

Distortion Product Otoacoustic Emissions (DPOAEs) In Tinnitus Patients

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Abstract

Introduction Tinnitus is the perception of sound in the absence of external sound stimulation. There is a general agreement that it is a direct consequence of irreversible and permanent cochlear damage.

Objectives The present work is designed to study the distortion product otoacoustic emissions (DPOAEs) in tinnitus patients with normal hearing in comparison with normal hearing control and to study any possible correlation between DPOAEs recording and patients' complaints.

Methods The present study included 80 subjects divided into 2 groups: Control group: consisted of 30 normal-hearing adults not complaining of tinnitus and Study group: consisted of 50 normal-hearing adults complaining of tinnitus. The methodology includes full audiological history, otoscopic examination, basic audiological evaluation, DPOAEs including both DP-gram and DPOAEs input/output functions.

Results Basic audiological evaluation showed within normal hearing sensitivity in both groups, however, with significant higher hearing thresholds in tinnitus patients at all frequency ranges. The Tinnitus Handicap Inventory Questionnaire showed mean scores of 35.2 ± 16.9 in the study group. The DP-gram showed higher amplitudes in the control group when compared with tinnitus patients. The DPOAEs input-output functions at different frequencies (1, 2, 4 and 6kHz) also showed higher amplitudes at all frequencies and different input levels. The slope of the I/O function tends to be steeper in tinnitus cases.

Conclusion Patients with tinnitus might have neural dysfunction at either the level of the cochlea, as shown in reduced DPOAE levels, and changes in the normal DP-I/O function recorded in the present work.

Keywords

- ▶ tinnitus
- ▶ otoacoustic emissions
- ▶ cochlear outer hair cells

Introduction

Tinnitus may be defined as an unwanted auditory perception of internal origin.¹ The prevalence of tinnitus increases with age, peaking in the 7th decade of life.^{2–4}

Tinnitus that is not associated with an identifiable sound source is assumed to be associated with damage to the auditory system anywhere between the cochlea and the auditory cortex.⁵ However, the majority of cases are triggered by or associated with cochlear damage.^{6,7} Recent

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studies have shown how cochlear damage can lead to unexpected functional changes in the central auditory system that may be related to hyperacusis and tinnitus.⁸ Tinnitus can also cause various somatic and psychological disorders that interfere with the quality of life, including concentration difficulties or insomnia.⁹

As mentioned before, the cochlear function may play an important role in the generation of tinnitus perception. So, the assessment of the inner ear is important for the evaluation of tinnitus patients. Cochlear function can be tested objectively and noninvasively using otoacoustic emissions, including distortion product otoacoustic emissions (DPOAEs).¹⁰ Distortion product otoacoustic emissions amplitudes were significantly reduced in 93.3% of the normal hearing tinnitus cases.¹¹ This suggested an altered functional state of the outer hair cells (OHCs) in the majority of the tinnitus ears with normal hearing.¹² Different studies used DPOAEs to assess cochlear function in tinnitus patients; however, few studies assessed the loudness growth pattern in those cases. This will be addressed in the present work using DPOAEs input/output function (DP-I/O function).

Objectives

This is a case-controlled study that was designed to study the DP-gram and DPOAEs input/output function in tinnitus patient with normal hearing in comparison with normal hearing subjects not suffering from tinnitus. The present study also aimed at studying the possible correlation between DPOAEs recording and complaints by the patients.

Method

In the present study, we recruited 80 subjects with bilateral normal peripheral hearing to participate. They were divided into two groups:

Group 1 (control group): composed of 30 subjects free from tinnitus.

Group 2 (study group): composed of 50 subjects suffering from tinnitus.

Inclusion criteria: Subjects with bilateral normal peripheral hearing thresholds (≤ 25 dBHL at all frequencies) with age range between 18 and 50 years old. All participants had no history of current external or middle ear disorders, history of noise exposure, systemic diseases or psychiatric problems

Exclusion criteria: Subjects with hearing impairment, history of ototoxic medication, chronic disorders such (as diabetes mellitus or hypertension), cervical spondylosis, history of head injury or cerebrovascular accident, psychiatric disorders or endocrinal diseases.

The present study was conducted in the Audiovestibular unit, Otolaryngology, Head and Neck Surgery Department, Kafrelsheikh University Hospitals, Egypt. Consents were obtained from all participants in the present work after explaining the test procedure. All cases were recruited from cases attending the Audiovestibular unit at Kafrelsheikh

University Hospitals. The present work was approved by the Ethical committee at the faculty of Medicine, Kafrelsheikh University Hospitals (Approval code: 17-7-2018).

All cases were submitted to:

Full history taking

Otосcopy examination

Basic audiological tests, including: air conduction pure tone audiometry along the frequency range of 250–8,000Hz, in addition to mid-octave frequencies (750Hz, 1,500Hz, 3,000Hz and 6,000Hz) and bone conduction pure tone audiometry along the frequency range of 500–4,000Hz, speech audiometry (including both speech reception thresholds and word discrimination %), immittanceometry (including tympanometry and acoustic reflexes thresholds).

Tinnitus matching for the study group including:

1. **Pitch matching:** It is measured by varying the frequency of a pure tone or narrow band noise so that it is matched with the pitch of the tinnitus
2. **Loudness matching:** The patient is instructed to raise his/her hand whenever the stimulus is equal in loudness to his/her tinnitus. Loudness is expressed in dB. In the present study, the ascending method was used.

Arabic version of Tinnitus Handicap Inventory Questionnaire¹³ to assess the psychological impact of tinnitus. This questionnaire includes 10 questions, and the patient should answer with no (score = 0), sometimes (score = 5), or always (score = 10). At the end of the questionnaire, the total score was calculated and the psychological impact of tinnitus was calculated accordingly.

Distortion Product Otoacoustic Emissions (DPOAEs):

The stimulus composed of a pair of primary pure tones (f_1 and f_2) at f_2/f_1 frequency ratio equal to 1.22, presented at two levels (L1 and L2), where L2 is higher than L1 by 10dB. Two methods of DPOAEs recording were used:

3. **DP-gram:** in this modality, we measure the $2f_1 - f_2$ DPOAEs amplitudes at various f_2 frequencies along the frequency range of 1,000- 6,000Hz with fixed stimulus intensities (L1 =65 dB and L2 = 55 dB SPL).

Distortion product otoacoustic emissions were considered present if the DP-signal to noise ratio (SNR) exceeded the noise floor by > 3 dB.

4. **DPOAEs Input/output function (DP-I/O):** this function is recorded by measuring the DPOAE amplitude as a function of a change of stimulus level at a particular f_2 frequency of 1,000, 2,000, 4,000, and 6,000 Hz. At each frequency, the stimulus levels started at 75dB for L1 and 65dB for L2 then decreased in 5dB until reaching 50dB for L1 and 40dB for L2.

The collected data were organized, tabulated and statistically analyzed using IBM SPSS Statistics for Windows, version 19 (IBM Corp. Armonk, NY, USA). Qualitative data were presented as number and percentage. Quantitative data were described using minimum and maximum, mean and standard

deviation (SD). The level of significance was adopted at $p < 0.05$. The used tests were: the Chi-squared test for categorical variables, to compare between different groups, the Student t-test for normally quantitative variables to compare between two studied groups, and the Mann Whitney test for abnormally quantitative variables to compare between two studied groups, and the Spearman coefficient to correlate between two normally quantitative variables.

Results

The present study was performed from July, 2018 to January, 2020, and included 80 participants: 50 as study cases and 30 as controls, with an age range between 18 and 50 years old. The mean age of the control group was 33.5 ± 1.3 years old, while that of the study group was 37.3 ± 3.3 years old, with no significant difference between both groups ($p < 0.05$). Regarding gender, the female percentages were higher in both groups, and represented 62 and 76% in the study and control groups, respectively, with no significant difference between both groups ($p < 0.05$).

In the study group, tinnitus was found to be bilateral in 56% of the cases and unilateral in 44% of the cases (left-sided in 32% and right-sided in 12% of the cases).

The results of the basic audiologic evaluation were within normal hearing sensitivity along the frequency range of 250–8,000Hz, in addition to mid-octave frequencies (except at 6,000Hz, where it did not reach a significant level). However, there was a significant higher hearing threshold in tinnitus patients at all frequency ranges, especially in high frequency ($> 2\text{kHz}$). The results of immittancemetry showed type A tympanograms in both ears with normal ipsilateral and contralateral acoustic reflex (AR) thresholds in both ears in both groups (\rightarrow Figure 1).

Tinnitus matching for frequency test was performed, and the results revealed that the minimum tinnitus frequency was 1kHz, and that the maximum frequency was 8kHz (Median = 1 kHz; IQR = 1–4KHz). In more details, the tinnitus frequency was ≥ 4 KHz in 8 ears, at the mid frequency range (1–3 KHz) in 10 ears, at the low frequency range (< 1 KHz) in 10 ears, and noise in 22 ears. Tinnitus matching for intensity revealed low intensity tinnitus (< 40 dB) in 25 ears (8 ears at 20dB and 17 ears at 30dB), moderate intensity level (40–60 dB) in 21 ears (9 ears at 40dB, 8 ears at 50dB, 4 ears at 60dB), while 4 ears suffered from loud tinnitus > 60 dB (3 ears at 70dB and one ear at 90dB).

The Arabic version of the Tinnitus Handicap Inventory Questionnaire was applied in order to assess the disability caused by tinnitus, and the results showed mean scores of 35.2 ± 16.9 in the study group. Thirty cases (60% of the total) had mild impairment, 17 cases had moderate impairment (34%), while 3 cases (6%) had severe impairment.

Distortion product optoacoustic emissions were recorded using two techniques. The first one is recording of DP-gram along the frequency range of 1,000–6,000Hz. The second technique is recording DP-I/O function. Regarding DP-gram in the right ear, the amplitudes of the DPOAEs were higher in the control group when compared with tinnitus patients at all frequencies, except 1 kHz, with the largest difference between both groups at 2 kHz when compared with other frequencies. In the left ear, the amplitudes of DP were significantly higher in the control group as compared with tinnitus patients, with the largest difference between 2 groups at 4 KHz for amplitudes (\rightarrow Table 1).

The DPOAEs input-output functions were studied at different frequencies (1, 2, 4 and 6kHz), starting at L2/L1 primary levels of 75/65dB and descending in 5dB steps till reaching primary levels of 50/40dB. At each level, the amplitudes of the DPOAEs were calculated and compared

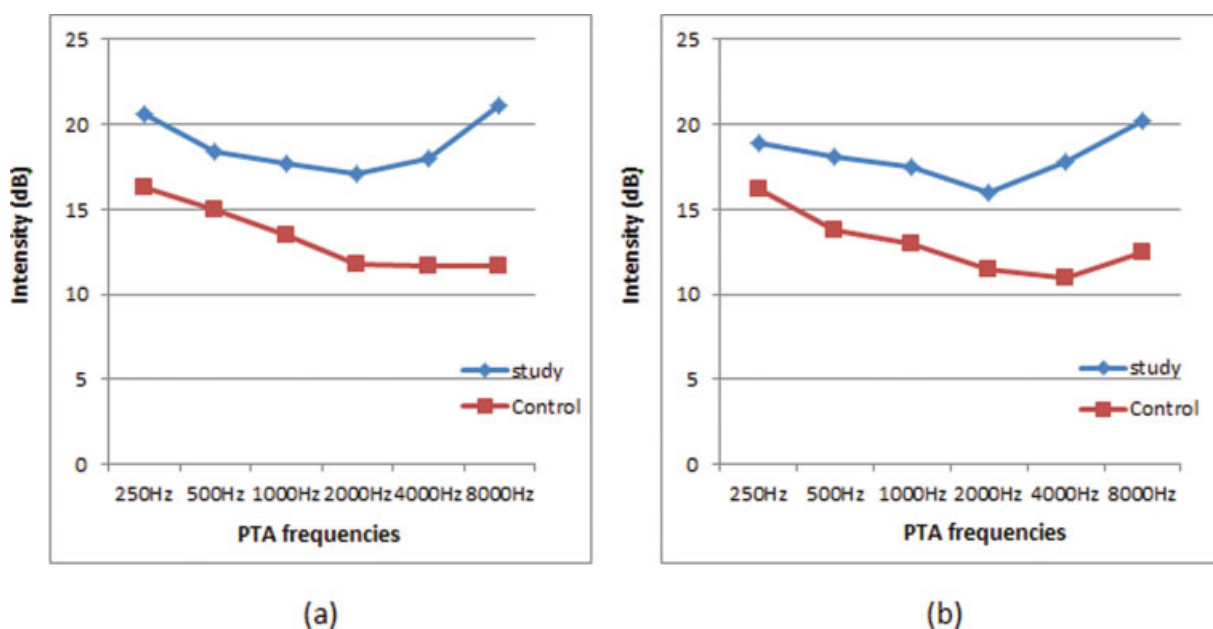


Fig. 1 Comparison of PTA thresholds between the control and study group in the right ear (a) and the left ear (b) at different frequencies.

Table 1 Comparison of DPOAEs amplitudes between control and study groups in right and left ears

			Right Ear			Left Ear			
			Group I	Group II		Group I	Group II		
DP Amplitude	1 kHz	Mean	9.5	7.4	$t = 1.020$ $p = 0.312$	Median	6.7	11.3	$Z_{mw} = 2.34$ $p = 0.019^*$
		IQR				1.1–10.4	6.3–15.4		
		SD	8.6	8.4		Mean rank	32.67	44.58	
	2 kHz	Median	13.1	4.6	$Z_{mw} = 2.281$ $p = 0.023^*$	Median	7.6	11.1	$Z_{mw} = 2.99$ $p = 0.003^*$
		IQR	3.7–18.2	2.5–11.1		IQR	3.4–10.3	7.5–19.1	
		Mean rank	40.97	25.03		Mean rank	31.32	46.57	
	4 kHz	Median	8.8	4.3	$Z_{mw} = 2.146$ $p = 0.032^*$	Median	3.0	9.2	$Z_{mw} = 2.74$ $p = 0.006^*$
		IQR	3.8–13.7	-3.1–9.1		IQR	-1.3–9.5	3.5–13.5	
		Mean rank	38.15	27.51		Mean rank	31.83	45.82	
	6 kHz	Median	-2.5	-2.8	$Z_{mw} = 3.417$ $p = 0.001^*$	Median	-9.7	-3.9	$Z_{mw} = 2.23$ $p = 0.026$
		IQR	-5.8–-0.2	-16.6–-4.9		IQR	-18.5–-2.5	-9.4–-2.4	
		Mean rank	37.82	27.81		Mean rank	32.90	44.25	

Abbreviations: DP, Distortion product; IQR, interquartile range; SD, standard deviation.

*significant at $p < 0.05$, t ; Independent t -test, Z_{mw} ; Mann-Whitney U test

between both groups in each ear. At 1 kHz, both the right and left ears showed higher DPOAEs amplitudes in the control group, which were significant only at 65/55dB (► **Table 2**; ► **Fig. 2**).

At 2 kHz, the DP-I/O function showed significant higher amplitudes at all primary levels in the right and left ears of the control group when compared with tinnitus patients. Similar results were found in the left ear at 4 kHz, while the right ear showed significant higher amplitudes at high input levels only in the same frequency (75/65, 70/60, 65/55) (► **Tables 3, 4**; ► **Figures 3 and 4**).

At 6 kHz, the DP-I/O function showed significant higher amplitude at all primary levels in the right ear of the control group when compared with tinnitus patients, except at 50/40, which did not reach a significant level. In the left ear, there were significantly higher amplitudes only at high input levels (75/65, 70/60, 65/55) (► **Table 5** and ► **Figs. 5, 6**).

To quantify the DP-growth function, the slope(s) of the I/O functions were calculated at different frequencies between 40–65 dB SPL level of L2 and compared between both groups. In the control group, the I/O function at 1 and 2 KHz tends to be more flattened at L2 level ≥ 55 dB SPL, while at 4 and 6 kHz, the I/O function tends to be steeper along all L2 levels. In the study group, the steeper I/O function tends to be preserved along all L2 levels at all frequencies, except at 1 kHz, where it tends to be flatter (► **Figures 6 and 7**).

In the present work, we studied the possible correlation between tinnitus questionnaire results and tinnitus frequency, tinnitus intensity and DP-gram amplitudes along different frequencies (1–6 kHz). The results showed no correlation between any of these parameters ($p > 0.05$).

Discussion

Tinnitus is a common disorder with hearing of unpleasant sounds; however, it is poorly understood. The expected increase in knowledge about the mechanism involved in tinnitus and potential treatment strategies will help in providing relief to this annoying disease. There are several hypotheses regarding the mechanisms of tinnitus generation. Most of the authors consider the origin of tinnitus as cochlear, such as lesions of the hair cells after acoustic trauma, presbycusis or sudden hearing loss. In 1990, Jastreboff¹⁴ had proposed that tinnitus probably starts in the cochlea and then the abnormal activity is generated in the central pathways that prolong the symptoms.

In the present work, we recruited 80 subjects to participate: 30 subjects (23 females and 7 males) constituted the control group, and 50 subjects with normal hearing and suffering from tinnitus constituted the study group (31 females and 19 males). The comparison between both groups showed no significant difference regarding age or gender ($p > 0.05$).

Studying the laterality of tinnitus in the present study showed that tinnitus was bilateral in 56% of the cases, left-sided in 32% of the cases, and right-sided in 12% of the cases. This is consistent with other studies^{15,16} that reported a similar higher percentage of left-sided tinnitus than right-sided tinnitus. This could be due to anatomical and physiological differences in the structures of the right and left central nervous system (CNS). For example, the left ear seems to be more susceptible to a wide range of cochlear insults, such as noise and ototoxic drugs.^{15,17,18}

Table 2 Comparison of DPOAEs I/O function amplitudes between the control and study groups at 1,000Hz in the right and left ears

1,000 Hz		Right Ear			Left Ear			Test of significance
		Group I	Group II	Test of significance	Group I	Group II	Test of significance	
DP amplitude	75/65	Mean	9.0	6.2	t = 1.81 p = 0.075	Median	8.4	Z = 1.27 p = 0.201
		SD	7.0	5.6		IQR	5.4-11.5	
		Median	10.6	5.6	Z = 1.65 p = 0.098	Mean rank	41.37	34.86
	70/60	IQR	4.8-14.2	7.7		IQR	6.1-13.7	3.7-10.1
		Mean rank	36.60	2.2-10.6		Mean rank	43.07	33.70
		Mean	8.4	3.7	t = 2.36 p = 0.021*	Median	11.4	7.4
	65/55	SD	6.5	9.0		IQR	7.8-14.1	2.7-10.8
		Median	9.8	5	z = 1.90 p = 0.057	Mean rank	43.88	33.15
		IQR	1.2-8.0	3.1-12.9		Median	9.5	5.0
	60/50	Mean rank	28.34	37.22		IQR	1.7-13.7	-0.9-10.6
		Mean	4.8	2.7	z = 0.932 p = 0.355	Median	7.3	4.1
		SD	9.3	8.8		IQR	3.8-10.1	-0.2-8.9
	55/45	Median	3.2	0.9	z = 1.60 p = 0.108	Mean rank	40.70	35.32
		IQR	0.4-6.2	-3.2-5.6		Median	3.0	3.8
		Mean rank	36.48	28.9		IQR	0.1-7.0	1.4-7.7
						Mean rank	36.08	38.47

Abbreviations: DP, Distortion product; IQR, interquartile range; SD, standard deviation.
*significant at $p < 0.05$, t: Independent t-test, Z_{m-w} : Mann-Whitney U test

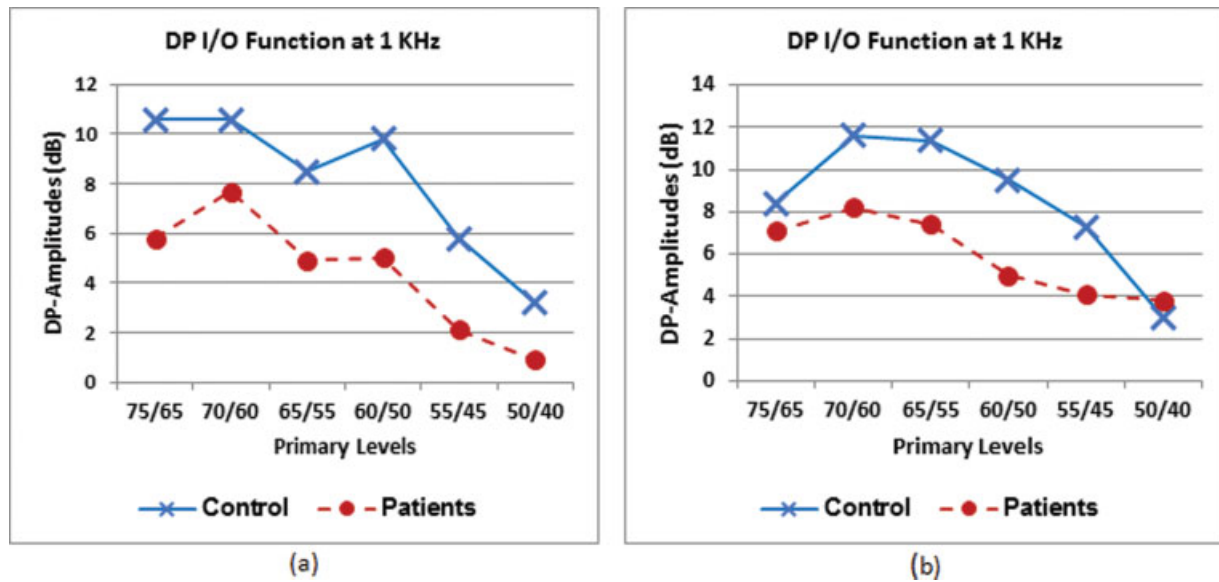


Fig. 2 Comparison of DPOAEs I/O function amplitudes between the control and study groups in the right ear (a) and left ear (b) at 1 kHz.

Despite the presence of normal pure tone audiometry (PTA) results in tinnitus patients in the present study, their hearing thresholds were significantly elevated when compared with the control group. This suggested that normal PTA does not necessarily exclude cochlear damage. Kujawa et al.¹⁹ supported the possibility of the presence of a sub-clinical hearing loss with normal hearing thresholds, or what is called “missing hearing loss”²⁰. Additionally, tinnitus may be a primary symptom of diseases that are only diagnosed after the occurrence of hearing loss.²¹

In the present study, the possibility of cochlear dysfunction as a cause of tinnitus generation was studied using DPOAEs recording in tinnitus patients with normal hearing. The selection of DPOAEs was based on its current use as an efficient tool for the objective evaluation of the inner ear function, especially of the outer hair cells of the cochlea.²² The DP-gram was recorded in both groups at 1, 2, 4 and 6 kHz. The results in the right ear showed significantly higher DPOAEs amplitudes in the control group at all frequencies, except at 1 kHz. In the left ear, the amplitude of the DP was significantly higher in the control group when compared with tinnitus patients. These findings suggest the possibility of subtle damage to the OHCs in tinnitus patients, which can be detected early with DPOAEs even before it is manifested as a shift in audiometric thresholds.²³ Some studies suggested that the basal region of the cochlea may contribute to some extent to DPOAEs measured at lower frequencies. Traditional audiometric data usually do not include higher frequencies (> 8 or 10 kHz). Therefore, normal conventional audiometry does not exclude higher frequencies affection. Additionally, OHC impairment in the most basal cochlear region may result in reduced contribution to more apically generated DPOAEs.^{24,25} Similar data were reported by Clark et al.,²⁶ who found that OHCs damage of ~20% might not be detected in the behavioral threshold measures. Another hypothesis suggested the presence of OHC impairment along with other subclinical pathologies, such as loss of normally high-thresh-

old spiral ganglion cells with subsequent generation of tinnitus.²⁷

Results of DP-growth function showed higher DPOAEs amplitudes in control cases, which were significant at the majority of frequencies and intensity levels (► **Tables 3–5**; ► **Figures 3–7**). Regarding the slope of the DP-growth function, there was a tendency of a steeper slope of the I/O functions mainly at high frequencies (4 and 6 kHz) in both groups. At lower frequencies, the I/O function tends to be more compressive, especially at high input levels (1 and 2 kHz), which were more evident in normal cases (► **Figure 7**). These findings were consistent with earlier observations of differences in cochlear processing at the base, compared with the apex. Fibers with high characteristic frequency (CF) innervating hair cells at the cochlear base had sharper tuning (with long low-frequency tails where the threshold remained relatively constant regardless of the frequency) compared with low-CF fibers innervating more apically located hair cells (with more symmetrical tuning, and low-frequency).²⁸ On using DPOAE I/O functions in human ears with normal hearing, these functions are characterized by a linear segment as the response emerges from the noise floor, followed by a compressive region over which the output is no longer linearly related to the input.²⁹

The sharp slope of the I/O function in tinnitus patients, especially at high frequencies, suggested diminished sensitivity and tuning of the cochlear amplifier, which alters the auditory processing that already occurs at the cochlear level. The linear growth function seen in tinnitus patients also might suggest the possibility of deficient efferent inhibition. This, in turn, might affect cortical activity, leading to hyperactivity in the OHCs.³⁰ It could be also due loss of the normal loudness growth, where auditory sensitivity might be rescaled as a function of the mean level of auditory sensory inputs.³¹ Additionally, tinnitus is usually associated with increased central gain as a result of reduction of auditory input, even when hearing loss is still not detectable on the audiogram.³²

Table 3 Comparison of DPOAEs I/O function amplitudes and SNR between the control and study groups at 2kHz in the right and left ears

2,000 Hz		Right ear			Left ear			Tests statistic	Group II	Tests statistic
		Group I	Group II	Tests statistic	Group I	Group II	Tests statistic			
DP amplitude	75/65	Median	15.1	10.1	Z = 2.13 P = 0.034*	Mean	14.9	t = 2.91 P = 0.005*	10.0	
		IQR	5.8-19.6	5.6-12.8		SD	7.8		5.7	
		Mean rank	37.77	27.85						
	70/60	Median	15.5	9.2	Z = 2.20 P = 0.027*	Mean	14.7	t = 3.18 P = 0.005*	9.3	
		IQR	6.5-20.3	4.5-13.1		SD	7.9		6.1	
		Mean rank	37.97	27.68						
	65/55	Median	15.7	6.4	Z = 2.38 P = 0.017*	Median	11.1	Z = 2.67 P = 0.008*	7.9	
		IQR	2.3-18.7	.6-10.2		IQR	5.4-20.6		2.5-11.2	
		Mean rank	38.40	27.29		Mean rank	45.58		31.99	
	60/50	Median	12.0	.8	Z = 2.92 P = 0.004*	Median	6.6	Z = 2.75 P = 0.006*	3.9	
		IQR	.6-15.5	-3.5-7.8		IQR	4.1-18.7		-9-7.3	
		Mean rank	39.73	26.12		Mean rank	45.85		31.81	
	55/45	Median	4.7	-3.4	Z = 2.69 P = 0.007*	Mean	4.8	t = 2.96 P = 0.004*	-7	
		IQR	-4.7-10.7	-7.5-2.6		SD	8.8		7.2	
		Mean rank	39.17	26.62						
	50/40	Median	2.6	-6.3	Z = 3.57 P = <0.001*	Mean	-4.6	t = 2.83 P = 0.006*	-4.8	
		IQR	-4.1-6.9	-12.6--1.5		SD	7.6		8.8	
		Mean rank	41.35	24.96						

Abbreviations: DP, Distortion product; IQR, interquartile range; SD, standard deviation.
*significant at $p < 0.05$; t; Independent t-test; Z_{mnw} ; Mann-Whitney U test

Table 4 Comparison of DPOAEs I/O function amplitudes and SNR between the control and study groups at 4kHz in the right and left ears

4,000 Hz		Right ear			Left ear			Tests statistic
		Group I	Group II	Tests statistic	Group I	Group II	Tests statistic	
DP amplitude	75/65	Median	13.4	9.1	Z =	14.4	9.7	Z = 2.15
		IQR	9.5-19.9	5.4-12.9	2.69	8.1-20.5	4.8-14.4	p = 0.031*
		Mean rank	39.17	26.92	0.007*	44.02	33.06	
70/60	Median	12.1	7.6	Z	11.7	7.8	Z = 1.99	
	IQR	7.1-17.7	0.3-11.2	2.08	5.2-18.2	1.3-12.6	p = 0.047*	
	Mean rank	37.67	27.94	0.037*	42.92	32.87		
65/55	Median	6.9	4.1	Z =	7.1	4.3	Z = .94	
	IQR	2.6-12.8	- 3.1-8.0	1.60	1.7-15.0	- 2.2-9.0	p = 0.045*	
	Mean rank	36.47	29.0	0.01*	43.08	33.69		
60/50	Mean	2.1	- 1.8	t =	2.8	- 2.1	Z = 2.081	
	SD	8.8	9.3	1.71	- 1.3-11.3	- 7.3-4.3	p = 0.037*	
	Mean	- 1.5	- 5.6	0.091	43.80	33.20		
55/45	SD	8.2	9.0	t =	-2.1	-6.6	Z = 2.26	
	Mean	- 5.2	- 9.1	1.91	-6.0-7.5	-12.6-1.2	p = 0.024*	
	SD	8.1	8.5	0.061	44.35	32.83		
50/40	Mean	- 5.2	- 9.1	t =	-3.4	-10.9	Z = 2.05	
	SD	8.1	8.5	1.86	-12.3-2.9	-14.8-(-5.2)	p = 0.039*	
	Mean	8.1	8.5	0.067	43.73	33.25		

Abbreviations: DP, Distortion product; IQR, interquartile range; SD, standard deviation. *significant at $p < 0.05$, t; Independent t-test, Z_{mw} ; Mann-Whitney U test

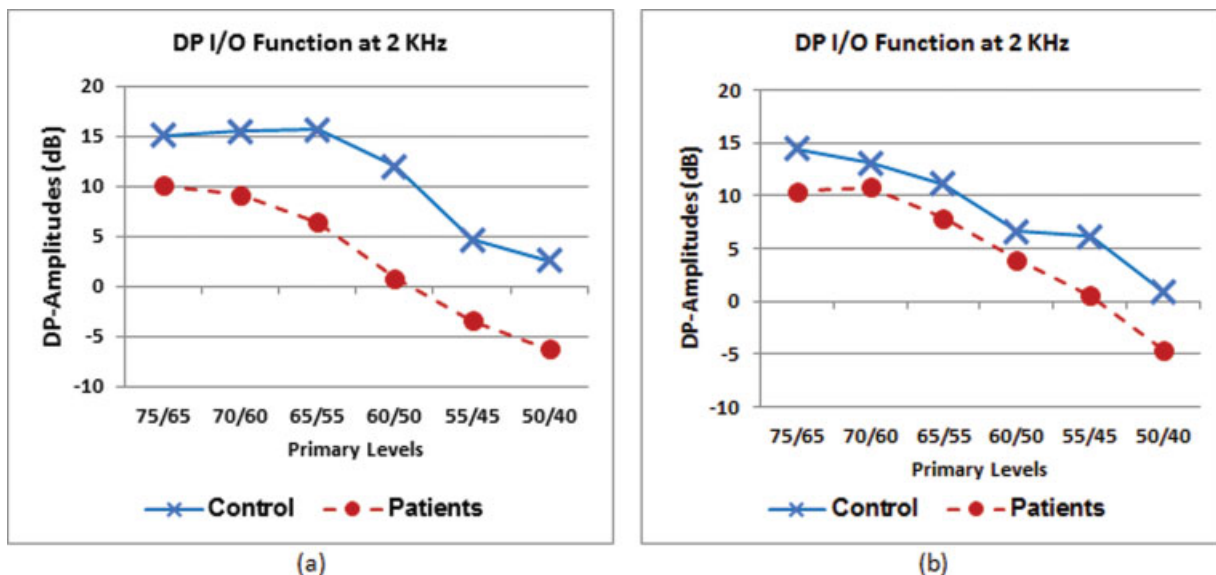


Fig. 3 Comparison of DPOAEs I/O function amplitudes between the control and study groups in the right ear (a) and left ear (b) at 2kHz.

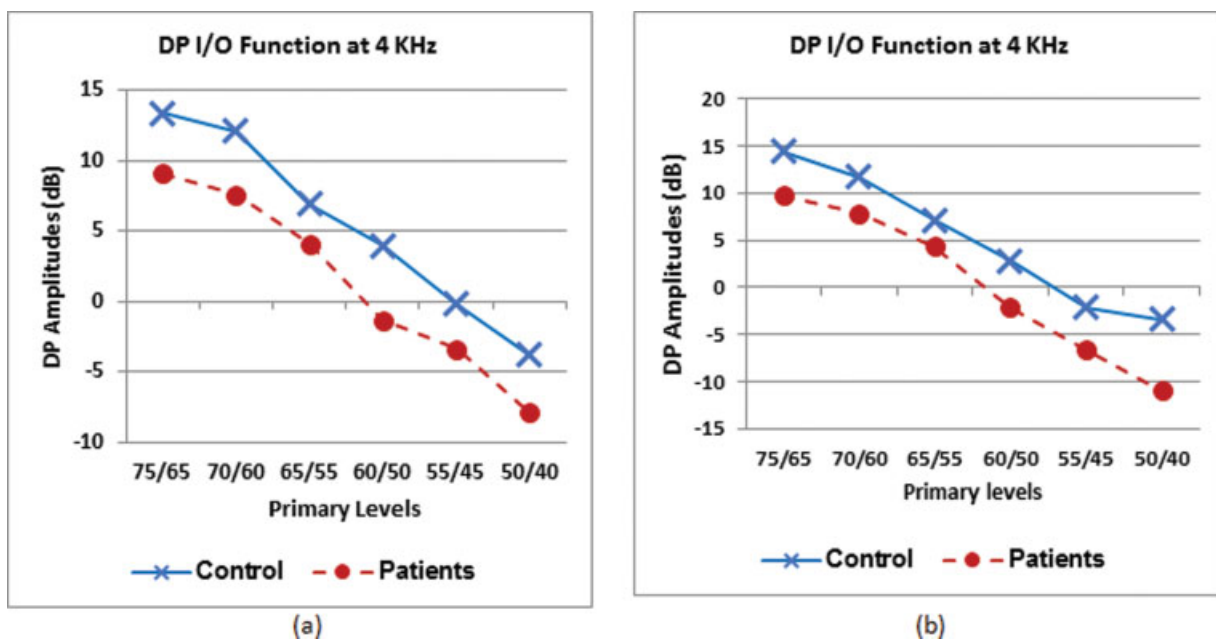


Fig. 4 Comparison of DPOAEs I/O function amplitudes between the control and study groups in the right ear (a) and left ear (b) at 4 kHz.

Conclusion

In conclusion, patients with tinnitus might have neural dysfunction at either the level of the cochlea, of the auditory nerve, or of the brainstem. In the present work, we indirectly assessed the integrity of the afferent auditory pathway by using DPOAEs in tinnitus cases with normal hearing. The results showed that those affected by tinnitus show reduced

OHC activity, as detected by reduced DPOAE levels and change in the normal DP-I/O function, which may manifest as tinnitus even before there is a shift in the hearing threshold.

Conflict of Interests

The authors have no conflict of interests to declare.

Table 5 Comparison of DPOAEs I/O function amplitudes and SNR between the control and study groups at 6kHz in the right and left ears

6,000 Hz		Right Ear			Left Ear			Tests statistic
		Group I	Group II	Tests statistic	Group I	Group II	Tests statistic	
DP amplitude	75/65	Mean	5.5	- 3.1	$z = 3.76$ $p < 0.001^*$	4.7	-2.1	$T = 3.44$ $p = 0.001^*$
		SD	8.5	9.7		7.5	9.4	
70/60		Median	2.7	-5.2	$z = 4.07$ $p < 0.001^*$.1	5.0	$z = 2.34$ $p = 0.019^*$
		IQR	- 0.5-5.8	- 15.3- -1.3		- 3.4-5.8	- 12.1-1.0	
		Mean rank	42.58	23.60		44.58	32.67	
65/55		Median	- 1.6	- 11.4	$z = 3.34$ $p = 0.001^*$	- 4.4	- 10.2	$t = 2.94$ $p = 0.004^*$
		IQR	- 6.0-1.7	- 15.2- -4.9		7.5	9.0	
		Mean rank	40.78	25.19				
60/50		Mean	- 8.3	- 12.5	$t = 2.08$ $p = 0.042^*$	- 9.7	- 12.9	$t = 1.46$ $p = 0.147$
		SD	8.9	7.4		8.7	9.4	
		Mean	- 11.4	- 15.9	$t = 2.02$ $p = 0.047^*$	- 13.5	- 15.0	$z = 1.09$ $p = 0.237$
55/45		SD	9.1	8.6		40.82	35.24	
		Mean	- 14.1	- 17.4	$t = 1.68$ $p = .098$	- 15.8	- 16.9	$z = 0.69$ $p = 0.488$
		SD	9.2	6.2		- 21.1- -9.4	- 22.2- -12.7	
		Mean rank	39.60	36.07		39.60	36.07	

Abbreviations: DP, Distortion product; IQR, interquartile range; SD, standard deviation.
^{*}significant at $p < 0.05$, t; Independent t-test, Z_{mnw} ; Mann-Whitney U test.

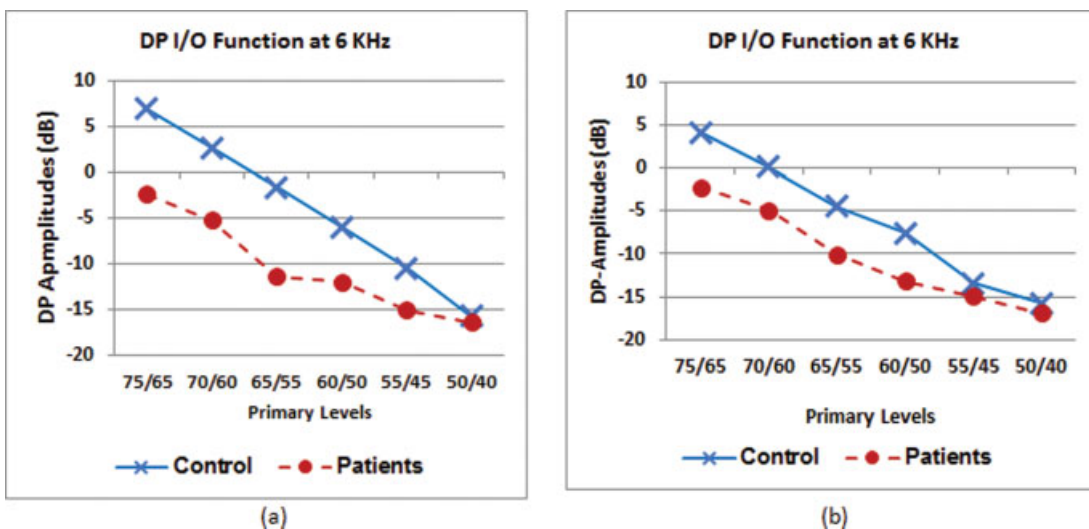


Fig. 5 Comparison of DPOAEs I/O function amplitudes between the control and study groups in right ear (a) and left ear (b) at 6 kHz.

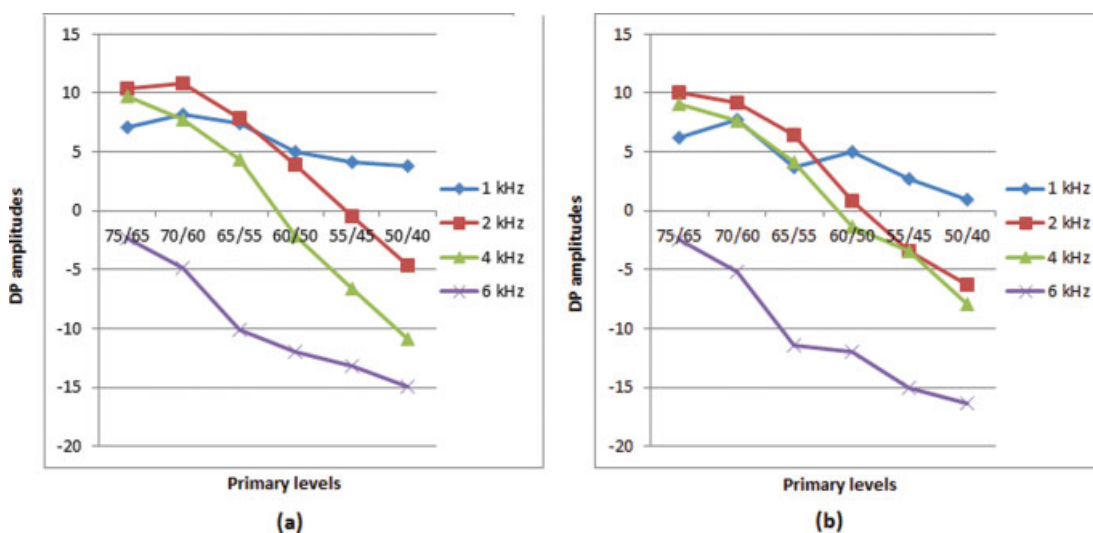


Fig. 6 DP-I/O function at different frequencies in the right ear (a) and left ear (b) of the control group.

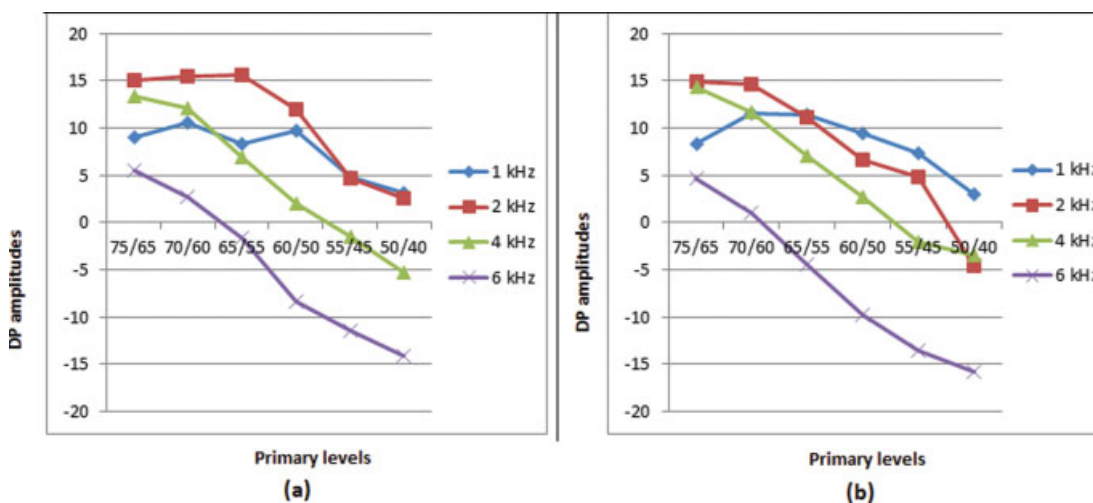


Fig. 7 DP-I/O function at different frequencies in the right ear (a) and left ear (b) of the study group

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