Adaptation of Distortion Product Otoacoustic Emission in Humans

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ABSTRACT

Previous studies of animals observed a phenomenon of adaptation of distortion product otoacoustic emission (DPOAE) and found that the phenomenon was mediated to a large extent by the medial olivocochlear (MOC) reflex. The present study investigated DPOAE adaptation in humans. The following stimuli were used: $f_2/f_1 = 1.2$; $f_2 = 2, 4$, or 5.65 kHz; $L_2 = 50$ – 65 dB SPL re $20 \mu\text{Pa}$ rms, $L_1 - L_2 = 0$ – 15 dB, where L_1 and L_2 represent levels of the f_1 and f_2 tones, respectively; duration of two-tone burst = 5.5 s; interburst gap = 20 or 30 s; number of repetitions = 40 or 64 . We analyzed the $2f_1 - f_2$ DPOAE as a function of time using a method of heterodyne envelope detection. The subjects were 20 humans aged from 15 to 54 years (median = 21 years) with normal hearing. We observed that (1) humans exhibited DPOAE adaptation phenomenon; (2) the time course of DPOAE level was characterized by a 2-exponential function; (3) distributions of the fast and slow time constants were well separated with their median values being 69 ms and 1.51 s, respectively; (4) distributions of the magnitudes of the fast and slow adaptation components were largely overlapped with their median values being 0.65 and 0.40 dB, respectively; and (5) the combined magnitude of the adaptation ranged from 0.4 to 3.0 dB with a median of 1.10 dB. To our knowledge, the present study is the first published article to describe adaptation of DPOAE in humans. These

results should help advance the basic knowledge of human cochlear mechanics operating under the control of the MOC feedback system and contribute to the development of practical applications such as identifying people at high risk of acoustical injury and a clinical test of the functional status of the MOC system.

Keywords: olivocochlear, efferent, reflex, feedback, cochlear mechanics, auditory, hearing

INTRODUCTION

Medial olivocochlear (MOC) neurons in the brain stem make descending projections onto outer hair cells (OHCs) of the cochlea, forming a feedback or reflex system (e.g., Warr and Guinan 1979). The MOC system is believed to influence the mechanics of OHCs mechanically because activation of the efferent system was found to produce changes in distortion product otoacoustic emissions (DPOAEs), a mechanical signal (Mountain 1980; Siegel and Kim 1982). This notion is consistent with the subsequent finding that OHCs are electromotile (Brownell et al. 1985; Zenner et al. 1985) and thus potentially able to influence the mechanics of the cochlea, as has been postulated theoretically in “cochlear amplifier” models (e.g., Davis 1983; Neely and Kim 1983).

Effects of the MOC acoustic reflex have often been demonstrated with changes in various measures of cochlear responses produced by contralateral stimulation (e.g., Buño 1978; Warren and Liberman 1989; Folsom and Owsley 1987; Collet et al. 1990), including a change in DPOAE by contralateral stimulation (Puel and Rebillard 1990; Kujawa et al 1993; Moulin et al.

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1993; Williams and Brown 1995; Puria et al. 1996). The contralateral influences were eliminated when the olivocochlear bundle was transected (Warren and Liberman 1989; Puel and Rebillard 1990; Liberman 1990).

Recently, a method has been introduced to observe an ipsilateral effect of the MOC-system reflex on DPOAE. Liberman et al. (1996) observed a phenomenon of adaptation of DPOAE in cats where the $2f_1 - f_2$ DPOAE level changed gradually over several seconds after the onset of the primary stimulus tones. This phenomenon was interpreted to be mediated mainly by the MOC system (further discussed in the Discussion section). The ipsilateral effect of the MOC reflex is an inherent, inseparable part of the response of the cochlea–brain-stem feedback system which comprises the cochlea, cochlear nucleus, and MOC neurons. Whenever the cochlea–brain-stem system of an animal (or a human) is acoustically stimulated, the ipsilateral reflex of the MOC system is potentially activated.

The phenomenon of DPOAE adaptation has subsequently been observed in other animal species, i.e., guinea pigs, mice, and gerbils (Kujawa and Liberman 1998; Sun and Kim 1999; McGee et al. 2000). Investigation of this phenomenon in humans should be helpful in (1) advancing basic knowledge of the dynamics of the human cochlea–brain-stem feedback system; (2) contributing to the development of methods of practical applications such as prediction of vulnerability to acoustical injury and a noninvasive clinical test of the functional status of MOC neurons in the human brain stem. The goals of the present study were (1) to determine whether humans exhibit the phenomenon of DPOAE adaptation and (2) to determine time constants and magnitudes of DPOAE adaptation in humans. Early results of this study were reported by Neely et al. (1999) and Kim et al. (2000).

METHODS

Subjects

Responses of 24 ears of 20 normal-hearing human subjects were examined in this study. All subjects had auditory thresholds less than or equal to 20 dB HL for octave frequencies from 500–800 Hz. The subjects did not have a history of exposure to noise, ototoxic medications, middle ear pathology, or ear surgery. For 10 subjects, middle-ear function was determined to be normal by standard tympanometry on the day of the DPOAE recording. The ages of the subjects were from 15 to 54 years (median = 21 years).

Stimulus

The following two-tone stimuli were used: $f_2 = 2, 4$, or 5.65 kHz; $f_2/f_1 = 1.2$; $L_2 = 50$ –65 dB SPL re 20 μ Pa rms, $L_1 - L_2 = 0$ –15 dB, where L_1 and L_2 represent levels of the f_1 and f_2 tones, respectively; duration of two-tone burst = 5.5 s; interburst gap = 20 or 30 s; number of repetitions = 40 or 64; sample rate = 48 kHz. The stimulus waveform was smoothly gated on and off over 10-ms rise–fall times by multiplying the stimulus waveform with a raised-cosine function.

Analysis of DPOAE level and phase versus time

A time-domain averaging of the ear-canal pressure waveform (duration = 5.5 s) was performed with a sample rate of 48 kHz. Initially, we performed a fast Fourier transform (FFT) of the complete pressure waveform, 262144 points representing 5.5 s. We obtained the magnitude and phase of the DPOAE component as a function of time as follows. We selected a band of (positive) frequencies surrounding a particular DPOAE frequency and shifted these frequency components down such that the DPOAE frequency was positioned at the zero frequency. A Blackman-shaped low-pass filter extending ± 120 Hz around the zero frequency was applied to the shifted spectrum. Then an inverse FFT was performed. The result was a complex-valued signal spanning the duration of the original waveform. This signal represents the magnitude and phase of the DPOAE component as a function of time. The magnitude-versus-time function, in this case, corresponds to the temporal “envelope” of the DPOAE component (e.g., Oppenheim and Shafer 1975, p. 361), sometimes called a “Hilbert” envelope.

The magnitude and phase of the DPOAE component obtained by the present method represent an analytic signal. An analytic signal has the property that its Fourier transform is zero for “negative” frequencies (e.g., Oppenheim and Shafer 1975, p. 358). Instead of computing the analytic signal directly by zeroing the negative frequency components, we heterodyned a band of spectral components around the DPOAE as described above. Thus, we refer to the present method as a “heterodyne” method. The advantages of the heterodyne method over direct computation of the analytic signal are that (1) the inverse FFT size is much smaller than the size of the original waveform buffer (4096 vs. 262144), and (2) the phase deviation is smaller because the phase of the center frequency has effectively been subtracted out. Talmadge et al. (1999) used other, similar signal processing methods to obtain analytic-signal representations of DPOAEs. Relkin et al. (1999) used a phase-locked amplifier, the analog equivalent of the heterodyne method, to obtain DPOAE envelopes.

FIG. 1. Level (a) and phase (b) of distortion product otoacoustic emission (DPOAE) vs. time for results from normal human subject No. 1.

The DPOAE envelope magnitude (in Pa) was then converted into DPOAE envelope level (in dB SPL). DPOAE envelope level and phase were displayed as functions of time as illustrated in Figure 1. In an analogous way, the f_1 and f_2 primary components in the ear-canal pressure were also analyzed as functions of time.

1- and 2-exponential fits

A fitting function was applied to a function of DPOAE envelope level (in dB SPL) versus time as follows. A nonlinear (simplex) fitting procedure was performed to obtain the least-squared difference between the DPOAE envelope level and an exponential fitting function. For this step, a short offset period (typically 20–40 ms) of the DPOAE envelope level at the beginning and the same period at the end of the stimulus duration were excluded to remove transients at the two ends.

One of the following fitting functions was applied:

$$\text{1-exponential fit: } L(t) = L_{ss} + m \cdot \exp(-t/\tau) \quad (1)$$

where $L(t)$ is the fit for DPOAE envelope level (in dB SPL) as a function of time t (in ms), L_{ss} is the steady-state level of DPOAE (in dB SPL), m is the magnitude of adaptation (in dB), and τ is the time constant of adaptation (in ms).

$$\begin{aligned} \text{2-exponential fit: } L(t) = & L_{ss} + m_f \cdot \exp(-t/\tau_f) \\ & + m_s \cdot \exp(-t/\tau_s) \quad (2) \end{aligned}$$

where m_f and m_s are the magnitudes of the fast and slow components of adaptation (in dB) and τ_f and τ_s are the time constants of the fast and slow components of adaptation (in ms).

$$m_{com} = |m_f| + |m_s| \quad (3)$$

where m_{com} is the combined adaptation magnitude representing the sum of the absolute values of m_f and m_s .

For the single-exponential fit, the initial estimate for the time constant was always 0.1 s. The initial estimate for the two-exponential fit was based on the results of a single-exponential fit, so that it would always be an improvement over the single-exponential fit. The “variance accounted for” (VAF) is a metric for the goodness of fit, defined as:

$$\text{VAF} = 1 - r \quad (4)$$

where r is the ratio of (1) the mean-squared difference between a fitting function and the DPOAE envelope level and (2) the mean-squared deviation of the time-varying DPOAE envelope level from its time-averaged value. The value of VAF ranges from 0 (a poor fit) to 1 (a perfect fit).

Figure 2 illustrates exponential fits for results from subject No. 1. A 1-exponential fit (Fig. 2a) provided a fit for the response over most of the time period except for the peak at the beginning. In contrast, a 2-exponential fit (Fig. 2b) provided an improved fit for both the initial peak and the later part of the response. The value of VAF increased from 0.58 with the 1-exponential fit to 0.60 with the 2-exponential fit. Figure 2c displays the response, together with the 2-exponential fit, over the full duration of stimulus (5.5 s), whereas Figure 2a, b display the response over the initial 2 s.

RESULTS

This article describes responses of 24 ears of 20 normal-hearing human subjects to three different f_2 frequencies and several different L_2/L_1 values as stated in the Methods section. The time courses of DPOAE levels were variable among subjects, with several representative examples illustrated in Figure 3. Each case in Figure 3 is shown with a 2-exponential fit. Some exhibited a slower time course (panel a), some faster time courses (panels b and c). Most of the cases exhibited a decreasing time course (panels a–c), while some exhibited a biphasic time course (panel d), where DPOAE level showed an initial decrease followed by an increase.

Distributions of the fast and slow time constants of

FIG. 2. DPOAE level vs. time with a 1-exponential fit (a) or 2-exponential fit (b, c). The abscissa in c covers a longer range than in a and b.

DPOAE adaptation (τ_f and τ_s , respectively) are shown in Figure 4. Note that a logarithmic scale of the time constants was chosen for the abscissa in this figure in order to show both τ_f and τ_s in the same graph. The data of this figure demonstrate that the distributions of the two time constants are clearly separated with little overlap between them. This observation of a separation of the two distributions supports the concept of two temporally distinct components of DPOAE adaptation. The median values of τ_f and τ_s were 69 ms and 1.51 s, respectively. The fact that there were many cases with $\tau_s = 5.5$ s (i.e., the rightmost bar in Fig. 4) suggests that the 5.5-s stimulus duration used in this study probably was not long enough to determine τ_s accurately. That is, data with a longer stimulus duration (perhaps 10 or 20 s) are expected to be necessary to determine accurately the distribution of τ_s .

FIG. 3. A variety of time courses of DPOAE level together with 2-exponential fits. The subject # is shown for each panel. The stimulus conditions were (a) $f_2 = 5.7$ kHz, $L_2/L_1 = 60/68$ dB SPL; (b) $f_2 = 5.7$ kHz, $L_2/L_1 = 65/73$ dB SPL; (c) $f_2 = 4.0$ kHz, $L_2/L_1 = 60/68$ dB SPL; (d) $f_2 = 4.0$ kHz, $L_2/L_1 = 60/75$ dB SPL.

Distributions of the magnitudes of the fast and slow components of DPOAE adaptation (m_f and m_s respectively) are shown in Figure 5. The two distributions have a large overlap. The values of m_f and m_s ranged from -0.3 to 2.2 dB. Their median values were 0.65 and 0.40 with the fast component being larger. All of the m_f and most of the m_s values were positive, corresponding to decreases of DPOAE level with time. In two cases, m_s values were negative, corresponding

FIG. 4. Distributions of the fast and slow time constants of DPOAE adaptation, i.e., τ_f and τ_s respectively.

FIG. 5. Distributions of the magnitudes of the fast and slow components of DPOAE adaptation, i.e., m_f and m_s respectively.

to increases of DPOAE level with time (as shown in Fig. 3d).

The relationships between the magnitudes and time constants of the adaptation are examined in Figure 6. In the top panel, filled and open circles represent the fast and slow components, respectively. The graph shows that larger/smaller magnitudes tend to be associated with shorter/longer time constants, both within each group and across the two groups combined. The two groups of symbols are separated such that the filled circles are concentrated in an upper-left area and the open circles in a lower-right area. One measure of separation between the fast and slow components in individual records is τ_s/τ_f . The median value of this measure among the data set was 24, indicating a clear separation between the two time constants. The median value of $m_f - m_s$ was 0.25 dB indicating that the fast component tended to have larger magnitudes. Figure 6 (bottom panel) illustrates the relationship between the fast and slow components in individual records for a representative subset of the data. (Only a subset of the data are shown in this panel to make the individual lines more visible. The method of selection of the data in Figure 6 bottom panel is explained

FIG. 6. **Top:** Magnitude of the fast or slow adaptation component (m_f or m_s) vs. the corresponding time constant (τ_f or τ_s). Filled and open symbols represent the fast and slow components, respectively. **Bottom:** m_f or m_s vs. τ_f or τ_s for a representative subset of the data. Each pair of data symbols for an individual record is connected by a straight line. The data for the bottom panel represents every fifth record in the data set where the data records were rank-ordered with respect to τ_s/τ_f .

in the figure caption. Here, each pair of data symbols for an individual record is connected by a straight line. The graph shows that, in individual records, (1) the lines connecting each pair of symbols are long and (2) the lines tend to have negative slopes. These characteristics which are visible in the individual records are consistent with those visible in the scatter plot of the data indicated above.

The distribution of the combined magnitude of DPOAE adaptation is shown in Figure 7. It ranged from 0.4 to 3.0 dB with a median of 1.10 dB. A typical time course of DPOAE adaptation in humans, as derived from a 2-exponential function using the median values of the parameters indicated above, is shown in Figure 8. It exhibits an initial fast decline of 0.65 dB followed by a slow decline of 0.4 dB, reaching a steady-state level by about 4.5 s.

For each record of DPOAE, the present analysis yielded both phase and level of DPOAE as functions of time as indicated in the Methods section. Changes of DPOAE phase were recognizable in some cases, and the polarity of a phase change was either in the leading or in the lagging Figure 9 illustrates an example where the phase of DPOAE gradually changed in the leading

FIG. 7. Distribution of the combined magnitude of DPOAE adaptation.

FIG. 8. A typical time course expected for DPOAE adaptation in humans as derived from a 2-exponential function using the median values of the parameters shown in the inset.

direction by about 4.5° as the level of DPOAE decreased by about 1 dB. In the example of Figure 1, the phase of DPOAE underwent a change of about 1.3° where the time course of phase was suggestive of a biphasic type, i.e., an initial lag followed by a lead.

In most of the cases, the observed phase change of DPOAE was less than 7.2° . However, in some cases much larger phase changes (70° – 80°) were also observed. Those large phase changes were associated with sharp notches of DPOAE level at the onset, analogous to the observation of Talmadge et al. (1999, Fig. 8) (see the Discussion section for further discussion.) Systematic analysis of time-varying DPOAE phase characteristics, e.g., distributions of the amount and polarity of DPOAE phase change, have not been performed yet. Such results will be reported in the future.

DISCUSSION

Main findings and comparison with other studies

To our knowledge, the present study is the first published article to describe changes of DPOAE level as

FIG. 9. Level (a) and phase (b) of DPOAE vs. time for results from normal human subject No. 4, illustrating a gradual change of phase in the leading direction.

a function of time, i.e., DPOAE adaptation, in humans. The time course of the human DPOAE adaptation was well characterized by a 2-exponential function. The fast component typically had a 69-ms time constant with a 0.65-dB decreasing magnitude. The slow component typically had a 1.51-s time constant with a 0.4-dB decreasing magnitude. Thus, the total DPOAE adaptation in humans was typically 1.1 dB.

Agrama et al. (1998) described preliminary results of a study of DPOAE adaptation in humans. Their observations are consistent with our results. A limitation of their method, however, is that it did not make a continuous measurement of the DPOAE level versus time. Rather, they sampled the DPOAE level at certain designated 46-ms-long time windows, e.g., a window at the beginning and another at the end of the stimulus-burst duration, 1.7 s. They observed that the DPOAE level of humans sampled in the 1.7-s window was 0.5–1.0 dB lower than that sampled in the initial window. Another limitation is that the 1.7-s stimulus-burst duration would be too short to reveal the slow component of DPOAE adaptation in view of the present observations.

The fast and slow time constants of DPOAE adaptation in animals (Liberman et al. 1996; Sun and Kim 1999; McGee et al. 2000) are comparable to those of humans (Figs. 3, 4). The main difference between humans and animals regarding DPOAE adaptation is that the adaptation magnitudes observed in humans

are smaller than those observed in animals. Although the reason for this difference is not clear, it may be related to the fact that the absolute level of DPOAE of humans is much lower than that of nonprimate animals. Whether the fact that ear-canal cavities of humans are larger than those of animals fully accounts for lower levels of DPOAE in humans than in animals is not known. The observation that humans exhibit more prominent, transiently evoked OAEs than animals suggest that, beyond differences in ear-canal cavities, there may be differences in OAE mechanisms between humans and animals. It is desirable that a theory of mammalian cochlear mechanics should explain both of the differences, i.e., those in the absolute level and in the adaptation magnitude of DPOAE between humans and nonprimate animals.

Another difference between humans and animals regarding DPOAE adaptation is that animals show increasing (Liberman et al. 1996; Sun and Kim 1999) and biphasic types of time courses (McGee et al. 2000) more prominently than humans. The biphasic-type adaptation (Fig. 3d) was rare and the increasing-type adaptation was absent in the present data from humans (see below).

In a study of DPOAE in guinea pigs, adaptation magnitude and polarity were much affected by stimulus parameters, particularly $L_1 - L_2$ (Kujawa and Liberman 1998). It is possible that the stimulus parameters of the present study differed from those that produce maximal magnitudes of DPOAE adaptation in humans. The recording time was much longer in humans (25–30 min per record) because of a lower signal/noise ratio and a need to do more averaging compared with the recording in animals (typically 2.5–8 min). Consequently, we have not had the opportunity to explore the stimulus-parameter space systematically. The information that was available in the present data regarding the effect of $L_1 - L_2$ on adaptation magnitude was not sufficient to reveal a general trend. A systematic exploration of the stimulus-parameter space in future studies of humans should help determine whether larger magnitudes of DPOAE adaptation can be observed in humans under certain stimulus conditions. In another study of guinea pigs, adaptation magnitude was observed to be larger in an awake condition than when anesthetized (Boyev et al. 2000). An effect of anesthesia cannot be a possible explanation for the smaller magnitude of human DPOAE adaptation because the human subjects of the present study were not anesthetized.

Different methods of observing DPOAE adaptation

Earlier studies of DPOAE adaptation (Liberman et al. 1996; Sun and Kim 1999) used trains of 64-ms bursts

of two tones as stimuli. The equipment used in those studies could not provide stimulation, recording, and DPOAE analysis continuously over several seconds. In contrast, the system used in the present study [the early results of which were reported by Neely et al. (1999) and Kim et al. (2000)] did provide these features. Since a study of adaptation normally employs a steady and continuous stimulus with a correspondingly continuous analysis of the response, the present system represents an improvement over those used in previous studies.

Middle-ear muscle and olivocochlear systems

The middle-ear muscle reflex may mediate DPOAE adaptation. This reflex, however, does not appear to be a major source of DPOAE adaptation, e.g., DPOAE adaptation in cats with completely severed middle-ear muscles was not substantially different from DPOAE adaptation in cats with intact middle-ear muscles (e.g., Fig. 9 of Liberman et al. 1996). The observation that DPOAE adaptation was mostly abolished by olivocochlear transection (Liberman et al. 1996) supports the view that DPOAE adaptation is mainly mediated by the olivocochlear system.

Liberman et al. (1996) also observed that DPOAE adaptation included a component that had a slower time constant and a smaller magnitude and that remained after olivocochlear transection. This observation suggests that the slower component of DPOAE adaptation, in part or in whole, is mediated by a local cochlear process, possibly associated with generation of the distortion product involving OHC motility. In the present study of humans, it was not possible to ascertain how much of the DPOAE adaptation is mediated by the olivocochlear system and how much by a local cochlear process. However, we interpret the DPOAE adaptation of humans described in this study, at least the fast component, to be mediated by the olivocochlear system. Our reason is that DPOAE adaptations of humans and cats are qualitatively similar. Caution is needed here because the slow-adaptation component was also affected by olivocochlear transection in some cases (in Liberman et al. 1996). Therefore, the slow-adaptation component should not be automatically interpreted to be mediated entirely by a local cochlear process.

MOC vs. LOC

The olivocochlear system consists of the medial and lateral olivocochlear (MOC and LOC) neurons, which project to the outer hair cells (OHCs) and to afferent fibers beneath the inner hair cells (IHCs), respectively (e.g., Warr 1992; Guinan 1996). The MOC subsystem, rather than the LOC subsystem, is believed to underlie

DPOAE adaptation for the following reasons. Liberman et al. (1996) found that sectioning only the crossed olivocochlear bundle (COCB) at the midline was as effective in disrupting the ipsilaterally evoked DPOAE adaptation as sectioning the complete olivocochlear bundle. This finding suggests that LOC neurons that are spared by the midline section do not contribute to the adaptation. In addition, the present view is consistent with the observations of OHC electromotility and of the influence on DPOAEs by electrical activation of the COCB cited in Introduction.

Implications of the biphasic- and increasing-type adaptation of DPOAE

In some cases of the present data, the time course of DPOAE adaptation was biphasic (Fig. 3d). In animals, both biphasic-type (McGee et al. 2000) and increasing-type adaptations of DPOAE (Liberman et al. 1996; Sun and Kim 1999) have often been observed. Such time courses may arise as a result of an interaction between contributions from two sources of DPOAE. It is believed that two sources underlie the DPOAE signal measured in the ear canal, i.e., one at the primary-frequency location and the other at the distortion-frequency location, as originally suggested by Kim (1980, p. 312) and supported by many other studies (e.g., Kemp and Brown 1983; Kummer et al. 1995; Brown et al. 1996; Heitmann et al. 1998; Talmadge et al. 1998; Shera and Guinan 1999; Stover et al. 1999; Knight and Kemp 2000; Moulin 2000; Parham et al. 2001).

To explain various types of DPOAE time courses, one may use a model of the type described by Talmadge et al. (1998, 1999) and Shera and Guinan (1999). The distortion product (DP) at the $2f_1 - f_2$ frequency is initially generated at the primary-frequency location and propagated basally, constituting one component of the DPOAE. The DP signal generated at the primary location is also propagated apically and reflected at the $2f_1 - f_2$ distortion-frequency location, constituting the second component of DPOAE. (To be accurate, one also needs to include a contribution from multiple reflections involving both a reflection at the cochlear base and a reflection at the distortion-frequency location.) One can represent the DPOAE signal as a sum of two vectors corresponding to the two main components of DPOAE.

Even if the effect of the MOC reflex on the DPOAE component contributed by the primary location is *always* a decrease of magnitude over time, one can get a decreasing, increasing, or biphasic time course of DPOAE adaptation depending upon the phase relationship between the two DPOAE components. Future efforts to convert the experimental observations of DPOAE adaptation in humans and animals into

parameters of the above type of model should be useful. In this regard, combined information about phase and level of DPOAE as functions of time should be more useful in inferring the model parameters than information about DPOAE level alone. The pattern of a notch in the level and a large abrupt change in the phase of DPOAE at the stimulus onset, which was observed by Talmadge et al. (1999, Fig. 8) and in the present study (data not shown), has been interpreted by Talmadge et al. to correspond to a destructive interaction between a smaller contribution from the source at the primary-frequency location and a larger and delayed contribution from a source at the distortion-frequency location. Compared with the studies of Talmadge et al. (1999), our study extends information about changes of DPOAE phase and level over longer periods of time, i.e., over several seconds as opposed to 200 ms.

In view of the above theoretical consideration, the fact that nonprimate animals show increasing- and biphasic-type adaptations of DPOAE more prominently than humans implies a large difference between humans and animals regarding the relative DPOAE contributions from the two sources. From the above discussion, the following emerges as a viable hypothesis: All of the several differences mentioned above between humans and nonprimate animals, i.e., those regarding (1) the absolute level of DPOAE, (2) the magnitude of DPOAE adaptation, and (3) the prevalence of biphasic and increasing time courses of DPOAE adaptation, have a common origin, i.e., a large difference in the relative contributions to DPOAE from the two sources of DPOAE (at the primary-frequency and distortion-frequency locations). Efforts to evaluate this hypothesis should be worthwhile.

Prediction about basilar membrane motion

A combined hypothesis about OHCs and MOC neurons (e.g., Kim 1984; Kim et al. 1998) postulates that, when the ear is subjected to a steady-state stimulus lasting several seconds, the cochlear amplifier gain is controlled by reflex activities of MOC neurons. Under such a condition, the cochlear mechanical response is postulated to undergo a gradual change reflecting the activities of MOC neurons. DPOAE adaptation provides strong support for this hypothesis. A prediction of the hypothesis is that the amplitude of basilar membrane motion (e.g., in response to one or two tones) should undergo an adaptation over a few seconds, analogous to the DPOAE adaptation. To our knowledge, there are no reports of such adaptation in basilar membrane motion. A reliable measurement should reveal such an adaptation in basilar membrane motion.

Practical applications of DPOAE adaptation in humans

Maison and Liberman (2000) observed that, in guinea pigs, DPOAE adaptation magnitude typically underwent a pattern of change that included a transition from a negative value (i.e., DPOAE level increasing with time) to a positive value (i.e., DPOAE level decreasing with time) when the stimulus-level condition changed from $L_1 - L_2 = 15$ dB to 0 dB while L_1 was fixed. They interpreted the full range of the DPOAE adaptation magnitude (i.e., the sum of the absolute values of the most negative and the most positive magnitudes of the adaptation) to be an indication of the strength of the MOC reflex. They found that this measure of the reflex strength was negatively correlated with the degree of hearing loss produced by exposure to an intense sound. Accordingly, a measure derived from DPOAE adaptation magnitude may serve as a useful noninvasive predictor of vulnerability to acoustical injury.

Applying the above concept to humans is desirable since the variability in noise-induced hearing loss among humans makes it difficult to predict such loss. One practical approach may be to screen normal-hearing people with a protocol of DPOAE adaptation and to identify individuals with a particularly small measure of DPOAE adaptation (i.e., weak MOC reflex) to be at high risk of acoustical injury. Such individuals can then be warned to avoid intense sounds more restrictively than the population at large. Results from the present study should be helpful in applying the above approach to humans by demonstrating that humans do indeed exhibit DPOAE adaptation and by indicating the range of adaptation magnitudes among normal-hearing people.

Another potential practical application of DPOAE adaptation is the development of a clinical test of the functional status of the MOC system. For example, patients who are suspected of having dysfunction of the brain stem (e.g., Musiek and Lamb 1994) may be subjected to a test of DPOAE adaptation. An abnormally small magnitude of adaptation would suggest dysfunction of the MOC system. Measurements in subjects known to lack MOC efferents, e.g., patients who have undergone a vestibular neurectomy, would be helpful in establishing the expected reduction in DPOAE adaptation. Since there is no existing clinical test, to our knowledge, that is specifically designed to assess the MOC system, such a test would be useful.

One major obstacle to implementing practical applications such as the above examples will be the requirement of a long recording time. The present study employed a stimulus paradigm with a long silent gap (20 or 30 s) and 40 or 60 repetitions for a total

recording time of 25–30 min for one particular stimulus. Efforts that attempt to obtain adequate information more rapidly by reducing the number of repetitions, the silent gap, or both should be helpful. Another obstacle to practical applications will be that the human adaptation magnitude is small and variable among a group of subjects. Stimulus conditions that yield larger DPOAE adaptations should help reduce the required measurement time.

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