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RESEARCH ARTICLE

Auditory evoked potential P300 characteristics in adults with and without idiopathic bilateral tinnitus

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Abstract

Background and Aim: Based on neurophysiological measurements, auditory and non-auditory pathways are involved in tinnitus. People who experience tinnitus may suffer from several problems such as attention disorder. The auditory evoked potential P300 is an endogenous response and depends on cognitive processes like attention. The purpose of this study was to compare the auditory P300 characteristics (amplitude and latency) in adults with and without tinnitus.

Methods: Participants were 20 adults with idiopathic bilateral tinnitus with mean duration of 8.4 ± 4.73 months, and 20 healthy adults. The P300 was recorded using oddball paradigm consisted of two standard (1000 Hz) and target stimuli (2000 Hz). To reduce eye blink during recording, all participants was instructed to look at and fixate on a dot sign located in front of them. The tinnitus handicap inventory (THI) was completed and pitch matching (PM) and loudness matching (LM) were measured in tinnitus group.

Results: P300 amplitude was lower at both Fz and Cz electrode placements in tinnitus patients compared to the normal group, but it was not statistically significant (p = 0.57). Tinnitus patients had delayed latency at Fz and Cz, but this difference was not significant either psychometric and psychoacoustic assessment had no statistically significant correlation with P300 amplitude and latency.

Conclusion: It seems that P300 characteristics are not different between adults with and without idiopathic bilateral tinnitus, may be due to using low sample size.

Keywords: Tinnitus; auditory evoked potential P300; attention

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Introduction

Tinnitus, derived from the Latin word *tinnier*, is the feeling of sound in the head or ears without any external auditory sources [1,2], and is distinctly different from schizophrenia [3]. Epidemiologic studies have shown that, on average, 17.5% of the world population has tinnitus with 5.3% having severe tinnitus, which reduces the quality of life [4]. In most cases, etiology of tinnitus is still unknown [5]. Several models and theories have been introduced for tinnitus. Based on neurophysiologic model, tinnitus may

be originated from an auditory or non-auditory system like limbic system [6,7], while some studies have suggested that various networks are involved in perception and generation of tinnitus, such as frontal cortex and limbic system, which may be responsible for distress and attention disorders in patients with tinnitus [6,8,9].
Attention may have an important role in tinnitus development in some patients. In a systematic review, Mohamad et al. showed that tinnitus may have impact on different types of attention (e.g. divided attention) and working memory [9]. Different subjective and objective tests have been introduced for assessment of auditory attention [10]. In recent years, objective tests such as auditory P300 test have been more common [11]. The P300 is an endogenous response and depends on cognitive processes like attention [12]. Some different cortical and subcortical regions are involved in P300 generation [12,13]. The P300 test has two standard and target stimuli; for better and reliable recording, attention to target stimuli is necessary [13]. Selective attention to target stimuli may generate P3b peak, which is a good indicator of attention among different populations [13]. Given that auditory attention is affected in patients with tinnitus, this study aimed to compare the P300 characteristics between patients with and without tinnitus matched for age, gender and educational level. Moreover, the correlation of P300 test amplitude and latency with tinnitus handicap inventory (THI), pitch matching (PM), and loudness matching (LM) was evaluated in patients with tinnitus.

Methods

Participants
This is a cross-sectional study. This study had two difference study groups of tinnitus and normal; the tinnitus group consisted of 20 participants (15 male and 5 female) aged from 18−36 years (mean age and SD: 23.40 ± 4.79 years), and normal group consists of 20 participants (15 male and 5 female) aged from 18−33 years (mean and SD: 24.25 ± 4.65 years). For sample selection, we used a convenience sampling method based on inclusion criteria from among those referred to the Audiology Clinic of Iran University of Medical Sciences (IUMS) in Tehran, Iran. Inclusion criteria were: normal tympanogram (Type An) and normal hearing (hearing threshold level > 25 dB HL in audiometric test frequencies) for both groups, and the presence of bilateral chronic subjective tinnitus for at least three months for tinnitus group. Both groups were right-handed and matched for age, gender and education. This study obtained an ethical approval from the Ethics Committee of IUMS. All participants signed a written informed consent form prior to study. They were evaluated in the morning and at the same session.

Procedure
After taking the demographic information of the participants and completion of the Persian version of the Edinburgh handedness inventory [14] by both groups, typanometry and acoustic reflex test using immittance audiometer (Zodiac 901, Madsen^{TM}, Denmark) and pure tone audiometry (PTA) using a GSI audiometer (GSI Inc., USA) were carried out. The Persian version of THI [15] and psychoacoustic assessments (PM and LM) were used for evaluation of tinnitus group. For PM testing, the type of tinnitus (tonal or non-tonal) was first determined by presenting pure tone and narrow-band noise. Then, the PM test was performed as a two-forced choice; that is, the participants were asked which one of the presented sounds was like their tinnitus sound. This process continued until the subject's tinnitus frequency was obtained repeatedly and recorded per Hz. For LM testing, the intensity of the tinnitus frequency was increased by 1 dB steps until the level of sound and tinnitus intensity was reported similar by the subject. The LM was recorded per dB SL [16].
P300 was tested for all participants using the two-channel bio-logic device (Navigator Pro, Natus Co., USA). For electrode placement, the skin was cleaned using Nuprep gel. Non-inverting (active) electrodes were placed at Fz and Cz; inverting (passive) electrodes at M1 and M2 (connected to each other through jumper lead); and ground electrode at Fpz. The

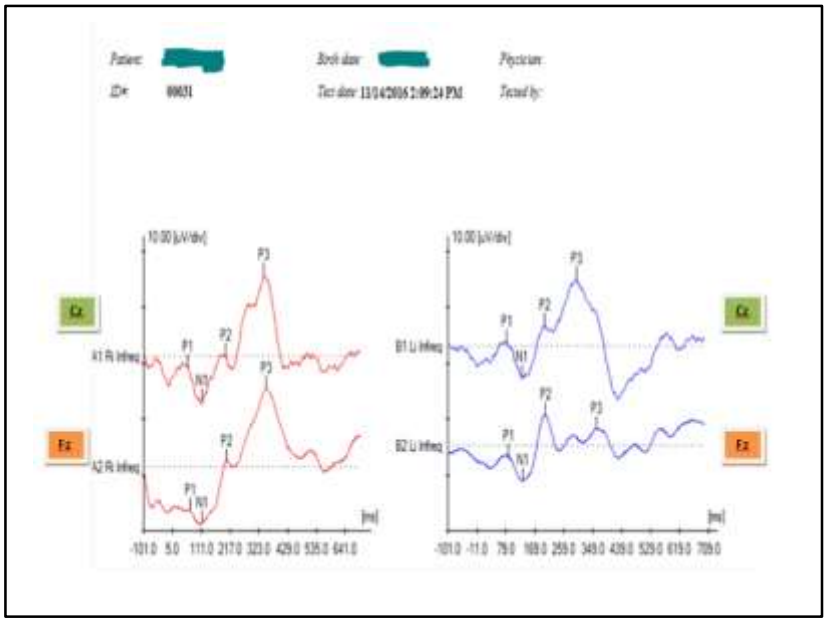

Fig. 1. One sample P300 response which recorded in two active placement (Fz and Cz).

impedance of each electrode was not exceed 5 kΩ and the inter electrode impedance difference was < 2 kΩ [13]. The P300 was recorded with oddball paradigm using standard stimuli (1000 Hz) and target stimuli (2000 Hz), presented with an intensity of 70 dB nHL [13]. The occurrence probability of target stimuli was 20% with a pseudo-random paradigm, and participants were instructed to count only the target stimuli silently and ignore other stimuli. The frequency of presentation was 0.7 Hz, and a total of 200 stimuli were presented [13]. The time epoch length was 100 ms at pre-stimulus and 700 ms at post-stimulus periods. We used band-pass filter of 0.1 to 30 Hz. To reduce blink during recording, participants were instructed to look and fixate on a dot sign located in front of them. The analyzed parameters of P300 were amplitude and latency. For measuring latency, a peak within the appropriate latency range (250−400 ms) was determined. For measuring amplitude and labeling it, a baseline-to-peak assessment in the appropriate latency range was performed [13]. Fig. 1 presents a P300 sample recorded by placement of two active electrodes (Fz and Cz).

Data analysis

Statistical analysis was performed in SPSS 22 software. For examining the normality of data distribution, Kolmogorov-Smirnov test was used whose results showed a normal distribution. Independent t-test and Pearson's correlation test were used to compare the data between groups. For all tests, the significance level was set at $p < 0.05$.

Results

In this section, we present the results of P300 parameters at different electrode placements (Fz and Cz) in both tinnitus and normal groups. At Fz, the mean ± SD of P300 amplitude was 4.74 ± 1.95 µv in tinnitus group and 5.49 ± 1.75 µv and in normal group. In the right and left ears, it was reported 5.34 ± 1.47 µv and 5.67 ± 2.30 µv, respectively. At Cz, the mean ± SD of P300 amplitude was 7.96 ± 2.62 µv in tinnitus group and 7.75 ± 2.8 µv in normal group. Its value in the right and left ears was 7.43 ± 2.61 µv and 7.38 ± 2.73 µv, respectively (Fig. 2). This indicates that patients with tinnitus had lower P300 amplitude at Fz and higher amplitude at Cz compared to the normal group; however,

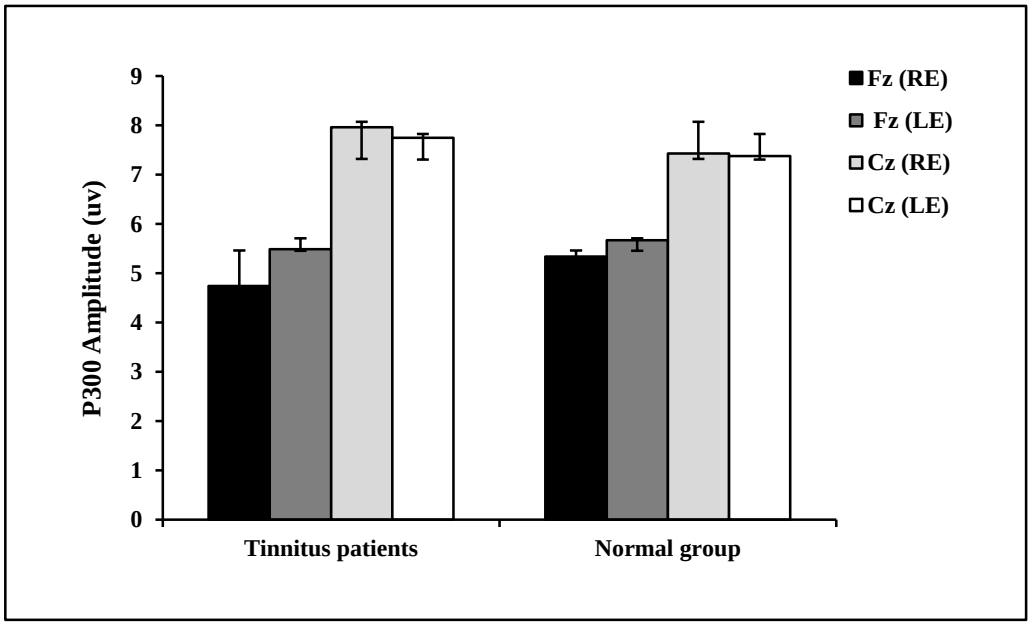

Fig. 2. P300 amplitudes in both Cz and Fz placements, in tinnitus patients and normal adults. RE; right ear, LE; left ear.

these differences were not statistically significant ($p > 0.05$).

Regarding the P300 latency at Fz, the mean ± SD was 337.44 ± 22.16 ms in tinnitus group and 331.91 ± 21.13 ms in normal group. Its value in the right and left ears was 330.93 ± 25.58 ms and 329.52 ± 29.25 ms, respectively. At Cz, the mean ± SD of P300 latency was 335.41 ± 24.07 ms in tinnitus group and 326.98 ± 24.81 ms in normal group. Its value in the right and left ears was reported 325.19 ± 21.34 ms and 320.29 ± 21.56 ms, respectively (Fig. 3). Tinnitus group had delayed P300 latency at both Fz and Cz electrode placements than the normal group, although it was not statistically significant ($p > 0.05$).

There was no significant correlation between P300 amplitude and duration of tinnitus and between P300 latency and duration of tinnitus at Fz and Cz in patients ($p > 0.05$). Moreover, P300 amplitude and latency had no significant correlation with THI score ($p > 0.05$). The mean ± SD of PM value was reported 4137.50 ± 2602.47 Hz (ranged 500−8000 Hz). For LM, it was 3.10 ± 1.25 dB (ranged 1−6 dB SL). Results showed no significant correlation of P300 amplitude and latency with PM and LM.

Discussion

Patients with tinnitus may suffer from several problems in their daily life [10]. In some cases, tinnitus may affect attention [9]. Several tests have been proposed for assessment of auditory attention [9]. One of them is P300 test. The P300 is an endogenous response which depends on several factors, like attention [13]. The P300 has a centro-parietal scalp distribution with its maximum over midline scalp sites, like Fz, Cz and Pz [13]. Given that auditory attention may be affected by tinnitus, in present study we applied P300 test placement of two Fz and Cz active electrodes.

The results showed that patient with tinnitus had lower amplitude at Fz but larger amplitude at Cz compared to controls, although these differences were not statistically significant. This result is in contrast with the results of Attias et al. [17], Attias et al. [18], dos Santos Filha and Matas

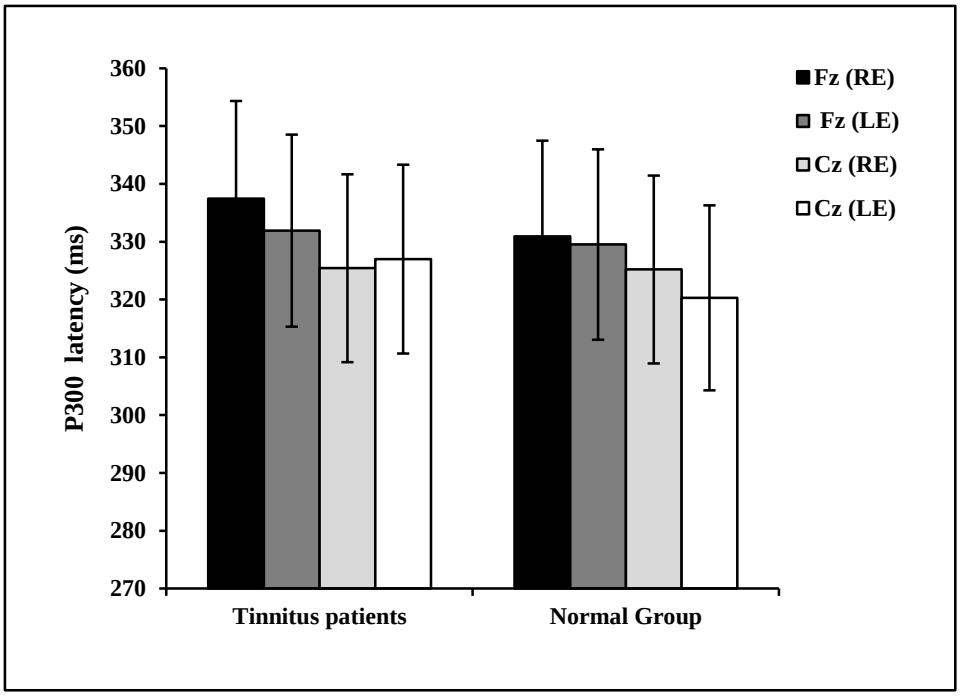

Fig. 3. P300 latencies in both Cz and Fz placements, in tinnitus patients and normal adults. RE; right ear, LE; left ear.

[19], Said [20], and Elmorsy and Abdeltawwab [21] who showed that tinnitus patients had lower amplitude at both Fz and Cz than the normal adults. This discrepancy may be because the tinnitus patients in our study had a mild degree of tinnitus handicap (based on THI results) and, therefore, they could better react to both standard and target stimuli. This finding was in agreement with the results of Zeinun et al. According to them, P300 amplitude may not provide important information about central impairment in tinnitus patients [22]. Nevertheless, De Ridder et al. suggested that the reason for lower amplitude at Fz channel in tinnitus group may be the input processing disorder and frontal lobe involvement, because dorsolateral prefrontal cortex (DLPFC) has an important role in auditory attention and has a direct connection with primary auditory cortex; involvement of DLPFC may cause the reduction of amplitude in tinnitus group [23].

This study showed that tinnitus patients had delayed latency at both Fz and Cz channels, although it was not statistically significant. This is in agreement with the results of Attias et al. [17] and Elmorsy and Abdeltawwab [21], but against the findings of Attias et al. [18], dos Santos Filha and Matas [19], Said [20], and Lima Do et al. [24] who reported a statistically significant difference. One main reason for this result in our study is the low sample size in both tinnitus and normal groups. However, these results may signify the theory presented by Andersson et al. [25] suggesting that tinnitus patients had a slower processing speed and poor attention ability.

In the current study, we conducted psychometric and psychoacoustic assessments of tinnitus to assess their relationship with P300 characteristics. Results showed that P300 amplitude and latency had no statistically significant correlation with tinnitus duration.

With higher scores in THI questionnaire, severity and handicap of tinnitus can be increased which may be due to abnormal activity in limbic, amygdale and hippocampus systems.

Results of our study showed that with higher total THI score, P300 amplitude and latency increased, but it was not statistically significant. This finding is in agreement with the results of Wang et al. [26]. Furthermore, with an increase in the LM, P300 amplitude and latency was increased but it was not statistically significant. This is somehow in agreement with the results of Riga et al. [27] which reported deficits in reticular formation in efferent nerve fiber through cortical connection may create impairment in central inhibition which produce abnormal high loudness in patients with tinnitus. Moreover, the P300 amplitude and latency had no significant correlation with PM. In overall, P300 characteristics had no significant correlation with duration of tinnitus, total THI score, PM, and LM. One of the limitations of this study was its low sample size. It is suggested to use larger sample size in future studies.

Conclusion

It seems that auditory P300 characteristics in tinnitus patients are not different from those in people with no tinnitus. P300 characteristics had no significant correlation with duration of tinnitus, tinnitus handicap inventory total score, pitch matching, and loudness matching. The P300 test may be a useful tool for objective assessment of tinnitus patients.

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Conflict of interest

The authors state that there was no conflict of interest.

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