Developing Distortion Product Emission Measurements for Clinical Applications

Élaboration de méthodes de mesure des émissions de distorsion à des fins cliniques

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Abstract

Recently, distortion-product emissions (DPEs) have become an important area of both pure and applied research. In this paper, we focus upon possible clinical applications of distortion-product emissions. In particular, the prediction of pure tone hearing sensitivity and issues relevant to the achievement of this goal are discussed. Factors that may have confounded previous correlational studies, such as noise rejection and signal analysis, are reviewed. The potential clinical applications of DPEs are identified and examples of various audiometric configurations and associated DPE recordings are also provided.

Résumé

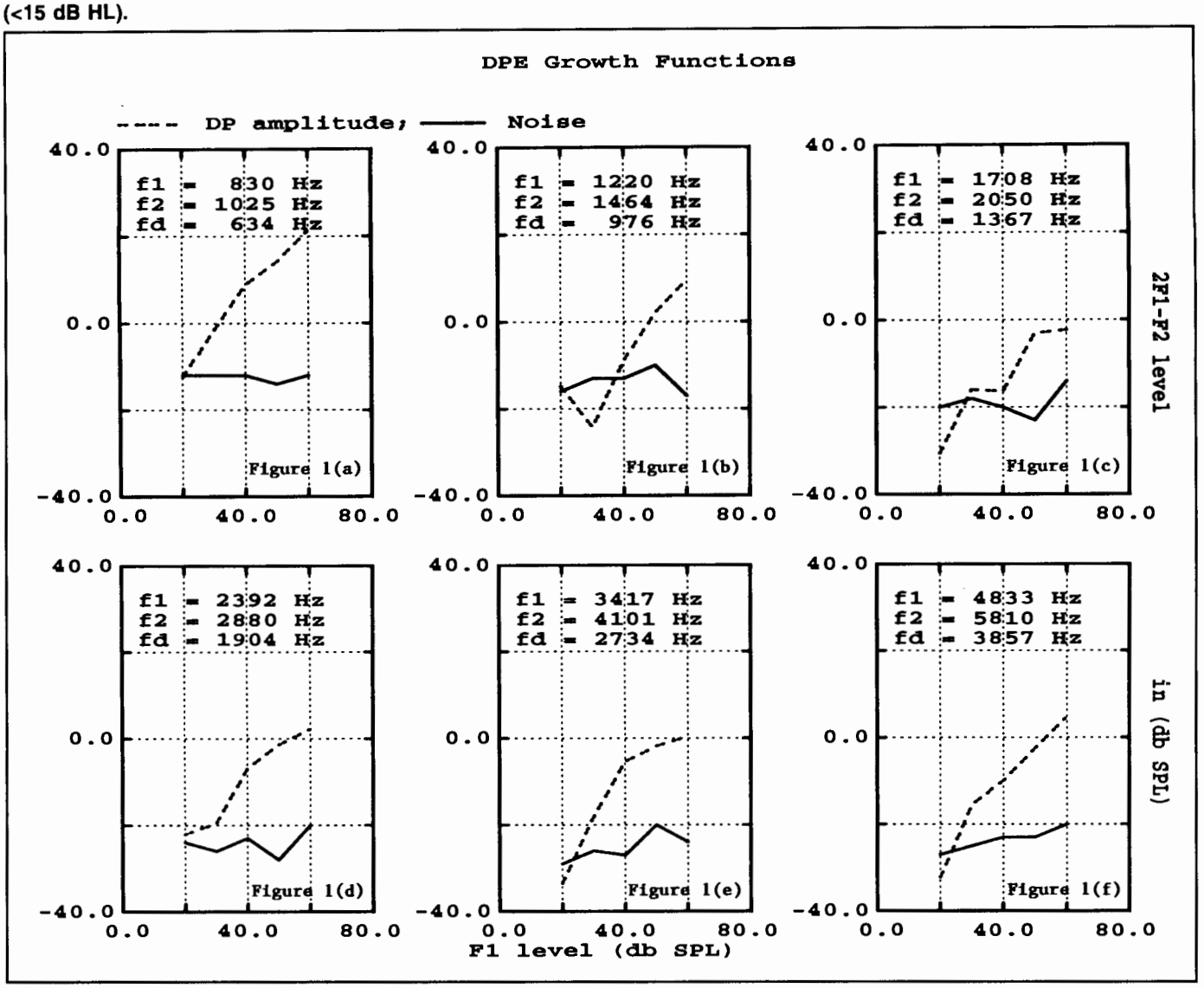
Les émissions de produits de distorsion acoustique sont devenues récemment un sujet important en recherche fondamentale et appliquée. Dans le présent document, nous énonçons des applications cliniques possibles des émissions de produits de distorsion acoustique. En particulier, la prédiction des seuils d'audibilité des sons purs et les questions relatives à l'atteinte de cet objectif sont abordées. Des facteurs qui auraient pu entraîner des erreurs dans des études de corrélation déjà effectuées, notamment sur l'élimination du bruit et l'analyse du signal, sont évalués. Suivent une description des applications cliniques possibles des émissions de produits de distorsion acoustique et des exemples de diverses configurations audiométriques et d'enregistrements d'émissions de produits de distorsion acoustique.

Introduction

The discovery that the cochlea actively generates acoustic energy, known as otoacoustic emissions, represents an exciting advancement in our understanding of cochlear physiology. Otoacoustic emissions are low intensity acoustic signals arising from mechanical vibration of the basilar membrane and can be recorded using a very sensitive microphone placed in the ear canal. A great deal of evidence supports the notion that otoacoustic emissions are a result of outer hair cell motility (Brownell, 1990). Ototoxic drugs, well-defined cochlear pathologies, and intense noise exposure have been shown to have deleterious effects on otoacoustic emissions (Brown, McDowell, & Forge, 1989; Long & Tubis, 1988). In the assessment of cochlear (outer hair cell) function and hearing sensitivity, the clinical application of evoked otoacoustic emissions offers the audiologist and otologist differential diagnostic power that has been previously unattainable. Additionally, otoacoustic emission recordings may be obtained non-invasively, objectively, and very rapidly (5 - 20 minutes to test both ears, depending upon the type of emission being recorded). Presently, there are several published reports that address the use of emissions in the differential diagnosis of various cochlear and retrocochlear pathologies (Kemp, Bray, Alexander, & Brown, 1986; Lutman, Mason, Sheppard, & Gibbon, 1989; Ohlms, Lonsbury-Martin, & Martin, 1991). We will show that one type of otoacoustic emission, namely distortion product otoacoustic emissions (DPEs), appears best suited to relate to pure tone behavioral thresholds.

In 1978, Kemp identified two types of otoacoustic emissions: (1) spontaneous otoacoustic emissions (SOEs), and (2) transiently-evoked otoacoustic emissions (TEOEs), which may be elicited by clicks or tone bursts. In that report, Kemp also described the general relationship between the TEOEs and hearing sensitivity, that is, that TEOEs were generally reduced in amplitude or absent in damaged cochleae and were present and robust in most healthy ears. Numerous researchers subsequently have confirmed this positive, though imperfect, correlation between TEOE amplitude and hearing sensitivity (Kemp, Ryan, & Bray, 1990; Kemp et al., 1986; Probst, Lonsbury-Martin, Martin, & Coats, 1987; Stevens, 1988; Tanaka, Suzuki & Inoue, 1990). Data obtained from subjects with various patterns and degrees of hearing impairment generally demonstrate high DPE thresholds or the absence of DPEs at any frequency at which behavioral thresholds are impaired (poorer than approx. 20 dB HL). A second type of

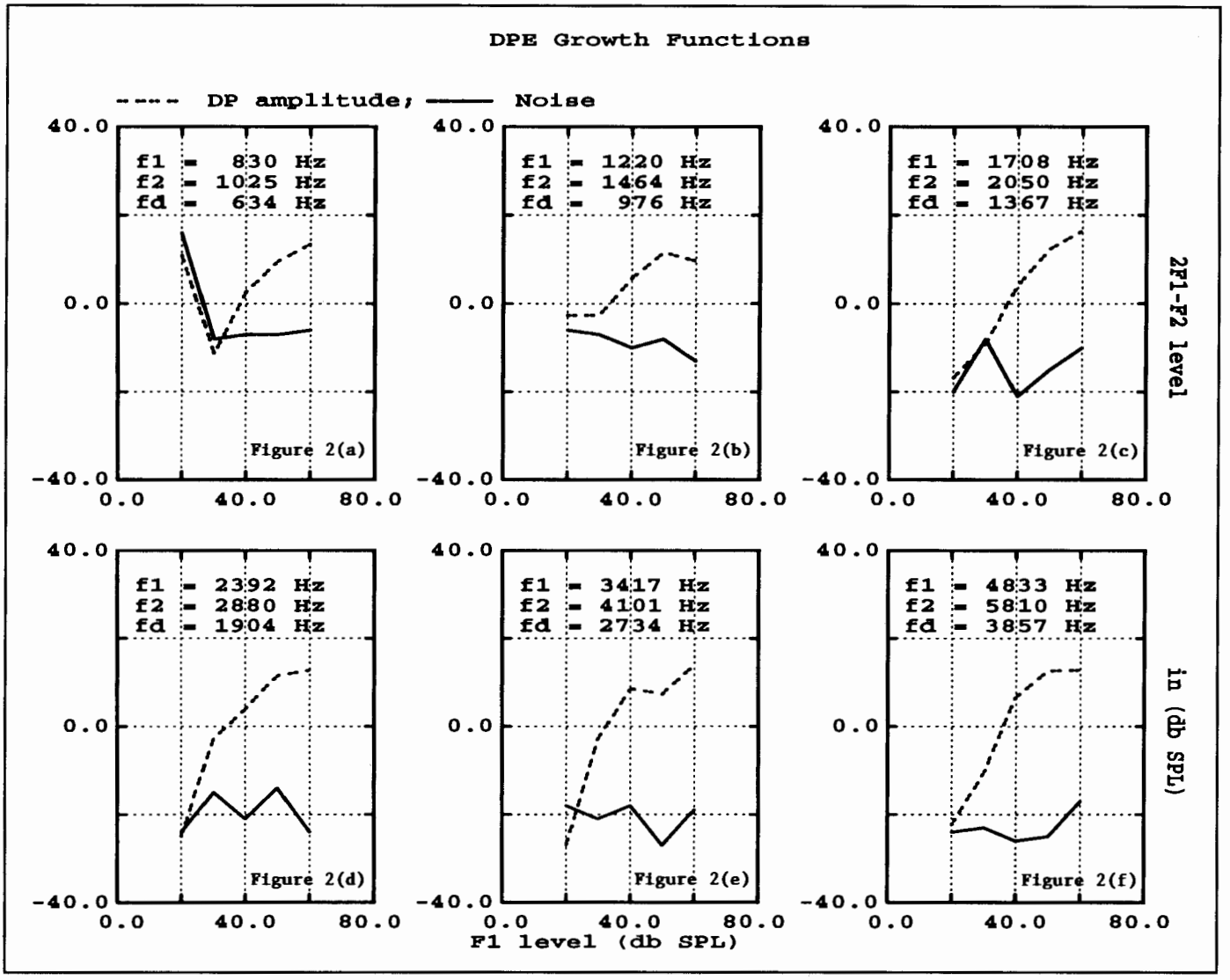
Figure 1. Low DPE thresholds are evident in the ear of an adult male whose pure tone thresholds were excellent (<15 dB HL).



evoked emission is the stimulus frequency otoacoustic emission (SFOE) which may be evoked using a single continuous low-amplitude pure tone stimulus and results in an emission that is identical in frequency to the stimulus, but differs in amplitude and phase (Kemp & Chum, 1980). SFOEs have not been as thoroughly investigated due to the technical difficulties encountered in separating the SFOE from the stimulus (Lonsbury-Martin, Whitehead, & Martin, 1991; Martin, Probst, & Lonsbury-Martin, 1990).

In 1979, Kemp defined another type of evoked emission, the distortion-product otoacoustic emission (DPOE or DPE). DPEs are elicited by simultaneously presenting two *continuous* pure tone stimuli to the ear. The outcome of this stimulus presentation is an emission of a frequency, amplitude, and phase differing from those of the two stimuli. Of the DPEs, the 2f1-f2 DPE (also known as a cubic difference tone, cubic distortion product, combination tone), where f1 < f2, is the most prominent acoustic distortion product in humans and has received the most scientific scrutiny to date. While DPEs have been less thoroughly investigated than TEOEs, extant research strongly supports the conclusion that DPEs are a normal phenomenon of healthy human ears in that they can be recorded in virtually 100% of normal ears (Harris, 1990; Kemp et al., 1986; Lonsbury-Martin & Martin, 1990).

Figure 2. DPE recordings obtained from a healthy neonatal ear demonstrate the qualitative similarity between healthy neonatal and healthy adult ear DPE recordings.

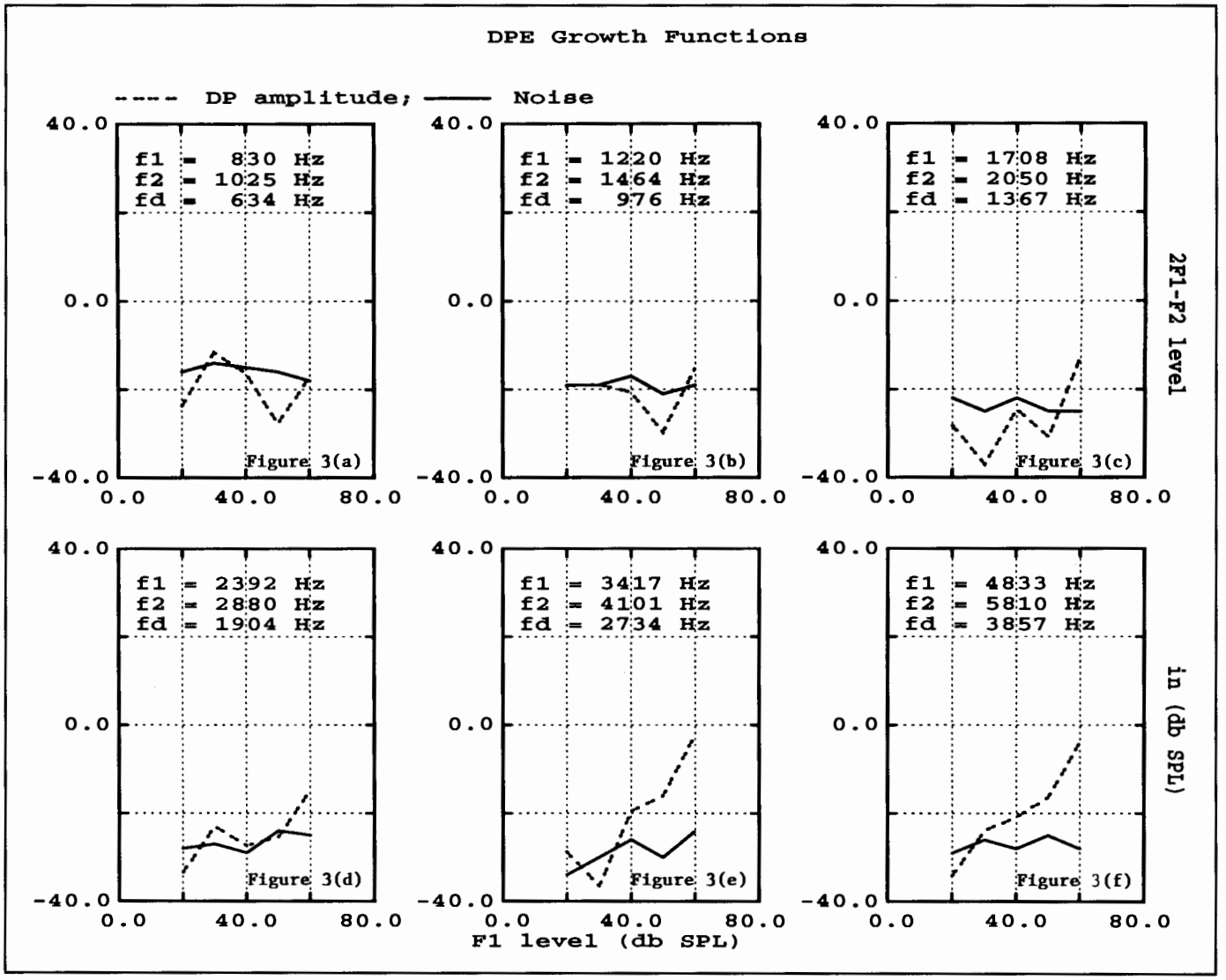


Frequency Specificity of DPEs

The stimuli employed to evoke DPEs and TEOEs differ fundamentally, and it is this difference that results in the relatively improved frequency specificity of DPEs over TEOEs. Any brief stimulus, such as an acoustic click or tone burst, used to obtain TEOE recordings, has broad spectral qualities. Such stimuli excite relatively broad regions of the basilar membrane. In contrast to TEOEs, DPEs are evoked using two continuous pure tones. Thus, relatively discrete regions of the cochlea are stimulated (Lonsbury-Martin & Martin, 1990), and inferences regarding both auditory sensitivity and localized OHC function may be made with greater precision. The better frequency specificity of DPEs, in comparison to TEOEs, has been predicted by a number of researchers (Lafreniere et al., 1991; Spektor et al., 1991). Some frequency-specific information can be obtained from TEOE recordings by either examining the spectral distribution of a click-evoked response or by using pure tone pips as the transient stimuli. However, to date, investigators have had difficulty making comparisons between frequency-specific audiometric (behavioral) thresholds and the frequency-specific information provided by TEOEs (Bonfils, Avan, Francois, Marie, Trotoux, & Narcy, 1990; Collet, Veuillet, Chanal, & Morgon, 1991; Lonsbury-Martin & Martin, 1990). Thus TEOEs appear to provide a measure of cochlear physiology and grossly infer audiometric sensitivity.

Another clinical advantage of DPEs over TEOEs relates to the range of hearing losses for which emissions can be recorded. While TEOEs are generally absent in ears in which

Figure 3. DPE recordings are highly consistent with the audiometric results. Highest DPE thresholds and lowest amplitudes are apparent for DPE test frequencies associated with this subject's highest behavioral thresholds. (See Figure 4 for audiometric results.)



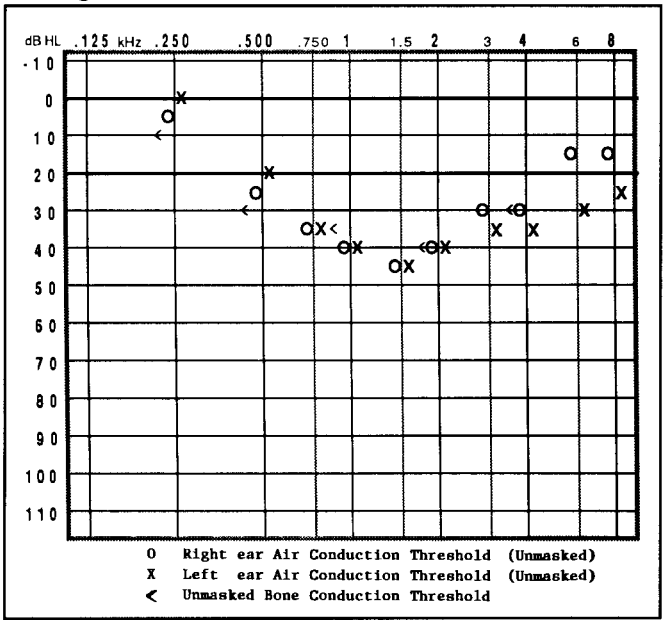
a hearing impairment of as little as 25-30 dB HL is present, DPEs may be assessed in patients whose audiometric thresholds are elevated to as much as 45 dB HL. In addition, DPEs show greater growth in amplitude with increases in stimulus intensity than do TEOEs (Lonsbury-Martin & Martin, 1990). Thus, DPEs may be used to study cochlear function at both threshold and suprathreshold levels. One clinical advantage of TEOEs over DPEs may be that transient stimuli may be somewhat more robust in compromised recording situations. Thus TEOEs, while not providing as much information, may have application for screening purposes.

Among the goals of our research is the identification of the precise relationship between DPE detection thresholds and pure tone hearing sensitivity. An understanding of that relationship is essential if DPE measurement is to gain acceptance as an objective diagnostic test in audiologic and otologic settings. Of the DPEs, the 2f1-f2 DPE has received the most investigation and is central to our research as well. A great deal of information remains unknown regarding the stimulus parameters necessary to elicit optimal DPE recordings and the nature of the subsequent analysis of the results.

Correlations Between DPE and Pure Tone Audiometric Thresholds

While emissions reflect cochlear physiology, pure tone behavioral thresholds not only reflect the auditory physiology at numerous parts of the auditory system, but also involve

Figure 4. Conventional audiometric results obtained from an adult male reveal a mild mid-frequency sensorineural hearing loss.



auditory perception as well. Despite these fundamental differences, attempts to define a relationship between DPE detection threshold (itself definable in various manners) and pure tone behavioral thresholds have yielded largely consistent results. Most published reports have revealed a positive relationship: that DPE thresholds are elevated in subjects demonstrating elevated audiometric thresholds and that DPEs are absent (i.e., not detectable above the noise floor) whenever hearing sensitivity in a given frequency band is moderately or more significantly impaired.

Spektor et al. (1991) studied DPEs in 19 children and 7 adults with normal hearing or sensorineural hearing loss. They described a close qualitative relationship between pure tone audiometric thresholds and DPE thresholds. A consistently positive qualitative relationship between DPE thresholds and behavioral thresholds in children (age 4-10 years) was also demonstrated. However, those authors did not quantitatively correlate DPE thresholds with behavioral thresholds. Lonsbury-Martin and Martin (1990) assessed DPE thresholds and behavioral thresholds in subjects with OHC damage (noise-induced hearing loss) and observed that every 1 dB increase in behavioral hearing sensitivity was associated with a 1 dB increase in DPE threshold. They also observed that pure tone audiometric thresholds were greater than 20 dB HL when DPE threshold was greater than 63 dB SPL. Harris and Probst (1991) concluded that DPE threshold (which they defined as the first point in the DPE growth function which was no less than 5 dB above the level of the noise floor) provided a closer approximation to audiometric thresholds than either (1) DPE level at two pre-selected suprathreshold levels, or (2) the configuration of DPE growth functions at each frequency.

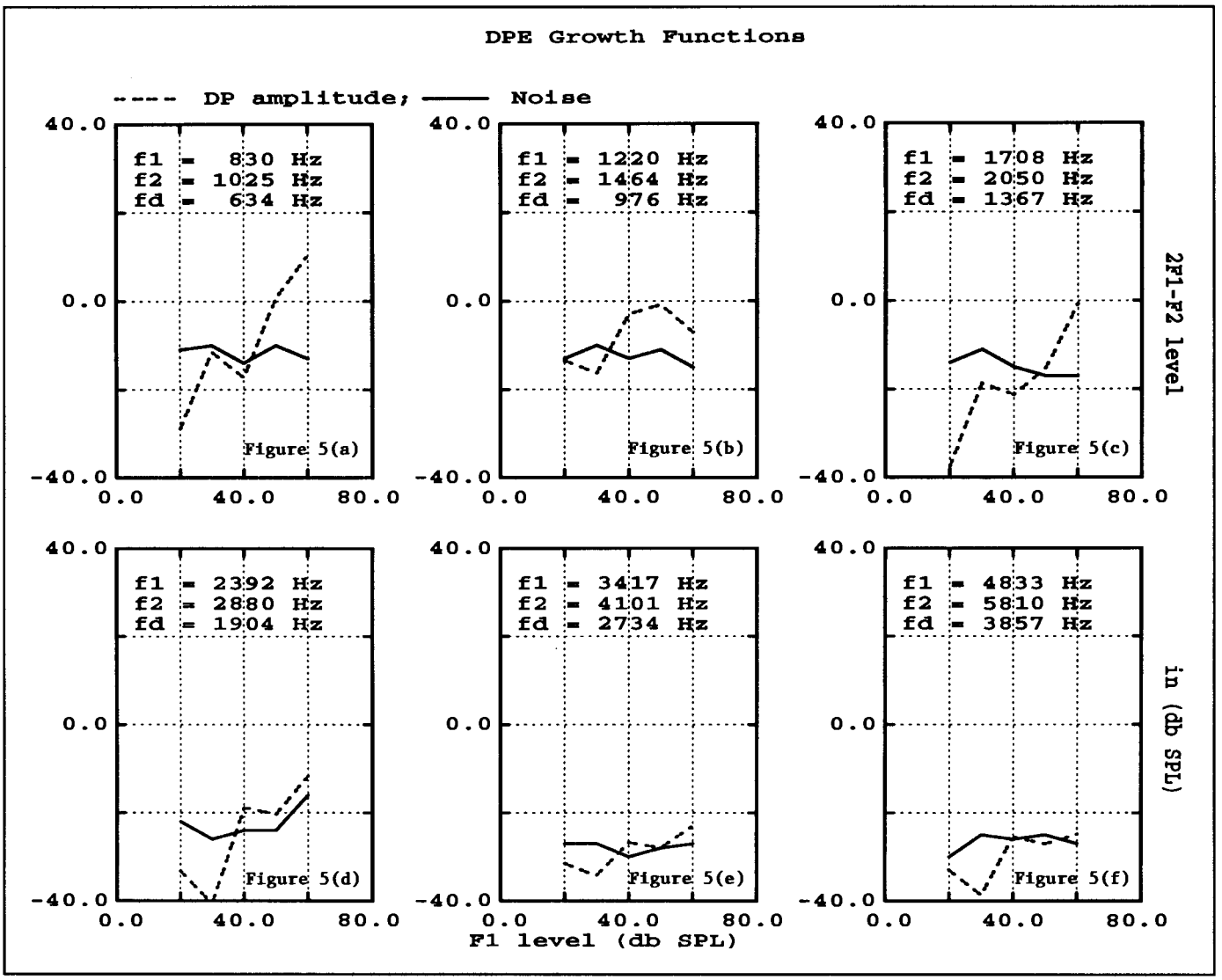
In their study of DPEs in subjects who presented with noise-induced hearing loss, Martin, Ohlms, Franklin et al., (1990) reported correlations (between DPE threshold and behavioral threshold above 1000 Hz) of +0.84 to +0.91 whenever a significant hearing loss was present. Kimberley and Nelson (1989) assessed DPE thresholds in 21 ears (11 subjects) across a frequency range of 700 to 6000 Hz. A linear fit to their data revealed a slope of 1 and correlation coefficients of up to +0.86 at some frequencies. Qualitative examination of their data suggested that frequency-specific auditory thresholds could be predicted to within 10 dB across a 60 dB range of hearing sensitivity. Thus, limited though consistent qualitative and quantitative evidence demonstrating the relationship between behavioral and DPE thresholds is available. However, at the present time, there are no quantitative studies identifying a precise mathematical relationship such that behavioral thresholds may be accurately predicted. DPE measurements are of obvious clinical value as a hearing screening device and as a way of categorizing pure tone hearing sensitivity into general classes (e.g., normal, borderline to mildly impaired (20-30 dB), and moderately {> 45 dB HL} or more significantly impaired). However, additional research in this area is needed in order to predict behavioral thresholds from DPE threshold values.

Technical Aspects of Recording DPEs

As is the case when conducting auditory brainstem response (ABR) assessments, there are numerous technical and analytical factors that must be taken into consideration when conducting DPE assessments. Among the relevant factors are the placement depth and acoustic seal of the probe assembly in the ear canal, calibration procedures, standards of acceptable noise levels, approaches to signal averaging and noise rejection, the absolute and relative frequencies and levels of the primaries, and definitions of DPE threshold. Presently, there are no universally accepted standards in these areas, nor is there sufficient research to support the selection of standards in some of these areas.

Given the low amplitude of otoacoustic emissions, typically between -30 dB SPL and +25 dB SPL, it is not surprising that noise has deleterious effects on the accuracy of DPE measurements, particularly DPE threshold. The type of averaging used during signal analysis affects the accuracy of DPE threshold measurement. Kimberley and Nelson (1990) were the first investigators to demonstrate the efficacy of time-averaged DPEs. Previously, root-mean-square (RMS) averaging was employed routinely. RMS averaging, also

Figure 5. A pattern of progressively diminishing DPE amplitudes with increased stimulus frequency is apparent in this ear. (See Figure 6 for audiometric results.)

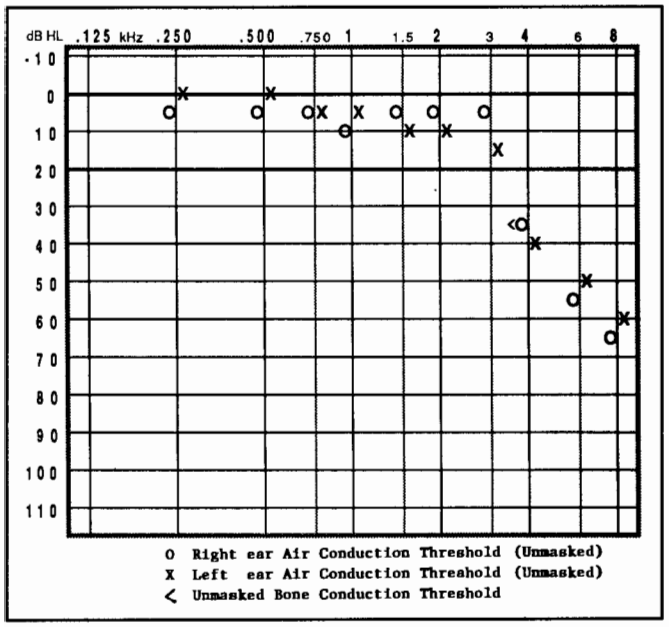


known as spectral averaging, "smooths" the noise floor but does not improve the signal-to-noise ratio. Typical noise floor values using RMS averaging are in the -10 dB SPL range, whereas time averaging results in noise floor values in the -25 to -30 dB SPL range. Time-averaging accomplishes both a reduction in the noise floor and permits measurement of the DPE across an extended amplitude range. Another method of minimizing the effects of noise on the collection of DPEs (and thus maximizing the accuracy of DPE feature measurements) is through the use of noise rejection algorithms. In the course of our research, we continually experiment with various noise rejection algorithms and have observed significant improvements in the quality of our DPE recordings. Details regarding these algorithms will be published in the near future.

The amplitude of a DPE depends upon the ratio of the primaries (f1, f2), the absolute frequencies of the primaries, and the primary tone levels (Probst, Lonsbury-Martin, & Martin, 1991). Distortion product emissions are evoked using two continuous pure tones, f1 and f2, where f1 < f2, and two levels (amplitudes), L1 and L2, where L1 > or = L2. Presently, an f2:f1 ratio of 1.2 to 1.3 appears to be most effective in eliciting DPEs of maximal amplitude (Harris, Lonsbury-Martin, Stagner, Coats, & Martin 1989).

The DPE measurement system in use at our facility includes the ARIEL 16 digital signal processing board, the Etymotics ER-10B microphone, and the Etymotics ER-2 insert ear phones. We have implemented a modified version of

Figure 6. Conventional audiometric results obtained from an adult male demonstrate a mild to moderately-severe high frequency sensorineural loss. (DPE results shown in Figure 5.)



the Cubdisp Version 2.10 program (c AT & T Bell Labs) on a Packard Bell 386 computer (Dos 5.0; 25 MHz processor speed; 4MB RAM memory). The modified software is fully described in the User Manual for the CUBEDIST distortion product measurement system Version 2.40 from Etymotic Research (August, 1992). Briefly stated, the modified software (Cubdisg) requires the user to specify starting frequency and a multiplier to be used for subsequent frequences (default = 1.41). The user also specifies the range of primary level (L1) and the incremental step size. The frequency ratio of the primaries may also be user-selected. A noise rejection routine rejects measurements made when the noise floor level exceeds the user-selected maximum value. Growth functions are measured by holding f1 and f2 constant, while systematically increasing their amplitudes, and recording the amplitudes of both the noise floor and the DPE. DPE "detection" threshold may be defined in various manners: The primary level at which the DPE is 2 - 5 dB above the noise floor is frequently chosen to represent DPE detection threshold. For the purpose of quantifying the DPE detection threshold - pure tone behavioral threshold relationship, DPE detection threshold and the behavioral threshold nearest the f2 frequency associated with the DPE are correlated. Other researchers believe that the cochlear place near the geometric mean frequency (f_{gm}) of the primaries is responsible for the generation of the emission and therefore associate pure tone behavioral data with f_{gm} instead of f2 (Smurzynski, Leonard, Kim, Lafreniere, & Jung, 1990; Martin, Probst, & Lonsbury-Martin, 1990).

Qualitative Examination of DPE Recordings

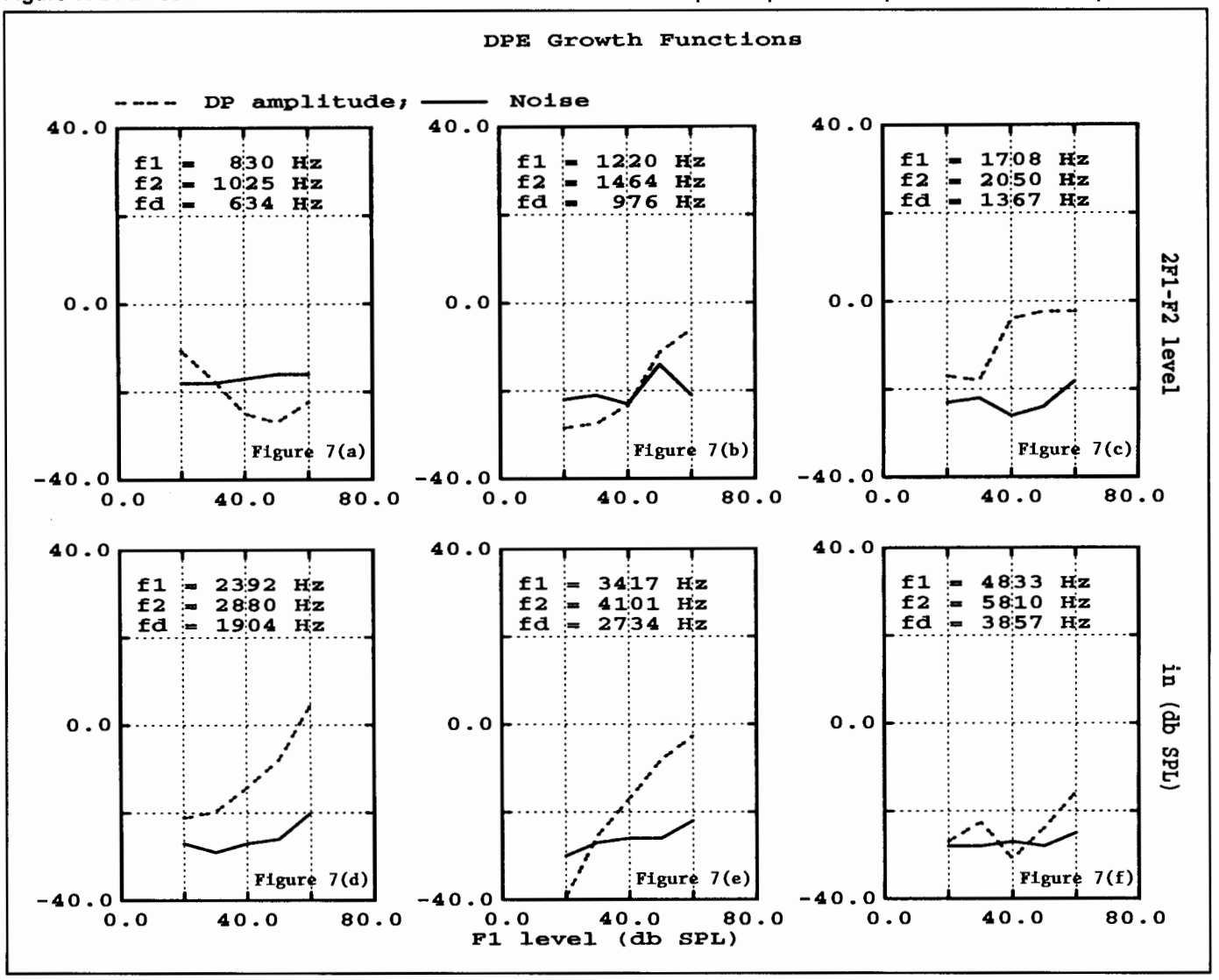
Some examples of DPE I/O functions in adults and in a full-term neonate are presented below. They serve to demonstrate the qualitative resemblance between DPE thresholds and pure tone audiograms of various configurations. In all of these examples, the frequency ratio was between 1.19 and 1.24, L1 exceeded L2 by 10 dB, and L2 ranged from 30-60 dB SPL in 10 dB steps. Pure tone audiometric results were obtained using a Virtual model 320 (Version 2.1) audiometer. Time-averaging and advanced noise-rejection algorithms were employed in the recording of these results. The noise floor is given by the solid line, and the DPE is represented by the dashed line. The frequency of the DPE is noted within each graph and abbreviated as "fd." Wherever applicable, qualitative examination will reveal a DPE threshold just above the noise floor on the positive slope of the DPE function. Adult data were obtained in a sound booth, while the neonate data were collected in a small, untreated room in the maternity ward of a hospital.

Normal hearing (Figure 1). Audiometric thresholds (250-8000 Hz) in this subject's right ear were all better than 15 dB HL. Examination of the DPE data reveals strong emissions at all test frequencies. In Figure 1(a), the DPE threshold for f2 = 1025 Hz, which is associated with pure tone results in the 1000 Hz range, is approximately 20 dB SPL. Note the non-linear growth in DPE amplitude with stimulus amplitude. In Figure 1 (b), the DPE threshold for 1464 Hz is approximately 39 dB SPL. Figure 1 (c) reveals a DPE threshold of approximately 30 dB SPL and a non-monotonic pattern of growth in the response. Figures 1 (d) and (e) show low DPE thresholds with evidence of saturation in the growth function at higher stimulus levels. Figure 1(f) also shows a low DPE threshold and a non-linear growth function.

Neonatal screening (Figure 2). These DPE recordings were recorded in the right ear of a healthy, 3-day-old full-term infant. Note the low thresholds (20 dB SPL) and high amplitudes of the emissions, which are clearly present at all test frequencies and suggestive of excellent hearing between 1025 and 5800 Hz and normal middle ear function. As expected, the noise floor (dotted line) was higher in the low frequencies than in the high frequencies (Figure 2a). Note that the high DPE amplitudes obtained from this neonate are typical of normal hearing neonates.

Mild sensorineural loss (Figures 3 and 4). These DPEs were recorded in the right ear of an adult male with a mild, bilateral, familial hearing loss (see audiogram in Figure 4). DPEs are absent at 1025 Hz and 1464 Hz (Figure 3a and b), and DPE threshold is quite elevated at 2050 Hz (Figure 3c). This finding is consistent with the elevated (40-45 dB HL) behavioral

Figure 7. DPE results obtained from an adult female ear in which a patent pressure equalization tube was present.



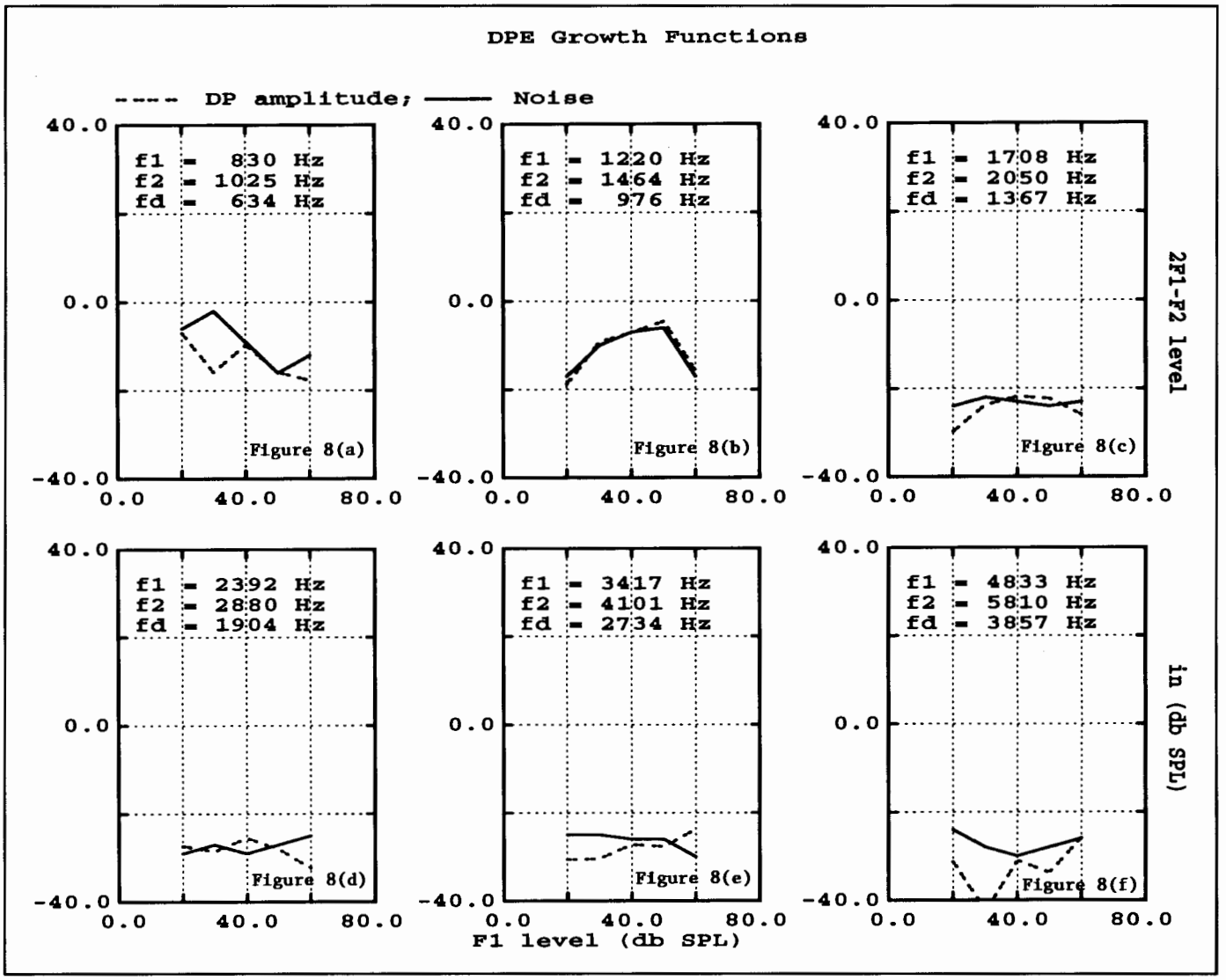
thresholds in the 1000 to 2000 Hz range. Figures 3(d), (e), and (f) demonstrate increasingly strong emissions and decreasing DPE thresholds, consistent with the increasingly lower behavioral thresholds (< 30 dB HL) obtained behaviorally from 2800 to 5700 Hz.

High frequency sensorineural loss (Figure 5 and 6). DPEs were recorded from the right ear of an adult male whose audiometric thresholds are presented in Figure 6. Figures 5 (a) and (d) demonstrate clear though progressively diminishing DPE amplitudes. Consistent with the elevated behavioral threshold at 4000 Hz, DPE testing at 4101 Hz (Figure 5e) reveals poor emissions, barely above the noise floor at the highest level of stimulation, and no DPEs at 5810 Hz (Figure 5f).

Normal hearing & Pressure Equalization Tube (Figure 7). These DPE results were obtained from an adult female whose left eardrum contained a PE tube. Her hearing was well within normal limits in that ear. Note that DPEs were not measurable at 1025 Hz, but were measurable at and above 1400 Hz (Figure 7b). This is an interesting finding given the anticipated use of DPEs in hearing assessments of young children—an age group in which middle ear pathology often necessitates the use of PE tubes. Additional testing of persons with normal hearing and PE tubes will reveal if this pattern of results is consistently obtained.

Moderate flat sensorineural loss (Figure 8). These DPE results were recorded from the left ear of an adult male who

Figure 8. DPEs could not be measured above the noise floor at any frequency. This subject's audiometric evaluation revealed a moderate (50-60 dB HL) flat-configuration sensorineural hearing loss.



presented with a moderate (50-60 dB) bilateral hearing loss from 250 Hz to 8000 Hz. DPE results are consistent with the configuration and severity of the hearing loss because the DPEs cannot be measured above the noise floor at any of the test frequencies.

Future Research

There are a number of DPE features that may be clinically valuable in the prediction of behavioral sensitivity. The use of DPE threshold to estimate behavioral hearing sensitivity has received considerable attention from researchers and has given rise to the concept of a "DPE audiogram." We believe that the use of time-averaging and certain noise rejection algorithms will improve the signal-to-noise ratio such that improved DPE feature extraction will lead to better correlations, and greater predictive strength will be achieved. Other DPE features or other approaches to the task also may prove to be of value.

Subcategorizations of DPE growth functions have been made (Nelson & Kimberley, 1992), but additional research in this area is indicated because the clinical value of such information is not yet apparent. This approach may offer new insights into normal or pathological cochlear processes.

Another approach may be using normative data, based upon DPE amplitudes at a pre-selected suprathreshold level, to make inferences regarding hearing sensitivity instead of seeking an equation that predicts behavioral thresholds from DPE threshold values. Research indicates that DPE amplitudes tend to decrease with increasing age (Kemp et al., 1990; Lonsbury-Martin et al.,1990; Spektor et al., 1991) and that DPE recordings from newborns are qualitatively similar to adult data (Lafreniere et al., 1991; Spektor et al., 1991). Results obtained from newborns also show similar test-retest reliability to that which has been observed in recordings from adults (Spektor et al., 1991).

A number of factors may account for the larger amplitudes of DPEs obtained from neonates. Differences in neonate external and middle ear properties (canal length, canal volume, tissue density, probe placement and acoustic seal, middle ear reverse transmission efficiency) may affect both the evoking stimuli and the emissions. Differences between neonatal and mature cochlear mechanics and the deleterious effects of socioacusis, which may become evident in adult ears, may also account for such findings. Reports describing changes in DPEs with advanced age (> 60 years) are not yet available. However, one study demonstrated the systematic decrease in DPE amplitude at every frequency with increased age up to the age of 60 (Lonsbury-Martin, Cutler, & Martin, 1991). Bonfils, Bertrand, and Uziel (1988) studied click-evoked emissions in persons up to the age of 88 years in whom hearing sensitivity was considered normal-for-age. Their results revealed increased absolute and relative (dB SL) emission thresholds with increased age above 40 years and 30 years respectively, and a much reduced incidence of emissions (35%) in persons aged 60 years and over as compared with a 100% incidence below the age of 60. Only additional research will identify the cause(s) of the high DPE amplitudes in neonates and young children, and the cause of changes in DPE features in older adults. However, given age-related differences, it is likely that normative data will be necessary if DPE thresholds and amplitudes are to be employed clinically.

Another potentially relevant factor may be the existence of gender-based differences in emission features or thresholds. These authors are aware of only one published study in which gender-based differences in evoked emissions were assessed (Lonsbury-Martin, Harris, Stagner, & Hawkins 1990).

The clinical applications of DPEs are not restricted to hearing screening and the eventual prediction of behavioral thresholds. Other applications include the monitoring of cochlear function in progressive or fluctuating hearing loss, the monitoring of the effects of medical treatments, and the differential diagnosis of cochlear from retrocochlear pathologies, possibly including acoustic neuromas. Lonsbury-Martin and Martin (1990) demonstrated that, in a patient with a surgically confirmed 2 cm acoustic neuroma and a mild flat hearing loss, DPEs were present and showed normal growth functions as per the authors' norms. Lutman et al. (1989) used click-evoked emissions, ABR, electrocochleography (ECoG), and magnetic resonance imaging (MRI) in the assessment of a child with a profound unilateral neural hearing loss. TEOEs were present, ECoG results were suggestive of eighth nerve pathology, and MRI results were negative. Clinical research will identify the hit rate of DPEs in this application.

Conclusions

The clinical potential of DPEs is great. In one rapid, non-invasive, and objective tool there is the opportunity to: (1) objectively and rapidly conduct hearing screenings; (2) objectively and rapidly obtain general estimates of frequency-specific auditory thresholds in the absence of reliable behavioral data (e.g., for infants, toddlers, mentally/multiply-handicapped persons, in cases of non-organic hearing loss, and in suspected malingerers) or to supplement behavioral data; (3) objectively monitor fluctuating or progressive cochlear pathologies or the deleterious effects of noise exposure; (4) perhaps differentially diagnose cochlear from retrocochlear pathologies and one cochlear pathology from another; and (5) develop a greater understanding of the complex processes comprising the peripheral auditory system.

Recently, hardware and software designed to assess click-evoked and distortion-product emissions in clinical settings have become commercially available. This is a positive development because the utilization of evoked emission measures in many clinics and across a wide variety of clinical populations will surely enhance our understanding of evoked emissions and their clinical value. Nonetheless, in light of the numerous factors discussed above, it appears unlikely that optimal DPE recordings and valid clinical interpretations of DPE results will be achieved without additional basic and applied research.

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