

Received: 2015.12.17
Accepted: 2016.04.25
Published: 2016.06.14

Relationship Between Distortion Product – Otoacoustic Emissions (DPOAEs) and High-Frequency Acoustic Immittance Measures

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Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
Literature Search F
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Source of support: This work was supported by the project "Integrated system of tools for diagnostics and telerehabilitation of sensory organs disorders (hearing, vision, speech, balance, taste, smell)" (INNOSNESE) co-financed by the National Center for Research and Development (Poland) within the STRATEGMED program

Background: Pathologies that alter the impedance of the middle ear may consequently modify the DPOAE amplitude. The aim of this study was to correlate information from 2 different clinical procedures assessing middle ear status. Data from DPOAE responses (both DP-Gram and DP I/O functions) were correlated with data from multi-component tympanometry at 1000 Hz.

Material/Methods: The subjects were divided into a double-peak group (DPG) and a single-peak group (SPG) depending on 1000 Hz tympanogram pattern. Exclusion criteria (described in the Methods section) were applied to both groups and finally only 31 ears were assigned to each group. The subjects were also assessed with traditional tympanometry and behavioral audiometry.

Results: Compared to the single-peak group, in terms of the 226 Hz tympanometry data, subjects in the DPG group presented: (i) higher values of ear canal volume; (ii) higher peak pressure, and (iii) significantly higher values of acoustic admittance. DPOAE amplitudes were lower in the DPG group only at 6006 Hz, but the difference in amplitude between the DPG and SPG groups decreased as the frequency increased. Statistical differences were observed only at 1001 Hz and a borderline difference at 1501 Hz. In terms of DPOAE I/O functions, significant differences were observed only in 4 of the 50 tested points.

Conclusions: The 1000-Hz tympanometric pattern significantly affects the structure of DPOAE responses only at 1001 Hz. In this context, changes in the properties of the middle ear (as detected by the 1000 Hz tympanometry) can be considered as prime candidates for the observed variability in the DP-grams and the DP I/O functions.

MeSH Keywords: **Acoustic Impedance Tests • Multifrequency Tympanometry • Otoacoustic Emissions**

Full-text PDF: <http://www.medscimonit.com/abstract/index/idArt/897157>

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Background

Tympanometry measures the middle ear function by assessing middle ear admittance [1]. A probe tone frequency of 226 Hz distinguishes a healthy middle ear from one presenting conducting hearing impairment. When an individual has a high impedance pathology such as otitis media with effusion (OME), the 226 Hz admittance tympanogram is frequently flat; therefore, it is not possible to measure the tympanometric width and peak pressure. In these cases, a higher frequency admittance probe at 1000 Hz can capture the changes not identified by the standard 226-Hz tympanogram [1,2].

With a 1000-Hz probe, normal ears display different tympanometric patterns than those of the 226-Hz probe. Frequently, the peak compensated static acoustic admittance is double-shaped (double-peak). Because the middle ear resonance is approximately 1000 Hz [2–4], it is plausible that the 1000-Hz admittance probe might offer more specific information about the condition of the middle ear and detect subclinical alterations. According to Zhiqi et al. [5] and Abou-Elhamd et al. [6], the probe tone frequency of 1000 Hz better discriminates middle ear status in otitis media than the 226-Hz frequency. Shahnaz [7] suggests that higher probe tone frequencies (in relation to 226 Hz) are more accurate for detecting otosclerotic ears, but they considered a probe tone frequency of 630 Hz to be more sensitive in the pathologies they examined.

Many authors have studied the influence of the middle ear on distortion product – otoacoustic emissions (DPOAE) measurements [8–12]. DPOAEs are generated by non-linear cochlear processes, when the ear is stimulated simultaneously by 2 pure tones (stimuli f_1 and f_2). DPOAEs can detect outer hair cell (OHC) function and their active mechanism of vibration [13]. In clinical terms, the most robust DPOAE response is located at the $2f_1-f_2$ [14] frequency. DPOAEs can be measured either by changing the frequency and having the stimulus amplitude L1 and L2 fixed (DP-gram), or fixing the frequency and changing the stimulus amplitude (DPOAE Input/Output function, I/O). For the latter, the most accepted relationship between the amplitudes of the 2 tones (code-named as the scissor paradigm) is defined as $L1=0.4L2+39$ dB [15–18] with a $f_2/f_1=1.22$ [19].

Data in the literature have suggested that it is possible to extrapolate DPOAE I/O functions to estimate hearing threshold [20,21]. In this context, the compressive characteristics of the basilar membrane can be studied in a healthy or damaged cochlea [16,23]. However, some criteria must be considered, such as the presence of DPOAE responses at L2 levels=65 dB SPL and normal middle ear conditions [16]. The non-inclusion of these criteria is a result of the great variability inherent in this method, which has high specificity but low sensitivity [17,23].

Gehr et al. [22] studied DPOAE I/O functions in pigmented guinea pigs with induced middle and inner ear alterations. They found a DPOAE amplitude reduction in the presence of middle ear alterations, but without modification of the slope. They assumed that this information could be useful to distinguish middle and inner ear alterations by considering that inner ear alterations usually present steeper slopes in DPOAE I/O functions.

Pathologies that alter the impedance of the middle ear consecutively modify the DPOAE amplitude because the stimulus to the inner ear is drastically altered. For a better diagnostic evaluation, it is necessary to have a better description of the middle ear status. The latter is feasible by using a 1000 Hz tympanometry probe.

The aim of this study was to provide more information on the relationship between clinical procedures that offer detailed descriptions of the middle ear. Data from 2 DPOAE protocols (DP-gram, DP Input/Output functions) were compared with tympanometric data from patients assessed with a 1000-Hz probe. The data were compared in the context of elucidating whether the tympanometric pattern, caused by a modification of the middle ear resonance, could have any effect on the DPOAE data.

Material and Methods

Subjects

Subjects were assigned into 2 groups according to their 1000 Hz tympanometry patterns: 20 subjects (mean age 22.6 ± 4.02 y) presenting double-peak 1000 Hz tympanograms were assigned to the double-peak group (DPG), and 16 subjects (mean age 23.5 ± 3.93 y) presenting single-peak tympanograms were assigned to the single-peak group (SPG). Exclusion criteria (for both groups) were: alcohol and drug dependence, vertigo, and treatment with salicylates. In addition, ears which did not present a single or a double tympanometry peak were not considered. After the application of the exclusion criteria, only 31 ears were assessed in each group. All participated subjects presented:

- Normal audiometric thresholds at 250, 500, 1000, 2000, 3000, 4000, 6000, and 8000 Hz (≤ 20 dB HL);
- Type “A” 226 Hz tympanometry patterns and tympanometric peak pressures from -50 to $+50$ daPa;
- Acoustic reflexes of 70–100 dB HL at 1000 Hz;
- DPOAE responses with signal/noise ratios ≥ 6 dB at 2002, 3174, and 4004 Hz.

Procedures and data collection

The details of the testing procedures were explained to all subjects who provided written informed consent. Each subject was assessed for approximately 1 h, following this protocol:

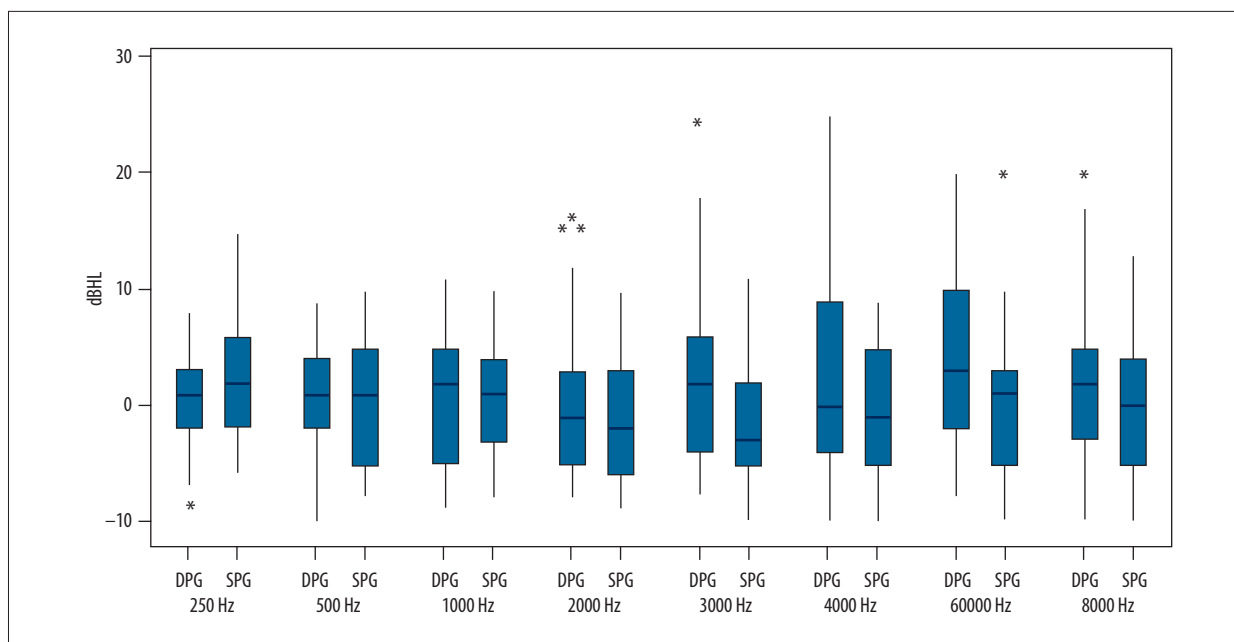


Figure 1. Boxplots showing the distribution of the audiometric thresholds in the double- (DPG) and single-peak (SPG) groups. For the double-peak group, higher threshold spreads were observed at frequencies ≥ 3000 Hz and the opposite at frequencies ≤ 500 Hz. The single-peak group maintained a relative threshold spread at all tested frequencies. Multiple stars represent outlier values, while single stars indicate significant differences at the 0.05 level.

- Medical history compilation;
- Tympanometry measurements to assess middle ear status using the GSI33 middle ear analyzer (v2; Grason-Stadler, Madison, WI) with a probe tone of 226 Hz and 1000 Hz;
- Determination of the acoustic reflex thresholds at 1000 Hz;
- Pure-tone audiometry with a GSI 61 audiometer (Grason-Stadler, Madison, WI) at frequencies of 1000 Hz, 2000 Hz, 3000 Hz, 4000 Hz, 6000 Hz, 8000 Hz, 500 Hz, and 250 Hz, with a 5-dB HL resolution;
- DPOAEs (DP-grams) were measured in an audiometric cabin using the ILO 92 system (Version 6, Otodynamics Ltd, Hatfield, UK) at 1000, 1501, 2002, 3174, 4004, and 6384 Hz (f2). The L1 was set=65 dB SPL and the L2=55 dB SPL, the f1/f2 ratio=1.22 and the noise floor was set to ≤ -5 dB;
- DPOAE I/O functions were estimated at 1501, 2002, 3174, 4004, and 6384 Hz. The stimulus paradigm proposed by Kummer et al. (1998) “L1=(0.4×L2)+39 dB SPL” was used, with L2 starting at 75 dB SPL and decreasing in 5-dB SPL steps until reaching 30 dB SPL.

Statistical analysis

Descriptive and comparative methods were used in the data analysis. Variables were compared using analysis of variance (ANOVA). Values of $p \leq 0.05$ were considered statistically significant.

Results

Figure 1 shows boxplots with the distribution of the pure-tone thresholds data from the 2 groups. A higher threshold variability was observed at frequencies ≥ 3000 Hz in the double-peak group. In comparison, in the single-peak group, the thresholds at frequencies between 1000 and 8000 Hz presented lower values. Significant between-group differences were observed at 3000, 6000, and 8000 Hz ($p=0.040$ and 0.038 , $p=0.047$, respectively).

The subjects assigned to the 1000 Hz double-peak group presented higher values of ear canal volume, peak compensated static acoustic admittance (in mmho), and peak pressures (daPa) than in the single-peak group. Statistical differences were observed for the admittance values between the 2 groups. The data are summarized in Table 1.

Figure 2 shows the boxplot data with the distribution of the DPOAE amplitudes for the 2 tested groups. Overall, the double-peak group presented higher mean DPOAE values (except at 6384 Hz). Statistical differences were observed only at the frequency of 1001 Hz ($p=0.01$). The DPOAE amplitude in the double-peak group showed a decreasing pattern with increasing frequency in comparison to the single-peak group. For example, at 1001 and 1501 Hz, the double-peak group had a DPOAE amplitude 8.86 dB and 4.68 dB higher than in the single-peak group. At the next 3 tested frequencies (2002, 3174,

Table 1. Means and p-values of the tympanometric measures (226 Hz admittance probe tone – Y) of ear canal volume, peak pressure, and peak compensated static acoustic admittance (in mmho) in the single-peak and double-peak groups. The star symbol indicates statistical significance at the 0.05 level.

| Tympanometry | Double peak | Single peak | p-value |
|------------------------|-------------|-------------|---------|
| Ear canal volume (ml) | 1.14 | 1.08 | 0.48 |
| Peak pressure (daPa) | -0.95 | -1.81 | 0.85 |
| Admittance peak (mmho) | 0.97 | 0.57 | 0.02* |

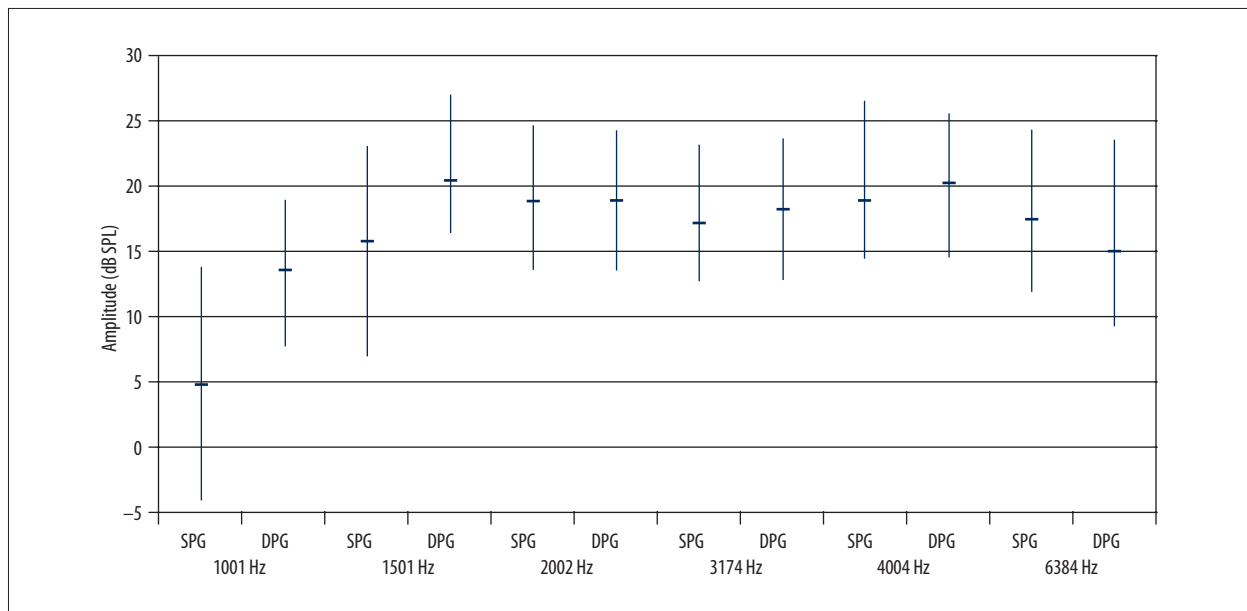


Figure 2. Boxplots of DPOAE amplitude per tested frequency and group. With increasing f_2 , the values of the DPOAE amplitude from the single-peak group (SPG) response move closer to the values from the double-peak group (DPG). The horizontal short lines show the position of the mean DPOAE value. Significant differences at the 0.05 level were observed only at 1001 Hz.

and 4004 Hz), the differences become smaller. The DPG group presented DPOAE amplitudes 0.14, 1.17, and 1.18 dB higher than the SPG. At the frequency of 6384 Hz, the subjects of the SPG group showed a mean DPOAE amplitude 2.39 dB higher than the corresponding DPG value.

The DPOAE I/O functions were analyzed with reference to the L2 stimulus values. At low stimuli (30 and 35 dB) and at all tested frequencies, the SPG's DPOAE amplitudes were higher. At the frequency of 1501 Hz, the SPG presented higher amplitudes at inputs from 40 to 75 dB, but significant differences were observed at 65, 70, and 75 dB ($p=0.05$, 0.01, and 0.03, respectively). At 2002 Hz, the input intensities of 45, 50, 55, and 75 dB demonstrated higher amplitudes in the SPG. At 3174 Hz, higher amplitudes in the SPG were observed at input intensities between 30 to 55 dB and 65 dB. At 4004 Hz, the SPG demonstrated higher values from 30 to 60 (input intensities). Finally, the frequency of 6384 Hz demonstrated higher responses to all input intensities tested.

Figure 3 show the means of DPOAE I/O functions of both groups. Despite the amplitude differences between groups, the significant differences were observed only in 4 of the 50 tested points (5 tested frequencies x 10 steps per frequency).

Discussion

The objective of this study was to evaluate the middle ear information as derived from 2 different clinical procedures. In this context, we have evaluated the effect of 2 distinct 1000-Hz tympanogram patterns (single and double) on the DPOAE amplitude and I/O functions.

Tympanometric data from Table 1 show that the 2 groups of tested subjects are characterized by a significant difference in admittance (Y). This could suggest that there is an association between the double-peak data and the middle ear's increased mobility (higher admittance). It is uncertain what

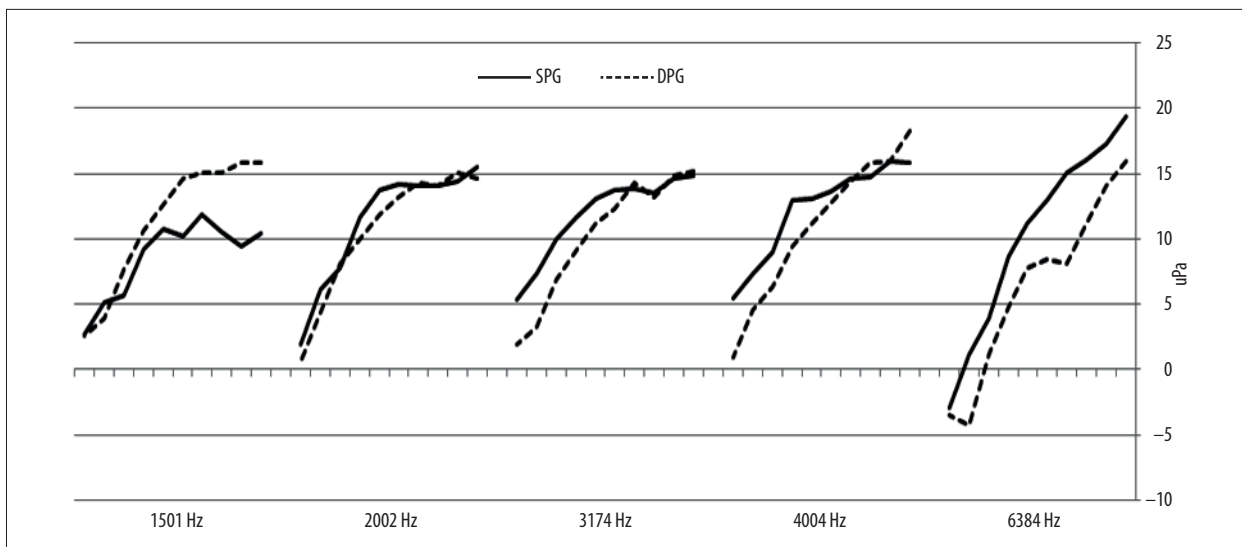


Figure 3. Mean DPOAE I/O function amplitudes from the 2 groups. Contrary to the DPOAE data (shown in Figure 2) the SPG group shows higher values at lower stimulus intensities. This observation is valid across all tested frequencies, but it is more evident from 3174 Hz. The data from Figure 2 refer to the fixed L_2 stimulus intensity of the DP-GRAM protocol (55 dB SPL).

is the source/cause of this mobility. A probable contribution might be related to a normal physiological variability, but the sequelae of high-impedance pathologies (such as otitis media) should also be considered because they might alter admittance at high frequencies.

In terms of audiometric thresholds, the double-peak group presented higher threshold variability (distribution spread) at frequencies >3000 Hz and the opposite at frequencies ≤ 500 Hz. The single-peak group maintained a relative threshold variability at all tested frequencies. Statistical differences were observed at 3000, 6000, and 8000 Hz. At 4000 Hz, a borderline difference ($p=0.06$) was also observed. At frequencies ≤ 500 Hz, the DPG group presented lower threshold values than the SPG, but the differences were not significant.

Surprisingly, the data showing threshold patterns reported in previous studies were not from normal subjects, but rather from patients presenting middle-ear complications, probably because the subjects in this study were classified (to a double- or single-peak group) according to their 1000 Hz tympanometry pattern profiles. Olusesi et al. [24] examined types of otitis media in a Nigerian population, reporting higher thresholds at high frequencies in ears with chronic suppurative otitis media and higher thresholds at low frequencies in ears with otitis media with effusion. Vallejo et al. [25] studied the impedance of the middle ear to evaluate its active function. They suggested that the middle ear may, through the contraction of the tympanic muscles, change its own resonance to increase its admittance at high frequencies, primarily in noisy environments. The reduction in transmission of high frequencies may modify this pattern and deteriorate this function in

relation to speech comprehension. Job and Nottet [11], who studied DP-grams and history of otitis media, reported that the group with middle ear antecedents presented lower audiometric thresholds at 500 Hz; however, compared with the control group (without antecedents), as the frequency increased, the thresholds increased as well.

The 1000 Hz tympanometric pattern was shown to influence DPOAEs, but not by the same degree, as observed in the threshold differences. Depending on the DPOAE stimulus paradigm (DP-grams or DP I/O functions) different aspects were observed. The DPOAE amplitudes of the DP-gram represent a quasi-linear context because it is assumed that at 65 and 55 dB the cochlear OAE generators are almost saturated. Lower stimuli are connected with active non-linear DPOAE generators; therefore, different relationships were observed.

DPOAE amplitudes were lower in the DPG only at 6006 Hz, but the amplitude difference between the DPG and SPG groups decreased as the frequency increased (see data in Figure 2). Statistical differences were observed only at 1001 Hz and a borderline difference at 1501 Hz ($p=0.06$). This pattern has been reported in a study by Garner et al. [26], who found great variability at low frequencies (500 and 1000 Hz) and at high frequencies (5656 and 8000 Hz), suggesting that the low frequencies suffered from a noise effect and that the variability at high frequencies could be a consequence of middle ear transmission characteristics.

DPOAE I/O functions presented a different pattern than the DP-grams. At low frequency stimuli (35 dB and 30 dB) and across all tested frequencies (with the exception of 1501 Hz), the SPG

presented higher DPOAE amplitudes. This finding can be associated with the DPOAE thresholds. Sun and Shaver [27] studied the effect of negative middle ear pressure on DPOAE, and they concluded that negative middle ear pressure substantially decreases DPOAE levels at low frequencies and some mid-frequencies, but tends to increase DPOAE levels at high frequencies. Because negative pressure induces middle ear stiffness, the stiffness modifies the admittance at high frequencies and increases the impedance of low frequencies. Our findings agree with these conclusions, assuming that the decrease in stiffness considerably alters the DPOAE measures. The data from this study agree with results of Gorga et al. [16] who reinforced the need to consider a middle ear condition when predicting hearing thresholds from extrapolated DPOAE I/O functions.

The data suggest that alterations of the middle ear resonant properties (as revealed by the admittance differences between the 1000 Hz pattern groups) are reflected in the attenuation of the recorded DPOAEs. Similar data from human and animal studies have been widely reported in the literature [8,15,17,28–31]. Nevertheless, the totality of factors influencing the induced changes of the middle ear still remain to be defined.

The data in this study show an interesting conflict. Differences in DPOAEs between the 2 groups were significant only at 1001 Hz and for high-amplitude stimuli (≥ 65 dB SPL). It is important to emphasize that despite the observed threshold differences at 3000, 6000, and 8000 Hz, the DPOAE data did not verify these differences. The DPOAE amplitudes showed an erratic/alternating behavior between the DP-grams in comparison to the data from the I/O curves, but no significant differences

were detected. In the first case (differences at 1001 Hz), one might assume that the tested subjects present subclinical threshold alterations, but in the second case the data offer no explanation. It is well documented that DPOAEs are more sensitive indicators of alterations in the cochlear function and gain [28–30] than the corresponding behavioral measurements. The only plausible hypothesis is that the observed behavioral differences have a retrocochlear origin, but the available data do not confirm this.

To elucidate this clinical finding, further studies must be conducted. As new data in the literature support the efficacy of middle ear-power-analysis (MEPA) [32,33], certain factors can be better defined. MEPA measures wideband power reflectance, which is an index of middle ear inefficiency, as a function of frequency. MEPA measurements in parallel with DPOAE and high-frequency tympanometry can more accurately describe the relationships observed.

Conclusions

The 1000 Hz tympanometric pattern (single or double) significantly affects the structure of DPOAE responses only at 1001 Hz. In this context, changes in the resonance properties in the middle ear (as detected by the 1000 Hz tympanometric probe) can be considered as prime candidates for the observed variability in the DP-grams and the DP I/O functions. Nevertheless, the data cannot reveal the mechanism connecting the double-peak tympanometric pattern to the higher middle ear admittance.

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