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Original Article

Assessment of Hidden Hearing Loss in Normal Hearing Individuals with and Without Tinnitus

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OBJECTIVES: To evaluate the functions of cochlear structures and the distal part of auditory nerve as well as dead regions within the cochlea in individuals with normal hearing with or without tinnitus by using electrophysiological tests.

MATERIALS and METHODS: Nine individuals (ages: 21-59 years) with normal hearing with tinnitus were included in the study group. Thirteen individuals (ages: 25-60 years) with normal hearing without tinnitus were included in the control group. Immitancemetric examination, pure-tone audiometry (125Hz-16kHz), speech audiometry in quiet and noise environments, transient evoked otoacoustic emissions (TEOAEs), distortion product otoacoustic emissions (DPOAEs), threshold equalizing noise (TEN test (500Hz–4kHz), and ECochG tests, Beck Depression Questionnaire, Tinnitus Handicap Questionnaire, and Visual Analog Scale were performed.

RESULTS: In the study group, three patients were found to have a minimal depression and six were found to have a mild depression. In pure-tone audiometry, the threshold (6-16 kHz) in the study group was significantly higher than that of the control group at all frequencies. In the study group, lower performance scores were obtained in speech discrimination in noise in both ears. In the control group, no dead region was detected in the TEN test whereas 75% of subjects in the study group had dead regions. DPOAE and TEOAE responses between study and control group subjects were not different. In the ECochG test, subjects in the study group showed an increase in the summating potential/action potential (SP/AP) ratio in both ears.

CONCLUSION: Determination of the SP/AP ratio in patients with tinnitus may be useful in diagnosing hidden hearing loss. Detection of dead regions in 75% of patients in the TEN test may indicate that inner hair cells may be responsible for tinnitus.

KEYWORDS: Cochlear synaptopathy, tinnitus, ECochG, TEN test, hidden hearing loss, high-frequency audiometry

INTRODUCTION

Tinnitus is a hyperactive hearing disorder and is one of the most diverse and complex disorders of the hearing system and occurs in approximately 10-15% of the population [1, 2]. The proportion of individuals with tinnitus complaints in the absence of hearing loss ranges from 8% to 30% [3]. Cochlear damage is usually manifested by increase of hearing thresholds, but the absence of hearing loss does not eliminate cochlear damage [2, 4]. The cochlear function is likely to play an important role in the etiology of tinnitus perception and objective and noninvasive methods such as distortion product otoacoustic emissions (DPOAEs) and transient evoked otoacoustic emissions (TEOAEs) can be used to detect cochlear dysfunction [3].

It is known that many patients with tinnitus show no signs of hearing loss up to 8 kHz in the audiometric test, which is routinely performed using pure tone sound stimuli. It is thought that one of the possible causes of tinnitus in these patients may be related to the cochlear disorder in the basal region [3]. Therefore, it was thought that it would be useful to extend this range to 16 kHz in audiometric tests when evaluating patients with tinnitus [5].

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Another factor in the development of tinnitus may be the cochlear synaptopathy, which is described as the loss of inner hair cell synapses without any evidence of increased hearing thresholds [6]. Non-invasive assays can be named as ABR, envelope-following response amplitude, and middle ear muscle reflex [7].

Diagnosis of cochlear synaptopathy may be done with ABR, which demonstrates reduced wave 1 amplitude [6] but as ABR waves vary considerably in humans, this test may not be used reliably to diagnose cochlear synaptopathy [8].

Another method in the diagnosis of cochlear synaptopathy is electrocochleography. Liberman et al. [9] showed that the summating potential/ action potential (SP/AP) ratio for subjects with higher risk of cochlear synaptopathy was significantly higher than that for low risk subjects. Fabijańska et al. [3] and Ambrosetti and Del Bo [10] have shown that tinnitus patients with normal audiograms up to 8 kHz may have cochlear synaptopathy. According to Fabijańska and Ambrosetti, pure-tone audiometry, speech audiometry, hearing in noise tests, otoacoustic emission, and some other electrophysiological tests are useful and necessary to diagnose cochlear synaptopathy.

Hearing difficulty in noise is another feature of cochlear synaptopathy and speech testing in noise may be another way to test cochlear damage [9]. In addition, self-reported hearing difficulties in normal audiograms may be helpful in patients with suspected cochlear synaptopathy. There are studies that reported difficulties in speech perception and tinnitus toleration in patients with normal hearing levels, which can be revealed by some questionnaires [11, 12].

A different interesting feature of the auditory system is the dead regions in cochlea or hidden hearing loss. Dead region is the region of cochlea where inner hair cells or neurons are not functioning. Vibration of the basilar membrane in this region is not detected by the IHC or neurons but is detected by the normal functioning neighboring regions, if the sound stimuli are high enough to produce displacement of the basilar membrane. Hence true hearing loss at a given frequency may be higher than the detected hearing thresholds by conventional techniques [13]. Dead regions may occur in patients with cochlear synaptopathy or may result from cochlear damage due to noise or ototoxicity. Moore et al. [14] developed a clinical test to diagnose dead regions by using TEN-threshold equalizing noise. This test can be used in normal hearing individuals with tinnitus to screen dead regions in the development of tinnitus.

In this study, several electrophysiological tests including electrocochleography, audiometric tests (TEN, OAE, high-frequency audiometer, and speech tests), and questionnaires were used to evaluate the functions of distal part of the cochlear nerve, cochlear sensorial structures, and cochlear regions in tinnitus patients with normal hearing and to compare with the control group (normal hearing patients without tinnitus). ECochG was also used to determine the cochlear synaptopathy in tinnitus patients with normal hearing.

MATERIALS AND METHODS

Participants, Groups, and Questionnaires

This study was approved by the Ethics Committee of Cerrahpasa Medical Faculty under protocol 83045809-604.0101-154065 and has been carried out in accordance with the Declaration of Helsinki. Informed consent was obtained from all subjects.

The study group comprised nine individuals who applied to Cerrahpasa School of Medicine, Department of Ear, Nose and Throat with tinnitus complaints (5 females, 4 males) aged between 21 and 59 years (SD: 48.8), with normal otoscopy examination, normal middle ear functions, no history of ear operation, no history of neurological and psychiatric disorders, unexposed to noise, and with normal audiometric hearing thresholds between 125 Hz and 8 kHz (<15 dBHL).

The control group comprised 13 individuals without tinnitus complaints (7 females, 6 males) aged between 25 and 60 years (mean=48.3) with normal otoscopy examination, normal middle ear functions, no history of ear operation, no history of neurological and psychiatric disorders, unexposed to noise, and with normal audiometric hearing thresholds between 125 Hz and 8 kHz (<15 dBHL).

The study group participants reported tinnitus: three of them in left ear, three of them in right ear, and three of them in both ears. All patients were able to determine in which ear tinnitus was present. For all participants in our study, visual analog scale (VAS) was used to measure the subjective perception level of tinnitus, tinnitus handicap questionnaire (THQ) was used to assess handicap, and Beck depression scale was used to assess quality of life and depression level.

Audiometric Thresholds, Immitancemetric Measurements, and Hearing in Noise Tests

Audiometric thresholds 125 Hz to 16000 Hz were measured using a calibrated (GSI AudioStar Pro-Grason-Stadler Inc. 10395 West 70th St. Eden Prairie, MN 55344, USA) clinical audiometer. The frequencies between 125 Hz and 8 kHz were measured using TDH-39P headphones and 9, 10, 11.2, 12.5, 14, and 16 kHz frequencies were measured using HDA200 high-frequency circumaural headphones. The average of frequencies of 500 Hz-1 kHz-2 kHz is 15 dBHL or less and is considered normal hearing. Bone conduction thresholds were obtained for frequencies from 250 to 4000 Hz using a Radio Ear B71 bone vibrator placed in the mastoid outcrop of the temporal bone. Tympanometry, acoustic reflex, and Eustachian tube function tests were carried out using a (GSI Tympstar -Grason-Stadler Inc. 10395 West 70th St. Eden Prairie, MN 55344, USA) middle ear analyzer to rule out middle ear pathology.

The GSI AudioStar Pro instrument used for hearing in noise test and room calibration was used before testing. Hearing in noise test stimuli were presented using EARLINK 3A inserts at 25 dB, 20 dB, 15 dB, 10 dB, dB, and 0 dB signal-to-noise ratios using the Adobe Audition program. As a stimulus, phonemic-balanced six sentences with five words chosen from the International Matrix Test are presented.

TEOAEs and DPOAEs

TEOAEs were recorded at 1.4, 2, 2.8, and 4 kHz in all subjects using Otodynamics Echoport ILO 288 (Otodynamics Ltd. 30-38 Beaconsfield Rd, Hatfield, Herts AL 10 8 BB, UK). DPOAEs were recorded using GSI Audera (Grason-Stadler Inc. 10395 West 70th St. Eden Prairie, MN 55344, USA) at 504, 844, 996, 1184, 1418, 1688, 2004, 2379, 2824, 3363, 3996, 4758, 5660, 6727, 8004, 8496, 9516, 11.309, and 12.000Hz frequencies with stimuli f1=65 dBSPL and f2=55 dBSPL (f1/f2=1.22).

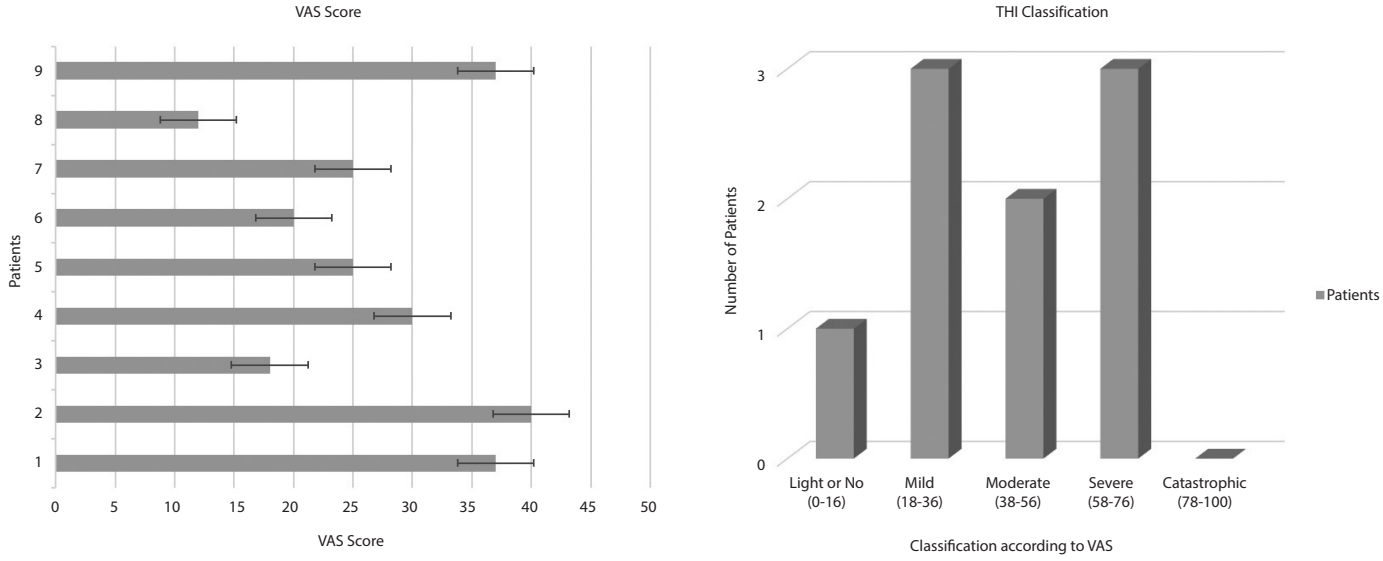

Figure 1. Graph on the left shows visual analog scale (VAS) scores in the patient group with tinnitus and graph on the right shows the results of the tinnitus handicap questionnaire (THA) in the patient group with tinnitus.

TEN Test

Thresholds of TEN test were measured with the EARLINK 3A (www.etymotic.com) insert at 500, 1000, 2000, and 4000 Hz frequencies using the GSI AudioStar Pro. For each frequency, 60 dBHL noise was used. Two dB steps were used to measure masked thresholds (Moore, Glasberg, & Stone, 2004). If the masked threshold is at a particular frequency at least 10 dB above the absolute threshold and 10 dB above the nominal noise level, this frequency region is considered a dead region [15].

Electrocochleography (ECochG)

ECochG is measured using the GSI Audera device. The ear canals of the subjects were cleaned up using Q-type long ear buds, cleaning solution, and gel. Before placing the ER3-26A (www.etymotic.com) electrodes in the ear canal, an EEG conductive gel was applied over the gold coating. The impedance values of the electrodes were <5 kΩ. A click stimulus of 100 μs was delivered at 94.5 dBnHL via a silicone tube attached to the ER-3A (www.etymotic.com) headphones. The electrical responses amplification was ×100.000. A band-pass filter (10-3,000 Hz) was used for recording and 2000 sweeps were received.

Statistical Analysis

All data analyses were carried out with the Statistical Packages for the Social Sciences (SPSS) software version 21.0 (IBM Corp.; Armonk, NY, USA). In comparison of subjects with normal hearing, with and without tinnitus, non-parametric Mann-Whitney U test (independent group comparisons test) was applied. Correlations were compared using a nonparametric Spearman test.

RESULTS

Questionnaire

In the study group, according to the results of the Beck depression questionnaire, three patients were found to have a minimal depression level and six were found to have a mild depression level. When the visual analog scale and tinnitus handicap surveys were compared, there was a correlation between the two surveys (p=0.41) (Figure 1).

Standard and High-Frequency Audiometry

According to pure-tone audiometric test results, hearing thresholds between 6 kHz and 16 kHz in the study group were obtained higher than the control group. This difference was statistically significant at all frequencies (p<0.05).

Speech in Noise Test

In the study group, lower performance scores were obtained in speech discrimination in noise in both ears. This decrease was statistically significant (left ear; p<0.01, right ear; p<0.05) (Figure 2).

TEN Test

In the control group subjects, no dead region was detected in the TEN test applied between 500 and 4 kHz. In the study group, in the TEN test between 500 and 4 kHz, dead regions were detected in nine of 12 tinnitus ears (75%). In the right ear, 33.3% of the dead regions were detected and in the left ear, 41.6% were detected. Of the dead regions, 36.5% were obtained at 500 Hz, 45.5% at 1 kHz, 9% at 2 kHz, and 9% at 4 kHz. In the tinnitus ears, a total of 11 frequency regions have been identified as dead regions.

TEOAEs and DPOAEs

In the DPOAE test in the study group, DPOAE responses were not different statistically (p>0.05) (Figure 3). In the TEOAE test, the study group showed no difference in TEOAE responses in both ears compared to the control group (p>0.05). (Figure 4).

Electrocochleography (ECochG)

In the ECochG test, when compared to the control group, the study group showed an increase in the SP/AP ratio in both ears (mean SP/AP ratio in subjects: left ear 0.32±0.09, right ear 0.38±0.08, mean

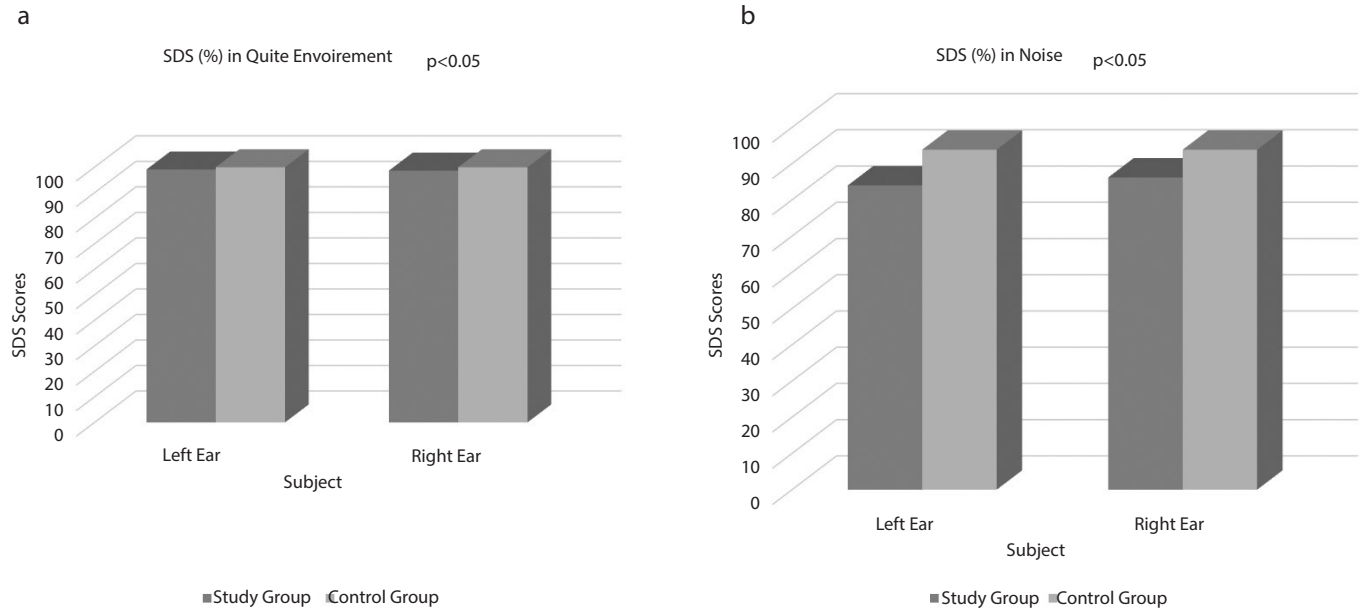

Figure 2. a, b. a) Graph showing the comparison of speech test scores (in quiet environment). b) Graph showing the comparison of speech scores (in noise).

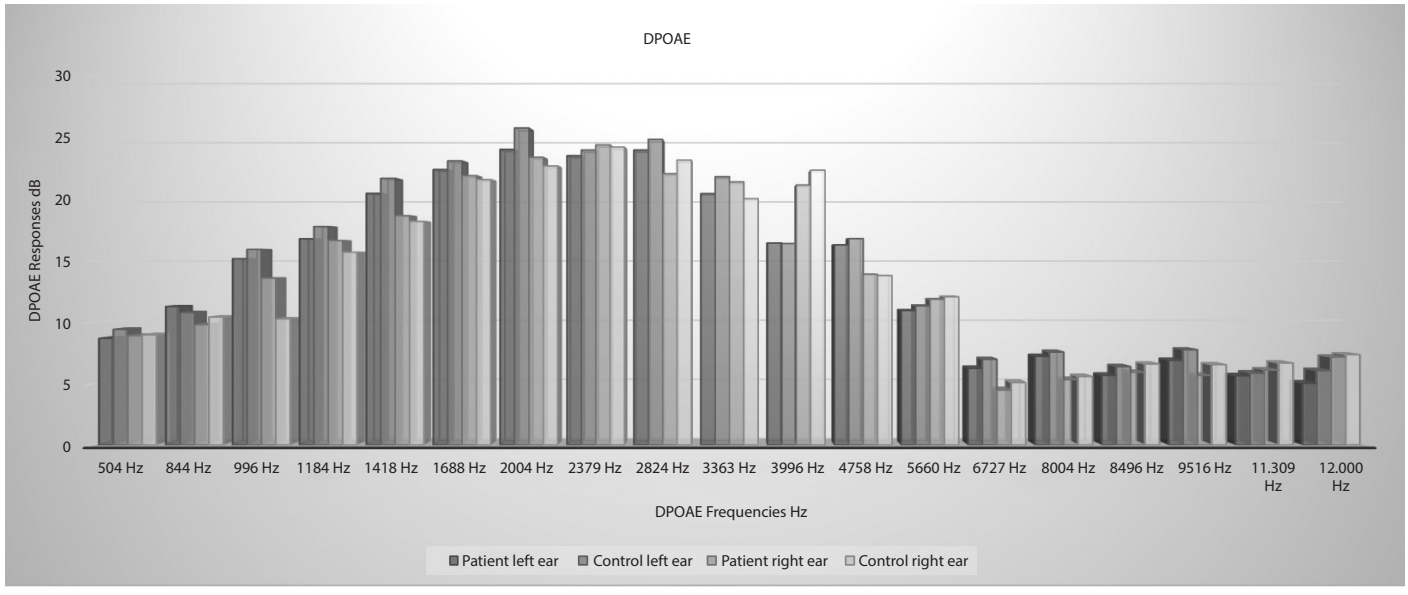

Figure 3. Graph showing DPOAE results compared to ears in patients and control.

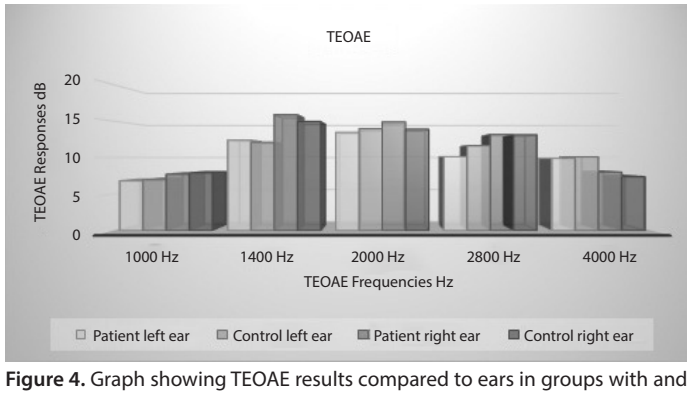

Figure 4. Graph showing TEOAE results compared to ears in groups with and without tinnitus.

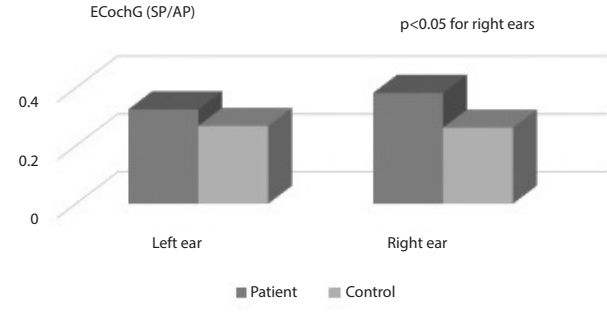

Figure 5. Graph showing SP/AP ratios in ears with and without tinnitus.

SP/AP ratio in the control group: left ear 0.26+/−0.05, right ear 0.26+/−0.05). While this increase was not statistically significant for the left ear (p=0.144), it was statistically significant for the right ear (p=0.01) (Figure 5).

DISCUSSION

Tinnitus is most commonly related to hearing loss that triggers neuroplastic changes in central auditory pathways [16]. However, absence of hearing loss in patients with tinnitus does not necessarily rule out cochlear damage. Cochlear synaptopathy and/or dead regions in the cochlea may be responsible for generation of tinnitus in normal hearing individuals. To determine hidden cochlear damage in these patients along with conventional audiologic evaluation, sophisticated electrophysiological tests such as OAE, TEN test, high-frequency audiometry, speech perception in noise, etc. are mandatory.

In the study of Thabet et al. [1], TEOAE and TEN tests were applied to 20 patients with normal hearing and unilateral tinnitus complaints. In the study, the other ear of the patients was used as the control ear. Abnormal TEOAE responses were obtained in 85% of the ears with tinnitus complaints, compared to control ears where TEOAE responses were found to be abnormal in 20%. Dead regions were detected in only 15% of the tinnitus ears in which the TEN test was performed. In the study performed by Gilles et al. [16], TEN test was applied to hearing impaired subjects with tinnitus and they could not find cochlear dead regions and concluded that the TEN test was not reliable to detect cochlear dead regions [17]. However, in the study of Weisz et al. [17], cochlear dead region was detected in 9 of 11 subjects. In our study, dead regions were detected in 75% of the tinnitus ears in the dead region evaluation using the TEN test. Unlike the study by Gilles et al. [16], our study included only subjects with normal hearing. Although inner hair cells are physically and physiologically more resistant than outer hair cells, this finding suggests that inner hair cells may play a more active role in the development of tinnitus than outer hair cells. These contradictions in the literature show that more studies are needed to achieve more consistent results.

Shiomi et al. [18] measured DPOAE amplitudes between 500 Hz and 8 kHz, and significantly lower DPOAE amplitudes were detected in 93.3% of nine patients with normal hearing tinnitus patients. The results of the study suggest that in some cases tinnitus may be related to cochlear mechanical activities. In our study, in evaluating the cochlear mechanical activities using DPOAE between 500 Hz and 12 kHz, the study group showed no difference than the control group. In the test using TEOAE, in the study group, the responses were not significantly different when compared to the control group. These results suggest that in both groups outer hair cell functions were similar and outer hair cell dysfunctions were not contributing to tinnitus. However, in some cases, the frequency of the tinnitus is determined outside the frequency range in which the decrease in the DPOAE is determined, and the frequency regions in which the dead regions are located, and the tinnitus frequency are inaccurate. These findings suggest that the tinnitus mechanism is still unclear [19].

Studies have shown that acoustic tests are not sufficient in diagnosis and treatment of tinnitus and it is necessary to evaluate the psychosomatic perception of tinnitus in patients [20]. Jain et al. [20] investigated the effect of tinnitus on psychoacoustic skills in 20 patients with tinnitus in normal hearing patients. The authors detected that tinnitus had negative effects on auditory perception skills like temporal resolution, discrimination of speech in noise, and temporal discrimination. They reported that this effect might be due to some changes in the central auditory system that was not apparent in the audiogram. In our study, when comparing the ability to discriminate speech in a silent environment, very similar results were obtained in both groups. However, in the speech test performed in the presence of background noise, the significant decrease ($p<0.05$) in the study group suggested that tinnitus affected auditory perception skills in these subjects, even though they had normal results in the standard audiometry test [21].

ECochG is an electrophysiological test that measures cochlear SP that arises from hair cells and AP, which is equivalent to wave I of the ABR produced by cochlear nerve [22]. The test has been traditionally used for the diagnosis of endolymphatic hydrops but some authors used the test for determining the risk of cochlear synaptopathy. Liberman et al. [9] detected that the SP/AP ratio was significantly higher in individuals with high risk of synaptopathy.

Stuermer reported that cochlear microphonic (CM) and summating potential (SP) thresholds were significantly lower than compound action potential (CAP) thresholds in patients with synaptopathy and concluded that ECochG could be used in differential diagnosis of synaptopathy [23].

In our study, we found increase in the SP/AP ratio in the study group when compared to the control group. These results suggest that determining SP/AP ratio may be useful in diagnosing hidden hearing loss (cochlear synaptopathy) in patients with normal hearing who suffer from tinnitus. The damage to synapses may affect hearing ability, even if the hearing thresholds are normal in frequencies between 250 and 8,000 Hz. In addition, DPOAE and TEOAE responses, which mostly assess outer hair cell functions, were normal in each group. This finding supports that the outer hair cell functions were not different in patients with tinnitus from the control subjects. The detection of dead regions in 75% of patients in the TEN test of our study may indicate that in our patient group inner hair cells may play a role in the emergence of tinnitus. In order to avoid hearing loss of hidden hearing in patients who have normal hearing with tinnitus complaints, detailed electrophysiological (ECochG, DPOAE, and TEOAE) and subjective tests (TEN test, high-frequency audiometry, and speech test on noise) should be done in detail to make the diagnosis clearer and tinnitus source. This will help to make more accurate projections about tinnitus.

CONCLUSION

In this study, electrocochleography, an electrophysiological test that has not previously been used to determine the rate of hidden hearing loss in tinnitus suffering patients along with other test methods, was used to determine cochlear synaptopathy. Our results suggest that the determination of the SP/AP ratio in patients with normal hearing with tinnitus may be useful in diagnosing hidden hearing loss (cochlear synaptopahy), and that damage to synapses may affect hearing ability, even if the hearing threshold is normal in standard audiometric frequencies. The detection of dead regions in 75% of patients in the TEN test supports the possibility that the inner hair cells

may play a role in the development of tinnitus in our study group. Detailed electrophysiological (ECochG, DPOAE, and TEOAE) and subjective tests (TEN test, high-frequency audiometry, and speech test in noise) are needed to diagnose hidden hearing loss in tinnitus patients with normal hearing and will help to make more accurate projections about the source of tinnitus.

Ethics Committee Approval: Ethics committee approval was received for this study from the Ethics Committee of İstanbul University-Cerrahpaşa, Cerrahpaşa School of Medicine (83045809-604.0101-154065

Informed Consent: Informed consent was obtained from the patients who participated in this study.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept - E.K.; Design - E.K., H.M.Y.; E.D.G., H.Ç.K.; Supervision - E.K., H.M.Y.; Resource - E.K., K.A., A.A.A., S.K., S.D.; Materials - E.K., K.A., A.A.A., H.M.Y.; Data Collection and/or Processing - E.K., K.A., A.A.A., S.K., S.D.; Analysis and/or Interpretation - E.K., H.M.Y., E.D.G., K.A., H.K.; Literature Search - E.K., K.A., A.A.A., S.K., S.D. ; Writing - E.K., H.M.Y., A.A.A., K.A.; Critical Reviews - E.K., H.M.Y.

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

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