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# Distortion Product Otoacoustic Emission Suppression in Subjects with Auditory Neuropathy

Carolina Abdala, Yvonne S. Sininger, and Arnold Starr

**Objective:** The objective of this experiment was to address: 1) whether normal efferent system function is required for normal cochlear tuning as measured by distortion product otoacoustic emission (DPOAE) suppression in humans and 2) whether cochlear function, assessed by DPOAE suppression tuning, is normal in a small group of patients with auditory neuropathy.

**Design:** DPOAE suppression tuning curves (STCs) are similar to other physiologic measures of tuning. They are generated by evoking a DPOAE with two simultaneously presented pure tones and then suppressing the distortion product with a third tone of varying frequency and level. In this study, DPOAE STCs were generated with f2 frequencies of 1500, 3000, and 6000 Hz in 15 normal-hearing adults and four subjects with documented auditory neuropathy. Tuning curve width, slope and tip characteristics, as well as rate of suppression growth were measured in each group. Contralateral suppression of otoacoustic emissions (OAEs) was also recorded as an index of medial efferent function.

**Results:** Results show that the four subjects with auditory neuropathy lacked efferent suppression of OAEs. However, these four subjects showed normal estimates of cochlear tuning as measured by DPOAE suppression results.

**Conclusions:** This finding suggests that normal efferent system function is not required at the time of test for normal DPOAE suppression tuning. It also suggests that cochlear function as evaluated by detailed measures of DPOAE suppression, is normal in these "typical" patients with auditory neuropathy.

(Ear & Hearing 2000;21:542-553)

## Efferent Influence on Cochlear Tuning

The role of the olivo-cochlear efferent system in functional audition is not clearly understood. Neurons originating in the superior olivary complex travel in the medial olivo-cochlear (MOC) pathway to innervate outer hair cells (OHCs) of the cochlea. OHCs have a significant functional role in auditory sensitivity and frequency resolution, thus it is not

unreasonable to postulate that the efferent system influences audition via this route. It is clear that OHCs are required for normal cochlear processes such as frequency resolution; when OHCs are damaged, it results in hearing impairment and loss of tuning (Evans & Harrison, 1976; Liberman & Dodds, 1984). However, the relationship between MOC innervation of OHCs and normal cochlear processes is less clear.

It has been shown that when the efferent system is stimulated either acoustically or electrically, cochlear physiology can be altered (Berlin, Hood, Hurley, & Wen, 1994; Mountain, 1980; Puel & Rebillard, 1990; Siegel & Kim, 1982; Warren & Liberman, 1989). However, although efferent stimulation can influence the cochlea, it does not appear that efferent activity is required for normal cochlear processes and coding. Many investigators have failed to find changes in neural or cochlear frequency selectivity in laboratory animals after the interruption of MOC bundle (Igarishi, Cranford, Nakai, & Alford, 1979; Littman, Cullen, & Bobbin, 1992; Rajan, Robertson, & Johnstone, 1990; Zheng, Henderson, McFadden, Ding, & Salvi, 1999).

Auditory neuropathy is a pathology so named because it appears to involve dysfunction of VIIIth nerve fibers and/or the inner hair cell-VIIIth nerve synapse (Sininger, Hood, Starr, Berlin, & Picton, 1995; Starr, Picton, Sininger, Hood, & Berlin, 1996). This pathology provides a naturally occurring condition in humans where OHCs of the cochlea are normal but both afferent activity and efferent regulation of the cochlea are impaired. In individuals with auditory neuropathy, otoacoustic emissions (OAEs) and cochlear microphonics are typically present. However, the auditory brain stem response (ABR) is either absent or grossly abnormal, beginning with wave I, which reflects VIIIth nerve activity. The abnormal ABR is felt to reflect poor synchrony in the auditory nerve (Starr et al., 1996).

The lesion site for auditory neuropathy is not completely understood. Many patients with this hearing disorder have concomitant peripheral neuropathy, which makes the auditory nerve a logical site of lesion. For patients without peripheral neuropathy, the possibility exists that the inner hair cell synapse is the site of lesion. Animal models of neuropathy have been generated that induce inner

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hair cell lesions and these animals show a pattern of auditory response similar to human subjects with auditory neuropathy (Harrison, 1998; Salvi, Wang, Ding, Stecker, & Arnold, 1999).

If the auditory nerve is dysfunctional in patients with auditory neuropathy as hypothesized, both the afferent and efferent pathway could be disrupted. Consistent with this pathology, patients with auditory neuropathy characteristically show an abnormal olivo-cochlear reflex measured by contralateral suppression of OAEs (Berlin, Hood, Cecola, Jackson, & Szabo, 1993; Collet, Kemp, Beuillet, Duclaux, Moulin, & Morgon, 1990; Starr et al., 1996). It is not clear if the efferent reflex arc is dysfunctional due to the disruption of the afferent leg of the auditory nerve only or a combination of afferent and efferent portions of the arc. Hood, Berlin, Bordelon, Goforth-Barter, Tedesco, and Hurley (Reference Note 1) have reported on one subject with unilateral neuropathy who did show contralateral suppression of the OAE on the affected side when noise was presented to the normal-hearing side. In this particular individual, the efferent pathway on the side with neuropathy was obviously functional and intact; however, it could only be accessed or stimulated from the unaffected side.

By examining cochlear frequency resolution in subjects with auditory neuropathy, it is possible to investigate the relationship between efferent system function and cochlear tuning in humans. Distortion product otoacoustic emission (DPOAE) ipsilateral suppression has been well tested and studied as a technique for exploring cochlear filtering. It has been studied in nonhuman species (Brown & Kemp, 1984; Martin, Lonsbury-Martin, Probst, Scheinin, & Coats, 1987) and more recently in humans (Abdala, 1998; Abdala, Sininger, Ekelikd & Zeng, 1996; Harris, Probst, & Xu, 1992; Kummer, Janssen, & Arnold, 1995). This technique includes the routine generation of a DPOAE using two stimulating tones ( $f_1$ ,  $f_2$ ), and the simultaneous presentation of a third ipsilateral pure tone (suppressor tone). When using an  $f_2$  frequency of 6000 Hz, for example, an ipsilateral suppressor tone is presented at a frequency around 6000 Hz and increased in level until a criterion amount of DPOAE amplitude reduction is achieved. The level of suppressor required to produce the criterion suppression is plotted as a function of suppressor frequency. When this procedure is repeated for many suppressor tones with frequencies around  $f_2$ , a DPOAE suppression tuning curve (STC) is generated.

DPOAE STCs are very similar in morphology to other physiologic tuning curves generated from the auditory system (Brown & Kemp, 1984). For this reason, they are presumed to provide an accurate

estimate of cochlear tuning or frequency resolution. This type of tuning curve is most likely outlining the DPOAE generation site. This site is determined by the overlap region of traveling waves produced by  $f_1$  and  $f_2$ . Thus, abnormalities involving active cochlear mechanics and traveling wave motion should be apparent using this paradigm.

### **Auditory Neuropathy and Cochlear Function**

A second aspect of this experiment addresses recent speculation that the cochlea may actually be impaired in patients with auditory neuropathy. Although patients with auditory neuropathy are presumed to have normal cochlear function, this aspect of the disorder has not been carefully studied. OAEs, which provide a reliable metric of OHC function, are typically present in individuals with auditory neuropathy. However, a simple categorical statement of OAE absence/presence provides limited and somewhat superficial information about cochlear function. Recent work has indicated that another metric of cochlear function, the cochlear microphonic, may be abnormal in patients with auditory neuropathy. Results suggest that the ear canal-recorded cochlear microphonic is higher in amplitude when neuropathy is present, than the microphonic from nonauditory neuropathy patients (Starr, Sininger, Nguyen, Michalewski, Oba, & Abdala, in press). Starr and colleagues hypothesize that cochlear microphonic amplitude may be enhanced due to a change in the OHC resting membrane potential.

Other recently reported data indicate that approximately 20% of patients with auditory neuropathy show a decrease in OAE amplitude over time (Abdala, Reference Note 2), again suggesting that cochlear function may be affected or become affected as auditory neuropathy progresses. Even though this information was gathered for only a small group of 24 patients, there was no consistent factor such as hearing aid use, exposure to ototoxins or patient age that could easily account for this deterioration of OHC function in this subset of subjects.

In the present study, DPOAE ipsilateral suppression tuning was recorded in four subjects with auditory neuropathy and compared with ipsilateral suppression tuning previously generated from a group of normal-hearing young adults (Abdala, 1998). The objective of this study was to assess cochlear frequency selectivity as revealed by DPOAE suppression tuning in subjects with compromised efferent system function. The specific research questions addressed: 1) whether normal efferent system function is required for normal cochlear tuning as measured by DPOAE suppression and 2) whether cochlear function, assessed by DPOAE suppression

**TABLE 1. Age of diagnosis (Dx Age), age of testing conducted for this experiment (Test Age), Absence/Presence of middle ear acoustic reflexes (AR), auditory brain stem response (ABR), cochlear microphonic (CM), and otoacoustic emissions (OAE).**

	Dx Age	Test Age	AR	ABR	CM	OAE
Subject 1	5	7	A	A	P	P
Subject 2	3	4	A	A	P	P
Subject 3	8	23	A	A	P	P
Subject 4	12	15	A	Abnl	P	P

A = Absent; P = present; Abnl = present but abnormal.

tuning is normal in these patients with auditory neuropathy.

## METHODS

### Subjects

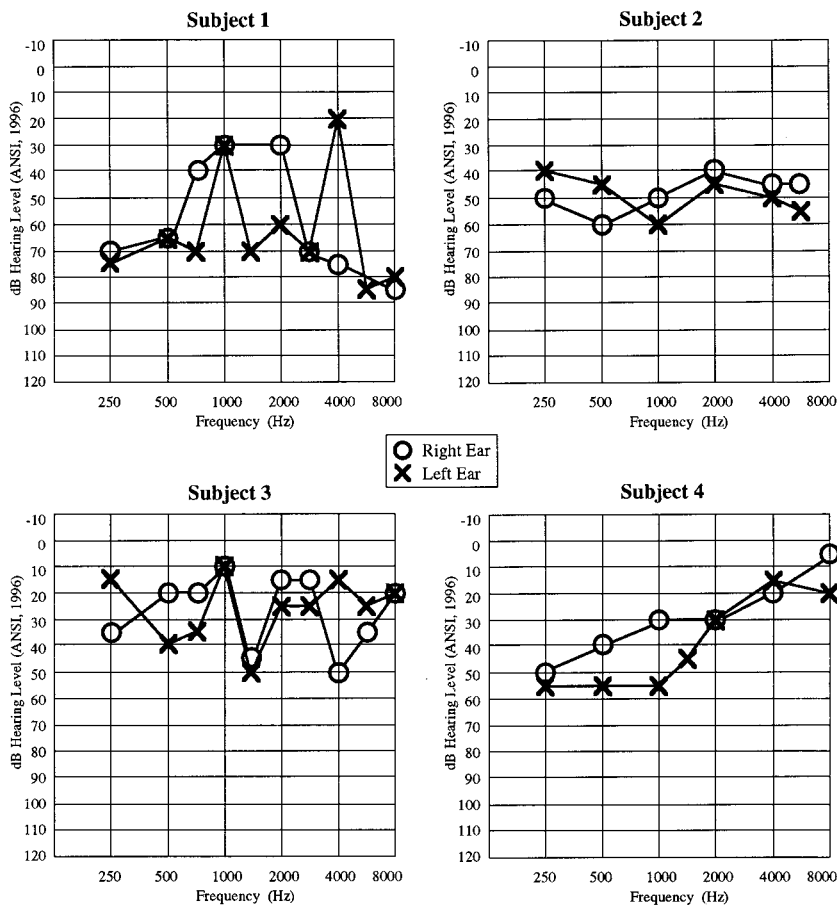
Four subjects with auditory neuropathy participated in this study. Table 1 summarizes their ages when first diagnosed with auditory neuropathy and their ages at test. Also included are basic test results, such as the acoustic reflex test and ABR, confirming their status as patients with auditory neuropathy. All four patients were seen by a neurologist to probe for any additional medical symptoms or peripheral neu-

ropathies that might be present. None of the four subjects with auditory neuropathy were found to have any other neurologic dysfunction at the time of test.

Their audiograms are shown in Figure 1. As is evident from Table 1, three of the four subjects were children; two were very young children, and one was an adolescent. Only one subject was a young adult. Testing included one session lasting anywhere from 2 to 4 hr. For the young children, testing was conducted during chloral-hydrate induced sedation. Subjects 3 and 4 sat quietly and read during testing. The ear selected for test in each case was dependent on practical issues like ear access (during sleep) and subject comfort. The right ears of subjects 1 and 2 were tested; the left ears of subjects 3 and 4 were tested. The 15 normal-hearing young adults used as control subjects are fully described in another report (Abdala, 1998). These subjects had normal audiograms (<15 dB HL) and a negative history of otologic disease or noise exposure.

### Instrumentation and Signal Analysis

An Ariel DSP16+ signal processing and acquisition board housed within a Compaq Prolinea 590 personal computer with Pentium processor was used



**Figure 1. Audiograms from four subjects with documented auditory neuropathy. Details about each subject are provided in Table 1.**



to generate DPOAE stimuli and acquire DPOAE data. The Ariel board was connected to an Etymotic Research ER-10C probe system and to an analog high-pass filter (12 dB/octave; 710 Hz high-pass cut-off). The ER-10C probe contains two output transducers and a low-noise microphone. The two primary tones and the suppressor tone were generated by the DSP processor. 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 produced by the second D/A-converter and output through the second transducer.

Energy at the ER-10C probe microphone was high-pass filtered and 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 comprised one block for  $f_2 = 3000$  and 6000 Hz. Due to elevated noise in the low-frequencies, 50 sweeps were added to make up one block at 1500 Hz. Two blocks of data were summed, averaged and the power spectrum was obtained by applying a 4096-point FFT.

The broadband noise (BBN) used in the DPOAE contralateral suppression paradigm for the measurement of efferent reflex was generated by a Grason-Stadler 16 Audiometer in the White Noise modality and delivered through an Etymotic Research, ER-2 transducer. Noise level was calibrated by routing output of the ER-2 insert transducer to a Zwislocki coupler and then to a half-inch microphone coupled to a sound level meter. Noise level was set to 60 dB SPL for all subjects. This is below the levels of noise known to evoke the middle ear reflex in adults (Silman, 1984).

### Data Acceptance Criteria

Acceptance criteria were as follows: 1) Noise measurements for three frequency bins (12.2 Hz wide) on either side of the  $2f_1$ - $f_2$  frequency had to be  $< 0$  dB SPL to ensure appropriate subject state. Preliminary work has shown that subjects with noise of 0 dB SPL or lower are more likely to generate DPOAE data with low amplitude variability and, 2) The measured DPOAE level must be at least 5 dB above the average noise measured in the same six bins around the distortion product frequency to be accepted into the grand average.

The program attempted up to six blocks of either 25 or 50 sweeps to achieve the absolute noise criteria of 0 dB SPL and the signal to noise ratio of 5 dB. If both of these criteria were not met after six attempted blocks, no data were collected and the next condition was initiated. In addition, sweeps were accepted into a block of data only when the esti-

mated RMS level in that sweep did not exceed a user-controlled artifact rejection threshold. This level was set for each subject based on observations of baseline activity level determined early in the test session, and modified if necessary during the experiment.

### Calibration

Inter-modulation distortion produced by the recording 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. The recording system noise floor was determined using a similar method with no tones present. The level of system noise floor ranged between  $-22$  and  $-27$  dB SPL.

An initial in situ 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.

### Procedure

Each subject was evaluated with the DPOAE suppression tuning paradigm to measure cochlear frequency resolution and with either transient evoked otoacoustic emissions (TEOAEs) or DPOAEs contralateral suppression paradigm to measure medial efferent system function. Subjects 1 and 2 were initially identified and diagnosed with auditory neuropathy at the Children's Auditory Research and Evaluation Center of the House Ear Institute. The clinical protocol at that time was to record TEOAE contralateral suppression as a measure of medial efferent system function. Subjects 3 and 4 were diagnosed at a later time when alternative measures of medial efferent function were available. Thus, DPOAE contralateral suppression was used to probe function of the medial efferent function in these two patients.

**DPOAE Suppression Tuning** • The custom-designed software used for the collection of DPOAE STCs was developed at the Children's Auditory Research and Evaluation Center, House Ear Institute. The ratio between primary tone one ( $f_1$ ) and two ( $f_2$ ) was kept constant at 1.2 and primary tone levels were presented at 65 and 50 for L1 and L2, respectively. Three  $f_2$  frequencies were presented: 1500, 3000, and 6000 Hz. An unsuppressed DPOAE was initially measured for a given  $f_2$  frequency. An ipsilateral suppressor tone ( $f_s$ ) then was presented

simultaneously with the primary tones and its level increased in 5 dB steps over a 30 to 40 dB range of intensities. As  $f_s$  level was increased, DPOAE amplitude typically decreased.

An average of 14 ipsilateral suppressor tones were presented at frequency intervals of between 25 and 150 cents (one octave = 1200 cents). Suppressor frequencies ranged from one octave below  $f_2$ , to 1/4 octave above  $f_2$  and were presented in finer intervals near the tip of the tuning curve compared with the sides. By following this procedure, each subject had a series of approximately 12 suppression growth functions for a given  $f_2$  frequency. A suppression growth function is a plot of DPOAE amplitude as a function of  $f_s$  level.

To generate DPOAE iso-STCs, the suppressor level that reduced DPOAE amplitude by 6 dB was determined from the suppression growth function using linear interpolation, and then plotted as a function of suppressor frequency. Six dB was chosen as the suppression criteria because it ensures a reasonable signal to noise ratio, and results in sharp, narrow STC in normal-hearing adults (Abdala et al., 1996; Kummer et al., 1995).

**Contralateral Suppression** • There is strong evidence that contralateral suppression of OAEs reflects an efferent-mediated effect (Puel & Rebillard, 1990). Thus, it serves as an effective assay of the olivo-cochlear reflex. To record DPOAE contralateral suppression, an  $f_2$  frequency of 1500 Hz was presented with 10 dB separation between L1 and L2 ( $L_1 > L_2$ ) and a constant  $f_2/f_1$  ratio of 1.22. DPOAE amplitude was recorded at 12 stimulus levels ranging from 30 to 85 dB SPL in 5 dB intervals. Three growth functions were collected with BBN (+BBN) presented at 60 dB SPL and three without BBN (-BBN) in an alternating fashion for a total of six growth functions per ear. Only the mean of three growth functions for +BBN and three for -BBN was entered into the data set. This initial averaging of DPOAE amplitude data from any one ear was conducted to reduce the influence of intra-subject, run to run variability.

TEOAE contralateral suppression was conducted by recording a click-evoked OAE in response to nonlinear 80 to 82 dB pSPL clicks, first in the absence of BBN and then with BBN presented contralaterally at 60 dB SPL.

## Data Analysis

The DPOAE suppression data were analyzed in the following way: 1) tuning curve width was quantified using a Q10 value. Q is determined by dividing the center frequency of the tuning curve by the bandwidth of the tuning curve 10 dB above the tip; 2) Slope

(dB/octave) of low- and high-frequency sides of the tuning curve was determined by fitting a regression line from the tip or center frequency of the STC to the data point representing the lowest- and highest-frequency  $f_s$  (excluding a low-frequency "tail" if present); 3) tuning curve tip frequency (Hz) was defined as the suppressor frequency at which criterion suppression was achieved with the lowest suppressor level; and 4) tuning curve tip level was defined as the level of the suppressor tone at tuning curve tip frequency.

The suppression growth function also was analyzed by fitting a regression line to the linear portion of the suppression growth function (on average, 1 to 3 dB down from unsuppressed DPOAE to the last point on the function with adequate signal to noise ratio) for six to eight representative suppressor tones within a given  $f_2$  category. This provided a measure of the slope (dB/dB) of suppression growth. DPOAE STC characteristics were analyzed at each  $f_2$  frequency separately with nonparametric Mann-Whitney *U* tests due to the small number of neuropathy subjects tested. The alpha level was set at 0.05.

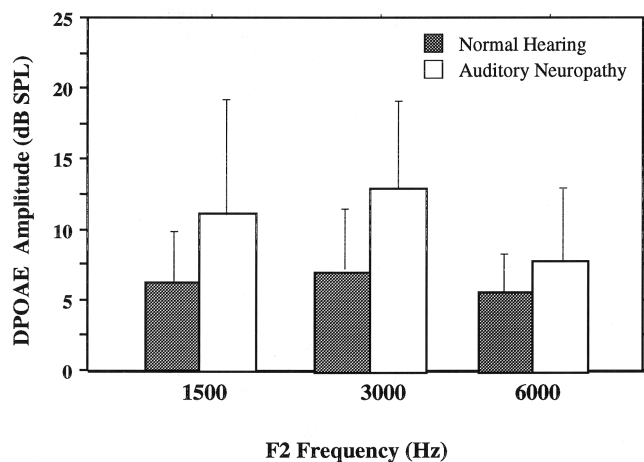
DPOAE contralateral suppression data were measured by subtracting DPOAE amplitude in +BBN condition from DPOAE amplitude in -BBN. This produced a difference score reflecting the impact of contralateral noise on the ipsilaterally evoked DPOAE. Difference scores obtained for four primary tone levels, 55, 65, 75 and 85 dB SPL were averaged and used in data analysis because they were compared with data previously collected in this manner.

TEOAE contralateral suppression was measured by subtracting overall amplitude of the TEOAE in the +BBN condition from amplitude in -BBN condition. This test was initially conducted in these neuropathy patients for clinical purposes and therefore, it was not administered with research parameters now understood to be optimal (i.e., using linear click modality and analyzing specific time segments of the response). Because only two observations were included for each technique (subjects 3 and 4 with DPOAE contralateral suppression and subjects 1 and 2 with TEOAE contralateral suppression), statistical analyses were not conducted on the difference scores. However, average results from previously collected normative samples were used as a comparison with these data (Abdala, Ma, & Singinger, 1999; Hood, Berlin, Hurley, & Wen, 1996).

## RESULTS

### DPOAE Amplitude

Subjects with neuropathy consistently showed higher level DPOAE amplitude than normal-hearing subjects (Fig. 2). However, differences between



**Figure 2.** Mean distortion product otoacoustic emission (DPOAE) amplitude as a function of  $f_2$  frequency for subjects with auditory neuropathy and normal-hearing subjects. Error bars represent 1 SD

the groups can be easily attributed to age because several studies have shown that infants and young children have higher level DPOAEs than adults (Abdala, 1996; Norton & Widen, 1990; Prieve, Fitzgerald, Schulte, & Kemp, 1997). When DPOAE amplitude values reported in the two children with auditory neuropathy in this study were compared with the mean data of age-matched normal-hearing children reported in a recent study (Prieve et al., 1997), their amplitude was within the normal range. Initial amplitude of the DPOAE does not influence the ipsilateral suppression tuning paradigm because each patient's unsuppressed amplitude is used as his or her own control.

### Contralateral Suppression

Figure 3 shows TEOAE contralateral suppression results from subjects 1 and 2 and DPOAE contralateral suppression results from subjects 3 and 4. Contralateral suppression from a normal-hearing subject is also illustrated for comparison in each column. Subject 1 had an average decrease in TEOAE amplitude of 0.1 dB when noise was presented. Subject 2 had a difference score of  $-0.1$  dB. Thus, using the range of 1.0 to 1.5 dB suppression derived from previous work documenting the magnitude of the efferent effect in normal-hearing individuals (Hood et al., 1996), neither subject 1 or 2 had present olivo-cochlear suppression of TEOAEs.

The amount of DPOAE suppression (averaged across subjects and four primary tone levels from 55 to 85 dB) in a group of normal-hearing young adult subjects with a mean age of 28 yr is 1.2 dB at 1500 Hz (Abdala et al., 1999). Subject 3 showed an aver-

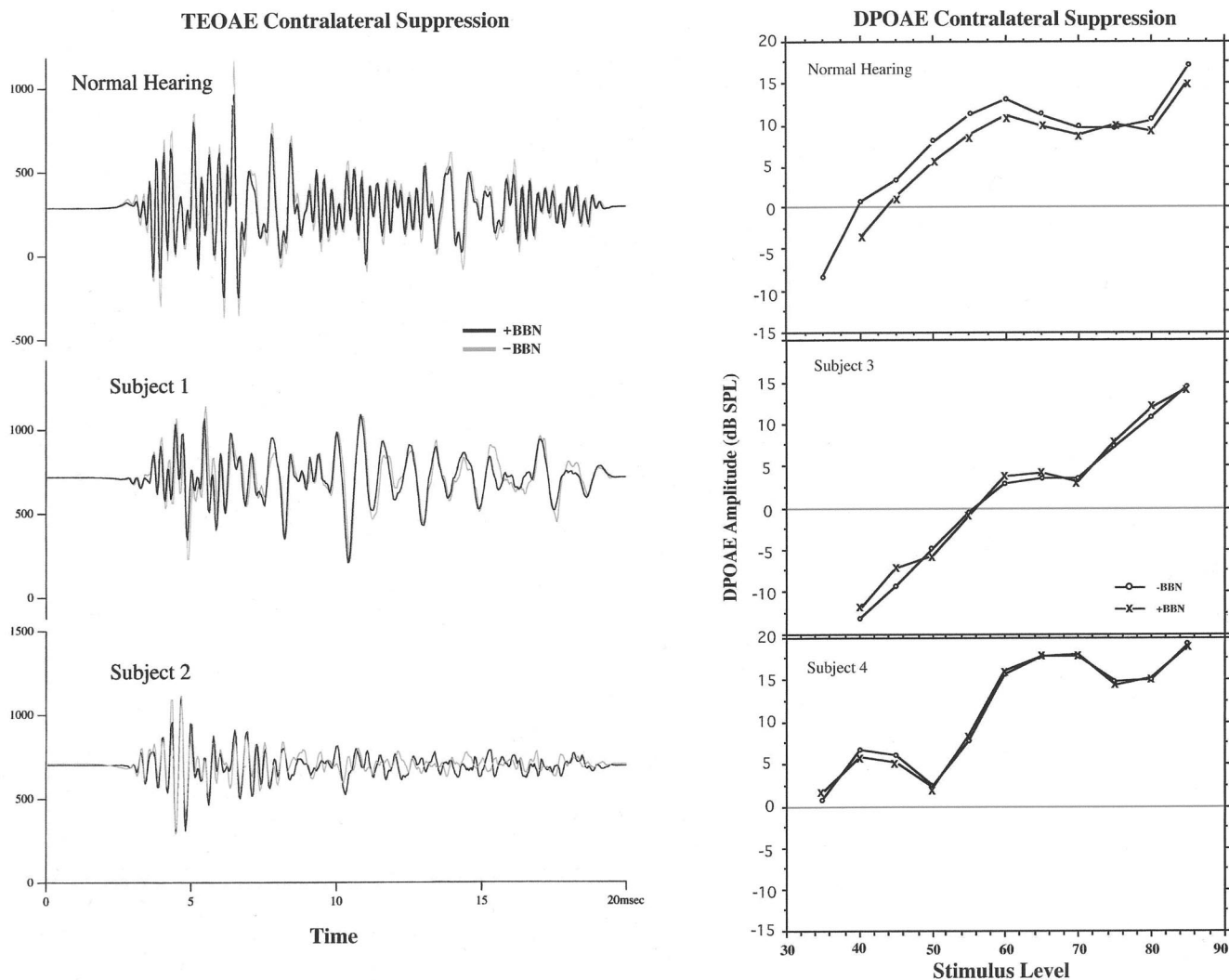
age difference between DPOAE amplitude recorded in quiet and with contralateral BBN of  $-0.13$  dB. Subject 4 showed a 0.01 dB difference score. Although it was not possible to conduct a statistical analysis of TEOAE or DPOAE contralateral suppression (with only an  $n$  of 2 in each category), the reduction in either DPOAE or TEOAE amplitude with presentation of contralateral noise was unequivocally absent in this small group (range of  $-0.13$  to 0.1 dB). Additionally, the literature has aptly documented the lack of this efferent reflex in other patients with auditory neuropathy (Berlin et al., 1993; Hood et al., 1996; Sininger et al., 1995; Starr et al., 1996).

### DPOAE Suppression Tuning

Ten DPOAE ipsilateral STCs were recorded from the four subjects with confirmed auditory neuropathy: two STCs for  $f_2 = 1500$  Hz, four STCs for  $f_2 = 3000$  Hz and four for  $f_2 = 6000$  Hz. Figure 4 is a logarithmic display of the individual STCs from neuropathy patients (solid lines). The dashed line for each  $f_2$  frequency is a representative STC from a normal-hearing child for visual comparison. DPOAE STCs from neuropathy patients look typical in morphology; that is, they are asymmetrically shaped (steeper high- versus low-frequency side), show a sharp tip and are generally centered around the  $f_2$  frequency in all cases. Figure 5 displays these same tuning curves using a linear scale to show detail. The individual STCs from neuropathy patients are superimposed on a gray background representing the average STC  $\pm 1$  standard deviation for 15 normal-hearing adult subjects. Although portions of the tuning curves from auditory neuropathy patients extend outside of the gray region, their general shape and width appears to be like those of their normal-hearing peers.

Tuning curve Q value is shown in Figure 6 for neuropathy patients and the group of normal-hearing adults. Figure 7 is a bar graph showing the mean slope of the low- and high-frequency flank of the tuning curve for both groups ( $\pm 1$  SD). Separate Mann-Whitney  $U$  tests were conducted for STC Q and slope at 3000 and 6000 Hz. Neither factor was found to be different between subjects with auditory neuropathy and normal-hearing control subjects.

Figure 8 displays STC tip level (i.e., suppressor level at the lowest point of the tuning curve) as a function of tip frequency. At 3000, the two groups are indistinguishable from one another. At 1500 and 6000 Hz, the points are more scattered; however, subjects with auditory neuropathy overlap with normal-hearing patients. Again, nonparametric Mann-



**Figure 3.** Transient evoked otoacoustic emission (TEOAE) time waveform with (black line) and without (gray line) broadband noise (BBN) presented to the contralateral ear (Left). The black line is consistently below the gray line for the normal-hearing subject; black and gray lines overlap randomly for subjects 1 and 2, indicating the lack of efferent-mediated contralateral suppression. Distortion product otoacoustic emission (DPOAE) growth function with (X) and without (O) broadband noise to the contralateral ear (Right). The normal-hearing subject shows a consistent decrease in DPOAE amplitude recorded in noise; no such decrease in DPOAE amplitude was observed for subjects 3 and 4, indicating lack of efferent-mediated contralateral suppression.

Whitney *U* tests indicated no STC tip level/frequency differences between groups.

### DPOAE Suppression Growth

Figure 9 shows the slope of suppression growth at various suppressor frequencies. The normal pattern (dashed line) shows that there is near linear growth of suppression for points lower in frequency than the  $f_2$  frequency (i.e., to the left of the dashed vertical line) and compressive growth of suppression for frequencies higher than  $f_2$  (to the right of the dashed vertical line). This frequency-related pattern of DPOAE suppression growth has been reported previously (Abdala, 1998; Kummer et al., 1995). As is

evident from Figure 9, neuropathy patients show a comparable configuration of frequency-related asymmetry in suppression growth.

### DISCUSSION

Individuals with auditory neuropathy, as a group, do not show normal efferent effects on cochlear function (Berlin et al., 1993; Sininger et al., 1995; Starr et al., 1996). Consistent with this observation, the four subjects with auditory neuropathy in the present study did not have efferent-mediated suppression of OAEs by contralateral BBN or middle ear acoustic reflexes. Thus, cochlear function measured in this study with ipsilateral suppression



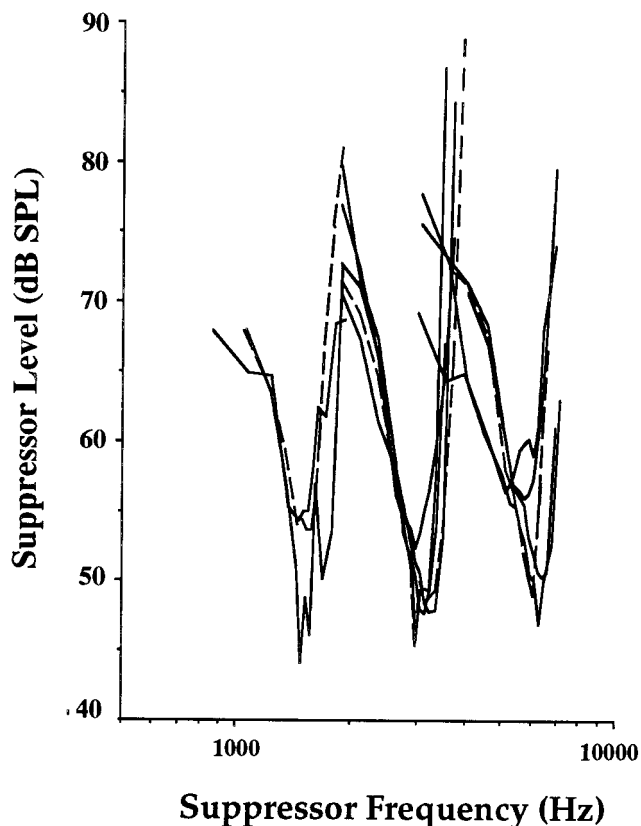


Figure 4. Logarithmic display of 10 distortion product otoacoustic emission (DPOAE) suppression tuning curves (STCs) generated from four subjects with auditory neuropathy. Dashed line represents DPOAE STCs generated from one normal-hearing child for comparison.

tuning, was reflective of cochlear function in the absence of normal efferent influence. All measures of cochlear function assessed by DPOAE suppression tuning were normal in these subjects with compromised access to the efferent system.

### DPOAE Suppression Tuning

The DPOAE tuning curves from patients with auditory neuropathy showed normal morphology; they were narrow with a sharp tip region, asymmetrically shaped showing steeper flank of the tuning curve on the high-frequency side, and their tip frequency was always centered around the  $f_2$  frequency. The center frequency or tip frequency of an STC always reflects the frequency/cochlear region where suppression occurs most easily, i.e., with minimal suppressor level. The region that allows for the “easiest” suppression of the DPOAE is typically the region where the DPOAE is generated. That is, a suppressor tone at nearly the same cochlear region as the DPOAE generation site will be maximally effective. The fact that the DPOAE STCs from auditory neuropathy patients had tip frequencies centered around  $f_2$  frequency, strongly suggests that their DPOAEs are being generated at the same site as distortion from normal-hearing individuals.

The findings from tuning curve width (Q) and slope data also indicate that active mechanical processes in the cochlea were normal for these subjects with auditory neuropathy. The DPOAE suppression paradigm probes basilar membrane motion and frequency selectivity. DPOAE suppression occurs when

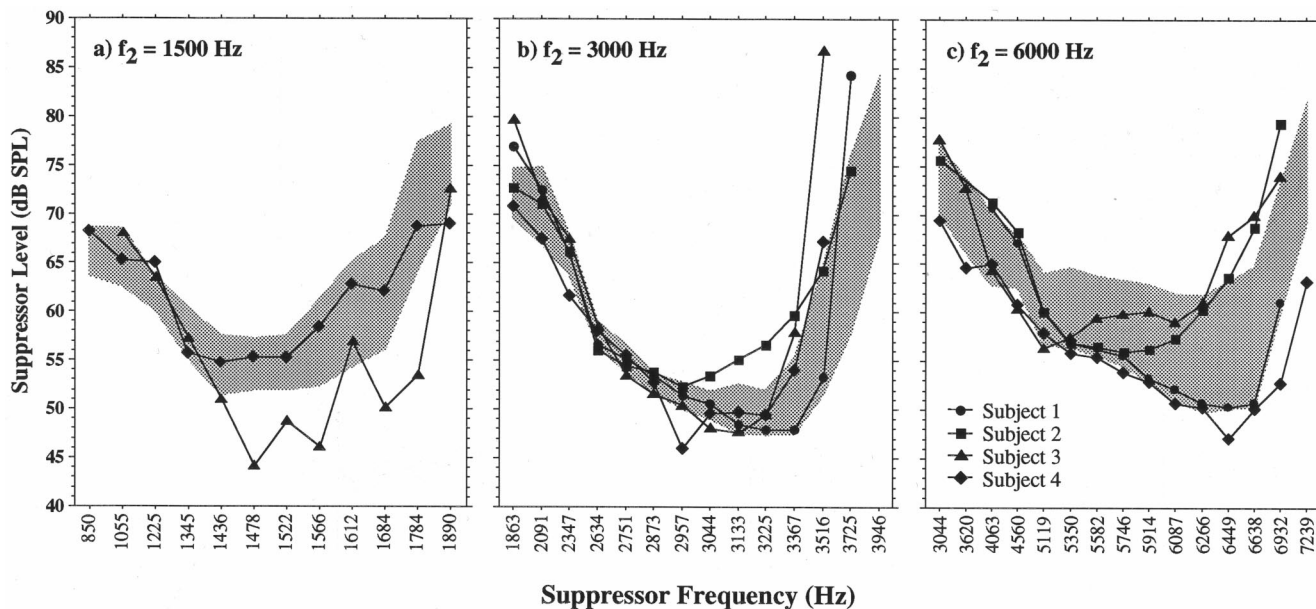


Figure 5. Linear display of two distortion product otoacoustic emission suppression tuning curves (STCs) generated at  $f_2 = 1500$  Hz and four at 3000 and 6000 Hz each from subjects with auditory neuropathy. The gray shaded region represents mean STCs  $\pm 1$  SD from 15 normal-hearing young adults.

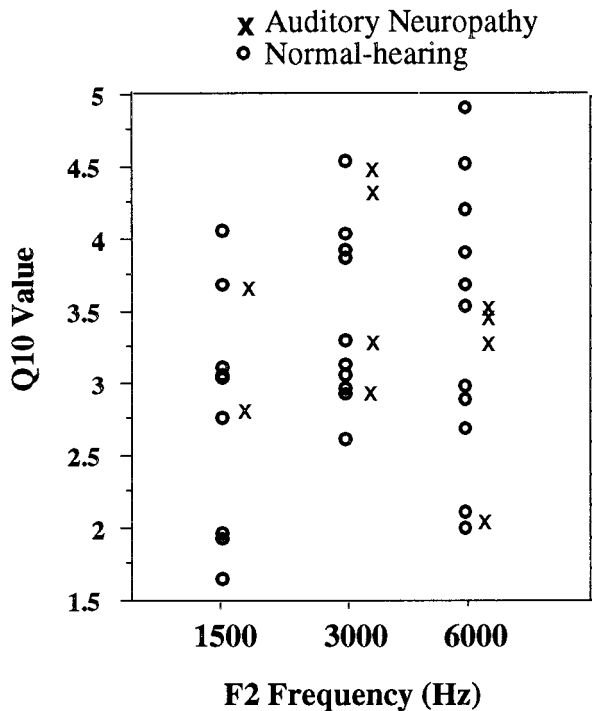


Figure 6. Q10 value as a function of f2 frequency for 10 distortion product otoacoustic emission suppression tuning curves (STCs) generated from four subjects with auditory neuropathy (X). Open circles represent Q10 values from a normal-hearing group of adults.

the suppressor tone interrupts the normal interaction between the traveling waves produced by f1 and f2. In doing so, the suppressor tone interrupts generation of the distortion product, which is known to occur at the region of maximum overlap between the primary tones. If the f2- and f1-evoked traveling waves are abnormally broad or low in amplitude (as

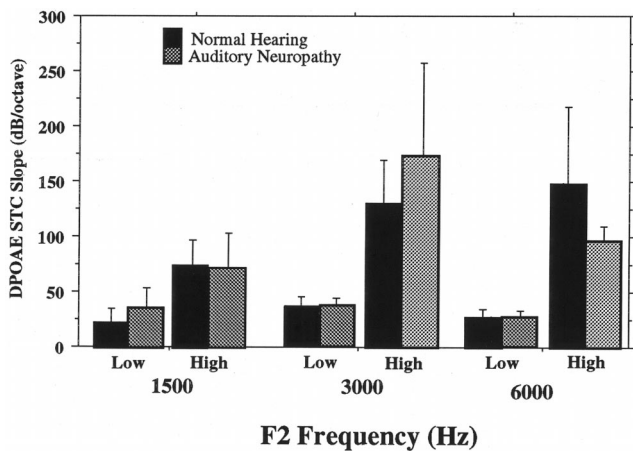


Figure 7. Mean slope (dB/octave) values as a function of distortion product otoacoustic emission (DPOAE) suppression tuning curve side (low/high) and f2 frequency for four subjects with auditory neuropathy and normal-hearing adults. Error bars represent 1 SD

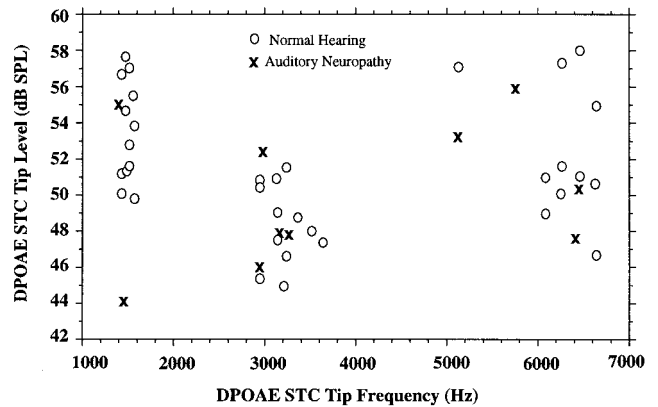


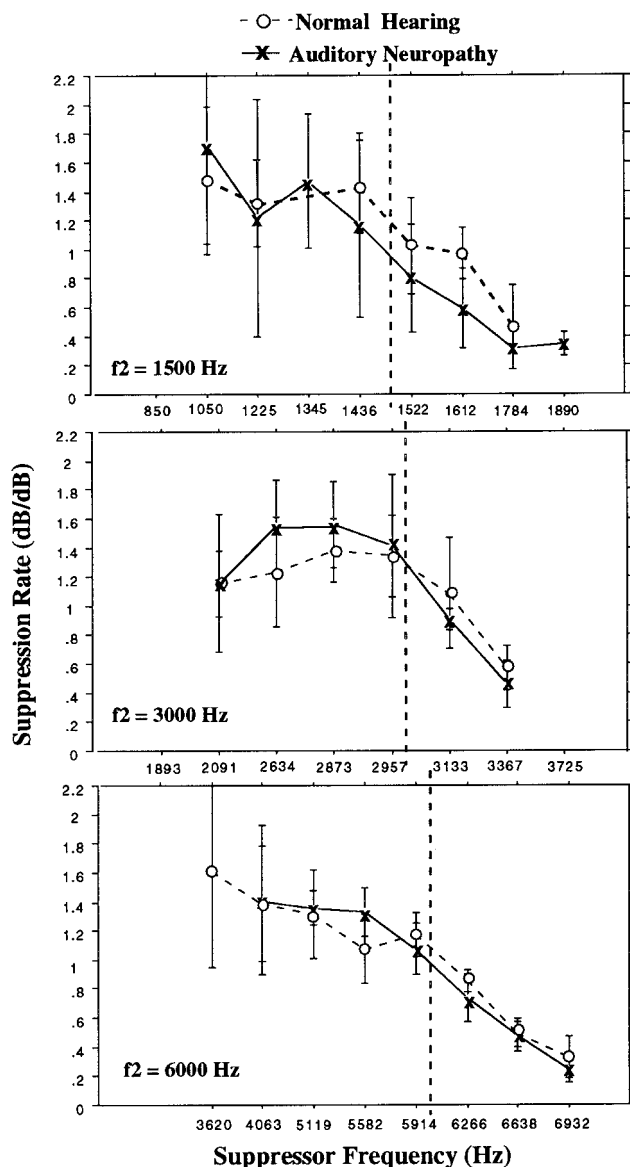
Figure 8. Distortion product otoacoustic emission (DPOAE) suppression tuning curve (STC) tip level as a function of STC tip frequency for three f2 frequencies: 1500, 3000, and 6000 Hz. Data are plotted for four subjects with auditory neuropathy (X) and a group of normal-hearing adults (O).

we would expect with dysfunction of cochlear mechanics), a suppressor tone would have an atypical pattern of effectiveness in reducing DPOAE amplitude. Therefore, although it is not clear exactly which aspect of the auditory filter DPOAE suppression measures, it is clearly reflecting mechanical aspects of cochlear function and the interaction of traveling wave activity on the basilar membrane.

Basilar membrane motion and filtering appear to be normal in these subjects with auditory neuropathy even though efferent influence on these aspects of auditory physiology is dysfunctional in all four subjects. These results indicate that the OHCs do not require normal efferent input to function efficiently and to provide sharp tuning as measured by DPOAE ipsilateral suppression. This conclusion, however, can only be extended to the particular stimulus environment created in this experiment. Under more taxing situations of competing background noise, for example, it may be that the efferent system does influence cochlear tuning in a significant manner and we were simply unable to observe this effect using this experimental paradigm.

### DPOAE Suppression Growth

Evaluation of suppression growth provides a more detailed probe of cochlear function because the DPOAE STC represents only a static, horizontal slice through suppression growth functions at 6 dB of amplitude reduction. In normal cochleae, the effectiveness of a suppressor, (i.e., suppression growth) is known to depend on the frequency of the suppressor tone (Fig. 9) (Costalupes, Rich, & Ruggero, 1987; Rhode & Cooper, 1993). Suppressor tones lower in frequency than the f2 tone produce



**Figure 9.** Mean rate at which suppression occurs (dB/dB) with increasing level of suppressor tone, as a function of suppressor tone frequency. Mean data are plotted for four subjects with auditory neuropathy (X) and a group of normal-hearing adults (O). Error bars represent  $\pm 1$  SD. The dashed vertical line is at f2 frequency.

rapid, effective suppression of the DPOAE ( $>1$  dB/dB). Suppressor tones higher in frequency than f2 produce slow, shallow rates of suppression ( $<1$  dB/dB).

The asymmetry in suppression growth is due to the nature of traveling wave motion. Motion near the peak of the traveling wave is compressive whereas motion basal to this peak, in the "tail" region grows linearly with increases in level. Therefore, low-frequency side suppressors (suppressor tones lower in frequency than f2 and f1) produce traveling waves that easily and effectively mask or

suppress the cochlear region of f2 as their level is raised. However, when the suppressor tones are higher in frequency than the f2 (high-frequency side suppressors), they are very ineffective suppressors because there is minimal downward spread of masking as level is raised (Ruggero, Rich, Recio, Narayan, & Robles, 1997). Thus, a high-frequency suppressor should not suppress the generation site of the DPOAE (around f2) effectively and should produce shallow suppression growth.

As a result of the above-described traveling wave properties for a three tone complex, normal-hearing individuals show asymmetry in suppression growth as displayed in Figure 9 and previously described for DPOAE data. It is significant that subjects with auditory neuropathy show the same asymmetry for low- and high-frequency side suppressors. These results suggest that spread of excitation on the basilar membrane and subsequent frequency coding is normal in these subjects even in the absence of a normal olivo-cochlear reflex.

## SUMMARY

These four subjects with auditory neuropathy were found to have normal cochlear function as defined by DPOAE suppression techniques. DPOAE generation site, degree of suppression tuning and growth of suppression were found to be normal in these four subjects with auditory neuropathy, providing detailed evidence of normal mechanical processes in the cochleae of these "classic" or typical patients with auditory neuropathy. This finding does not rule out the possibility that there are variations of this disease process that do cause OHC dysfunction.

Considering the fact that the contralateral suppression of OAEs was absent in all four subjects, the DPOAE suppression results can be assumed to exist in the absence of normal efferent influence to the OHCs of the cochlea. This suggests that normal efferent innervation to the OHCs is not necessary for normal cochlear tuning as defined by DPOAE suppression. However, it is not clear when efferent function became abnormal in these experimental subjects because it is difficult to pinpoint the exact onset of auditory neuropathy. All of the subjects in this study were diagnosed with auditory neuropathy as children (i.e., beyond the neonatal period). Thus, it is not known whether the pathology was present congenitally.

If the disease process began after the innervation of OHCs by efferent fibers during the third trimester of human fetal life, appropriate innervation of the cochlea may have occurred during a critical developmental period. This early innervation could have

established normal cochlear physiology and later disruption of the efferent fibers (onset of auditory neuropathy) may have been inconsequential to cochlear function. Recent results reported with cat have shown that cochlear and VIIIth nerve fiber tuning of kittens is abnormal when the efferent pathway is disrupted before appropriate innervation of OHCs by MOC fibers (Walsh, McGee, McFadden, & Liberman, 1998). However, when efferent fibers of adult cats are severed, auditory function appears to be unaltered. Thus, although our study supports the idea that efferent innervation is not required at the time of test for normal cochlear tuning in humans, it may be required during a critical developmental period in fetal life to ensure normal cochlear tuning as an adult.

In conclusion, although it has been unequivocally shown that the efferent system can influence cochlear physiology, results of this study suggest that it is not required once the cochlea is mature, for normal mechanical function and frequency resolution of the human cochlea as measured by DPOAE suppression.

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