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Alteration of distortion product otoacoustic emission input/output functions in subjects with a previous history of middle ear dysfunction

Authors' Contribution:
A Study Design
B Data Collection
C Statistical Analysis
D Data Interpretation
E Manuscript Preparation
F Literature Search
G Funds Collection

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Summary

Background: The aim of this study was to investigate the effects of sub-clinical alterations on the amplitudes and slopes of the DPOAE input-output responses from subjects with previous history of middle ear dysfunction.

Material/Methods: The study included 15 subjects with and 15 subjects without a history of otitis media in the last 10 years. All participants were assessed with acoustic immittance, pure-tone audiometry, and DPOAEs. For the later, I/O functions and I/O slopes were estimated at 1501, 2002, 3174, 4004 and 6384Hz.

Results: No statistically significant differences were found between the 2 groups in terms of behavioral thresholds. The group with a previous history of middle ear dysfunction presented significantly lower mean DPOAE amplitudes at 2002, 3174 and 4004 Hz. In terms of DPOAE slopes, no statistically significant differences were observed at the tested frequencies, except at 3174 Hz.

Conclusions: Middle ear pathologies can produce subclinical alterations that are undetectable with traditional pure-tone audiometry. The data from the present study show that reduced amplitude DPOAEs are associated with a previous history of middle ear complications. The corresponding DPOAE slopes were affected at only 1 tested frequency, suggesting that the cochlear non-linearity is preserved. Considering these results, it remains to be elucidated to what degree the DPOAE amplitude attenuation interferes with higher-order auditory tasks.

key words: **otoacoustic emissions • normal hearing • middle ear • middle ear dysfunction • distortion product otoacoustic emissions – Input/Output functions**

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Background

Otoacoustic emissions (OAEs) are routinely used in the assessment of the functional integrity of the cochlea [1]. The OAEs can be categorized by the invoking stimulus in 2 classes, namely in the evoked and in the spontaneous OAEs. A sub-category of the first class is called distortion product otoacoustic emissions (DPOAE) and refers to cochlear responses evoked by 2 pure tones – f_1 and f_2 – with stimulus amplitudes L_1 and L_2 [2,3]. The DPOAE response can be recorded in 2 modalities: (i) by varying the amplitude of the stimulus, keeping the frequency fixed (Input–Output or I/O-function protocol); or (ii) by fixing the amplitude of the stimulus and varying the frequency (DP-Gram protocol). The behavior of the I/O function is considered a good index of cochlear nonlinearity [4].

A number of variables are of critical importance for the analysis of DPOAE I/O functions, such as: (i) the DPOAE threshold; (ii) the DPOAE slope, and (iii) the DPOAE amplitude. The DPOAE threshold is defined as the lower level of L_2 stimulus associated with the presence of a valid DPOAE response [4]. The DPOAE slope can be defined as the growth rate of the DPOAE response, expressed in dB/dB units. The slope value decreases at higher stimulus intensities, especially in the range from 50 dB to 80 dB SPL, where cochlear compression is observed [5]. Although cochlear compression decreases with the increased severity of cochlear lesions, the observed variability makes the DPOAE slope determination a method with high specificity and low sensitivity [6,7]. Gehr et al. [8] investigated DPOAE I/O functions in relationship to middle and inner ear alterations in an animal model. The authors reported that the DPOAE slopes were steeper after noise exposure, suggesting a possible loss of cochlear compression, concluding that the estimation of the DPOAE slope could be useful in distinguishing conductive from sensorial hearing impairment. Campos et al. [9] studied DPOAE I/O functions in neonates to verify the contra-lateral acoustic suppression phenomenon. They suggested that it might be primarily a linear phenomenon, deprived of the cochlear compression and non-linear components seen in the healthy cochlea.

A middle ear dysfunction can alter the physical properties of sound conduction in the middle ear and can raise the audiometric threshold. However, data from the literature [1] suggest that minor alterations (ie, subclinical features) of the sound conduction are undetectable by traditional evaluation procedures. Carvallo [11] studied the relationship between the status of the middle ear and the OAE responses and concluded that detectable OAEs are 78 times more common in healthy ears than in ears with middle ear complications. Akdogan and Ozkan [10] studied OAEs in children with otitis media (OM) with effusion and concluded that DPOAE measurements are helpful in evaluating the middle ear during treatment. Prieve et al. [12] compared OAE responses from children with and without a negative tympanometric peak pressure. They reported that the OAE responses from the group with negative tympanometric peak pressure were characterized by lower amplitudes – approximately 4 dB across all frequency ranges. In a study involving American Indian infants [13], OM was found to be responsible for 30% of the fail rates of hearing screening.

The relationship between a previous history of middle ear dysfunction and the DP-gram was investigated by Yilmaz et al. [14] and Job and Nottet [15]. Both studies reported lower DP-gram amplitudes in individuals with history of OM compared to individuals without any previous OM incidence. The authors suggested that DPOAEs could be considered a sensitive instrument for the detection of a sub-clinical dysfunction, whatever its origin.

Data from the literature suggest that the standard clinical evaluation measurements, such as pure tone audiometry and acoustic immittance, are not sensitive enough to detect minor alterations in the middle ear sound conduction. Previous studies have reported that DPOAEs (in the form of DP-grams) can be used in the detection of these subclinical alterations [14,15]. The impact of sub-clinical middle ear complications on the DPOAE I/O functions (amplitude and slope) is still unknown. To elucidate this statement, this study was designed to generate evidence, from subjects with previous history of middle ear dysfunction, on the possible effects of sub-clinical threshold alterations on the amplitudes and slopes of the DPOAE Input-Output functions.

Material and Methods

Subjects

The study design was evaluated and approved by the Ethics Committee for the Analysis of Research Projects (process no. 0086/08). Forty subjects, all university students, participated in the study.

The medical history of each subject on previous incidents and occasional treatment of OM in the last 10 years was assessed by a detailed questionnaire. The subjects were screened by 8 criteria, including: (i) a normal audiometric threshold (≤25 dB HL) at 250, 500, 1000, 2000, 3000, 4000, 6000 and 8000Hz; (ii) a type A tympanometric curve with values comprised from 0.3 to 2 cc for the middle ear mobility and from –50 to +50 daPa for the pressure peak; (iii) presence of acoustic reflexes at 1000 Hz (evoked by 100 dB stimuli); (iv) DPOAE responses with signal/noise ratio (SNR) at least 3 dB SPL above the noise floor at the f2 frequencies 2002, 3174, 4004 and 6384 Hz; and as exclusion criteria: (v) alcohol and drug dependence; (vi) presence of vertigo; (vii) middle-ear complications in the last 12 month prior to the enrollment to the study; and (viii) recent treatment with salicylates.

Ten subjects did not meet the above criteria and were excluded from the study. The final sample consisted of 15 individuals (30 ears, mean age 22.67±2.55 years) without any previous history of middle ear complication in the last 10 years (control group), and 15 individuals (30 ears, mean age 23.89±2.67 years) with a previous history of middle ear complication (study group).

Procedures and data-collection

The hearing of each subject was assessed with the following standardized procedures:

- Acoustic immittance, using the GSI33 middle ear analyzer (v2; Grason-Stadler). For the impedance measurements a 226 Hz probe tone was used. For the acoustic reflex a tone of 1000 Hz at 100 dB SPL was employed.

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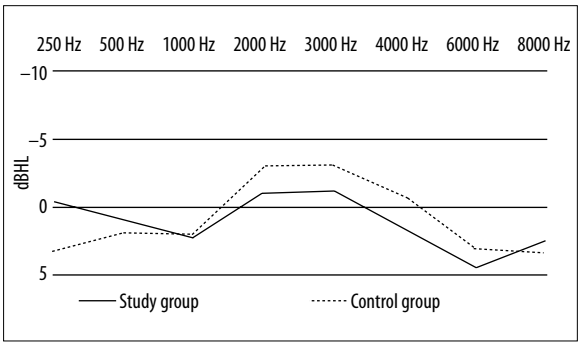

Figure 1. Mean audiometric thresholds in the control and study groups. The standard deviation varied from 3,95 to 7,68 dB in the study group and from 2.59 to 7.51 in the control group. * Significant difference.

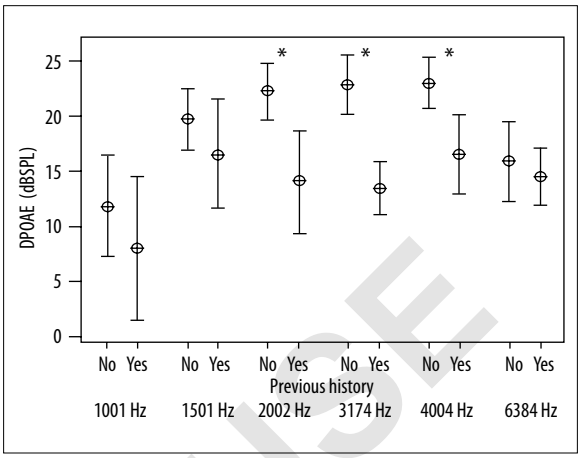

Figure 2. Average DPOAE SNRs (mean ± standard error), from the control and study groups, at the six tested frequencies. The star symbol indicates significant differences. The no–yes label refers to the presence (or no) of previous history of middle ear dysfunction.

- Pure-tone audiometry using the GSI 61 audiometer (Grason-Stadler, Madison, WI, USA). Frequencies were tested in this order: 1000, 2000, 3000, 4000, 6000, 8000, 500 and 250 Hz.
- DPOAEs (DP-Grams), using the ILO 292 – USB-II, V6 (Otodynamics Ltd, Hatfield, UK). Tested f_2 frequencies included 1001, 1501, 2002, 3174, 4004 and 6384 Hz. The primary tone stimuli were set to L_1=65 and L_2=55 dB SPL. The frequency ratio was adjusted to f_1/f_2=1.22. The acquisition stop-rule considered a "noise floor" ⩽–5 dB SPL.
- DPOAE I/O functions were recorded with the ILO 292 – USB-II, V6 (Otodynamics Ltd, Hatfield, UK) by sweeping 10 stimulus intensities between 75 and 30 dB SPL at 1501, 2002, 3174, 4004 and 6384 Hz. The stimulus paradigm proposed by Kummer et al. [16] was used, with the primary tone stimulus set to $L_1=(0.4 * L_2) +39$ dB SPL. For each frequency, 5 sweeps were averaged. Datasets were obtained by decreasing L_2 in –5 dB SPL steps. The rule for stopping data acquisition was determined by a minimum value of the noise-floor level, which was set to –5 dB SPL, at all tested intensities. Data were considered valid when the DPOAE amplitude was at least 3 dB higher than the noise floor level. For each I/O function, the ILO software calculated the value of the DPOAE slope.

Statistical analysis

Descriptive and comparative methods were applied to the data analysis. Variables were compared using ANOVA (Analysis of Variance) procedures and Student's t-test with bimodal analysis and unequal variance of 2 samples. Values of p⩽0.05 were considered as statistically significant.

Results

Behavioral data

Figure 1 shows the distribution of the audiometric thresholds for both groups. In the control group the mean audiometric thresholds ranged from –3.11 dB HL (3000 Hz) to 3.33 dB HL (8000 Hz). In the study group the mean thresholds ranged from –1.16 dB HL (3000 Hz) to 4.38 dB HL (6000 Hz). No statistically significant differences were observed between the 2 groups, except a border-line effect at the frequency of 2000 Hz (p=0.048).

The mean admittance peaks at 226 Hz were 0.47 and 0.69 cc for the control and study groups, respectively. No statistically significant differences were observed between the 2 groups.

Acoustical data

From the comparison of the DP-Gram data, statistically significant mean SNR differences were observed at 2002, 3174 and 4004 Hz (p<0.001, p<0.001 and p=0.002, respectively). At all tested frequencies the mean amplitudes of the DPOAE responses from the control group were larger than those from the study group. The data are summarized in Figure 2.

The comparison of the DPOAE I/O functions between the 2 groups revealed significant SNR differences at all frequencies except at 6384 Hz. As in the DP-Gram data, the control group was characterized by higher SNRs. At 1501 Hz, statistical differences were observed for the stimulus levels from 50 to 30 dB SPL. The 55 dB responses presented borderline differences. At 2002 Hz, all stimulus levels presented significant differences between groups, except at the 30 dB level. At 3174 and 4004 Hz all stimulus levels presented significant differences. At 6384 Hz only the stimulus levels of 40 and 35 dB SPL presented significant differences. Table 1 summarizes the I/O data from both groups.

The values of the DPOAE I/O slopes were slightly shallower in the study group than the control group, but the difference was significant only at 3174 Hz (p=0.001). The mean slope of the control group was closer to a 1 dB/dB value than the slope from the study group. Figure 3 summarizes these findings.

Discussion

This study investigated the variations of DPOAE responses in subjects with and without a history of middle ear dysfunction, in a time span of 10 years. The main reason for investigating these variations originates from the conclusions of a previous pilot study, where a group of normal hearing subjects demonstrated a very large DPOAE amplitude

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Table 1. Comparison between the control and study groups at 1501, 2002, 3174, 4004 and 6384 Hz. The columns show the presence or no of previous middle ear dysfunction, average S/N ratio, and the corresponding t-test probability value, at the 5 tested frequencies and stimulus levels (75–30 dB). Statistically significant differences are indicated by a star symbol.

	Previous history	Input Level									
		Freq	75 dB	70 dB	65 dB	60 dB	55 dB	50 dB	45 dB	40 dB	35 dB	30 dB
S/N	Yes	1501 Hz	13.18	11.26	11.63	11.09	10.22	7.95	6.88	2.99	–0.38	–1.35
	No		15.33	14.33	14.80	15.01	14.98	13.89	12.67	9.52	6.81	4.68
p- value			0.345	0.223	0.188	0.105	0.054	0.026*	0.019*	0.019*	0.013*	0.013*
S/N	Yes	2002 Hz	10.85	11.77	10.83	10.52	8.44	5.30	5.44	2.61	1.91	1.01
	No		19.13	18.22	17.35	18.32	17.46	15.92	13.94	10.15	6.90	4.38
p-value			0.004*	0.003*	0.003*	0.002*	0.001*	0.002*	0.005*	0.015*	0.033*	0.140
S/N	Yes	3174 Hz	11.27	12.00	8.70	9.45	6.89	5.18	1.59	2.32	0.01	–6.02
	No		19.19	17.97	17.54	17.21	16.45	16.46	12.84	11.69	8.85	5.52
p-value			0.002*	0.004*	0.001*	0.001*	0.001*	0.001*	0.003*	0.001*	0.002*	0.002*
S/N Means	Yes	4004 Hz	14.92	12.40	10.59	11.34	9.82	7.78	5.14	2.69	1.73	–0.91
	No		20.37	18.21	17.87	16.75	16.03	14.26	12.70	11.07	7.06	5.74
p-value			0.002*	0.028*	0.005*	0.007*	0.008*	0.012*	0.017*	0.022*	0.037*	0.014*
S/N Means	Yes	6384 Hz	16.52	13.93	11.32	6.29	5.39	4.57	–0.72	–2.19	–6.24	–4.64
	No		17.02	15.76	12.82	12.11	9.52	7.99	4.73	3.76	–0.83	–3.82
p-value			0.790	0.330	0.548	0.065	0.192	0.215	0.115	0.031*	0.027*	0.673

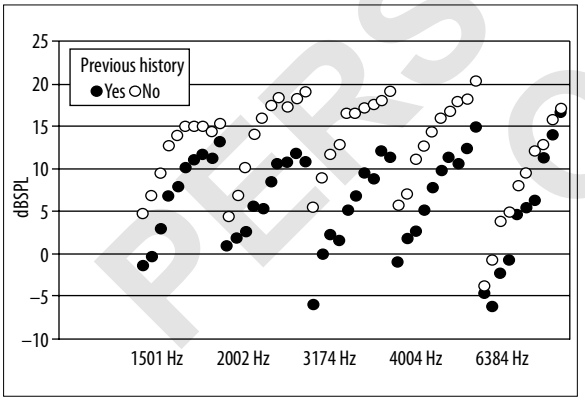

Figure 3. Average DPOAE I/O functions in the control and study groups at 1501, 2002, 3174, 4004 and 6384Hz. The star symbol indicates significant differences between the two groups.

variability. In order to understand the innate sources of the DPOAE variability, the detailed anamnesis of the tested subjects was re-evaluated. It was found that subjects with a normal tympanometry and normal behavioral thresholds, but with a previous history of middle-ear dysfunction, presented reduced DPOAE amplitudes. The collection of DPOAE I/O data in the present study serves as a means to further elucidate these previous observations.

The data of this study show that despite the absence of statistical differences between the pure tone audiometry and acoustic immittance measurements, from a DPOAE point of view statistical differences exist between the 2 tested groups. The subjects with a previous history of middle ear dysfunction present altered DPOAEs, probably caused by subclinical alterations of the stimulus conduction pathway.

In terms of the DP-Gram amplitudes, all frequencies in the control group presented higher amplitudes, with statistical significance at 2002, 3174 and 4004 Hz. The I/O function DPOAE amplitudes in the study group were reduced in approximately 80% of the recordings, mainly in the frequencies of 2002, 3174 and 4004 Hz. These findings are in accordance with results of previous studies [8,10,11,14,15] showing that minor middle ear dysfunctions can impair the proper detection of DPOAEs. At the frequencies of 1501 Hz and at 6384 Hz, the mean differences between groups were not significant for both the DP-Gram and the I/O function DPOAE amplitudes. Several factors might have contributed to these results, such as: (i) the higher ambient noise might have altered the response-detection of DP-Gram at 1501 Hz; or (ii) the non-linear frequency response of the ILO probe above 5 kHz might have influenced the 6384 Hz data values.

Previous studies have evaluated the effect of ventilation tubes on DPOAEs and TEOAEs, as well as the comparison between DPOAEs / TEOAEs before and after treatment of OM [8,17,18]. The data of the present study are in agreement with these studies, in which DPOAE determination was found to facilitate the evaluation of middle ear conditions, as well as that of treatment response and outcomes.

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Data from the literature [14,15] show that in subjects with a previous history of OM and normal behavioral hearing levels (≤20dB HL) the DPOAE amplitudes were reduced. It is even possible that the presence of OM could have an effect on the cochlear amplification mechanism, resulting in an additionally lower DPOAE detection. The present study reinforces the data of Yilmaz et al. [15] showing that even if the middle ear sound conduction alterations are undetected by traditional audiometry and/or by acoustic immittance, the presence of sub-clinical complications can interfere with and influence the DPOAE detection. In this context, normal hearing groups and control groups must be carefully selected with criteria including DPOAE measurements.

In the study group the slopes of the DPOAE I/O functions were shallower (ie, with smaller values) than slope values from the control group, but the mean group-difference was significant only at 3174Hz. The results corroborate data from previous studies [8] which assumed that the middle ear dysfunction resulted in a reduction of the DPOAE amplitude independent of the primary tone level and in this context the DPOAE I/O growth behavior should not be affected. According to Gehr et al. [8], DPOAE I/O-functions allow a differentiation between middle and inner ear dysfunction, but further studies would have to show the usability of this method for clinical diagnostics. The present results may be useful to in differentiating between middle and inner ear dysfunction, considering that DPOAE I/O functions slopes are affected only by inner ear conditions. However, in a study of tinnitus and DPOAE I/O functions at 4000 Hz, Sanches et al. [19] found that normal-hearing individuals with tinnitus presented shallower slopes (slope measured from 20 to 60 dB peSPL) than the control group. They suggested that both the shallower slope and the reduced response at 80 dB in the DPOAE I/O functions might be associated with subclinical inner ear damages that were not detected in pure-tone audiometry.

In the present study the measurement of DPOAE I/O functions was able to discriminate ears with and without minor middle ear dysfunction. It is necessary to investigate the influence of peripheral mechanisms, assessed by DPOAE amplitudes and I/O function, on the information sent to cortical areas. Smurzynski and Probst [20] demonstrated that there is a physiological aspect that alters performance on discrimination, temporal integration and gap detection tasks, especially for low-level stimulus spectral components that can be detected by means of OAE.

It remains unclear whether the distinct patterns found in the DPOAE I/O functions of the study group were related to cochlear dysfunction. Gunnarson and Finitzo [21] stated that electrophysiological differences among children are related to early transient hearing loss and that these differences are a central, rather than peripheral, effect. The authors suggested that physiological responses will be altered if the peripheral structures do not transmit adequate stimulation to the central nervous system.

Conclusions

Middle ear dysfunctions may produce subclinical alterations undetectable by traditional pure-tone audiometry or immittance audiometry. The data shows that reduced DPOAE (DP-Gram and I/O function levels) are associated with a previous history of middle ear dysfunction. The fact that the DPOAE slope is not greatly modified suggests that the cochlear non-linearity is preserved after a middle ear dysfunction. It still remains to be elucidated to what degree this sub-clinical DPOAE attenuation interferes with higher-order auditory tasks.

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