Auditory P300: Selective Attention to 2 KHZ Tone-Bursts in Patients with Idiopathic Subjective Tinnitus

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Abstract: *Objective*: To study whether a group of idiopathic subjective tinnitus (IST) has abnormal changes in auditory P300 and to compare these results with normal subjects.

Design: AuditoryP300 was done to thirty two patients with idiopathic subjective tinnitus and they were compared to normal. The elicited auditory P300 event-related potentials (ERPs) were analyzed in terms of peak amplitude and latency of the P300 waveforms. Basic audiological assessments that include pure tone audiometry and immittancemetry were done to the whole study group.

Results: The results showed that while P300 peak amplitudes were overall reduced for idiopathic subjective tinnitus but it was varied individually and the P300 peak latencies were statistically of non-significant values between the study group and normal subjects.

Discussion and Conclusion: Reduced waveform amplitudes were observed in IST than normal subjects. Possible mechanisms include that the processing of selective attention and its response to auditory tone burst stimuli associated with IST differ than that of the normal. The findings of our study are consistent with the hypothesis that IST patients differ in their response to auditory stimulus measured by P300 mainly auditory cortical area than normal subjects.

Keywords: P300, Event related potentials, idiopathic subjective tinnitus, Tinnitus, AEP; Auditory evoked potentials.

INTRODUCTION

Tinnitus is broadly defined as the perception of sound in the absence of acoustic events. This sound perception or noise emanating from the ears or head ranges from a barely noticeable annoyance to a debilitating chronic condition [1]. It is experienced by 10 to 15% of the adult population [2]. The severity of subjective tinnitus can only be assessed symptomatically by the patient and cannot be measured objectively. Idiopathic subjective tinnitus is the experience of noises in the ears or head without both aberrant etiology and external stimuli [1].

Despite the prevalence of tinnitus, the patho-physiology of the disorder is poorly understood [3]. For most of these individuals, the tinnitus is chronic, and their awareness of its presence generally increases in quiet environments [2]. Many different perceptual experiences of tinnitus result from many underlying neurophysiological and otological factors [4].

Tinnitus could be peripheral due to loose coupling between steriocilia and tectorial membrane, or to disruption of multiple interconnection between the nerve fibers and the sensory cells or to a vascular injury [5, 6]. On the other hand tinnitus could be central in origin following surgical procedures or viral infections and vascular lesions of the brain cortex [7, 8].

Although damage to the cochlea causes hearing loss and often initiates tinnitus, recent studies have established that it is the central nervous system that plays a key role in chronic tinnitus [9]. It has been hypothesized that increased hyperactivity in the dorsal cochlear nucleus may be associated with noise-induced tinnitus [10]. But, other auditory centers have been similarly implicated [4].

Auditory evoked potentials (AEPs) are used to examine the synchronous discharge of fibers in the auditory pathway and identify the presence of abnormal neuronal activity [11]. The middle latency response and the auditory long latency event related potentials are the two most common protocols for evaluation of the upper brainstem and auditory cortical areas [12]. The insula and auditory cortical areas of the superior temporal lobe are major sites of generation of the auditory P300 response [13].

The auditory P300 is an auditory event-related potential represented by a large, positive peak occurring approximately 300 msec post–stimulus onset [14]. It has multiple generator sites [15]. The auditory P300 is typically elicited using an oddball paradigm such that two different stimuli are used to generate the

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waveform. The standard oddball paradigm utilizes frequent and target (rare) acoustic stimuli that are perceptually different. It is of exogenous origin, external acoustic stimulus characteristics, such as intensity, can affect its amplitude and latency [16].

The purpose of this study was to investigate and measure auditory P300 responses in-patient with idiopathic subjective tinnitus and to compare it with normal subjects.

MATERIALS AND METHODS

Participants

The participants of this study were chosen from attendee of outpatient ENT and Audiology clinic from March to November 2011. The study was approved by the hospital research committee and all participants provided a written informed consent. A total of thirty-two right-handed patients were tested as a part of an ongoing study of measurement of auditory P300 in idiopathic subjective tinnitus as a function of side (right or left) and gender affection. Their age ranged from (21) to (58) years, (20) males and (12) females. The control group participants were matched for the age and sex of the study group. They consisted of 30 normal subjects aged from 22 to 57 years (17 males and 13 females) with absence of psychiatric or neurological problems.

The study group was subjected to thorough history taken, ENT, medical and neurological examinations to exclude other causes of tinnitus. Criteria of selection include special emphasis on the following items in the history taken: no history of exposure to noise, ototoxic drug medication, and no history of previous ear disease, diabetes mellitus, hypertension, cervical disc lesion or trauma.

Participants were included if conventional audiologic testing revealed within normal peripheral hearing at frequencies range 250-8000 Hz with no air bone gaps or other evidence of conductive hearing loss. They were excluded if evidence of active otologic or neurologic disease was present. Also, they were excluded if evidence of sensorineural hearing loss at frequencies ranges 250-8000 Hz was detected.

For females the auditory P300 was not done during the menstrual phase of menstrual cycle as the cognitive abilities fluctuates during it. The groups were approximately matched for educational level and they have no history of language abnormalities.

Auditory Assessment

The evaluations for all participants include otoscopy and pure tone audiometry. The pure-tone audiometry was tested in both ears for air and bone conduction thresholds using Interacoustic Clinical audiometer AC40. Calibrated headphone for conventional measurement was used for frequencies range 250-8000 Hz within sound treated booth.

Acoustic immitance testing was performed before the electrophysiological evaluation to rule out middle ear affection. Tympanometry and acoustic reflexes in the frequencies 500, 1 kHz, 2 kHz, and 4 kHz were done using middle ear analyzer Interacoustic AZ 26. The study groups showed evidence of normal-hearing with normal pure tone audiometric thresholds of 25 dB HL or better at all octave frequencies from 250 to 8000 Hz and normal middle ear function.

Auditory P300 Parameters

All participants in this study subjected to electrophysiological study using evoked potential testing, ICS Medical version 3.00 CHARTR, USA, coupled with a preamplifier (ICS medical CHARTR preamplifier PA-800), an output amplifier, computer and insert earphones (ICS medical, IL, USA) was used for both stimulation and recording of the auditory P300 event-related potentials testing.

P300 auditory stimuli were presented in a train of oddball paradigm pattern which consists of the presentation of a stream of two different frequency tone bursts one of them is rare deviants (2000Hz) and the others are frequent standards (1000Hz) to evoke the response. Insert earphones were used to deliver the stimuli. The portability was 20% for the rare tone (probability = 0.2) and 80 % for the frequent tones (probability = 0.8). Tones were presented at intensity of 75 dBnHL. The repetition rate was 1.1/second. 250 ipsi-lateral stimuli with artifact free tone presentation were presented monaurally (for tone burst: plateau time = 50 ms; rise/fall time= 10 ms). The participant was instructed to press a button in response to the rare tone. Two trials were done to ensure reproducibility.

Auditory P300 responses were recorded for each participant. All reliable measures were included for analysis. Active electrodes were placed on the Fz in reference to A2 and A1, the ground electrode was placed at the forehead. The time window for recording was 900 ms analysis time with 100 ms a pre-stimulus

baseline recording. The filter was set as 0.5 to 50 Hz band-pass filter.

Procedure

The test was conducted in sound treated booth with the participant sitting in reclining chair. The procedures were explained to the participants. They were instructed to sit calm and to keep their eyes open and remain awake. The skin where the electrodes were to be placed was cleaned with an abrasive paste to improve electrical conductivity. Responses were recorded using surface electrodes and separate averages were computed. Averaged waveforms were digitally filtered and baseline corrected. Recording was reproduced to assure reliability and waves were marked in tracings for easier replication. The impedance of each electrode did not exceed 5 kohms and the impedance difference between each electrode did not exceed 2 k ohms.

P300 amplitude was measured for each participant at the peak latency and the latency was measured at the midpoint of the component peak. Waves were identified based on consistency of wave component latency and amplitude values. The inter-amplitude value between the highest repeatable positive peak following 250 ms and the lowest negative peak following this peak was used to represent P300 amplitude measurement. The positive P300 and the following negative peak had to be present in both replication runs to be accepted.

The results were submitted to statistical analysis. This includes descriptive statistics (mean and standard deviation) and analysis of variance based on the t-test adopting a significant level of (<0.05). The statistical analysis was carried out in relation to the latency and amplitude values for P300 components for IST patients and normal subjects.

Table 1: The Mean Age in Years, Duration of Tinnitus in Months, Latencies in ms and Amplitude in µV for the IST Patients and Control Group

	IST		Normal subjects	
	Mean	SD	Mean	SD
Age in years	39.8	10.9	38.7	9.5
Latencies in ms	316.1	35.6	306.2	26.7
Amplitude in µV	8	3.5	9.4	3.7
Duration of tinnitus in months	36.7	14.9		

SD = standard deviation, IST = Idiopathic subjective tinnitus, ms = milliseconds, µV = microvolt.

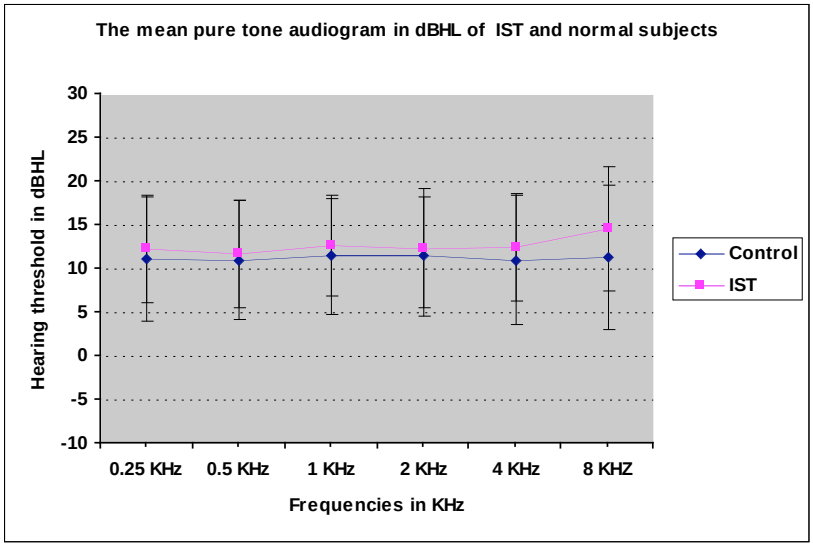

Figure 1: The mean pure tone audiogram in dBHL of IST and normal subjects. Error bars represent 1 SD above and below the mean.
SD = standard deviation, IST = Idiopathic subjective tinnitus.

RESULTS

In this study, the mean age for idiopathic subjective tinnitus was 39.8 ± 10.9 years and it was 38.7 ± 9.5 years for the normal subjects. The mean age did not differ between the patients with idiopathic subjective tinnitus and normal subjects. The duration of tinnitus was 36.7 ± 14.9 months (Table **1**).

Figure **1** reveals, the mean pure-tone audiogram for idiopathic subjective tinnitus patients and normal subjects at frequencies 0.25, 0.5, 1, 2, 4, and 8 kHz as a function of hearing threshold level in dBHL. No statistical significant difference between IST hearing threshold and normal subjects despite high threshold level for the tinnitus group.

Figures **2** and **3** show auditory P300 amplitude and latencies for the right and left affected and un-affected ears with tinnitus, there were no statistically significant difference between right and left affected and un-affected side respectively (T-test, $p > 0.05$).

Table **2** shows the auditory P300 for males and females as a function of the mean latencies and amplitude for IST and normal subjects. It was noticed that the amplitude was lower in IST than normal subjects but of no statistical significant value.

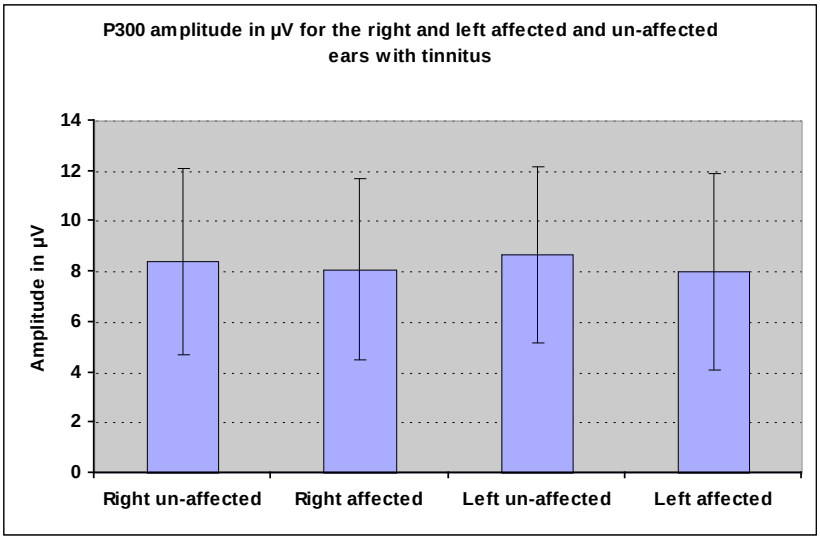

Figure 2: The mean P300 amplitudes in µV measured from the left and right affected and un-affected side with IST. Error bars represent 1 SD above and below the mean.
SD = standard deviation, IST = Idiopathic subjective tinnitus, µV = microvolt.

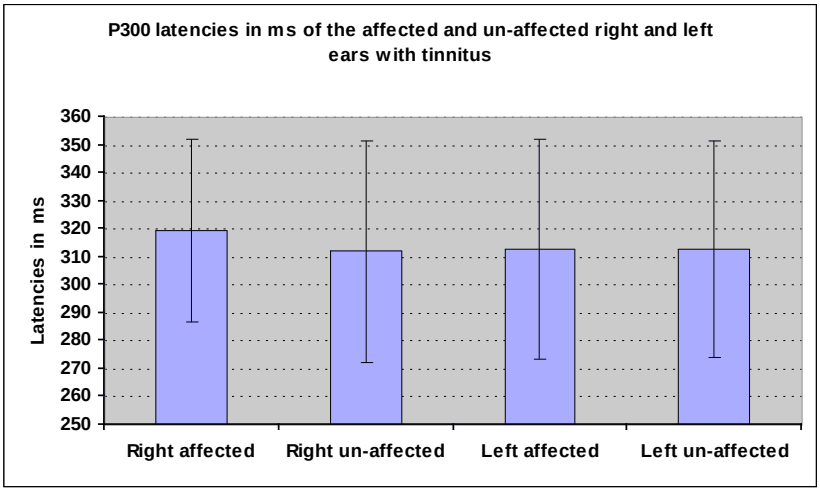

Figure 3: The mean P300 latencies in ms measured from the left and right affected and un-affected side with IST. Error bars represent 1 SD above and below the mean.
SD = standard deviation, IST = Idiopathic subjective tinnitus, ms = milliseconds.

Table 2: The Mean and SD of Latencies in ms and Amplitude in μV for (Males and Females) IST and Normal Subjects

	IST		Normal subjects	
	Mean	**SD**	**Mean**	**SD**
Latencies in ms				
Males	322	35.8	308	28.3
Females	306	34.4	303	24.7
Total	316.1	35.6	306.2	26.7
Amplitude in μV				
Males	8.3	3.1	9.1	4.1
Females	7.6	4.1	9.8	3.1
Total	8	3.5	9.4	3.7

SD = standard deviation, IST = Idiopathic subjective tinnitus, ms = milliseconds, μV = microvolt.

Table 3: *T* Test of the Affected Ear with Tinnitus Versus Normal Subjects, the Un-Affected Versus Affected Ears and Affected Side (Right Versus Left and Females Versus Males) as a Function of Latency and Amplitude of Auditory P300

	Latencies	**P value**	**Amplitude**	**P value**
Idiopathic tinnitus versus normal subjects	0.173	> 0.05	0.081	> 0.05
Idiopathic tinnitus patients				
Right versus left affected side	0.614	> 0.05	0.922	> 0.05
Males versus females affected side	0.063	> 0.05	0.599	> 0.05
Affected versus unaffected in tinnitus patients	0.692	> 0.05	0.568	> 0.05

Furthermore, the latencies in IST were longer than normal subjects but (P > 0.05). Whereas, Table **3** shows the T test of the affected ear with tinnitus versus normal subjects, the un-affected versus affected ears and affected side (right versus left and females versus males) as a function of latency and amplitude of auditory P300.

DISCUSSION

The prevalence of tinnitus with normal audiometry was found to be 7.5 % in a study by Barnea *et al*., 1990 [17]. Event related potential was first described by Picton *et al*., 1978 [18]. P300 is thought to be endogenous cognitive response that reflects higher level processing or classification of sounds [19, 20]. In the present study the elicited auditory P300 event related potentials were analyzed in terms of peak amplitude and latency of the response and it was compared with normal subjects.

Results of this study showed that despite the P300 peak amplitudes were overall reduced for IST than normal subjects; P300 peak latencies were of statistically non-significant values. These findings are consistent with the hypothesis that IST patients differ in their response to auditory stimuli.

Possible mechanism includes the possibilities of central origin of IST that causes different response to auditory tone burst and a processing of selective attention associated with it. This result was in agreement with that of Maurizi *et al*., 1985 in their study on differentiation of peripheral versus central tinnitus *via* auditory brain stem response evaluation in-patient with idiopathic tinnitus [21].

On the other hand, in this study no statistical significant difference was found as regards the auditory P300 latencies which may suggest that those patients do not have auditory problems at the level measured by P300 and so casting the doubt on affection of the hypothized origin of P300 mainly auditory cortical area for tinnitus origin.

Further studies are needed in which both linguistic and nonlinguistic stimuli of various types to be used to elicit the P300 response. Also the involvement of simultaneous collection of behavioral and physiological data should be pursued for idiopathic tinnitus evaluation.

CONCLUSION

Auditory P300 event related potentials to tone burst stimuli amplitude and to less extent latencies differ in patient with idiopathic tinnitus than normal subjects. This difference may suggest that P300 originating sites may be incriminated as an origin of IST, this can be due to the particular susceptibility of P300 generating sites to the changes that could be associated with it. But the latencies difference was statistically non-significant which necessitate further studies to accept the null hypothesis of the relation between P300 originating sites and idiopathic tinnitus.

CONFLICT OF INTEREST

There is no conflict of interest.

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