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Original Article

Impact of Tinnitus on Cochlear Dysfunction and Electromotile Responses of Outer Hair Cells

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ABSTRACT

Objective: Tinnitus is defined as the perception of sound in the absence of an external source. It affects a significant proportion of the adult population and can have a detrimental psychological influence even in people with normal hearing. The aim of this study was to investigate the possible changes in cochlear function in the presence of tinnitus despite normal hearing using the Distortion Product Otoacoustic Emission Input/Output function.

Methods: Thirty-two patients aged 18-45 years (26 ± 6.45), including 12 patients with chronic subjective tinnitus and 20 patients without tinnitus, with normal hearing were included in the study. After a detailed ENT examination, evaluations including pure tone audiometry, immittancemetric evaluation, tinnitus evaluation, and distortion product otoacoustic emission input/output tests were performed.

Results: In the chronic subjective tinnitus group, the mean tinnitus intensity was 45.58 ± 16.1 dB. When the distortion product otoacoustic emission input/outputt values of the individuals with chronic subjective tinnitus were compared with those of the control group, significantly reduced amplitude responses were obtained at all frequencies (500-10 000 Hz) and at all intensity levels (40-70 dB) in the individuals with tinnitus.

Conclusion: In conclusion, the distortion product otoacoustic emission input/outputt test, which is a valuable tool for the assessment of cochlear function and hearing sensitivity in normal hearing individuals, was shown to be useful in individuals with chronic subjective tinnitus. In our study, we demonstrated the effects of tinnitus-induced cochlear dysfunction by a decrease in the amplitude of distortion product otoacoustic emission input/output responses at all frequencies tested.

Keywords: Tinnitus, subjective, hearing, cochlea

Introduction

Tinnitus is defined as a sound that is heard in the ear in the absence of any stimulus from a source.[1] These sounds can be intense enough to affect a person's quality of life and can last for a long time. Although tinnitus is not a symptom of a life-threatening disease, the psychological effects of the condition can make it difficult for people to function socially.[2]

Tinnitus is classified into subjective and objective tinnitus. Tinnitus of unknown cause is called subjective tinnitus and is the most common type of tinnitus (95%). Subjective tinnitus can be caused by otological causes, metabolic disorders, neurological disorders, pharmacological causes, and psychological disorders. There is no specific treatment for subjective tinnitus.[3] Objective tinnitus, on the other hand, is defined as tinnitus caused by a known disease or condition. Objective tinnitus can be caused by vascular abnormalities and hypertension.[4] However, the majority of cases are idiopathic. The distinction between acute and chronic tinnitus is classified in the literature according to when the tinnitus first occurs. Acute tinnitus is defined as tinnitus of less than 6 months duration, while chronic tinnitus is tinnitus of more than 6 months duration.[5]

The source of mechanical energy in the ear was discovered to be sounds produced in the inner ear, called otoacoustic emissions (OAE). In the cochlea, low-level stimulus inputs were modulated quite sharply, and a nonlinear growth was detected as the sound level increased. These findings indicate that the cochlea has a nonlinear function. Outer hair cells (OHCs) actively alter cell length in response to changes in membrane

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potential.[6,7] Cochlear amplification is a process in which the OHCs in the cochlea, the auditory organ of the inner ear, mechanically amplify vibrations. Outer hair cells have a structure that can elongate and contract in response to depolarization and hyperpolarization currents.[8,9] This electromotility is considered to be the basis of cochlear amplification, and cell length variation is mediated by the motor molecule prestin.[10-12] Loss of OHCs results in reduced cochlear sensitivity and frequency selectivity.

Distortion product otoacoustic emissions (DPOAEs) are objective measures of cochlear function that can be used to assess hearing function.[13] The strength and structure of DPOAEs can provide valuable information about cochlear function.[14] They are widely used in various clinical applications, including cochlear screening of tinnitus, assessing the effects of ototoxic drugs, and studying the impact of noise on the cochlea.[15] Specifically, DPOAEs at certain input levels were found to be significantly higher in subjects with tinnitus and normal hearing thresholds compared to those with tinnitus and hearing loss, indicating a potential link between cochlear function and tinnitus perception.[16] Additionally, differences in DPOAE levels between individuals with and without tinnitus have been observed, suggesting a potential association between tinnitus and OHC function.[17]

Distortion product otoacoustic emissions are known to decrease with increasing hearing loss in patients without tinnitus.[18] In addition, altered DPOAE results were observed in patients with tinnitus and normal hearing, suggesting a role for cochlear dysfunction in tinnitus generation.[19] Moreover, the association of tinnitus with changes in the amplitude of DPOAEs has been reported, indicating a potential role of DPOAE in identifying subtle auditory deficits in tinnitus patients with normal audiometric thresholds.[20] In the study by Yenigün et al, patients with normal hearing and patients with hearing loss were assessed with DPOAE in tinnitus. The results showed that DPOAE responses may be reduced in patients with normal hearing and that these responses may be more pronounced in low-frequency tinnitus.[21] In the study by Satar et al, cochlear function was analyzed using the DPOAE test in patients with tinnitus and normal hearing. The results showed that patients with normal hearing but tinnitus had some degree of cochlear dysfunction.[22]

The aim of this study was to investigate the possible changes in cochlear function in the presence of tinnitus despite normal hearing using the Distortion Product Otoacoustic Emission Input/Output (DPOAE I/O) function.

Methods

Participants

A total of 32 individuals aged between 18 and 45 years (26 ± 6.45) were included in the study. The individuals consisted of 12 people with tinnitus for at least 6 months and normal hearing, and 20 people with normal hearing without tinnitus. In the study, individuals in the groups with and without tinnitus were determined according to the inclusion and exclusion criteria. Individuals in the group with tinnitus were formed according to the following inclusion criteria: (1) being between 18 and 45 years of age, (2) having bilateral normal hearing (0-25 dB HL), (3) having chronic subjective tinnitus (CST) for at least 6 months, (4) having not undergone ear surgery, and (5) having no ongoing middle ear pathology. Individuals in the group without tinnitus were selected according to the following inclusion criteria: (1) being between 18 and 45 years of age, (2) having bilateral normal hearing (0-25 dB HL), (3) having no tinnitus, (4) having not undergone ear surgery, and (5) having no ongoing middle ear pathology. The study was conducted in accordance with the Declaration of Helsinki and Good Clinical Practices, and informed consent was obtained from all individuals. The study was approved by the Trakya University Faculty of Medicine Clinical Research Ethics Committee (Approval no: 2022/126, Date: April 11, 2022).

Protocol of the Study

Detailed anamnesis and demographic information were obtained from all individuals enrolled in the study. A detailed physical examination was conducted by an otolaryngologist. The following assessments were completed on the same day and in a single session: audiological evaluation, which included tympanometry, pure tone audiometry, and DPOAE I/O test. Tinnitus evaluation comprised tinnitus frequency (TF) measurement, tinnitus level measurement, and the Tinnitus Handicap Inventory (THI).

Audiological Evaluation

Immittancemetry Test

Immitancemetric measurements were performed on Resonance R36M Middle Ear Analyser (Resonance, Gazzaniga, Italy) using TDH-39 (Telephonics, USA) headphones, and a tympanometry test was performed at 226 Hz prop tone at 75 dB SPL. Tympanograms with a "type A"peak curve between +100 daPa and −50 daPa pressure range were considered normal.[23,24] Acoustic reflex (AR) test was manually tested and recorded ipsilaterally and contralaterally at stimulus frequencies of 500, 1000, 2000, and 4000 Hz.

Pure Tone/Speech Audiometry Test

Audiometric evaluations were performed according to ANSI standards in standard soundproof cabinets following audiometric evaluation procedures. All pure tone air-conducted audiometric evaluations were performed on an Interacoustics AC-40 clinical audiometer (Interacoustics, Denmark) with a range of 0.25-8 kHz using Telephonic TDH-39 (Telephonics, USA) headphones, and bone conduction evaluations were performed with a Radioear B-71 (Radioear, USA) bone conduction vibrator with a frequency range of 0.5-4 kHz. Following the pure tone audiometric evaluation, speech discrimination scores (SDSs) were evaluated as a percentage (%) with speech stimuli in all individuals.[25] Participants with bilateral hearing in the range of 0-25 dB HL with "type A" normal tympanogram were considered to have normal hearing.[26]

Distortion Product Otoacoustic Emission Input/Output (DPOAE I/O) Test

Distortion Product Otoacoustic Emission tests were recorded in a quiet cabinet with an Eclipse EP25 Clinical ABR-OAE device (Interacoustics, Denmark). The stimulus consisted of 2 pure tones (f1 and f2; f2/f1 = 1.22) presented with L1 and L2 set to 60 and 50 dB SPL, respectively. Distortion Product Otoacoustic Emission Input/Output testing was performed in 2 stages. Individuals with a low TF (<4 kHz) underwent DPOAE I/O testing at 0.5, 1, 2, and 3 kHz, while individuals with high TF (>4 kHz) underwent DPOAE I/O testing at 4, 6, 8, and 10 kHz.

The responses of DPOAEs were considered "passed" if:

- The signal-to-noise ratio (SNR) was equal to or greater than 6 dB SPL for all f2 frequencies.
- Reliability was over 98%.

Tinnitus Evaluation

Measurement of Tinnitus Frequency

In individuals with unilateral tinnitus, the tinnitus TF was measured in the contralateral ear. In patients with bilateral tinnitus, the evaluation was performed in the ear with less tinnitus intensity; if the tinnitus intensity was the same in both ears, the evaluation was performed in the ear with less hearing loss. If the person's pure-tone hearing

thresholds and tinnitus intensity were the same in both ears, one of the ears was randomly selected and evaluated.

Measurement of Tinnitus Intensity

In patients with unilateral tinnitus, the severity of tinnitus was determined from the contralateral ear. In individuals with bilateral tinnitus complaints, the evaluation was performed in the ear with less tinnitus severity; if the tinnitus was bilateral and of the same severity, the evaluation was performed in the ear with less hearing loss. If the person's hearing thresholds and tinnitus severity were the same bilaterally, one of the ears was randomly selected and evaluated. The procedure was terminated when the intensity of the tinnitus was equal to the intensity of the stimulus.

Tinnitus Handicap Inventory

Tinnitus Handicap Inventory (THI) is a questionnaire developed in 1996 by Newman et al.[27] A Turkish validity and reliability study was conducted in 2007 by Aksoy et al.[28] The questionnaire consists of 25 questions and is scored between 0 and 100. Tinnitus Handicap Inventory is a questionnaire form that demonstrates high reliability in test repetitions, remains unaffected by gender, age, and hearing thresholds, and produces more psychometrically significant results.

Statistical Analysis

The power analysis for the individuals planned to be included in the study was determined using G*Power version 3.1.9.7 software. In a study conducted in the literature with a similar population and methodology, 10 individuals for each group were included in the study.[29] In our study, according to 95% confidence ($1 - \alpha$), 95% test power ($1 - \beta$), and an effect size of $d = 0.5$ for a one-tailed correlation coefficient, the number of samples to be taken was determined as at least 12 individuals for each group and 24 individuals in total.

Data were analyzed using the Statistical Package for Social Sciences version 22.0 software (IBM Corp.; Armonk, NY, USA). Values with a *P*-value below .05 were considered statistically significant. Mean and standard deviation were used for numerical data, and frequency values were used for categorical variables. Kolmogorov–Smirnov test was used to evaluate the conformity to normal distribution. Mann–Whitney U test was used to examine differences between groups, while the Wilcoxon signed-rank test was used for intra-group comparisons.

Results

A total of 32 adults, 20 female and 12 male, aged 18-45 years, were included in the study. The mean age of individuals was 31.2 ± 8.4 years in the CST group and 23.3 ± 1 years in the control group. The study group consisted of 12 individuals with tinnitus (17 ears) and 20 individuals without tinnitus (40 ears). Among the individuals with CST, bilateral tinnitus was observed in 5 individuals, while unilateral tinnitus was observed in 7 individuals (4 in the right ear and 3 in the left ear).

Pure-Tone Hearing Evaluation and Immittancemetric Analysis Results

All individuals were evaluated with pure-tone audiometry and immittance measurements. The results of the pure-tone audiometry tests are shown in Table 1. Tympanometry results for all individuals were obtained as bilateral type A. The results of the group comparison analysis of the results of the AR test evaluation are presented in Table 2.

Tinnitus Evaluation Results

As a result of the tinnitus intensity matching test, the mean tinnitus intensity value of individuals with CST was found to be 45.58 ± 16.1 dB. In the group of individuals with CST, as a result of tinnitus frequency matching, 10 ears with tinnitus frequencies of 4000 Hz and below were included, while 7 ears with tinnitus frequencies above 4000 Hz were included in the study. When the THI scores were analyzed, a mean score of 55 ± 20.5 was obtained.

Table 1. Pure-Tone/Speech Audiometry Results

	CST (n:17)	Control (n:40)	*P* value
AC-PTA (dB)	8.17 ± 4.4	9.62 ± 4.4	.265
BC-PTA(dB)	3.11 ± 3.5	2.72 ± 2.1	.914
SRT (dB)	7.94 ± 3	8.75 ± 4	.589
SDS (%)	88.47 ± 7	92.3 ± 3.3	.03*

AC, air conduction; BC, bone conduction; CST, chronic subjective tinnitus; PTA, pure tone average; SRT, speech reception threshold; SDS, speech discrimination score.

Table 2. Comparison Results of Acoustic Reflex Responses Between Groups

		CST (n:17)	Control (n:40)	*P*
İpsilateral (dB)	500 Hz	93.82 ± 4.1	95.5 ± 3.35	.114
	1000 Hz	92.64 ± 6.4	95.25 ± 3.9	.105
	2000 Hz	92.35 ± 4.3	94.87 ± 4.1	.063
	4000 Hz	94.7 ± 6.4	95.5 ± 4	.882
Contralateral (dB)	500 Hz	96.76 ± 4.6	96.25 ± 4	.517
	1000 Hz	97.64 ± 3.5	96.5 ± 3.7	.,26
	2000 Hz	96.47 ± 4.5	95.25 ± 4	.23
	4000 Hz	97.5 ± 2.3	95.5 ± 3.8	.11

CST, chronic subjective tinnitus.
*$P < .05$.

Distortion Product Otoacoustic Emission Input/Output Test Results

Individuals with CST were separated according to TF, and DPOAE I/O evaluations were completed. Individuals with TF < 4000 Hz (7 ears) were evaluated at stimulus frequencies of 500, 1000, 2000, and 3000 Hz, while individuals with TF ≥ 4000 Hz (10 ears) were evaluated at frequencies of 4000, 6000, 8000, and 10 000 Hz at stimulus intensities of 40, 50, 60, and 70 dB.

When the DPOAE I/O values of the individuals with CST were compared with those of the control group, the amplitude responses of the individuals with CST were lower than those of the control group at all intensity levels (40, 50, 60, and 70 dB) at 500, 1000, 4000, 6000, and 8000 Hz, and the difference was statistically significant. At 10 000 Hz, the amplitude responses of individuals with CST were lower than those of the control group only at 40 and 50 dB stimulus intensity levels, and the difference was statistically significant. At 2000 and 3000 Hz, there was no statistically significant difference between the groups at any stimulus level. The results of the statistical significance of the difference between the CST group and the normal group in the DPOAE I/O evaluation are presented in Tables 3 and 4.

Discussion

The main finding of this study showed that the presence of tinnitus at all frequencies except 2000 and 3000 Hz decreased DPOAE I/O responses and led to cochlear dysfunction. In addition, the reduction in DPOAE I/O responses in the presence of normal hearing suggests that the presence of CST may have a negative effect on the linear function of the cochlea.

When the AR thresholds of normal hearing individuals were evaluated, AR thresholds were observed in the range of 70-100 dB SPL.[30,31] In another study, AR thresholds were obtained at an average level of 80-90 dB SPL in normal individuals.[32] In our study, when analyzing the

Table 3. Distortion Product Otoacoustic Emission Input/Output Amplitude Comparisons of Individuals with Tinnitus Frequency <4000 Hz

		500 Hz		1000 Hz		2000 Hz		3000 Hz	
		Mean ± SD	*P*	Mean ± SD	*P*	Mean ± SD	*P*	Mean ± SD	*P*
40 dB	CST	2.47 ± 5.13	.00*	8.95 ± 7.83	.005*	15.89 ± 9.61	.077	15.46 ± 5.92	.146
	Control	9.49 ± 1.1		16.02 ± 3.91		16.72 ± 4.79		18.05 ± 4.58	
50 dB	CST	2.1 ± 6.3	.00*	10 ± 7.08.	.001*	16.55 ± 6.28	.619	15.38 ± 7.74	.884
	Control	10.33 ± 1.52		17.63 ± 4.43		18.08 ± 4.55		17.73 ± 4.71	
60 dB	CST	1.99 ± 5.66	.00*	11.8 ± 10.1	.017*	16.7 ±9.06	.56	15.44 ± 7.79	.085
	Control	11.74 ± 2.29		17.69 ± 4.24		16.72 ± 5.24		16.34 ± 4.84	
70 dB	CST	2.67 ± 6.1	.00*	13.09 ± 6.78	.039*	17.98 ± 13.37	.104	16.9 ± 4.02	.075
	Control	13.07 ± 2.64		17.43 ± 4.58		17±5.04		17.04 ± 4.69	

CST, chronic subjective tinnitus; SD, standard deviation.
*P <.05.

Table 4. Distortion Product Otoacoustic Emission Input/Output Amplitude Comparisons of Individuals with Tinnitus Frequency ≥4000 Hz

		4000 Hz		6000 Hz		8000 Hz		10 000 Hz	
		Mean ± SD	*P*	Mean ± SD	*P*	Mean ± SD	*P*	Mean ± SD	*P*
40 dB	CST	5.21 ± 4.61	.00*	1.5 ± 10.34	.00*	0.4 ± 3.47	.00*	6.41 ± 7.05	.001*
	Control	17.94 ± 4.7		15.67 ± 5.1		15.38 ± 4.82		17.38 ± 4.78	
50 dB	CST	5.38 ± 6.04	.00*	4.54 ± 3.97	.00*	4.38 ± 8.49	.001*	10.78 ± 3.59	.007*
	Control	17.12 ± 5.27		16.68 ± 4.37		16.26 ± 5.18		16.04 ± 4.08	
60 dB	CST	7.51 ± 4.5	.00*	5.5 ± 6.87	.001*	6.41 ± 7.98	.001*	14.17 ± 3.16	.172
	Control	17.07 ± 4.3		15.98 ± 4.09		17.73 ± 4.73		16.63 ± 4.36	
70 dB	CST	10.77 ± 8.8	.00*	8.85 ± 9.81	.001*	8.4 ± 6.32	.00*	16.54 ± 4.65	.851
	Control	17.71 ± 3.96		17.89 ± 4.93		18.04 ± 4.08		18.63 ± 4.56	

CST, chronic subjective tinnitus; SD, standard deviation.
*P < .05.

ipsilateral and contralateral AR thresholds in the normal group, we obtained mean AR responses at mean levels of 90-100 dB SPL. When we analyzed the AR results of individuals with normal hearing and tinnitus, it was shown that the presence of tinnitus had no effect on the mean AR thresholds, both ipsilateral and contralateral, in individuals with normal hearing. Our results are consistent with the literature and support previous studies. We think the reason for this is the low severity of tinnitus in the people included in the study.

Several studies have investigated the effect of tinnitus on SDS in individuals with hearing loss and normal hearing. The frequency of CST that individuals have may influence SDS to decrease with hearing loss.[33] When we looked at the comparison of the SDS of the groups in our study, it was observed that SDS decreased in individuals with CST despite normal hearing, and our findings were in agreement with the literature. Decreased SDS is one of the symptoms that can negatively affect us in many environments in our daily life.

Studies support the finding that tinnitus-induced cochlear dysfunction can lead to a decrease in the amplitude of DPOAE I/O responses at all frequencies tested. Gehr et al and Shiomi et al both observed a reduction in DPOAE amplitude in tinnitus patients, with Gehr et al specifically linking this to cochlear impairment.[34,35] Paglialonga et al[36] further confirmed this finding, noting abnormal DPOAEs in tinnitus subjects with normal hearing sensitivity, suggesting a role for outer hair cell dysfunction. Job et al[37] provided additional evidence, identifying lower DPOAEs in normal hearing subjects exposed to noise and susceptible to tinnitus, indicating a potential marker of susceptibility to tinnitus. The relationship between tinnitus and DPOAEs has been investigated in the literature. Özimek et al found that tinnitus patients had lower DPOAE amplitude levels compared to normal hearing controls.[18] Similarly, Ami et al[38] reported decreases in DPOAE responses in both normal hearing and tinnitus patients with hearing loss. Shekhawat et al[39] showed that tinnitus is associated with hearing loss and DPOAEs can be used to estimate hearing sensitivity. In the findings of our study, it was observed that there was a decrease in responses and significant differences at many frequencies analyzed in the comparison of DPOAE I/O results with normal individuals. Distortion product otoacoustic emission input/output responses provided us with findings to differentiate conditions such as impaired/started deterioration of the linear function of the cochlea.

Limitations of the Study

Our study has a limitation. High-frequency audiometry evaluation of the individuals included in the study was not performed. The reason for this is that the individuals were from the young population and the tinnitus frequency values were 8 kHz and below.

Conclusion

In conclusion, the DPOAE I/O test, which is a valuable tool for evaluating cochlear function and hearing sensitivity in individuals with normal hearing, has been shown to be useful in individuals with CST. As a result, we demonstrated the effects of tinnitus-induced cochlear dysfunction with a decrease in the amplitude of DPOAE I/O responses at all frequencies tested. Our study predicts that the DPOAE I/O test will be a valuable tool for investigating the effects of tinnitus in clinics in the future.

Ethics Committee Approval: Ethics committee approval was received for this study from the Ethics Committee of Trakya University (Approval no: 2022/126; Date: April 11, 2022).

Informed Consent: Written informed consent was obtained from patients and patients' parents who participated in this study.

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References

1. Merve A. Subjektif Tinnituslu Bireylerde Kefir Tüketiminin Tinnitus Derecesi Üzerine Etkisi. Dissertation. *Aydın Adnan Menderes Üniversitesi*. 2021.
2. Welch D, Dawes PJ. Personality and perception of tinnitus. *Ear Hear*. 2008;29(5):684-692. [CrossRef]
3. Tanrıöver Ö. Approach to the patient with tinnitus in primary care. *Türkiye Aile Hekimliği Dergisi*. 2011;15(1):24-28.
4. Tunkel DE, Bauer CA, Sun GH, et al. Clinical practice guideline: tinnitus executive summary. *Otolaryngol Head Neck Surg*. 2014;151(4):533-541. [CrossRef]
5. Esmaili AA, Renton J. A review of tinnitus. *Aust J Gen Pract*. 2018;47(4):205-208. [CrossRef]
6. Russell IJ, Nilsen KE. The location of the cochlear amplifier: spatial representation of a single tone on the guinea pig basilar membrane. *Proc Natl Acad Sci U S A*. 1997;94(6):2660-2664. [CrossRef]
7. Withnell RH, Shaffer LA, Lilly DJ. What drives mechanical amplification in the mammalian cochlea? *Ear Hear*. 2002;23(1):49-57. [CrossRef]
8. Brownell WE, Bader CR, Bertrand D, de Ribaupierre Yd. Evoked mechanical responses of isolated cochlear outer hair cells. *Science*. 1985;227(4683):194-196. [CrossRef]
9. Kileny PR, Zwolan TA. Diagnostic audiology. In *Cummings Otolaryngol Head Neck Surg*. Amsterdam: Elsevier; 2010:1887-1903.
10. Cooper NP, van der Heijden M. *Dynamics of Cochlear Nonlinearity*. Berlin: Springer International Publishing; 2016:267-273.
11. Oliver D, He DZ, Klöcker N, et al. Intracellular anions as the voltage sensor of prestin, the outer hair cell motor protein. *Science*. 2001;292(5525):2340-2343. [CrossRef]
12. Moore R, *Head and Neck Surgery? Otolaryngology*. 3rd ed. Philadelphia: Byron J. Bailey, Lippincott Williams & Wilkins. [CrossRef]
13. Bhagat SP, Bass JK, White ST, et al. Monitoring carboplatin ototoxicity with distortion-product otoacoustic emissions in children with retinoblastoma. *Int J Pediatr Orl*. 2010;74(10):1156-1163. [CrossRef]
14. Dhar S, Abel R, Hornickel J, et al. Exploring the relationship between physiological measures of cochlear and brainstem function. *Clin Neurophysiol*. 2009;120(5):959-966. [CrossRef]
15. Dağli AŞ, Ankara KK. *Distortion Product Otoakustİk Emİsyonlar* (UYARI/CEVAP EĞRİLERİ).
16. Zhou X, Henin S, Long GR, Parra LC. Impaired cochlear function correlates with the presence of tinnitus and its estimated spectral profile. *Hear Res*. 2011;277(1-2):107-116. [CrossRef]
17. Modh D, Katarkar A, Alam N, Jain AK, Shah P. Relation of distortion product otoacoustic emission and tinnitus in normal hearing patients: A pilot study. *Noise Health*. 2014;16(69):69-72. [CrossRef]
18. Ozimek E, Wicher A, Szyfter W, Szymiec E. Distortion product otoacoustic emission (DPOAE) in tinnitus patients. *J Acoust Soc Am*. 2006;119(1):527-538. [CrossRef]
19. Granjeiro RC, Kehrle HM. Oliveira TSCd, Sampaio ALL, Oliveira CACPd. Is the degree of discomfort caused by tinnitus in normal-hearing individuals correlated with psychiatric disorders? *Otolaryngology*. 2013. [CrossRef]
20. Ishak WS, Zhao F, Rajenderkumar D, Arif M. Measurement of subtle auditory deficit in tinnitus patients with normal audiometric thresholds using evoked otoacoustic emissions and threshold equalizing noise tests. *Int Tinnitus J*. 2013;18(1):35-44. [CrossRef]
21. Yenigün A, Doğan R, Aksoy F, Akyüz S, Dabak H. Assessment of tinnitus with tinnitus severity index, tinnitus handicap inventory and distortion product otoacoustic emissions in patients with normal hearing and hearing loss. *Kulak Burun Bogaz Ihtis Derg*. 2014;24(1):11-16. [CrossRef]
22. Satar B, Kapkin O, Özkaptan Y. Evaluation of cochlear function in patients with normal hearing and tinnitus: a distortion product otoacoustic emission study. *Kulak Burun Bogaz Ihtis Derg*. 2003;10(5):177-182.
23. Lidén G. The scope and application of current audiometric tests. *J Laryngol Otol*. 1969;83(6):507-520. [CrossRef]
24. Jerger J. Clinical experience with impedance audiometry. *Arch Otolaryngol*. 1970;92(4):311-324. [CrossRef]
25. Thornton AR, Raffin MJ. Speech-discrimination scores modeled as a binomial variable. *J Speech Hear Res*. 1978;21(3):507-518. [CrossRef]
26. Suutarla S, Rautio J, Ritvanen A, Ala-Mello S, Jero J, Klockars T. Microtia in Finland: comparison of characteristics in different populations. *Int J Pediatr Orl*. 2007;71(8):1211-1217. [CrossRef]
27. Newman CW, Weinstein BE, Jacobson GP, Hug GA. The HEARing Handicap Inventory for Adults: psychometric adequacy and audiometric correlates. *Ear Hear*. 1990;11(6):430-433. [CrossRef]
28. Aksoy S, Firat Y, Alpar R. The Tinnitus Handicap Inventory: a study of validity and reliability. *Int Tinnitus J*. 2007;13(2):94-98.
29. Sobhy O, Elbanby N, Elmoazen D. Study of auditory brainstem response in tinnitus patients with normal hearing. *Egypt J Ear Nose Throat Allied Sci*. 2020;22(22):1-9. [CrossRef]
30. Sm P. Acoustically elicited stapedial reflex in cochlear implanted patients. *Biology. Eng Med*. 2020;5(1). [CrossRef]
31. Block M, Wiley T. Overview and basic principles of acoustic immitance. *Handbook of Clinical Audiology*. 1994:271-282.
32. Mazlan R, Kei J, Hickson L. Test-Retest Reliability of the acoustic stapedial Reflex Test in healthy neonates. *Ear and Hearing*. 2009;30(3):295-301.
33. Oh JH, Lim T, Joo JB, Cho JE, Park P, Kim JY. The relationship between tinnitus frequency and speech discrimination in patients with hearing loss. *Korean J Otorhinolaryngol-Head Neck Surg*. 2023;66(3):156-161. [CrossRef]
34. Gehr DD, Janssen T, Michaelis CE, Deingruber K, Lamm K. Middle ear and cochlear disorders result in different DPOAE growth behaviour: implications for the differentiation of sound conductive and cochlear hearing loss. *Hear Res*. 2004;193(1-2):9-19. [CrossRef]
35. Shiomi Y, Tsuji J, Naito Y, Fujiki N, Yamamoto N. Characteristics of DPOAE audiogram in tinnitus patients. *Hear Res*. 1997;108(1-2):83-88. [CrossRef]
36. Paglialonga A, del Bo L, Ravazzani P, Tognola G. Quantitative analysis of cochlear active mechanisms in tinnitus subjects with normal hearing sensitivity: multiparametric recording of evoked otoacoustic emissions and contralateral suppression. *Auris Nasus Larynx*. 2010;37(3):291-298. [CrossRef]
37. Job A, Raynal M, Kossowski M. Susceptibility to tinnitus revealed at 2 kHz range by bilateral lower DPOAEs in normal hearing subjects with noise exposure. *Audiol Neurootol*. 2007;12(3):137-144. [CrossRef]
38. Ami M, Abdullah A, Awang MA, Liyab B, Saim L. Relation of distortion product otoacoustic emission with tinnitus. *Laryngoscope*. 2008;118(4):712-717. [CrossRef]
39. Shekhawat GS, Searchfield GD, Stinear CM. The relationship between tinnitus pitch and hearing sensitivity. *Eur Arch Otorhinolaryngol*. 2014;271(1):41-48. [CrossRef]