



‘Is It Brain Talking to the Ear’: Neuro-otological Evaluation of Tinnitus Using Auditory Brainstem Response Audiometry

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Abstract Tinnitus is hypothesized to be an auditory phantom phenomenon resulting from spontaneous neuronal activity somewhere along the auditory pathway. The neural abnormalities underlying tinnitus are largely unknown. We evaluated the functional characteristics and the auditory system synchronization using Auditory Brainstem Response (ABR) in normal hearing tinnitus patients. In this observational comparative cross-sectional study, patients with chief complaints of Tinnitus and equal number of age and sex matched controls without hearing loss and tinnitus were enrolled. All patients underwent a full ENT assessment, pure tone audiometry and Brainstem evoked response audiometry (BERA) tests. The study population consisted of 100 patients with tinnitus, 55 controls without tinnitus and 45 controls with tinnitus. Statistical analysis showed significant relation ($p < 0.05$) between hearing loss and tinnitus between cases and controls with tinnitus, between absolute latency of wave III amongst cases and controls without tinnitus, Interpeak Latency between wave III and V amongst cases and controls with tinnitus and interpeak latency of wave I and wave III amongst controls without and with tinnitus. Brainstem evoked response

audiometry results that we obtained from the patients of tinnitus and controls with and without tinnitus are different from one person to another. This suggests impaired neural firing synchronization and transmission in the central auditory pathway in tinnitus patients. These findings also indicate that the pathology underlying tinnitus is not the same in every individual, with possible brainstem involvement in some cases.

Keywords Tinnitus · Auditory brainstem response · Tinnitus laterality · Hearing loss · Inter-peak latency · Inter-aural latency

Introduction

Background

“Yes, it was about the mid-1950s. I took 100 people with normal hearing and placed them in the sound booth for some 15 min or so. As you can imagine, more than 90 percent of them heard whistling, buzzing, and other sounds. Then I did the same thing with 100 people with hearing loss. The obvious conclusion was simply even people with normal hearing hear tinnitus, but because their hearing is so good, the everyday acoustic environment masks their ability to perceive their tinnitus.”—Bergman.

Tinnitus (Latin *tinnire* “to ring”) is the perception of sound for more than five minutes at a time, in the absence of any external acoustical or electrical stimulation of the ear and not occurring immediately after exposure to loud noise, phantom auditory perception or head noise. Tinnitus has been one of the bugbears of humanity for as long as medical records have been kept ancient Babylonian clay tablets from more than 600 years BC contain multiple

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references to tinnitus together with instructions on how to treat the condition using incantations and charms [1].

Many experiments on tinnitus have been conducted so far to determine the causes, pathophysiology, co-morbidities and therapeutic interventions. The commonly performed tests in tinnitus patients include tympanometry, pure-tone audiometry (PTA), distortion-product otoacoustic emissions (DPOAEs) measured with high frequency resolution, and click-evoked auditory brainstem responses (ABRs). More than 40% of tinnitus sufferers have normal pure-tone audiograms and the characteristics of tinnitus in subjectively normal-hearing individuals have been found to be significantly different from those observed in tinnitus patients with sensorineural hearing loss [2]. The optimal audiological test battery for tinnitus characteristics includes assessment of subjective tinnitus loudness, pitch, and minimum masking level [3].

Aim

Even if tinnitus patients have normal pure-tone audiograms, their DPOAEs results frequently disclose abnormalities. The Brainstem evoked response audiometry (BERA) technique provides information about the integrity of the central auditory system and can be a valuable diagnostic tool. This study aimed to evaluate the functional characteristics and the auditory system synchronization using auditory brainstem response (ABR) in normal hearing tinnitus patients. It is also designed to assess brainstem involvement in those patients. Further, this study addressed the laterality effect of perceived tinnitus on ABR response in those patients through comparing patients with right, left sided or bilateral tinnitus with healthy normal hearing controls.

Materials and methods

Study group

This study was conducted in the Department of Otorhinolaryngology for a period of 19 months from 15th September 2017 to 15th April 2019 in tertiary care hospital in New Delhi. The study population included patients with tinnitus and normal subjects. Total number of 100 cases and 100 controls were included in the study. The Institutional Ethics Committee reviewed and approved the study proposal prior to commencement of this study. The subjects were divided into three groups:

Group A: Patients with tinnitus (The inclusion criteria were: adults with chief complaint of tinnitus and the exclusion criteria were: not known case of any psychiatric or neurological disorders and not below 12 years).

Group B: Controls without tinnitus (They were age and sex matched individuals who had bilateral normal middle ear function with no past history of any otological, psychological or neurological problems).

Group C: Controls with tinnitus (They were age and sex matched individuals who never had any otological, psychological or neurological complaints, but could hear sounds in a sound proof room.)

Evaluation

The study was conducted after taking an informed written consent by both the cases and the controls. History of exposure to excessive noise, treatment with potentially ototoxic drugs including aspirin, circumstances of tinnitus onset, and accompanying complaints like vertigo and hypersensitivity to sound were asked. A detailed clinical examination of the subjects was conducted including thorough aural examination. Subjects underwent PTA to determine the type and magnitude of hearing loss. All the subject groups matched for age and sex underwent BERA for assessment of cochlear function.

Statistical analysis

A *p* value of < 0.05 was considered statistically significant. The data was entered in MS EXCEL spreadsheet and analysis was done using Statistical Package for Social Sciences (SPSS) version 21.0. Categorical variables were presented in number and percentage (%) and continuous variables were presented as mean \pm SD and median. Normality of data was tested by Kolmogorov–Smirnov test. When the normality was rejected then non-parametric test was used.

Statistical tests applied were

1. Quantitative variables were compared using unpaired t-test/Mann–Whitney Test (when the data sets were not normally distributed) between the two groups.
2. Qualitative variables were compared using Chi-Square test /Fisher's exact test.

Results

This work included three groups of patients: Group A which included 100 patients with tinnitus as chief complaint (61 males and 39 females), Group B which included 55 controls without tinnitus (27 males and 28 females) and Group C which includes 45 controls with tinnitus (24 males and 21 females). In our study, it was seen that there are more number of males than females among the cases and controls with tinnitus as compared to controls without

tinnitus were they are almost equally numbered (p value = 0.34) and we did not find any statistically significant differences amongst the groups in relation to sex.

Mean age of group A, group B and group C varies between 16 and 66 years with mean age being 40.26 years, 31.69 years and 37.28 years respectively. There is a statistically significant difference between the group A and B and groups B and C in relation to age (p value < 0.01).

On studying the correlation between hearing loss and tinnitus we found that 32.0% of cases had some form of hearing loss and only 11.1% of controls with tinnitus had some form of hearing loss and it was found to be statistically significant (p value < 0.01). (Table 1).

The average frequency of tinnitus among cases was 5097.50 Hz and the average frequency among controls with tinnitus was 4238.67 Hz.

In this study, the laterality of tinnitus amongst cases (−12.30) compared to controls (−4.62) was more lateralized to Left Ear i.e., there were more cases of bilateral tinnitus among controls with tinnitus.

The mean latency of Wave I among the 3 groups was more for left ear as compared to right ear.

The Absolute latency of wave III among all the groups was more for left ear compared to right ear and there is a statistically significant difference between absolute latency of wave III amongst cases and controls without tinnitus (p value = 0.041).

The absolute latency of Wave V in left ear was more as compared to the right ear.

The mean inter aural latency for wave V among Cases was −0.17 which was more than inter aural latencies for wave V among Controls without tinnitus (−0.05) and Controls with tinnitus (−0.12).

The interval latency between waves I –III for cases (1.78) was less than controls without tinnitus (1.94) and controls with tinnitus (1.81).

The Inter peak latency between waves III-V for cases is 2.04 which were more than controls without tinnitus (1.90) and controls with tinnitus (1.75). There is a statistically significant difference between cases and controls with tinnitus.

Table 1 Hearing Loss amongst different groups

Hearing loss	Group			Total
	A	B	C	
No	68	55	40	163
	68.0%	100.0%	88.9%	81.5%
Yes	32	0	5	37
	32.0%	0.0%	11.1%	18.5%
Total	100	55	45	200
	100.0%	100.0%	100.0%	100.0%

The Inter peak latency between wave I and V for cases was 3.82 which was less than controls with tinnitus (3.57). There is a statistically significant difference between the Inter peak latency between waves I and V between Controls without tinnitus (3.84) and controls with tinnitus (3.57). (Table 2).

Discussion

Tinnitus is a frequent and ruinous symptom of auditory system disorders and a variety of other pathological condition which affects the quality of life. In our study we were concentrated on the patients with normal hearing with tinnitus. Since there is a common agreement that tinnitus can be also due to an impaired brain process, and there is lack of scientific evidence to prove that tinnitus arises from cochlear damage in normal-hearing patients has encouraged us to investigate whether patients with tinnitus show changes in the central auditory pathways. The sensation of tinnitus may be associated with perceptual impairments at various levels of the auditory processing. The only clinical available measure of tinnitus is the psycho-acoustical description of pitch and loudness which is based on subjective match between tinnitus and external sounds. Since there is a common agreement that tinnitus can be also due to an impaired brain process, researchers tried to support this assumption with electrophysiological evidences. One such method is Auditory brainstem response (ABR) audiometry [4].

According to Jastreboff, the limbic system is responsible for the impairment experienced by tinnitus patients. He emphasized the role of the limbic system in affecting a participant's attention, memory, detection and processing of auditory stimuli. Chronic tinnitus is caused by compromised limbic-cortico-striatal circuit, the same network is linked with emotional state in mood disorders, reward, averseness, addictions [5].

In our study, the mean age amongst the cases was 40.26 years which was more than the mean age amongst the controls with tinnitus (31.691 years) and the mean age amongst the controls without tinnitus (37.289 years). There was a statistically significant differences between the group A and B and groups B and C in relation to age (p -value < 0.01).

Also, in a study by Baguley et al. it was seen that the prevalence of troublesome tinnitus increases with age to 70 years; results of some studies show that it continues to increase thereafter, although others have shown it to diminish [6].

We found statistically significant relation between hearing loss and tinnitus. It was found out that 32.0% of cases had some form of hearing loss and only 11.1% of

Table 2 Analysis of Auditory Brainstem Responses in the three groups

	A (cases)	B (controls without tinnitus)	C (controls with tinnitus)	<i>p</i> -value
Distribution	100	55	45	
L1R	2.03 ± 0.35	2.05 ± 0.28	2.04 ± 0.41	0.948
L1L	2.17 ± 0.44	2.08 ± 0.33	2.19 ± 0.46	0.282
L3R	3.80 ± 0.49	3.99 ± 0.34	3.83 ± 0.48	0.041 (A vs. B)
L3L	4.04 ± 0.51	4.06 ± 0.29	4.11 ± 0.48	0.676
L5R	5.86 ± 0.61	5.88 ± 0.36	5.77 ± 0.59	0.526
L5L	6.09 ± 0.58	5.93 ± 0.37	5.93 ± 0.58	0.117
IAD VR-VL	− 0.17 ± 0.77	− 0.05 ± 0.21	− 0.10 ± 0.62	0.528
IPL I-III	1.78 ± 0.50	1.94 ± 0.28	1.81 ± 0.49	0.1
IPL III-V	2.04 ± 0.63	1.90 ± 0.52	1.75 ± 0.57	0.024 (A vs. C)
IPL I-V	3.82 ± 0.70	3.84 ± 0.48	3.57 ± 0.58	0.045 (B vs. C)

Abbreviation in Table 2: *L1R* Latency of Wave I in right ear, *L1L* Latency of Wave I in left ear, *L3R* Latency of Wave III in right ear, *L3L* Latency of Wave III in left ear, *L5R* Latency of Wave V in right ear, *L5L* Latency of Wave V in left ear, *IPL I-III* Inter peak latency between waves I and III, *IPL III-V* Inter peak latency between waves III and V, *IPL I-V* Inter peak latency between waves I and V

controls with tinnitus had some form of hearing loss (p value < 0.01). Various studies in the past support our findings. Baguley et al. stated the main risk factor of tinnitus is hearing loss [6]. Fowler suggested there is relation between hearing loss and tinnitus [7–10]. According to a study by Chul Won Yang et al., 42% of patients with tinnitus had experienced sensorineural hearing loss (SNHL) and 33% had experienced conductive hearing loss (CHL), whereas 20% had normal hearing.

The average frequency of tinnitus among cases was 5097.50 Hz and the average frequency among controls with tinnitus was 4238.67 Hz i.e., it is more among cases than in controls with tinnitus (p -value = 0.104). The finding is confirmed by a study by Meikle et al. in 1984 it was seen that many of the frequency matches are at fairly high levels (above 3 kHz), they conjectured that the pitch of the tinnitus might be related to its severity. It seems reasonable to suggest that high pitched tinnitus might be more aversive than low pitched tinnitus [11].

We found the laterality of tinnitus amongst cases (−12.30) compared to controls (−4.62) is more lateralized to left ear i.e., there are more cases of bilateral tinnitus among controls with tinnitus (p -value = 0.179). This finding is supported by a study by Reiss and Reiss whereby sixty per cent of the sample heard tinnitus only in the left ear, 21% only in the right ear and 19% in both ears. They also reviewed 7 studies (altogether 4634 patients) on laterality, it was inferred that tinnitus occurs more often bilaterally (48.8%) than on the left side (28.0%) or the right (23.2%). There is no general predominance of the left ear [12].

In our study the mean latency of Wave I among the 3 groups is more for left ear and there is no significant difference in the mean latency of wave I among all 3 groups.

(p -value = 0.948 and 0.282 for right and left ear respectively).

We found statistically significant increase in the latency of Wave III amongst cases when compared to controls without tinnitus. It indicates aberrant neural activity in cochlear nucleus and cochlear nerve nucleus complex. (p -value = 0.041 and 0.676 for right and left ear respectively).

Also, the absolute latency of Wave V in left ear is more as compared to the right ear and there is no significant difference among all 3 groups. (p -value = 0.526 and 0.117 for right and left ear respectively).

Rosenthal and Axelsson found significant prolongation in waves I and V in females and III and V in males [13]. In a study by Ravikumar et al. different patterns of ABR abnormalities were found in normal hearing tinnitus patients suggesting central auditory pathway affection. The first pattern was the statistically significant prolongation of wave I, III and V absolute latencies which occurred in 18, 17 and 23% of ears respectively and the P values were 0.020, 0.027 and 0.011 respectively [14].

In our study, interval latency between waves I–III for cases (1.78) was less than controls without tinnitus (1.94) and controls with tinnitus (1.81). (p -value = 0.1).

But, we found statistically significant difference in the inter peak latency between waves III-V of cases (2.04) and controls with tinnitus (1.75) with a p -value of 0.024. Increase in the inter peak latencies signifies increased neural conduction time in auditory nerve pathway and brainstem.

We also found statistically significant difference between the inter peak latency of waves I and V between Controls without tinnitus (3.84) and controls with tinnitus (3.57) with a p -value of 0.045. Increase in inter peak

latencies between waves III-V and waves I and V indicates purely brainstem dysfunction. This could be due to permanent activation of auditory system by tinnitus, which might change central transmission at upper brainstem further modifying external stimuli transmission as suggested in a by Jastreboff [15].

The brainstem evoked response audiometry results that we obtained from the patients of tinnitus and controls with and without tinnitus are different from one person to another. This suggests impaired neural firing synchronization and transmission in the central auditory pathway in tinnitus patients. These findings also indicate the pathology underlying tinnitus is not the same in every individual, with possible brainstem involvement in some cases.

Conclusion

The exact origin and pathophysiological pathways of tinnitus is not that well known. All structures of the auditory system from periphery to auditory cortex have been suggested as possible sites of tinnitus. Therefore, to objectify this subjective perception, auditory electrophysiological response parameters are used. The brainstem evoked response audiometry results that we obtained from the patients of tinnitus and controls with and without tinnitus are different from one person to another. This suggests impaired neural firing synchronization and transmission in the central auditory pathway in tinnitus patients. These findings also indicate the pathology underlying tinnitus is not the same in every individual, with possible brainstem involvement in some cases. Thus ABRs can be used not only to understand the pathophysiology of tinnitus but also objectify its presence in individuals.

In recent years, there has been a major resurgence of scientific and clinical interest in tinnitus. This increased interest is of great potential benefit for the millions of individuals who are distressed by this common symptom. Activity in tinnitus research is slowly answering questions regarding the best way to undertake tinnitus management. Within the large number of studies that have been published, however, there are many with unique and

sometimes idiosyncratic design, so that comparison between test results or treatments is often difficult.

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