To the Graduate Council:

I am submitting herewith a thesis written by Erin L. Wendover entitled "Effects of Intravenous Hypertonic Urea on Distortion Product Otoacoustic Emissions in Cats." I have examined the final copy of this thesis for form and content and recommend that it be accepted in partial fulfillment of the requirements for the degree of Masters of Arts, with a major in Audiology.

James W. Thelin, Major Professor

We have read this thesis and recommend its acceptance:

Accepted for the Council:

Associate Vice Chancellor and
Dean of the Graduate School

EFFECTS OF INTRAVENOUS HYPERTONIC UREA ON DISTORION PRODUCT OTOACOUSTIC EMISSIONS IN CATS

A Thesis

Presented for the

Master of Arts

Degree

The University of Tennessee, Knoxville

Erin Wendover

May, 1998

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ABSTRACT

The present study was conducted to measure the effects of IV hypertonic urea on cochlear function in seven normal cats as measured using distortion product otoacoustic emissions (DPOAEs). DPOAE measurements were made at 1/12 octave intervals from 1000 - 8000 Hz on cats sedated with ketamine and xylazine. Three measurement trials (8 minutes per trial) were made before the infusion of hypertonic urea and four measurements trials were made while urea was being infused at a rate of 2-7 mg/kg. The infusion of urea resulted in a mean reduction of 45% in intraocular pressure (IOP), which remained constant over the four post-infusion periods.

The mean results indicated that hypertonic urea produced small but significant (3.1 dB) reductions on DPOAE levels in the 1-2 kHz octave-frequency band. In the 2-4 kHz and 4-8 kHz octave-frequency band, the mean DPOAE levels were 4.6 and 1.7 dB, respectively; but these mean differences were not significant. However, for one subject, DPOAE levels decreased very substantially at all frequencies. For another subject, DPOAE levels changed in two well-defined regions; they increased in one region and decreased in the other. Urea did not appear to produce DPOAE changes that could be characterized as shifts in place of stimulation or in frequency selectivity.

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1. INTRODUCTION

Hypertonic mannitol, glycerol, and urea have osmotic effects that reduce intracranial and intraocular pressure (Larsen, Angelborg, & Hultcrantz, 1982). In the cochlea, they have the effect of osmotically drawing endoylmph from the scala media into the stria vascularis (Duvall, Santi, & Hukee, 1981). The effects of these drugs have been studied in humans with behavioral tests of hearing and in animals with measures of blood flow and histologic descriptions of cochlear structures. The present study extends this work by examining the effects of intravenous (IV) hypertonic urea on DPOAEs in cats.

Effects Of Oral Hypertonic Glycerol, Urea, and Mannitol on the Hearing of Humans with Meniere's Disease

Angelborg, Klockhoff & Stahle (1977) demonstrated that oral hypertonic glycerol temporally improves the hearing in patients with Meniere's disease. The average changes in thresholds of audibility that occur in ears with Meniere's disease are shown in Figure 1 (Slattery, Synder, & Thelin, 1986). The ears with Meniere's disease are represented by circles. At 2000 Hz and below, the average threshold shifts were negative, indicating improvements in hearing thresholds. The average improvement in threshold is significant over the frequency range of 250 Hz through 2000 Hz. However, at 4000 Hz and 8000 Hz, oral glycerol does not have a significant effect on thresholds of audibility in ears with Meniere's disease.

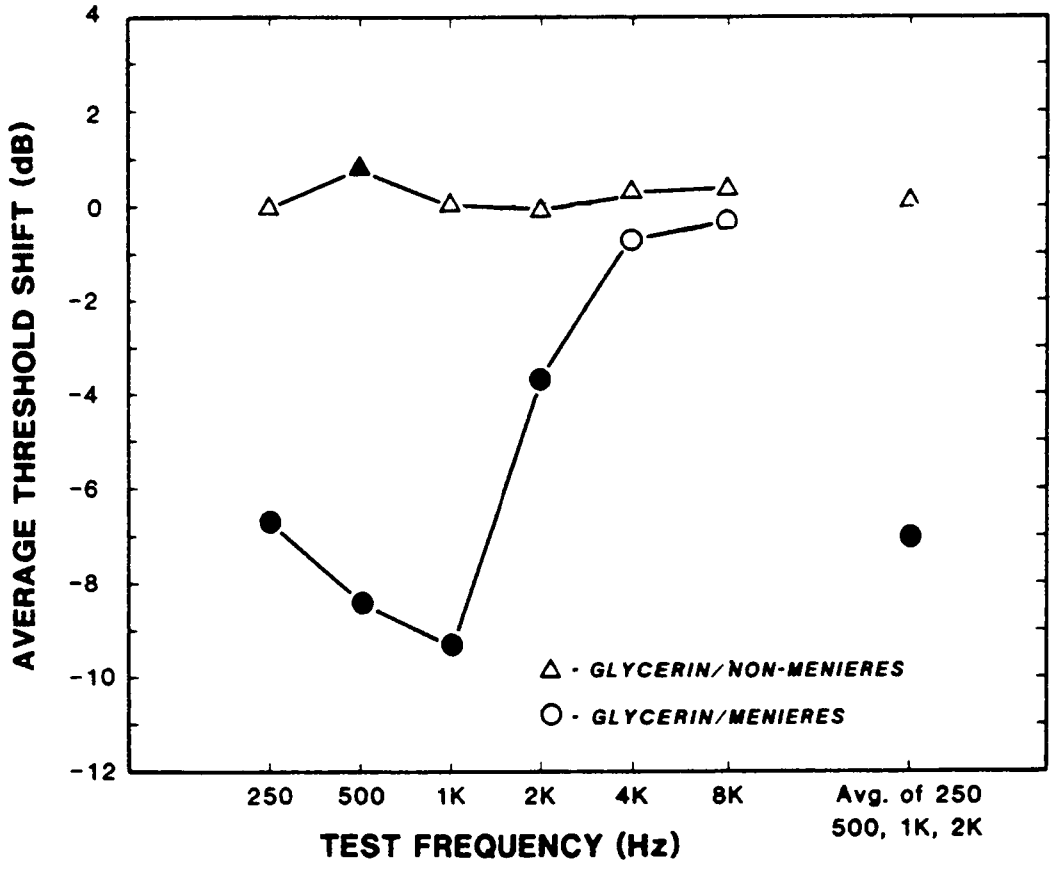


FIGURE 1. Changes in pure tone thresholds of hearing with oral glycerol for ears with Meniere's disease (circles) and the non-involved ear (triangles) in patients with unilateral Meniere's disease. The filled symbols represent significant changes in hearing thresholds.

Source: Slattery, W. H., Synder, J.M., & Thelin, J.W. (1986). Glycerin test: method for analysis of pure tone threshold shifts. *Corti's organ,* 11,7.

In Figure 2, the audiometric data for a patient with Meniere's disease shows that the effects of oral glycerol are more complex than improving thresholds alone (Thelin, Barbero, Templer, & Christiansen, 1983). Though improvements in threshold can be seen in the frequency range from 250 - 2000 Hz, the disease caused the cochleas to function as narrow band filters. Post-glycerol results show broadening of these filters, which may be due to the changes in fluid pressure in the cochleas and possibly to changes in stiffness mass relations within the cochlea that govern the place of stimulation on the basilar membrane. Further evidence that oral glycerol effects more than hearing thresholds can be seen in the speech discrimination data. Speech discrimination scores improved in both ears following the use of oral glycerol, even when speech levels were reduced to compensate for improvements in hearing thresholds. These data suggest that in ears with Meniere's disease, frequency selectivity and sensitivity of the cochlea may be improved and the place of stimulation may be altered with oral glycerol.

Hearing in patients with Meniere's disease has also been studied using oral mannitol and oral urea. Oral urea was found to produce similar results to glycerol, but oral was mannitol less effective in producing improvements in thresholds of audibility (Angelborg, Klockhoff, & Larsen, 1982; Angelborg, et al., 1977).

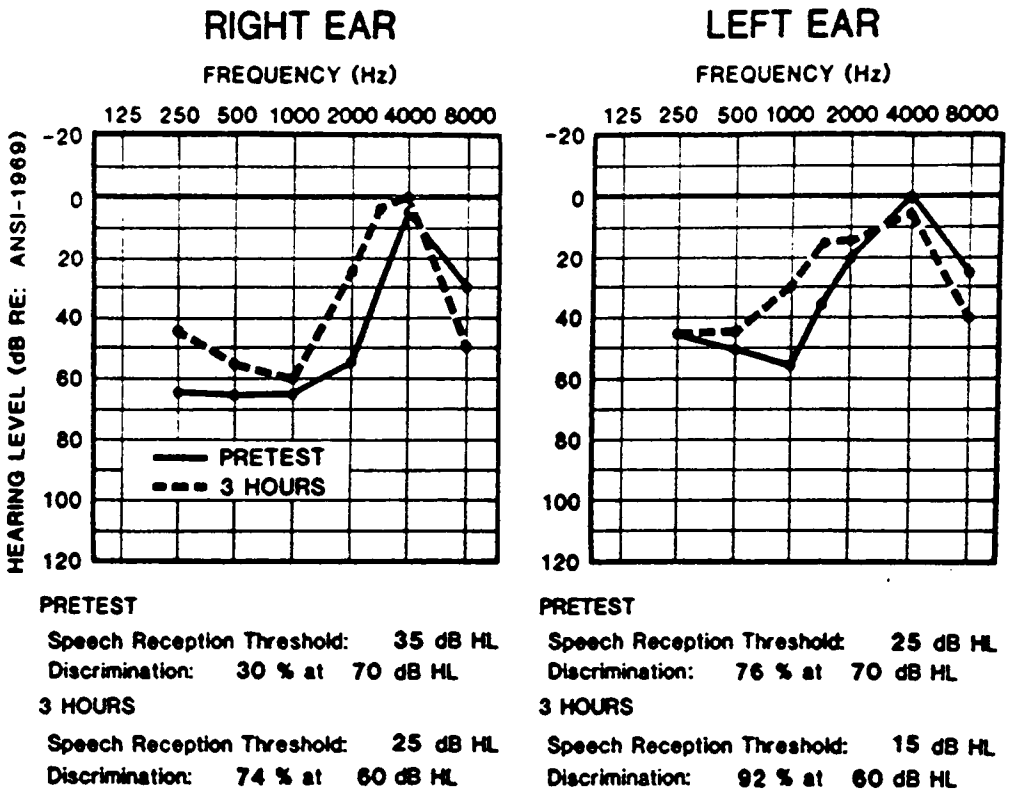


FIGURE 2. Audiometric effects of oral glycerol in a patient with Meniere's disease. Results are shown for pre-test conditions and for three hours following ingestion of oral glycerol.

Source: Thelin, J.W., Barbero, G.J., Templer, J.W., & Christiansen, S.G. (1983). Audiometric findings in a child with rapidly progressing Meniere's disease. *Asha*, 25, 114.

Effects of Oral Glycerol on Human Ears Without Meniere's Disease

When the effects of oral glycerol have been measured in the non-involved ear of patients with unilateral Meniere's disease, the results have shown small changes or no changes in thresholds of audibility (Slattery et al., 1986). In Figure 1, post-glycerin results show no significant changes in thresholds of audibility except at 500 Hz. At that frequency, which is a relatively low frequency, thresholds were reduced slightly but significantly.

Effects of IV Glycerol, Mannitol, and Urea in Animals

In animal experiments, IV mannitol, glycerol and urea have been shown to reduce intracranial pressure and increase cochlear microcirculation (Takeda, Hukee, & Santi, 1981). Moderate increases in cochlear blood flow following IV administration of mannitol, glycerol, and urea have been documented in the guinea pig and rabbits (Baldwin, Ohlsen, Miller, & Nuttal, 1992). The use of IV glycerol in the guinea pig (Baldwin et al., 1992), IV mannitol (Duvall et al., 1981), and IV urea (Wright, Lee, Meyerhoff, & Roland, 1988) in the chinchilla, caused morphological changes and edema of the stria vascularis. Angelborg et al. (1977), found that IV glycerol and IV urea in the chinchilla caused an almost immediate collapse of Reissner's membrane; no collapse was found after IV mannitol.

In animal studies with IV administration of these drugs, blood flow effects have been shown to depend on dosage and time after infusion of the drug. In a comparison of effects on arterial relaxation, the time course

of the effects for each of the three drugs was similar but the pattern of effects differed. The effects were similar for glycerol and urea but different for mannitol (Takeda et al., 1981). Carlborg and Farmer (1983) also found that IV glycerol and urea had cochlear effects that were similar while those for IV mannitol were different. In the present study, the decision was made to use either IV glycerol or IV urea, based on the similarity of the results obtained with the two drugs. Intravenous urea was selected because their were existing protocols regarding dosage and administration for cats at the University of Tennessee College of Veterinary Medicine, but not for IV glycerol.

Another reason for selecting IV urea was that it produced effects of sufficient magnitude and duration to study possible changes in DPOAEs over time. The data of Balwin et al. in Figure 3, showed the effects on cochlear blood flow for IV urea infused for five minutes at a rate of 0.6 mL/minute. These data show that blood flow effects are greatest between 5 to 10 minutes after onset of the infusion and extend for 10 to 15 minutes after termination of the urea infusion.

Otoacoustic Emissions as Measures of Cochlear Function

The anatomical and physiological data of Brownell (1990) provide evidence that otoacoustic emissions (OAEs) are generated by outer hair cells that are electrically activated. The outer hair cells are situated in an electrical field with a silent current arising from the stria vascularis. When an outer hair cell is activated acoustically, the silent current is altered and the electromotile movement of the outer hair cell begins and

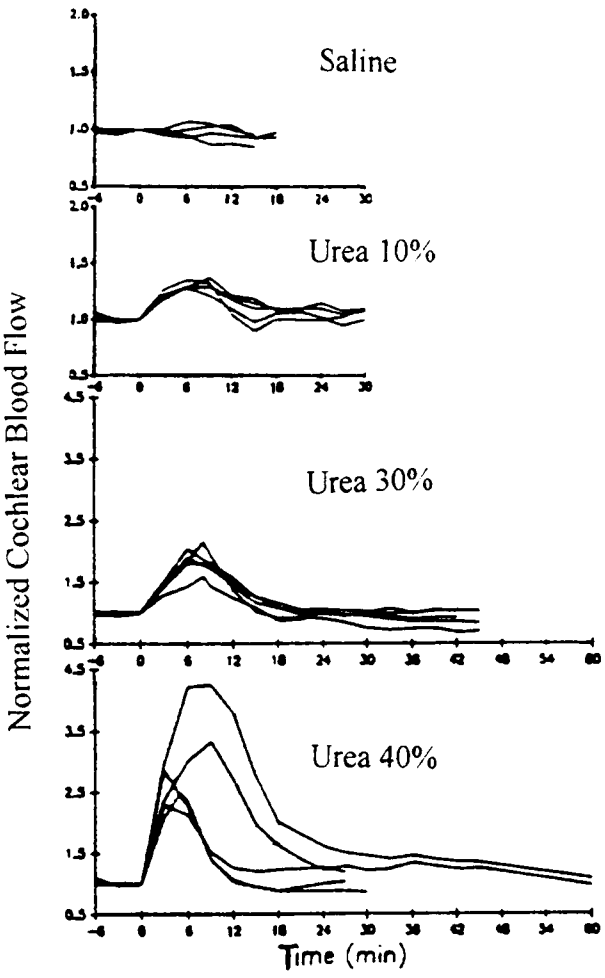


FIGURE 3. Changes in normalized cochlear blood flow following infusions of saline and urea at 10%, 30%, and 40% in five animals. Magnitude and duration of blood flow responses increase with concentration of solute administration. Time 0 indicates time of drug administration.

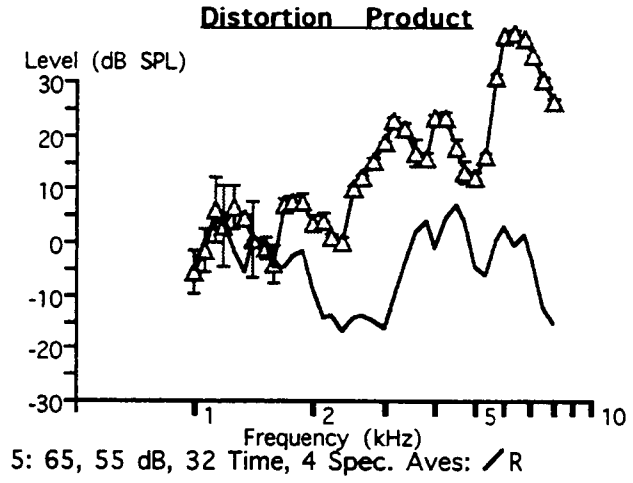
Source: Baldwin, D.L., Ohlsen, K.A., Miller, J.M., & Nuttal, A.L. (1992). Cochlear blood flow and microvascular resistance changes in response to hypertonic glycerol, urea, and mannitol infusions. *Archives of Otology, Rhinology, and Laryngology,* 011, 168-175.

enhances the movement of the hair cells, basilar membrane and tectorial membrane.

Data on ears with noise-induced hearing loss and Meniere's disease, indicate that if hearing loss is present at specific frequencies, OAEs are also not present at those frequencies (Harris, 1990; Probst, Lonsbury-Martin, & Martin, 1990). Since OAEs appear to depend on the function of specific hair cells related to the frequency of activation, then DPOAE responses could be used to measure changes in activity related to specific hair cells. In the present study, DPOAEs were measured at a large number of frequencies to determine if IV urea changed DPOAEs in a manner that might be attributed to specific hair cells or in the location of stimulation within the cochlea.

Distortion Product Audiogram

The procedure used to measure DPOAEs in the present study was the distortion product (DP) audiogram. An example of a DP audiogram for a normal-hearing cat is shown in Figure 4. The ordinate on the graph is the level of the 2F1-F2 DPOAE in dB SPL, and the abscissa is the geometric center frequency of the tone pairs used to elicit the DPOAE. The signals and response measurement procedures are described in the legend of Figure 4. The center frequencies of the signal pairs were at 1/12 octave intervals and were chosen to provide a detailed description of DPOAEs as a function of frequency. It was hypothesized that hypertonic IV urea would have an effect on place of stimulation within the cochlea, that would result in changes in pattern of the DPOAE response, either



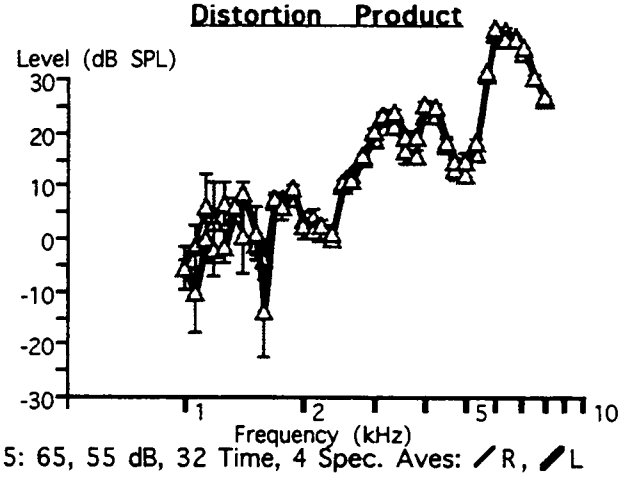


FIGURE 4. Example of distortion product audiograms using F1= 65 dBSPL and F2= 55dBSPL, 32 temporal averages and 4 spectral averages. Data were obtained at 1/12 octave intervals from 1000 - 8000 Hz. The top figure shows a single trial and the lower figure shows the superimposition of the two trials.

higher or lower in frequency. The close 1/12 octave intervals were selected to permit the detection of small frequency-related DPOAE effects. The frequency range from 1000 - 4000Hz was selected because robust DPOAEs can be recorded in this frequency range and maximum oral glycerol effects from Meniere's patients are also centered in this frequency range. The signal levels (F1=65 dB SPL; F2=55 dB SPL) were selected as the highest level signals to produce DPOAEs due to hair cells distortion rather than other forms of distortion.

Effects of IV Urea on DPOAE Response Patterns

Based on the effects measured in humans and animals, there is evidence to suggest that urea alters cochlear sensitivity, frequency selectivity, and place of stimulation within the cochlea. With DPOAE data, as shown in Figure 4, these phenomena may be manifested in the following ways:

1) changes in cochlear sensitivity: increase or decrease in DPOAE levels at some or all frequencies.
2) changes in frequency selectivity: if there were a broadening of the traveling wave, then the abrupt changes at different frequencies might be lessened, resulting in a smoother DP audiogram; sharpening of the tuning might create a more irregular DP audiogram.
3) changes in place of stimulation: changes in stiffness mass relations within the cochlea may alter the place of stimulation on the basilar membrane which may result in displacement of the

DP audiogram higher or lower in frequency with minimal changes in the DPOAE pattern.

Purpose of the Present Study

The purpose of this study was to determine the effects of IV hypertonic urea on cochlear function as measured by DPOAEs in cats. Specifically, three research questions were asked:

1) Does IV hypertonic urea alter the amplitude of activation within the cochlea?
2) Does IV hypertonic urea alter the frequency selectivity within the cochlea?
3) Does IV hypertonic urea alter the place of activation within the cochlea?

2. REVIEW OF LITERATURE

Gold and Pumphrey (1948) proposed that an unstable feedback system in the cochlea was responsible for enhancing movement of the basilar membrane and for increasing frequency selectivity in the cochlea. The first evidence of such a mechanism was shown by Kemp in 1978. He developed the signal averaging equipment to measure spontaneous and evoked acoustic responses from the cochlea in the external auditory canal. These responses have become to be known as otoacoustic emissions (OAEs).

Since Kemps' discovery in 1978, experimental studies of OAEs have been carried out and indicate that the emissions are produced as normal by-products of micromechanical actions within the cochlea. The structures that are believed to be involved in this generation of the OAE are the outer hair cells (OHC) which are driven by the silent current from the stria vascularis (Brownell, 1990). This action is called electromotility of the OHCs and the entire mechanism is called the cochlear amplifier (Lonsbury-Martin, Whitehead, & Martin, 1991).

Mechanisms for Otoacoustic Emissions

The cochlear amplifier or active source of mechanical energy amplifies the traveling wave and exists as a series along the basilar membrane (Lonsbury-Martin et al., 1991). The idea that the active mechanical enhancement is produced by movements by the OHC, is based on the findings from tuning curve data. When the OHCs are

healthy, the basilar membrane is sharply tuned and nonlinear; tuning curves are not present when OHC have been destroyed (Norton, 1992). Liberman and Dodds (1984) showed than inner hair cells (IHC) are involved only in the detection of the movement of the basilar membrane, and did not produce sharp tuning. From this information, it is believed that OHCs are the elements that make up the cochlear amplifier.

The OHCs are believed to be the generators of the OAEs and act as enhancers of IHCs (Brownell). The tallest row of OHCs are coupled apically to stereocilia, which make contact in the tectorial membrane, such contact is absent for the IHC. Because OHCs are in contact with the tectorial membrane, stimulation of the OHCs depends primarily on the displacement of the tectorial membrane which is directly proportional to the displacement of the basilar membrane (Dallos, Durrant, & Raynor, 1972). OHCs are excited by this mechanical coupling whereas IHC are displaced by subtectorial flow created by the tectorial membrane. This flow provides mechanical force to bend the IHC stereocilia. Movement or shearing displacement of the stereocilia initiates the activation and excitation of hair cells (Burch-Sims & Ochs, 1992).

Measurement of Otoacoustic Emissions

OAEs arise in the cochlea and are transmitted through the middle ear, and measured as acoustic responses in the ear canal. Middle ear transmission affects the OAEs in two ways. For evoked OAEs, stimulus level at the cochlea is reduced if the middle ear transmission is adversely affected by disease or damage. Also, when the OAE travels to the

external ear, its level is reduced if reverse transmission though the middle ear is poor. Kemp (1978) found that, in four subjects with immobile middle ears, OAEs were absent. In animal experiments OAE amplitude has been shown to be extremely susceptible to changes in middle ear status. Mass loading of the tympanic membrane in the cat reduced outward transmission of the DPOAE (Whitehead, Lonsbury-Martin, & Martin, 1992). For this reason, in the present study, tympanometry was performed to determine if middle ear mobility was grossly within normal limits and to ensure that there was no significant evidence of eustachian tube dysfunction.

In the reverse transduction process, OAEs can be recorded in response to acoustic stimulation and also when there is no acoustic stimulation. Spontaneous OAEs are OAEs that are continuously present in the absence of external stimulation (Lonsbury-Martin, Harris, Stagner, Hawkins & Martin, 1990). Bonfils (1989), found in humans, spontaneous OAEs to be absent in frequency regions for which hearing thresholds exceed about 20 dB HL. In humans, they are most commonly detected in the 1- to 2-kHz region, where reverse transmission through the middle ear is most efficient (Kemp, 1978). Lonsbury-Martin et al. (1991) found about 50% of normally hearing subjects generate spontaneous OAEs. Evoked OAEs are the by-products of stimulating the cochlea with acoustical stimuli. One type of evoked OAE is the distortion product OAE (DPOAE). DPOAEs arise from the intermodulation of two pure tones, referred to as F1 and F2. The amplitude of the DPOAE is greatest when the level of F1 is greater that the level of F2 by 5 to 15 dB. The most

prominent distortion product occurs at the cubic difference frequency-2F1-F2 (Lonsbury-Martin et al., 1991). DPOAE level depends on the frequency separation of the pure tones; the highest levels occur with F2/F1=1.22 (Whitehead et al., 1992). In humans, DPOAEs can be recorded in well over 90% of normal ears (Kemp, 1979; Lonsbury-Martin et al., 1990; Harris, 1990). In the present study, when DPOAEs are referred to, it will be taken unless otherwise stated to refer to the DPOAE of 2F1-F2.

OAEs have been measured for clinical and experimental purposes. One clinical DPOAE procedure is to present signals of constant amplification at different frequencies. In this procedure, the level of the DPOAE is plotted as a function of signal frequency for several or many frequencies. This procedure has been called a "DP audiogram" (Lonsbury-Martin, McCoy, Whitehead, & Martin, 1992). A second clinical procedure is the measurement of the growth of DPOAE responses for signals that are fixed in frequency and systematically increased in level. The responses of DPOAE levels are called input-output (I/O) functions (Lonsbury-Martin, McCoy, Whitehead, & Martin, 1993). Using I/O functions, procedures have been developed to measure minimum detection levels or the OAE "thresholds".

Experimental procedures have been explored in which a third tone has been used as a suppression to measure the cochlear tuning (Brown & Kemp, 1984). Similar experiments have been done in which tuning has been measured by separating the pure tones activating signals (Rogers, 1994; Whicker, 1995).

One of the benefits provided by the discovery of cochlear-based acoustic signals in the ear canal has been the opportunity to evaluate the similarity of human and animal subjects with respect to the same phenomenon (Zurek, Clark, & Kim, 1983). Otoacoustic emissions can be measured using identical procedures and equipment in humans and animals with the exception of anesthetizing the animal. Studies with and without anesthetics have been shown to have identical results (Wilson & Evans 1983). In small animals, such as cats and rabbits, DPOAEs are considerably larger than in humans, whereas monkeys have responses that are identical to those of humans (Whitehead et al.). DPOAEs exceeding 20 dB SPL are routinely measured from the small animals (Zurek et al. 1983).

Conditions That Affect Otoacoustic Emissions

Support for the cochlear origin of OAEs was obtained in studies showing that agents known to damage the cochlea and reduce or eliminate OAEs (Lonsbury-Martin et al., 1993). Some of the agents that cause the reduction of OAEs are hypoxia/anoxia, over exposure to noise, an ear with Meniere's disease, and drugs.

Anoxia/Hypoxia. Temporary hypoxia causes rapid, reversible reduction of spontaneous OAEs and lethal anoxia rapidly abolishes spontaneous OAEs in small mammals (Whitehead et al.). Evans, Wilson & Borerwe (1981), found that after two minutes of inducing hypoxia, the spontaneous OAE in the cat and guinea pig rapidly ceased and after two minutes of restoration of oxygen, the spontaneous OAE recommenced.

Anoxia/Hypoxia. Temporary hypoxia causes rapid, reversible reduction of spontaneous OAEs and lethal anoxia rapidly abolishes spontaneous OAEs in small mammals (Whitehead et al.). Evans, Wilson & Borerwe (1981), found that after two minutes of inducing hypoxia, the spontaneous OAE in the cat and guinea pig rapidly ceased and after two minutes of restoration of oxygen, the spontaneous OAE recommenced. Other experiments in a variety of laboratory animals have also shown the dependence of DPOAE levels on oxygen (Kim, Neeley, Molinar, & Matthews 1980; Kemp & Brown, 1984).

Permanent noise induced hearing loss. The effects of noise on OAEs have been demonstrated in studies in which permanent threshold shifts have occured. Kemp (1979) studied humans with sensorineural hearing loss and found that OAEs became unmeasurable when hearing loss exceeded 30 dB. The OAE has been shown to be frequency dependent in that the emission will be absent only in the frequency range of the hearing loss (Probst, Lonsbury-Martin, & Martin, 1990; Whitehead et al.). Experiments on chinchillas and rabbits have shown permanent reductions of DPOAEs resulting from chronic-noise overexposure (Zurek et al.; Stainback, Lonsbury-Martin, Stagner, & Coats, 1987).

Temporary noise induced hearing loss. Experiments have shown that noise or exposure to sound in humans which have induced a temporary threshold shift have also reduced levels of OAEs (Whitehead et al.). Temporary reductions of OAEs by noise overexposure have been reported in gerbils, cats and rabbits (Lonsbury-Martin et al., 1993,; Kim, 1980; Schmeidt, 1986; Weiderhold, Mahoney, & Kellogg, 1986). Results

et al., 1992). However, in some patients, DPOAE amplitudes were normal even when thresholds were increased. Interpretation of these findings suggested that, only in some cases of Meniere's disease, that is, those demonstrating reduced OAEs, is the motile action of OHC compromised (Whitehead et al.). Experimental endolymphatic hydrops have been surgically induced in guinea pigs and rabbits to use as a model for Meniere's disease. It was found that DPOAEs were reduced when stimulus tones fell into regions of elevated thresholds. Horner and Cazals (1989) showed that in hydrops-induced hearing losses, DPOAEs are reduced because of OHC dysfunction.

Drugs That Affect Otoacoustic Emissions

Aspirin. Aspirin has been shown to affect OAEs in animals and humans. This drug can produce prominent but reversible effects (Lonsbury-Martin et al., 1993). Doses of aspirin sufficient to change hearing have been shown to block the OAE (Long & Tubis, 1988; McFadden & Plattmeir, 1984). The fact that aspirin blocks both OHC electromotility and OAEs is one of the strongest arguments for the role of healthy OHC in the generation of OAEs (Brownell).

Loop diuretics. Acute doses of the loop diuretics furosemide and ethacryanic acid, which are used in the treatment of kidney failure, produce temporary hearing loss. Loop diuretics are thought to work by effecting the stria vascularis (Norton, 1992). They produce a rapid, reversible reduction of the endolymphatic potential, the effective energy supply for the organ of Corti, and corresponding decreases in the sound-

evoked responses in the cochlea. (Whitehead et al.). Kemp (1979) found that furosemide in monkeys caused a substantial reduction in the OAE after two minutes. Wilson & Evans (1983) found that in the cat, furosemide abolished the OAE after one minute.

Osmotic agents. Mannitol, glycerol, and urea are used for the purpose of reducing intracranial pressure (Takeda et al., 1981). They have not been used for the purpose of studying DPOAEs . In the present study, use of these drugs was considered as a means of altering intracochlear pressure in normal-hearing cats. The following review deals with data on IV use of these drugs in animals.

Mannitol, glycerol, and urea have been used to alter cochlear blood flow in the guinea pig and rabbit (Baldwin et al.). All three produce increases in blood flow, however serum osmolarity is increased more with glycerol than mannitol and urea. Of the three drugs, only glycerol and urea have significant changes in hearing sensitivity (Baldwin et al.). These investigators, though, believe that changes in blood flow cannot account for the auditory effects.

All three of these drugs have been shown to create morphological changes in the stria vascularis (Baldwin et al.; Duvall et al., 1981; Wright et al., 1988). They found that these drugs produce edema of the stria vascularis that is rapid in onset and reversible. The change is believed to be indicative of metabolic stress, and not of toxicity (Wright et al.).

Basilar and labyrinthine arteries have also been studied using these drugs (Takeda et al., 1981). It was found that the tension of the vascular smooth muscles without spontaneous contractions could be suppressed by

these substances. All three substances had similar time course effects, but the relaxation process was temporary with urea and glycerol, but stable when mannitol was used.

Johnstone, Patuzzi, & Yates (1982) and Angelborg et al. (1982) have studied the penetration of these drugs into the perilymph. They found that there is greater penetration with glycerol and urea than with mannitol. Mannitol has been shown to have a restricted ability to penetrate into the perilymph. As a result of this rapid penetration, glycerol and urea create an osmotic effect that results in the collapse of Reissner's membrane.

The effects of osmotic agents can not be measured in the cochlea directly. However, the effects can be measured as a change in intraocular pressure (IOP). Intraocular pressure is maintained by an equilibrium that occurs as the result of the balance between aqueous humor and inflow (Green, 1990). Small variations in either the rate of production or in the rate of outflow from the eye can result in large changes in IOP (Hart, 1992).

IOP can be measured by flattening the cornea with pressure, which is called applanation. The instrument used to apply the force and measure the pressure is called an applanation tonometer. In the cat, the normal IOP range is 15-30 mm Hg (Wilkie & Latimer, 1991). IOP depends on long-term factors (age, blood pressure, and season), and short-term factors (body posture, exercise, eye movement, and drug effects) (Hart, 1992).

In the present study, IV urea was used to induce osmotic changes within the cochlea. As was stated in the introduction, urea was chosen

because present protocols for use of IV urea in the cats exists at our laboratory, it is more effective in producing improvements in thresholds of audibility, it produces an immediate collapse of Reissner's membrane, and the similarities of urea to glycerin.

3. METHOD

Subjects

Seven healthy adult cats were used. None of the subjects had evidence of auditory dysfunction in the test ear as determined in the subject qualification procedures described below.

Sedation

None of the procedures would have been painful in conscious subjects, but to eliminate movement artifacts, cats were sedated. Each cat was given an intramuscular injection of ketamine (2.5 mg/lb.) and xylazine (0.3 mg/lb.). This protocol was intended to induce sedation times lasting 60 - 90 minutes. A supplementary dose of ketamine was given to all subjects part way through the procedure to ensure a proper state of relaxation.

Subject Qualification Procedures

After sedation, the following procedures were used to measure auditory function. The results of these procedures can be found in Appendix B.

1) Otoscopy. Otoscopy was performed to ensure that the ear canals were free from excessive cerumen. Those with excessive cerumen were cleaned.

2) Tympanometry. Tympanograms were obtained from both ears using an acoustic admittance measuring system (Amplaid Model 702)

with a 220-Hz probe signal. An ear was qualified as a test ear only if the admittance maximum was within 100 daPa of room pressure and the admittance of the middle ear was between 0.2 and 1.0 mmhos.

3) Auditory brainstem responses (ABRs). ABRs were obtained from both ears using an evoked potential recording system (Nicolet Compact Four). The signals were 90 dB nHL and 40 dB nHL alternating polarity clicks. A montage of three subcutaneous electrodes were used; the active (+) electrode was placed at the vertex and the reference (-) and ground electrodes were placed just rostral to the base of the pinnas. ABR waveforms were based on 512 responses. For the 90 dB nHL signals, wave V latencies for all test ears ranged from 4.00 - 4.08 ms, which was within laboratory norms; waveform morphology was good. For the 40 dB nHL signals, wave V responses were present in all test ears.

4) Intraocular pressure (IOP) measurement. IOP measurements were obtained from the cornea of one eye from each of the subjects prior to testing using an applanation tonometer (Tono-Pen XL). Baseline IOP measurements were established by making two consecutive measurements and computing an average IOP. The IOP measurements from the seven subjects ranged from 18.5 - 33 mm Hg.

5) Qualifying DPOAEs. DP audiograms were measured in one ear to determine if there were strong DPOAE responses at a sufficient number of frequencies to justify use of the ear for experimental purposes. In all cases, the first ear was an acceptable test ear.

DP audiograms were obtained using an OAE test instrument (Virtual, Model 330). This system included probe assembly and probe tips

designed for use with human beings. The system was suitable for use with cats without modification. The signals were tone pairs, F1 and F2; the signal pair was labeled using the geometric center frequency between F1 and F2. In each DP audiogram, frequencies from 1000 - 4000 Hz in one-octave intervals were evaluated. The frequency ratio of the tones in each pair was held constant at F2/F1=1.21.

For DPOAE measurements, the cats were placed in a sound-treated chamber designed especially for animals (Industrial Acoustics). Background noise levels within the chamber were below the maximum permissible ambient noise levels for ears covered in audiometric test rooms in accordance with ANSI S3.1 (1991) (Measurements in Appendix A).

The DPOAE response for each tone pair was the average level for 2F1-F2 DPOAE obtained from four response frequency spectra. Each response frequency spectrum was based on the average of 32 time waveforms. For the seven test ears, the DPOAE responses were at least 3 dB above the noise floor as measured by the DPOAE system.

Experimental Procedures

The purpose of the experiment was to measure changes in DPOAEs due to IV hypertonic urea. The effects of urea were monitored using IOP as an indirect measure of changes occurring in the distrubution of body water.

Signals and responses. DPOAE measurements were made using the same apparatus as was used in the DPOAE qualification procedures.

The experimental signals were the same as used in subject qualification except that there were 36 tone pairs at geometric center frequencies from 1-8 kHz in 1/12 octave intervals.

The response measures were different than from the qualification procedures. Responses were derived from a single frequency spectrum based on the average of 64 time waveforms. This enabled the noise floor to be reduced by 18 dB.

At each frequency, a determination was made as to whether the measurement was a DPOAE response or whether it was deemed to be indistinguishable from noise. The procedure for determining whether the DPOAE was sufficient was made by considering noise measured in frequency bands near 2F1-F2. With the DPOAE measurement system, noise was measured in 10 Hz wide bands. The noise in the 10 Hz wide bands above and below the 2F1-F2 were disregarded. The levels of the noise bands were examined at 20 and 30 Hz above and below the frequency of 2F1-F2. The response measured at 2F1-F2 was considered to be a valid response if it was at least 3 dB greater than the noise measured in each of the four bands. If the DPOAE met the criterion, it was considered to be a valid response and its level was specified in dB SPL. If the response level did not meet the criterion, the response was considered to be noise and was represented as a missing data point. The results of this analysis are shown as the raw date for each subject in Appendix B.

Experimental protocol. There were seven experimental trials. Each trial was begun with an IOP measurement, taking approximately one minute, and followed by presentation of experimental signals taking

approximately 5 1/2 minutes. For completion of the procedures and data collection, each trial began at eight minute intervals. The sequence of trials is shown in Figure 5.

The IOP measurement in Trial 1 was the average of the two measurements made during the qualification procedures and was considered to be the baseline IOP. The first three trials were the pre-urea trial conditions. After Trial 3 was completed, the IV drip was begun and continued through the end of Trial 7. Urea (30% urea in 10% invert sugar) was infused through an IV catheter. The urea was delivered at a rate of 2-7 mL/kg over approximately 30 minutes.

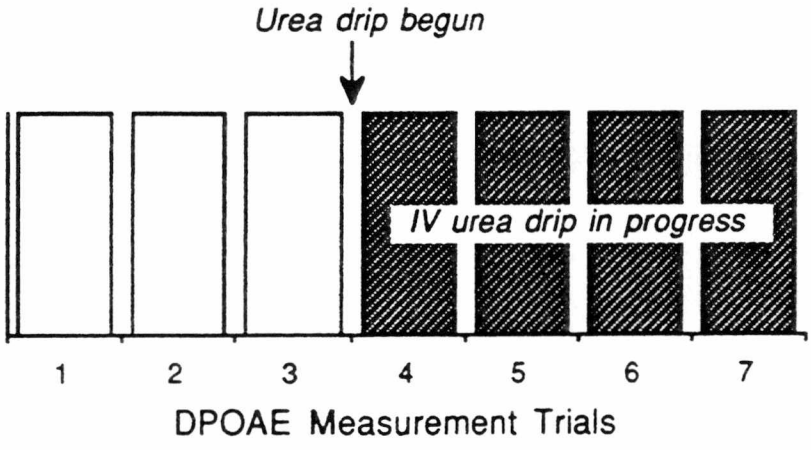


FIGURE 5. Representation of DPOAE measurement trials; each block represents one of seven DPOAE trials. Each trial was approximately eight minutes in duration. Each tic mark on the abscissa represents an IOP measurement.

4. RESULTS

Overview of Data Analysis

DPOAE measurements were made for 36 frequencies for seven trials and for seven subjects. In the analyses, the 36 frequencies were reduced to three one-octave bands and trials were reduced to pre- and post-urea conditions. However, it was useful to represent the data in forms not used in the final analyses. Figure 6 is a representation of the data that best describes the overall effects. In this figure, median DPOAEs for seven subjects are shown for pre- and post- infusions. The ordinate is DPOAE level; and the abscissa is signal frequency. Each plotted datum was computed in the following manner: at each frequency, a median DPOAE level was computed for each subject for three pre- or post- trials and then at each frequency, a median DPOAE was obtained for the seven subjects. Thus, each plotted datum is a median of medians for a pre- or post-urea conditions at that frequency. There are some frequencies for which no DPOAE responses are shown. For those frequencies, the median response did not satisfy the criteria to be classified as a DPOAE response.

As seen in Figure 6, from 1.06 - 7.13 kHz, DPOAE levels increase systematically from approximately -10 dB SPL to approximately 35 dB SPL (excepting frequencies from 4.49 - 5.66 kHz); at higher frequencies (7.56 kHz to 8.01 kHz), DPOAE levels are slightly reduced. In the frequency region from 4.49 - 5.66 kHz, DPOAE levels are reduced substantially (10 - 20 dB). These reduced DPOAE levels are most likely

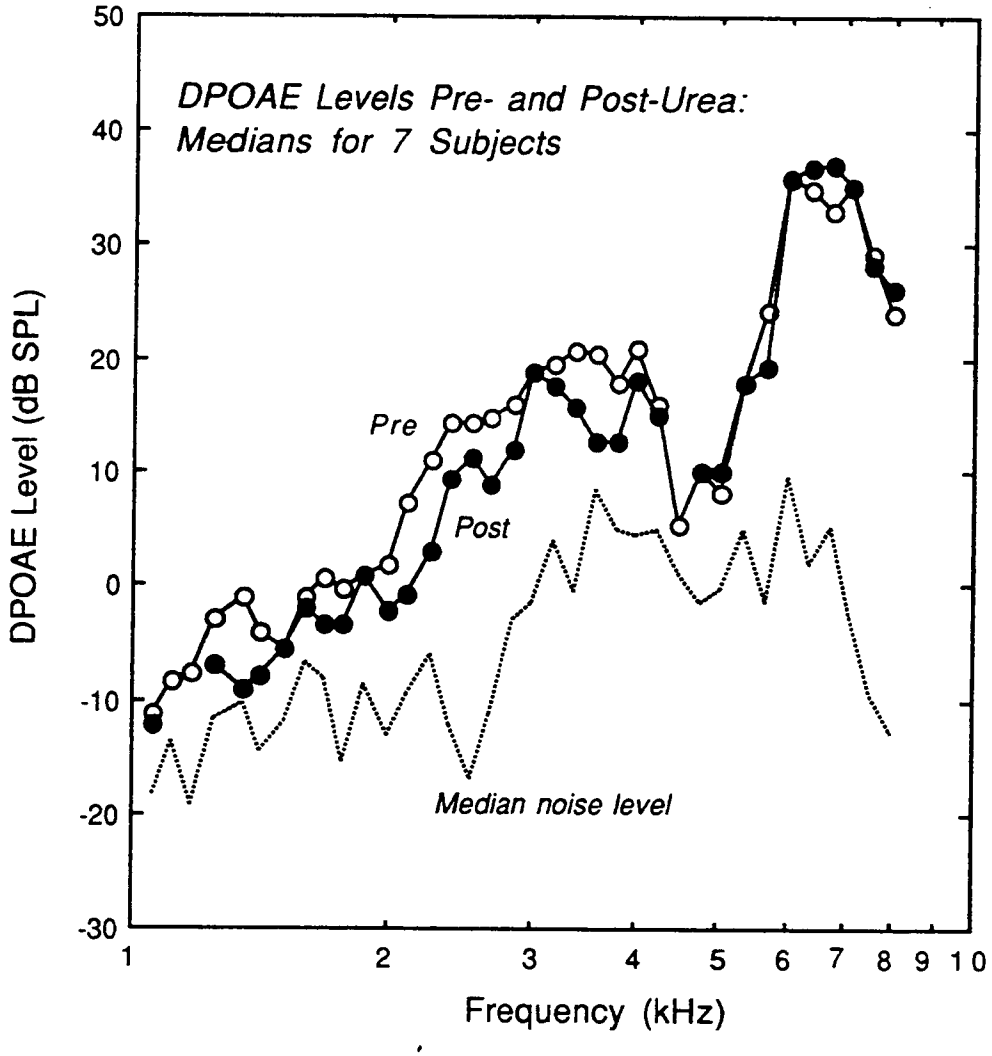


FIGURE 6. Pre- and post-urea DPOAE levels are presented as a function of frequency for all seven subjects. The open circles represent pre-urea conditions and the filled circles represents post-urea conditions. Each plotted datum is a median of medians across trials and subjects. The median noise level was computed across subjects in Trial 2.

artifacts caused by standing waves generated in the measurement process.

In addition to the DPOAE data in Figure 6, a median noise floor is shown based on noise measurements obtained from all subjects in Trial 2. It can be seen that noise levels range from approximately -10 dB SPL in the octave-frequency range from 1-2 kHz to approximately 5 dB SPL in the octave-frequency range above 3 kHz.

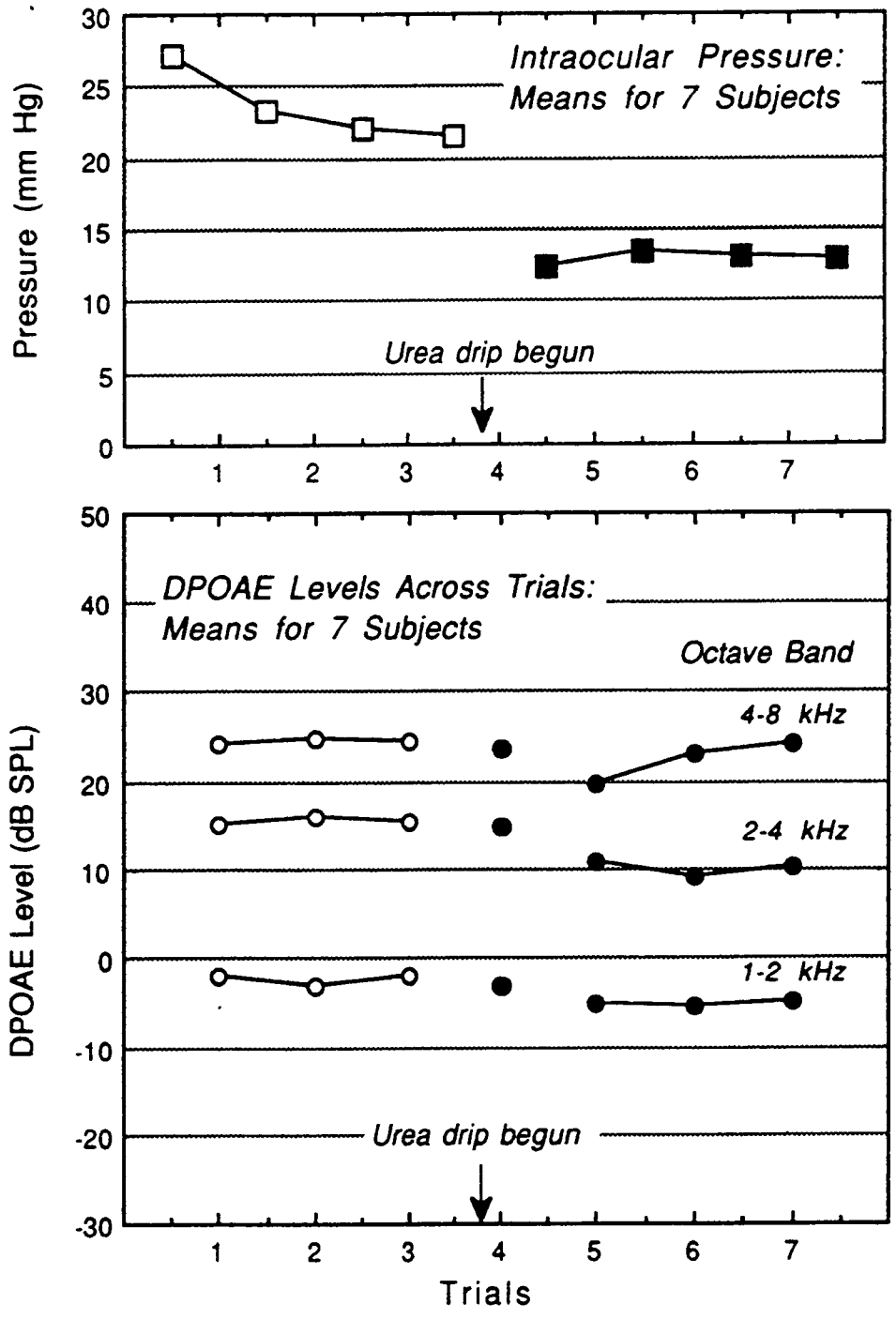
The important result illustrated in Figure 6 is the comparison of pre- and post- urea DPOAE levels. In general, median post-urea DPOAE levels were reduced slightly in the octave bands of 1-2 kHz and 2-4 kHz. In the 4-8 kHz octave band, mean DPOAE levels were not altered systematically by urea infusion.

Effects of Urea on Intraocular Pressure

IOP measurements were used to determine if IV hypertonic urea produced systemic dehydration effects. The mean IOP measurements made before and after each trial are shown in the top part of Figure 7. The ordinate is the mean IOP and the abscissa represents trials. The four pre-urea IOPs (open squares) were all substantially greater than the four post-urea IOPs (filled squares). Pre-urea mean IOP was 23.5 mm Hg, and the post-urea mean IOP was 12.9 mm Hg, which is a mean reduction of 45%. (Range = 40-53%).

A repeated measures analysis of variance was performed using the split-plot approach: the four IOP measurements made before the infusion

FIGURE 7. Intraocular pressure and DPOAE levels over experimental trials. The top part of the figure shows mean IOP measurements plotted as a function of trial. The open squares represent the pre-urea condition and the filled squares represent the post-urea condition. The bottom figure shows mean pre- and post-urea DPOAE levels as a function of trials for the three octave frequency bands. The open circles represent the pre-urea condition and the filled circles represent the post-urea condition. The isolated filled circles represent the transitional trial in which IV urea infusion was begun.


Intraocular Pressure:
Means for 7 Subjects
Pressure (mm Hg)
30
25
20
15
10
5
0
Urea drip begun
1
2
3
4
5
6
7
DPOAE Levels Across Trials:
Means for 7 Subjects
Octave Band
4-8 kHz
2-4 kHz
1-2 kHz
DPOAE Level (dB SPL)
50
40
30
20
10
0
-10
-20
-30
Urea drip begun
Trials

of urea were compared in a pair-wise manner with the four IOP measurements made after the infusion of urea. Use of the split-plot approach was used because the data were found to be normally distributed using a Q-Q plot. The results of this analysis which are shown in Table 1, indicate that IOP depends on the infusion of urea (Pre/Post), and that there is a significant interaction between urea infusion effects and trials effects. The interaction may be due to sedation. In the top part of Figure 7, the first IOP measurement (the baseline measurement) was obtained at approximately 20 minutes following administration of the sedative. The mean baseline IOP was 27.1 mm Hg. Approximately ten minutes later (after Trial 1) the mean IOP decreased by 3.8 mm Hg to 23.3 mm Hg. The next two IOP measurements also decreases systematically but at a much slower rate, suggesting that the effects of the sedative on IOP became small after Trial 1. However, the difference between the baseline IOP and the mean of the IOPs obtained after Trials 1,2, and 3 was significant ($t(6)=.001$).

In summary, early in the pre-urea measurement trials, IOP decreased significantly, probably due to sedation effects, and then stabilized. Following infusion of urea, IOP decreased substantially and remained stable for the duration of the experiment.

DPOAE Data Grouped into Octave Bands

For purposes of statistical analyses, the data obtained at 36 frequencies were grouped into three one-octave bands: the 1-2 kHz band contained 12 frequencies from 1.06 - 2.00 kHz; the 2-4 kHz band

Table 1. Repeated measures analysis of variance for IOP measurements.

Source	F	df	df error	ms	p
Pre/Post	163.240	1	6	1596.446	.000
Trial	20.409	3	18	23.345	.000
Pre/Post x Trial	1.304	3	18	22.411	.001

contained 12 frequencies from 2.12 - 4.00 kHz; and the 4-8 kHz band contained 12 frequencies from 4.24 - 8.01 kHz. A median DPOAE level was computed for each band and for each subject for use in the analyses.

Dependence Of DPOAE Levels On Trials

The dependence of DPOAE level on trials was examined for the three one-octave frequency bands. This analysis was performed using the means for each subject and for each octave band computed as described in the preceding section. The mean DPOAE levels for each trial are shown in the bottom half of Figure 7. The ordinate represents DPOAE level and the abscissa represents trials. Each datum is a mean of medians for seven subjects. The open circles designate the three trials used as pre-urea conditions. The filled circles represent the post-urea conditions. The data from Trial 4 is isolated because the urea drip was begun at the beginning of this trial and DPOAE effects may have varied throughout the trial.

In the pre-urea trials (Trials 1, 2, and 3), urea effects were virtually invariant for all three octave-frequency bands across the three trials. In the post-urea trials (Trials 5, 6, and 7), where urea effects were maximum and constant, the DPOAE effects appeared to be different for the three one octave bands. In the 1-2 kHz and the 2-4 kHz bands, the mean DPOAE levels were reduced and did not change over the trials. In the 4-8 kHz band, the mean DPOAE level was reduced and then recovered to pre-urea levels by Trial 7.

The dependence of DPOAE level on trials and octaves was examined using a repeated measures analysis of variance. This analysis was conducted using data from the three pre-urea trials (Trials 1, 2, and 3), and from the three post-urea trials (Trials 5, 6, and 7). Data from the transitional trial (Trial 4) were omitted from this analysis. Since assumptions of sphericity could not be met, the Huynh-Feldt correction was applied. The results of this analysis (Table 2) indicate that DPOAE levels depend on octave-frequency bands, but not on trials. Also, there was no interaction between trials and octave frequency bands. The implication of these results is that hypertonic urea did not effect DPOAE levels.

DPOAE Pre/Post Urea Difference Scores

However, the DPOAE data were reanalyzed using a more sensitive measure of effects due to urea. For each subject, a median pre-urea and post-urea DPOAE level was computed for each octave band. Then, for each subject, the median pre-urea DPOAE level was subtracted from the median post-urea DPOAE level, to obtain a DPOAE difference score for each octave band. The data obtained in this manner are shown in Figure 8; change in DPOAE level is plotted on the ordinate and octave-frequency band are shown on the abscissa. The results are shown for each of the seven subjects. For five of the seven subjects, infusion of IV urea resulted in only small changes in DPOAE level across all three octave-frequency bands. The results for the other two subjects (Subject 1 and Subject 3) are discussed after the statistical analysis for all subjects.

Table 2. Repeated measures analysis of variance for DPOAE levels over Trials. The Huynh-Feldt correction was used.

Source	F	df	df error	ms	p
Octave	96.561	1.356	8.137	121.851	.000
Trials	2.806	1.290	7.743	81.204	.130
Octave/Time	1.304	3.473	20.838	16.539	.301

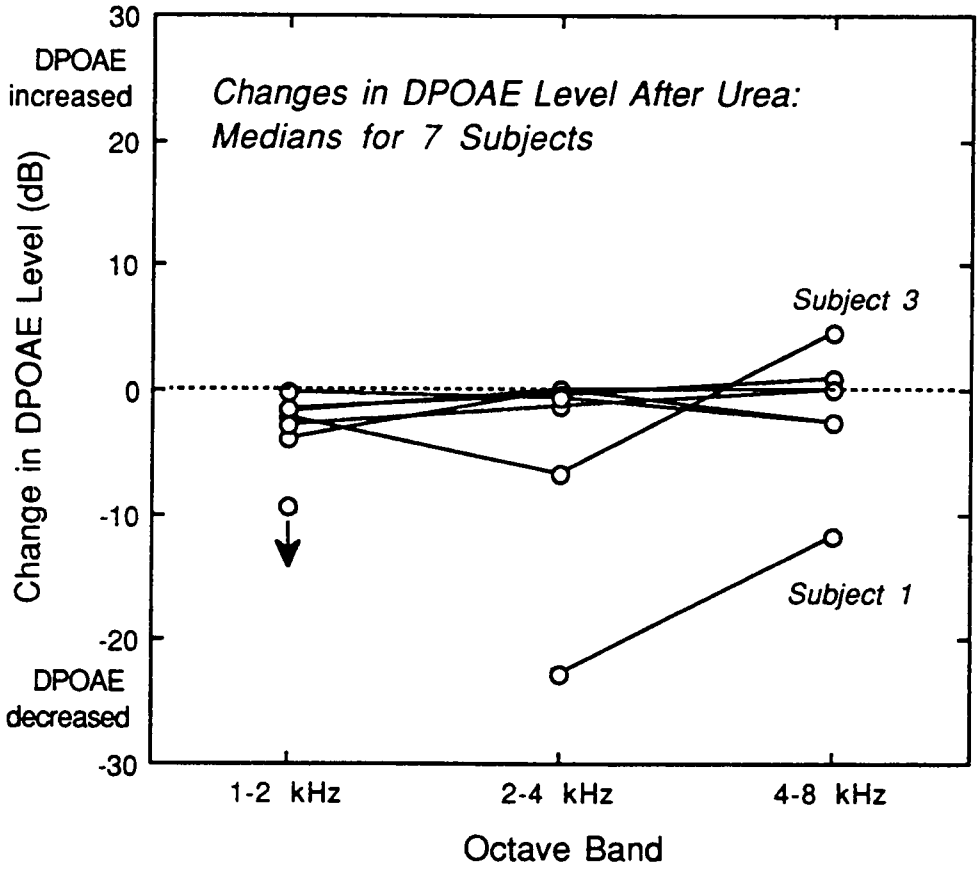


Figure 8. DPOAE difference scores between the pre- and post- urea conditions for the three octave frequency bands for the seven subjects.

The effects of IV urea for the seven subjects and for each octave band were evaluated using t-tests (Table 3). For the 1-2 kHz band, urea decreased the DPOAE by an average of 3.1 dB. This decrease was small but significant. In this octave band median DPOAE levels decreased in 80% of the frequency conditions. In the 2-4 kHz band, the mean decrease was 4.6 dB, but was not significant because of the large variability. In this octave band, the median DPOAE level decreased in 68% of the frequency conditions. In the 4-8 kHz band, urea reduced the DPOAE level by an average of 1.7 dB which was not significant, and the median DPOAE level was reduced in 42% of the frequency conditions. These findings indicate that DPOAE levels are typically reduced a small amount by the infusion of IV urea in the low and middle frequencies.

There were two subjects that were atypical. Figure 9 shows the pre- and post- urea results, for individual frequencies, in Subject 1. At many frequencies, the effects of the urea were so great that DPOAEs were eliminated. It is possible that reductions in DPOAE levels obtained for Subject 1 were due to substantial dehydration effects caused by urea. Subject 1 had the largest reduction (53%) in IOP of any of the seven subjects. However, Subject 6 had the next largest decrease (50%) in mean IOP, and only showed slight reductions in DPOAE levels in the 1-2 kHz band and no changes in the 2-4 and 4-8 kHz band. This suggests that the DPOAE changes seen for Subject 1 maybe due to individual hypersensitivity in sensitivity to urea.

For Subject 3, pre-and post-urea DPOAE levels are shown as a function of frequency Figure 10. For most of the frequencies, DPOAE

Table 3. Analysis of DPOAE difference scores for pre- and post- urea conditions. Mean DPOAE difference scores and standard deviations are also reported.

Source	df	t	p	Mean difference scores	Mean standard deviations
1-2 kHz band	6	-3.064	.022	-3.1	2.7
2-4 kHz band	6	-1.433	.202	-4.6	8.4
4-8 kHz band	6	- .895	.405	-1.7	5.1

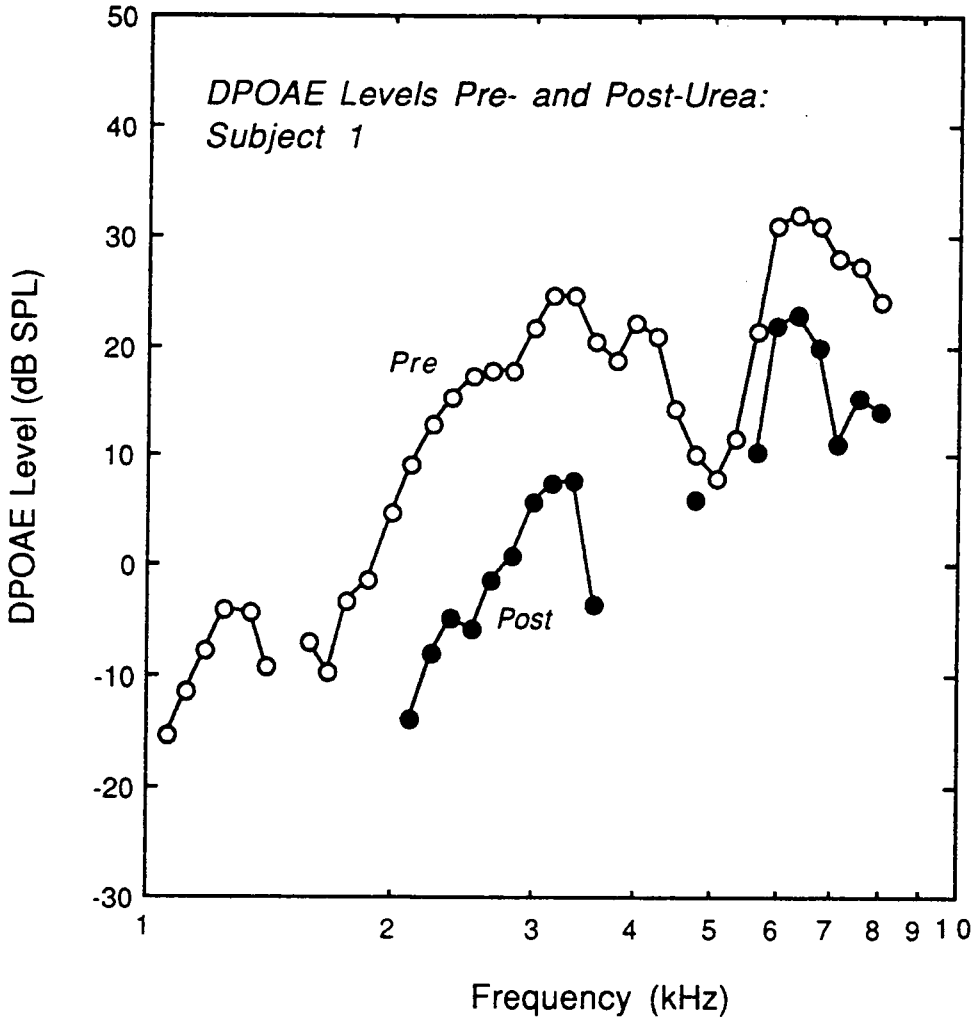


Figure 9. Pre-and post-urea DPOAE levels are presented as a function of frequency for Subject 1. Data are presented in the same format as in Figure 6.

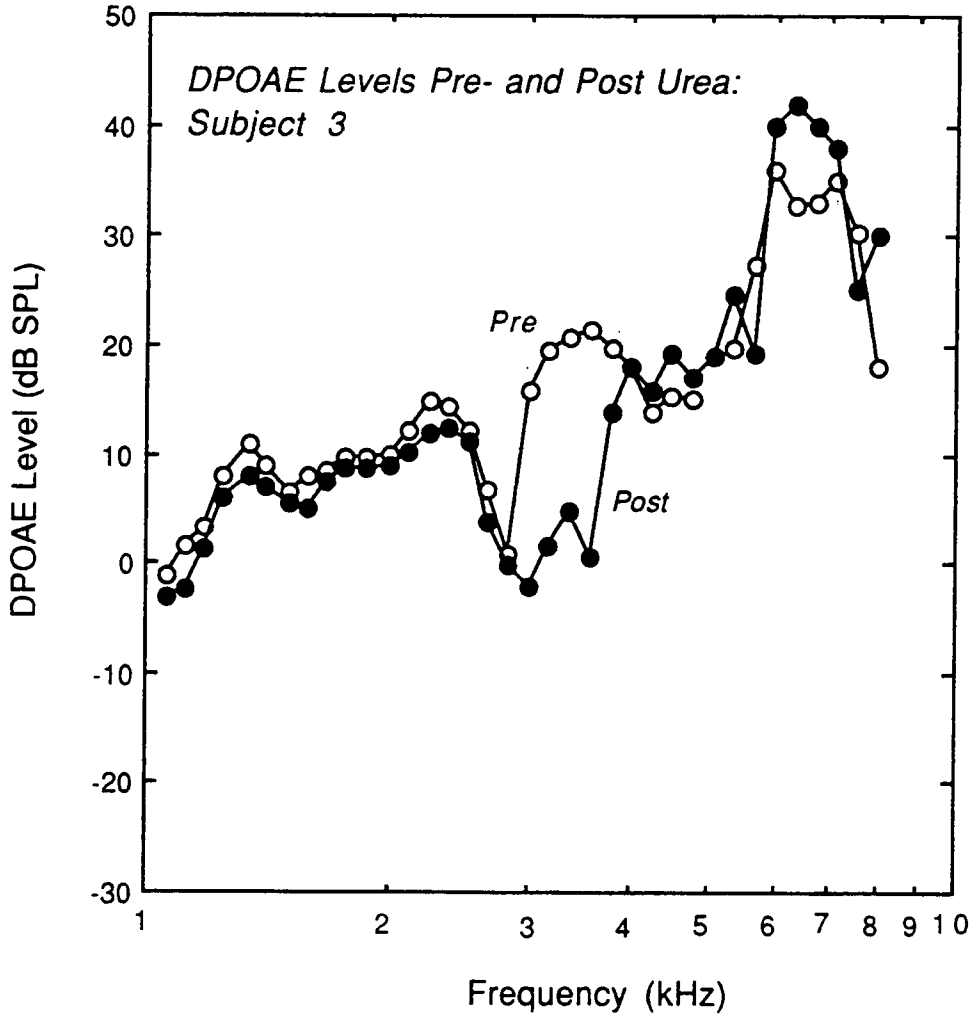


Figure 10. Pre-and post-urea DPOAE levels are presented as a function of frequency for Subject 3. Data are presented in the same format as in Figure 6.

levels were very similar or slightly reduced after infusion of urea. However, from 3.00 -3.78 Hz, the DPOAE level dropped by an average of 20 dB, while in the frequency region from 5.99 - 7.13 Hz, it increased by an average of 10 dB. For Subject 3, the mean IOP reduction of 40% was less that the average reduction of 45% for the group.

5. DISCUSSION

With endolymphatic hydrops, such as occurs in Meniere's disease, the scala media is inflated due to an excess of endolymph. The greatest effects are marked by reduction in low frequency sensitivity. These changes are most likely due to increases in the stiffness reactance of the basilar membrane. When ears with Meniere's disease are dehydrated with hyperosmotic agents such as glycerol, there is a temporary improvement in low frequency sensitivity, this is likely due to decreases in stiffness reactance of the basilar membrane or possibly the entire scala media.

When hyperosmotic agents have been used with normal ears, a variety of effects related to dehydration of the cochlea have been measured. These effects are listed in Table 4. They include anatomic and physiologic effects measured in laboratory experiments, as well as behavioral effects measured as changes in hearing. In the present study, hyperosmotic urea was used in doses that were equal to or greater than the doses used to obtain the effects shown in Table 4. Indirect evidence of cochlear dehydration was obtained from substantial changes measured in IOP following infusion of urea. As a result, it is believed that the DPOAE effects measured in the present study were obtained when the scala media was dehydrated, when the stria vascularis was swollen, and when arterial flow in the cochlea was increased.

Table 4. Physiological and anatomical effects of osmotic agents.

Osmotic Agent	Effect
Oral glycerol (Slattery et al., 1986)	A small but significant decrease in thresholds of audibility at 500 Hz in normal hearing individuals
IV urea, mannitol, glycerol (Takeda et al., 1981)	Reduced intracranial pressure and increased cochlear microcirculation
IV urea, mannitol, glycerol (Baldwin et al., 1992)	Moderately increased cochlear blood flow
IV urea, mannitol, glycerol (Duvall et al., 1981)	Morphological changes and edema in the stria vascularis
IV urea, glycerol (Angelborg et al., 1982)	Immediate collapse of Reissners membrane
IV urea, glycerol (Takeda et al., 1981)	Arterial relaxation

Typical DPOAE Effects

At the outset of the experiment, it was hypothesized that IV urea would affect the place of stimulation within the cochlea, the frequency selectivity of the cochlea, and/or the sensitivity of the cochlea. The major finding of the present study is that, for five of the seven subjects, substantial dehydration produced small reductions in DPOAE levels.

Place of Stimulation. Using the data shown in Figure 6, attempts were made to determine if the pattern of DPOAE changes was better characterized as a reduction in level or as a shift in frequency. If the pattern appeared to shift in frequency, it would provide some evidence that dehydration caused a change in place of stimulation within the cochlea. Shifting the data in frequency did not improve the correlation between pre- and post- infusion results as would be expected if this hypothesis had been correct.

Frequency Selectivity. If frequency selectivity had been a significant factor, it was expected that the pattern of the post-urea responses would have become noticeably more jagged or smoothed. From visual inspection of data for individual subjects, and for the group (Figure 6), it is difficult to conclude that the pattern of the DPOAE was altered in this manner. Thus, it was not possible to conclude that frequency selectivity had been affected by the dehydration.

Sensitivity. For all seven subjects, there was a systematic reduction in DPOAE response levels in the 1-2 kHz octave band (Figure 8). These findings suggest that with this method of dehydration there is a loss of

sensitivity that is confined to the low frequency regions. Though the reasons for these effects are not known, two hypotheses are proposed. The first hypothesis is that water is pulled into the stria vascularis and it becomes engorged. This engorgement causes the basilar membrane to stiffen which results in an increase of the stiffness reactance of the basilar membrane and reduces the sensitivity progressively--minimally at the base and maximally at the apex of the cochlea. A second hypothesis is that the dehydration of the scala media creates negative pressure within the cochlea that stiffens the scala media, which in turn increases the stiffness reactance in the apical portion of the cochlea. Both of these phenomenon may account for the reduction in DPOAE response levels seen in the low frequencies for the present study and for the behavioral threshold data at 500 Hz presented by Slattery et al., 1986 (Figure 1).

Atypical DPOAE Effects

The results for the two atypical subjects provide evidence that dehydration produced amplitude-related effects rather than effects due to changes in place of stimulation or frequency selectivity. For Subject 1 (Figure 9), dehydration markedly reduced or eliminated DPOAE responses across the entire experimental frequency range. After dehydration, the pattern of responses had been altered so radically that it was difficult to associate the response pattern with changes in place of stimulation or frequency selectivity. One possible explanation for the dramatic reductions is that Reissners membrane collapsed completely on top of the tectorial membrane as described by Angelborg et al. (1981)

under similar conditions of dehydration. If the consequence of the collapse of Reissners membrane is reduction in DPOAE response levels, or elimination of DPOAE responses across a wide range of frequencies, then there is the implication that Reissners' membrane did not collapse for the other subjects in the study. One possible explanation of the unique results for Subject 1 is that this subject was dehydrated at the outset of this experiment due to illness that was compounded by the infusion of hypertonic urea.

For Subject 3 (Figure 10), the response pattern after dehydration is very similar to the median response pattern (Figure 6), except for two discrete frequency regions. In one frequency region, or location in the cochlea, DPOAE levels were reduced by approximately 20 dB and in another, they were increased by approximately 10 dB. These findings indicate that there was considerable suppression or enhancement of activity in specific regions of the cochlea with no changes in function in adjacent regions. The results for Subject 3 do not suggest that Reissners membrane collapsed across a large range of frequencies as was postulated for Subject 1. Instead, the large changes due to dehydration were confined to discrete regions and the effects of the changes (response enhancement or supression) were not predictable.

Implications for Future Research

Osmotic agents have been used to dehydrate cochleas as part of the process for the diagnosis of Meniere's disease and endolymphatic hydrops. The measures of cochlear function have been thresholds of audibility and

word recognition ability. The results of the present study suggest that DPOAE measurements may also provide useful information. The evidence to support this idea is based on the similarity of the results obtained on the hearing in normal ears (Slattery et al.,Figure 1), and the DPOAE results found in this study. In both studies, small changes in sensitivity were found for lower frequency signals as the result of dehydration. However, before this tool can be used clinically, there is the need to establish the relationship between hearing threshold data and DPOAEs for hydropic ears.

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APPENDICES

APPENDIX A

BACKGROUND NOISE LEVELS

Background noise levels in the sound treated chamber (Industrial Acoustics) were measured in one-third octave bands using a precision sound level meter (Quest Electronics, Model 1800) with a one-half inch condensor microphone, Measurements were made with only the sound level meter in the chamber.

One-third octave band center frequency (Hz)	--One-third octave band levels-- Permissible levels (dB SPL)	Measured levels
250	28.5	22.2
315		17.0
400		12.0
500	14.5	12.5
630		12.5
800	16.5	10.0
1000	21.5	9.0
1250		7.5
1600	21.5	7.3
2000	23.0	7.0
2500		6.7
3150	28.5	7.9
4000	29.5	8.6
5000		9.0
6300	33.0	8.0
8000	38.5	12.5
10000		7.3

* ANSI 3.1-1991, Table III, ears covered, test frequencies from 500-8000 Hz.

APPENDIX B

SUBJECT QUALIFICATION DATA

QUALIFICATION DATA LEGEND

Qualifying Data	Description
Qualification Session Date	Date of procedure
Weight	Measured in pounds
Test Ear	Right or left
IOP Average	Pre-test average of two measurements. Measured in mmHg.
Tympanometry (226 Hz)	The ear canal pressure (daPa) at which middle admittance was greatest.
ABR	
Wave I @ 90 dB	{Click levels
Wave V @ 90 dB	{are specified
Wave V @ 40 dB	{in dB nHL.
Probe Color	Color of probe tip
Anesthesia (ml):	Dose/Time of administration
Supplementary Dose	Dose/Time of administration
DPOAE	The qualification DPOAE shown below are required to have been categorized as "pass". is defined as a significant DPOAE response at 1,2,4, and 8 kHz.

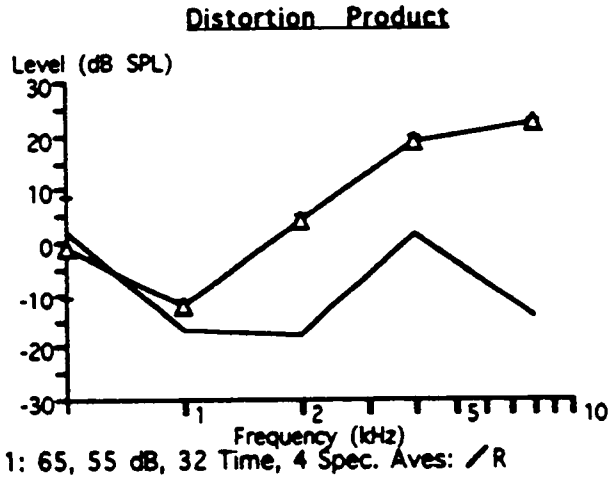
Distortion Product Otoacoustic Emission:

DP Audiogram

SUBJECT #1-BARRACUDA

Qualification Session Date	6/6/97
Weight (lbs.)	7
Test Ear	R
IOP Average	25
Tympanometry (226 Hz @ 0 daPa)	1.0
ABR (ms.)	
Wave I @ 90 dB	1.76
Wave V @ 90 dB	4.04
Wave V @ 40 dB	4.42
Probe Color	blue
Anesthesia (ml): Dose/Time	1.0 @ 8:30
Supplementary Dose	.05 @ 9:12
DPOAE	pass

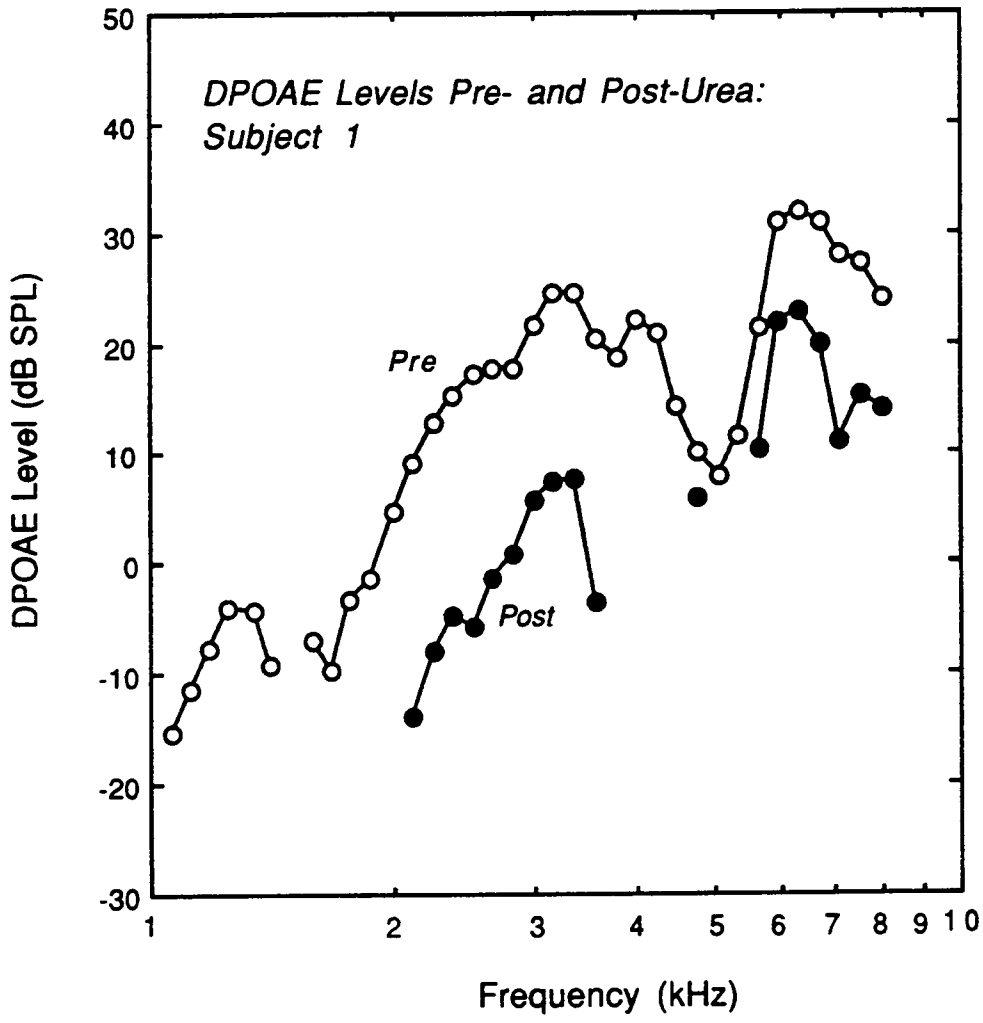
Distortion Product Otoacoustic Emission



SUBJECT #1- BARRACUDA

RAW DATA

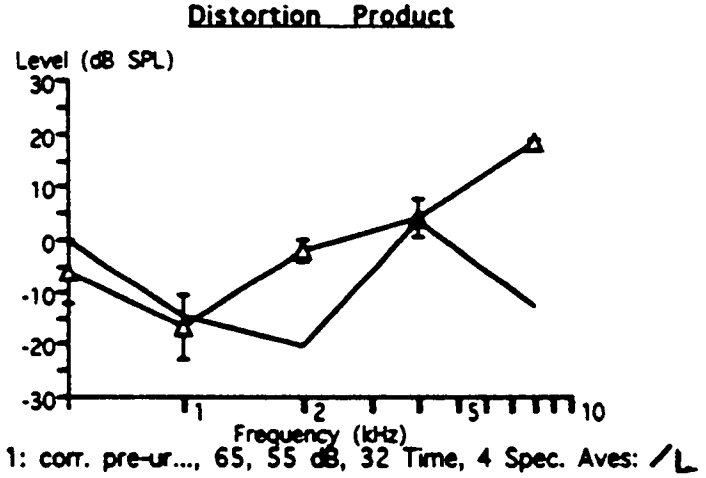
k Hz	Barr 1	Barr 2	Barr 3	Barr 4	Barr 5	Barr 6	Barr 7
1	-10.8	-7.8			-14.8		
1.06	-15.2		-7.2	-22.2			
1.12	-11.4	-2.4					
1.18	-7.7		-3.7				-13.7
1.25	-3.1		-4.1	-10.1			
1.34	-4.2		-4.2	-6.2			
1.41	-9.1	-11.1	-5.1	-6.1			
1.5	-4.6						
1.59	-7.1	-4.1				-10.1	
1.68	-9.6	-10.6	-9.6	-4.6	-16.6		
1.77	-3.4	-3.4	-4.4	-1.4	-10.4		
1.88	-1.3	-0.3	-2.3	-0.3		-13.3	
2	2.8	4.8	5.8	3.8		-11.2	
2.12	8.2	9.2	9.2	6.2	-9.8	-13.8	
2.25	12.9	11.9	12.9	8.9	-8.1	-4.1	
2.38	15.3	15.3	15.3	11.3	-8.7	-3.7	-4.7
2.52	16.2	17.2	17.2	14.2	-5.8	-2.8	-5.8
2.66	17.7	17.7	18.7	15.7	-3.3	-1.3	-1.3
2.83	15.8	17.8	17.8	14.8	-0.2	0.8	0.8
3	20.7	22.7	21.7	18.7	5.7	7.7	5.7
3.17	23.5	24.5	24.5	21.5	7.5	7.5	6.5
3.37	23.6	24.6	24.6	20.6	7.6	10.6	1.6
3.56	20.5	20.5	21.5	17.5	-3.5	4.5	
3.78	17.7	18.7	18.7	13.7			
4	20	22	23	17		6	
4.24	19.9	20.9	20.9	17.9			
4.49	13.3	15.3	14.3				
4.76	9	10	11	13		8	6
5.04		8	8	11			
5.34	9.7	11.7	11.7	6.7			
5.66	22.3	20.3	21.3	17.3		10.3	15.3
5.99	28.9	30.9	30.9	26.9	15.9	21.9	22.9
6.35	30.8	31.8	31.8	29.8	17.8	23.8	22.8
6.73	27	32	31	26	16	20	22
7.13	24	28	28	24	4	11	16
7.56	25.2	27.2	28.2	24.2	8.2	15.2	16.2
8.01	23	24	24	21	6	14	16


DPOAE Levels Pre- and Post-Urea:
Subject 1
Pre
Post
DPOAE Level (dB SPL)
50
40
30
20
10
0
-10
-20
-30
1
2
3
4
5
6
7
8
9
10
Frequency (kHz)

SUBJECT #2- TAPPER

Qualification Session Date	6/12/97
Weight (lbs.)	13
Test Ear	L
IOP Average	18.5
Tympanometry (226 Hz @ 0 daPa)	.8
ABR (ms.)	
Wave I @ 90 dB	1.72
Wave V @ 90 dB	4.06
Wave V @ 40 dB	4.76
Probe Color	blue
Anesthesia (ml): Dose/Time	1.0 @ 8:30
Supplementary Dose	.05 @ 9:28
DPOAE	pass

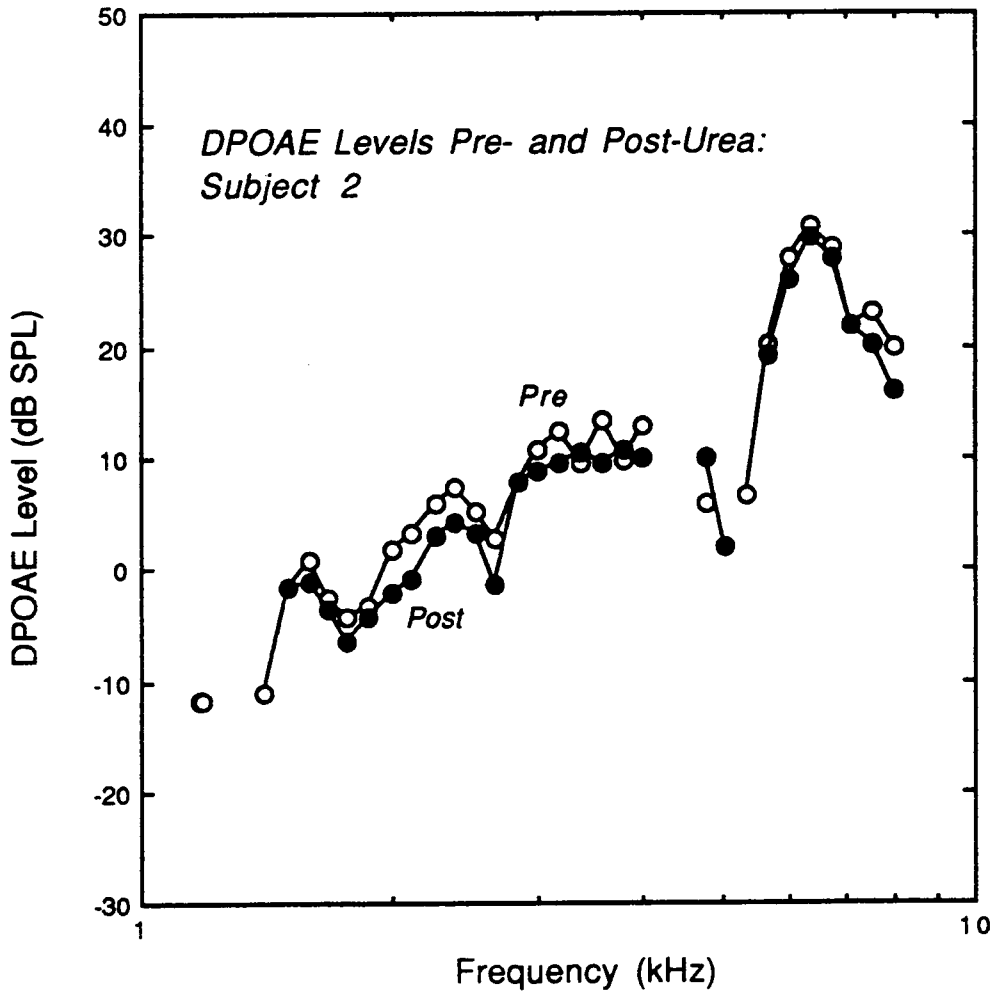
Distortion Product Otoacoustic Emission



SUBJECT #2- TAPPER

RAW DATA

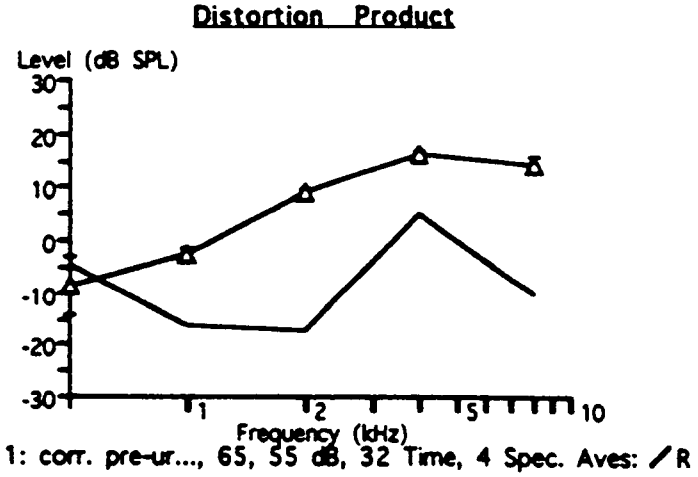
k Hz	Tapper 1	Tapper 2	Tapper 3	Tapper 4	Tapper 5	Tapper 6	Tapper 7
1			-12.8	-12.8			
1.06	-13.2						-11.2
1.12							
1.18	-9.7	-11.7			-8.7		
1.34							-5.2
1.41	-11.1	-12.1	-8.1	-9.1		-12.1	
1.5	-1.6	-0.6	-2.6	-0.6	-1.6	-2.6	-1.6
1.59	0.9	0.9	0.9	0.9	-0.1	-1.1	-1.1
1.68	-4.6	0.4	-2.6	-4.6	-0.6	-3.6	-5.6
1.77	-3.4	-5.4	-4.4	-3.4	-9.4	-6.4	-5.4
1.88	-3.3	-5.3	0.7	-0.3	-5.3	-4.3	-2.3
2	-0.2	1.8	1.8	0.8	-8.2	-1.2	-2.2
2.12	3.2	3.2	4.2	5.2	-2.8	2.2	-0.8
2.25	2.9	5.9	6.9	6.9	3.9	2.9	2.9
2.38	4.3	7.3	7.3	7.3	3.3	5.3	4.3
2.52	5.2	5.2	5.2	5.2	4.2	3.2	2.2
2.66	0.7	2.7	3.7	1.7	-1.3	-2.3	-0.3
2.83	7.8	8.8	7.8	8.8	4.8	7.8	8.8
3	9.7	10.7	10.7	10.7	8.7	9.7	7.7
3.17	12.5	11.5	13.5	13.5	9.5	11.5	9.5
3.37	9.6	7.6	11.6	12.6	10.6	10.6	11.6
3.56	13.5	13.5	14.5	13.5		9.5	14.5
3.78		9.7	10.7	10.7		10.7	13.7
4	7	13	14	15		14	10
4.24				10.9	6.9		
4.49							
4.76	6	5	10	9	7	12	10
5.04	8					4	2
5.34	6.7		13.7				
5.66	17.3	20.3	21.3	20.3	19.3	19.3	21.3
5.99	27.9	27.9	28.9	29.9	27.9	23.9	25.9
6.35	28.8	31.8	30.8	32.8	30.8	25.8	29.8
6.73	25	31	29	31	28	27	29
7.13	21	22	24	22	24	20	22
7.56	23.2	23.2	24.2	24.2	19.2	20.2	22.2
8.01	20	20	21	20	16	16	17


DPOAE Levels Pre- and Post-Urea:
Subject 2
Pre
Post
DPOAE Level (dB SPL)
50
40
30
20
10
0
-10
-20
-30
1
10
Frequency (kHz)

SUBJECT #3- RICKY

Qualification Session Date	6/26/97
Weight (lbs.)	10
Test Ear	R
IOP Average	24.5
Tympanometry (226 Hz @ 0 daPa)	.4
ABR (ms.)	
Wave I @ 90 dB	1.68
Wave V @ 90 dB	4.06
Wave V @ 40 dB	4.80
Probe Color	blue
Anesthesia (ml): Dose/Time	1.0 @ 9:30
Supplementary Dose	.05 @ 10:08
DPOAE	pass

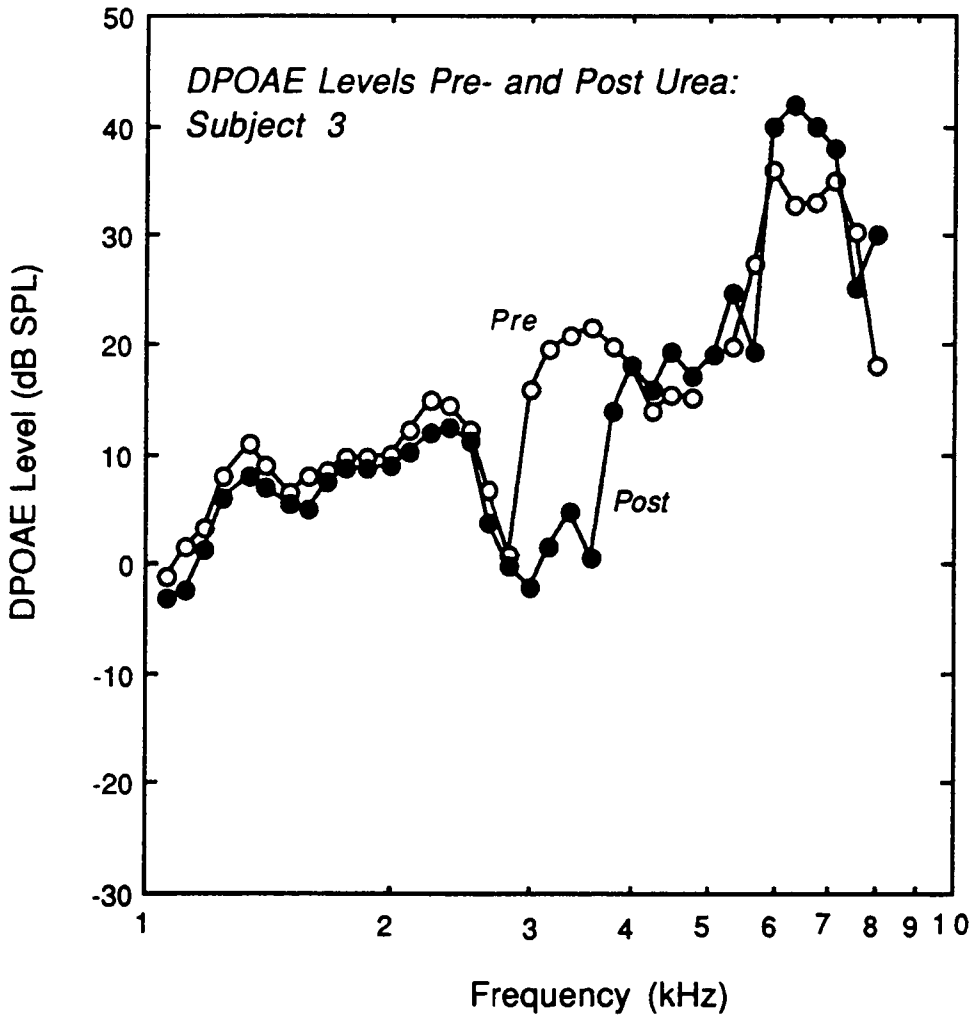
Distortion Product Otoacoustic Emission



SUBJECT #3- RICKY

RAW DATA

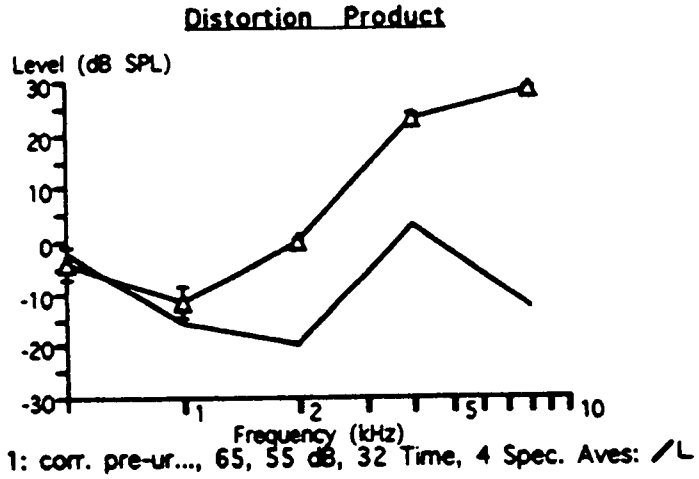
k Hz	Ricky 1	Ricky 2	Ricky 3	Ricky 4	Ricky 5	Ricky 6	Ricky 7
1	-3.8	-3.8	-2.8	-7.8	-6.8	-4.8	-3.8
1.06	-1.2	-2.2	-0.2	-9.2	-3.2	-5.2	-0.2
1.12	0.6	1.6	3.6	-1.4	-1.4	-2.4	-2.4
1.18	4.3	3.3	3.3	1.3	1.3	1.3	0.3
1.25	7.9	7.9	7.9	5.9	7.9	5.9	4.9
1.34	10.8	10.8	10.8	8.8	9.8	7.8	7.8
1.41	9.9	8.9	8.9	7.9	8.9	5.9	6.9
1.5	6.4	7.4	6.4	5.4	5.4	5.4	3.4
1.59	7.9	6.9	7.9	4.9	5.9	4.9	2.9
1.68	8.4	8.4	8.4	6.4	7.4	8.4	5.4
1.77	9.6	9.6	9.6	5.6	8.6	8.6	5.6
1.88	9.7	9.7	9.7	2.7	8.7	8.7	6.7
2	9.8	9.8	8.8	1.8	8.8	8.8	6.8
2.12	13.2	12.2	12.2	9.2	10.2	11.2	10.2
2.25	14.9	14.9	13.9	12.9	12.9	11.9	11.9
2.38	14.3	14.3	14.3	13.3	13.3	11.3	12.3
2.52	12.2	12.2	12.2	13.2	9.2	11.2	11.2
2.66	7.7	6.7	4.7	6.7	1.7	3.7	6.7
2.83	2.8	0.8	-6.2	-0.2		-0.2	1.8
3	15.7	15.7	10.7	11.7	4.7	-4.3	-2.3
3.17	19.5	20.5	18.5	15.5	9.5	-3.5	1.5
3.37	21.6	20.6	19.6	19.6	11.6	0.6	4.6
3.56	21.5	21.5	21.5	20.5	16.5	0.5	-0.5
3.78	18.7	19.7	19.7	16.7	17.7	13.7	10.7
4	18	18	18	15	16	20	18
4.24	14.9	12.9	13.9	11.9	11.9	15.9	15.9
4.49	16.3	15.3	12.3			19.3	21.3
4.76	15	15	15			19	17
5.04			7			21	19
5.34	17.7	19.7	19.7			24.7	30.7
5.66	26.3	27.3	27.3	21.3	15.3	19.3	26.3
5.99	35.9	35.9	35.9	24.9	25.9	39.9	39.9
6.35	23.8	32.8	32.8	30.8	31.8	41.8	41.8
6.73	33	34	33	20	38	40	42
7.13	34	35	35	28	31	38	40
7.56	30.2	29.2	32.2	22.2	25.2	34.2	4.2
8.01	8	19	18	16	22	31	30


DPOAE Levels Pre- and Post Urea:
Subject 3
Pre
Post
DPOAE Level (dB SPL)
50
40
30
20
10
0
-10
-20
-30
1
2
3
4
5
6
7
8
9
10
Frequency (kHz)

SUBJECT #4- TAB

Qualification Session Date	6/27/97
Weight (lbs.)	12.5
Test Ear	L
IOP Average	27
Tympanometry (226 Hz @ 0 daPa)	.2
ABR (ms.)	
Wave I @ 90 dB	1.76
Wave V @ 90 dB	4.00
Wave V @ 40 dB	4.70
Probe Color	blue
Anesthesia (ml): Dose/Time	1.0 @ 8:20
Supplementary Dose	.05 @ 9:04
DPOAE	pass

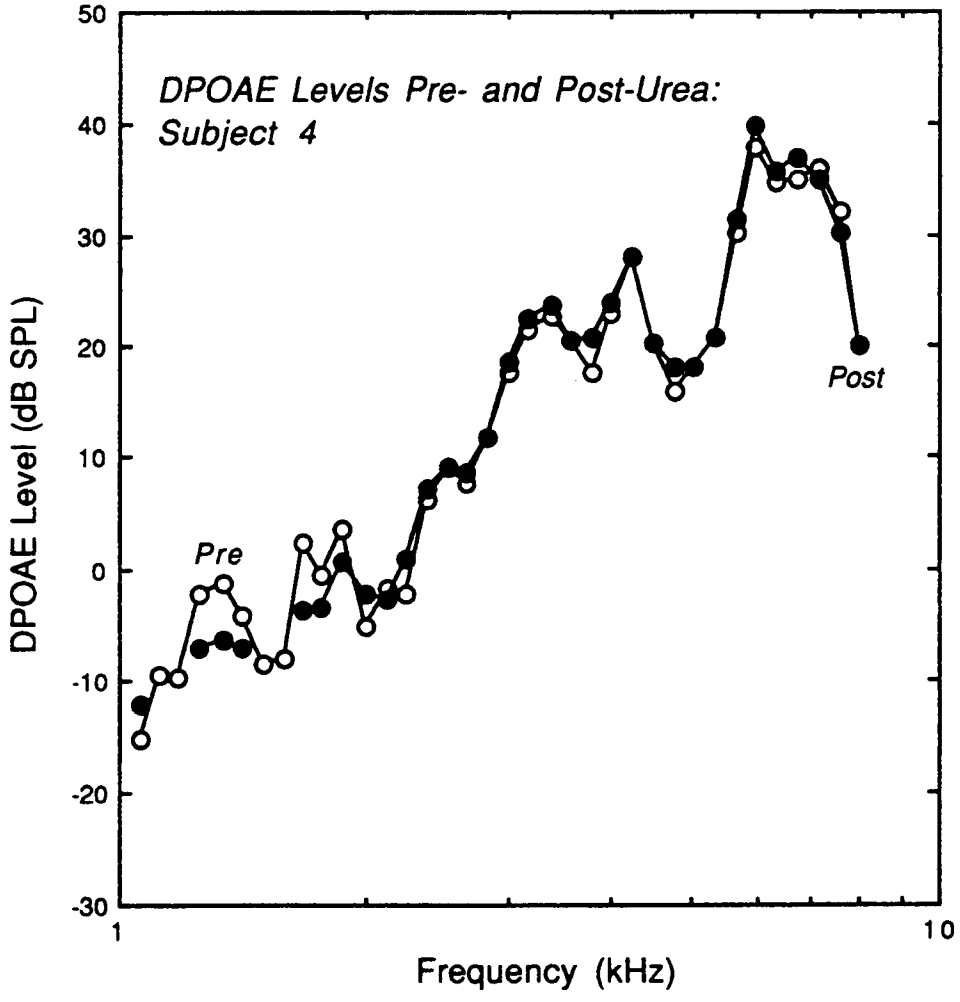
Distortion Product Otoacoustic Emission



SUBJECT #4- TAB

RAW DATA

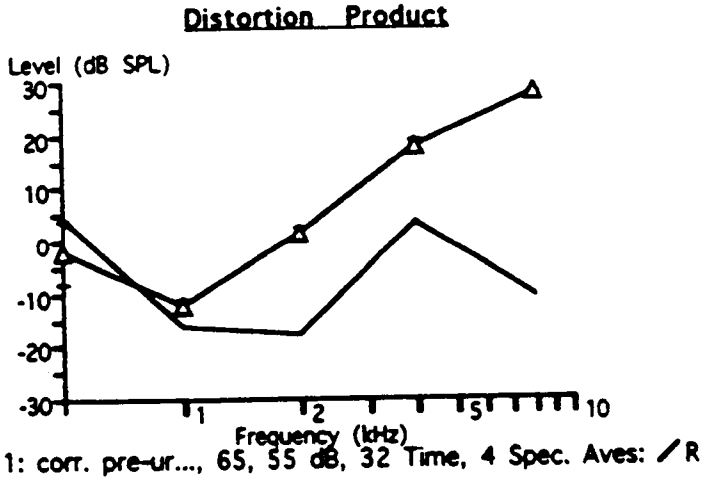
k Hz	Tab 1	Tab 2	Tab 3	Tab 4	Tab 5	Tab 6	Tab 7
1			-10.8	-6.8		-12.8	
1.06		-9.2	-15.2		-12.2	-10.2	-12.2
1.12	-9.4	-8.4					
1.18	-9.7	-9.7	-9.7	-3.7			
1.25	2.9	-2.1	-4.1		-7.1		-6.1
1.34	-2.2	-1.2	1.8	-1.2	-3.2	-6.2	-8.2
1.41	-6.1	-2.1	-4.1	-5.1	-4.1	-7.1	-8.1
1.5	-8.6	-6.6					
1.59	-5.1	-8.1	-15.1	-11.1			-10.1
1.68	2.4	2.4	0.4	1.4	-3.6	-0.6	-6.6
1.77	0.6	-0.4	-2.4	1.6	-3.4	-1.4	-3.4
1.88	5.7	3.7	3.7	0.7	0.7	1.7	0.7
2	-5.2	-5.2	-2.2	-2.2	-2.2	-1.2	-3.2
2.12	-0.8	-1.8	-1.8	-3.8	-2.8	-1.8	-2.8
2.25	-0.1	-2.1	-2.1	-0.1	1.9	-0.1	0.9
2.38	6.3	5.3	8.3	7.3	8.3	6.3	7.3
2.52	7.2	9.2	10.2	9.2	10.2	8.2	9.2
2.66	8.7	7.7	7.7	7.7	8.7	7.7	8.7
2.83	11.8	11.8	11.8	11.8	11.8	11.78	12.8
3	17.7	17.7	18.7	18.7	17.7	18.7	18.7
3.17	21.5	21.5	21.5	22.5	21.5	22.5	22.5
3.37	21.6	22.6	23.6	23.6	23.6	23.6	23.6
3.56	19.5	20.5	21.5	20.5	20.5	21.5	20.5
3.78	17.1	17.7	19.7	20.7	19.7	20.7	21.7
4	23	24	23	24	24	24	24
4.24	27.9	27.9	27.9	27.9	27.9	27.9	25.9
4.49	19.3	20.3	20.3	21.3	20.3	21.3	18.3
4.76	17	16	15	17	20	18	15
5.04	18	17	19	18	18	18	17
5.34	19.7	20.7	20.7	20.7	20.7	21.7	19.7
5.66	29.3	30.3	30.3	31.3	31.3	31.3	31.3
5.99	36.9	37.9	37.9	37.9	38.9	39.9	39.9
6.35	34.8	34.8	35.8	34.8	34.8	35.8	38.8
6.73	35	35	36	35	36	37	38
7.13	36	35	36	35	36	34	35
7.56	32.2	32.2	32.2	31.2	30.2	29.2	32.2
8.01	20	22	14	24	20	20	28


DPOAE Levels Pre- and Post-Urea:
Subject 4
Pre
Post
DPOAE Level (dB SPL)
50
40
30
20
10
0
-10
-20
-30
1
10
Frequency (kHz)

SUBJECT #5-DOLPHIN

Qualification Session Date	7/11/97
Weight (lbs.)	13
Test Ear	R
IOP Average	30.5
Tympanometry (226 Hz @ 0 daPa)	.2
ABR (ms.)	
Wave I @ 90 dB	1.86
Wave V @ 90 dB	4.04
Wave V @ 40 dB	4.40
Probe Color	blue
Anesthesia (ml): Dose/Time	1.0 @ 8:35
Supplementary Dose	.01 @ 8:48
Supplementary Dose	.02 @ 9:15
DPOAE	pass

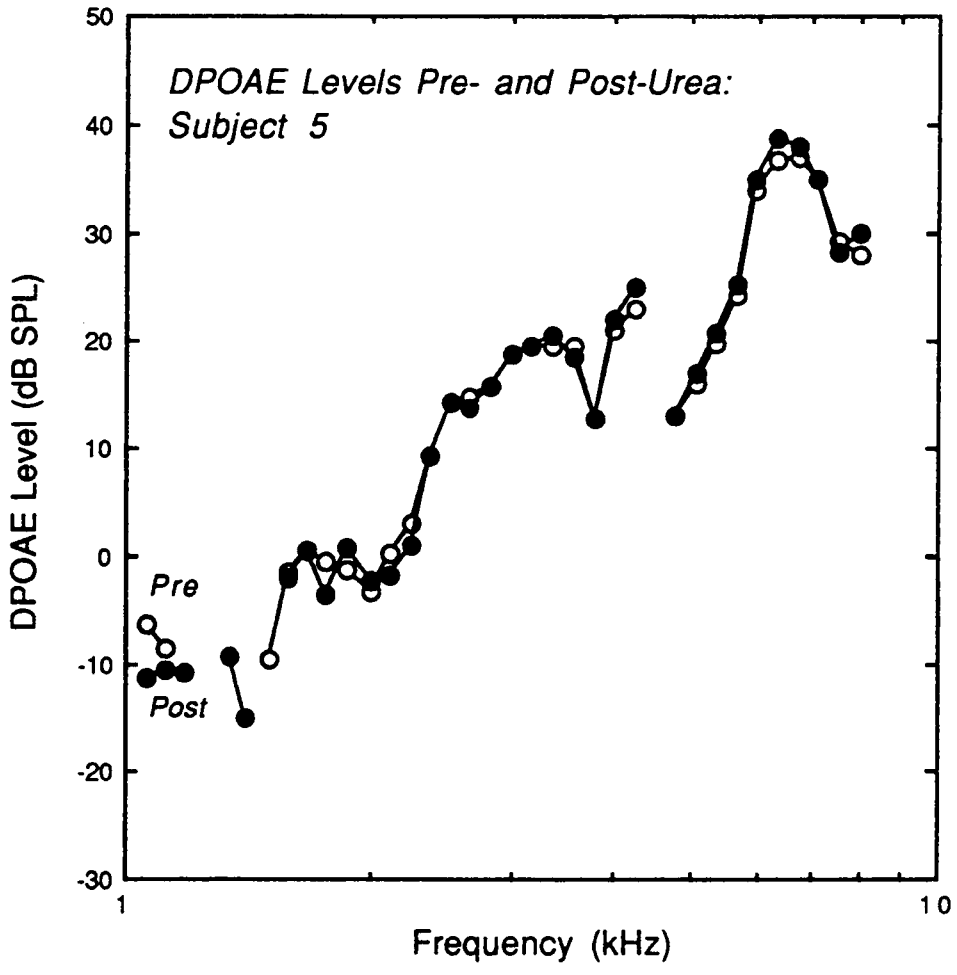
Distortion Product Otoacoustic Emission



SUBJECT #5- DOLPHIN

RAW DATA

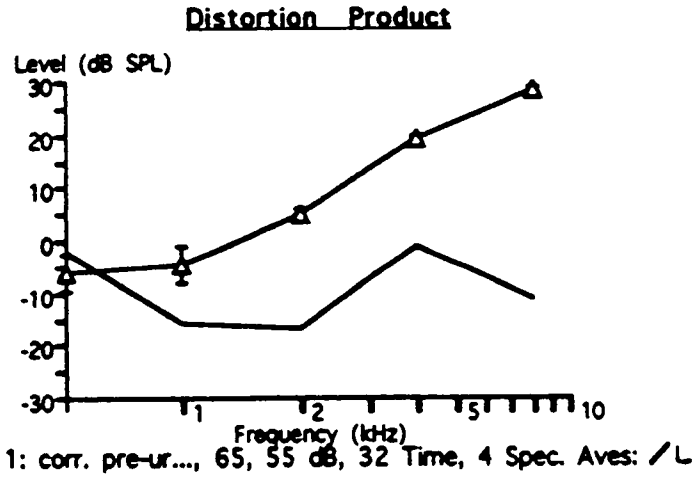
k Hz	Dolphin 1	Dolphin 2	Dolphin 3	Dolphin 4	Dolphin 5	Dolphin 6	Dolphin 7
1	-10.8	-11.8		-7.8	-7.8	-12.8	-11.8
1.06	-6.2		-6.2		-11.2	-10.2	
1.12	-8.4	-2.4	-8.4	-7.4	-10.4	-11.4	-7.4
1.18	-5.7				-10.7	-6.7	-12.7
1.25				-4.1			
1.34		-9.2	-5.2			-9.2	-7.2
1.41						-15.1	-10.1
1.5		-0.1	-9.6			-5.6	
1.59	-3.1	-1.6	-1.1	-6.1	-0.1	-4.1	-2.1
1.68	0.4	0.6	1.4	-0.6	1.4	0.4	-2.6
1.77	-1.4	2.7	-0.4	-1.4	-1.4	-3.4	-4.4
1.88	-1.3	-3.2	2.7	-0.3	0.7	1.7	-0.3
2	-3.2	-3.8	-3.2	-5.2	-2.2	-4.2	-2.2
2.12	0.2	1.9	-1.8	-3.8	-1.8	-0.8	-3.8
2.25	2.9	10.3	-1.1	-0.1	1.9	-0.1	0.9
2.38	9.3	15.2	8.3	9.3	9.3	9.3	8.3
2.52	15.2	13.7	14.2	15.2	15.2	14.2	14.2
2.66	14.7	15.8	13.7	13.7	13.7	13.7	13.7
2.83	15.8	18.7	14.8	15.8	14.8	15.8	15.8
3	18.7	18.7	18.7	18.7	18.7	18.7	19.7
3.17	19.5	20.5	18.5	18.5	18.5	19.5	19.5
3.37	19.6	21.6	19.6	20.6	19.6	20.6	20.6
3.56	17.5	19.5	19.5	17.5	18.5	18.5	16.5
3.78	8.7	12.7	12.7	12.7	12.7	14.7	11.7
4	20	21	22	22	22	22	20
4.24	22.9	24.9	22.9	23.9	24.9	25.9	23.9
4.49			13.3		12.3		
4.76	9	13	15	13	13		15
5.04	16	13	16	17	14	17	17
5.34	17.7	19.7	19.7	22.7	19.7	20.7	21.7
5.66	24.3	23.3	24.3	25.3	25.3	25.3	25.3
5.99	33.9	34.9	33.9	34.9	33.9	34.9	34.9
6.35	36.8	36.8	36.8	37.8	37.8	38.8	38.8
6.73	37	37	37	37	37	38	38
7.13	35	34	35	36	35	35	35
7.56	28.2	29.2	29.2	27.2	27.2	28.2	29.2
8.01	28	29	27	28	29	30	31


DPOAE Levels Pre- and Post-Urea:
Subject 5
DPOAE Level (dB SPL)
50
40
30
20
10
0
-10
-20
-30
Pre
Post
1
10
Frequency (kHz)

SUBJECT #6- TUNA

Qualification Session Date	7/17/97
Weight (lbs.)	14
Test Ear	L
IOP Average	28.5
Tympanometry (226 Hz @ 0 daPa)	.9
ABR (ms.)	
Wave I @ 90 dB	1.86
Wave V @ 90 dB	4.08
Wave V @ 40 dB	4.80
Probe Color	blue
Anesthesia (ml): Dose/Time	1.0 @ 8:50
Supplementary Dose	.01 @ 9:15
Supplementary Dose	.02 @ 10:08
DPOAE	pass

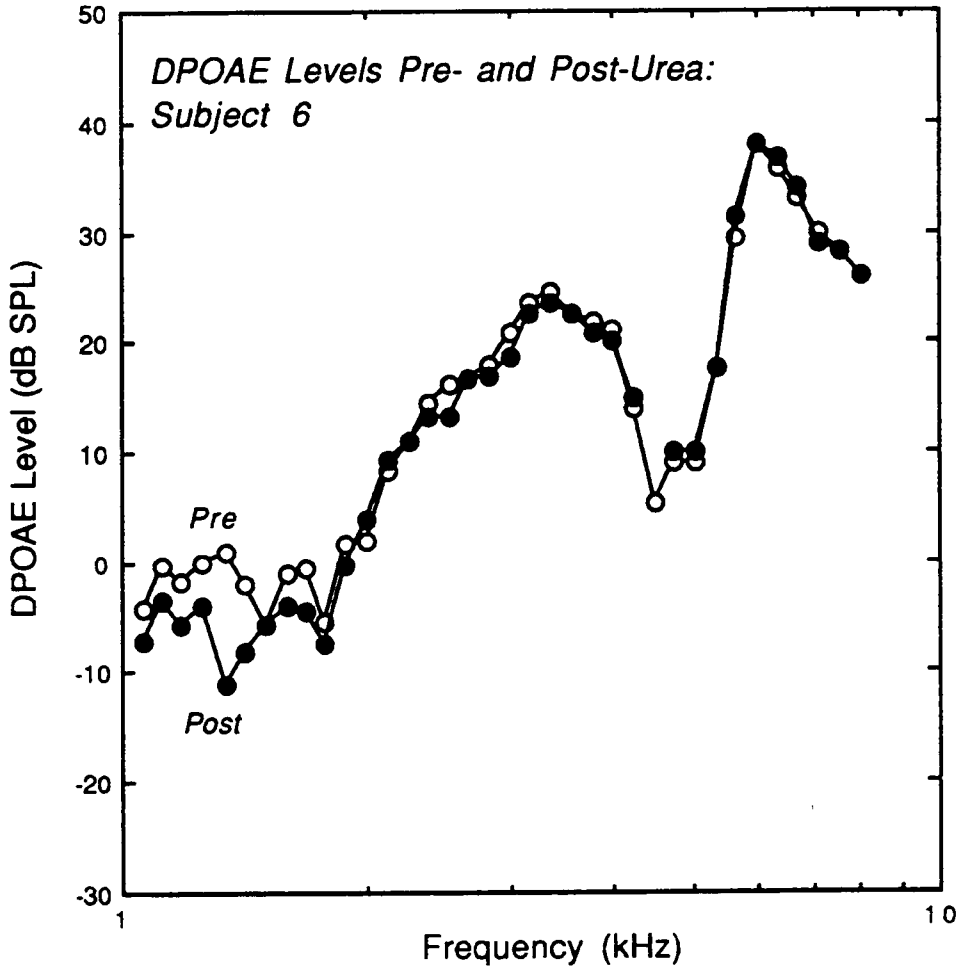
Distortion Product Otoacoustic Emission



SUBJECT #6- TUNA

RAW DATA

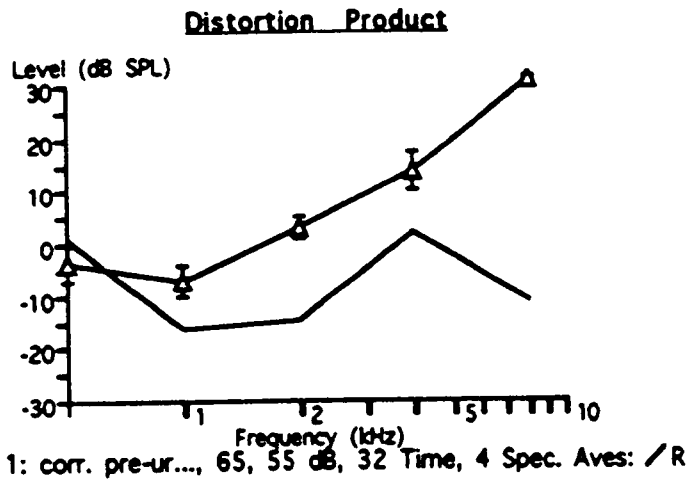
k Hz	Tuna 1	Tuna 2	Tuna 3	Tuna 4	Tuna 5	Tuna 6	Tuna 7
1	-4.8	-4.8	-7.8	-3.8	-3.8	-3.8	-7.8
1.06	-2.2	-4.2	-5.2	-5.2		-6.2	-7.2
1.12	-0.4	-2.4	-0.4	-0.4	-1.4	-3.4	-6.4
1.18	-1.7	-3.7	-0.7	-2.7	-5.7	-8.7	-3.7
1.25	-0.1	-4.1	-0.1	-2.1	-4.1	1.9	-7.1
1.34	0.8	0.8	-3.2	-0.2	-8.2	-11.2	
1.41	0.9	-2.1	-3.1	-3.1	-7.1		-8.1
1.5	-5.6	-5.6	-3.6	-6.6	-7.6	-4.6	-5.6
1.59	0.9	-1.1	-5.1	-6.1	-4.1	-5.1	-4.1
1.68	1.4	-0.6	-1.6	-2.6	-4.6	-6.6	-4.6
1.77	-2.4	-5.4	-9.4		-8.4	-7.4	-3.4
1.88	2.7	1.7	-0.3	-0.3	-0.3	-1.3	0.7
2	0.8	1.8	1.8	3.8	3.8	2.8	3.8
2.12	7.2	8.2	9.2	10.2	8.2	9.2	9.2
2.25	10.9	10.9	11.9	11.9	10.9	10.9	10.9
2.38	13.3	14.3	14.3	13.3	14.3	13.3	13.3
2.52	16.2	16.2	15.2	15.2	14.2	13.2	13.2
2.66	16.7	17.7	16.7	16.7	16.7	16.7	14.7
2.83	17.8	17.8	17.8	16.8	16.8	16.8	14.8
3	20.7	19.7	20.7	19.7	19.7	18.7	17.7
3.17	22.5	23.5	23.5	23.5	22.5	22.5	20.5
3.37	24.6	24.6	25.6	25.6	24.6	23.6	21.6
3.56	22.5	22.5	22.5	22.5	22.5	22.5	19.5
3.78	20.7	21.7	21.7	20.7	20.7	20.7	19.7
4	21	21	21	21	21	20	16
4.24	15.9	13.9	12.9	14.9	14.9	15.9	12.9
4.49	5.3		7.3	8.3		6.3	
4.76	7	9	9	8	12	10	7
5.04	15		9		11	9	10
5.34	16.7	17.7	17.7	17.7	18.7	17.7	17.7
5.66	29.3	29.3	30.3	30.3	31.3	31.3	28.3
5.99	37.9	37.9	37.9	37.9	37.9	38.9	37.9
6.35	35.8	35.8	35.8	35.8	36.8	36.8	35.8
6.73	33	34	33	34	34	34	33
7.13	29	30	30	30	29	29	29
7.56	28.2	28.2	28.2	28.2	28.2	28.2	28.2
8.01	25	27	26	27	27	26	24


DPOAE Levels Pre- and Post-Urea:
Subject 6
DPOAE Level (dB SPL)
50
40
30
20
10
0
-10
-20
-30
Pre
Post
1
10
Frequency (kHz)

SUBJECT #7- LUTHER

Qualification Session Date	7/18/97
Weight (lbs.)	9
Test Ear	R
IOP Average	33
Tympanometry (226 Hz @ 0 daPa)	.3
ABR (ms.)	
Wave I @ 90 dB	1.88
Wave V @ 90 dB	4.00
Wave V @ 40 dB	4.50
Probe Color	blue
Anesthesia (ml): Dose/Time	1.0 @ 8:25
Supplementary Dose	.05 @ 8:58
DPOAE	pass

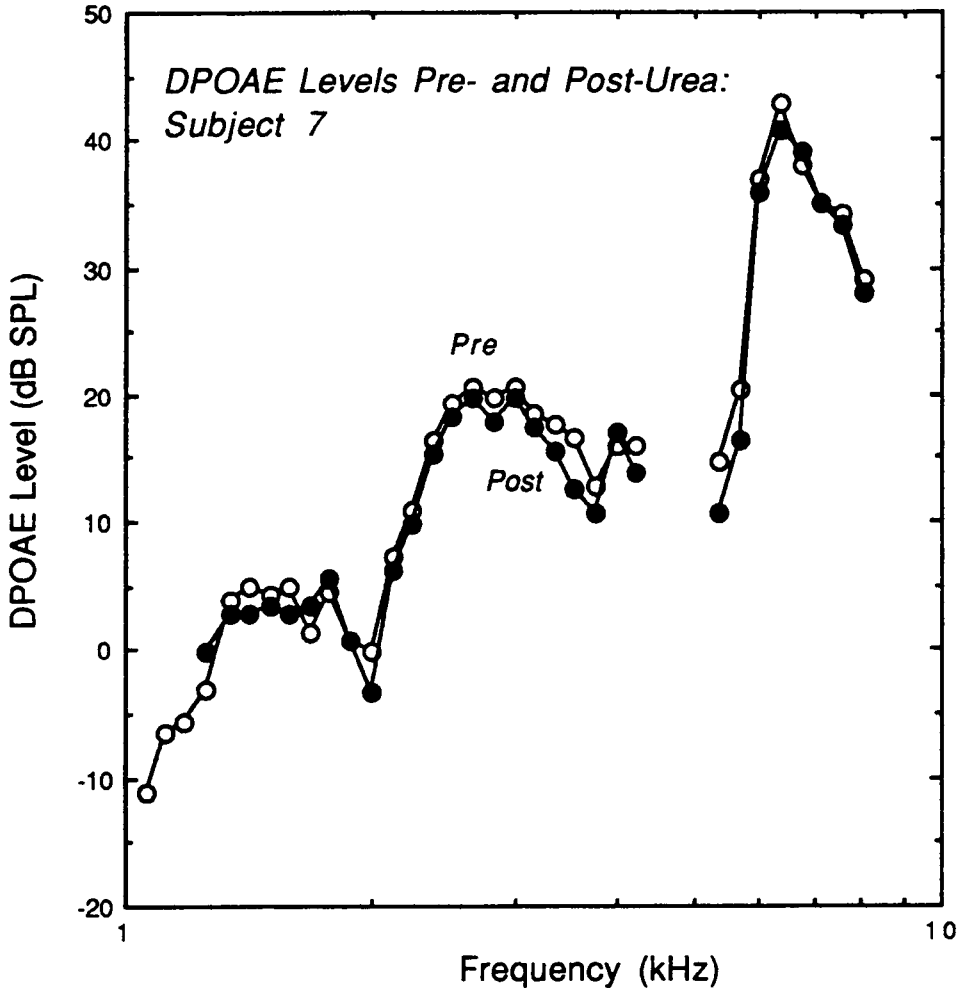
Distortion Product Otoacoustic Emission



SUBJECT #7- LUTHER

RAW DATA

k Hz	Luther 1	Luther 2	Luther 3	Luther 4	Luther 5	Luther 6	Luther 7
1	-14.8		-11.8	-0.8		-12.8	
1.06	-11.2	-3.2		-9.2		-13.2	
1.12	-6.4	-7.4	-1.4	-6.4		-6.4	
1.18	-2.7	-5.7	-9.7	-3.7		-7.7	
1.25	-2.1	-3.1	-4.1	1.9	-6.1	-0.1	3.9
1.34	3.8	2.8	4.8	2.8	3.8	2.8	-0.2
1.41	4.9	4.9	2.9	2.9	3.9	2.9	1.9
1.5	3.4	4.4	5.4	0.4	1.4	3.4	3.4
1.59	4.9	3.9	4.9	0.9	2.9	1.9	3.9
1.68	1.4	-2.6	2.4	4.4	3.4	3.4	2.4
1.77	4.6	4.6	4.6	6.6	6.6	3.6	5.6
1.88	2.7	0.7	0.7	6.7	3.7	0.7	0.7
2	0.8	-4.2	-0.2	7.8	-0.2	-3.2	
2.12	4.2	8.2	7.2	9.2	7.2	6.2	3.2
2.25	11.9	10.9	10.9	10.9	12.9	9.9	7.9
2.38	16.3	16.3	16.3	16.3	16.3	15.3	13.3
2.52	20.2	19.2	19.3	17.2	20.2	18.2	17.2
2.66	20.7	20.7	20.7	18.7	20.7	19.7	18.7
2.83	19.8	19.8	19.8	17.8	17.8	19.8	17.8
3	20.7	20.7	21.7	18.7	19.7	20.7	19.7
3.17	17.5	18.5	19.5	15.5	17.5	17.5	15.5
3.37	17.6	17.6	16.6	15.6	16.6	15.6	15.6
3.56	16.5	14.5	16.5	11.5	12.5	11.5	14.5
3.78	11.7	12.7	13.7	12.7	16.7	10.7	9.7
4	16	16	17	16	18	17	14
4.24	17.9	13.9	15.9	8.9	13.9	13.9	14.9
4.49		3.3					
4.76	4			1			
5.04	9			12	7		
5.34	15.7	12.7	14.7	14.7	10.7		13.7
5.66	24.3	20.3	16.3	20.3	15.3	16.3	16.3
5.99	32.9	36.9	37.9	37.9	37.9	35.9	30.9
6.35	40.8	42.8	42.8	40.8	42.8	40.8	35.8
6.73	39	38	38	38	39	39	40
7.13	35	35	34	35	35	35	33
7.56	35.2	34.2	34.2	34.2	33.2	34.2	33.2
8.01	29	28	29	28	28	27	31


DPOAE Levels Pre- and Post-Urea:
Subject 7
Pre
Post
DPOAE Level (dB SPL)
50
40
30
20
10
0
-10
-20
1
10
Frequency (kHz)

APPENDIX C

INTRAOCULAR PRESSURE MEASUREMENTS

INTRAOCULAR PRESSURE (mm Hg)

		--------Measurements made after--------						
Subject	Qualification	T-1	T-2	T-3	T- 4	T- 5	T- 6	T- 7
1	26	21	19	19.5	7.5	10.5	11.5	10.5
2	18.5	18.5	15.5	15	12	10.5	9	9
3	27.5	23	20.5	20	12.5	12	15.5	12.5
4	27	27	26	22.5	15.5	15	16	17
5	31	24.5	24.5	25	16	15.5	14.5	13.5
6	27	24	23	23	12	13	13	10.5
7	33	25	26	26	14	14.5	14	13

VITA

Erin Lee Wendover was born in North Miami Beach, Florida on September 12, 1974. After graduating from North Miami Beach Senior High School in 1992, she attended Miami Dade Community College. She then transferred to Florida State University. At Florida State she was captain of the Varsity cheerleading squad, and received her Bachelor of Arts degree in Communication Disorders. Upon graduating, she began the graduate program at The University of Tennessee in Audiology. In May 1998, she received a Masters of Arts degree in Audiology. Future plans include completing a Clinical Fellowship Year in Audiology.