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Contralateral Suppression of Transient Evoked Otoacoustic Emissions: Normative Data for a Clinical Test Set-Up

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Hypothesis: Contralateral suppression of transient evoked otoacoustic emissions (TEOAEs) can be used in a clinical set-up using a procedure based on a unique and robust parameter to quantify the magnitude of suppression for a subject.
Background: TEOAEs can be suppressed by delivering contralateral white noise (WN). This suppression is thought to be mediated via the efferent nerve fibers that innervate the outer hair cells. The ipsilateral TEOAE-eliciting click stimulus level and the contralateral WN level have a strong impact on the recorded level of suppression.
Methods: TEOAEs were recorded using the nonlinear stimulation mode in two conditions (with and without contralateral WN). An optimal TEOAE-eliciting click stimulus level and contralateral WN level were defined to obtain a unique and robust parameter to quantify the magnitude of suppression.
Results: Suppression of TEOAEs with contralateral WN can be measured in a clinical set-up using nonlinear stimulation, and the level of suppression is of the same order of magnitude as measures using the linear stimulation recording mode. The level of suppression appears to be "locked" to the interaural difference between ipsilateral TEOAE-eliciting broadband click stimulus level and the contralateral WN level.
Conclusions: A procedure is proposed to record contralateral suppression in a clinical set-up, and normative data are given for a normal-hearing population (n = 60). **Key Words:** Otoacoustic emissions—Contralateral suppression—Cochlear mechanics—Outer hair cell—Efferent system.
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The level of transient evoked otoacoustic emissions (TEOAEs) was found to increase nonlinearly with increasing stimulus level and to reach saturation at high levels (1–4). This led Kemp et al. (5) to introduce the "nonlinear stimulation mode" that records only the differential nonlinear response of the cochlea. A possible loss of signal-to-noise ratio is traded for a near total elimination of meatal and probe-linked acoustic artifacts and thus insures recording of exclusive cochlear responses, which is essential for a clinical application (5). The nonlinear response is believed to result mainly from the outer cell function. These cells are innervated by efferent nerve fibers of the medial olivocochlear bundle, stimulation of which causes a slow voltage-dependent motility of the hair cells and consequently a reduction in their Ca^{++}-dependent motility (6,7). This is speculated to result in a reduction of the click-evoked response of the outer hair cells, a phenomenon that has been called *suppression of TEOAEs* (8). The efferent innervation is in part contralateral (9), and stimulation of one ear causes efferent stimulation of the contralateral ear and thus contralateral suppression of TEOAEs. Measures of this level of contralateral suppression are thought to give an indication of the status of the functioning of these efferent nerve fibers of the olivocochlear bundle (10). This test has been applied to patients with acoustic neuroma with preserved TEOAEs and to patients who underwent a vestibular nerve section; it could also become a clinical audiologic investigation tool in the evaluation of tinnitus, acoustic trauma, and hyperacusis (11–14).

The existence of contralateral suppression of TEOAEs has mainly been documented for TEOAEs that were elicited using the "linear stimulation mode" (10,15,16). The magnitude of this suppression was shown to increase with increasing contralateral noise levels and to decrease with increasing ipsilateral stimulation levels (10). These findings are consistent with reports of greater suppression of auditory nerve responses when using lower stimulation intensities (17–19).

This study had four goals:

To develop for a procedure for obtaining a unique and robust parameter that quantifies the magnitude of

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contralateral suppression for a subject in a clinical set-up
- To identify the optimal noise and stimulation level to measure contralateral suppression
- To obtain normative data using this optimal procedure for a large population with normal hearing
- To determine if the magnitude of contralateral suppression depends mainly on the stimulus level, on the suppressor level, or on the difference between both.

MATERIALS AND METHODS

Three experiments were conducted, and the methodology is described below.

Subjects

In the first experiment, TEOAEs were recorded from 30 subjects (mean age, 24±8 years; range, 11–47 years); in the second experiment from 60 subjects (mean age, 24±9 years, range, 11–52 years); and in the third experiment from 29 subjects (mean age, 21±3 years; range, 11–30 years).

All test persons had hearing thresholds better than 20 dB HL on all test frequencies (1.25 to 8 kHz in octave multiples). They also presented with normal TEOAEs to nonlinear click stimulation at 80±3 dB peak sound pressure level (SPL). This means that the signal-to-noise ratio in at least three of the four highest frequency bands (1.6, 2.4, 3.2, and 4 kHz) exceeded 6 dB. The TEOAEs were recorded in only one ear, and this side was determined at random. To obtain a certain level of arousal, all test subjects were instructed to read during the entire test (20).

Apparatus

Nonlinear clicks of 80-microsecond duration were presented routinely according to the nonlinear differential method to the test ear at peak SPL ranging from 37 to 78 dB and at a rate of 50 clicks per second through the standard probe of an Otodynamics (London, U.K.) ILO88 otoacoustic emission analyzer. Nonlinear stimulation consisted of the standard four-stimulus sets that were combined into the 260 subsets used to compute each of the two averages for buffers A and B, respectively.

All tests were performed in a sound-treated room. To keep the noise level as low as possible, the personal computer running the ILO V5.60 software (Otodynamics) was stationed outside the sound-treated booth.

White noise (WN) was generated using a Madsen (Taastrup, Denmark) OB 822 clinical audiometer and delivered to the contralateral ear through an EAR-LINK 3A insert earphone (Aearo, Indianapolis, IN, U.S.A.).

Contralateral stapedial reflexes were analyzed using a Grason Stadler (Milford, NH, U.S.A.) middle ear analyzer (GSI 1723). Acoustic reflex threshold (ART) for WN was determined using a "1-dB-up, 2-dB-down" paradigm.

Methods

In all the experiments, the TEOAEs were recorded in two conditions. The only difference between these conditions was the presence or absence of WN delivered to the contralateral ear. The level of suppression was then determined by subtracting the overall TEOAE response in the absence of WN from the TEOAE response with the WN present.

As the level of suppression was shown to depend on the ipsilateral eliciting click level (10), there was a need for some reference click level that would be applicable to all test subjects. To this end, a "TEOAE threshold" was determined for each tested ear and was defined as the emission click level (using a 3-dB step) for which the overall response level increased to just above the overall noise level while delivering WN (at 40 dB sensation level [SL]) to the contralateral ear. After this "TEOAE threshold determination," all other TEOAE-eliciting click levels were referenced to this threshold, and the dimension "dB thr" is used here to denote the number of decibels above this threshold. Suppression measures were obtained at click levels ranging from 0 to 15 dB above an individual's threshold (0 to 15 dB thr).

Experiment 1

The aim of the first experiment was to identify both the optimal WN suppressor level and the optimal click level to be used in suppression measures.

Previous work showed that the level of suppression increases as the WN suppressor level increases (10). On the other hand, the level of the WN suppressor should not be too high to avoid eliciting a contralateral acoustic stapedial reflex. Thus, the ART for the contralateral WN suppressor was determined for 30 subjects and was expressed in decibels above a person's sensation level (dB SL). The optimal suppressor level was defined as the highest level at which, statistically, less than 1% of the subjects showed contralateral acoustic reflexes.

The "TEOAE threshold" determination was performed using this optimal WN suppressor level. To determine the optimal TEOAE click level, suppression was subsequently measured using the optimal WN suppressor level and click level stimuli of 0, 3, 6, 9, 12, and 15 dB thr. The optimal TEOAE click level was derived from the normal distributions of these suppression measures at different click levels and was defined as the click level yielding the best "suppressible responses."

Experiment 2

The aim of experiment 2 was to obtain normative data for suppression of TEOAEs for a larger population (n = 60). Using the optimal WN suppressor level and the optimal click level from experiment 1 (40 dB SL suppressor level and 12 dB thr click level), a subject's TEOAE threshold was determined and suppression measured. This procedure was repeated four times, and statistical analysis was performed on the mean of these four suppression measures.

Experiment 3

The aim of the third experiment was to determine if the level of suppression depended mainly on the TEOAE click level, on the WN suppressor level, or on the difference between both. Suppression was measured in two conditions: first, using the optimal parameters from the first experiment (40 dB SL suppressor level and 12 dB thr click level) and second using a 10 dB higher suppressor level (50 dB SL) combined with a 10 dB higher click level (22 dB thr). In this way, the interaural signal-to-noise ratio was "locked" to the same level in the two conditions. This approach was adopted to evaluate the trade-off between two antagonist effects: increasing the stimulus level should decrease suppression level, while increasing the suppressor level should increase this suppression level (10). In the case that the stimulus effect should predominate the suppressor effect, one might expect the suppression level to be lower in the second condition. On the other hand, in the case that the suppressor effect should predominate the stimulus effect, one might expect suppression to be higher in the second condition. Should there be no predominance, one might expect suppression to be the same in both conditions.

Statistics

Paired *t* tests with a significance level of 0.05 were used to compare dependent data, such as the emissions with and without suppression in experiment 1 and the suppression in the two settings of experiment 3. A linear regression analysis by the least squares method was used for the correlation between the stimulus and the suppression level in experiment 1. A Shapiro-Wilk's W test with significance level at 0.05 was used to evaluate whether the data distribution of experiment 2 was normal (21).

RESULTS

Experiment 1

The mean ART for WN was 62.3 dB SL, with a standard deviation (SD) of 8.6 dB SL. The optimal safe noise level was defined such that the risk of eliciting an ART was less than 0.005. This means a level of 2.58 SDs (p = 0.005 for one-tailed evaluation) below the mean, which was in this case a level of 40 dB SL. Using this optimal noise level of 40 dB SL, the results of the level of suppression for nonrepeated measures at different TEOAE click levels are given in Table 1 and shown in Figure 1.

The optimal TEOAE click level was defined as the level that showed the statistically most pronounced suppression as evaluated by a paired *t* test. This was found to be the TEOAE click level of 12 dB thr (p= 0.046). At all other click levels the p value was less significant and exceeded 0.05.

The linear regression curve of suppression level versus TEOAE click level is also shown in Figure 1. The level of suppression shows a tendency to decrease with increasing TEOAE click level, although this negative correlation is poor and not significant.

Experiment 2

The mean suppression level for four repeated measures was determined for 60 test persons using the optimal parameters from experiment 1. The ranked test results are shown in Figure 2. Shapiro-Wilk's W test for normality showed that these data are not normally distributed ($p<0.05$). Therefore, similar to the method used in ISO 7029 for audiometric data, the statistical distribution of a subject's suppression is approximated by the halves of two normal (Gaussian) distributions (22). One half lies above the median value (the high group) and has a larger dispersion reflected by the upper SD, s_u; the other half (the lower group) lies below the median and has a smaller dispersion reflected by the lower SD, s_l.

TABLE 1. *Results from experiment 1: suppression level at different click levels (stimulus) in terms of population mean, SD, and its significance (p value) for the different TEOAE click levels*

Stimulus	0 dB thr	3 dB thr	6 dB thr	9 dB thr	12 dB thr	15 dB thr
Mean	1.85	1.76	2.02	1.62	1.69	1.43
SD	1.28	1.41	1.34	0.99	1.00	1.07
p Value	0.075	0.107	0.067	0.052	0.046	0.092

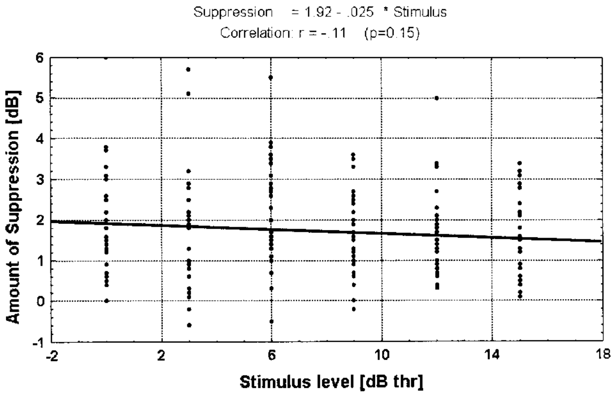

FIG. 1. Suppression amount measured at different TEOAE click levels and a linear regression function fit to these data. (For the definition of dB thr, see Materials and Methods).

The median suppression level was 1.18 dB, with an s_u of 1.16 dB and an s_l of 0.65 dB. Figure 3 shows the normal distribution functions of the halves of the two normal distributions. The percentile values of these normative data are given in Table 2 and are calculated using formula (1). Subsequently, they identify the corresponding p value in a normal distribution table.

$$\text{If } x \leq 1.18 \text{ dB then } z = (x - 1.18)/s_l$$

$$\text{If } x > 1.18 \text{ dB then } z = (x - 1.18)/s_u$$

Experiment 3

The recorded TEOAE levels with WN, without (no noise, NN), and the addition of contralateral WN are shown in Figure 4 for the two recording conditions. The corresponding suppression levels are also shown. The mean level of suppression was 1.52 dB (SD, 1.09) at a stimulus level of 12 dB thr and 1.44 dB (SD, 1.00) at a stimulus level of 22 dB thr. Paired *t*-tests showed no significant differences between these two levels of suppression (p=0.66).

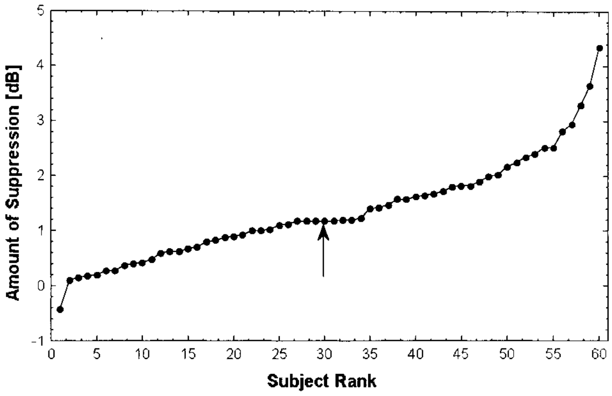

FIG. 2. Raw data from experiment 2 ranking subjects according to their amount of suppression. The arrow indicates the median value.

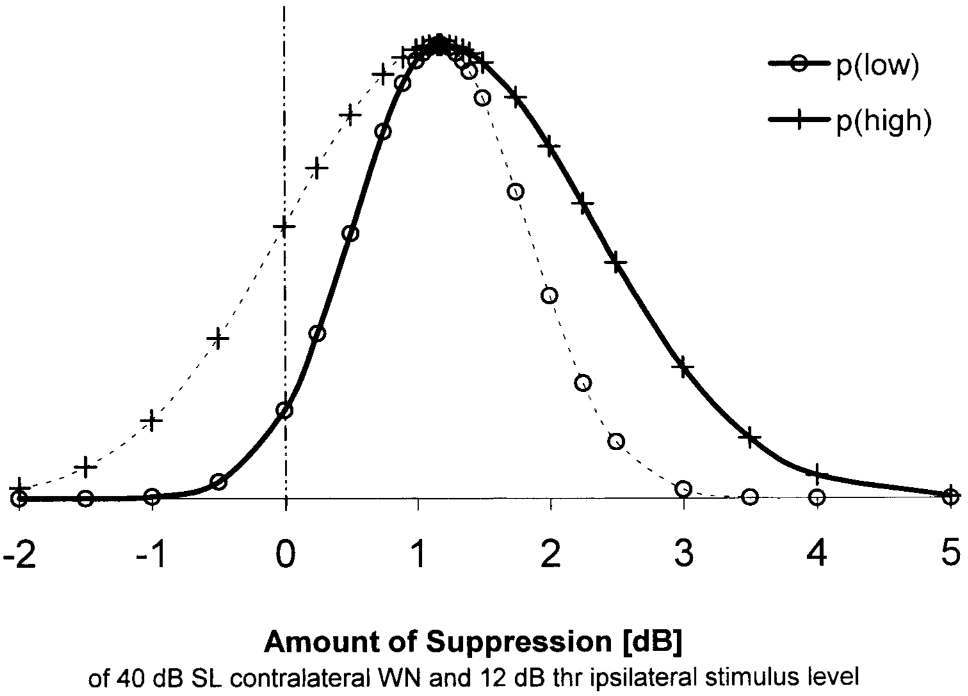

FIG. 3. Probability distribution functions for the low ("p(low)") and high ("p(high)") group. The continuous bold line combines the two complementary halves into a new asymmetric distribution.

DISCUSSION

This study showed that TEOAEs obtained with the nonlinear stimulation mode were suppressed by adding WN to the contralateral ear. This mode of recording was selected because it ensured a near total elimination of meatal and probe-related acoustic artifacts, which is essential in clinical applications.

Two major observations make it difficult to obtain a single robust test parameter to express the level of suppression:

The level of suppression is thought to depend on the TEOAE click stimulus level, i.e., suppression has been shown to be higher at lower click levels (10,23).

A given TEOAE stimulus level yields different TEOAE responses in different individuals. This intersubject variability is in consequence reflected in the level of suppression (23).

TABLE 2. *Normative data for the percentile values of suppression level for a click level of 12 dB thr and a contralateral white noise at 40 dB SL calculated using formula (1)*

Percentile	Suppression level (dB)
1	−0.35
5	0.10
10	0.34
20	0.63
30	0.83
40	1.01
50	1.18
60	1.47
70	1.79
80	2.15
90	2.67
95	3.09
99	3.89

To overcome these difficulties, the current study defined a "TEOAE threshold" for each individual ("0 dB thr") and set the individual stimulus level in reference to this threshold. The threshold was determined in the presence of 40 dB SL WN, which has been shown to be the optimal suppressor level. Likely, using this reference stimulus, suppression will always be measured at the same point of operation of the outer hair cells.

In the first experiment, the optimal measurement parameters were determined. A combination of a WN suppressor of 40 dB SL and a TEOAE click level of 12 dB thr appeared to be the best condition for subsequent suppression measures. Linear regression statistics on the level of suppression versus the TEOAE click level failed to show a significant (negative) correlation. There is, however, evidence of a negative correlation between suppression level and click level, as has been shown by Veuillet et al. (10) for linear stimulation.

Using these optimal recording parameters, normative data were obtained for a group of 60 normal-hearing subjects. The median suppression level of 1.18 dB is of the same order of magnitude as those obtained in other comparable studies using the linear stimulation mode (12,23). This result means that the "suppressible" part of

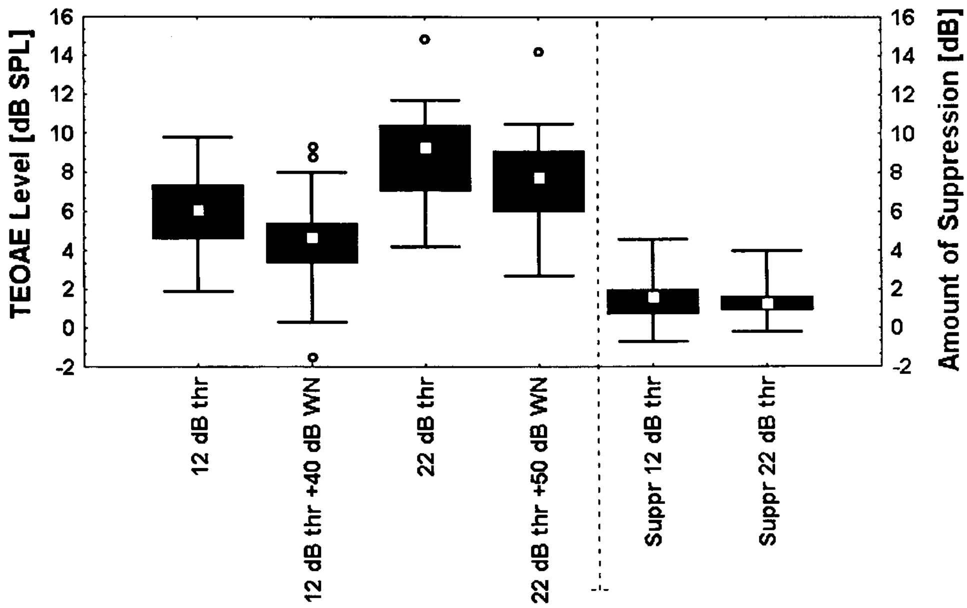

FIG. 4. Box and whisker plots representing the results of experiment 3. Bars: minimum to maximum; large rectangles: 25% to 75%; small white squares: median values; black open dots: outliers. The first four variables show the TEOAE responses (left Y-axis) of the four different test conditions, i.e., a stimulus of 12 and 22 dB thr in the absence and presence of a contralateral WN locked at 28-dB interaural difference. The last two variables represent the calculated amount of suppression (right Y-axis) at the two stimulus levels (12 and 22 dB thr).

the TEOAE probably lies mainly within its nonlinear characteristic part.

From the last experiment, it can be inferred that the level of suppression mainly depends on the difference between the WN suppressor level and the TEOAE click level. Suppression seems to be "locked" to a certain level when the ipsilateral TEOAE click level and the contralateral WN suppressor level are varied to the same extent. It appears that only the interaural difference between ipsilateral stimulus and contralateral suppressor levels determines the level of suppression.

Considering these results, the following clinical test procedure for measuring the suppression level of TEOAEs by contralateral WN can be proposed:

Determine the subject's threshold for the WN suppressor in the contralateral ear (0 dB SL WN).

Determine the subjects "TEOAE threshold" ("0 dB thr") by delivering a 40 dB SL WN in the contralateral ear and identifying the ipsilateral TEOAE click level for which the TEOAE just increases above the noise level (>A-B). The click level (gain) is varied with a 3-dB step.

Set the TEOAE click level to 12 dB above the TEOAE threshold (12 dB thr) and obtain four TEOAE recordings with and four without contralateral WN (random order).

Compute the suppression level by averaging the difference between four paired recordings (with and without WN).

Determine the corresponding percentile value based on formula (1).

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