

Changes in Distortion Product Otoacoustic Emission Caused by Contralateral Broadband Noise

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The main purpose of this investigation was to measure the effect of contralateral acoustic stimulation (CAS) on distortion product otoacoustic emission (DPOAE) in twenty human ears, for a ratio of primary tones $f_2/f_1 = 1.22$ and a wide frequency range of f_2 (1.4–9 kHz), for two intensity levels of primary tones ($L_1 = 60$ dB SPL; $L_2 = 50$ dB SPL and $L_1 = 70$ dB SPL; $L_2 = 60$ dB SPL) and two intensity levels of CAS (50 and 60 dB SPL). It was found that in the presence of CAS, in the majority of cases the DPOAE level decreased (suppression), but it might also increase (enhancement) or remain unchanged depending on the frequency. The mean suppression level of the component of the frequency $f_{DP} = 2f_1 - f_2$ might be approximated by a linearly decreasing function of the f_2 frequency of primary tones. The slope of this function was negative and increased with an increase of the contralateral stimulation level. The higher was the contralateral noise level the greater was the suppression. For the f_{DP} level below about 15 dB SPL, suppression was observed in a substantial number of measurement cases (in about 85% of all measured cases on average). When the f_{DP} level was higher than 15 dB SPL, only suppression (not enhancement) was observed.

Keywords: distortion product otoacoustic emissions (DPOAEs), contralateral acoustic stimulation (CAS), contralateral suppression.

1. Introduction

Otoacoustic emissions (OAEs) are low-level sounds produced by the cochlea which can be measured in the outer ear canal. There are several types of OAEs such as spontaneous OAEs, evoked OAEs and distortion product OAEs (DPOAEs) (for a review see (PROBST *et al.*, 1991)). The DPOAEs considered in the present paper are assumed to be caused by the compressive nonlinearity of cochlear micromechanics and originate when two pure-tone stimuli (primary tones) of different frequencies (f_1 and f_2) are supplied to the ear canal. When this happens, nonlinear components occur, the strongest of which is the cubic¹ distortion component of the frequency $f_{DP} = 2f_1 - f_2$. It is assumed that DPOAEs are a result of the superposition of two components from different cochlear sources. The first distortion component is generated by the cochlear non-

linear mechanisms and arises in the region of maximum excitation of the basilar membrane caused by two primary tones, near the characteristic site of f_2 . The second component, known as the reflection component, results from a reflection source which is located at the characteristic site of $2f_1 - f_2$ (KNIGHT, KEMP, 2001; KONRAD-MARTIN *et al.*, 2002). The two DPOAE components have different phase and level characteristics because they are generated by different mechanisms. It is usually assumed that DPOAE results from a vector sum of the reflection and distortion components. The difference in relative phases between those components causes either constructive or destructive interaction between them. The constructive interaction leads to an increase of DPOAE amplitude at some frequencies, while destructive interaction leads to amplitude decrease at other frequencies. This variation in the sound pressure level of DPOAEs is quasi-periodic *versus* frequency and produces peaks and dips in the fine structure of a DPgram (MAUERMANN *et al.*, 1999; REUTER, HAMMERSHOI, 2006).

¹A cubic nonlinearity can produce many difference tones. The difference tone of interest in this study corresponds to the cubic distortion component of the $2f_1 - f_2$ frequency.

DPOAEs are often measured in the presence of additional tonal or noise stimuli which are presented ipsilaterally, contralaterally or binaurally (WILLIAMS, BROWN, 1995; 1997; ZHANG *et al.*, 2007; SUN, 2008). There have been many reports on OAEs suppressed by contralateral stimulation in both animals (MANLEY *et al.*, 1999; JAMES *et al.*, 2005) and humans (CHERY-CROZE *et al.*, 1993; MOULIN *et al.*, 1993; JAMES *et al.*, 2002; LISOWSKA *et al.*, 2002; ZHANG *et al.*, 2007; SUN, 2008). Reports on DPOAEs suppressed by contralateral stimulation showed reduction of the cubic distortion components by amounts of 0.5 to 2 dB with large intersubject variability (MOULIN *et al.*, 1993; WILLIAMS, BROWN, 1997; SUN, 2008). This reduction is often called contralateral suppression (HOOD, 2002; GUINAN *et al.*, 2003). The contralateral mode is the most commonly used method to study suppression; however, the binaural mode of suppressor presentation results in greater suppression. Furthermore, broad-band noise (BBN) appears to be the most effective suppressor (MAISON *et al.*, 2000). Some other investigations have demonstrated that the effects of contralateral stimuli on distortion product OAEs appear more variable and can both increase and decrease DPOAE amplitude (LISOWSKA *et al.*, 2002; OZIMEK, WICHER, 2006; SUN, 2008).

The qualitative differences in DPOAE contralateral suppression data are presumably a result of different measurement procedures and the variability in DPOAE amplitude due to stimulus parameters. For example, measurements of DPOAE suppression clearly depend on the frequency resolution of the primary tones. DPgrams measured with primary tones with high frequency resolution show quasi-periodic variations in level (peaks and dips), which are called DPOAE fine structure (HE, SCHMIEDT, 1993; MAURMANN *et al.*, 1999; MULLER *et al.*, 2005; REUTER, HAMMERSHOI, 2006; SUN, 2008; ABDALA *et al.*, 2009). More contralateral suppression usually occurs at the peaks and less suppression or enhancement occurs at the dips in DPOAE fine structure (WILLIAMS, BROWN, 1997; ZHANG *et al.*, 2007; SUN, 2008; ABDALA *et al.*, 2009).

Contralateral suppression of DPOAEs has been used as a marker of efferent activity which could change the operating state of the cochlear amplifier. In measuring DPOAE suppression, the efferent system has been activated using a variety of stimuli such as pure tones, clicks, and narrow- and broad-band noises (COLLET *et al.*, 1990; PUEL, REBILLARD, 1990; MOULIN *et al.*, 1993; COLLET *et al.*, 1994; GIRAUD *et al.*, 1997; MAISON *et al.*, 2000; JAMES *et al.*, 2005; SUN, 2008; DEETER *et al.*, 2009). There are two types of efferent fiber that originate in the superior olivary complex of the brainstem: medial olivocochlear (MOC) fibers, which in general project to the contralateral

side, and lateral olivocochlear (LOC) fibers, which mainly project to the ipsilateral side (for details on the anatomy and physiology of the MOC and LOC see (GUINAN, 2006)). The MOC system plays an important role in hearing, e.g. by controlling the sensitivity and frequency selectivity of the cochlea, shifting the dynamic range of hearing, increasing the discriminability of transient sounds in a noisy background, protecting from an acoustic trauma, and aiding the detection of signals in noise.

The ipsilateral or contralateral sound stimulation causes amplitude changes in various types of otoacoustic emissions (PUEL, REBILLARD, 1990; BERLIN *et al.*, 1993; MOULIN *et al.*, 1993; COLLET *et al.*, 1994; GIRAUD *et al.*, 1995). Bilateral stimulation produces changes which approximately correspond to the sum of ipsilateral plus contralateral stimulation (LILAONITKUL, GUINAN, 2009). Since OHC function and the generation of DPOAEs are related, decrease in gain of the cochlear amplifier changes the level of the measured distortion products. In other words, DPOAE contralateral suppression is the consequence of a control mechanism in the auditory system which is mediated by MOC efferents. Typical MOC effects (in the form of suppression) on DPOAEs range from a fraction of a decibel to a few decibels. For sound level ranges, where OAEs monotonically increased, MOC-induced suppression of the OAEs was observed. However, for the OAEs measured at DPOAE dips, MOC effects often show enhancement of the OAEs for some frequencies (MOULIN *et al.*, 1993; MULLER *et al.*, 2005; ABDALA *et al.*, 2009). The reason for this is that if the contralateral acoustic stimulation (CAS) induced effects on DPOAEs are measured at dips (where DPOAE components are out of phase), CAS (activating the MOC) can suppress one of the components more than the other and produce a release of cancellation; this in turn produces some sort of enhancement (ABDALA *et al.*, 2009; DEETER *et al.*, 2009). However, this enhancement is not a true MOC reflex and this is a very important fact. Measuring at peaks ensures that the MOC is being measured at a frequency where the two DPOAE components are adding in phase. Generally, the MOC effect is strongest in the low frequencies and low stimulus levels and it gets stronger with higher levels of contralateral noise. These facts were reported and established in normal hearing humans, in newborns and older infants and in laboratory animals (MOULIN *et al.*, 1993; BACKUS, GUINAN, 2006).

There has been a great deal of research on the effect of CAS on the DPOAE level when the suppressor frequency range is located around the primary tone frequencies. For example, (CHERY-CROZE *et al.*, 1993) observed that contralaterally presented narrow-band noise, centered around 1–2 kHz, produced a large sup-

pression of DPOAEs elicited by the primary tones of frequencies corresponding to the suppressor frequency region. Recently, (FRANCIS, GUINAN, 2010) showed decreasing suppression of click-evoked otoacoustic emissions across the frequency range from 1 to 5 kHz. However, a quantitative dependency of the CAS effect *versus* wide frequency range is not well-documented in the literature and further investigations are needed. That is why the basic question posed in this study is how contralateral broad-band noise affects the DPOAE level in humans for a wide frequency range. Additionally, the effect of CAS on DPOAEs, for two levels of contralateral stimulus and primary tones, was also considered.

2. Materials and methods

2.1. Stimuli and apparatus

DPOAEs were measured using the Tucker-Davis Technologies system 3, in conditions without and with the presence of broad-band noise (BBN) applied as a suppressor to the contralateral ear. Pairs of primary tones of frequencies f_1 and f_2 ($f_2/f_1 = 1.22$) were used at one-eighth octave steps and the f_2 frequency ranged from 1.4 kHz to 9 kHz (this corresponds to $2f_1 - f_2$ frequency changes from 1.14 kHz to 7.38 kHz).

The primary tones were generated using a 24-bit digital real-time signal processor RP2.1 at a 44 kHz sampling rate. Each signal was sent to the programmable attenuator and then to the headphone buffer. Signals from the output of the headphone buffer, via insert earphone (Etymotic Research, ER-2), were finally delivered to the ear canal. A low noise microphone (ER-10B+) was inserted into the external auditory meatus in soft plastic foam in order to measure the ear canal sound pressure waveform. A bandpass filtering (8 Hz bandwidth, centered at frequency $2f_1 - f_2$) was performed and the $2f_1 - f_2$ component level changing over time was recorded. The $2f_1 - f_2$ component was accepted as a physiological response when the 20 log of the signal-to noise ratio of the DPOAE exceeded 6 dB.

The level of the noise floor was estimated as an average of the ten FFT frequency components (10 spectral lines adjacent to the $2f_1 - f_2$ component, five above and five below) (SUN, 2008). The noise level was the mean plus one standard deviation from the signal average.

Primary tones were presented at two sound pressure levels: $L_1 = 60$ dB SPL, $L_2 = 50$ dB SPL and $L_1 = 70$ dB SPL, $L_2 = 60$ dB SPL, and calibrated with a low noise microphone (ER-10B+) inserted into the ear. In the condition “with contralateral stimulation”, the broad-band noise (bandwidth 0.2–10 kHz) was generated by a 24-bit digital real-time signal pro-

cessor RP2.1, sent to a headphone buffer and then to the earphone (Etymotic Research, ER-2) inserted in the contralateral ear. The contralateral noise was presented at 50 and 60 dB SPL. The CAS (broad-band noise) was monitored by a low-noise probe microphone (ER-10B+) placed in the external ear canal. The microphone was connected to the FFT analyzer; it was thus possible to ensure that the CAS presented to the subjects was flattened and had an appropriate level each time the contralateral stimulus was used.

Real-time recordings of DPOAE signal amplitude lasted 8 seconds (JAMES *et al.*, 2002). They were extracted with a bandpass filtering (8 Hz bandwidth, centered at frequency $2f_1 - f_2$). In this way a 4-second recording in the absence of CAS and a 4-second recording in the presence of CAS were measured.

Three independent recordings of the DPOAE signal were made for different experimental conditions (i.e. various f_2 frequencies and levels of contralateral noise). To obtain reliable and comparable data, it was necessary to fix the time interval in which the amount of suppression would be measured. The DPOAE levels, without and with CAS, were measured in time intervals (2.2 s) which excluded transient intervals and corresponded to relatively steady rms values of the DPOAE temporal record. The suppression value was defined as the averaged (across recordings) difference between the DPOAE levels without and with CAS.

Measurements were made for all f_2 frequencies without changing the probe position in the ear canal to minimize its possible influence on the DPOAEs. The data obtained were visualized in the form of DPgrams, both in the absence and in the presence of CAS. DPgrams at octave frequencies from 1 to 8 kHz were preliminarily measured in both ears of each subject and the ear showing higher DPOAE levels was used in basic measurements to get more accurate DPgrams (22 data points) in the range from 1.5 to 9 kHz.

The amount of nonlinear distortion produced by the apparatus used was checked separately by placing the ear probe in a 2.5 cm³ test cavity and each primary tone pair was presented at 60 and 70 dB SPL. The signal from the measuring setup was analyzed in the frequency domain by an Ono Sokki FFT analyzer (Japan Research Systems). It was found that none of the nonlinear components for the primary tone pairs tested were above the noise floor.

2.2. Subjects

Measurements of DPOAEs, in conditions without and with CAS, were performed for 10 normal-hearing adults (6 males and 4 females) with ages ranging from

19 to 24 years. All the subjects were volunteers and the experiments were conducted with their informed consent. Before data collection, clinical pure-tone basic audiometric and middle-ear testing had been performed for all subjects. The audiometric testing, determined by means of a clinical audiometer (AC 40 Interacoustics), comprised measurements of hearing thresholds at half-octave frequencies from 250 to 8000 Hz, with a minimum step size of 5 dB. Subjects had no history of ear diseases, occupational noise exposure or use of ototoxic drugs, and they had hearing thresholds at or better than 15 dB HL in both ears for the audiometric test frequencies (0.5, 1, 2, 3, 4, 6, and 8 kHz). The middle-ear testing concerned immittance measurements, by means of a Siemens SD-30 tympanometer, and comprised peak middle-ear pressure, compliance and base volume (ear-canal volume).

The middle ear reflex (MER) threshold to contralateral noise was tested for all subjects in both ears. MER was defined as the lowest noise level that produces a measurable change in acoustic admittance. The subjects' MER thresholds ranged from 80 to 85 dB SPL and were on average 10 dB above the level of the contralateral elicitor sound.

Preliminary testing and basic DPOAE measurements for each subject lasted for about 2 hours. During the DPOAE measurements the subjects were seated in a sound-treated room.

3. Results

3.1. Cross-over effect and DPOAE change versus time

The effect of cross-over during CAS was checked prior to the basic DPOAE measurements. An ear probe was placed in the ear canal in which DPOAE was

measured and broad-band noise was presented to the contralateral ear at 80 dB SPL. No significant differences between the averaged spectra of the noise floor obtained without and with CAS were found, demonstrating that the effect of acoustic cross-over of CAS on the DPOAE values might be negligible in this study. A one-way analysis of variance ANOVA revealed that the effect of acoustic cross-over $\{F(1, 88) = 1.5026, p = 0.2235\}$ was not statistically significant. All statistical analyses were performed with IBM SPSS Statistics (ver. 21) software.

Real-time recordings of the f_{DP} were examined from the point of view of the DPOAE level change when the CAS was applied. Off-line data analysis involved comparing the amplitude levels of the f_{DP} , without and with contralateral stimulus. Figure 1 depicts an exemplary envelope trace for an f_{DP} recording for f_2 of 2840 Hz at $L_{sup} = 60$ dB SPL.

As can be seen, a certain variation of amplitude is evident in the time-course measures. At the beginning of the recording, the f_{DP} amplitude slightly decreased when the primary tones were turned on. After this effect, which is called rapid onset adaptation, the amplitude of the f_{DP} fluctuates within a certain range, and when the contralateral broad-band noise is turned on, f_{DP} exhibits a post-onset transient state (decay) and finally reaches a lower level.

3.2. DPOAE change versus f_2 frequency

DPOAEs, evoked by two primary tones of intensity levels ($L_1 = 60$ dB SPL, $L_2 = 50$ dB SPL and $L_1 = 70$ dB SPL, $L_2 = 60$ dB SPL) under two intensity levels (50 and 60 dB SPL) of the contralateral stimuli, were measured. The obtained DPOAE values are presented in the form of DPgrams showing f_{DP} levels (y -axis) as a function of the f_2 frequency (x -axis).

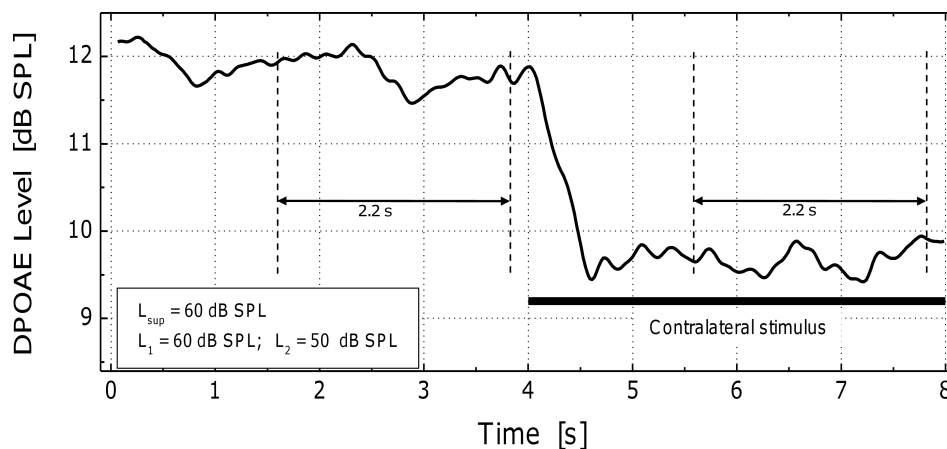


Fig. 1. Envelope of the f_{DP} for chosen frequency $f_2 = 2840$ Hz of the primary tones at $L_{sup} = 60$ dB SPL. The time interval (4 s) of contralateral stimulus presentation (thick solid line), the 2.2 s intervals in which the rms value of the f_{DP} were determined without and with contralateral stimulation (thin solid lines).

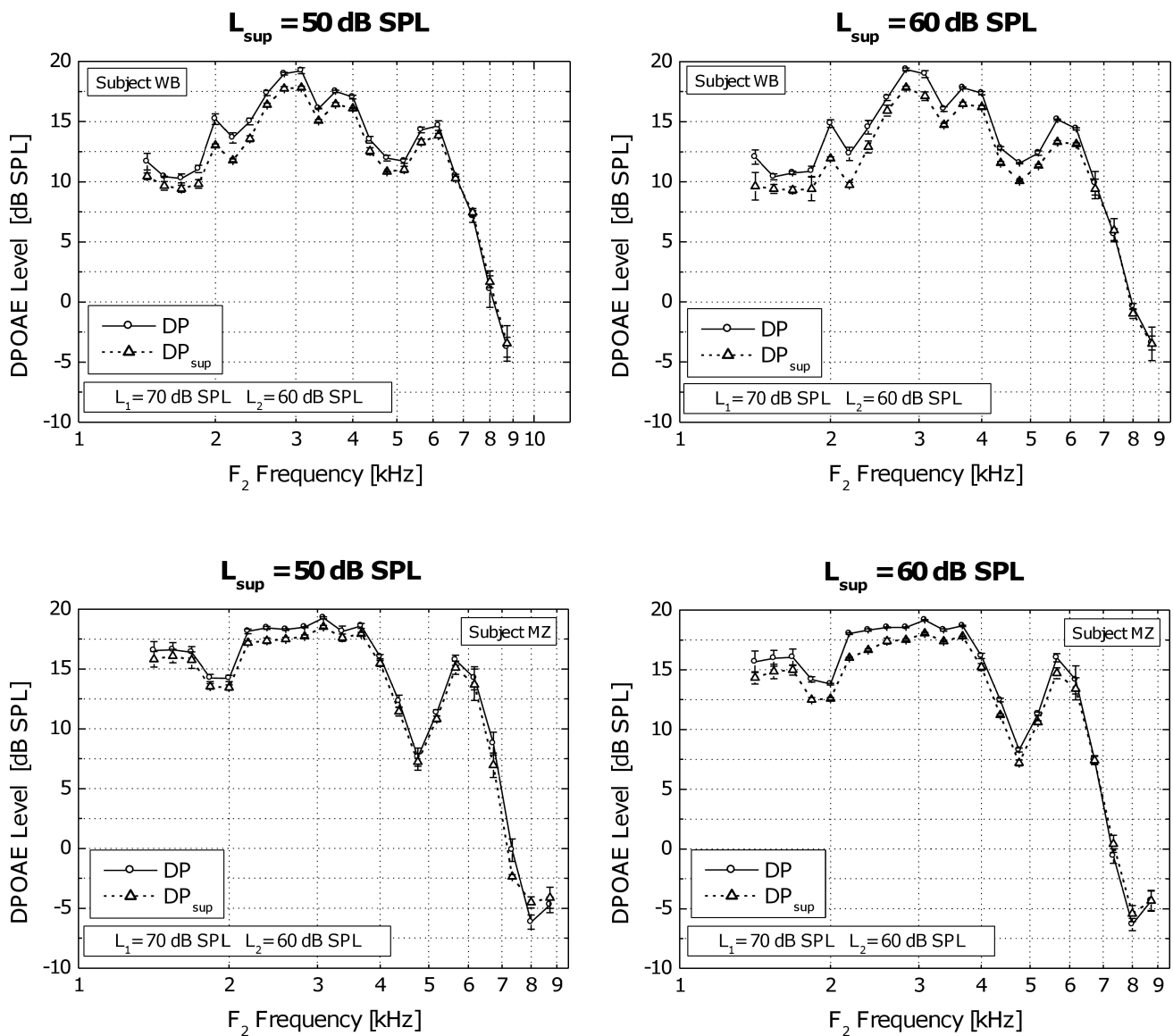


Fig. 2. Examples of DPgrams without (solid line) and with (broken line) contralateral broad-band noise stimulation for two subjects WB and MZ. The contralateral noise was presented at two intensity levels: 50 and 60 dB SPL. The intensity levels of the primary tones evoking DPOAE were $L_1 = 70$ dB SPL, $L_2 = 60$ dB SPL.

Figure 2 presents examples of DPgrams without and with CAS for two subjects: MZ and WB.

The two columns correspond to two contralateral noise levels (50 and 60 dB SPL) and the two rows present data for the two subjects and the intensity of the primary-tone levels of $L_1 = 70$ dB SPL, $L_2 = 60$ dB SPL. Visual inspection of Fig. 2 indicates that the f_{DP} levels differ, depending on the f_2 frequency, between measurement conditions, with lower levels occurring with contralateral broad-band noise when compared to the measurement condition without contralateral noise. The changes of f_{DP} suppression ranged from a fraction of a dB to approximately 3 dB depending on both the f_2 frequency and the contralateral noise level. The suppression of the f_{DP} in

the lower frequency range is greater than in the higher one, which is usually insignificant and for which sometimes a slight f_{DP} enhancement is observed. It should be added that, although all the subjects tested had normal hearing thresholds, a considerable variability in DPOAE levels and suppression values was found between subjects.

The suppression was stronger when the level of the CAS was 60 dB SPL than that obtained with the 50 dB SPL.

The effectiveness of the f_{DP} suppression was determined by subtracting the DPOAE level recorded without CAS from the level with CAS. In this way a positive DPOAE difference indicated suppression, while a negative value indicated enhancement. The

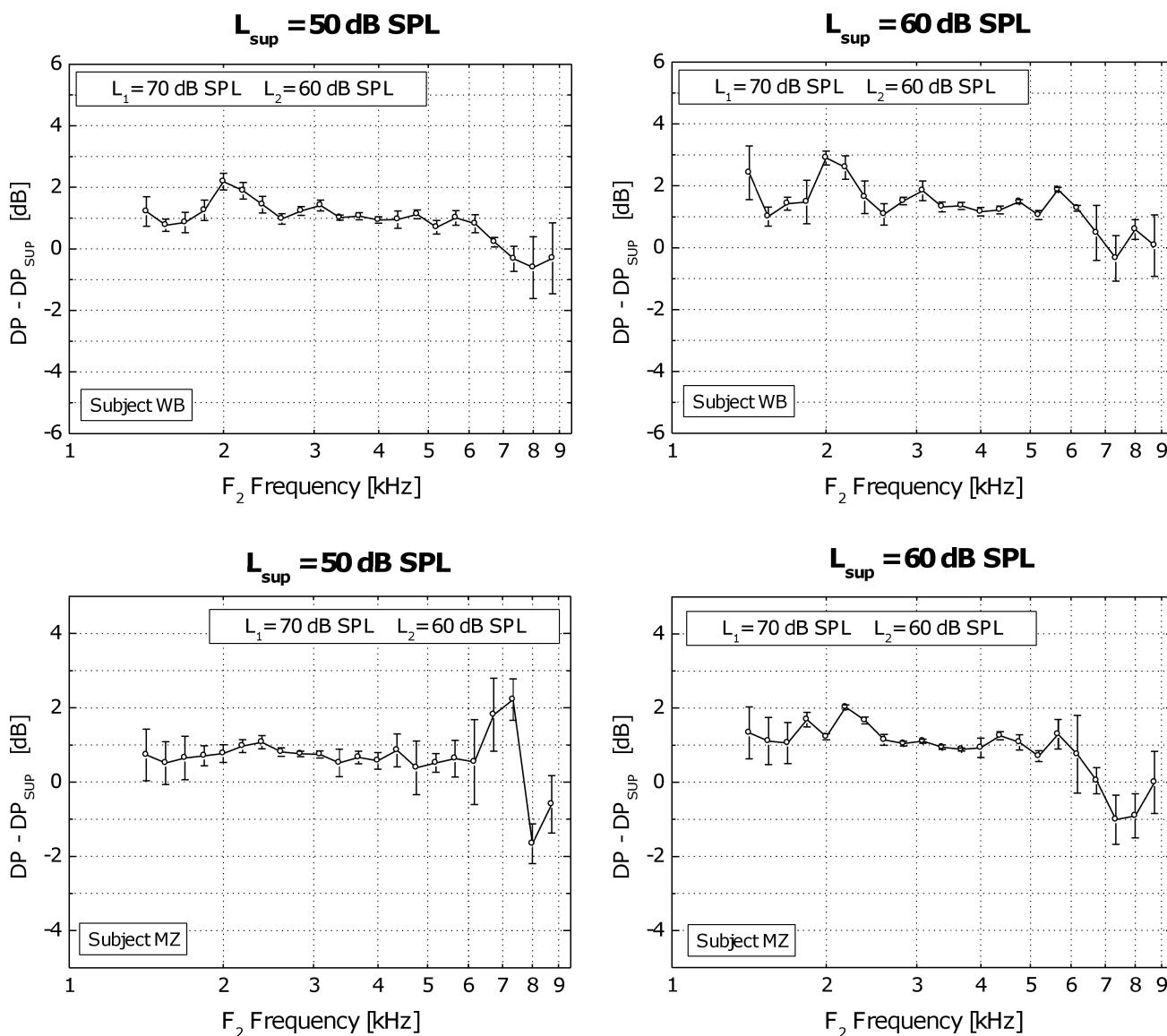


Fig. 3. Differences between DPgrams (shown in Fig. 2) without and with contralateral broad-band noise stimulation for two subjects WB and MZ. The contralateral noise was presented at two intensity levels: 50 and 60 dB SPL. The intensity levels of the primary tones evoking DPOAE were $L_1 = 70$ dB SPL, $L_2 = 60$ dB SPL.

obtained data are presented in Fig. 3 as a function of the frequency f_2 and as an example for the subjects MZ and WB. The y -axis presents the difference $\Delta DP = DP - DP_{sup}$ in dB, while the x -axis shows the frequency f_2 in kHz. The greater suppression is demonstrated with a larger positive number on the y -axis. A rough inspection of Fig. 3 reveals a fluctuating change of the ΔDP versus f_2 frequency. It appears that in a significant majority of cases, positive ΔDP s (suppression) are observed; however, zero or negative ΔDP s can also be noticed.

The pooled data from 10 subjects, two suppressor levels (50 and 60 dB SPL) and two primary tone levels ($L_1 = 60$ dB SPL, $L_2 = 50$ dB SPL and $L_1 = 70$ dB SPL, $L_2 = 60$ dB SPL) are shown in Fig. 4.

The f_{DP} suppression is clearly dependent on the f_2 frequency, with higher suppression occurring at the low frequencies compared to that of the highest frequencies. There are substantial intersubject ΔDP variabilities for almost all frequencies of f_2 resulting from large individual differences in the DPOAE values obtained for the tested subjects. The differences between the f_{DP} levels without and with CAS are in the majority of cases positive (i.e. the f_{DP} level decreases during CAS), but in some cases, instead of f_{DP} suppression, a f_{DP} enhancement of the order 1–2 dB occurred. Figure 4 shows that the suppression is generally stronger when the level of the contralateral stimulus is 60 dB SPL, compared to that obtained with the 50 dB SPL.

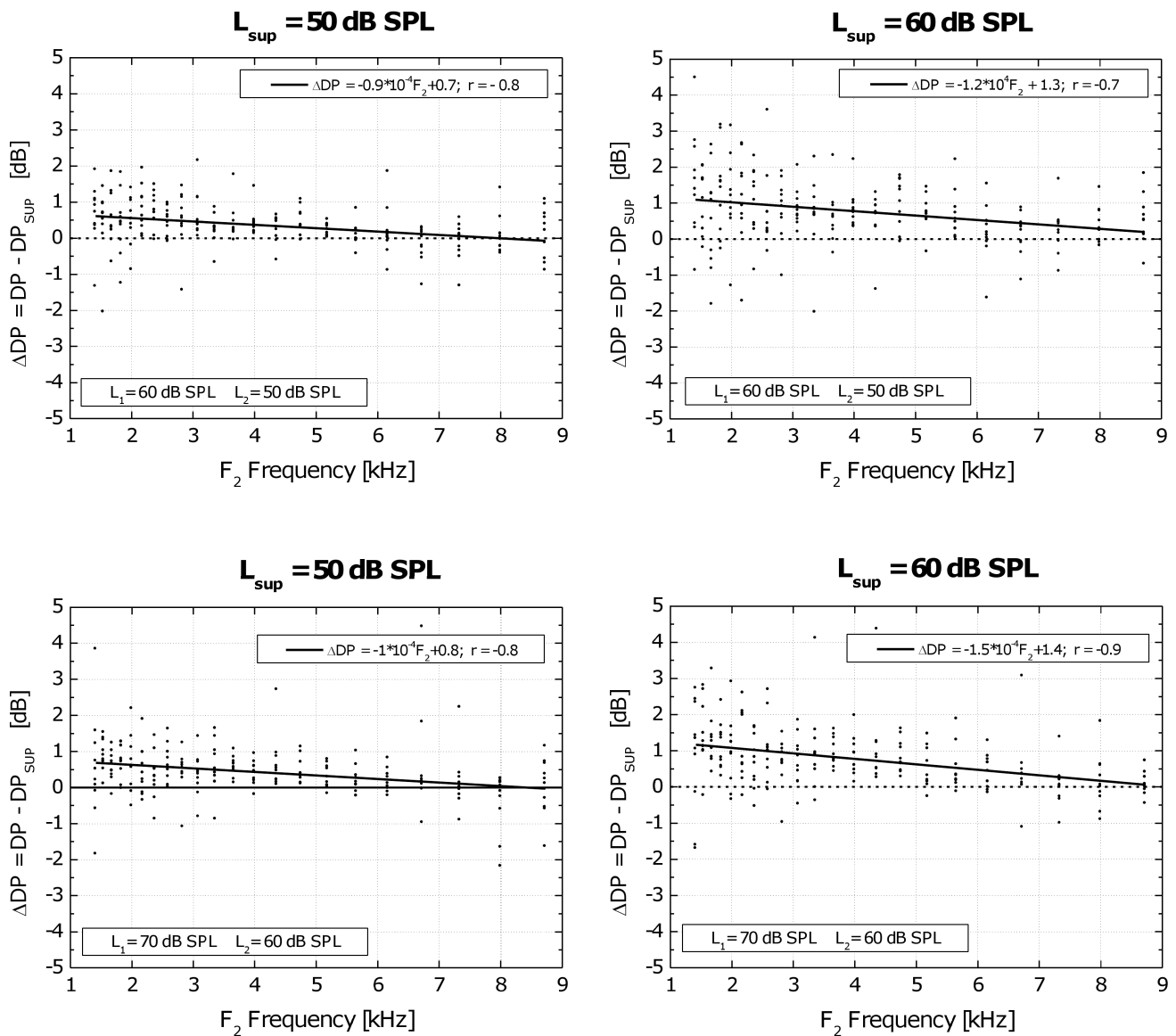


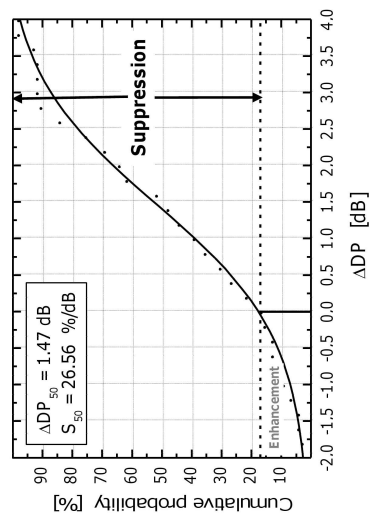
Fig. 4. Scatterplot of the DPOAE suppression against f_2 frequency, measured for 10 subjects. Each point represents the suppression value for a given subject and determined f_2 . The linear regression equation and correlation coefficient r are given in the top right legend of each panel. The contralateral noise was presented at two intensity levels: 50 and 60 dB SPL. Two intensity levels of the primary tones were used (the first row, $L_1 = 60$ dB SPL, $L_2 = 50$ dB SPL; the second row, $L_1 = 70$ dB SPL, $L_2 = 60$ dB SPL).

Linear regression analysis was done to apply a line of best fit to a spread of data points presented at each panel and to determine the regression equation and regression parameters (i.e. the slope and intercept). The best fitting line for the DPOAE suppression *versus* the f_2 frequency, for intensity levels of primary tones equal to $L_1 = 60$ dB SPL, $L_2 = 50$ dB SPL, was characterized by the negative slope -0.9×10^{-4} dB/Hz for $L_{sup} = 50$ dB SPL ($r = -0.8$) and -1.2×10^{-4} dB/Hz for $L_{sup} = 60$ dB SPL ($r = -0.7$) as the intercept increased from 0.7 to 1.3. For the 10 dB higher intensity level of primary tones (i.e. for $L_1 = 70$ dB SPL and

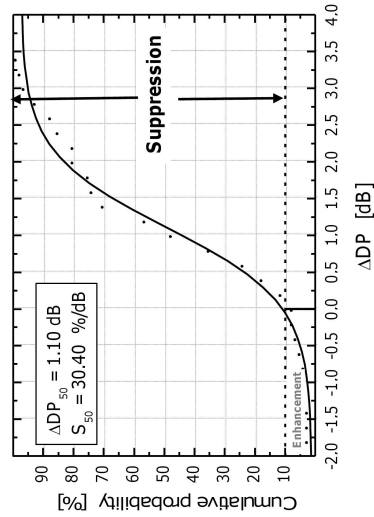
$L_2 = 60$ dB SPL) the corresponding data are equal to, respectively: -1×10^{-4} dB/Hz for $L_{sup} = 50$ dB SPL ($r = -0.8$); and -1.5×10^{-4} dB/Hz for $L_{sup} = 60$ dB SPL ($r = -0.9$), with almost the same increasing intercept value from 0.8 to 1.4. Relatively high negative values of the Pearson coefficient r indicate that f_{DP} suppression and the f_2 frequency are dependent. Calculating the r^2 one can estimate the extent to which variability in DPOAE suppression can be explained by the variability in the f_2 frequency. The r^2 values for the upper row are 0.7 and 0.5 and for the lower row 0.8 and 0.6, respectively.

$L_{sup} = 60$ dB SPL

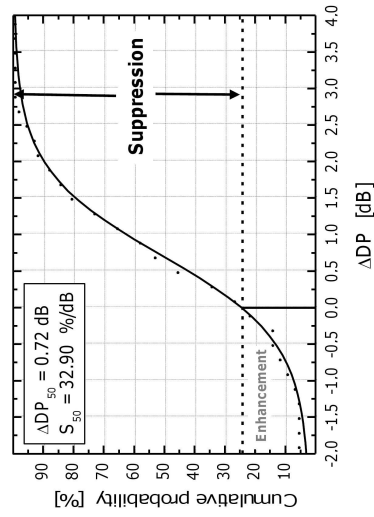
f_2 bandwidth 1.4 - 2.5 kHz



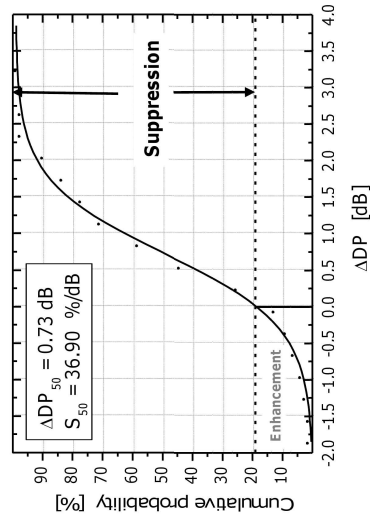
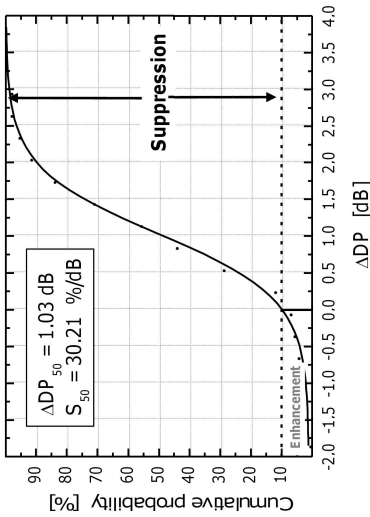
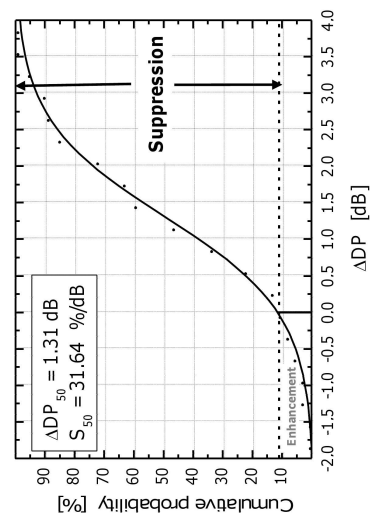
f_2 bandwidth 2.5 - 5 kHz



f_2 bandwidth 5 - 8.8 kHz



$L_1=60$ dB SPL, $L_2=50$ dB SPL



$L_1=70$ dB SPL, $L_2=60$ dB SPL

Fig. 5. Cumulative probability functions for three ranges of f_2 frequency and two intensity levels of the primary tones (first row, $L_1 = 60$ dB SPL, $L_2 = 50$ dB SPL; second row $L_1 = 70$ dB SPL, $L_2 = 60$ dB SPL) at $L_{sup} = 60$ dB SPL. Suppression and enhancement regions are denoted.

To determine the significance of the difference in f_{DP} levels without and with CAS across the experimental conditions, a two-way within-subjects analysis of variance (ANOVA) was conducted. A p value of < 0.05 was considered significant. The within-subjects factors were: the f_2 frequency and the level of the contralateral noise. The ANOVA revealed that the effects of the f_2 frequency $\{F(21, 1188) = 6.744, p < 0.0001\}$ and the contralateral noise level $\{F(2, 1188) = 61.358, p < 0.00001\}$ were statistically significant. The interaction effects of the f_2 frequency with the level of the contralateral noise were not statistically significant $\{F(42, 1188) = 0.6270, p < 0.9704\}$.

The probability of the differences of the DPOAE levels without and with CAS was approximated by the standardized cumulative distribution function of the form (1)

$$\Phi(\Delta DP) = \frac{100}{\sqrt{2\pi}} \int_{-\infty}^{(\Delta DP - P_{50})/\sigma} e^{-x^2/2} dx, \quad (1)$$

where $\Delta DP = DP - DP_{sup}$, P_{50} corresponds to the ΔDP value at 50% probability, σ is a standard deviation (SD) and x is an integral variable. The cumulative distribution $\Phi(\Delta DP)$ was characterized by two parameters: P_{50} and steepness S_{50} at the P_{50} point. Having ΔDP data, it was possible to apply an iterative procedure for finding the ΔDP_{50} (at P_{50}) and the corresponding steepness S_{50}^2 . The iterative procedure searched for the P_{50} and S_{50} by means of minimizing the mean square error between the empirical data and the fitted cumulative function.

Figure 5 presents examples of the cumulative probability functions of ΔDP values for three ranges of the f_2 frequency and two intensity levels of the primary tones (first row $L_1 = 60$ dB SPL, $L_2 = 50$ dB SPL, second row $L_1 = 70$ dB SPL, $L_2 = 60$ dB SPL) at $L_{sup} = 60$ dB SPL. The data in the legend to Fig. 5 provide values of the basic parameters (ΔDP_{50} , S_{50} , σ) of the cumulative probability.

The ΔDP_{50} suppression, assigned to 50% probability, clearly decreases when the f_2 frequency increases (from $\Delta DP_{50} = 1.47$ dB for bandwidth 1.4–2.5 kHz to $\Delta DP_{50} = 0.72$ dB for 5–8.8 kHz for $L_1 = 60$ dB SPL, $L_2 = 50$ dB SPL and from $\Delta DP_{50} = 1.31$ dB for bandwidth 1.4–2.5 kHz to $\Delta DP_{50} = 0.73$ dB for 5–8.8 kHz for $L_1 = 70$ dB SPL, $L_2 = 60$ dB SPL). The steepness

²There is a direct relationship between S_{50} and σ characterizing a spread of data at the P_{50} point. The two parameters are easily convertible by the expression:

$$S_{50} = \frac{100}{\sigma\sqrt{2\pi}}. \quad (2)$$

Since the steepness S_{50} of the cumulative probability function increases when the standard deviation σ decreases, S_{50} indirectly describes the spread of the ΔDP values for the determined measurement condition.

of the cumulative function generally increases as the f_2 frequency increases.

This means, according to formula (2), a decrease of the σ value *versus* the f_2 frequency range. Comparing data between rows, i.e. for different levels of the primary tones, one can see that for the first two frequency bandwidths, the higher the level of the primary tones, the lower ΔDP_{50} ; however, this is not the case for the 5–8.8 kHz range. The point of intersection of the x -coordinate at $\Delta DP = 0.0$ dB with the cumulative function allows separation of two parts: suppression (right part) and enhancement (left part). As can be seen in Fig. 5, the position of the intersection point slightly fluctuates on the y -axis as frequency bandwidths change, but on average it corresponds to 14% probability. On this basis one can say that 85% of the data obtained can be assigned to the suppression and 14% to the enhancement, given that the above percentage values refer to a situation when the DPOAE level was lower than 15 dB SPL. For the DPOAE levels higher than 15 dB SPL, only suppression was observed.

3.3. Effect of contralateral noise level and three-dimensional diagrams

For the tested frequency range of stimulating primary tones, the DPOAE mean suppression increased with the increasing level of the contralateral suppressor. This relationship depended on the f_2 frequency range of the primary tone. For 1.4–2.5 kHz, the mean suppression ranged from 0.6 dB to approximately 1.2 dB for an increase of the contralateral noise level from 50 to 60 dB SPL. For a higher frequency range, the change of mean suppression was respectively lower (for 2.5–5 kHz, 0.4–0.8 dB and for 5–8.8 kHz, 0.2–0.4 dB). Suppression variability expressed by SD of the mean for two suppressor levels ranged from 0.1 dB to about 0.3 dB. Figure 6 shows three-dimensional diagrams of DPOAE mean suppression averaged across subjects. In this figure ΔDP differences are plotted as a joint function of f_2 frequencies and a ratio of DPOAEs to noise floor amplitudes (S/N ratio), for two contralateral stimulus levels (50 and 60 dB SPL) and two levels of the primary tones ($L_1 = 60$ dB SPL, $L_2 = 50$ dB SPL and $L_1 = 70$ dB SPL, $L_2 = 60$ dB SPL).

As can be seen, DPOAE mean suppression distribution is a complex function of f_2 frequency, S/N ratio and the contralateral noise level. The mean suppression at low f_2 frequency and high S/N ratio is larger than at the higher f_2 and low S/N ratio. In the range of the latter parameters, the effect of DPOAE enhancement can be seen (shaded area). The three-dimensional diagrams of DPOAE distribution highlight a complex mechanism of distortion product generation *versus* f_2 frequencies, S/N ratio and L_{sup} .

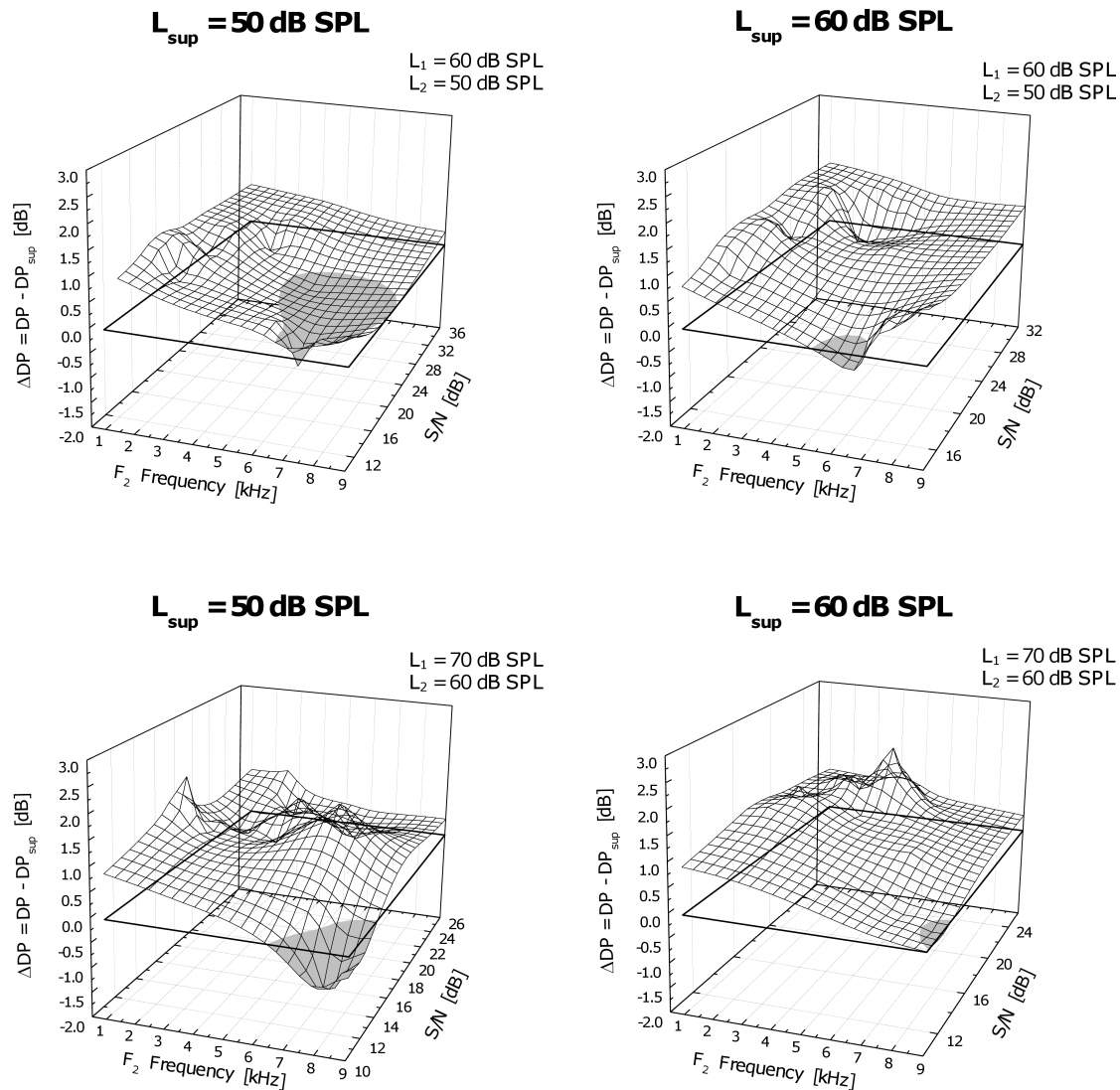


Fig. 6. DPOAE amplitude levels plotted as a function of frequency f_2 and S/N ratio, in a three-dimensional diagram. Measurements were taken at one-eighth octave steps in the range from 1.5 to 9 kHz and at two contralateral noise levels (50 and 60 dB SPL) and at two levels of stimulating primary tones ($L_1 = 60$ dB SPL, $L_2 = 50$ dB SPL and $L_1 = 70$ dB SPL, $L_2 = 60$ dB SPL). Data were fitted using a surface fitting algorithm.

4. Discussion

A quantitative estimation of the effect of contralateral noise stimulation was made in the current study by comparing the amplitude levels of the f_{DP} before and during presentation of contralateral broad-band noise. Three main findings resulted from the present study. The first one was that the f_{DP} suppression proved to be a decreasing function of the f_2 frequency for a wide frequency range of 1.4–9 kHz. The second finding was that for the f_{DP} lower than 15 dB SPL, suppression was observed in about 85% of cases, whereas DPOAE enhancement occurred in about 14% of cases. When the f_{DP} level was higher than 15 dB SPL, only suppression was observed. The third finding was that the f_{DP} suppression depended on the level of the con-

tralateral wideband noise – the higher the level, the greater the suppression.

As regards DPOAE frequency dependence, the data of the present study clearly showed that the suppression was much greater at lower f_2 , starting from 1.4 kHz, and substantially smaller at the highest frequencies (above 5 kHz). Apart from that, significant intra- and intersubject variabilities of the DPOAE contralateral effect were found for all tested subjects. At frequencies below 1.4 kHz, random variations in DPOAE level due to physiological noise prevented a reliable detection of suppression. The negative slope of this function depended on the contralateral noise level in the sense that the higher the level, the larger the slope. Additionally, the bipolar changes (suppression and enhancement) in the DPOAE level by CAS were

observed in the DPOAE *versus* frequency which enlarged the dynamic range of the DPOAE contralateral suppression.

Our data on DPOAE frequency dependence are generally consistent with the results presented in previous studies. The majority of investigators have reported DPOAE suppression during the presentation of contralateral noise in humans and amplitude level reduction in f_{DP} within the range from 1 to 4 dB, depending on the frequency tested (MOULIN *et al.*, 1993; WILLIAMS, BROWN, 1995; JAMES *et al.*, 2002; 2005; OZIMEK, WICHER, 2006; ZHANG *et al.*, 2007; SUN 2008; ABDALA *et al.*, 2009). However, the range of primary frequency changes was much narrower and chosen rather arbitrarily. It has been confirmed so far that a greater suppression occurs at the lower frequency range (CHERY-CROZE *et al.*, 1993; MOULIN *et al.*, 1993). Some other results indicated that DPOAE suppression is greater at frequencies corresponding to the peaks of the DPOAEs located within the frequency range 1–2 kHz than that corresponding to dips (ZHANG *et al.*, 2007; SUN, 2008; ABDALA *et al.*, 2009). As shown in literature, DPgram frequency resolution clearly effects changes in DPOAE level at selected points of maxima and minima. For high frequency resolution, suppression occurs more often and is larger at fine-structure maxima, whereas enhancement of level is more likely to occur near the minima (SUN, 2008; ABDALA *et al.*, 2009). Frequency dependence of the DPOAE suppression is a consequence of the MOC effects providing frequency-specific inhibitory feedback in the wide frequency region. It probably results from the fact that the firing rates of medial efferent fibers *versus* fiber characteristic frequency (CF) decreases when CF increases (LIBERMAN, 1988; GUINAN, 1996). FRANCIS and GUINAN (2010), considering the MOC effect, showed that the MOC inhibition of the click-evoked OAE amplitudes tended to be smaller at higher frequencies than at lower frequencies. This is in line with our data, which, however, refer to a broader frequency range (1–9 kHz).

As regards second finding, the data in the present study generally show that the DPOAE level measured in the contralateral presentation mode may be suppressed, enhanced, or remain almost unchanged. In a substantial majority of measurement cases (85%), DPOAE suppression was measured. However, DPOAE enhancement (14%) was also found for some frequencies and ranged from -0.1 to -3 dB. For about 1% of measurement cases, DPOAEs were almost unchanged. More cases of enhancement were observed in the higher frequency range than in the lower one. Additional information on DPOAE enhancement might be obtained from the cumulative distribution function determining the probability of the differences of the DPOAE levels without and with CAS. The point of intersection of the x -coordinate at $\Delta DP = 0.0$ dB with the

cumulative function made it possible to separate the areas of suppression and enhancement. On this basis, on average, 14% of all DPOAE level changes could be classified as enhancement. Some authors have reported that DPOAE level differences, determined by subtracting the DPOAE level recorded without CAS from the level with CAS, usually demonstrated suppression, but in some cases, at certain frequencies, manifested as enhancement (WILLIAMS, BROWN, 1997; LISOWSKA *et al.*, 2002; MULLER *et al.*, 2005; SUN, 2008; ABDALA *et al.*, 2009).

ZHANG *et al.* (2007) reported that suppression was significantly greater at the peaks than at the dips for any tested CAS level. According to SUN (2008), at the peaks of the DPgram, DPOAEs were mostly suppressed with a larger change, while those at the dips had greater variance, with increased occurrence of enhancement or no change. The fact that at the peaks mostly suppression was observed is in line with our data indicating that for high enough DPOAE peaks (above 15 dB SPL), only suppression has been measured. The difference between the peak and the dip frequencies in the DPOAE level change was significant. A switch from suppression to enhancement of the DPOAE level, or vice versa, with a small change in frequency, was noted. These results imply that DPOAE fine structure is the main source of the variability in DPOAE contralateral suppression measurement. Those studies, however, did not take into account possible frequency shifting of the deep minima in DPOAE fine structure in certain frequency regions during CAS. DPOAE fine structure is known to shift with primary-tone levels (HE, SCHMIEDT, 1993).

According to the third finding, an increase in f_{DP} suppression with higher CAS levels for a wide frequency range is observed. When the levels of the primary tones were held constant and the level of contralateral suppressor was increased from 50 to 60 dB SPL, the suppression value increased on average by 0.5 dB. This was the case for two levels of the primary tones used. The finding is consistent with previous reports that have demonstrated a similar influence of the contralateral suppressor level on OAE suppression (COLLET *et al.*, 1990; MOULIN *et al.*, 1993; ZHANG *et al.*, 2007).

It was also shown that DPOAE suppression increased as the primary-tone levels decreased. Comparing the ΔDP_{50} results given in Fig. 5 for the primary-tone levels of $L_1 = 60$ dB SPL, $L_2 = 50$ dB SPL and $L_1 = 70$ dB SPL, $L_2 = 60$ dB SPL, it can be seen that for the first two frequency bandwidths (1.4–2.5 kHz and 2.5–5 kHz), the higher the level of the primary tones, the lower the ΔDP_{50} .

Additionally, the ΔDP_{50} values were found to decrease when the f_2 frequency bandwidth increased. The primary-tone level induced suppression change is in line with the literature reports, which have shown

that suppression is proportionately greater for lower intensity stimuli than for higher ones (WILLIAMS, BROWN, 1997).

DPOAE suppression is usually discussed in the light of MOC activity. Our data generally suggest that the bigger the baseline DPOAE, the clearer the effect of suppression by the MOC system. Activating the MOC reflex system leads, firstly, to inhibiting gain of the cochlear amplifier around the $2f_1 - f_2$ position and consequently to some attenuation of the reflection component and also its phase changes. A vector sum of the two components at the ear canal may cause constructive or destructive interaction between them. Such interaction, which has such a strong effect, depends on frequency and leads to the ripple shapes of DPOAE fine structure, and accordingly to a large inter- and intra-subject variability of DPOAEs. This mechanism contributes to the complex differences in the DPOAE levels measured with or without CAS which may manifest themselves in the form of suppression or enhancement (ABDALA *et al.*, 2009).

To measure DPOAE suppression, one must ensure that the middle ear reflex (MER), which is most effective at low frequencies, does not influence the data. It is known that MER contraction, by increasing the impedance of the middle ear and changing middle-ear transmission, can have an effect on OAEs (GUINAN, 2006). Thus, the level of contralateral noise and the level of primary tones should be kept below the MER threshold. According to GELFAND and PIPER (1984), the MER threshold for broad-band noise was around 75 dB SPL. MOULIN *et al.* (1993) claimed that it was not likely that the MER could contribute to DPOAE suppression, since CAS up to 70 dB SPL could cause similar suppression in subjects with and without the MER. HENIN *et al.* (2011) showed that MER contractions were not a significant source of contamination. According to our data, the middle ear reflex could not have been involved in DPOAE suppression, since for all subjects participating in the study MER thresholds were measured and none of them exhibited a meaningful MER neither for contralateral noise stimulation nor for primary tone levels.

Another problem is whether an interaural crossover can contribute to a reduction in the DPOAE level. The interaural crossover was measured in the present study and no evidence of this phenomenon was observed. We have found no statistically significant differences $\{F(1, 88) = 1.5026, p = 0.2235\}$ between the estimates of the average noise floors in the conditions without and with CAS even at the level of 80 dB SPL. Similarly, COLLET *et al.* (1990) showed that the acoustical crossover of the contralateral noise suppressor presented at the level near 80 dB SPL may be assumed to be negligible. The acoustic crossover is fairly unlikely if an insert earphone is used, due to the 60–90 dB interaural attenuation.

Finally, it is worth commenting on discrepancies in the results of DPOAE contralateral studies found in the literature. These may be for a number of reasons. One of them is the observed variability in DPOAE level and its fine structure with stimulus parameters. A change in the frequency ratio of primaries, for example, causes complex changes in the level and phase of the cubic distortion products (ABDALA *et al.*, 2009). The reasons for these changes are not well established. Moreover, DPOAE fine structure is clearly dependent on various stimulus parameters such as level and f_2/f_1 ratio (HE, SCHMIEDT, 1993; SUN, 2008). It is also not clear how to apply DPOAE fine structure to measure the DPOAE contralateral effect since the optimal frequency resolution is not known. ABDALA *et al.* (2009) suggested recording the MOC reflex only at fine structure peak frequencies. One can expect that the higher the resolution, the more rippled and complex the DP-gram would be. Thus, the choice of the optimal parameters in the evaluation of DPOAE contralateral suppression constitutes a basic problem in the implementation of this method in clinical practice to measure the MOC function. This implementation is basically limited by the necessity of applying many discrete primary frequencies to get reliable DPOAE data. In literature (SUN, 2008; HENIN *et al.*, 2011), however, there are some suggestions for how to improve the DPOAE contralateral suppression measurement for clinical purposes to evaluate the MOC reflex effect.

Also, the temporal recording of the f_{DP} suppression may have made a contribution to the final data. As shown in this study, during the CAS onset there was a build-up of f_{DP} suppression over time, comprising differentiated transient states which were frequency and intensity dependent, until f_{DP} reduction reached a relatively fixed plateau. Such an observation implies that the suppression mechanism involves, among other things, a temporal integration process.

The following conclusions can be drawn from the present study:

- Mean suppression of the f_{DP} might be approximated by a linearly decreasing function of the f_2 frequency of primary tones. The slope of this function was negative and increased with an increase of the contralateral stimulation level.
- Suppression of the f_{DP} depended on the level of the contralateral wideband noise. The higher the contralateral noise level, the greater the suppression.
- For f_{DP} levels lower than 15 dB SPL, suppression was observed on average in about 85% of all measured cases; however, f_{DP} enhancement also occurred (in about 14% of cases on average). The value of suppression or enhancement usually fluctuated around a fraction of a dB but in extreme cases reached 2–3 dB. When the f_{DP} level was higher than 15 dB SPL, only suppression was observed.

More work is needed to determine unequivocal experimental parameters and conditions for normative measuring of the DPOAE contralateral effect. Such work will contribute to the development of a method for non-invasive clinical assessment of the olivocochlear mechanism as well as cross-brainstem functioning.

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