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Distortion product otoacoustic emission suppression tuning curves in human adults and neonates

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Abstract

Distortion product otoacoustic emission (DPOAE) iso-suppression tuning curves (STC) were generated in 15 normal-hearing adults and 16 healthy term-born neonates for three f_2 frequencies. The $2f_1$-f_2 DPOAE was elicited using $f_2/f_1 = 1.2$, L1 = 65 and L2 = 50 dB SPL. A suppressor tone was presented at frequencies ranging from 1 octave below to 1/4 octave above f_2 and varied in level until DPOAE amplitude was reduced by 6 dB. The suppressor level required for 6 dB suppression was plotted as function of suppressor frequency to generate a DPOAE STC. Forward-masked psychoacoustic tuning curves (PTC) were obtained for three of the adult subjects. Results indicate that DPOAE STCs are stable and show minimal inter- and intra-subject variability. The tip of the STC is consistently centered around the f_2 region and STCs are similar in shape, width (Q_{10}) and slope to VIIIth-nerve TCs. PTCs and STCs measured in the same subject showed similar trends, although PTCs had narrower width and steeper slope. Neonatal STCs were recorded at 3000 and 6000 Hz only and were comparable in shape, width and slope to adult STCs. Results suggest: (1) suppression of the $2f_1$-f_2 DPOAE may provide an indirect measure of cochlear frequency resolution in humans and (2) cochlear tuning, and associated active processes in the cochlea, are mature by term birth for at least mid- and high-frequencies. These results provide significant impetus for continued study of DPOAE suppression as a means of evaluating cochlear frequency resolution in humans.

Keywords: Otoacoustic emission; Distortion product; Suppression; Tuning curve

1. Introduction

Otoacoustic emissions (OAE) are low-level acoustic signals generated within the cochlea. They are thought to be by-products of an active cochlear mechanism or cochlear amplifier that works to enhance low-level sensitivity and frequency selectivity of the basilar membrane (Kim, 1986; Lim, 1986). Because they are generated solely in the cochlea, OAEs provide a window into preneural, cochlear function. They travel from their point of generation on the basilar membrane towards the place corresponding to their characteristic frequency and, at the same time, towards the cochlear base. OAEs travel through the middle ear and can be measured in the ear canal with a sensitive insert microphone.

There are two broad classes of OAEs: spontaneous and evoked. Distortion product OAEs (DPOAE) are evoked intermodulation products created by the cochlea when it is stimulated with two tones ($f_1 < f_2$) simultaneously. DPOAEs are present in normally functioning ears and occur at predictable frequencies related to the frequency of the primary tones (Lonsbury-Martin and Martin, 1990; Probst et al., 1991). The most robust DPOAE is observed at $2f_1$-f_2. Because DPOAEs are relatively narrow-band responses, they are considered by many to be the most valuable otoacoustic emission for investigating frequency-related phenomena, such as cochlear frequency resolution (Brown and Kemp, 1984; Lonsbury-Martin et al., 1987; Martin et al., 1987; Harris et al., 1989; Gaskill and Brown, 1990; Lonsbury-Martin and Martin, 1990; Whitehead et al., 1990, 1992a,b; Popelka et al., 1995).

Suppression occurs when the response of the cochlea to a stimulus is modified by presenting a second stimulus that falls within certain frequency and amplitude boundaries (Harris and Glattke, 1992). Suppression techniques have been used to confirm the cochlear origin of otoacoustic emissions and to a lesser extent for probing peripheral frequency resolution. Suppression experiments have been

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conducted with transient OAEs (Kemp, 1979; Wit and Ritsma, 1980; Folsom et al., 1995), spontaneous OAEs (Wilson, 1980; Zurek, 1981; Bargones and Burns, 1988; Long et al., 1993) and stimulus frequency OAEs (Kemp and Chum, 1980). However, sparse data are available to describe the characteristics of DPOAE suppression in the human auditory system (Brown and Kemp, 1984; Harris et al., 1992; Kummer et al., 1995). Suppression of distortion product OAEs is produced by presenting a third tone (within a given frequency range) simultaneously with the two stimulating tones, f_1 and f_2, and varying the level of the suppressor tone until the amplitude of the DPOAE is reduced. The suppressor level required for criterion amount of DPOAE suppression as a function of suppressor frequency, is known as a DPOAE iso-suppression tuning curve (STC).

Brown and Kemp (1984) conducted the initial study investigating iso-suppression of the $2f_1$-f_2 DPOAE in gerbils and in a limited sample of human adult subjects. They generated DPOAE STCs with 13–18 suppressor tones in a few human ears with limited primary tone frequency combinations. Suppressor tones close in frequency to the stimulating tones (particularly near f_2) were most effective in suppressing the distortion product, thus forming the tip of the STC. The tip is the frequency at which criterion suppression is achieved with the lowest suppressor level; it presumably reflects the frequency region where stimulating tones interact and generate the distortion product (Brown and Kemp, 1984; Martin et al., 1987). When Brown and Kemp presented suppressor tones at frequencies close to $2f_1$-f_2 (DP-place), high levels of the suppressor were needed to reduce emission amplitude, suggesting minimal importance for this region in the generation process.

Consistent with the work of Brown and Kemp, Harris et al. (1992) found that adult human DPOAE STCs typically had tips centered around f_2 rather than at the DP-place and Q_{10} and slope values were similar to other types of physiological tuning curves. Based on this similarity, Harris and colleagues concluded that ear canal measurements of DPOAEs can be used as an indirect measure of cochlear frequency resolution. However, these investigators generated DPOAE STCs using only 7–8 suppressor frequencies per STC, presented at frequency intervals as large as 500 Hz, consequently, tuning curve resolution was limited.

More recently, Kummer et al. (1995) conducted a detailed analysis of fine-resolution DPOAE STCs recorded from human adults for four f_2 frequencies. They observed STC shape, width and tip characteristics comparable to previously reported results. They also documented the growth and threshold for suppression and addressed questions about the influence of suppression criteria on tuning, multiple sources of DPOAE energy and complexities inherent in the DPOAE suppression paradigm. Despite well-founded cautions offered in this research report, they cite their findings of asymmetry in suppression growth, and broadened tuning with increasing stimulus levels as evidence that DPOAE STCs reflect suppression of the basilar membrane mechanical response.

DPOAE suppression paradigms have been applied effectively to rodents, bat and lizard as well (Brown and Kemp, 1984; Martin et al., 1987; Koppl and Manley, 1993; Frank and Kossl, 1995). In non-human mammals, the frequency region around the primary tones is also most critical to the DPOAE generation process (Brown and Kemp, 1984; Martin et al., 1987, 1995). Recently, Frank and Kossl (1995) investigated DPOAE suppression in the mustached bat (*Pteronotus parnelli*). The bat has regions of cochlear specialization where the basilar membrane is thickened relative to non-specialized regions. DPOAE STCs generated from these specialized cochlear areas were found to be considerably different in shape and tip form than the STCs generated in the same animal from non-specialized regions in the cochlea. These results strongly suggest that DPOAE STCs can provide an accurate reflection of cochlear function and structure.

The cumulative research suggests that DPOAE suppression tuning curves in non-human mammals and human adults reflect cochlear frequency resolution around the region of primary tone stimulation; however, additional studies are needed to replicate and confirm human findings. Also, DPOAE STCS from humans have not been compared to tuning curves generated with an established methodology such as a psychoacoustic paradigm. Finally, there have been no studies of DPOAE suppression in human neonates.

The present report describes two sequential experiments conducted to further investigate DPOAE suppression in the human auditory system; Experiment I evaluated DPOAE iso-suppression tuning curves in normal-hearing adults and Experiment II evaluated DPOAE STCs in healthy term-born neonates. The objectives were: (1) to investigate the nature of DPOAE iso-STCs recorded with fine resolution from normal-hearing human adults and compare the adult DPOAE STCs to forward-masked psychoacoustic tuning curves (PTC) in the same subjects and, (2) to record DPOAE STCs in term-born human neonates and evaluate the maturity of cochlear tuning in this population.

2. Methods

2.1. Subjects

2.1.1. Experiment I

Fifteen normal-hearing adults with thresholds between 250 and 8000 Hz < 15 dB HL, ranging in age from 21 to 33 years were used as subjects in this study (9 female, 6 male). Three of the 15 adults also served as subjects for the generation of PTCs. None of the adult subjects had a history of noise exposure or otologic pathology.

2.1.2. Experiment II

Sixteen newborn infants (9 male, 7 female) were used as subjects after obtaining parental consent. Infants were tested between 24 and 108 h (mean hours = 63) after term birth (36–41 weeks gestation) at Women and Children's Hospital, Los Angeles County University of Southern California Medical Center. The infant subjects had no high-risk factors for hearing loss and were delivered after a normal pregnancy. The mean 1-min APGAR score was 8 and mean 5-min APGAR score was 9.1. Birthweight ranged from 2320 to 4855 g with a mean of 3249 g.

2.2. Instrumentation and signal analysis

A custom-designed system was used to obtain suppression tuning curves. The hardware included an Ariel DSP16 + signal processing and acquisition board connected directly to an Etymotic Research ER-10C probe system. The ER-10C probe contains two output transducers and a low-noise microphone. The probe was coupled to the subject's ear via a foam tip.

The two primary tones and the suppressor tone were generated by the DSP board. The primary tone at f_1 was generated by one D/A-converter and delivered via one transducer. The primary tone at f_2 and the suppressor tone (f_s) were both generated by the second D/A-converter and output through the second transducer. Energy at the probe microphone was sampled at a rate of 50 kHz with a sweep length of 4096 samples, giving a frequency resolution of 12.2 Hz. Twenty-five sweeps of the microphone signal were added and the sum stored as 32-bit integer values. An average of the sweeps was computed and the power spectrum was obtained by applying a 4096-point FFT. The level of the DPOAE was computed using the summed 32-bit data directly and 8-byte IEEE-format floating-point computations in the discrete Fourier transform.

An initial calibration procedure was conducted on both output transducers before each subject was tested. Tones of fixed voltage were presented to the transducers at 250 Hz intervals from 500 to 10000 Hz and the resulting SPL of these tones was recorded in the ear canal. Based on this information, an equalization of output levels was performed for each subject to achieve target stimulus and suppressor levels across all test frequencies.

Intermodulation distortion produced by the system at $2f_1$-f_2 was measured with the probe in a Zwislocki coupler for all test conditions. The mean level of distortion was −21 dB SPL. In no case did the level exceed −17 dB SPL. This is well below the level of the lowest amplitude emission recorded (−3 dB SPL). The system noise floor was determined using a similar method with no tones present. The level of the noise floor was −27 dB SPL for $f_2 = 3000$ and 6000 Hz and −22 dB SPL for $f_2 = 1500$ Hz. System distortion and the noise floor levels were between 82 and 92 dB below the f_1 primary-tone level.

2.3. Recording parameters and procedure

2.3.1. DPOAE suppression tuning curves in adults

The $2f_1$-f_2 DPOAE was elicited in all subjects with primary tones presented at 65 and 50 dB SPL for L1 and L2, respectively, and a 1.22 frequency ratio ($f_1 < f_2$). Previous experiments have found 10 to 15 dB level separation between primary tones and an average of 1.2 frequency ratio to be optimal in eliciting large amplitude DPOAEs in human adults (Harris et al., 1989; Gaskill and Brown, 1990). Low-moderate level primaries were selected because recent research has suggested that high-level DPOAEs may be produced by the passive mechanical properties of the basilar membrane rather than the action of the cochlear amplifier (Brown, 1987; Norton and Rubel, 1990; Whitehead et al., 1990). Three f_2 frequencies were chosen to represent tuning in the low- (1500 Hz), mid- (3000 Hz) and high-frequency (6000 Hz) regions of the human cochlea.

Initially, an unsuppressed emission was recorded. Following this, a suppressor tone was introduced at frequencies ranging approximately 1 octave below f_2 to 1/4 octave above f_2. The number of suppressor tones presented varied slightly among subjects due to practical constraints such as subject availability and cooperation. Suppressors were presented with 200–250 Hz spacing for the low and high segments of the tuning curve and 100 Hz spacing near the tip region. The level of the suppressor was increased in 2 dB steps until a 6 dB reduction in amplitude was obtained. Brown and Kemp (1984) recommended a 6 dB suppression criterion to generate DPOAE STCS because it provides good immunity from noise and allows for speed of data collection. Suppressor tones ranged from 30 to 84 dB SPL.

As the suppressor level was increased in 2 dB steps, DPOAE amplitude was gradually reduced. Input/output graphs (I/O) were constructed by plotting DPOAE amplitude as a function of suppressor level (Fig. 1a). The suppressor level that reduced DPOAE amplitude by 6 dB was determined from the I/O graph and was then plotted as a function of suppressor frequency. In order to construct a DPOAE STC, this process was repeated for 15–19 suppressor frequencies (Fig. 1b).

2.3.2. Psychoacoustic tuning curves

Forward-masking PTCs were obtained at 1500, 3000 and 6000 Hz from three of the 15 adult subjects for a total of seven PTCs. Stimuli were digitally generated by an IBM-PC computer and output through a 16-bit D/A converter at a sampling rate of 20 kHz (TDT model QDA2, Tucker-Davis Technologies). The stimuli were smoothed by an anti-aliasing filter (TDT model FLT3) with a cutoff frequency of 8 kHz. For measurement of the PTC at 6000 Hz, a 50 kHz sample rate was used and no anti-aliasing filter was necessary because of filtering imposed by the transducer. The levels of the probe tone and the masker

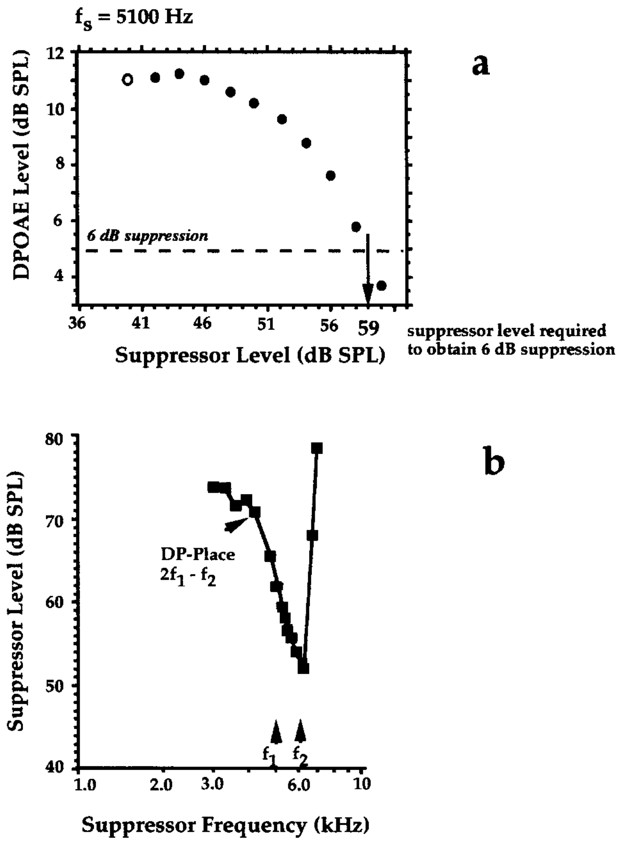

Fig. 1. a: I/O function of DPOAE level as a function of suppressor level for $f_2 = 6000$ Hz, $f_1 = 5000$ Hz and $f_s = 5100$ Hz. As the suppressor level is raised in 2 dB steps, DPOAE amplitude decreases. The dashed horizontal line and arrow indicate which suppressor level corresponds to 6 dB suppression in DPOAE. b: DPOAE iso-suppression tuning curve (STC) for $f_2 = 6000$ Hz.

were separately controlled by programmable attenuators (TDT model PA3). Monaural stimulation was used in the same ear that had provided DPOAE STCs in the initial experiment.

PTC probe stimuli were 20 ms pure tones of 1500, 3000 and 6000 Hz. The forward masker was of 100-ms duration, with a 1.0-ms delay between the offset of the masker and the onset of the probe. Stimuli were turned on with 5.0-ms cosine-squared ramps. The masker was presented at 1/8 octave intervals around the tip region of the PTC and 1/4 octave intervals for the low- and high-frequency segments. PTC masker frequencies reflect larger intervals than those used for DPOAE suppression. This was due to the excessive time requirements involved in generating PTCs relative to DPOAE STCs. Between 9 and 13 masker frequencies were used to construct each PTC.

The probe was presented at a level 5 dB below the level of the suppressor tone representing the tip of that own subject's DPOAE STC. Using this criterion, probe levels were ± 5 dB from the level of the f_2 primary tone (50 dB SPL) and ranged from 45–52 dB SPL. The PTC probe tones were presented at these levels to obtain better correspondence with the moderate-level primary tones used to generate DPOAE STCs. This adjustment brought PTC tip levels within 5 dB of DPOAE STC tip level in 5 out of 7 cases.

A 2-interval, 2-alternative forced-choice adaptive procedure was employed. All three subjects had 4–6 h of practice before test sessions were initiated. Each interval contained the masker stimulus and one of the randomly chosen intervals also included the probe tone. During test sessions, the subject was asked to indicate whether the probe tone was present in interval 1 or in interval 2. Subjects received trial-by-trial feedback on the correct response. The masker level was increased after three consecutive correct responses and decreased after one incorrect response. The step size was 10 dB for the first four reversals and 2 dB for subsequent presentations. The 3-down, 1-up procedure resulted in a 79% level of correct response for each run. The masker level in each run was estimated from the arithmetic mean of the last eight reversals in a 14-reversal sequence. The reported masker levels were the average of 3–4 such runs.

2.3.3. DPOAE suppression tuning curves in human infants

Informed consent was obtained from the mother prior to testing infant subjects. Following this, the infant was then taken from the mother's room into the Auditory Research Laboratory for the test session. The infant was fed if necessary, swaddled, and placed in a covered, but not acoustically shielded, isolette for sleep. The ER-10C probe was inserted firmly into the infant's ear canal and the test was conducted in the same manner described for adult subjects.

To conserve test time, the DPOAE STC acquisition program was automated for the collection of infant data; an adaptive procedure was implemented to search for target suppression (6 dB $\pm$ 0.5 dB). In addition, the interval between suppressor tones was decreased for finer resolution. Fifty to 75 cent intervals were used in the tip region and 100–200 cent intervals were presented for the low- and high-frequency segments of the DPOAE STC (1 octave = 1200 cents). A single-point noise estimation technique was implemented for rejection of noisy data (Elberling and Don, 1984). The single-point technique uses activity repeatedly measured at a single point in time to generate an estimate of noise. The rejection level for noisy data was under user control. Infant data were only collected for $f_2 = 3000$ and 6000 Hz conditions due to excessive biologic and ambient noise in the low-frequency condition ($f_2 = 1500$ Hz).

2.4. Data analysis

Two quantitative measures were used to describe suppression tuning curves. (1) Q_{10}, a measure of STC width, was obtained by measuring the bandwidth 10 dB above the tip of the tuning curve and then dividing the tip frequency of the STC by this bandwidth value; (2) Slope was calculated by fitting a linear regression equation to the following STC segments. (a) Low-frequency slope was measured from the tip (or lowest tip frequency if multiple peaks were present) to the lowest frequency suppressor tone presented. If a tail was present, slope was measured from tip to the beginning of the tail portion. The tail was identified as a flattening of the low-frequency side and had to meet the following criteria: a change in suppressor frequency failed to elicit change in suppressor level of greater than 5 dB for at least three consecutive data points. (b) High-frequency slope was measured from the tip (or highest tip frequency) to the highest frequency suppressor tone presented.

The Q_{10} values and slope were analyzed with analyses of variance (ANOVA) to test for age, frequency and side (low/high frequency) effects. Although some subjects had more than one STC measured, a repeated-measures design could not be employed because the majority of subjects did not provide more than one STC. When necessary, paired post-hoc comparisons (Scheffè) were subsequently conducted to identify which contrasts were significant. The tip frequency (frequency at which criterion suppression was achieved with the lowest suppressor level) and level were also recorded. A descriptive comparison of width, slope and overall shape was also conducted between DPOAE STCs and PTCs for three adult subjects.

3. Results

3.1. Experiment I: DPOAE suppression tuning curves from adults

In adult subjects, the mean level of unsuppressed DPOAEs for f_2 = 1500 Hz was 7.9 dB SPL; for f_2 = 3000 Hz was 8.7 dB SPL and for f_2 = 6000 Hz was 6.8 dB SPL. Ninety-three percent of unsuppressed DPOAE amplitudes were between 35 and 45 dB below the f_2 level.

Eleven 1500 Hz, ten 3000 Hz and seven 6000 Hz DPOAE STCs were generated from adult subjects for a total of 28 DPOAE STCs. Data from all three f_2 frequencies were obtained in three of the 15 subjects whereas partial sets (1 or 2 frequencies) were collected in the remaining 12 subjects. Fig. 2a–c displays individual adult STCs superimposed for the three f_2 frequencies. The DPOAE STCs are narrow in width, there is a sharply tuned tip component for all tuning curves, and the high-frequency slope is markedly steeper than the low-frequency slope. In addition, DPOAE STCs are highly replicable across subjects as shown by the superimposition of tuning curves. A tail was present on the low-frequency side of many of the 3000 and 6000 Hz STCs (44 and 86% respectively) and less frequently present on the 1500 Hz DPOAE STC (20%).

Fig. 3 shows results from one adult subject tested 4 times over a 4-month period. The DPOAE STCs in this figure demonstrate relative consistency in width and slope although tip frequency shifted from 5850 to 6300 Hz across the four test sessions. Q values ranged from 4.06 to 4.5 while low- and high-frequency slope ranged from 22

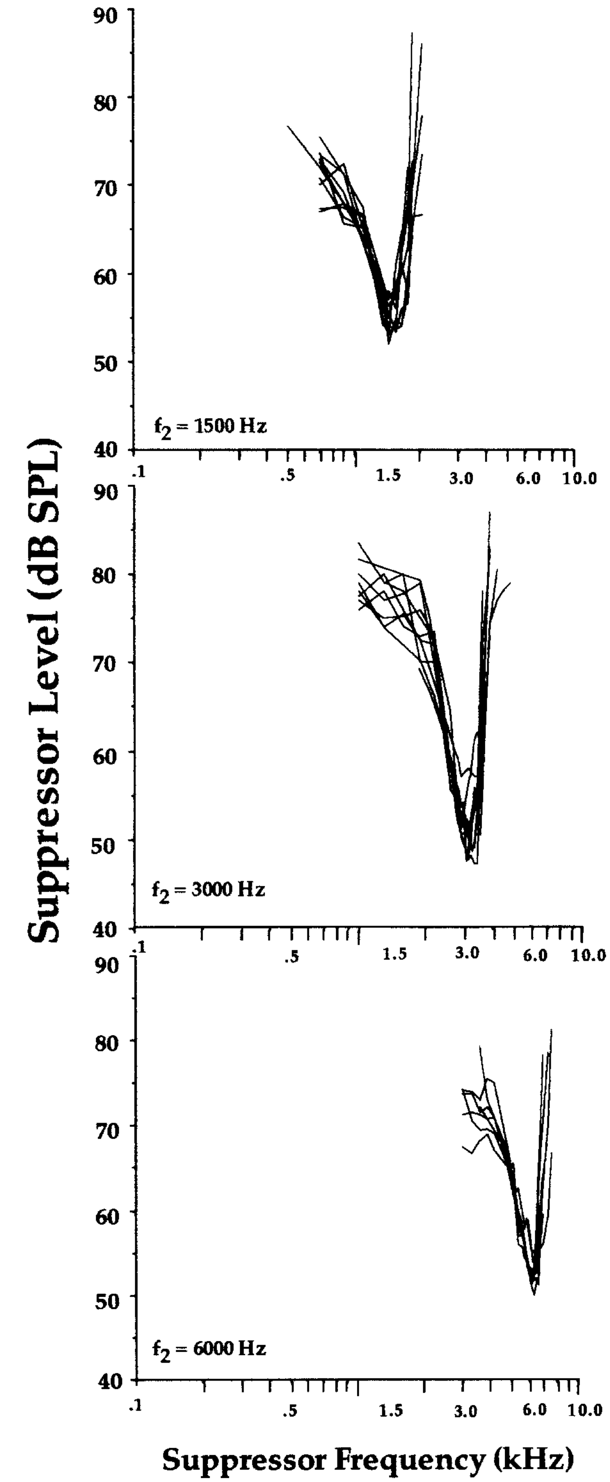

Fig. 2. 28 DPOAE STCs generated from 15 normal-hearing adult subjects for f_2 = 1500, 3000 and 6000 Hz.

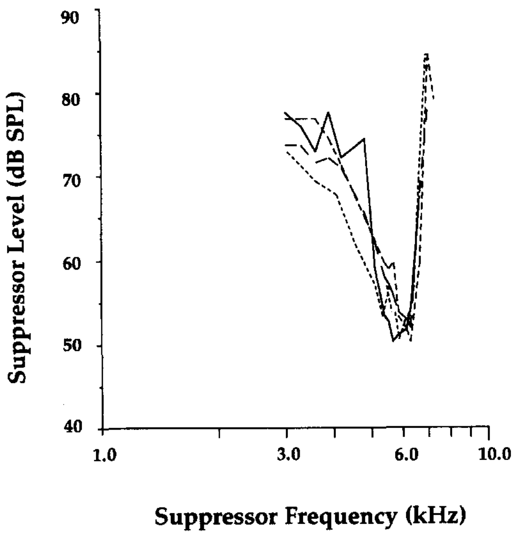

Fig. 3. Four superimposed DPOAE STCs generated from one adult subject over a 4-month time period at 1-month intervals. Each test session can be distinguished by STC line pattern.

to 29 dB/octave (7 dB range) and 128 to 171 dB/octave (43 dB range) respectively across the four sessions.

Fig. 4 shows examples of two individual STCs chosen randomly from each of the three f_2 frequency categories. This display gives an indication of variability in shape among subjects. The tip region of the STC was clearly defined in most adults although a small percentage showed perturbations or multiple peaks around the tip region. The suppressor frequency representing the tip of the STC (i.e., the point of maximum suppressibility) varied slightly with f_2 frequency. 1500 Hz STCs had a tip centered close to the f_2 frequency (mean = 1508 Hz). In contrast, at 3000 and 6000 Hz, the tip of the STC shifted to frequencies beyond f_2 in all but two cases (3000 Hz, mean = 3160 Hz; 6000 Hz, mean = 6308 Hz). The range of tip frequencies among subjects was 700 Hz for 3000 and 6000 Hz STCs and 225 Hz for 1500 Hz STCs. The mean level of the suppressor tone at the tip was not substantially different among the three f_2 conditions and ranged from 49 to 54 dB SPL. Fig. 5 displays tip frequency and level for the three f_2 frequencies.

3.1.1. Q_{10} results

The adult Q_{10} values obtained ranged from 1.7 to 4.4. Mean Q values were as follows: 2.4 (SD = 0.51) for 1500 Hz, 3.2 (SD = 0.51) for 3000 Hz and 3.86 (SD = 0.62) for 6000 Hz. Q values became progressively larger as f_2 frequency increased. These differences were significant as shown by an ANOVA of Q_{10} by f_2 frequency ($F_{2,25} = 12.97$, $P < 0.0001$). Subsequent paired comparisons found significant differences between the Q_{10} values at 6000 and

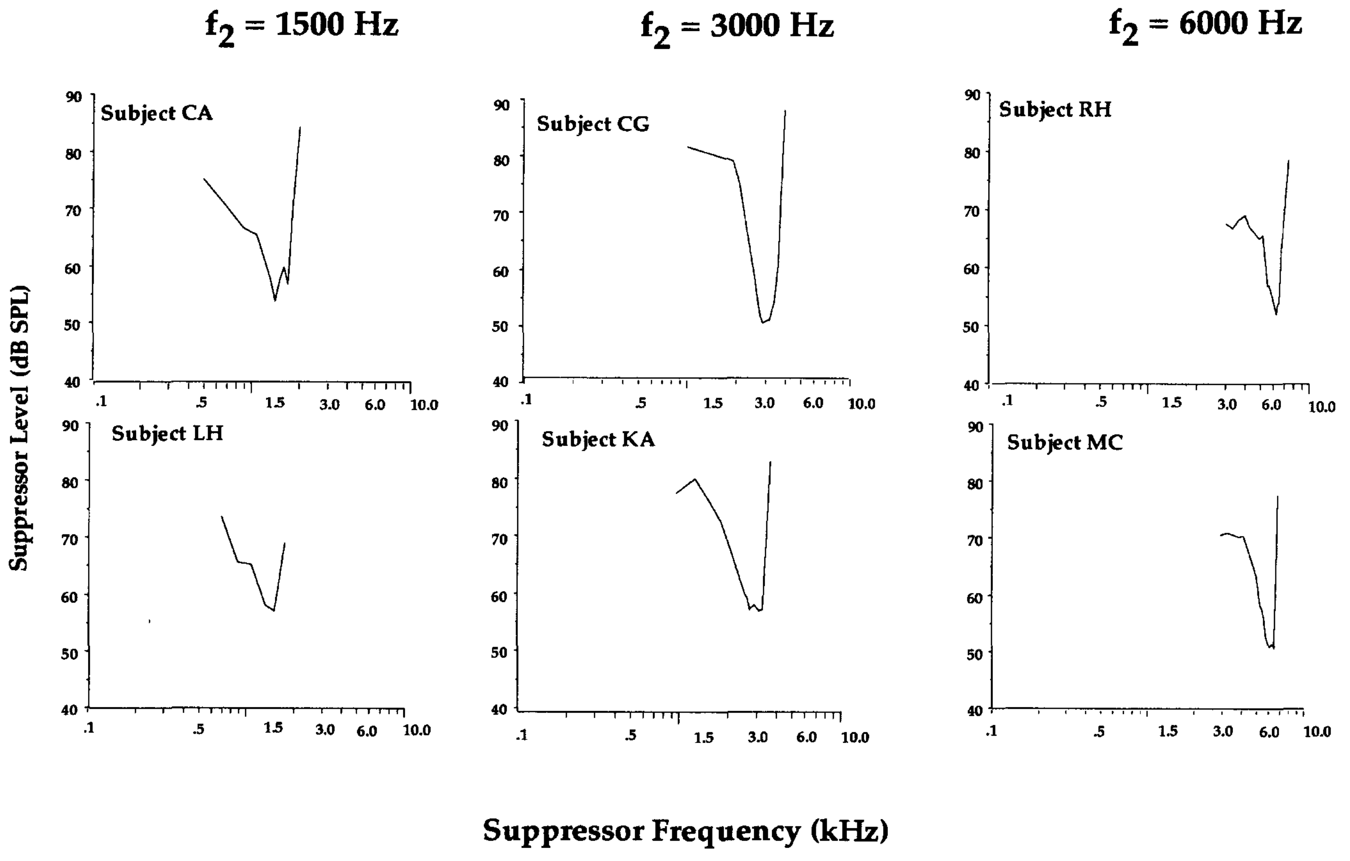

Fig. 4. Examples of two adult DPOAE STCs chosen at random from each of the three f_2 conditions.

1500 Hz ($P < 0.0002$) and between 3000 and 1500 Hz ($P < 0.02$). The difference between Q_{10} values for 3000 and 6000 Hz was not significant ($P < 0.07$) possibly due to the relatively small number of subjects tested. Fig. 6 is a scatterplot of the Q_{10} values for all of the adult STCs generated at each f_2 frequency. The general increase in Q_{10} with f_2 frequency is evident from this graph.

3.1.2. Slope results

Adult slope data are presented in Table 1. The high-frequency slope is steeper than the low-frequency slope for the three f_2 frequencies. Consistent with the Q_{10} results, slope values increased, indicating steeper slope, as f_2 frequency increased. A 2-way ANOVA of slope (low/high-frequency side $\times$ f_2 frequency) was conducted and showed significant frequency ($F_{2,48} = 5.83$; $P < 0.005$) and side effects ($F_{1,48} = 35.5$; $P < 0.0001$) with no interaction between these two variables ($F_{2,48} = 1.94$; $P < 0.15$).

Paired comparisons were subsequently conducted to further define the frequency effect on slope. Slope differences were observed between 1500 Hz and both 3000 ($P < 0.04$) and 6000 Hz ($P < 0.007$), but not between 3000 and 6000 Hz. These findings are consistent with: (1) an increase in slope steepness as f_2 frequency increases and (2) an asymmetrical tuning curve shape (steeper high than low-frequency slope) for all three f_2 frequencies. The tail portions of both 3000 and 6000 Hz STCs were predictably shallow ranging from 1 to 14 dB/octave (mean = 5 dB/octave).

3.1.3. Psychoacoustic tuning curves

Forward-masked PTCs were generated in 3 of the 15 adult subjects. Fig. 7 displays the 7 PTC and DPOAE STCs obtained from these subjects. Both types of tuning curves demonstrated similar trends; that is, narrower width and steeper slope as probe/f_2 frequency increased. The shape of the two types of tuning curves was also comparable; both showed a sharp tip region and shallower low- compared to high-frequency slope. The PTC, however, was consistently narrower in width than the DPOAE STC at all three frequencies. Fig. 8 shows the mean Q_{10} and high-frequency slope values obtained from PTCs and STCs. The mean PTC Q_{10} values were at least double the values obtained for DPOAE STCs in the same subject.

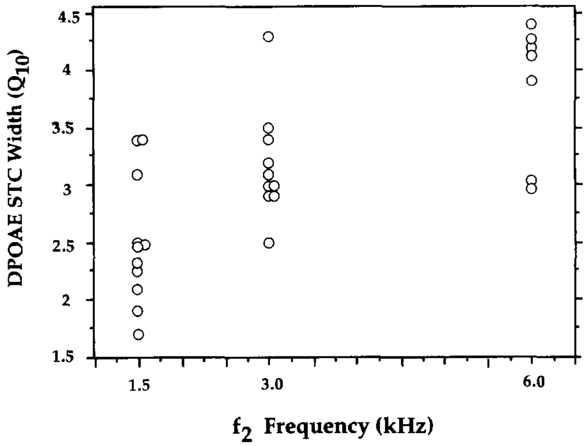

Fig. 6. Q_{10} values measured from adult DPOAE STCs for f_2 = 1500, 3000 and 6000 Hz. The Q_{10} values increase with increasing f_2 frequency.

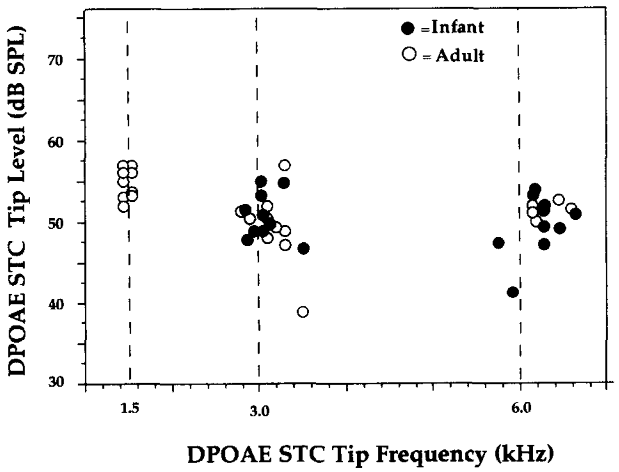

Fig. 5. Suppressor level at DPOAE STC tip as a function of suppressor frequency at DPOAE STC tip for adults and neonates. Note: There is overlap among data points, consequently, not all values can be observed in this figure.

3.2. Experiment II: DPOAE suppression tuning curves from neonates

In infants, mean DPOAE amplitude for f_2 = 3000 Hz was 13 dB; for f_2 = 6000 Hz, it was 11.3 dB SPL. These levels are between 4 and 5 dB greater than the adult levels for the same stimuli.

Ten 3000 Hz and eleven 6000 Hz DPOAE STCs were generated from 16 human neonates for a total of 21 DPOAE STCs (Fig. 9). Each infant STC was made up of between 13 and 15 data points. The shape of the tuning curves is very similar to adult DPOAE STCs and to other physiological measures of tuning. The tip region was well defined in most cases although there was a greater number of multi-peaked DPOAE STCs in the infant relative to adult data. Fig. 10 presents three examples of multi-peaked DPOAE STCs from the infant data. Forty-three percent of infant DPOAE STCs had multiple peaks around the tip region while only 21% of adult tuning curves showed this pattern.

Consistent with adult data, the tip of the infant DPOAE STC was located slightly higher than the f_2 frequency for both 3000 and 6000 Hz (3000 Hz, mean = 3064 Hz; 6000 Hz, mean = 6218 Hz). The range of tip frequencies among neonates was 660 Hz. The mean suppressor level at the tip of the STC was 50 dB SPL for 3000 Hz and 49 dB SPL for 6000 Hz. Fig. 5 displays the tip frequency and level across f_2 frequency for infant subjects. As is evident from this figure, the suppressor levels at the tip of the infant STCs overlap with adult values.

3.2.1. Q10 results

The Q_{10} values for infant DPOAE STCs ranged from 2.3 to 5.6 . Mean values were 3.3 for 3000 Hz (SD = 0.67) and 3.7 for 6000 Hz (SD = 0.74). The infant Q_{10} values

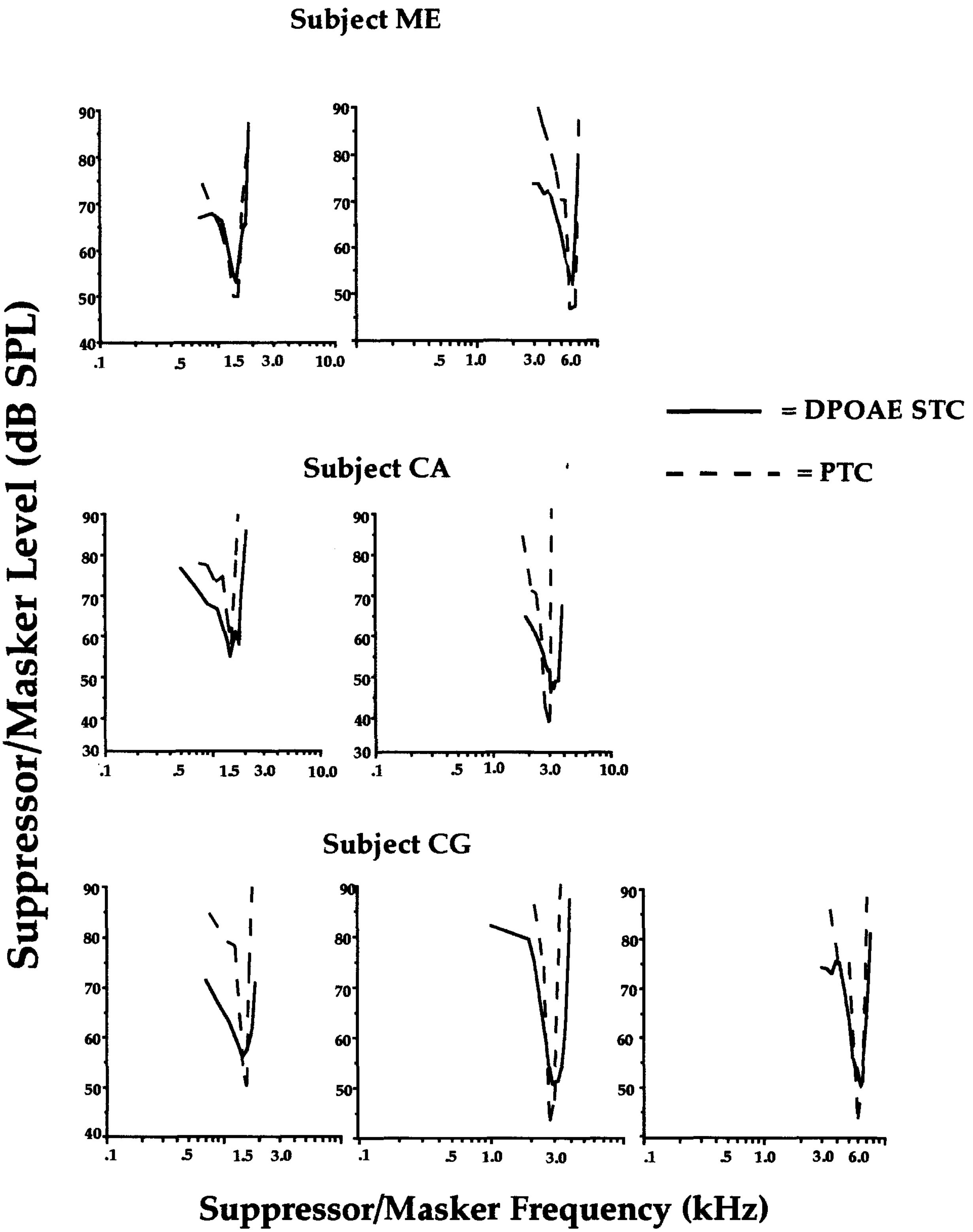

Fig. 7. Psychoacoustic tuning curves (dashed lines) and DPOAE suppression tuning curves (solid lines) superimposed for three adult subjects.

Table 1
Mean, median and individual slope values measured from DPOAE STCs generated with f_2 = 1500, 3000 and 6000 Hz in 15 normal-hearing adult subjects

Subject	DPOAE STC slope					
	1500		3000		6000	
	Low	High	Low	High	Low	High
1			77	186	42	146
2	35	83			34	173
3	41	83				
4			30	61		
5	23	52	42	112	37	323
6	21	90				
7			23	115	45	115
8	15	39	54	106	45	126
9	18	53	36	77		
10	18	91				
11	18	33	22	163		
12			57	48		
13	14	37				
14	14	49	42	43	33	44
15					23	92
Mean	22	61	40	107	42	139
Median	18	52.5	42	106	37	126
SD	9.0	23	18	48	8.0	94

were within the adult range of Q values for these same f_2 frequencies as shown in Fig. 11. The data presented in this figure demonstrate that Q_{10} increases (DPOAE STC becomes narrower) as f_2 frequency increases. A 2-way ANOVA of adult and infant Q_{10} (age $\times$ f_2 frequency) found no age difference between infant and adult tuning curve width at either f_2 frequency, however, Q_{10} across frequency did vary significantly ($F_{1,36} = 7.35$; $P < 0.01$).

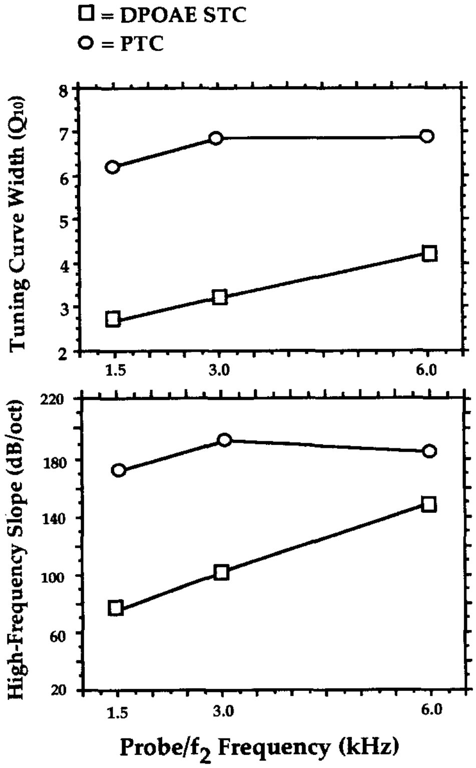

Fig. 8. Mean Q_{10} and high-frequency slope at f_2 = 1500, 3000 and 6000 Hz for seven forward-masked psychoacoustic tuning curves (○) and DPOAE suppression tuning curves (□) recorded from three adult subjects.

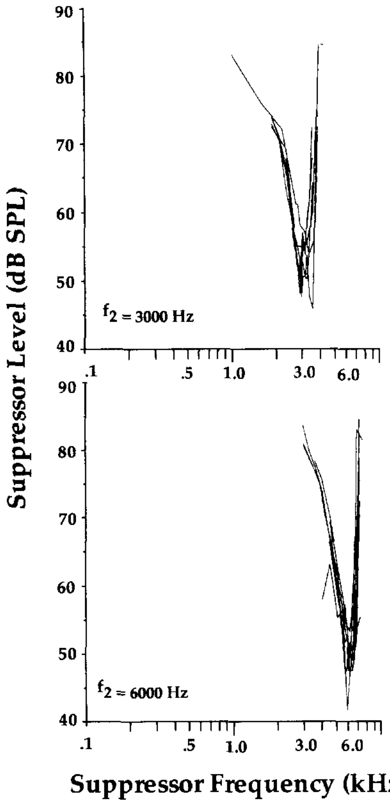

Fig. 9. Twenty-one DPOAE STCs generated from 16 healthy term-born neonates for f_2 = 3000 and 6000 Hz.

3.2.2. Slope results

Table 2 provides the slope values measured from infant DPOAE STCs. A 2-way ANOVA of slope (low/high-frequency side $\times$ f_2 frequency) was conducted. A significant interaction between frequency and side was observed ($F_{1,38} = 5.42$; $P < 0.02$). Post-hoc analyses subsequently showed that only the high-frequency side became significantly steeper as f_2 frequency increased ($P < 0.02$). In addition, the high-frequency side of the STC was significantly steeper than the low-frequency side ($P < 0.000$).

Age comparisons between infant and adult slope data were also conducted. A 3-way ANOVA (age $\times$ side $\times$ f_2 frequency) showed no interaction among these factors. There was no effect of age or frequency (between 3000 and 6000 Hz) on slope. The only main effect was for side ($F_{1,68} = 75$; $P < 0.0001$). The high-frequency side was significantly steeper than the low-frequency side for both ages and all f_2 frequencies.

3.3. Summary

In summary, high-resolution DPOAE iso-STCs generated from the $2f_1$-f_2 distortion product in human adults

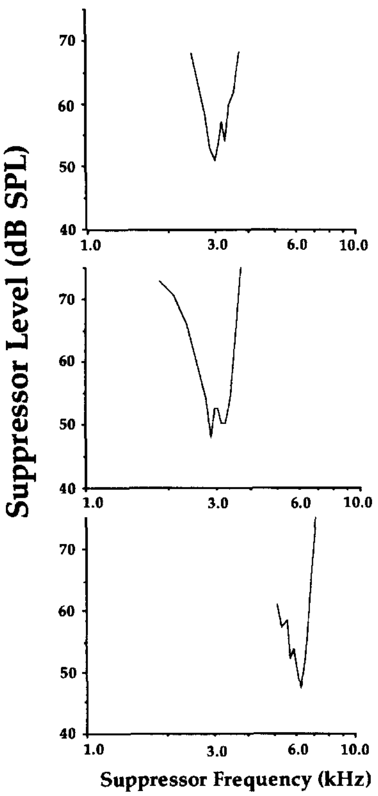

Fig. 10. Three examples of mutli-peaked DPOAE STCs from the infant data. As shown in these data, the peaks or perturbations occurred on both the low- and high-frequency side and around the tip region.

Table 2
Mean, median and individual slope values measured from DPOAE STCs generated with f_2 = 3000 and 6000 Hz in 16 term-born neonates

Subject	DPOAE STC slope			
	3000		6000	
	Low	High	Low	High
1			33	106
2	29	118		
3	39	142	29	169
4			33	187
5			42	102
6			90	144
7	60	54		
8	36	201	36	195
9	30	70		
10			36	119
11	40	82		
12	61	77	37	116
13			43	145
14	42	85	40	165
15	35	142	19	132
16	46	139		
Mean	42	101	40	143
Median	39.5	82	36	144
SD	11	49	17	32

show inter- and intra-subject consistency, a typical shape and a high degree of tuning. In addition, DPOAE STCs became narrower and had steeper high-frequency sides as probe (f_2) frequency was increased. The tip frequency of the tuning curves was always located near the f_2 frequency rather than the DP-place. Similar trends were observed in PTCs and DPOAE STCs generated in the same individual, however, absolute Q_{10} and slope values were consistently greater in psychoacoustic compared to distortion product tuning curves. DPOAE STCs generated from human neonates were comparable to adult tuning curves in their stability, shape, degree of tuning and distribution of tip frequency/level.

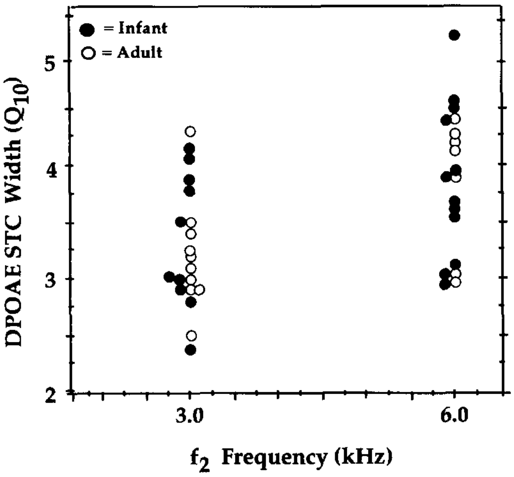

Fig. 11. Q_{10} values measured from infant (●) and adult (O) DPOAE STCs for f_2 = 3000 and 6000 Hz. The Q_{10} values from infants and adults show substantial overlap and a general trend for increasing Q_{10} value with increasing f_2 frequency.

4. Discussion

4.1. Experiment I

In the present experiment adult DPOAE levels were typically recorded at 35–45 dB below the f_2 level. These levels are higher than other reported DPOAE amplitudes (Kemp and Brown, 1983a; Harris et al., 1989). Earlier investigations reported DPOAE amplitude to be between 55 and 65 dB below primary tone levels. However, a recent investigation employing moderate level primary tone stimuli (< 60 dB SPL) and a 15 dB level difference between f_1 and f_2 reported findings consistent with those observed here (Gaskill and Brown, 1990). It is probable that the use of equi-level primary tones contributed to lower amplitude emissions observed in the initial studies.

4.1.1. Do DPOAE STCs reflect cochlear tuning?

DPOAE STCs obtained in this study showed characteristics that are typical of physiological tuning curves generated from the basilar membrane, hair cells, VIIIth nerve and spontaneous OAEs (Russell and Sellick 1978; Zurek, 1981; Brown and Kemp, 1984; Bargones and Burns, 1988; Pickles, 1988; Ruggero and Rich, 1991; Harris et al., 1992). Narrow tuning curve width, asymmetric, and sharper tuning with increased f_2 frequency were all clearly present.

Several studies have reported results suggesting that DPOAE STCs reflect the mechanical response of the basilar membrane. DPOAE STCs: (1) strongly resemble other established physiologic measures of tuning in the auditory system, such as the VIIIth-nerve frequency threshold curves; (2) accurately reflect structural specialization areas in the cochlea (Frank and Kossl, 1995), (3) behave like other physiologic TCs; that is, they become narrower as probe frequency is increased and as probe level is decreased (Harris et al., 1992; Abdala et al., 1995; Kummer et al., 1995) and (4) show expected asymmetry in suppression patterns for low- and high-frequency suppressors. These observations suggest that DPOAE STCs reflect cochlear frequency resolution to some extent. It is not known how these tuning curves might reflect auditory immaturity or pathology. Subsequent investigations applying the DPOAE suppression paradigm to other subject populations, such as premature infants, the elderly or mild to moderately hearing impaired individuals are warranted to answer these questions.

4.1.2. Effect of stimulus / recording parameters

Stimulus parameters such as primary tone level and suppression criterion were not varied in the present experiment. However, the human data reported thus far indicate that several recording variables will affect DPOAE STC shape, width and slope. For example, with lower primary-tone levels, STCs become narrower (Harris et al., 1992; Kummer et al., 1995). In contrast, they become broader as the frequency ratio between the primary tones is increased (Brown and Kemp, 1984). Suppression criterion can greatly influence STC characteristics as well (Brown and Kemp, 1984; Kummer et al., 1995). With increasing criterion, the tip of the DPOAE STC typically shifts downward and tuning curve width becomes narrower. Also, a small dip that alters STC shape is sometimes observed at f_1 when the suppression criterion is high (Kummer et al., 1995).

It has been hypothesized that suppression criterion will influence the experimenter's ability to observe multiple DPOAE sources (Kummer et al., 1995). Kummer and colleagues observed a secondary dip in DPOAE STCs at the DP-place in approximately 30% of their subjects, only when very small suppression criterion and low-level primary tones were used. With higher suppression criterion (> 4–5 dB), this dip disappeared and only the f_2-related tip remained. They interpret the double-tipped STC as an indication of contribution from the DP-place to the ear canal response. This issue will be discussed further in the following section.

The potential influence of recording and stimulus parameters when generating DPOAE STCs may explain some of the differences among reports. Our mean high-frequency slope data at 6000 Hz for example (mean = 139–143 dB/octave) are consistently lower than the high-frequency slope reported by Kummer and colleagues (≈ 225 dB/octave), although low-frequency slope and *Q* values are comparable between studies. This slope difference between studies may reflect a level effect since Kummer and colleagues used low-level primary (55–40) tones and low-moderate level tones (65–50) were employed in the present study. Differences may also be related to varying suppression criteria, as other investigators have found high-frequency slope particularly susceptible to changes in criterion (Brown and Kemp, 1984). It is evident that choice of parameters will affect measures of STC width, slope, tip frequency and possibly, observation of multiple DPOAE sources. The potential impact of stimulus and recording factors must be considered when comparisons among studies are conducted.

4.1.3. DPOAE generation site

Resolution of DPOAE STCs recorded in the present study was excellent as each tuning curve was composed of between 15 and 19 data points representing suppression of the distortion product at various frequencies. The tip of the DPOAE STC is thought to reflect the frequency region at which the two primaries interact and generate the distortion product. When interference (i.e., a third tone) is presented in this region, generation of the emission is most effectively disrupted and DPOAE amplitude is reduced with low-level suppressor tones.

The tip of the DPOAE STCs for both adults and neonates was always centered around the f_2 region or slightly above, consistent with other reports (Brown and Kemp, 1984; Harris et al., 1992; Kummer et al., 1995). STC tips occurred an average of 0.07 octaves above f_2, which agrees well with the data of Kummer et al. (1995). STCs generated from spontaneous OAEs also have tips located above the SOAE frequency in adults (Wilson, 1980; Zurek, 1981) and infants (Bargones and Burns, 1988). The reason for this tip phenomenon is not clear; however, it has been observed in all reports of human DPOAE suppression to varying degrees.

The existing data strongly suggest that the frequency region around f_2 is the generation site of the $2f_1$-f_2 DPOAE (Kemp and Brown, 1983a; Brown and Kemp, 1984; Martin et al., 1987; Harris et al., 1992; Abdala et al., 1995). However, evidence also exists suggesting that a contribution from the DP-place to the ear canal recording of apical emissions can occur and be detected when using certain recording parameters (Kemp and Brown, 1983b; Kummer et al., 1995; Piskorsi et al., 1995). After the DPOAE is generated near the f_2 place, it travels basally, through the middle ear and into the external ear canal where it is detected by the probe microphone. It is also mechanically propagated to the DP-place, amplified and reflected back towards the base of the cochlea (Kemp and

Brown, 1983b; Martin et al., 1987). The distortion product reflected from the DP-place may sum in phase with the initial response generated around the primary tone region and enhance the level of the DPOAE recorded in the ear canal. Consequently, the final ear canal measurement may include contribution from both sites in the cochlea.

Identifying a DP-place contribution to DPOAE has proven to be elusive. Brown and Kemp (1984), for example, were unable to extract any contribution from the DP-place in gerbils using even a 1 dB suppression criterion. They concluded that if a contribution exists from the DP-place, it reflects a small part of the ear canal recording. Other experiments have found a contribution and attributed it to a stimulus frequency emission at the DP-place (Kemp and Brown, 1983b). As mentioned previously, Kummer et al. (1995) reported that primary tone level and suppression criterion determined whether contribution from the DP-place was detected in their DPOAE suppression data. They reported some cases where sensitivity to suppressor tones near the DP-place was observed when L2 = 55, L2 = 40 and a 4–5 dB suppression criterion was employed. In these cases, the resulting DPOAE STCs had two regions of suppressibility, one centered near the f_2 frequency and another near the DP-place, suggesting two sources or components to the ear canal recording.

We did not see any evidence that the DPOAE was susceptible to a suppressor tone in the $2f_1$-f_2 region, perhaps due to the stimulus parameters employed. Based on these data, and the data of other investigators reporting similar results, we have applied a conventional interpretation to the DPOAE findings and consider that suppression tuning curves reflect cochlear integrity and frequency resolution around the f_2 regions at 1500, 3000 and 6000 Hz.

4.1.4. Psychoacoustic tuning curves and DPOAE suppression tuning curves

Narrower tuning curves with steeper slopes were consistently observed for psychoacoustic data compared to DPOAE suppression data. Finer tuning in psychoacoustic compared to physiological tuning curves has been observed previously in non-human mammals as well (Dallos et al., 1977). Dallos and colleagues reported that Q_{10} values measured from forward-masked PTCs in guinea pigs were approximately twice the size of Q values generated from frequency threshold tuning curves of single VIIIth-nerve fibers in the same species. Our comparisons between physiologic and psychoacoustic tuning curves in adult subjects agree well with Dallos' data.

The reason for the finer tuning observed with the psychoacoustic versus DPOAE paradigm may be related to off-frequency listening. Off-frequency listening occurs during a psychophysical task, when a subject detects the signal through side-lobe energy associated with the short-duration probe tone (Moore and O'Loughlin, 1986). When subjects utilize cues from the spectral splatter, threshold for the probe tone is lowered and the signal-to-noise ratio is maximized (Patterson, 1976). Several investigators have found that off-frequency listening alters tuning curve shape and can result in an increase in Q_{10} values (Johnson-Davies and Patterson, 1979; O'Loughlin and Moore, 1981; Moore and O'Loughlin, 1986). Because masking was not presented in this experiment to control for off-frequency listening, it may account for the sharper tuning seen in psychoacoustic relative to DPOAE data.

Another critical difference between experiments relates to masking methodology. Forward-masking methodology is frequently used to generate PTCs because the effect of suppression, which is thought to enhance tuning, is not revealed when using simultaneous masking. Simultaneous PTCs are broader than non-simultaneous PTC, presumably because the influence of suppression cannot be observed. In contrast to the forward-masking used to generate PTCs in the present study, DPOAE STCs were obtained by presenting an interference tone simultaneously with the eliciting stimuli. Consequently, DPOAE STCs may not include enhancement or sharpening of tuning from suppression effects. It is possible that simultaneous PTCs would have provided a more accurate comparison to DPOAE STCs.

A third difference between psychoacoustic and DPOAE methodology involves probe level. PTCs are generated with a single low-level stimulus. In contrast, DPOAE STCs are generated by two moderate-level stimuli. Although a gross attempt was made to match probe levels, it is not possible to rule out level effects contributing to the difference in width for the two types of tuning curves.

Finally, differences in anatomical generators of DPOAE and psychoacoustic data may contribute to width and slope results observed here. The PTC includes activity from many nerve fibers and fiber tracts in the central auditory system whereas the DPOAE STCs are generated solely in the cochlea. Because the PTC is generated with neural contribution from various levels of the auditory pathway, it is possible that it benefits from additional sharpening that takes place in the central auditory system (Katsuki et al., 1959; Dallos et al., 1977). This idea has not been equivocally accepted. Calford et al. (1983) recorded threshold tuning curves from single units in the cat at various levels of the auditory pathway and found no difference in tuning among the data collected at different neural levels. The issue has not been clearly defined; however, if additional sharpening occurs at more central stages of the auditory system, DPOAE STCs would not benefit from this process since they are preneural responses.

In the past, it has been assumed that non-simultaneously masked PTCs are a reflection of single fiber VIIIth-nerve tuning curves and are similar in shape and width. Although these two types of tuning curves demonstrate similar trends across frequency and generally similar shape, our results, as well as the results reported by Dallos et al. (1977), suggest fundamental differences in tuning curve width and slope between PTCs and physiologic tuning curves. The relationship between physiologic and psychoacoustic measures of tuning in the human auditory system warrants further investigation.

4.2. Experiment II

4.2.1. Development of cochlear function and structure

Although low-frequency DPOAE STCs were not obtained in Experiment II, the recording of 3000 and 6000 Hz DPOAE tuning curves adequately addressed the critical issue of tuning development for mid- to high-frequency stimuli. A high-pass filter is currently being implemented in the DPOAE STC system and a sound-treated isolette is being utilized to decrease low-frequency noise and facilitate the collection of data at $f_2 = 1500$ Hz.

The results in this study suggest that at least for mid- and high-frequencies, the human cochlea is tuned in an adultlike manner at term birth. Infant and adult DPOAE STC shape, width, slope and tip frequency/level are comparable. Results of other otoacoustic emission studies conducted with infants also support early adultlike cochlear function. Bargones and Burns (1988) reported adultlike SOAE STCs in human infants at 2–3 weeks of age. Brown et al. (1994) found that the most robust neonatal DPOAEs are generated using an f_2/f_1 frequency ratio similar to the optimal adult ratio. The f_2/f_1 ratio presumably reflects the filtering properties of the cochlea (Allen and Fahey, 1993). More recently, Popelka et al. (1995) described adultlike patterns of DPOAE amplitude as a function of stimulus level in a preterm infant population and Eggermont and colleagues reported adult-like travel times measured using DPOAE latency and phase data (Eggermont et al., 1996). In addition to OAE data, microscopic observations of postmortem fetal cochleae support the idea that the cochlea is anatomically mature and shows adult-like innervation patterns by the second trimester (Bredberg, 1968; Lavigne-Rebillard and Pujol, 1987, 1988).

When using auditory brainstem response (ABR) paradigms or behavioral techniques to measure tuning, immaturities in the frequency resolving abilities of infants as old as 6 months of age have been reported (Folsom and Wynne, 1987; Schneider et al., 1990; Spetner and Olsho, 1990; Abdala and Folsom, 1995). The results of the present study suggest that ABR and behavioral reports of broad tuning in 3–6-month-old infants are probably due to central auditory immaturities rather than cochlear immaturities. There is ample evidence from evoked potential studies and studies of postmortem fetal tissue to indicate that the auditory brainstem is immature in structure and function postnatally (Salamy and McKean, 1976; Hecox and Burkard, 1982; Morgan et al., 1987; Ponton et al., 1992, 1994; Werner et al., 1994; Abdala and Folsom, 1995; Moore et al., 1995).

4.2.2. Development of active cochlear processes

The presence of mature cochlear tuning at term birth provides developmental information about other aspects of cochlear function and structure as well. Cochlear tuning has been intricately linked with the cochlear amplifier. When active elements within the cochlea are disabled after death, ototoxic treatment or anoxia, sharp tuning and cochlear non-linearity disappear rapidly (Kiang et al., 1970; Liberman and Dodds, 1984; Khanna and Leonard, 1986; Norton and Rubel, 1990). Normal function of the cochlear amplifier appears to be necessary for the presence of sharp frequency resolution and non-linear phenomenon.

Moderate to low-level stimuli were used as primary tones in this study in order to ensure that DPOAE generation was based in activity of active cochlear mechanisms. Several studies have suggested 60–70 (Whitehead et al., 1992a,b) or 70–80 dB (Mills et al., 1995) as transition regions for active to passive cochlear function in small mammals. F_2 was presented at 50 dB SPL, consequently, it is assumed that the cochlear amplifier was functional in the subjects tested here. Considering the similarity of adult and neonatal DPOAE STCs reported, it is reasonable to assume that active elements within the cochlea which regulate and sharpen frequency resolution are functional by term birth in the human auditory system. This suggests that processes associated with normal functioning of the cochlear amplifier, such as outer hair cell motility, maintenance of an appropriate endocochlear potential, and mature frequency-place organization are also mature or approaching maturity at birth.

4.3. Limitations of DPOAE suppression

Although our data show excellent inter-subject stability and are consistent with previously reported physiological tuning curves, DPOAE suppression data should be interpreted with considerable caution due to the presence of confounding factors. Suppression within the cochlea does not only involve the intended suppression effect on the $2f_1$-f_2 DPOAE but probably includes multiple interactions among secondary distortion products generated from combination of primary with suppressor tones and, possibly, combinations of the suppressor with other distortion products.

The presence of spontaneous OAEs may also affect DPOAEs if they are present around the DP-place or at one of the primary tone frequencies (Burns et al., 1984; Wier et al., 1988; Long et al., 1993). When a spontaneous OAE is near the DP-place, it can enhance level of the distortion product measured in the ear canal by phaselocking to the DPOAE (Long et al., 1986; Harris et al., 1992). Harris et al. (1992) reported larger DPOAE amplitude in four subjects showing SOAEs near $2f_1$-f_2 than subjects without spontaneous emissions in this region.

Since spontaneous OAEs were not monitored in the subjects here, it is not possible to assess how they might have affected DPOAE STCs. However, it does not appear that the presence of SOAEs alters suppression tuning curve shape or width. Harris et al. (1992) found that, although their subjects with SOAEs near the DP-place generally had larger amplitude DPOAEs, there was no significant difference with respect to DPOAE suppression patterns between subjects with and without SOAEs. Their data, however, may not have provided sufficient resolution to observe such a relationship. More recently, Kummer et al. (1995) studied the relationship between SOAEs and fine-resolution DPOAE STC shape and could not find a consistent relationship.

The data from our laboratory also argue against SOAEs altering STC shape. DPOAE STCs have been successfully obtained in 21 adult subjects and 29 neonates in our laboratory, resulting in a total of 56 DPOAE STCs. As shown in Figs. 2 and 7, the inter-subject consistency and replicability is excellent. If SOAEs were disruptive to STC shape, it is likely that tuning curves generated in subjects with and without SOAEs at $2f_1$-f_2, would show different morphology.

Small perturbations or multiple-peaks were observed around the tip region in some tuning curves and these may be the result of SOAEs around $2f_1$-f_2. Interestingly, these multiple-peaked STCs were more prevalent in the infant population where we would expect higher level SOAEs (Bright and Glattke, 1986; Burns et al., 1991). It is possible that the presence of SOAEs alters the fine structure of the DPOAE STC slightly, introducing some'roughness' or 'peakiness' into STC data, but in most cases does not disrupt the basic shape or pattern across suppressor frequencies.

In infrequent cases where a large SOAE near $2f_1$-f_2 interferes with DPOAE suppression, it should be apparent once the suppression paradigm is initiated. We would observe a general lack of expected suppression and, possibly, the inability to achieve 6 dB amplitude reduction in the DPOAE even at high levels. Only two prospective adult subjects (out of 20) have demonstrated lack of suppression or irregular suppression patterns and were eliminated from the study. It is possible that high-level, intrusive SOAEs were present in these two subjects that disrupted the DPOAE suppression paradigm. All other subjects evaluated thus far have shown predictable suppression patterns.

4.4. Summary

These experiments demonstrated the stability and replicability of fine-resolution STCs generated from the $2f_1$-f_2 DPOAE recorded in the external ear canal of normally hearing adults and healthy term-born neonates. The DPOAE STCs generated here were similar in shape to physiological and psychoacoustic tuning curves, shared many of the same characteristics and showed excellent replicability and stability. The DPOAE suppression paradigm may provide a non-invasive, indirect measure of cochlear frequency resolution in humans.

The similarity between adult and neonatal data suggest that cochlear frequency resolution is adultlike at term birth for, at least, the mid- and high-frequency regions of the cochlea. These findings provide significant impetus for continued study of DPOAE suppression as a means of evaluating cochlear frequency resolution in humans.

References

Abdala, C. and Folsom, R. (1995) The development of frequency resolution as revealed by the auditory brainstem response recorded with notched-noise masking. J. Acoust. Soc. Am. 98, 921–930.

Abdala, C., Sininger, Y., Ekelid, M. and Zeng, F.-G. (1995) Distortion product otoacoustic emission suppression tuning curves in human adults. Abstr. Assoc. Res. Otolaryngol. 18: 120.

Allen, J. and Fahey, P. (1993) A second cochlear frequency map that correlates distortion product and neural tuning measurements. J. Acoust. Soc. Am. 94, 809–816.

Bargones, J. and Burns, E. (1988) Suppression tuning curves for spontaneous otoacoustic emissions in infants and adults. J. Acoust. Soc. Am. 83, 1809–1816.

Bredberg, G. (1968) Cellular pattern and nerve supply of the human organ of Corti. Acta Oto-laryngol., Suppl. 236, 1–135.

Bright, K. and Glattke, T. (1986) Spontaneous otoacoustic emissions in normal ears. In: M. Collins, T. Glattke and L. Harker (Eds.), Sensorineural Hearing Loss, Univeristy of Iowa, Iowa City, IA, pp. 201–208.

Brown, A. (1987) Acoustic distortion from rodent ears: a comparison of responses from rats, guinea pigs and gerbils. Hear. Res. 31, 25–38.

Brown, A. and Kemp, D. (1984) Suppressibility of the 2f1-f2 stimulated acoustic emissions in gerbil and man. Hear. Res. 13, 29–37.

Brown, A., Sheppard, S. and Russell, P. (1994) Acoustic distortion products (ADP) from the ears of term infants and young adults using low stimulus levels. Br. J. Audiol. 28, 273–280.

Burns, E., Strickland, B., Tubis, A. and Jones, K. (1984) Interactions among spontaneous otoacoustic emissions. I. Distortion products and linked emissions. Hear. Res. 16, 271–278.

Burns, E., Arehart, K. and Campbell, S. (1991) Prevalence of spontaneous otoacoustic emissions in neonates. Abstr. Assoc. Res. Otolaryngol. 14, 66.

Calford, M., Webster, W. and Semple, M. (1983) Measurement of frequency selectivity of single neurons in the central auditory pathway. Hear. Res. 11, 395–401.

Dallos, P., Ryan, A., Harris, D., McGee, T. and Ozdamar, O. (1977) Cochlear frequency selectivity in the presence of hair cell damage. In: E. Evans and J. Wilson (Eds.), Psychophysics and Physiology of Hearing, Academic Press, London, pp. 249–257.

Eggermont, J., Brown, D., Ponton, C. and Kimberley, B. (1996) Comparison of DPE and ABR traveling wave delay measurements suggests frequency specific synapse maturation. Submitted.

Elberling, C. and Don, M. (1984) Quality estimation of averaged auditory brainstem responses. Scand. Audiol. 13, 187–197.

Folsom, R., Burns, E., Morrison, R. and Zettner, E. (1995) Comparison of peripheral vs. central tuning in human adults and infants. Abstr. Assoc. Res. Otolaryngol. 18, 120.

Folsom, R. and Wynne, M. (1987) Auditory brainstem responses from human adults and infants: wave-V tuning curves. J. Acoust. Soc. Am. 81, 412–417.

Frank, G. and Kossl, M. (1995) The shape of 2f1-f2 suppression tuning curves reflects basilar membrane specializations in the mustached bat, *Pteronotus parnellii*. Hear. Res. 83, 150–160.

Gaskill, S. and Brown, A. (1990) The behavior of the acoustic distortion product, 2f1-f2, from the human ear and its relation to auditory sensitivity. J. Acoust. Soc. Am. 88, 821–839.

Harris, F. and Glattke, T. (1992) The use of suppression to determine the characteristics of otoacoustic emissions. Sem. Hear 13, 67–80.

Harris, F., Lonsbury-Martin, B., Stagner, B., Coats, A. and Martin, G. (1989) Acoustic distortion-products in humans: systematic changes in amplitude as a function of f2/f1 ratio. J. Acoust. Soc. Am. 85, 220–229.

Harris, F., Probst, R. and Xu, L. (1992) Suppression of the 2f1-f2 otoacoustic emission in humans. Hear. Res. 64, 133–141.

Hecox, K. and Burkard, B. (1982) Developmental dependencies of the human brainstem auditory evoked response. Ann. NY Acad. Sci. 388, 538–556.

Johnson-Davies, D. and Patterson, R. (1979) Psychophysical tuning curves: restricting the listening band to the signal region. J. Acoust. Soc. Am. 65, 765–770.

Katsuki, Y., Watanabe, T. and Maruyama, N. (1959) Activity in auditory neurons in upper levels of brain of cat. J. Neurophysiol. 22, 343–359.

Kemp, D. (1979) Evidence of mechanical nonlinerarity and frequency selective wave amplification in the cochlea. Arch. Otorhinolaryngol. 224, 37–45.

Kemp, D. and Brown, A. (1983a) An integrated view of cochlear mechanical nonlinearities observable from the ear canal, In: E. de Boer and M. Viergever (Eds.), Mechanics of Hearing, Martinus Nijhoff, The Netherlands, pp. 75–82.

Kemp, D. and Brown, A. (1983b) A comparison of mechanical nonlinearities in the cochlea of man and gerbil from ear canal measrements. In: R. Klinke and R. Hartmann (Eds.), Hearing - Physiological Bases and Psychophysics, Springer, Berlin, pp. 82–88.

Kemp, D. and Chum, R. (1980) Properties of the generator of stimulated acoustic emissions. Hear. Res. 2, 213–232.

Khanna, S. and Leonard, D. (1986) Measurement of basilar membrane vibrations and evaluation of cochlear condition. Hear. Res. 23, 37–53.

Kiang, N., Moxon, E. and Levine, R. (1970) Auditory nerve activity in cats with normal and abnormal cochleas. In: G. Wolstenholm, and J. Knight. (Eds.), Sensorineural Hearing Loss, Ciba Symposium, London, pp. 241–273.

Kim, D. (1986) Active and nonlinear cochlear biomechanics and the role of outer-hair-cell subsystem in the mammalian auditory system. Hear. Res. 22, 105–114.

Koppl, C. and Manley, G. (1993) Distortion-product otoacoustic emissions in the bobtail lizard. II. Suppression tuning characteristics. J. Acoust. Soc. Am. 93, 2834–2843.

Kummer, P., Janssen, T. and Arnold, W. (1995) Suppression tuning characteristics of the 2f1-f2 distortion product otoacoustic emission in humans. J. Acoust. Soc. Am. 98, 197–210.

Lavigne-Rebillard, M. and Pujol, R. (1987) Surface aspects of the developing human organ of corti. Acta Oto-laryngol, Suppl. 436, 43–50.

Lavigne-Rebillard, M. and Pujol, R. (1988) Hair cell innervation in the fetal human cochlea. Acta Oto-laryngol. 105, 398–402.

Liberman, M. and Dodds, L. (1984) Single-neuron labeling and chronic cochlear pathology. II. Sterocilia damage and alterations of threshold tuning curves. Hear. Res. 16, 55–74.

Lim, D. (1986) Cochlear micromechanics in understanding otoacoustic emission. Scand. Audiol., Suppl. 25, 17–25.

Long, G., Sun, C. and Talmadge, C. (1993) Interactions between spontaneous emissions and external tones: suppression, frequency shifting and distortion product generation. In: H. Duifuis, J. Horst, P. van Dijk and S. van Netten (Eds.), Biophysics of Hair Cell Sensory Systems, World Scientific Publ., Singapore, pp. 40–47.

Long, G., Tubis, A. and Jones, K. (1986) Changes in spontaneous and evoked otoacoustic emissions and corresponding psychoacoustic threshold microstructures induced by aspirin consumption. In: J. Allen, J. Hall, A. Hubbard, S. Neely and A. Tubis (Eds.), Peripheral Auditory Mechanisms, Springer, Berlin, pp. 213–220.

Lonsbury-Martin, B. and Martin, G. (1990) The clinical utility of distortion-product otoacoustic emissions, Ear Hear. 11, 144–154.

Lonsbury-Martin, B., Martin, G., Probst, R. and Coats, A. (1987) Acoustic distortion products in rabbit ear canal. I. Basic features and physiological vulnerability. Hear. Res. 28, 173–189.

Martin, G., Lonsbury-Martin, B., Probst, R., Scheinin, S. and Coats, A. (1987) Acoustic distortion products in rabbit ear canal. II. Sites of origin revealed by suppression contours and pure-tone exposures. Hear. Res. 28, 191–208.

Martin, G., Whitehead, M., Stagner, B. and Lonsbury-Martin, B. (1995) Suppression and enhancement of DPOAEs by interference tones above f2 in rabbits. Abstr. Assoc. Res. Otolaryngol. 18, 124.

Mills, D., Norton, S., Rubel, E. (1995) Development of active and passive mechanics in the mammalian cochlea. Aud. Neurosci. 1, 77–99.

Moore, B. and O'Loughlin, B. (1986) The use of non-simultaneous masking to measare frequency selectivity and suppression. In: B. Moore (Ed.), Frequency Selectivity in Hearing, Academic Press, London, pp. 179–250.

Moore, J. Perazzo, L. and Braun, A. (1995) Time course of axonal myelination in the human brainstem auditory pathway. Hear. Res. 87, 21–31.

Morgan, D., Zimmerman, M. and Dubno, J. (1987) Auditory brainstem evoked response characteristics in full-term newborn infant. Ann. Otol. Rhinol. Laryngol. 96, 142–151.

Norton, S. and Rubel, E. (1990) Active and passive ADP components in mammalian and avian ears. In: P. Dallos, D. Geisler, J. Matthews, M. Ruggero and C. Steele (Eds.), Mechanics and Biophysics of Hearing, Springer, New York, pp. 219–265.

O'Loughlin, B. and Moore, B. (1981) Off-frequency listening: effects on psychoacoustical tuning curves obtianed in simultaneous and forward masking. J. Acoust. Soc. Am. 69, 1119–1125.

Patterson, R. (1976) Auditory filter shapes derived with noise stimuli. J. Acoust. Soc. Am. 59, 640–654.

Pickles, J. (1988) An Introduction to the Physiology of Hearing, Academic Press, London, pp. 297–320.

Piskorsi, P., Long, G., Talmadge, C. and Tubis, A. (1995) Origin of the fine structrue of distortion product emissions in the human ear. Abstr. Assoc. Res. Otolaryngol. 18, 119.

Ponton, C., Eggermont, J., Coupland, S. and Winkelaar, R. (1992) Frequency-specific maturation of the VIIIth-nerve and brainstem auditory pathway: evidence from derived auditory brainstem responses (ABRs) J. Acoust. Soc. Am. 91, 1576–1586.

Ponton, C., Moore, J. , Eggermont, J., Wu, B.J. and Huang, J. (1994) The relation between auditory brainstem size and auditory brainstem response (ABR) interpeak latency during human development. Abstr. Assoc. Res. Otolaryngol. 17, 57.

Popelka, G., Karzon, R. and Arjmand, E. (1995) Developmental characteristics of the 2f1-f2 distortion product otoacoustic emission (DPOE) in human neonates. Ear Hear. 16, 159–165.

Probst, R., Lonsbury-Martin, B. and Martin, G. (1991) A review of otoacoustic emissions. J. Acoust. Soc. Am. 89, 2027–2065.

Ruggero, M. and Rich, N. (1991) Furosemide alters organ of Corti mechanics: evidence for feedback of outer hair cells upon the basilar membrane. J. Neurosci. 11, 1057–1067.

Russell, I. and Sellick, P. (1978) Intracellular studies of hair cells in the mammalian cochlea. J. Physiol. 284, 261–290.

Salamy, A. and McKean, C. (1976) Postnatal development of human brainstem potentials during the first year of life. Electroenceph. Clinical Neurophysiol. 40, 418–426.

Schneider, B., Morrongiello, B. and Trehub, S. (1990) The size of the critical band in infants, children and adults. J. Exp. Psychol.: Hum. Percep. Perform. 16, 642–652.

Spetner, N. and Olsho, L. (1990) Auditory frequency resolution in human infancy. Child Dev. 61, 632–652.

Werner, L., Folsom, R. and Mancl, L. (1994) The relationship between auditory brainstem response latencies and behavioral thresholds in normal hearing infants and adults. Hear. Res. 77, 88–98.

Whitehead, M., Lonsbury-Martin, B. and Martin, G. (1990) Actively and passively generated acoustic distortion at 2f1-f2 in rabbits. In: P. Dallos, C. Geisler, J. Matthews, M. Ruggero and C. Steele (Eds.), Mechanics and Biophysics of Hearing, Springer, New York, pp. 243–250.

Whitehead, M., Lonsbury-Martin, B. and Martin, G. (1992a) Evidence for two discrete sources of 2f1-f2 distortion-product otoacoustic emission in rabbit. I. Differential dependence on stimulus parameters. J. Acoust. Soc. Am. 91, 1587–1607.

Whitehead, M., Lonsbury-Martin, B. and Martin, G. (1992b), Evidence for two discrete sources of 2f1-f2 distortion product otoacoustic emission in rabbit. II. Differential physiological vulnerability. J. Acoust. Soc. Am. 92, 2662–2682.

Wier, C., Pasanen, E. and McFadden, D. (1988) Partial dissociation of spontaneous otoacoustic emissions and distortion products during aspirin use in humans. J. Acoust. Soc. Am. 84, 230–237.

Wilson, J. (1980) Evidence for a cochlear origin for acoustic re-emissions, threshold, fine-structure and tonal tinnitus. Hear. Res. 2, 233–252.

Wit, H. and Ritsma, R. (1980) Evoked acoustical responsese from the human ear: some experimental results. Hear. Res. 2, 253–261.

Zurek, P. (1981) Spontaneous narrowband acoustic signals emitted by human ears. J. Acoust. Soc. Am. 69, 514–522.