

Jutta Roede^a
Frances P. Harris^b
Rudolf Probst^b
Li Xu^b

Repeatability of Distortion Product Otoacoustic Emissions in Normally Hearing Humans

^a Department of
Otorhinolaryngology,
Regensburg, FRG;

^b Department of
Otorhinolaryngology,
Kantonsspital Basel, Switzerland

Abstract

Distortion product otoacoustic emissions (DPOAEs) at the frequency of $2f_1 - f_2$ were measured in one or both ears of 12 young adults during 4 test sessions over a 6-week period. The purpose was to determine the variability in DPOAE amplitudes and 'detection thresholds' over repeated measurements using a computer-based time-averaging system. DPOAEs were generated with f_1 and f_2 relative to $(f_1 f_2)^{1/2}$ in two basic paradigms: (a) fixed levels of $L_1 = L_2$ of 70 and 55 dB SPL over a stimulus range from 0.8 to 8 kHz in 0.2-octave intervals; (b) input-output functions in stimulus regions of 0.8, 1, 1.5, 2, 3, 4 and 6 kHz, L_1 from 35 to 70 dB SPL changing in 5-dB steps and L_2 at 6 dB below the amplitude of L_1 . The mean variability of DPOAE amplitudes with equilevel stimuli was 1.8 dB (SD = 1.8) for $L_1 = 70$ dB SPL and 2.9 dB (SD = 2.7) for $L_1 = 55$ dB SPL. It was 1.7 dB (SD = 1.7) and 2.4 dB (SD = 2.0) for comparable levels of L_1 with L_2 at 6 dB below L_1 . Variability in amplitude of the DPOAEs for the fixed-level condition was greatest overall above 6 kHz and below 1 kHz and in the 2-kHz region for one third of the subjects. Neither individual differences in emission amplitudes nor the presence of spontaneous otoacoustic emissions had a significant influence on the amount of amplitude variability within ears. Variability was not influenced by the length of time between measurements from 1 to 6 weeks. Median variability in detection threshold was from 0 to 5 dB SPL. According to these results, a change in DPOAE amplitude of more than 6-9 dB, depending upon stimulus levels, would indicate a significant change in cochlear status if recording conditions and middle-ear status are stable.

Key Words

Otoacoustic emission
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Dr. Frances P. Harris
Research Scientist
HNO-Klinik
Kantonsspital Basel
CH-4031 Basel (Switzerland)

Introduction

Since the discovery of otoacoustic emissions by Kemp [1] in 1978, the possibility of their use for clinical applications has been increasingly recognized. Transiently evoked otoacoustic emissions (TEOAEs) are already established as a screening method in pediatric audiology [2-4]. Distortion product otoacoustic emissions (DPOAEs) are still undergoing evaluation for clinical use. These emissions can be measured over a broader frequency range than TEOAEs when measured with current techniques and instrumentation. Acoustic distortion products result from the nonlinearity of the cochlea, and it is likely that the outer hair cells are involved in their generation [5, 6]. Stimulating the cochlea with two pure tones at frequencies f_1 and f_2 leads to the generation of intermodulation distortion. The frequency $2f_1 - f_2$ is the most prominent component that can be detected in almost all normally hearing humans [7]. Although there is high intersubject variability in DPOAE amplitudes and frequency dispersion, these emissions are stable over time within individual ears [8, 9]. Results from animal studies using manipulations known to damage outer hair cells, such as chronic noise exposure, drug administration and acoustic trauma, have revealed that DPOAEs are reduced in amplitude or can no longer be measured following such manipulations [for a review, see 7]. Because of the dependence of DPOAEs on cochlear integrity, their measurement should be well suited as an objective method for monitoring cochlear function. However, towards this end, it is important to determine the amount of variability of DPOAEs when repeated measurements are made in human ears with normal hearing. The purpose of this investigation was to assess the amount of this variability over a 6-week period when using an automatic, computer-based system used for making routine measurements.

Methods

Six women and 6 men (mean age: 26.3 years) who were in good general health were paid to participate as subjects. Ears were selected for repeated measurements of DPOAEs if they had normal middle-ear status by otoscopy and immittance procedures and if pure-tone air conduction thresholds were ≤ 20 dB HL from 0.5 to 8 kHz. Twelve right and 10 left ears were included. Two left ears were excluded: one did not meet the audiometric test criteria at one frequency, and test results for the other could not be used because of technical difficulties during one session. Subjects were tested during 4 sessions separated by 1-week intervals for the first 3 sessions and by a 4-week interval for the last test session. They were seated comfortably in a sound-treated room during measurements.

DPOAEs were generated using two main conditions. In the first, L_1 and L_2 were equal in level and were fixed at either 70 or 55 dB SPL. The geometric mean of f_1 and f_2 was at frequencies between 0.8 and 8 kHz ($f_2/f_1 = 1.21$ [10]) and changed in 0.2-octave steps. In the second condition, input-output (I/O) functions were generated at geometric mean frequencies of 0.8, 1, 1.5, 2, 3, 4 and 6 kHz ($f_2/f_1 = 1.22$) and $L_1 = L_2 + 6$ dB SPL. Stimulus levels were decreased in 5-dB steps from $L_1 = 70$ to 35 dB SPL for each stimulus frequency region. Spontaneous otoacoustic emissions were measured in the first test session according to methods described previously [11].

A computer-based system (Macintosh IIfx) was used for DPOAE measurements. Stimuli at f_1 and f_2 were generated digitally by a two-channel 16-bit processor board (Audiomedia) and were delivered separately to two ER-2 (Etymotic Research) earphones. These were connected to an ER-10A probe system, which was placed securely in the subject's outer ear canal using a foam eartip. The ear canal sound pressure was recorded by the probe's microphone system, and the signal was led to an ER-72 preamplifier followed by a custom-built low-noise amplifier with 10 dB of additional gain and a high-pass filter with a cut-off frequency of 400 Hz. The amplified microphone signal was fed to the analog/digital board within the computer. The signals were time averaged for 65 samples with stimuli at 0.8 and 1 kHz and for 32 samples for the other frequencies. A noise rejection feature was used to eliminate any responses that occurred during noise that exceeded a reference criterion level. The initial reference noise floor level was determined at the beginning of a test series by taking 3 samples of the noise and setting the reference level at the lowest of the 3 samples. When the noise floor exceeded the reference

level by 6 dB during measurements, then the sample was rejected. Measurements then continued successively until the criteria were satisfied. Samples of the level of the noise floor were continuously revised during testing to account for reductions in noise level with increasing frequency. Probe fit was monitored throughout testing by observing a running display of the spectrum of the bitonal stimuli.

Five measurement intervals were used for comparison of response parameters: 1 week (test 1 → test 2, test 2 → test 3), 2 weeks (test 1 → test 3), 4 weeks (test 3 → test 4), 5 weeks (test 2 → test 4) and 6 weeks (test 1 → test 4). With the time-averaging system as described, it was determined that a response was present if its amplitude exceeded the noise floor by 6 dB. Therefore, only levels of $2f_1 - f_2$ meeting this criterion were analyzed. For the I/O functions, the last stimulus level resulting in a criterion response was designated as the 'detection threshold' of the response series. Amplitudes of the responses and detection thresholds from the I/O functions were evaluated.

Results

DPOAEs could be recorded from all ears during each test session; however, responses were not always present for the lowest levels used to generate the I/O functions. The mean DPOAE amplitude for the 17 frequencies measured with $L_1 = L_2 = 70$ dB SPL was 9 dB SPL (SD = 5.9), and for stimuli at 55 dB SPL it was -2.6 dB SPL (SD = 6.7) for the right ears. Mean DPOAE amplitudes for the left ears were lower: 7.5 dB SPL (SD = 5.6) and -4.6 dB SPL (SD = 6.1) for the stimulus conditions of 70 and 55 dB SPL, respectively. The differences in mean amplitude of responses from right and left ears were not significant (t test, $p < 0.05$). Amplitude maxima appeared in the frequency regions of 1.5 and 5–8 kHz. Figure 1 displays the mean DPOAE amplitudes across frequency for the two fixed stimulus levels for the right ears. For the I/O functions, the mean DPOAE amplitudes for comparable levels of L_1 were 10.4 dB SPL (SD = 5.1) and -1.3 dB SPL (SD = 6.5) for the right side and 9.2 dB SPL (SD = 5.8) and -3.3 dB SPL (SD = 6.5) for the

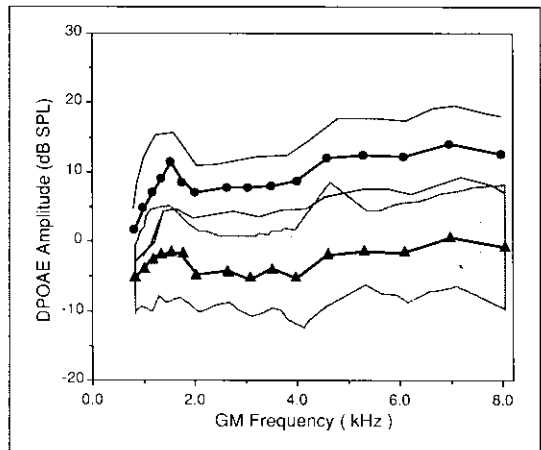


Fig. 1. Mean DPOAE amplitude (± 1 SD) for 16 frequencies with fixed levels of L_1 and L_2 . The solid lines with symbols represent the responses for $L_1 = L_2 = 70$ dB SPL (\bullet) and for $L_1 = L_2 = 55$ dB SPL (\blacktriangle). The solid lines without symbols (upper curve) and shaded area (lower curve) represent ± 1 SD for the conditions of 70 and 55 dB SPL, respectively ($n = 12$ right ears). GM = geometric mean.

left side, for stimuli of 70 and 55 dB SPL, respectively. Because there were no significant differences in inter- and intra-subject variability between the right and left ears for the majority of the parameters considered, the results for the right ears are presented primarily.

Some subjects had markedly greater variability than did others. The range of individual mean variability in DPOAE amplitudes over all frequencies measured with stimuli at $L_1 = L_2 = 70$ dB SPL was from 0.8 to 3.3 dB and for $L_1 = L_2 = 55$ dB SPL from 1.8 to 4.4 dB. The individual results in figures 2 and 3 for the fixed-level condition illustrate these extremes. The results from the subject with the most variability are displayed in figure 2, and the least variable results are reproduced as figure 3. Both of these results are from the right ear of female subjects who had spontaneous otoacoustic emissions in both ears. In addition to demonstrating individual differences, the results

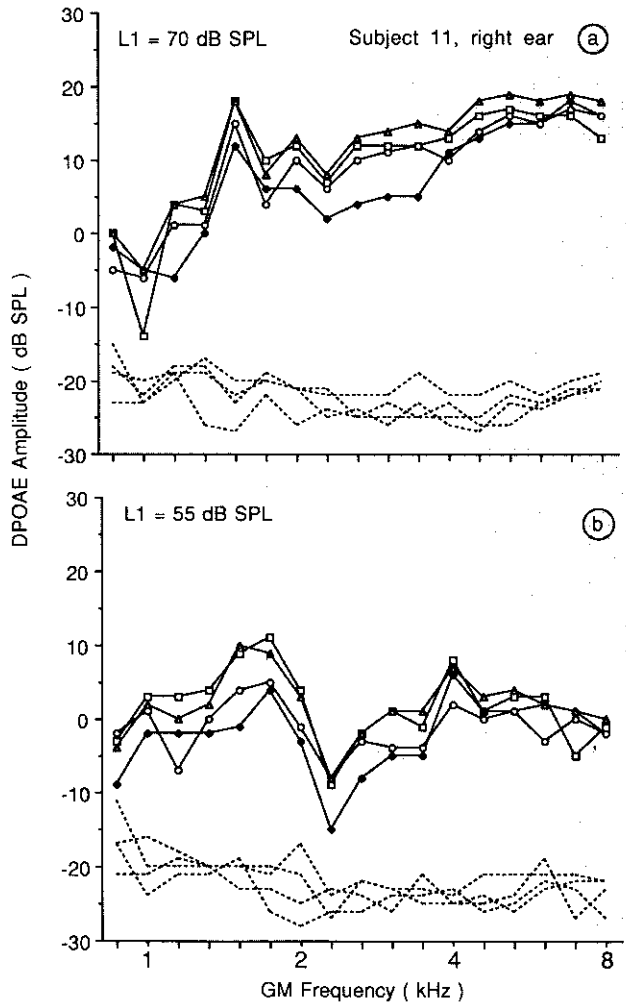


Fig. 2. Four measurements of DPOAEs for the subject with the greatest amount of amplitude variability. GM = Geometric mean. The solid lines with symbols represent the responses by frequency: \square = measurement 1; \blacklozenge = measurement 2; \circ = measurement 3; \triangle = measurement 4. The dotted lines represent the noise floor: $L_1 = L_2 = 70$ dB SPL (a), $L_1 = L_2 = 55$ dB SPL (b).

in figure 3 also illustrate the overall finding of greater variability for the lower stimulus levels and for the extreme low and high stimulus frequency regions. Overall, there was more variation in DPOAE amplitudes at frequencies below 1 kHz and above 6 kHz than for frequencies in the midfrequency region. However, greater variability around 2 kHz was noted in about one third of the subjects. This variability increased at lower stimulus levels. Despite the variations in amplitude, the overall

shapes of the curves were generally reproduced with great accuracy, as figures 2 and 3 illustrate.

Overall variability was determined by averaging the amplitude differences between successive measurements. The amount of this variability was not influenced by the length of time between measurements. However, there were differences as a function of the levels of the stimuli. Both of these trends can be appreciated by the results displayed in figure 4. With

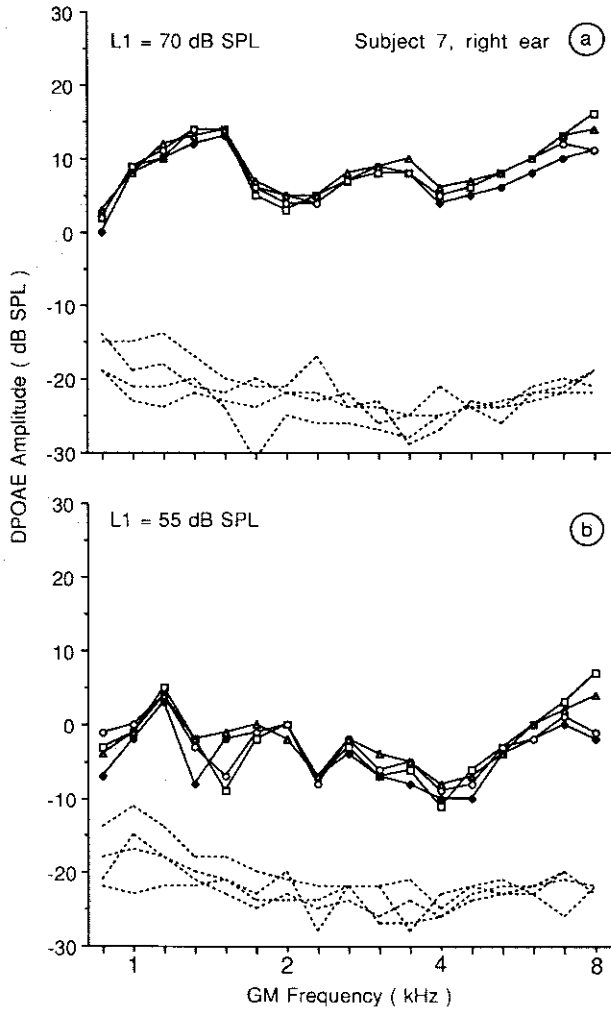


Fig. 3. Four measurements of DPOAEs for a subject with minimal variability in emission levels. GM = Geometric mean. The solid lines with symbols represent the responses by frequency. The symbols are the same as those described for figure 2. The dotted lines represent the noise floor: $L_1 = L_2 = 70$ dB SPL (a), $L_1 = L_2 = 55$ dB SPL (b).

fixed levels of either 70 or 55 dB SPL for L_1 and L_2 , the mean variability for the right ears over all measurement intervals was 1.1 dB greater for $L_1 = L_2 = 55$ dB SPL than for the stimuli of 70 dB SPL. The left side revealed the same trend with a 0.9-dB difference of mean variability between low and high stimulus conditions. Changes in variability as a function of stimulus level were also found for the I/O functions. For comparable stimulus levels of $L_1 = 70$ and 55 dB SPL ($L_2 = 64$ and 49

dB SPL), the mean variability for the right ears was 1.7 and 2.4 dB and for the left side 1.9 and 2.4 dB, respectively. As stimulus levels were reduced below 55 dB SPL, the trend for greater variability continued, as illustrated by the results for the right ears displayed in figure 5. The number of responses available for making these determinations decreased as the stimulus level decreased. Therefore, sufficient data were not available for $L_1 = 35$ dB SPL to obtain valid estimates of variability.

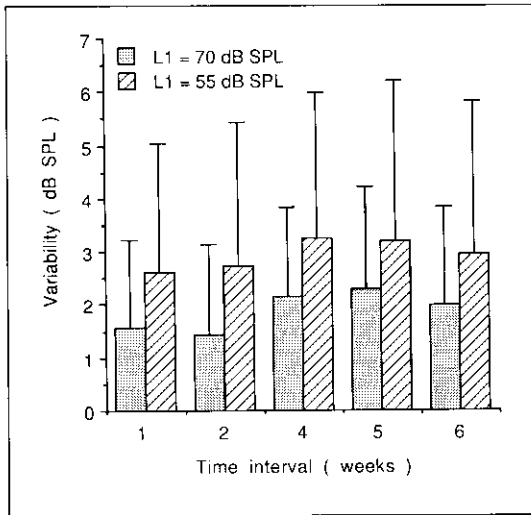


Fig. 4. Mean variability of the DPOAE response amplitudes with respect to the two fixed primary-tone levels over 6 measurement intervals. Error bars indicate 1 SD.

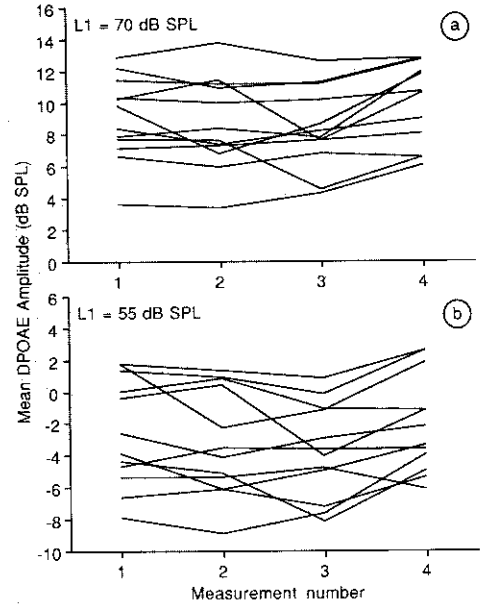


Fig. 6. Mean response levels obtained from 12 right ears during each of the 4 test days: $L_1 = L_2 = 70$ dB SPL (a), $L_1 = L_2 = 55$ dB SPL (b).

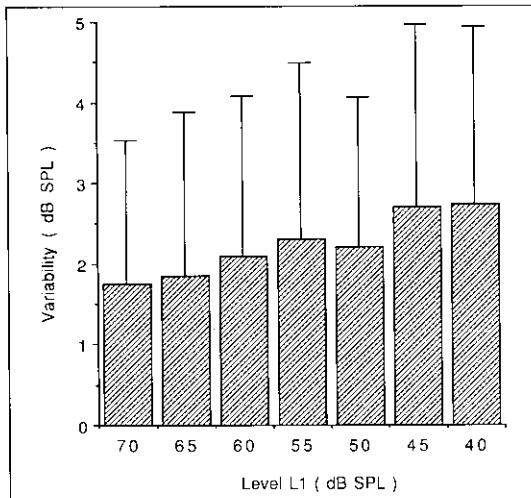


Fig. 5. Mean variability of the I/O functions with respect to stimulus levels from $L_1 = 70$ dB SPL to $L_1 = 40$ dB SPL in 5-dB steps. L_2 was 6 dB lower in level than L_1 ($n = 12$ right ears). Error bars indicate 1 SD.

Despite the influence of stimulus level on DPOAE amplitude variability, the variability was largely independent of the absolute amplitude of DPOAEs in individual ears. Figure 6 illustrates this finding from the mean DPOAE amplitudes for the fixed-level condition for all right ears. Mean results for each test session for each ear are plotted.

Changes that occurred in the overall configuration of the I/O functions were considered as either parallel or nonparallel in form. A shift was considered as parallel if an entire function moved either upward or downward from the reference function. That is, the general pattern of the function did not change, but the relative levels of the entire function were shifted. Nonparallel shifts were those that had inconsistent differences in levels over the course of the function. Parallel shifts were

identified in 85 of the 432 (6 frequencies, 12 ears, 6 comparisons) possible comparisons (20%). Nonparallel shifts occurred in 56% of the comparisons, and 24% had essentially no change in the overall configuration of the I/O functions. Variability in the DPOAE detection thresholds determined from the I/O functions was also evaluated. The median detection threshold variability was from 0 to 5 dB across frequency. However, individual detection threshold variation of 15–20 dB was present in 16 (4%; 14 had 15-dB, 2 had 20-dB differences) of the 432 comparisons of the measurements from the right ears. The amount of variation in amplitude, configuration or detection threshold did not vary significantly with stimulus frequency region.

Discussion

TEOAE measurements are used clinically as an addition to traditional audiological screening and monitoring methods. These emissions are stable in frequency composition and in amplitude over time with overall response levels varying approximately by 2.0 dB [12]. The clinical use of DPOAEs is not yet as established as that of TEOAEs. However, there are indications that the measurement of DPOAEs may provide specific advantages as a clinical test. The purpose of this study was to investigate the test repeatability of DPOAE measurements in normally hearing human ears.

The spectral patterns and amplitudes of the DPOAEs obtained in this study were similar to those reported in other comprehensive investigations of DPOAE amplitudes in normally hearing subjects [13]. DPOAEs could be recorded from all ears during each measurement session for the majority of stimuli. Within individual ears, DPOAEs were relatively stable across the four measurements

obtained at time intervals from 1 to 6 weeks. Variability was dependent on the stimulus level but not on the absolute amplitude of the DPOAE. Reduction of primary-tone amplitudes from 70 to 55 dB SPL ($L_1 = L_2$) resulted in an increase in variability of approximately 1 dB. The same trend was found when L_1 was 6 dB greater in amplitude than L_2 although the amount of variation was smaller. For this level condition, decreasing L_1 from 70 to 55 dB SPL led to an increase in mean variability of 0.7 dB and reducing L_1 to 40 dB SPL did not increase mean variability more than 1 dB. Therefore, the stimulus configuration $L_1 > L_2$ ($L_1 = L_2 + 6$ dB), which was used for generating the I/O functions, was associated with less variability than the $L_1 = L_2$ condition. It has been found previously that the stimulus configuration $L_1 > L_2$ elicits higher DPOAE amplitudes [14]. However, the individual differences in DPOAE amplitudes at fixed stimulus levels did not influence the test-retest variability significantly in this study. Therefore, even patients with low response levels can be monitored for clinical purposes.

In addition to amplitude differences, I/O functions were evaluated for morphologic changes (including the parameter 'detection threshold') over the 4 test sessions. Both parallel and nonparallel shifts occurred in the I/O functions with repeated measures. However, random irregularities were more common than were 'parallel' shifts. Influences of the instrumentation, including the placement of the probe, would be more likely to account for the 'parallel' changes than the test-retest differences in the cochlea. Median DPOAE detection threshold variability ranged from 0 to 5 dB across all frequencies. However, in a few ears, detection threshold changes of up to 20 dB were present for single frequencies from one test to another. As reported previously, DPOAE detection threshold tends to correspond more closely than do other parameters

with pure-tone threshold by frequency [15–17]. Therefore, although the detection threshold parameter was not highly variable for the majority of ears in this study, the few large deviations that were present should be considered when interpreting changes in clinical test findings. Careful testing with control for noise and probe placement should reduce this variability to a minimum.

The frequency region of the stimuli influenced the amount of variability in response amplitude. DPOAEs stimulated at 6–8 kHz had more variability than did those generated at lower frequencies. Ideally, a measuring system should be capable of detecting DPOAEs adequately in the entire audiofrequency range. However, the system used in this study probably had less than ideal sensitivity above 6 kHz. The increase in variability for one third of the subjects in the 2-kHz region was probably not related to the measuring system. This frequency region is known to have decreased response levels for reasons that are not yet fully understood [13]. The relatively large amount of variability at frequencies below 1 kHz was probably due to the greater influence of noise in this frequency region.

Measurement variability may be influenced by several factors external to the cochlea including middle-ear status, external and internal noise levels and instrumentation. Middle-ear influences, such as pressure changes or fluid, will alter the low- and mid-frequency components of the responses primarily and will have less effect on the high frequencies [18]. Changes in test procedure, instrumentation and environment can also lead to measurement differences. These factors were controlled in several ways in this study. A strict noise rejection level was used routinely. Probe fitting was monitored throughout testing. To determine the importance of probe fitting, measurements at fixed stimulus levels were made without replacing the probe during

4 repeated measurements for 2 subjects. Without probe replacement the mean variability in amplitude over all stimulus conditions was <1 dB.

It might be expected that spontaneous otoacoustic emissions would influence variability. However, this was not the case in our results. Subjects with and without spontaneous otoacoustic emissions did not differ significantly in the amount of variability in their responses. The finding of frequency stability of spontaneous otoacoustic emissions [7] may be important in this respect.

The $2f_1 - f_2$ DPOAE can be detected easily in an objective and noninvasive manner in almost all normally hearing human ears. Emission levels are relatively stable over time. In our study, the mean changes in amplitude of $2f_1 - f_2$ with repeated measurements over several time intervals were 1.8 dB (SD = 1.8) with stimuli at 70 dB SPL and 2.9 dB (SD = 2.7) with stimuli at 55 dB SPL for right ears. Under relatively stable test conditions and with removal and replacement of the probe, changes exceeding 5.4 dB (mean + 2 SD) for 70 and 8.3 dB (mean + 2 SD) for 55 dB SPL stimulus levels can be interpreted as due to clinically relevant changes within the cochlea. This variability is higher than determined previously for TEOAEs [12]. However, the measurement of DPOAEs can offer a method of monitoring cochlear status over a range of frequencies approximately an octave higher than is currently possible with TEOAEs.

La reproductibilité des produits de distorsion des émissions otoacoustiques chez les sujets humains à audition normale

Les produits de distorsion des émissions otoacoustiques (PDEOAs) à la fréquence de $2f_1 - f_2$ ont été mesurés dans une des deux oreilles de 12 jeunes adultes lors de 4 sessions pendant une période de 6 semaines. Le but de l'étude était de déterminer la variabilité des amplitudes des PDEOAs et les seuils de détection par des mesures répétées, en utilisant un système informatisé de moyennage. Les PDEOAs étaient générées avec f_1 et f_2 par rapport à $(f_1 f_2)^{1/2}$ dans deux protocoles principaux: (a) niveaux fixes $L_1 = L_2$ de 70 et 55 dB SPL sur une gamme de stimulations de 0,8 à 8 kHz par pas de 0,2-octave; (b) fonctions d'entrée/sortie dans les régions de 0,8, 1, 1,5, 2, 3, 4 et 6 kHz, L_1 de 35-70 dB SPL par pas de 5 dB, et L_2 à 6 dB en dessous de l'amplitude de L_1 . La variabilité moyenne des amplitudes des

PDEOAs avec des stimuli de même intensité était de 1,8 dB (c.t. = 1,8) pour $L_1 = 70$ dB SPL et 2,9 dB (e.t. = 2,7) pour $L_1 = 55$ dB SPL. Elle était de 1,7 dB (e.t. = 1,7) et 2,4 dB (e.t. = 2,0) pour des niveaux comparables de L_1 avec L_2 6 dB en dessous de L_1 . La variabilité dans les amplitudes des PDEOAs pour la condition niveaux fixes était plus grande au-dessus de 6 kHz et au-dessous de 1 kHz et dans la région de 2 kHz pour un tiers des sujets. Ni les différences individuelles dans l'amplitude des émissions ni la présence d'émissions otoacoustiques spontanées n'avaient d'influence significative sur l'importance de la variabilité de l'amplitude dans une même oreille. La variabilité n'était pas influencée par la durée de l'intervalle entre les mesures de 1-6 semaines. La médiane de la variabilité du seuil de détection était de 0 à 5 dB SPL. En fonction de ces résultats, une variation de l'amplitude des PDEOAs de plus de 6-9 dB, en fonction du niveau de stimulation, pourrait indiquer une modification significative de l'état de la cochlée, si les conditions d'enregistrement et l'état de l'oreille moyenne sont stables.

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