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Study of residual otoacoustic emissions in hearing loss with artifact differentiation and physiological responses

Estudo das emissões otoacústicas residuais nas perdas auditivas neurossensoriais com diferenciação de artefatos e respostas fisiológicas

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ABSTRACT

Purpose: To study the effect of stimulation intensity variation on the responses of distortion products in subjects with sensorineural hearing loss using a new protocol to register the otoacoustic emissions. **Methods:** This is a cross-sectional observational study. The following procedures were performed: anamnesis, otoscopy, pure tone audiometry, speech audiometry, tympanometry, distortion product and residual otoacoustic emissions. The residual DPOAE were collected with the Echodia equipment, Elios®. The protocol that was developed allows the variation of frequency and intensity parameters and the responses are analyzed by phase gradient test. Responses recorded in residual otoacoustic emissions were considered "present", "absent" or "artifact". **Results:** The total included ears was 72. On residual otoacoustic emissions test, at a frequency of 1300Hz and 2000Hz, there was statistically significant difference. By analyzing the average found in the audiometry and the results of residual emissions, only the frequency of 1300Hz showed a statistically significant association in all groups. By correlating the results of the audiometry and the stimulation intensity used to evoke the residual emission, there was positive correlation for the frequencies of 1000Hz and 4000Hz. The "artifact" was mostly recorded in the higher frequencies: 56.2% in 3000Hz and 58.2% in 4000 Hz. Residual EOAPD present was recorded as 18.6% at 1000Hz, 13.4% at 2000Hz, 6.3% at 3000Hz and 7.5% at 4000Hz. **Conclusion:** The increased stimulation intensity in the otoacoustic emissions test can aid in the study of residual outer hair cells, as long as a protocol is used to check the correctness of the responses.

Keywords: Spontaneous otoacoustic emissions; Hearing; Cochlea; Diagnosis; Outer hair cells

RESUMO

Objetivo: Avaliar o efeito da variação da intensidade de estimulação sobre as respostas das emissões otoacústicas produto de distorção em indivíduos com perda auditiva neurossensorial, utilizando um protocolo de gradiente de fase das emissões. **Métodos**: Estudo observacional transversal. Participaram 38 indivíduos com diagnóstico de perda auditiva neurossensorial de grau leve, moderado ou severo. Foram realizadas anamnese, meatoscopia, audiometria tonal liminar, logoaudiometria, imitanciometria, emissões otoacústicas produto de distorção e emissões otoacústicas residuais. As emissões otoacústicas residuais foram coletadas com o equipamento Echodia, modelo Elios®. O protocolo utilizado permite a variação dos parâmetros frequência e intensidade e as respostas são analisadas por meio do teste do Gradiente de Fase. As respostas registradas nas emissões residuais foram consideradas como "presente", "ausente" e "artefato", considerando a variação da fase em função de f1. **Resultados**: Foram incluídas 72 orelhas. Houve diferença estatisticamente significativa nas frequências de 1300 Hz e 2000 Hz, ao comparar os resultados das emissões residuais. Ao correlacionar o resultado da audiometria e a intensidade de estimulação que evocou a emissão residual, houve correlação positiva para as frequências de 1000 Hz e 4000Hz. O "artefato" foi registrado, principalmente, nas frequências mais agudas: 56,2% em 3000 Hz e 58,2% em 4000 Hz. A emissão otoacústica residual presente foi registrada em 18,6% em 1000 Hz, 13,4% em 2000 Hz, 6,3% em 3000 Hz e 7,5% em 4000 Hz. **Conclusão**: O aumento da intensidade de estimulação no exame de emissões pode auxiliar no estudo das células ciliadas residuais, desde que seja utilizado um protocolo capaz de diferenciar respostas fisiológicas de artefatos.

Palavras-chave: Emissões otoacústicas espontâneas; Audição; Cóclea; Diagnóstico; Células ciliadas externas

Study carried out at Observatório de Saúde Funcional em Fonoaudiologia, Faculdade de Medicina, Universidade Federal de Minas Gerais – UFMG e Ambulatório Bias Fortes, Hospital das Clínicas – HC, Universidade Federal de Minas Gerais – UFMG – Belo Horizonte (MG), Brasil.

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INTRODUCTION

In 1978, based on the theory of cochlear amplification, Kemp proposed a new hearing assessment method: the otoacoustic emissions (OAE)[1]. Since then, this method has been considered a window to the cochlea, and more specifically to the outer hair cells (OHC)[1,2].

The advantage of researching evoked otoacoustic emissions (EOAE) is that it is an easy, quick, and noninvasive procedure that effectively identifies peripheral hearing losses. Hence, it is ideal to screen and follow up on cochlear functions[3,4].

Transient and distortion-product are two different types of EOAE. These last ones, the DPOAE, provide more precise information on cochlear functioning because of their frequency specificity. DPOAE are evoked with two simultaneously presented pure tones – f1 and f2 –, in which f2 > f1. Oscillations generated by these tones in specific regions of the cochlea produce a distortion-product response that is picked up by a probe positioned in the external acoustic meatus (EAM)[2].

In clinical practice, the OAE help diagnose hearing losses, but they do not quantify them. Some studies report the presence of OAE in individuals with hearing thresholds better than 30 dBHL and DPOAE in individuals with hearing thresholds better than 50 dBHL[5-7].

A series of papers has already demonstrated the effective role of OHC in the production of OAE, establishing a relationship between OAE response and the presence of OHC[8,9]. Such affections may partly destroy OHC – i.e., a percentage of them is preserved, being called residual OHC. However, protocols used in current clinical practice do not research OAE generated in residual OHC. This would require stimulation at a higher intensity than the usual, leading residual OHC to generate distortion products that could be picked up by the probe in the EAM. In this regard, a study by Carvalho and Giraudet, 2014[10], presented a new approach to measure and analyze DPOAE, using strong-intensity stimulation in the equipment Elios, manufactured by Echodia®. The researchers named the protocol Phase Gradient and presented a two-case study in which they compared DPOAE responses with pure-tone audiometry results. They found that, in the absence of DPOAE responses with standard stimuli (L1 = L2 = 60 dB), the Phase Gradient is useful to identify the presence or absence of residual DPOAE.

It is important to point out that, when stimulation intensity is increased, the equipment may record distortion-product responses that are artifacts as if they were physiological[10]. Therefore, it is essential to use equipment capable of analyzing the origin of the responses.

Hence, aiming to study residual DPOAE, the objective of this paper was to assess with a protocol the effect of stimulus intensity variation on DPOAE responses in individuals with mild, moderate, and severe sensorineural hearing loss, distinguishing physiological responses from artifacts.

METHODS

This observational cross-sectional study with a convenience sample was approved by the Research Ethics Committee of the Federal University of Minas Gerais, under evaluation report no. 36403414.6.0000.5149.

Sample

A total of 38 individuals diagnosed with mild, moderate, or severe sensorineural hearing loss were invited to participate in the research. They received treatment at the Hearing Healthcare Service of the São Geraldo Hospital, part of the Clinics Hospital of the Federal University of Minas Gerais.

The study inclusion criteria were as follows: being 7 years or older; being diagnosed with mild, moderate, or severe sensorineural hearing loss through audiometry performed up to 6 months before the collection; having, on the day of the research, tympanometry results with type A curve bilaterally; having "absent" DPOAE in at least one frequency between 1 and 4 kHz. Participants who withdrew from the research or did not perform all procedures were excluded. All individuals involved in the research (or their parents/guardians) signed an informed consent form.

Procedures

The following procedures were conducted at the speech-language-hearing outpatient center of a university hospital: medical history, otoscopy, pure-tone threshold audiometry, speech audiometry, imitanciometry, DPOAE, and residual DPOAE.

Imitanciometry was performed on the day of collection to assess the integrity of the tympanic-ossicular chain with the tympanometric curve, static compliance, and contralateral acoustic reflexes. The tympanometry results were analyzed according to the normal standards suggested by Jerger[11]. The equipment used was the Interacoustics At235h Impedance, calibrated according to ANSI S3.6 (American National Standards Institute[12]).

Pure-tone audiometry and speech audiometry were performed up to 6 months before collection to verify the patients' hearing thresholds and confirm their sensorineural hearing loss. Air-conduction pure-tone audiometry was performed at 250 Hz, 500 Hz, 1 kHz, 2 kHz, 3 kHz, 4 kHz, 6 kHz, and 8 kHz, and bone-conduction at 500 Hz, 1 kHz, 2 kHz, 3 kHz, 4 kHz. Speech audiometry researched the speech recognition percentage index and speech recognition threshold. The examination was conducted in a sound booth, following the recommendation in ANSI S3.6[12]. Pure-tone threshold audiometry results were classified according to Silman and Silverman[13].

DPOAE were recorded with the equipment Echodia, model Elios®. Each ear's F2 frequency was recorded at 1300, 2000, 3000, 4000, and 5000 Hz. Both pure tones (f1 and f2) were presented in the examination at L1 = L2 = 60 dBSPL. The f1/f2 ratio was 1.22, and the 2f1-f2 product was analyzed.

If the examination indicated at least one "absent" frequency between 1 and 4 kHz after performing the examination at the standard intensity (60/60 dBSPL), residual DPOAE were researched.

Residual DPOAE were collected with the equipment Echodia, model Elios®, calibrated according to ANSI – S3.6[12]. The protocol applied, which had been developed exclusively for research, enables the variation of frequency and intensity parameters, and the responses are analyzed with the phase verification test.

In residual DPOAE protocol, the assessment is made at different intensities, in which L1 = L2. The initial stimulation intensity is 60 dBSPL, which is automatically increased every

3 dBSPL until finding a response or reaching the maximum stimulation intensity (95 dBSPL).

When either an artifact or physiological response is picked up, the equipment performs the phase verification test – which fixes the f2 value and varies the f1 value, generating five different f1/f2 ratios: 1.22, 1.24, 1.26, 1.28, and 1.30.

The responses are classified as follows:

- Present DPOAE: signal-to-noise ratio (SNR) > 3 dBSPL and phase difference between f1 variations (5 points) of at least 20º;
- Absent DPOAE: SNR < 3 dBSPL; in this case, the phase test is not performed;
- Artifact DPOAE: SNR > 3 dBSPL and phase difference between f1 variations (5 points) < 20º.

Besides the types of responses (artifact, absent, and present), the residual DPOAE threshold – i.e., the lowest stimulation intensity capable of evoking residual DPOAE – was also analyzed.

In artifacts, there is no difference between the response phases of the different f1/f2 combinations, as shown in Figure 1. In the physiological responses, the phases vary along with f1/f2 ratio changes, demonstrating that the responses originated in the various stimulated parts of the cochlea, as shown in Figure 2.

The frequencies tested in this research were 1300 Hz, 2000 Hz, 3000 Hz, and 4000 Hz. The phase verification test was performed at 1300 Hz because lower frequencies suffer greater interference from internal and external noises.

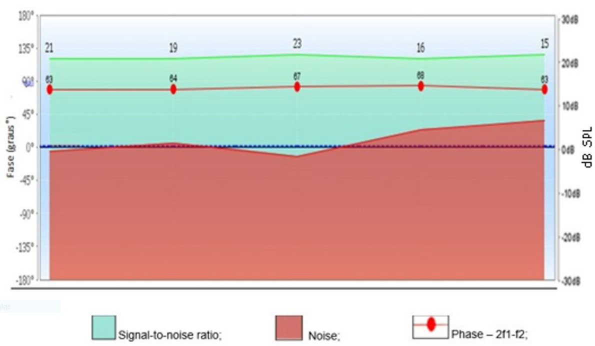

Figure 1. Result of an examination with an instrumental response for f2 = 1300 Hz
Subtitle: dBSPL = decibels of sound pressure level
Source: Adapted - Print screen from Elios® Echodia System

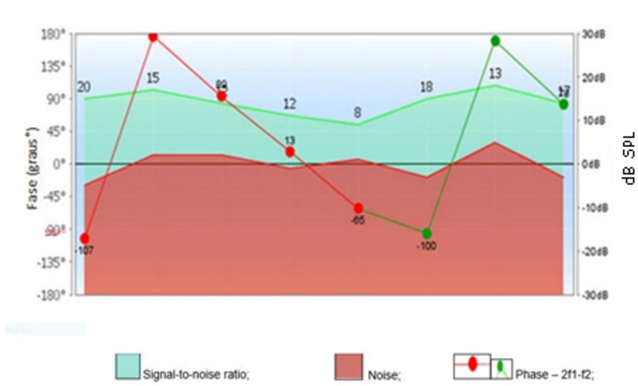

Figure 2. Result of an examination with a physiological response for f2 = 1300 Hz
Subtitle: dBSPL = decibels of sound pressure level
Source: Adapted - Print screen from Elios® Echodia System

Data analysis

The data were entered into an Excel spreadsheet and statistically analyzed in SPSS, version 18.

The categorical variables considered for analysis were the type of hearing loss and the residual DPOAE result (artifact, present, absent), and the continuous variables were the stimulation intensity level that evoked residual DPOAE (residual DPOAE threshold) and the audiometry threshold. In the absence of residual DPOAE, thresholds were set at 96 dBSPL for statistical analysis and representation (an intensity higher than the maximum output of the equipment).

The categorical variables were presented in frequency analysis and the continuous variables in measures of central tendency and variability.

The Mann-Whitney test and ANOVA test with Bonferroni correction were used. The correlation between the audiometry threshold (between 1 and 4 kHz) and the residual DPOAE threshold was presented in dispersion diagrams, and the degree of the correlation was measured with Spearman correlation.

RESULTS

The study comprised 38 participants – 23 (61%) females and 15 (39%) males. The participants' minimum age was 8 years, and the maximum was 90 years.

Altogether, 72 ears were assessed. Regarding the degree of hearing loss, 18 (25%) were mild, 45 (62.5%) were moderate, and 9 (12,5%) were severe, according to the classification by Silman and Silverman[13]. The descriptive analysis of hearing thresholds at each frequency assessed in audiometry is presented in Table 1.

DPOAE was researched in each ear at 1 kHz to 4 kHz. When an absence of response was recorded at any frequency, the residual DPOAE was researched. The results of this analysis are described in the flowchart in Figure 3. However, in the residual DPOAE assessment at 1300 Hz, one examination was not concluded due to environmental noise interference.

The residual DPOAE threshold results revealed a statistically significant difference at 1300 Hz between the groups with "absent" and "present" results, between the groups with "artifact" and "present" results, and, at 2000 Hz, between the groups with "absent" and "present" results. It is important to highlight that results were considered "absent" when the

Table 1. Descriptive analysis of audiometry thresholds per frequency assessed (N = 72)

Audiometry frequency	Minimum*	Maximum*	Mean*	Standard deviation*
1000 Hz	15	85	51.94	16.83
2000 Hz	10	95	58.89	16.19
3000 Hz	40	90	62.78	13.5
4000 Hz	35	90	67.01	13.36

*Value in decibels
Subtitle: N = number of ears

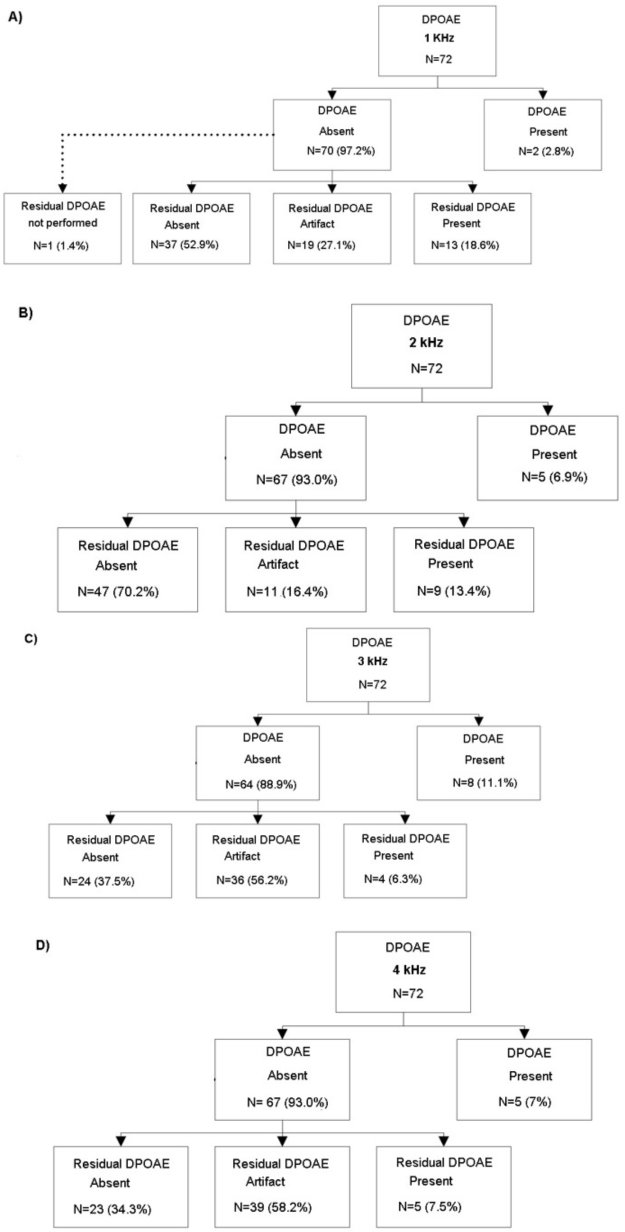

Figure 3. Descriptive analysis of the results of the distortion-product otoacoustic emissions and the residual otoacoustic emissions
Subtitle: (A) Frequency of 1300 Hz; (B) Frequency of 2000 Hz; (C) Frequency of 3000 Hz; (D) Frequency of 4000 Hz; DPOAE = distortion-product otoacoustic emissions; N = number of ears

maximum intensity of the equipment was reached without obtaining a response. The measures of central tendency and variability of the results found in the residual DPOAE thresholds are described in Table 2.

In the analysis of audiometry mean values and residual DPOAE results in the measures of central tendency and variability, the frequency of 1300 Hz was the only one with a statistically significant relationship in all groups. The frequency of 2000 Hz had a statistically significant relationship between "absent" and "present" results and between "artifact" and "present" results. The measures of central tendency and variability of the audiometry results in relation to the residual DPOAE results are described in Table 3.

Figure 4 indicates the correlation between audiometry thresholds and the residual DPOAE thresholds. There was a positive correlation only at 1000 Hz and 4000 Hz.

DISCUSSION

The objective of this study was to verify with a new protocol the effect of stimulation intensity variations on residual DPOAE responses. To this end, the audiometry thresholds and their correlation with DPOAE responses were also analyzed at high stimulation levels.

The audiometry results (Table 1) showed that the thresholds varied greatly, especially at 1000 Hz. This may be explained by sample heterogeneity, both in age (8 to 90 years) and degree and configuration of hearing loss. In this study sample, the mean audiometry threshold increased at higher frequencies. A recent study with 110 children found that a descending curve was the most frequent audiometry configuration[14]. It is also known that age-related hearing loss (presbycusis) damages first the OHC responsible for decoding higher frequencies[8].

The DPOAE results (Figure 3) revealed that "present" results were found at all tested frequencies. This is so because, in some cases, the DPOAE is present in thresholds of approximately 30 to 50 dB[5-7].

Further on residual DPOAE results (Figure 3), the "artifact" response was recorded in the equipment in 16.4% to 58.2%. The analysis of residual DPOAE results per frequency (Table 2) shows that the equipment recorded "artifacts" at higher frequencies: 56.2% at 3000 Hz and 58.2% at 4000 Hz. This may have happened because higher means – and therefore higher or absent residual DPOAE thresholds – were found in the audiometry thresholds at 4000 Hz (Figure 4). However, studies with larger samples, enabling analyses per hearing loss configuration, are necessary to confirm this hypothesis.

The intensity recorded as "artifact" ranged from 60 to 81 dBSPL, indicating that even at 60 dB (the routinely used intensity) the pieces of equipment available in the market may generate false physiological DPOAE responses, as they do not distinguish physiological responses from artifacts. Therefore, people must be cautious before stating that the DPOAE indeed originated in OHC, as mistaken diagnoses misdirect intervention, as in the case of hearing aid fitting.

The analysis of residual DPOAE results (Table 2) also found a statistically significant difference at 1300 Hz between the "present" and "absent" groups and between the "present" and "artifact" groups. The group with "present" residual DPOAE results had a mean intensity of 76 dBSPL in this examination, which was lower than in the groups with "absent" and "artifact" results (80 dBSPL). This was also observed at 2000 Hz, in which the "present" and "absent" groups had a statistically significant difference – the "present" group had responses at the mean intensity of 78 dBSPL.

No significant association was found between the groups at 3000 Hz and 4000 Hz. This result shows that it was not possible to obtain enough residual emission even at higher stimulation intensities because in some etiologies the OHC are the first ones to be damaged to high frequencies[8,9,15].

DPOAE frequency specificity has already been researched, particularly to monitor diagnosis control[16] and correlate audiograms with DPgrams[17]. Nevertheless, few studies have addressed high stimulation intensities in humans. These papers

Table 2. Description of the measures of central tendency and variability of the residual otoacoustic emission response thresholds

	Residual DPOAE threshold 1300 Hz					
	Absent (n=37)	Artifact (n=19)	Present (n=13)	p-value (Abs x Art)	p-value (Abs x Pre)	p-value (Art x Pre)
inimum	96	75	63			
Maximum	96	81	81			
Mean	96	80	76	0.233	0.002*	0.049*
SD	0	2	6			
Median	96	81	78			
Characteristics	Residual DPOAE threshold 2000 Hz					
	Absent (n=47)	Artifact (n=11)	Present (n=9)	p-value (Abs x Art)	p-value (Abs x Pre)	p-value (Art x Pre)
Minimum	96	78	72			
Maximum	96	81	81			
Mean	96	80	78	0.516	0.001*	0.065
SD	0	1	3			
Median	96	81	78			
Characteristics	Residual DPOAE threshold 3000 Hz					
	Absent (n=24)	Artifact (n=36)	Present (n=4)	p-value (Abs x Art)	p-value (Abs x Pre)	p-value (Art x Pre)
Minimum	96	69	72			
Maximum	96	81	75			
Mean	96	75	74	0.160	0.070	0.680
SD	0	4	2			
Median	96	75	74			
Characteristics	Residual DPOAE threshold 4000 Hz					
	Absent (n=23)	Artifact (n=39)	Present (n=5)	p-value (Abs x Art)	p-value (Abs x Pre)	p-value (Art x Pre)
Minimum	96	60	63			
Maximum	96	78	81			
Mean	96	71	72	0.222	0.193	0.347
SD	0	4	5			
Median	96	72	72			

Mann-Whitney test In the absence of responses, thresholds were represented at 96 decibels (a higher intensity than the maximum output). *p < 0.005
Subtitle: DPOAE = distortion-product otoacoustic emissions; Abs = absent; Pre = present; Art = artifact; n = number of ears; SD = standard deviation. In the absence of responses, thresholds were represented at 96 decibels (a higher intensity than the maximum output)

Table 3. Description of the measures of central tendency and variability of the audiometry thresholds in relation to residual otoacoustic emission results (absent, artifact, present)

Audiometry 1000Hz	Residual DPOAE 1300 Hz					
	Absent (n=37)	Artifact (n=19)	Present (n=13)	p-value (Abs x Art)	p-value (Abs x Pre)	p-value (Art x Pre)
Minimum	40	25	15			
Maximum	85	70	65	0.009*	0.000*	0.011*
Mean	60.95	49.21	34.62			
Standard deviation	13.32	14.16	12.65			
Audiometry 2000Hz	Residual DPOAE 2000 Hz					
	Absent (n=47)	Artifact (n=11)	Present (n=9)	p-value (Abs x Art)	p-value (Abs x Pre)	p-value (Art x Pre)
Minimum	35	40	20			
Maximum	95	95	60	1	0.001*	0.019*
Mean	63.51	61.36	43.89			
Standard deviation	13.14	17.04	12.44			
Audiometry 3000Hz	Residual DPOAE 3000 Hz					
	Absent (n=24)	Artifact (n=36)	Present (n=4)	p-value (Abs x Art)	p-value (Abs x Pre)	p-value (Art x Pre)
Minimum	45	40	45			
Maximum	90	90	55	1	0.068	0.13
Mean	66.88	64.72	51.25			
Standard deviation	12.4	12.81	4.78			
Audiometry 4000Hz	Residual DPOAE 4000 Hz					
	Absent (n=23)	Artifact (n=39)	Present (n=5)	p-value (Abs x Art)	p-value (Abs x Pre)	p-value (Art x Pre)
Minimum	50	50	45			
Maximum	90	90	65	1	0.172	0.125
Mean	69.35	69.74	58			
Standard deviation	12.81	11.69	7.58			

ANOVA test with Bonferroni correction *p < 0.005
Subtitle: DPOAE = distortion-product otoacoustic emissions; Abs = absent; Pre = present; Art = artifact; n = number of ears

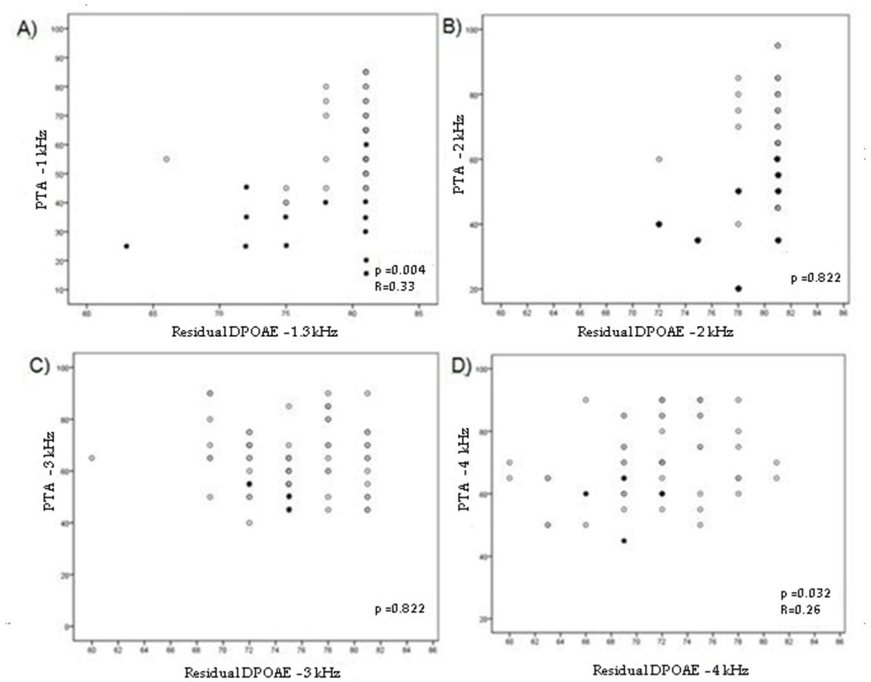

Figure 4. Dispersion diagram of audiometry thresholds and residual otoacoustic emission thresholds
Subtitle: DPOAE = distortion-product otoacoustic emissions; ● present residual otoacoustic emission; ◦ absent residual otoacoustic emission; p = p-value; r = degree of correlation

assessed the DPOAE input/output curve to analyze changes in OHC compression and estimate hearing thresholds[18,19]. It is important to point out that these papers did not use specific protocols to distinguish physiological responses from artifacts.

In Brazil, Kós et al. conducted a study in 2009[6] comparing DPOAE amplitudes between normal-hearing individuals and those with mild or moderate sensorineural hearing loss, using two protocols (L1 = 65 dBSPL and L2 = 55 dBSPL; L1 = L2 = 70 dBSPL). They also observed differences between the amplitudes found with the two protocols. The normal-hearing group had a significantly higher amplitude than the groups with mild and moderate hearing loss, whereas the group with mild hearing loss had a higher amplitude than the one with moderate hearing loss. The authors concluded that, as audiometry thresholds increased, OAE amplitudes decreased. In the present study, as thresholds worsened, the stimulation intensity necessary to evoke residual DPOAE responses also increased (Table 3).

The possibility of estimating residual DPOAE thresholds may contribute to quantitative DPOAE analysis, improving its sensitivity to diagnose hearing losses. Furthermore, cochlear monitoring may gain a promising quantitative and objective tool. Hence, the protocol must be applied to individuals with different audiometry configurations, ages, and hearing loss etiologies to consolidate the potential of the technique.

CONCLUSION

Residual DPOAE were observed especially at 1300 Hz and 2000 Hz in individuals with mild to severe sensorineural hearing loss. These results indicate that increasing the stimulation intensity in emission examination may help study residual OHC, as long as a protocol capable of distinguishing physiological responses from artifacts is used. The protocol used in this research made it possible to safely increase stimulation intensity in OAE examination.

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