.12	0.86		0.44	
Non test ear IPL difference of peak I-V	30	3.97	0.47	29	(NS)	< 0.05

Table 7. Two-sample t-test with equal variances of absolute latency of peak III and ILD-V value of multiple feature and single feature tinnitus ears.

Variables	Sample size	Mean ms	Std. Dev.	df	t-value	P-value
Test ear of single feature tinnitus of absolute latency of peak III	24	3.52	0.92			
Test ear of multiple feature tinnitus of absolute latency of peak III	6	4.41	0.29	28	0.033 (S)	< 0.05
Test ear of single feature tinnitus of ILD-V	30	5.56	1.49			
Test ear of multiple feature tinnitus of ILD-V	30	6.92	0.34	28	0.040 (S)	< 0.05

nature and longer duration tinnitus (> 12 months) than shorter duration and single nature tinnitus.

Table 5 showed a significant difference in absolute latency value of peak-I ($t = 0.001$, $p < 0.05$), peak III ($t = 0.033$, $p < 0.05$) and peak V ($t = 0.0137$, $p < 0.05$) between non-tinnitus ear and tinnitus ear. These findings are consistent with a lesion in the peripheral auditory system.

Table 6 showed IPLs difference in tinnitus ear were significant from non-tinnitus ear in only III-V ($t = 0.0253$, $p < 0.05$); however, IPL of I-V ($t = 0.44$, $p < 0.05$) and I-III ($t = 0.416$, $p < 0.05$) had no significant difference suggesting involvement of upper brainstem lesion in tinnitus patients. This prolongation of IPL in tinnitus ear may be caused by increased neural conduction time in the brainstem.

Table 7 showed a significant difference in absolute latency of peak III ($t = 0.0337$, $p < 0.05$) and ILD-V ($t = 0.04$, $p < 0.05$) between single feature tinnitus ear and multiple feature tinnitus ear suggesting whole brainstem involvement.

ABR absolute latency of peak I, III and V in tinnitus ear were significantly different from non-tinnitus ear ($t = 0.0000$, $p < 0.05$, $t = 0.033$ and $t = 0.0137$, $p < 0.05$). Inter aural Latency Difference -V was significantly prolonged when compared with tinnitus ear and multiple feature tinnitus ear ($t = 0.05$, $p < 0.05$). Therefore, severe tinnitus might be associated in the central nervous system[10].

DISCUSSION

Since there is a common agreement that due to some associated problem at various levels of auditory pathway including cochlea to brainstem level, there is a perception of tinnitus. However, no standard clinical objective measure of tinnitus is available, except pitch and loudness measure which is also based on subjective match between external sound and tinnitus. Therefore, researchers have tried to find out involvement of cochlear and auditory pathway in tinnitus perception with electrophysiological evidence. In this study, DPOAE was used to evaluate cochlear pathology and ABR to evaluate auditory pathway at brainstem level.

In this study, SNR value of DPOAE was significantly different in tinnitus ears and non-tinnitus ear at 4 kHz ($t = 0.000$, $p < 0.05$) and 5 kHz ($t = 0.000$, $p < 0.000$) (Table 1). Amplitude of DPOAE was significantly different in tinnitus ear and non-tinnitus ear at 4 kHz ($t = 0.000$, $p < 0.05$) and 5 kHz ($t = 0.000$, $p < 0.004$) (Table 2).

Significantly lower DPOAE was seen at high frequency in patients with tinnitus in comparison to non-tinnitus control participants, reflecting OHC dysfunction generally in high frequency cochlear regions. Similar results had been found by several investigators including Abo Jamous et al.[13]

Furthermore, SNR value was significantly different between longer duration tinnitus ear and shorter duration tinnitus ear at 4 kHz ($t = 0.004$, $p < 0.05$) and 5 kHz ($t = 0.000$, $p < 0.05$)(Table 3). It was also observed that there was significant difference in SNR value between single feature tinnitus and multiple feature tinnitus ear at 4 kHz ($t = 0.0038$, $p < 0.05$) and 5 kHz ($t = 0.0043$, $p < 0.05$) (Table 4). Dysfunction starts in the cochlea and then a weak imbalance of neural activity is generated in the central pathway; this is noticed at low level signal in the auditory systems and being a new signal it is enhanced by subcortical centres, transferred to the auditory cortex and perceived as an abnormal sound-tinnitus. Longer duration involvement of auditory system in tinnitus patients affect limbic system and autonomic nervous system also[7]. Thus DPOAE has potential weight in the assessment of tinnitus, providing information on the structural integrity of the cochlea, especially OHC functioning. Hence, more randomized trial with large sample size is required to clarify these arguments.

In the present study, abnormal prolonged absolute latencies of I, II and III were seen in the study group compared with the control group, concurring with the findings of Kehrle[14] and Gabr[12]. Abnormal prolongation of wave I, parallel to a lengthening of the latter ABR waves, occurs in ears with cochlear hearing loss[15]. Thus it suggests that patients of the study group might have sensorineural hearing loss at frequencies greater than 8000 Hz which were not measured. Prolonged IPLs of III-V in the study group compared with control group, suggest increased neural conduction time in the upper brainstem. These findings correlate with those of Gabr[12], Kehrle[14], Schaette and McAlpine[16], Rosenhall and Axelsson[17]. This may be attributed to impaired neural firing synchronization and transmission in the auditory pathways in these individuals.

Further, there was significant peak III latency difference between single feature tinnitus and multiple feature tinnitus ($t = 0.0337$, $p < 0.05$) (Table 7) and also there was significant ILD-V difference between single feature tinnitus and multiple feature tinnitus ($t = 0.040$, $p < 0.05$)(Table 7). Thus this evidence supports the viewpoint that in multiple feature tinnitus there is involvement of whole brainstem; also that multiple feature tinnitus are a result of abnormal activity within the central auditory pathway. These abnormalities due to abnormal activity in IC, CN, MSOC and brainstem, leads to changes in tonotopic organisation of auditory maps[18]. Thus original abnormalities trigger secondary abnormalities and this could explain why pitch, loudness and RI of tinnitus changes multiple feature tinnitus[19]. Shiomi et al.[20], and Gerken[21] reported that perception of tinnitus is also associated with several dysfunction of cochlear impairment, pathologic changes in the auditory nerve, cochlear nuclei, auditory cortex and associated area result in abnormal spontaneous hyperactivity along with the auditory pathway. Longer duration tinnitus perception involving Limbic system dysfunction[22] in tinnitus patient might be due to efferent pathway[23] disturbances which also alter OHC activity.

CONCLUSION

The results of the present study have important implications in designing proper assessment protocol by introducing ABR and OAE instruments and management protocols concerning the relief of tinnitus.

Limitation

As the sample size is less ($N = 30$), the findings have to be viewed with caution. Further research using randomised design with more number of participants is warranted.

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