Distortion product otoacoustic emission suppression tuning curves in normal-hearing and hearing-impaired human ears

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Distortion product otoacoustic emission (DPOAE) suppression measurements were made in 20 subjects with normal hearing and 21 subjects with mild-to-moderate hearing loss. The probe consisted of two primary tones (f_2, f_1), with f_2 held constant at 4 kHz and $f_2/f_1 = 1.22$. Primary levels (L_1, L_2) were set according to the equation $L_1 = 0.4L_2 + 39$ dB [Kummer *et al.*, J. Acoust. Soc. Am. **103**, 3431–3444 (1998)], with L_2 ranging from 20 to 70 dB SPL (normal-hearing subjects) and 50–70 dB SPL (subjects with hearing loss). Responses elicited by the probe were suppressed by a third tone (f_3), varying in frequency from 1 octave below to $\frac{1}{2}$ octave above f_2. Suppressor level (L_3) varied from 5 to 85 dB SPL. Responses in the presence of the suppressor were subtracted from the unsuppressed condition in order to convert the data into decrements (amount of suppression). The slopes of the decrement versus L_3 functions were less steep for lower frequency suppressors and more steep for higher frequency suppressors in impaired ears. Suppression tuning curves, constructed by selecting the L_3 that resulted in 3 dB of suppression as a function of f_3, resulted in tuning curves that were similar in appearance for normal and impaired ears. Although variable, Q_{10} and Q_{ERB} were slightly larger in impaired ears regardless of whether the comparisons were made at equivalent SPL or equivalent sensation levels (SL). Larger tip-to-tail differences were observed in ears with normal hearing when compared at either the same SPL or the same SL, with a much larger effect at similar SL. These results are consistent with the view that subjects with normal hearing and mild-to-moderate hearing loss have similar tuning around a frequency for which the hearing loss exists, but reduced cochlear-amplifier gain.
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I. INTRODUCTION

Distortion-product otoacoustic emissions (DPOAE) are a byproduct of normal nonlinear cochlear processes. Their generation is linked to the status of the outer hair cells (OHC). Recent findings, in which DPOAE data were collected in mice for which the putative ''motor'' molecule (prestin) was knocked out, are consistent with the view that DPOAEs are generated by OHC motility (Liberman *et al.*, 2002). Under appropriate stimulus conditions, the normal-hearing ear (having normal OHC function) produces these distortion products in response to pairs of primary tones. Because OHC damage results in a reduction or loss of normal nonlinear behavior (e.g., Dallos *et al.*, 1980; Kim, 1980), one manifestation of damage to the normal nonlinear system (i.e., the OHC system) is the reduction or loss of DPOAEs. It also is known that damage to OHCs results in auditory threshold elevation.

The relationships among OHC status, auditory function, and DPOAE levels have led to the application of DPOAE measurements to the task of identifying hearing loss. Several studies have described DPOAE measurements in normal-hearing and hearing-impaired ears (e.g., Martin *et al.*, 1990; Gorga *et al.*, 1993, 1996, 1997, 2000; Kim *et al.*, 1996). These studies have shown that DPOAEs accurately identify auditory status at mid- and high frequencies, performing less accurately at lower frequencies. These efforts have focused primarily on the ability of DPOAEs to identify auditory status, as defined by the pure-tone audiogram. As such, they have focused on dichotomous decisions in which DPOAE measurements were used to classify an ear as having either normal hearing or hearing impairment. To a lesser extent, others have described the relation between behavioral thresholds and DPOAEs, by relating DPOAE threshold and auditory thresholds (Martin *et al.*, 1990; Gorga *et al.*, 1996; Boege and Janssen, 2002; Gorga *et al.*, 2003), or by relating DPOAE level and auditory threshold (Martin *et al.*, 1990; Dorn *et al.*, 2001; Gorga *et al.*, 2002a).

Threshold elevation, however, is only one of several consequences of OHC damage. There are both mechanical and neural data from lower animals, indicating that frequency selectivity may be reduced and response growth may become more rapid when OHC damage exists (e.g., Evans, 1974; Kiang *et al.*, 1976; Dallos and Harris, 1978; Liberman and Dodds, 1984; Sewell, 1984; Gorga and Abbas, 1981b; Ruggero and Rich, 1991). Frequency selectivity in these studies typically is defined by the parametrization of tuning curves, using measures such as Q_{10} and differences in threshold at the tip and on the tail of tuning curves. Response growth refers to the rate at which either discharge rate (for single-unit studies), displacement or velocity (for basilar-membrane studies), or masking (for whole-nerve action po-

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tential studies) grows as stimulus level is increased. These ''suprathreshold'' effects may be related to perceptual phenomena such as the reduced speech-perception abilities or loudness recruitment that sometimes are associated with peripheral hearing loss. For example, compensating for abnormally rapid growth of loudness is the motivation for including compression in many hearing aids. In one sense, the compression circuit of the hearing aid is attempting to compensate for the loss of the compressive behavior of the normal cochlea.

While direct measurements of frequency selectivity or response growth are not possible in humans, indirect measures may provide insight into underlying properties related to cochlear processing. Psychoacoustic and electrophysiologic masking studies are motivated by a desire to indirectly estimate representations of cochlear properties that have been identified from more direct, invasive measurements in lower animals. Recently, for example, Oxenham and Plack (1997) related the growth of forward masking (measured behaviorally) to nonlinear cochlear processing, based on a comparison of on-frequency and low-frequency masking effects.

DPOAE measurements in a suppression paradigm have also been used to describe peripheral response properties in humans. Several studies have shown that DPOAE suppression measurements provide information related to the site of generation for DPOAEs and the tuning properties of the cochlea at the place(s) of DPOAE generation, at least for ears with normal cochleae (e.g., Brown and Kemp, 1984; Martin *et al.*, 1987). Furthermore, studies in humans have shown that the reductions in DPOAE levels in the presence of a suppressor (Abdala, 1998, 2001; Abdala *et al.*, 1996; Kummer *et al.*, 1995; Gorga *et al.*, 2002b) share a dependence on frequency that is similar to other measures of response growth such as single-unit rate-level functions (Sachs and Abbas, 1974; Schmiedt and Zwislocki, 1980) and measurements of basilar-membrane motion (Ruggero and Rich, 1991; Ruggero *et al.*, 1997), that were based on more direct measurements in lower animals. These similarities have led us to pursue DPOAE suppression measurements in patients with cochlear hearing loss in order to determine whether changes in response growth and tuning, evident in direct measurements from lower animals, can be indirectly observed in humans using the same noninvasive DPOAE techniques that have been applied with humans having normal auditory thresholds.

The present study describes our initial efforts to measure DPOAE suppression in human subjects with mild-to-moderate hearing loss. Subjects with normal hearing are included for comparison purposes. Of primary interest was determining whether reduced frequency selectivity and/or more rapid response growth, predicted from single-unit and basilar-membrane studies in lower animals, can be observed in indirect DPOAE measurements in humans. A long-term goal of our research program has always been to determine whether there are relationships between objective measurements of cochlear function (such as DPOAE and/or evoked potential (EP) measurements) and perceptual consequences of damage to the cochlea (such as threshold elevation or abnormal growth of loudness) so that eventually the perceptual consequences can be predicted from the objective measures. This long-term goal has clinical importance related to the identification and the rehabilitation of hearing loss (such as the selection of hearing-aid characteristics) in infants and young children who may be unable to provide behavioral responses to sound, especially subjective judgments such as loudness. While a great deal is already known about the relationship between DPOAE measurements and sensitivity loss (e.g., Martin *et al.*, 1990; Gorga *et al.*, 1993, 1997, 2000; Stover *et al.*, 1996; Kim *et al.*, 1996; Boege and Janssen, 2002), the present work is viewed as an initial step towards understanding the relationship between DPOAE measurements and suprathreshold consequences of cochlear damage. The primary aim is to determine whether DPOAE measurements of frequency selectivity and response growth are possible in subjects having hearing loss. This initial step is needed prior to efforts to correlate DPOAE data with suprathreshold perceptual phenomena because of the tendency for DPOAEs to be reduced or absent when hearing loss exists. If DPOAE suppression studies can be performed in humans with hearing loss, future work will determine the extent to which these measurements correlate with behavioral findings.

II. METHODS

A. Subjects

Twenty-two ears of 20 subjects with normal hearing and 29 ears of 25 subjects with hearing loss participated in these studies. The two subject groups differed in age, with the normal-hearing subjects being younger (mean=24.9 years, s.d.=13.4 years) than the group of subjects with hearing loss (mean=57.3 years, s.d.=14.6 years). It was difficult to recruit older normal-hearing subjects or younger hearing-impaired subjects, due to factors associated with subject availability. Thus, there is concern that some of the results reviewed below might have been influenced by age rather than hearing loss. As will be seen, however, it is not obvious how age could have affected the data in such a way as to result in the outcomes that were observed.

Normal hearing was defined as audiometric thresholds less than or equal to 15 dB HL (*re*: ANSI, 1996) at 4 kHz. The mean threshold for subjects in the normal-hearing group at 4 kHz (the probe frequency; see below) was 5.7 dB HL (s.d.=4.4 dB). Subjects with thresholds of 20 dB HL or greater at 4 kHz were classified as hearing impaired. It was assumed that the hearing losses in these subjects were of cochlear origin, based upon their case histories, pure-tone audiometry, acoustic immittance measures, and prior results of any additional diagnostic tests. However, a precise diagnosis of etiology was not available for the majority of the subjects with hearing loss. This ''diagnostic ambiguity'' highlights one of the issues that is confronted whenever studies are conducted in humans. Whereas in animal studies, cochlear damage is typically induced and, therefore, controlled, such control is frequently impossible in studies that involve humans with hearing loss. In fact, it is difficult to find a homogeneous group of human subjects with hearing loss.

Subjects with hearing loss were selected according to their thresholds at 4 kHz, which was the f_2 frequency that was used as the "probe frequency" during the DPOAE suppression experiments. Special efforts were made to include subjects for whom the magnitude of the loss was between 20 and 55 dB HL, on the assumption that it would be more likely that DPOAE level would be too reduced or the response would be completely absent for ears with hearing losses exceeding the upper limit of this range. Even so, DPOAE suppression experiments were not possible in four of the 25 subjects with hearing loss because they did not produce responses of sufficient level to permit reliable estimates of the suppression of that response. Thus, the data reported below are based on measurements from 23 ears of 21 subjects with mild-to-moderate hearing loss, who represent a subset of the potential subjects with hearing loss in this range. The mean thresholds at 4 kHz for the group of subjects with hearing loss was 36.3 dB HL (s.d.=9.1 dB). Thus, on average, the subjects with hearing loss had thresholds that were 30.6 dB higher than thresholds for the normal-hearing group.

B. Stimuli

DPOAE data were collected with custom-designed software (EMAV, Neely and Liu, 1994). This system controlled a sound card (CardDeluxe, Digital Audio Labs) that was housed in a PC. Separate channels of the sound card were used to output the two primary tones (f_1 and f_2) that were mixed acoustically in the ear canal. The channel that was used to generate f_2 was also used to generate the suppressor tone (f_3). The output of the sound card was delivered to a probe–microphone system (Etymotic, ER 10C). This system was modified in order to remove 20 dB of attenuation from each channel, thus permitting the presentation of suppressors at higher levels than would be otherwise possible. Separate loudspeakers in the probe were used to transduce the outputs from the two separate channels of the sound card. The probe's microphone was used to measure levels at the plane of the probe.

All DPOAE data were collected for the condition in which f_2 was fixed at 4 kHz, $f_2/f_1=1.22$, the level of f_2 (L_2) was varied from 20 to 70 dB SPL (in 10-dB steps), and, for each L_2, L_1 was set according to the equation, $L_1=0.4L_2+39$ dB (Kummer *et al.*, 1998). A third tone, f_3, was used to suppress the response elicited by the primary tones. Seventeen suppressor frequencies were used, ranging from 1 octave below (2 kHz) to $\frac{1}{2}$ octave above (5.6 kHz) f_2. Suppressor level (L_3) was varied in 5-dB steps from 5 dB SPL up to a maximum level of 85 dB SPL.

Prior to data collection, real-ear measurements at the plane of the probe were used to calibrate the stimuli. This calibration procedure may introduce errors, especially for frequencies close to the probe frequency used in the present experiment ($f_2=4$ kHz). These errors are a consequence of standing-wave problems introduced by an interaction between the quarter wavelength of the probe frequency and the dimensions of adult ear canals with a probe system in place (Siegel, 1994, 2002). However, the use of standard cavities for calibration also introduces errors related to the fact that these cavities may not provide a good model for individual ears. The best solution might be one in which acoustic intensity is measured (Neely and Gorga, 1998). That approach, however, has not been implemented in any widely available device or software system. Thus, while it is recognized that real-ear calibration measurements may introduce some errors, it is viewed as an acceptable compromise, given the current state of calibration methods.

C. Procedures

Both DPOAE and noise levels were estimated from the energy in the $2f_1-f_2$ frequency bin. During data collection, each 2-s sample was alternately stored in one of two buffers. In order to estimate DPOAE level, the contents of the two buffers were summed. Noise level was estimated by subtracting the contents of one buffer from the contents of the other buffer. This approach is attractive in that signal and noise are estimated within the same frequency bin. However, it has the disadvantage of providing a more variable estimate of noise level, compared to the case when noise levels are estimated from the contents of several bins adjacent to the $2f_1-f_2$ (signal) frequency bin.

Measurement-based stopping rules were used during DPOAE measurements. For each condition, averaging continued (1) until the noise floor was -25 dB SPL or less, or (2) for 32 s of artifact-free averaging, whichever occurred first. The noise-stopping rule allowed us to measure DPOAEs (and, therefore, suppression) over a wide dynamic range and still be confident that measured responses were above the level at which system distortion occurred (see Dorn *et al.*, 2001 for a more complete description of system distortion for the present measurement system). The time limit prevented data collection from continuing indefinitely for any single stimulus condition.

In each subject, a DPOAE input/output (I/O) function was measured when $f_2=4$ kHz. These initial measurements were needed in order to select the range of L_2 levels for each subject over which the suppression experiments could be conducted. Figure 1 shows mean DPOAE I/O functions for both normal-hearing and hearing-impaired subjects. The mean noise floor is also shown. Note that DPOAE levels were less in impaired ears at the same L_2 levels. The response levels at 50–70 dB SPL in impaired ears were more like the levels observed at 20–40 dB SPL in normal ears. Significant differences in DPOAE level were observed when normal and impaired responses were compared at the same SPL. Differences were not significant when the levels in impaired ears at 50–70 dB SPL were compared to the levels observed in normal ears at 20–40 dB SPL. That is, if the results are shifted in impaired ears by 30 dB (an amount that is nearly equivalent to the mean behavioral threshold difference between groups), the levels produced by both groups were similar. Another way of thinking about these findings is that normal and impaired ears produced different DPOAE levels when comparisons were made at similar SPL, but not when comparisons were made at levels that were approximately equivalent in terms of sensation level (SL). We will return to this SPL/SL comparison when considering the primary findings of the present study.

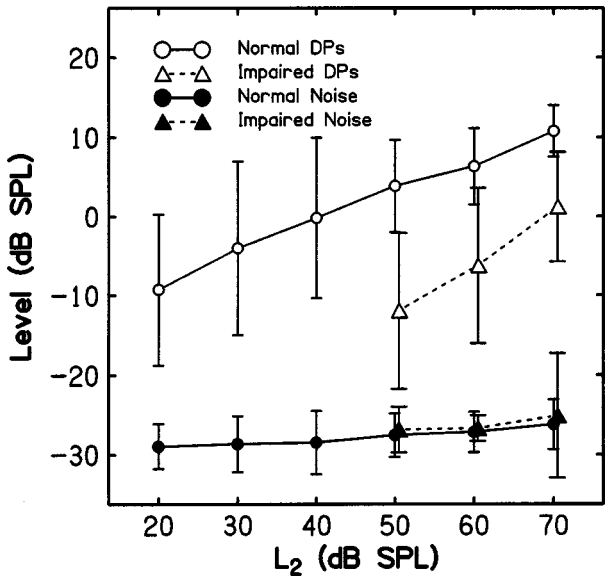

FIG. 1. Mean DPOAE and noise level (dB SPL) as a function of L_2 (dB SPL). Circles represent data from normal ears, while triangles represent data from ears with hearing loss. Open and filled symbols represent DPOAE and noise levels, respectively. Error bars represent 1 s.d. Data points were offset slightly in the L_2 dimension to help visualization.

The influence of the stopping rule is evident in the constancy of noise levels across L_2 and between the two subjects groups. For each subject, suppression experiments were performed at those L_2 levels for which at least a 10-dB signal-to-noise ratio (SNR) was evident in the previously measured I/O functions. As can be seen in Fig. 1, sufficient DPOAE level was measured over the range of L_2 levels from 20 to 70 dB SPL in subjects with normal hearing. The range of levels was more restricted in subjects with hearing loss, being limited to L_2 levels of 50–70 dB SPL.

In each set of suppression measurements, L_2 was fixed at one of six levels in normal ears (20–70 dB SPL, 10-dB steps) or one of three levels in impaired ears (50–70 dB SPL). Experimental conditions were then selected such that f_3 was fixed and its level was varied from 5 to 85 dB SPL (5-dB steps). DPOAE levels were measured for each of these 17 suppressor levels at each f_3 frequency. However, the initial condition prior to the presentation of each f_3 was a control condition, in which no suppressor was presented. Once an L_3 series had been completed for one f_3, a different f_3 was selected and the entire process was repeated. This approach continued until measurements were completed for each of 17 suppressor frequencies. For each subject, no more than 12 hours of data-collection time was required, depending mainly on the range of L_2 levels for which reliable DPOAEs could be measured. This means that data-collection time was greater for subjects with normal hearing (for whom measurements were possible at up to six L_2 levels), but less time was required for subjects with hearing loss.

Following data collection, DPOAE levels were converted to decrements (or amount of suppression) by subtracting the level measured in each suppressor condition from the level measured in the preceding control condition. There were several reasons why the data were converted into decrements. Decrements have the advantage of converting the DPOAE data into amount of suppression (in dB), and they partially account for variance in absolute DPOAE level across subjects. Decrement-versus-L_3 functions for each f_3 were fit with a linear equation in order to provide an estimate of response growth to the suppressor at the place where (presumably) the $2f_1-f_2$ distortion product was initially generated. The fits were restricted to conditions in which the SNR$\geqslant$3 dB, at least one decrement was required to be in the range from 3 to 15 dB, and, outside of this range, decrements were required to increase monotonically with respect to L_3. This combination of inclusion criteria prevented the inclusion of any conditions in the fits in which no suppression occurred or in which the response was completely suppressed. In an effort to include data points in the linear fits for which the SNR was high (i.e., points for which the decrement was as little as 1 dB), these data were transformed by the equation

$$D = 10\log(10^{\mathrm{decr}/10}-1). \tag{1}$$

When $D=0$, the decrement=3 dB. This transformation had the effect of linearizing the decrement functions. Finally, in order to reduce the influence of points with low SNRs, data points were weighted by the following equation:

$$\text{SNR weight} = (10^{\mathrm{signal}/10})/(10^{\mathrm{signal}/10}+10^{\mathrm{noise}/10}). \tag{2}$$

It should be noted, however, that there was little difference between weighted and unweighted fits to the data. In fact, the two fits superimposed for the majority of conditions. Figure 2 summarizes the effects of the above treatments to the data for one subject with normal hearing. Circles represent the unprocessed decrements with signal-to-noise ratios (SNR)$\geqslant$3 dB, triangles represent the same data after transformation by the above equation, and the lines represent the weighted fits to the transformed data. The small filled circles represent conditions not meeting the SNR criterion (SNR$\leqslant$3 dB). Thus, they represent conditions in which the DPOAE was at a level that was nearly or completely suppressed. The top, middle, and bottom panels show the data for the cases in which the suppressor (f_3) was below (2.2 kHz), close to (4.1 kHz), and above (4.8 kHz) f_2. As can be seen, the transformation's only effect was to extend the usable range of data, and the weighted functions provide good fits to the data. These trends were evident for decrement functions in both normal-hearing and hearing-impaired ears. The linear equations were solved for the suppressor level that resulted in a decrement of 3 dB (i.e., $D=0$, or 3 dB of suppression). These "threshold" decrements were plotted as a function of f_3 in order to generate DPOAE suppression tuning curves (STC). Because of the differences in L_2 conditions between subject groups, these tuning curves were constructed for L_2 levels from 20–70 dB SPL in normal-hearing subjects, but were restricted to probe levels of 50–70 dB SPL in subjects with hearing loss, due to the smaller responses for the control condition in hearing-impaired ears.

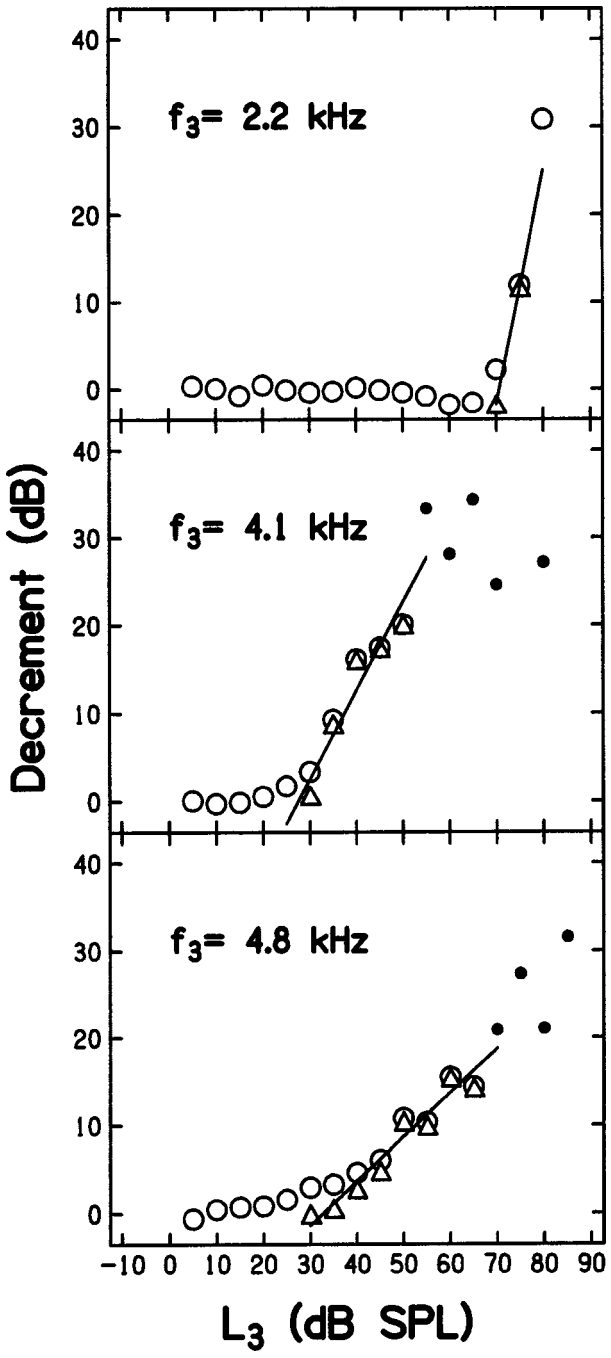

FIG. 2. Decrement (in dB) as a function of suppressor level (L_3) for a low-frequency (2.2 kHz, top), on-frequency (4.1 kHz, middle), and high-frequency suppressor (4.8 kHz, bottom), relative to f_2 for one normal-hearing subject. $L_2=30$ dB SPL. Open circles represent the decrements for which the SNR was at least 3 dB, small filled circles represent data for cases in which the SNR criterion was not met, triangles represent the transformed decrement data meeting the SNR criterion (see the text), and the lines represent linear fits after weighting data according to the SNR. Line fits were restricted according to the rules described in the text.

III. RESULTS

A. Decrement versus suppressor-level functions in normal-hearing ears

Figure 3 shows mean decrement-versus-L_3 functions for subjects with normal hearing. The left column represents data for the case when the suppressor was lower in frequency than the probe ($f_3<f_2$), while the right column represents data for the opposite case ($f_3>f_2$). Each row represents data for a different probe level (L_2). The heavy line represents data for the f_3 frequency closest to f_2 for the set of f_3 frequencies shown in each panel. Thinning lines represent data for f_3 frequencies that are increasingly distant from f_2. Consistent with previous data describing DPOAE suppression (e.g., Martin *et al.*, 1987; Kummer *et al.*, 1995; Abdala *et al.*, 1996; Gorga *et al.*, 2002b), suppression occurred at the lowest levels when f_3 was close to f_2, with increasing suppression "thresholds" as f_3 moved away from f_2 in either direction. In addition, the functions for lower f_3 frequencies relative to f_2 were steeper, compared to the functions when $f_3>f_2$. These trends were evident at all L_2 levels, although it became progressively more difficult to suppress the DPOAE as L_2 increased. An estimate of the dynamic range of the measurements can be obtained by examining the level at which the decrement functions "saturate." When this occurs, the DPOAE was completely suppressed into the noise floor. Examination of these decrement functions indicate that the dynamic range of the present measurements varied from about 20 dB ($L_2=20$ dB SPL) up to more than 30 dB ($L_2=50$, 60, and 70 dB SPL).

B. Decrement versus suppressor-level functions in hearing-impaired ears

In similar fashion, Fig. 4 presents mean decrements as a function of L_3 for subjects with hearing loss. In all respects, the conventions followed in this figure are identical to those used in Fig. 3. However, data collection was restricted to L_2 levels of 50 dB SPL or higher. Decrement functions from impaired ears tended to saturate at lower levels, compared to similar conditions in subjects with normal hearing. Thus, the dynamic range of these measurements was reduced, which probably is due to the same mechanisms that resulted in the reduced L_2 range (of unsuppressed conditions) over which measurable DPOAEs were observed. With the exception of differences in terms of the probe levels (L_2's) for which the experiments could be performed and the reduced dynamic range, there were no apparent differences between these decrement functions and those observed in subjects with normal hearing. That is, thresholds were lowest for f_3 frequencies close to f_2, and the decrement functions appear steeper when $f_3<f_2$, compared to the case when $f_3>f_2$.

C. Slopes of decrement versus suppressor-level functions

Each decrement versus L_3 function was fit with a linear regression in order to provide an estimate of the slope of these functions, as described previously. Figure 5 plots the mean slopes from these linear regressions as a function of f_3. In all cases, solid lines are used to depict the estimated slopes from ears with normal hearing and dotted lines are used to represent the data from ears with hearing loss. Each panel shows data for a different L_2. For the reasons described above, slope could be estimated for L_2 levels ranging from 20 to 70 dB SPL in subjects with normal hearing, but could be estimated only for levels from 50 to 70 dB SPL in subjects with hearing loss.

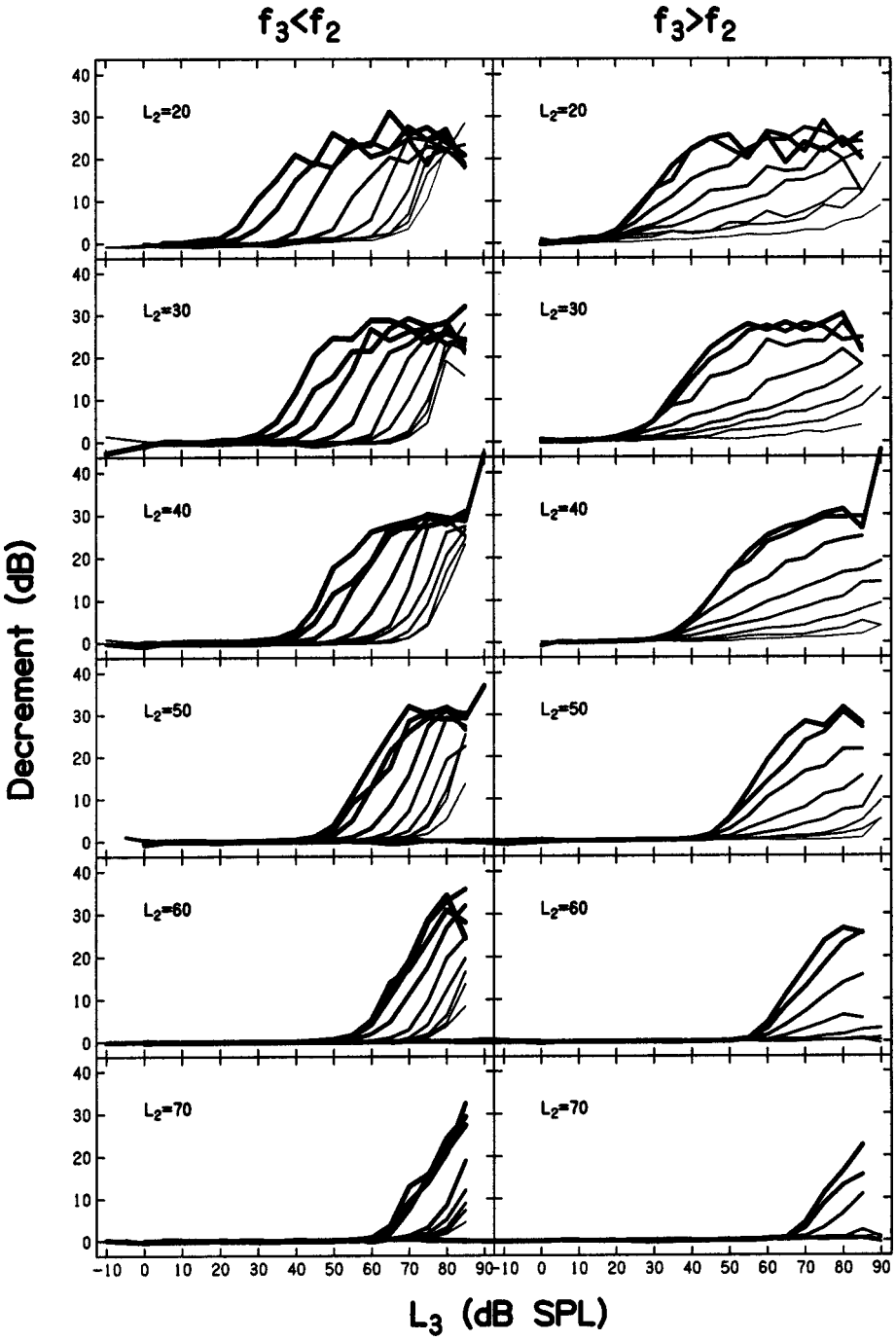

FIG. 3. Mean decrements (in dB) as a function of suppressor level (L_3) for subjects with normal hearing. The left column shows data for the case when the suppressor frequency (f_3) was less than the probe frequency (f_2), while the right column represents the results when f_3 was greater than f_2. Each row presents data for a different probe level (L_2), ranging from 20 to 70 dB SPL. Within each panel, the heavy lines represent decrements for the f_3 closest to f_2 of the set of f_3 frequencies represented in each panel. Thinning lines represent data for f_3 frequencies increasingly more distant from f_2.

These slope estimates were variable across f_3, but tended to decrease as f_3 increased both for normal and impaired ears. For subjects with normal hearing, the slopes were generally greater than 1 for f_3 frequencies below f_2, decreasing rapidly as f_3 moved towards frequencies just above f_2. A similar pattern was observed in subjects with hearing loss, although the apparent differences in slope as a function of frequency were less. Shallower slopes were observed for the highest f_3 frequencies in both subject groups; however, the functions were not always monotonic with frequency. The slopes of decrement functions in subjects with hearing loss appeared to be slightly shallower on the low-frequency side and slightly steeper on the high-frequency side, compared to similar data from ears with normal hearing.

In order to analyze these frequency effects on slope of the decrement functions, frequency was divided into two groups, $f_3<f_2$ and $f_3>f_2$. Within these groups, the slopes for individual f_3 frequencies were averaged to provide single estimates for low- and high-frequency suppressors. In addition, stimulus level was treated in two different ways. In the first analysis, average slopes for normal and impaired ears were compared when stimulus level (L_2) was constant for the two groups. This means that data were compared when L_2 was 50–70 dB SPL for both groups of subjects. In a second analysis, data for normal ears at L_2 levels of 20–40 dB SPL were compared to data from impaired ears when $L_2=50-70$ dB SPL. Two observations from the present study provide support for applying this 30-dB shift in the range of levels over which comparisons between the two

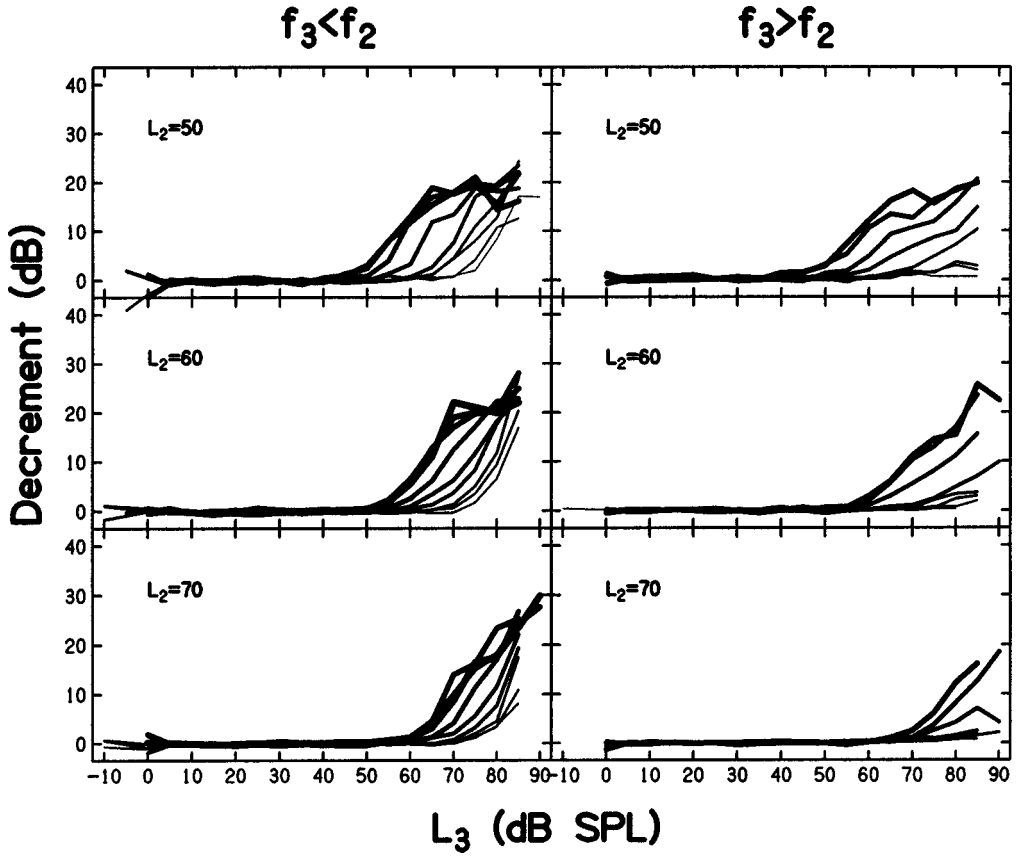

FIG. 4. Same as Fig. 3, only here data are shown for subjects with hearing loss. Note that data are shown only for L_2 levels of 50, 60, and 70 dB SPL, for the reasons described in the text.

groups were made. Recall that the mean normal audiometric threshold was 5.7 dB HL while the mean thresholds for the subjects with hearing loss was 36.3 dB HL, a 30.6-dB difference. In addition, the DPOAE levels differed between the two groups when these levels were compared at the same SPL, but did not differ when the levels produced by impaired ears at 50–70 dB SPL were compared to the levels produced by the normal-hearing group at 20–40 dB SPL, a 30-dB shift for the normal ears (see Fig. 1). Thus, we consider the 30-dB shift as something akin to making the comparison at equivalent SL, at least on average.

Analysis of variance (ANOVA) was used to evaluate the effects of frequency (either above or below f_2), level, and hearing-status group on estimates of slope. For both equivalent SPL and equivalent SL, the outcomes of the ANOVA were the same. Significant effects were observed for frequency and for a frequency×hearing-status group interaction. That is, the slopes were steeper for suppressors below f_2 compared to the slopes for suppressors above f_2 in both groups, but the differences depended on hearing status. Subjects with normal hearing had greater differences between slopes above and below f_2, compared to subjects with hearing loss. This occurred because there was less difference in slope for low- and high-frequency suppressors in subjects with hearing loss. This observation indicates that, at the place where the DPOAE was generated, the growth of response for off-frequency and on-frequency stimuli was more similar in ears with hearing loss.

D. DPOAE suppression tuning curves (STC)

For each L_2, the linear regressions were solved for the L_3 that resulted in 3 dB of suppression for each f_3 frequency. These levels were then plotted as a function of f_3 to produce DPOAE STCs, which are shown in Fig. 6 for one subject with normal hearing and three subjects with hearing loss. The parameter in each panel is L_2. The symbols represent the L_3 necessary for 3 dB of suppression for each f_3. Also shown are the values of Q_{10}, Q_{ERB}, and tip-to-tail differences for each STC. *Q*s were estimated from spline fits to the data, while tip-to-tail differences represent the dB differences between suppression thresholds at $f_3=2.2$ kHz and $f_3=4.1$ kHz. In the normal-hearing subject, sharp tuning was evident around the tip, and the difference between thresholds at the tip and on the low-frequency tail was 40 dB when $L_2=20$ dB SPL. For this subject, there was a systematic decrease in Q_{10}, Q_{ERB}, and tip-to-tail differences as L_2 increased, primarily as a result of changes in suppression threshold around the tip. Less change was evident on the tail. Data from three subjects with hearing loss are shown in the next three panels. While the data from impaired ears were less orderly compared to the data from the subject with normal hearing, the general patterns were similar. At the same SPL, the STCs from the impaired ears appeared similar, and *Q*- and tip-to-tail values were grossly in the range observed for the subject with normal hearing.

Figure 7 shows mean STCs for both normal-hearing and

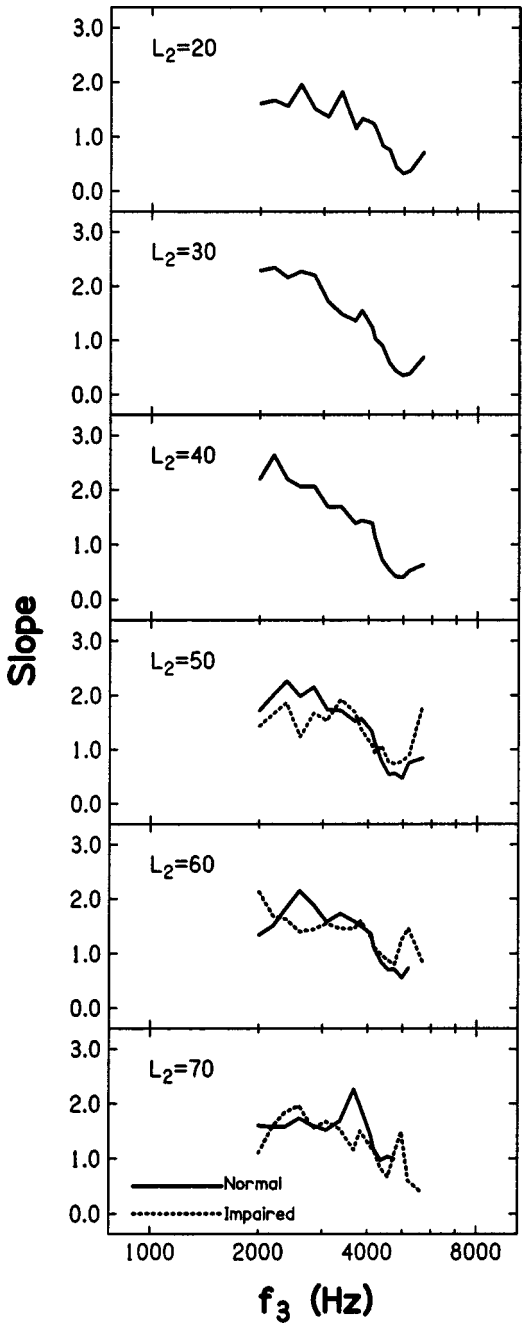

FIG. 5. Mean slopes of decrement versus suppressor level (L_3) functions as a function of suppressor frequency (f_3). Each panel represents data for a different L_2. Within each panel, data from normal-hearing subjects are shown as a solid line, and data from subjects with hearing loss are shown as a dotted line.

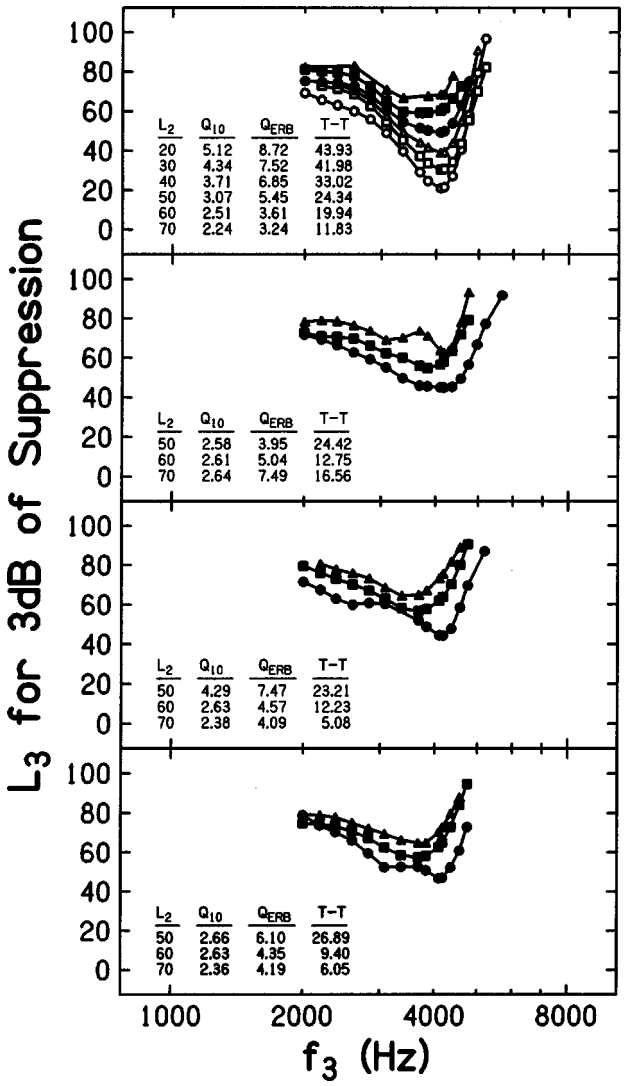

FIG. 6. Suppressor level (L_3) necessary for 3 dB of suppression as a function of f_3 for a subject with normal hearing (top) and for three subjects with hearing loss (bottom three panels). Within each panel, the parameter is L_2. Q_{10}, Q_{ERB}, and tip-to-tail differences for each tuning curve are given within each panel.

hearing-impaired subjects. Each panel represents data for a different L_2, with solid lines representing data for normal ears, and dotted lines representing data for ears with hearing loss. As expected from the previous discussion, DPOAE STCs could be constructed for L_2 levels ranging from 20 to 70 dB SPL in ears with normal hearing and from 50 to 70 dB SPL in ears with hearing loss.

STCs in normal and impaired ears appeared to be similar at the three absolute levels for which comparisons could be made. In the STCs from ears with normal hearing, there was a tendency for the best suppressor frequency to shift towards lower frequencies as level increased. Although less obvious in ears with hearing loss (primarily because there was a smaller range of L_2 levels to consider), the best frequency also shifted towards lower frequencies as L_2 increased. There was a tendency for the suppression thresholds on the tails of the STCs to occur at a lower level for ears with hearing loss, compared to thresholds for similar frequencies in normal ears.

E. Q_{10} and Q_{ERB}

Figure 8 provides a scatter plot of the individual values of Q_{10} and Q_{ERB} (top and bottom rows, respectively) as a function of audiometric threshold. Q_{10} is defined as the best frequency (f_3 frequency with the lowest suppression threshold) divided by the bandwidth at a level 10 dB above the suppression threshold at best frequency (BF). Q_{ERB} is defined as the BF divided by the equivalent rectangular bandwidth (ERB). For any filter, the corresponding ERB is the bandwidth of the rectangular filter with the same BF response that passes the same total power. The DPOAE STCs

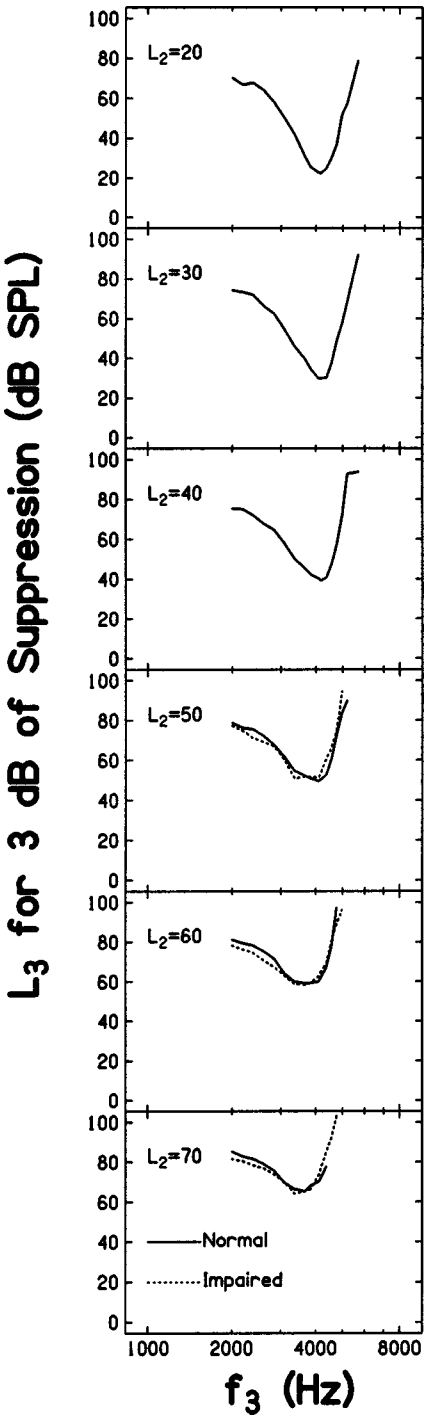

FIG. 7. Mean DPOAE STCs for normal-hearing and hearing-impaired ears plotted as the suppressor level in dB SPL for 3 dB of suppression as a function of f_3. Each panel shows the STC for a different L_2. STCs for subjects with normal hearing are shown as solid lines, while STCs for subjects with hearing loss are shown as dotted lines.

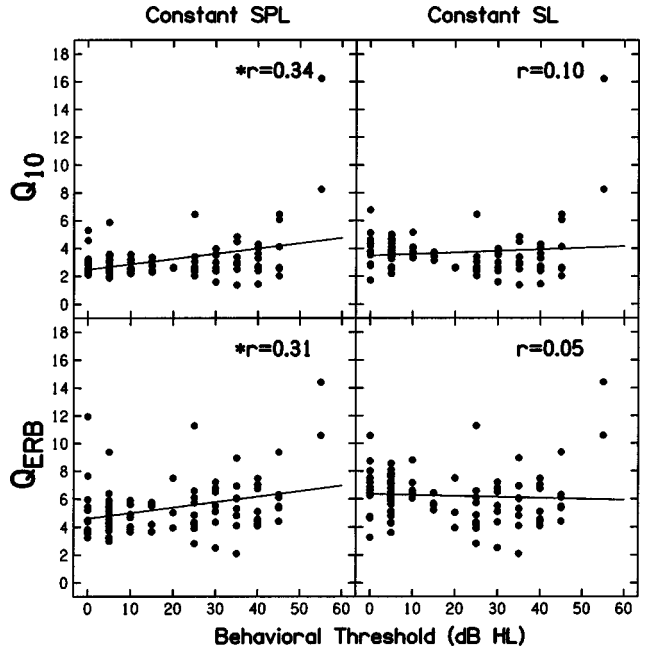

FIG. 8. Scatter plots of Q_{10} (top row) and Q_{ERB} (bottom row) as a function of audiometric threshold (dB HL) for the case when stimuli were presented at a constant SPL (left column) or constant SL (right column).

were inverted for the purpose of computing the ERB. While Q_{10} is the more common way of quantifying the sharpness of both neural and DPOAE tuning curves, Q_{ERB} has been used to estimate the tuning in behavioral estimates of frequency resolution (e.g., Shera, Guinan, and Oxenham, 2002).

The left column shows data from the two groups at constant SPL, but lumps together the data for the three L_2 levels summarized in each panel. Thus, it includes data from normal and impaired ears when $L_2=50$, 60, and 70 dB SPL. The right column similarly collapses data across three L_2 levels, but includes data when L_2 was more similar in SL. Thus, it includes data from normal ears when $L_2=20-40$ dB SPL, but includes data from impaired ears when $L_2=50-70$ dB SPL. As can be seen in Fig. 8, there was considerable overlap between normal and impaired Qs, and the relation between these values and audiometric thresholds was not obvious. This was true, whether the relation was evaluated at equivalent SPL or equivalent SL. Correlation analyses were consistent with this observation at equivalent SL (right column, Fig. 8). However, correlations ($r=0.34$ or 0.31) were significant for both Q_{10} and Q_{ERB} at equivalent SPL (left column, Fig. 8). In spite of these correlations, an examination of the actual data suggests that a strong relationship between tuning around the tip of the STC and audiometric threshold did not exist, at least for the data from the present group of subjects.

Figure 9 shows mean Q_{10} and Q_{ERB} in the top and bottom panels, respectively, as a function of L_2 for both normal and impaired ears. Regardless of which estimate was used, the sharpness of tuning decreased as L_2 increased for subjects with normal hearing. Mean Q_{10} values of about 4 were observed when L_2 was 20 or 30 dB SPL, decreasing to a value of 2.6 at the highest probe levels. Similarly, Q_{ERB} decreased from average values of 6.5 at low L_2 levels to about 4.4 for L_2 levels of 60 dB SPL or greater. For ears with hearing loss, Q_{10} was slightly larger, compared to values observed in ears with normal hearing, when the estimates were derived at the same absolute L_2 levels. Q_{ERB} estimates also were slightly larger in ears with hearing loss. For both Q_{10} and Q_{ERB}, the differences between groups were small; however, an ANOVA for constant SPL conditions revealed that these differences, although small, were significant. No significant differences were noted when the data for normal

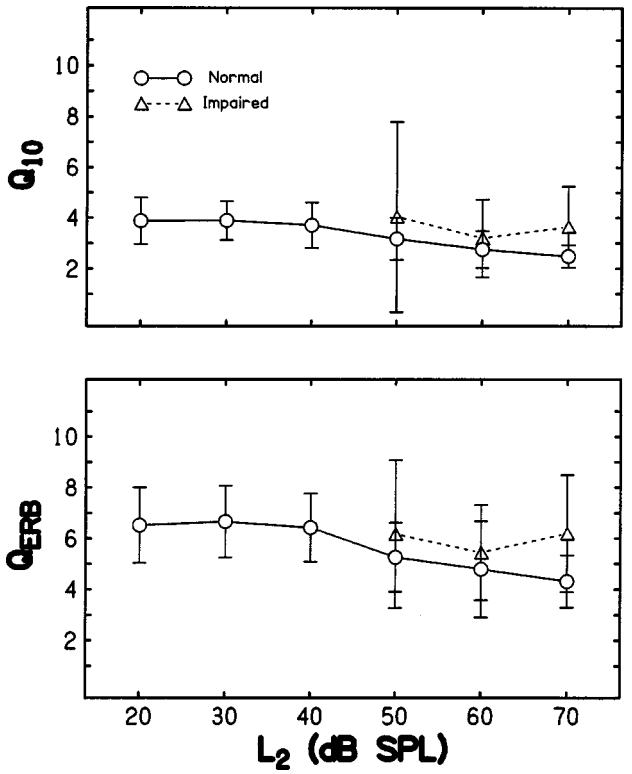

FIG. 9. Mean Q_{10} and Q_{ERB} as a function of L_2 in the top and bottom panels, respectively. Error bars represent ± 1 s.d. Data for subjects with normal hearing are shown as circles, while data for ears with hearing loss are shown as triangles.

ears at 20–40 dB SPL were compared to data from impaired ears at 50–70 dB SPL, which is the equivalent SL condition. Whether comparisons were made at constant SPL or SL, and in spite of the statistical observations, these estimates were variable in both normal and impaired ears, and the distributions of normal and impaired *Q*s overlapped, as can be seen in plots of individual (Fig. 8) and mean (Fig. 9) data.

F. Tip-to-tail differences (dB)

Following an approach initially proposed by Mills (1998), based on data from animal studies, and since used by Pienkowski and Kunov (2001) and Gorga *et al.* (2002b) to describe similar human DPOAE data, suppression thresholds were compared for a suppressor at the STC tip (i.e., close to f_2) and for a suppressor on the low-frequency tail of the STC. The differences between these suppression thresholds were estimated for the range of L_2 levels at which the measurements were made in each subject group. This quantity, which is specified in dB, is sometimes referred to as the tip-to-tail difference or the tip-to-tail ratio. The tails of the STCs were not completely flat, meaning that suppression threshold continued to slowly increase as f_3 decreased. As a consequence, the "tail" threshold was defined as the threshold for the 2.2–kHz suppressor because it was close to the lowest f_3 used in the present experiment and it was a suppressor frequency for which criterion suppression was measurable in the majority of cases. The tip-to-tail differences were derived for normal and impaired ears at all L_2 levels at which STCs could be measured.

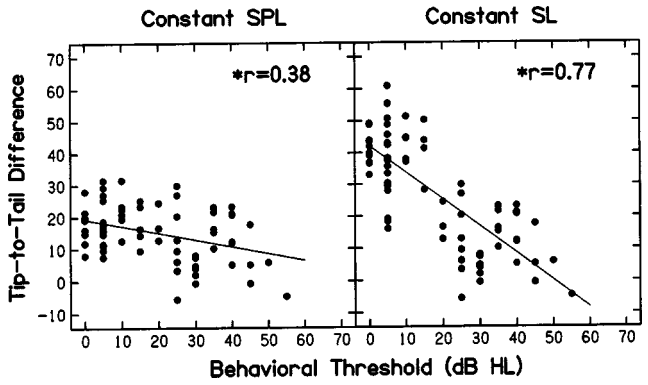

FIG. 10. Scatter plots of tip-to-tail difference (dB) as a function for audiometric threshold (dB HL). Left panel: data for stimuli presented at a constant SPL. Right panel: data for stimuli presented at a constant SL.

Figure 10 provides scatter plots of individual tip-to-tail differences as a function of audiometric threshold, following the convention that was used in Fig. 8. Thus, data are presented for equivalent SPL conditions (left panel) and equivalent SL conditions (right panel). Data are collapsed across the three L_2 levels represented in each panel, just as they were for the Q values represented in Fig. 8. A significant relationship was observed between tip-to-tail differences and audiometric thresholds, in that these differences decreased as audiometric thresholds increased, even though the data were variable at each audiometric threshold. Correlations ranged from 0.38 for the equivalent SPL condition to 0.77 for the equivalent SL condition. This represents a main observation in the present study. While tuning around the tip of the STCs did not depend strongly on audiometric threshold, the relationship between threshold at the tip and on the tail of the STC decreased systematically as threshold increased.

The results shown in Fig. 10 are summarized in Fig. 11, where the top panel plots the mean suppressor level (L_3) necessary for 3 dB of suppression as a function of L_2 for subjects with normal hearing. The parameter is f_3, with filled circles showing data for the case when $f_3 \approx f_2$ and open circles showing the results when $f_3 < f_2$. Note that when $f_3 \approx f_2$, the suppressor level necessary to achieve 3 dB of suppression was nearly equal to probe level (L_2), which also means that criterion suppressor level increased linearly with L_2. In contrast, a higher L_3 was required for 3 dB of suppression when the suppressor was 2.2 kHz, as expected from the individual STCs shown in Fig. 6 and the scatter plots in Fig. 10. For example, when $L_2 = 20$ dB SPL, an L_3 of about 65 dB SPL was needed in order for the criterion suppression to occur. However, L_3 increased at a slower rate, compared to L_2, for this low-frequency suppressor.

In similar fashion, the middle panel plots mean suppression thresholds as a function of L_2 for the same on-frequency and low-frequency suppressors in subjects with hearing loss. In this case, filled triangles represent results when $f_3 \approx f_2$, and open triangles represent data when $f_3 = 2.2$ kHz. As expected from previous results, suppression was measurable over a restricted range of L_2 levels in impaired ears, compared to ears with normal hearing, and data from impaired ears were characterized by greater variability. However, for those L_2 levels at which suppression could be measured, the

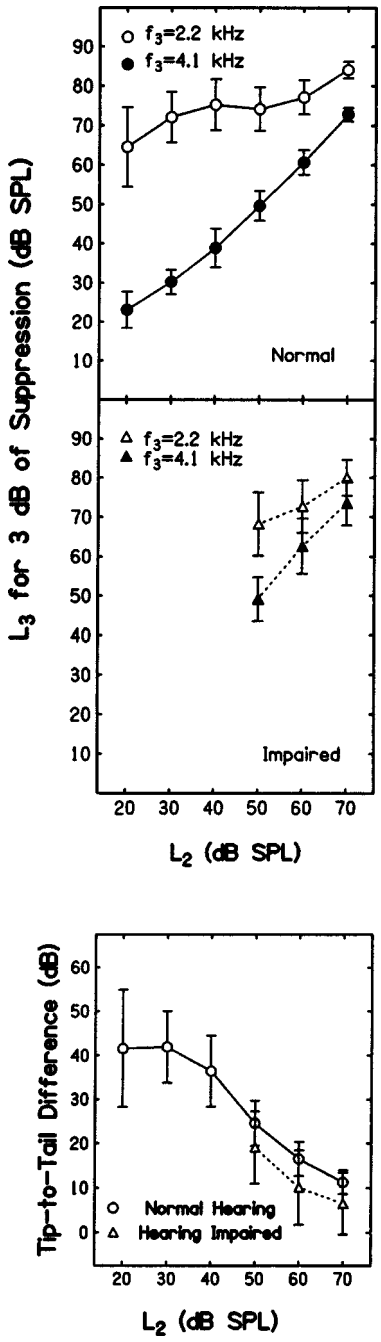

FIG. 11. Mean suppressor level (L_3) necessary for 3 dB of suppression (in dB SPL) as a function of probe level (L_2) for an on-frequency suppressor ($f_3=4.1$ kHz, filled symbols) and for a low-frequency suppressor ($f_3=2.2$ kHz, open symbols). Error bars represent ± 1 s.d. Top panel presents data from normal-hearing subjects; middle panel shows results for subjects with hearing loss. Bottom panel: The tip-to-tail difference (in dB as a function of L_2; data from subjects with normal hearing are shown as circles, while data from subjects with hearing loss are shown as triangles.

overall pattern of response for low- and on-frequency suppressors appears to be similar for the two groups. That is, the ''threshold'' suppressor level approximated L_2 and, thus, grew linearly with L_2 when $f_3 \approx f_2$. Higher suppressor levels were needed when $f_3=2.2$ kHz, while L_3 increased more slowly for this condition, compared to the case when $f_3 \approx f_2$.

The data shown in the top two panels are summarized in the bottom panel of Fig. 11, in which the mean levels for suppression thresholds when $f_3=4.1$ kHz were subtracted from the thresholds when $f_3=2.2$ kHz, and this quantity is plotted as a function of L_2. Thus, the bottom panel plots the mean tip-to-tail difference in dB for both subject groups. In normal-hearing ears, the tip-to-tail difference decreased as L_2 increased, going from a maximum of about 42 dB ($L_2=20$ dB SPL) to a minimum of about 12 dB ($L_2=70$ dB SPL). At the three L_2 levels at which data were obtained in impaired ears, tip-to-tail differences also systematically decreased with L_2. Ears with hearing loss, however, produced tip-to-tail differences that were 5–6 dB smaller than those produced by subjects with normal hearing at the same L_2 levels, although variability in these measurements was large, especially among ears with hearing loss. An ANOVA revealed significant effects for both L_2 and group, but no interactions between L_2 and group. This was true for both the constant SPL and the constant SL conditions.

IV. DISCUSSION

To summarize the results from the present experiment, threshold and growth of suppression (measured in the form of DPOAE decrement vs L_3 functions) depended on the relationship between suppressor frequency (f_3) and probe frequency (f_2) both in normal-hearing and hearing-impaired subjects (Figs. 3, 4, and 5). When $f_3<f_2$, suppression threshold occurred at higher levels and the slope of the decrement function was steeper, compared to cases when $f_3 \approx f_2$. While suppression threshold increased as f_3 increased above f_2, the slopes of the decrement functions decreased in both subject groups. There were differences, however, between normal and impaired ears in that the differences in slope between low-frequency ($f_3<f_2$) and high-frequency suppressors ($f_3>f_2$) were less in impaired ears. The decrement-vs-L_3 data were used to generate DPOAE STCs, in which the suppressor level necessary for 3 dB of suppression was plotted as a function of f_3 (Figs. 6 and 7). While STCs were measurable over a more limited range of absolute probe levels (L_2) in ears with hearing loss, at the same absolute probe levels, mean STCs in normal and impaired ears were similar in appearance. These similarities were noted around the tips of the STCs, in that there was overlap in the estimates of Q_{10} and Q_{ERB} for the two groups (Figs. 8 and 9). There was a tendency towards sharper tuning around the tip of the STC in ears with hearing loss, although this effect was significant only for conditions of equivalent absolute L_2 levels in normal and impaired ears. In contrast, ears with hearing loss produced smaller tip-to-tail differences, compared to subjects with normal hearing, with a larger effect for comparisons in which L_2 was presented at roughly equivalent SL (Figs. 10 and 11).

The relationship between the slopes of decrement functions as a function of suppressor frequency in normal ears has been observed in several previous DPOAE studies (e.g., Kemp and Brown, 1983; Kummer *et al.*, 1995; Abdala, 1998, 2001; Gorga *et al.*, 2002b). In turn, these data are consistent with previous animal studies in which it was shown that the response at any point along the cochlea grows more rapidly when that place is driven by a stimulus whose frequency is

lower than the best frequency for that place (Rhode, 1971; Sachs and Abbas, 1974; Schmiedt and Zwislocki, 1980; Ruggero and Rich, 1991; Ruggero *et al.*, 1997).

The observation that the slopes of these functions in ears with mild-moderate hearing loss were, in general, shallower for low-frequency suppressors, compared to data in normal hearing ears was not expected. Previous studies in animals suggest that response growth changes as a consequence of cochlear damage (Evans, 1974; Sewell, 1984; Gorga and Abbas, 1981a,b; Ruggero and Rich, 1991). A recent study in animals with noise-induced hearing loss described best-frequency rate-level functions that sometimes were shallower than normal, normal, or steeper than normal (Heinz *et al.*, 2003). They attributed the variation in slopes to differences in cochlear damage (IHC damage, OHC damage, or some combination of IHC and OHC damage), although cochlear status was not assessed directly. Likewise, the status of the OHCs and the IHCs cannot be known in the present study. In those studies that examined response growth for on- and off-frequency stimuli, however, little or no change in response growth was observed following cochlear damage for a stimulus that was lower than the best or probe frequency. Stated differently, the response to a low-frequency stimulus was relatively insensitive to the status of the cochlea at a high-frequency place. However, the slope of response-growth functions tended to increase (relative to the normal case) for stimuli close to the best frequency when cochlear damage existed. The present results appear, at least at face value, to differ from these previous findings. There was more similarity in the slope of these decrement functions for low- and high-frequency suppressors in impaired ears. This occurred because there was a small decrease in slope for suppressors below f_2 and perhaps an even smaller increase in slope for suppressors above f_2.

The differences between the present findings and predictions from studies in lower animals may be due to the differences in the measurement paradigms used to collect the data. Unlike previous animal experiments, in which response growth can be examined directly by presenting a single tone, such measurements are not possible in humans. In studies involving humans, a probe (the primaries in the present case) must be presented and response growth to another tone (the suppressor) must be inferred from the changes it causes to the probe response. The integrity of the OHCs presumably should not influence the response to a low frequency at a high-frequency place because the high-frequency place only responds nonlinearly when it is excited by frequencies close to its best frequency. Evidence in support of this view comes from single-unit studies in animals where OHC damage exists. Tail thresholds remain relatively constant (or perhaps even hypersensitive) so long as the damage is restricted to the OHCs (Dallos and Harris, 1978; Liberman and Dodds, 1984). Further support for this view comes from studies in which basilar-membrane motion was measured before and after treatment with furosemide, an agent known to reversibly impair cochlear function (Ruggero and Rich, 1991). While the response from a high-frequency cochlear place to best-frequency tones changed when furosemide was administered, there was little change at that same place when it was stimulated with a low-frequency tone.

It may be reasonable to assume, therefore, that the effects of the low-frequency suppressors were the same in normal and impaired ears. However, the response to suppressors must be inferred from the changes their presentation causes to the response to the probe. Perhaps the slope patterns observed in the present study are a consequence of the fact that our measures reflect the relative growth of response between suppressor and probe. If the growth of response was more alike in impaired ears for low- and on-frequency conditions, then differences in slope across frequency might be reduced, not because the low-frequency slope has become more shallow, but because the on-frequency slope has become more steep.

Measures of tuning, based on the present measurements, also revealed some interesting trends. DPOAE STCs in normal and mildly impaired ears appeared to be similar when they were compared at the same probe levels (L_2). In spite of the statistical outcome indicating that impaired ears produced larger Q_{10} and Q_{ERB} than normal-hearing ears when the probes were presented at equivalent SPL, it is difficult to consider the individual data presented in Fig. 8 and conclude that these differences are meaningful. That is, there was overlap between Q_{10} and Q_{ERB}, regardless of audiometric threshold. These results, at one level, are similar to those observed in two recent papers in which either loop diuretics (Martin *et al.*, 1998) or noise exposure (Howard *et al.*, 2002) was used to induce temporary, reversible effects in the cochleae of rabbits. This group recently observed similar effects when more permanent noise-exposure damage was induced in rabbits (Howard *et al.*, 2003). In all three studies, there was little difference in the DPOAE STCs prior to and soon after cochlear insult (although some STCs in impaired ears appeared more variable compared to the pre-exposure or pre-treatment cases). In fact, there may actually have been a tendency for some STCs reported in these previous studies to become more sharply tuned after insult. In any case, Martin *et al.* and Howard *et al.* observed little or no change in either Q or tip-to-tail differences following cochlear insult. As a result of these findings, they concluded that DPOAE suppression measurements do not provide the same information about cochlear tuning as do other measurements, such as single-unit frequency-threshold curves or direct measurements of basilar-membrane tuning. The present observation of little or no difference between the DPOAE STC sharpness around the tip (Q) in normal and impaired ears would be consistent with the observations made by Martin *et al.* and Howard *et al.* There are other physiological data in the form of single-unit frequency-threshold curves (Dallos and Harris, 1978; Liberman and Dodds, 1984) or forward-masking action potential (AP) tuning curves (Gorga and Abbas, 1981b), suggesting that tuning around the best frequency (single-unit studies) or probe frequency (AP studies) may be similar in ears with normal and impaired hearing, at least for ears with mild-to-moderate threshold elevations. Stated differently, hearing loss (by definition) causes an elevation of threshold at best frequency, but not necessarily a decrease in tuning around best frequency. Thus, the present observations in re-

gard to Q are consistent with previous DPOAE data and with the results of single-unit and AP masking studies in animals with induced lesions. While the present findings in relation to tip-to-tail differences are also in agreement with previous single-unit and AP data, they differ from DPOAE data in animals with induced cochlear damage that showed no change in tip-to-tail differences (Martin *et al.*, 1998; Howard *et al.*, 2002, 2003).

Conclusions about tuning at the tip in normal and impaired ears might be modified by examining level effects. In the present data, Q_{10} and Q_{ERB} (in addition to tip-to-tail differences) decreased as level increased, an observation that was more pronounced in ears with normal hearing. Larger Qs were seen at low probe levels (L_2 levels of 20–40 dB SPL), compared to L_2 levels at and above 50 dB SPL. Less systematic changes with level were observed in impaired ears. However, this may have occurred because of the restricted range of possible measurements in impaired ears. Hearing loss in these subjects increased DPOAE threshold and/or reduced DPOAE level (see Fig. 1). Because suppression experiments require an unsuppressed response of some level that subsequently will be reduced by the suppressor, it was necessary to perform the experiments in impaired ears only at the higher L_2 levels for which some reduction in tuning occurs in normal ears. This suggests that the lack of differences between Qs in normal and impaired ears might represent a level effect. Thus, the observation of differences between normal and impaired ears might depend on the way the level is chosen at which comparisons will be made. This argument, however, is not supported by the observation that the overlap in Qs was similar, regardless of whether normal and impaired data were compared at equivalent SPL or equivalent SL (see Fig. 8). The present data, therefore, suggest that Q is relatively insensitive to probe level (L_2) or audiometric threshold, at least among subjects with no worse than a moderate hearing loss, statistical results for Q notwithstanding.

The present estimates of Q_{ERB} in human ears with normal hearing are less than the values recently reported by Shera *et al.* (2002), whose estimates were based on stimulus-frequency otoacoustic emission (SFOAE) and behavioral forward-masking measurements in humans. For example, their SFOAE estimates of Q_{ERB} were 15–20 at 4 kHz, while their behavioral Q_{ERB} estimates were close to 15 at 4 kHz. Their measurements were made with a 40-dB SPL probe. At this level, the current estimates of Q_{ERB}, on average, were about 6.5. This value is closer to the values (about 8 or 9 at 4 kHz) observed in a number of other papers (as summarized by Glasberg and Moore, 1990), in which simultaneous masking techniques were used. Thus, the differences between our estimates and the recent estimates by Shera *et al.* might relate to the fact that the data reported by Shera *et al.* represent the excitatory response area, while the present measurements (as well as those summarized by Glasberg and Moore) include suppressive, as well as excitatory, areas in the response. The SFOAE measurements of Shera *et al.*, although derived in a suppression paradigm, represent the unsuppressed response to a single tone. Similarly, their forward-masking behavioral data presumably describe only the excitatory representation to the probe and not the wider representation due to suppression (see Sachs and Kiang, 1968, for a classic description of excitatory and suppressive regions in the responses of auditory neurons). This would be the case because suppression is memoryless, occurring only when the probe and suppressor (or masker) are on at the same time. In contrast to the paradigm used by Shera *et al.*, the present measurements were derived from suppression measurements, and thus would be expected to result in wider estimated bandwidths. In addition, the probe in the present study consisted of two tones, slightly different in frequency. Both tones contribute to the generation of the DPOAE, and, because of this, it is possible that a wider range of suppressors is effective in reducing the response. While both factors may account for the differences in Q estimates between the present study and the data reported by Shera *et al.*, it is uncertain how this distinction would impact the present comparisons between normal and impaired ears. Perhaps an effect of hearing status would have been observed (in Q_{10} and Q_{ERB}) if the data were derived from a paradigm that did not include the effects of suppression. A paradigm in which only the excitatory regions were evaluated might have resulted in sharper tuning (higher Q) in normal ears because the suppression region would not have been outlined, but might have had no effect on the tuning in impaired ears. Unfortunately, isolating the excitatory region in normal ears is not possible for measurements like those used in the present study.

In normal ears, it is assumed that nonlinear processing occurs at a specific place when that place is driven by its best or characteristic frequency. In suppression experiments like the present study or psychophysical masking studies (Oxenham and Plack, 1997), the growth of suppression (or masking) with probe level is linear when probe frequency approximates suppressor frequency because both the suppressor (or masker) and the probe are being processed through the same nonlinear mechanism. In contrast, low-frequency suppressors (or maskers) are processed more linearly at the place where the probe is primarily represented. Thus, a high-frequency probe is processed nonlinearly (compressively) at its characteristic place, while a low-frequency suppressor is processed linearly at the same place. As a consequence, functions relating suppressor level to probe level grow at a slow rate when suppressor frequency is well below probe frequency, reflecting the compressive processing for the probe, but not for the low-frequency suppressor (see the top two panels of Fig. 11).

These effects were explored further in the present study by estimating tip-to-tail differences (Figs. 10 and 11). Tip-to-tail differences decreased as either level or audiometric threshold increased. When grouped dichotomously according to hearing status, normal and impaired results differed significantly, regardless of whether comparisons were made at the same SPL or the same SL. These data suggest that one effect of hearing loss might be to cause more upward spread of excitation in ears with hearing loss, even if the tuning close to the best frequency (f_2 in the present experiment) does not differ between normal and impaired ears. These results are consistent with single-unit data (e.g., Dallos and

Harris, 1978; Liberman and Dodds, 1984), in which the differences in tip and tail sensitivity decreased as the extent of the cochlear lesion (and the amount of threshold elevation) increased. In addition, they are consistent with forward-masking AP data, in which tip-to-tail differences in normal ears were larger than those observed in ears with noise-induced hearing loss, regardless of whether the probe in the normal ears was presented at the same SL or the same SPL as was used in impaired ears (Gorga and Abbas, 1981b).

The influence of stimulus level appears to be consistent with data reported by Rubsamen *et al.* (1995), in which DPOAE levels and neuronal thresholds were correlated before and after administration of furosemide. At low and moderate primary levels, the DPOAE level decreased and the neuronal threshold increased synchronously. Decreases in DPOAE level of 30 dB or more and increases in unit thresholds of 50 dB or more occurred at essentially the same time. As the primary levels increased, however, the size of the reduction in DPOAE level decreased. At primary levels of 80 and 70 dB SPL (L_1 and L_2, respectively), smaller changes in DPOAE level were observed (see Fig. 5, Rubsamen *et al.*, 1995, for an example of these effects). Stated differently, changes in DPOAE level were more apparent when low-level primaries were used to elicit these responses, compared to the case when higher-level stimuli were used. This effect is consistent with other reports that have shown that the sensitivity of DPOAE measurements to hearing loss is greater for lower level primaries (e.g., Whitehead *et al.*, 1995; Stover *et al.*, 1996).

Mills (1998) described an approach in which DPOAE STCs were used to calculate differences between on-frequency and low-frequency thresholds, and proposed that these differences related to the ''gain of the cochlear amplifier.'' As stated above, this idea is based on the notion that active nonlinear processes occur when a given place in the cochlea is driven by its ''best'' or ''characteristic'' frequency (CF), and these nonlinear processes are absent when the same place is driven by a frequency much lower than CF. Pienkowski and Kunov (2001) applied this approach with humans whose audiometric thresholds fell within broad normal limits, using a single set of moderate-level primaries. We further explored this application by measuring tip-to-tail differences for a wide range of primary levels in humans with normal hearing (Gorga *et al.*, 2002b). The tip-to-tail differences previously observed by us decreased with primary levels in a manner that was similar to what was observed for normal-hearing subjects in the present study. One interpretation of these data might be that the gain of the cochlear amplifier (if that is what is being estimated by measurements of tip-to-tail differences) decreases as level increases. It is as if the need for amplification of low-level stimuli decreases as level increases. If this notion is correct, it might provide a framework for interpreting the present results. Specifically, both hearing status and probe level might be exerting an influence on the tip-to-tail difference in impaired ears. The ''gain'' in ears with hearing loss could only be measured for L_2 levels of 50–70 dB SPL, for the reasons described previously. These are levels for which, under normal circumstances, less gain is evident. Thus, differences between normal and impaired ears are reduced when compared at the same absolute levels because of changes with level to the nonlinear processing in ears with normal hearing. Added to this level effect is the effect of hearing loss. Thus, the small differences between normal and impaired ears (at equivalent SPL) relate to the fact that comparisons could be made only for high-level responses, with their attendant reduced gain under normal conditions. The further reduction in the tip-to-tail differences in ears with hearing loss might reflect an additional consequence of hearing loss, namely an increase in upward spread of excitation.

There are several potentially important differences between the way single-unit frequency-threshold curves (FTC) and psychophysical tuning curves (PTC) are measured, compared to how the present DPOAE STCs were derived. In the case of single-unit FTCs, ''threshold'' typically is defined as the stimulus level that results in a specified increase in discharge rate above the spontaneous rate (for example, see Liberman, 1978). Thus, the threshold represents a level that causes a small response on the nerve fiber. PTCs typically are measured by setting a probe tone slightly above its threshold, and then presenting maskers that render this barely audible sound inaudible. In contrast, DPOAE STCs typically are measured by presenting the probe (f_2 and f_1) at a level that produces a response well above its threshold. This suprathreshold response is then suppressed by some criterion amount (i.e., decrement) in order to produce a DPOAE STC. It may be an important distinction that both FTCs and PTCs are measured at near-threshold levels (either as an increase in discharge rate or as the masking of a low-level probe), while DPOAE STCs are measured as reductions in level for a suprathreshold response that typically is elicited by moderate level probes. Howard *et al.* (2002) made this point when noting the unexpected finding that DPOAE STCs in ears exposed to noise did not show changes in tuning-curve properties that might be predicted from FTCs measured at the level of an auditory neuron. Perhaps more similarity would be observed if DPOAE STCs were measured in paradigms more skin to the paradigms used in FTC or PTC measurements.

Another important difference relates to the levels in the auditory system that are assessed during DPOAE measurements, compared to either single-unit or psychophysical studies. It is reasonable to assume that DPOAE studies describe only OHC function, and are uninfluenced by the status of the IHCs, auditory nerve, or higher levels of the auditory system (admittedly ignoring influences from the efferent system). In contrast, single-unit studies provide information related to both OHC and IHC status, and psychophysical masking studies (although dominated by the status of the auditory periphery) also may be affected by more central phenomena.

Finally, there is perhaps a parsimonious (and less interesting) explanation for the present findings, related to subject selection criteria. Special effort was made to recruit subjects with mild-to-moderate hearing loss at 4 kHz. However, this inclusion criterion alone was insufficient. It was necessary that each ear produce a DPOAE of sufficient level in order to conduct these suppression studies. A total of 29 ears of 25

subjects with mild-to-moderate hearing loss was recruited, but DPOAE suppression experiments were possible in only 23 ears of 21 of these subjects. These subjects produced responses of sufficient level to permit measurements of suppression of that response. Thus, the subjects with hearing loss included in the study constitute a biased sample in that they produced larger DPOAEs than the excluded subjects. While this was necessary in order to conduct suppression experiments, it suggests the possibility that the present subjects are NOT entirely representative of patients with mild-to-moderate hearing loss. This caveat regarding bias in the selection of subjects with hearing loss may be unnecessary, given the fact that the majority of ears with mild-to-moderate hearing loss produced responses.

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