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I am submitting herewith a thesis written by Pritesh K. Pandya entitled "Evaluation of the Human Frequency Following Response Distortion Product at 2F1-F2." 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 Master of Arts, with a major in Audiology.

A.K. Ananthanarayan, Ph.D., Major Professor

We have read this thesis
and recommend its acceptance:

Accepted for the Council:

Associate Vice Chancellor and
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EVALUATION OF THE HUMAN FREQUENCY FOLLOWING RESPONSE DISTORTION PRODUCT AT 2F1-F2

A Thesis Presented for the Master of Arts Degree
The University of Tennessee, Knoxville

Pritesh K. Pandya
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DEDICATION

This thesis is dedicated to the faculty, staff, and students in the Audiology department at the University of Tennessee. From top to bottom, this is a first class operation. It has been my honor to have been given the opportunity to mature as an individual and develop life long relationships with the people at this institution.

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A special note of appreciation to my fellow students

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ABSTRACT

The present study evaluated certain response characteristics of the human frequency following response distortion product at 2F1-F2 (FFR-DP). The specific aspects evaluated included: (i) the Input-Output growth characteristics for three frequency pairs, (ii) the nature of the 2F1-F2 (FFR-DP) amplitude on primary tone level variations (L2-L1), and (iii) evaluation of a possible brainstem component contributing to the generation of the 2F1-F2 (FFR-DP).

The results indicate a trend of decreasing magnitude of F1, F2, and the 2F1-F2 (FFR-DP) components with increasing frequency. Second, there is a clear decrease in slope of the growth function of 2F1-F2 (FFR-DP) with increases in the distortion product frequency. In addition, the slope of F2 and 2F1-F2 components are essentially parallel for two of the stimulus pairs evaluated which may suggest a generation site consistent with the F2 place on the cochlea. Third, the percent detectability of the 2F1-F2 (FFR-DP) increases with intensity. Higher frequency distortion products were the most difficult to identify. An additional response

characteristic of the 2F1-F2 component was that there was a distinct region where the separation of the primary tone levels produced maximal distortion. Thus, the level differences generating the maximal distortion product component depends upon L1. Finally, there appears to be minimal brainstem contribution to the 2F1-F2 (FFR-DP).

An advantage of this mode of measurement is that it can be used in evaluating nonlinearities of the auditory system generated from apical regions of the cochlea. In addition, the neural response behavior at the primary frequencies as well as the distortion product frequencies can be assessed. Evaluation of these individual components and their interactions may provide insight to our understanding of the mechanisms governing these nonlinearities.

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CHAPTER I

INTRODUCTION AND REVIEW OF LITERATURE

OVERVIEW

It is well documented that the auditory system responds in a complex and nonlinear manner by the presence of harmonic and intermodulation distortion products (Dallos and Sweetman, 1969; Goldstein, 1967; Goldstein and Kiang, 1968; Humes, 1980; Kim, Molnar, and Matthews, 1980; Smoorenburg, 1971a, 1971b; Worthington and Dallos, 1971). Intermodulation distortions occur in response to the presentation of two tones in a nonlinear system. When two tones are presented at F1 and F2 (F1<F2), the measured output signals show energy at F1 and F2 and harmonics of each. In addition, energy at other frequencies known as combination tones are present as well. Combination tones occur at F2-F1 (the difference tone or DT), at F1+F2 (the summation tone or ST), and at 2F1-F2 (the cubic difference tone). The most prominent combination tone in the auditory system is present at 2F1-F2. These intermodulation distortion products are reflections of the nonlinearity of the auditory system. Of interest in this study is the cubic

difference tone distortion product recorded in neural responses.

Two techniques to assess the intermodulation distortion products reflecting cochlear nonlinearity in the auditory system are otoacoustic emissions and auditory evoked potentials (AEP). Distortion product otoacoustic emissions (DPOAE) provide a measure index of nonlinearity at the hair cell (cochlear) level and AEP distortion products provide neural reflections of, presumably, cochlear nonlinearity. Otoacoustic emissions reflect nonlinearities transmitted in reverse direction from the cochlea. AEP distortion products may reflect intermodulation distortion generated in the cochlea that is encoded in neural activity at the brainstem. Cochlear distortion products and neuronal distortion products should anatomically complement one another assuming there is no central component in distortion products recorded in AEP. Very few studies have been done on the AEP distortion products and to date, the growth rate of the distortion product at 2F1-F2 in AEP as a function of stimulus intensity has not been acquired. In addition, the dependance of relative level of the primary signals on AEP distortion product amplitude have not been investigated.

Finally, the determination of whether there is a central component to the 2F1-F2 neural distortion product as a potential generator has not been explored.

OTOACOUSTIC EMISSIONS

Otoacoustic emissions are a release of acoustic energy from the cochlea (reverse direction), transmitted through the middle ear into the ear canal (Kemp, 1978). They can be measured objectively as responses to click or tonal signals or as intermodulation products from stimulation with two tones (Kemp, 1979; Lonsbury-Martin, Martin, Probst, and Coats, 1987). Responses to clicks or tonal signals are referred to as Transient Evoked Otoacoustic Emissions (TEOAEs), whereas responses evoked from stimulation with two tones are called Distortion Product Otoacoustic Emissions (DPOAEs). Both types of emissions provide information about cochlear function in response to stimulations by sound energy. These emissions are a phenomenon in which outer hair cells generate an active mechanical metabolic response to stimulations by sound (Brownell, 1990). Biomechanical energy from the outer hair cells is transmitted in reverse fashion through the fluids in the cochlea, through the middle ear, and back into the external auditory canal where

it is measured as acoustic energy (Kemp, 1978). This active metabolic process may explain the very high sensitivity (i.e. low threshold) of the inner ear to sound stimulation, the sharp frequency selectivity, and the wide dynamic range of normal auditory systems.

DPOAE: Response Characteristics

The DPOAE can be recorded reliably for high frequency primaries, e.g., 2, 4, and 8 kHz (Chertoff and Hecox, 1992). Detectable DPOAEs have been shown to be present in a majority of normal ears (Probst, 1990; Harris, Lonsbury-Martin, Stagner, Coats, and Martin, 1990). Specific stimulus parameters are needed to evoke optimum DPOAEs in normal hearing individuals. These include i) frequency separation of the primary signals or the F2/F1 ratio and ii)the relative amplitudes or levels of the primary signals. These two parameters are interrelated in a complex manner.

The effects of F2/F1 ratio or the frequency separation of the primary signals required to find maximal 2F1 - F2 has been studied by several investigators. Harris, Lonsbury-Martin, Stagner, Coats, and Martin (1989) showed that larger ratios (i.e. greater separation of the primaries) were more effective at generating DPOAEs at 1kHz than at 4kHz. This

was because the F2/F1 ratio is inversely related to DPOAE frequency. They found a nonmonotonic change in DPOAE amplitude as F2/F1 ratio was increased. In their study, DPOAE were elicited using equilevel primary signals at 65, 75, and 85 dB SPL. They noted that DPOAE amplitude as a function of primary tone level was directly related to the frequency separation of the primary tones. Smaller F2/F1 ratios generated robust DPOAEs at 65 dB stimuli, whereas larger ratios elicited larger responses with primary signals at 75 and 85 dB SPL. When all stimulus conditions were considered, they concluded that a F2/F1 ratio of 1.22 on average yielded the maximal DPOAE.

Gaskill and Brown (1990) also explored the effects of primary signal separation (i.e. F2/F1 ratio) and primary signal levels on DPOAEs. Their results agreed with the those of Harris et al. (1989) showing a best average optimal frequency separation ratio to obtain the largest DPOAEs is 1.225 when all conditions are considered. Using this F2/F1 ratio, they varied the levels of the primary signals and evaluated the effects on the DPOAE. They observed that as the level of one stimulus is increased relative to the other, the DPOAE grows, saturates, and in most cases shows a

non-monotonic growth function.

DPOAE: Presumed Origins

The source of the OAE is thought to be the outer hair cells on the basilar membrane (Khanna, Ulfendahl, and Flock, 1990; Brownell, 1990). Studies utilizing ototoxic agents and high noise levels to damage the outer hair cells of the cochlea show a decrease or obliteration of OAEs (Kim, 1980; Kemp and Brown, 1984). In addition, suppression studies by Kemp (1979) have demonstrated a reduction in the level of OAEs due to the introduction of additional tones to the cochlea. These studies suggest that there is a strong correlation between OAE origin and outer hair cell function. Although DPOAEs originate from the cochlea, the specific origin of the 2F1-F2 cubic difference tone is unknown. An early study by Wilson (1980) suggested a generation site associated with the frequency of the 2F1-F2. Martin, Lonsbury-Martin, Probst, Scheinin, and Coats (1987) attempted to determine if DPOAE originated from activity at the place associated with the frequency of the distortion product (the place on the cochlea at 2F1-F2) versus the place associated with the area of maximum overlap between the primary signals F1 and F2 (i.e. near the geometric mean

of the two primaries). Using suppression and interference tone techniques, they found that the DPOAE at 2F1-F2 was suppressed most when the suppressor was in the area of the geometric center of the primary signals. Although the primary contribution is in the region of maximum overlap, the area surrounding F1 and F2 also contributed to the creation of the DPOAE. Suppression studies by Brown and Kemp (1984), however, show that 2F1-F2 DPOAE was suppressed most effectively when the suppressor tone was nearest to the higher primary frequency F2. In addition, latency studies by Stover, Neely, and Gorga (1994) support the 2F1-F2 origin more consistent with the F2 place on the cochlea.

FREQUENCY FOLLOWING RESPONSE (FFR) AND ITS RESPONSE CHARACTERISTICS

The frequency following response (FFR) is an auditory evoked potential that reflects sustained neural activity phase-locked to the individual cycles of the stimulus waveform (Worden and Marsh, 1968). The first report of the FFR recorded from the human scalp were published by Moushegian et al. in 1973. It is a true neural potential and is complex of many distinct components. Evidence suggests an upper brainstem source of the human FFR. For

example, the onset latency of the FFR recorded from the scalp and from the inferior colliculus (IC) brainstem nuclei was found to be similar (Smith, Marsh, and Brown, 1975). In addition, the FFR has been recorded bilaterally from the IC, the medial superior olive (MSO), and from the scalp. Cryogenic cooling of the IC resulted in reduced amplitude of FFR recordings at both IC and scalp FFR. The FFR recorded from the MSO remained at control amplitudes. Thus, the primary generator of the FFR seems to be the inferior colliculus (Smith, Marsh, and Brown, 1975). Variables affecting the FFR are stimulus frequency and intensity. The upper frequency limit of the FFR is about 1.5 kHz or 2kHz (Moushegian, Rupert, and Stillman, 1973; Glaser, Suter, Dasheiff, and Goldberg, 1976). As stimulus frequency increases, the amplitude of the FFR declines. In addition, the FFR increases in amplitude and decreases in latency with increases in stimulus intensity. The FFR is generally present at stimulus intensities greater than 25 to 50 dB SL (Moushegian, Rupert, and Stillman, 1973; Marsh, Brown, and Smith, 1975).

FREQUENCY FOLLOWING RESPONSE DISTORTION PRODUCT (FFR-DP)

An electrophysiological technique/paradigm which assesses intermodulation distortion in the auditory system has been introduced by Chertoff and Hecox (1990). Using spectral analysis of the FFR to two tone signals, they noted intermodulation distortion products at the difference tone and cubic difference tones which were not stimulus artifact and were definitely neural in origin. The Chertoff and Hecox paradigm has been introduced to measure the nonlinearity in neural responses. Since the intermodulation distortion product in this study is at 2F1-F2, the evoked potential distortion product will be referred to as the 2F1-F2 (FFR-DP) for the remainder of this document.

The Chertoff and Hecox Methodology for 2F1-F2 (FFR-DP)

The Chertoff and Hecox paradigm utilizes spectral analysis of evoked responses to two tone signals. Initial studies were done using alternating polarity, thereby eliminating odd-order distortion products such as the cubic difference tone at 2F1-F2. Odd-order distortion products using alternating polarity are canceled after averaging. Therefore, in order to enhance odd-order distortion products in the FFR, specifically at 2F1-F2, summed responses to

condensation onset polarity were subtracted from summed responses to rarefaction onset polarity (Rickman et al., 1991). Subsequently, a Fast Fourier Transform (FFT) was calculated on the resultant waveform.

2F1-F2 (FFR-DP): Response Characteristics

The 2F1-F2 (FFR-DP) was obtained 73% of the time with the greatest percentage of responses occurring for the 1400 Hz primary F1 (Chertoff and Hecox, 1992). They found that the 2F1-F2 (FFR-DP) increased with increasing F2/F1 ratios for the 500 Hz primary and remained constant for 800 Hz and 1700 Hz. The largest proportion of responses were at a frequency separation of 1.32 (85%). The 2F1-F2 (FFR-DP) was found 77% of the time with a F2/F1 ratio of 1.22. The two tone signals in their study were presented at equilevels (L1=L2) of 75 dB SPL. Their data showed that the 2F1-F2 (FFR-DP) was not prominent for a 2 kHz primary. The amplitude of the FFR decreases with increasing frequency (Moushegian, Rupert, and Stillman, 1973) and for the 2 kHz primary, the 2F1-F2 (FFR-DP) is high in frequency and was difficult to distinguish from the noise floor. The FFR is primarily a low frequency phenomenon, and thus the 2F1-F2 (FFR-DP) provides information about apical regions of the

cochlea.

Neural Response of Auditory Nerve Fibers at 2F1-F2

Nonlinearities have been found in the neural discharge patterns of auditory nerve fibers. Kim, Molnar, and Mathews (1980) demonstrated the extent to which each fiber was driven by the primaries and by a combination tone. They produced a "neurogram" which produced peaks of activity at the characteristic place of the two primaries and also noted that the combination tone produced a peak at its own characteristic place on the cochlea. Their results suggest that the 2F1-F2 combination tone produces its own travelling wave in the cochlea. It also implies that the combination tone is produced where the primaries overlap because when the cochlea is noise damaged in one region, the response to the combination tone was reduced in fibers tuned to the combination tone (Siegel, Kim, and Molnar, 1982).

2F1-F2 Response Characteristics

Specific stimulus parameters are needed to evoke optimum distortion products in normal hearing individuals. These include i) frequency separation of the primary signals or the F2/F1 ratio and ii) the relative amplitudes or levels of the primary signals. These two parameters have been

shown to be interrelated in a complex manner as documented in numerous distortion product otoacoustic emission studies (Harris et al.,1989;Gaskill and Brown, 1990; Hauser and Probst, 1991).

The F2/F1 ratio has been studied in 2F1-F2 (FFR-DP) by Chertoff and Hecox (1992) and their results have already been summarized. Findings in animals have suggested that primary levels are most effective when L1 is 5-10 dB larger than L2 in DPOAEs (Wiederhold, Mahoney, and Kellogg, 1986). In human ears, the relationship of L1 and L2 on the 2F1-F2 (FFR-DP) amplitude has not been explored since Chertoff and Hecox presented their signals at equilevels (L1=L2) of 75 dB SPL.

RATIONALE FOR THE PRESENT STUDY

Based on the limited number of studies done on auditory distortion products measured with averaged auditory evoked potentials, specifically at 2F1-F2, further characterization of this response is warranted. Systematic measurements in 2F1-F2 (FFR-DP) amplitude with increases in the level of the primary signals have not been generated. In addition, the magnitude of the 2F1-F2 (FFR-DP) as a function of primary tone level variation has not been explored. Finally, the

primary generator of this response has not been established. It is plausible that the 2F1-F2 (FFR-DP) is simply a propogated neural representation of cochlear intermodulation distortion at the brainstem level. However, a central component may exist. Therefore, the present study focuses on three different aspects of the 2F1-F2 (FFR-DP). First, the Input-Output (I-O) function of the 2F1-F2 (FFR-DP) will be determined and evaluated across three frequency pairs. The second experiment will be conducted to explore the effects of relative level of the primary tones on the amplitude of 2F1-F2 (FFR-DP). The final experiment will investigate whether the 2F1-F2 (FFR-DP) is primarily a cochlear phenomenon by presenting F1 and F2 dichotically.

CHAPTER II

METHOD AND PROCEDURES

SUBJECTS

Twelve human subjects ranging in age from 19 to 25 years participated in these experiments. The criteria for inclusion in the study included: (i) hearing sensitivity of 20 dB HL or better for octave frequencies from 500 Hz to 8000 Hz for both ears; (ii) normal appearance of the ear canal; and (iii) normal tympanograms. All subjects were unpaid volunteers.

STIMULUS

The tone burst stimuli used in this study were complex tones formed by two frequency components, F1 and F2. The overall duration of each tone burst was 80 msec, including the 10 msec rise and fall times and 60 msec plateau duration. The nominal frequency values of the experimental stimuli and the constant F2/F1 ratio of 1.225 was chosen to optimize recording of the 2F1-F2 (FFR-DP) and so that it can be used in future comparisons with DPOAE data. A cosine squared gating was utilized to minimize spectral splatter of the tone burst stimulus. These tone bursts were digitally

synthesized and controlled by a signal generation and data acquisition system (Tucker-Davis System II) interfaced to a microcomputer (Zenith, 486DX, 66MHz). The synthesized stimuli files were then routed through a dual channel digital-to-analog module. All tone bursts were presented through magnetically shielded TDH-49 earphones encased in Mu-metal.

2F1-F2 (FFR-DP) RECORDING SYSTEM

Subjects reclined comfortably in an acoustically shielded room after being instructed to be quiet and remain still during the recording session. The 2F1-F2 (FFR-DP) Input-Output function was recorded differentially between scalp electrodes placed on the midline of the forehead at the hairline (FpZ) and the 7th cervical vertebra (C7 location). Another electrode placed on the left mastoid (A1) served as the common ground for the vertical configuration. The interelectrode impedances were maintained below 3000 ohms. EEG inputs were amplified by 200,000 and band pass filtered from 100 to 3000 Hz (6 dB/octave roll-off, RC response characteristics). Each response waveform represented an average of 1500 stimulus presentations over a 90 msec analysis window using a

sampling rate of 25 kHz. Sound levels are expressed as the sound pressure level measured in a 6 cc calibration cavity using a 1 inch condenser microphone coupled to a sound level meter.

RESPONSE EVALUATION OF THE 2F1-F2 (FFR-DP)

Fast Fourier Transforms (FFTs) were performed on the derived frequency following response (i.e. the waveform resulting from the subtraction of the FFR to the condensation polarity from the FFR to the rarefaction polarity in a given experimental condition). The magnitude of the spectral peak at the 2F1-F2 frequency in the FFT was taken as the amplitude of the FFR-DP. Subsequently, an Input-Output function was generated for each stimulus pair for Experiment One. For Experiment Two, the 2F1-F2 (FFR-DP) magnitude as a function of the relative levels of the primary signals was noted in the same way as Experiment One. Finally, for Experiment Three, the presence or absence of a peak at the 2F1-F2 frequency for the binaural response was compared to the response obtained monaurally.

EXPERIMENTAL PROTOCOL

There were at least two experimental sessions for each subject. At the start of the first session, the otoscopic and audiologic qualification previously described in the Subjects section of this chapter was performed. Subjects then read and signed the informed consent form containing all pertinent information about the experiments and their participation in it. The remainder of this session was devoted to data collection. For each primary pair and for each level, waveforms were obtained for both condensation and rarefaction onset polarities. The order of the primary frequencies and stimuli were randomized both within and across subjects. The tone burst pairs comprising the primaries were presented at a rate of 7.12/second.

A. Experiment One

The 2F1-F2 (FFR-DP) Input-Output function was generated using tone bursts composed of two frequency components (F1 and F2). The primary frequencies of these stimuli were: (i) F1=500 Hz, F2=612 Hz; (ii) F1=1000 Hz, F2=1225 Hz; and (iii) F1=1400 Hz, F2=1715 Hz. The levels of the primary tones were set at L2-L1=-5. Stimuli were presented monaurally at 65, 75, 85, and 95 dB SPL.

B. Experiment Two

As in Experiment One, the 2F1-F2 (FFR-DP) was elicited using a two tone complex burst presented monaurally. For this experiment, the primaries of the two tone frequency pair were F1=500 Hz and F2=612 Hz. These were recorded at L1=75 or 85 dB SPL with L2 set:

1. Equal in level (L2-L1=0)
2. F2 lower in level than F1 by 5 dB (taken from the Input-Output function in Experiment One; L2-L1=-5)
3. F2 lower in level than F1 by 10 dB (L2-L1=-10)
4. F2 lower in level than F1 by 15 dB (L2-L1=-15)

C. Experiment Three

For the dichotic listening situation, F1 (500 Hz tone burst) was presented to the right ear and F2 (612 Hz tone burst) was presented at the left ear. As with Experiment One, L2-L1=-5. This response was recorded at L1=75 dB SPL and L2=70 dB SPL. These levels were chosen because they resulted in easily discernable/recognizable 2F1-F2 (FFR-DP) response amplitudes (pilot data) and usually did not show saturation.

CHAPTER III

RESULTS

EXPERIMENT ONE: INPUT-OUTPUT CHARACTERSITICS

Waveform Data

Representative derived FFR waveform data (from one subject) obtained at 75 dB SPL for the the three stimulus pairs, is shown in Figure 1. Each response waveform in this figure represents the result of subtracting the FFR to condensation onset polarity from the FFR to rarefaction onset polarity for a given stimulus condition. Visual inspection of these complex response waveforms reveals only the expected reduction in the amplitude of response as the frequency of the stimulus pairs are increased. Results of the spectral analysis of these waveforms, presented in the following section, provide a more complete quantitative characterization of the behavior of the individual response components (F1, F2, and 2F1-F2).

Spectral Data

The mean spectra for the three frequency pairs are shown in panels A (F1=500 Hz,F2=612 Hz), B (F1=1000 Hz, F2=1225 Hz), and C (F1=1400 Hz,F2=1715 Hz) of Figure 2. For

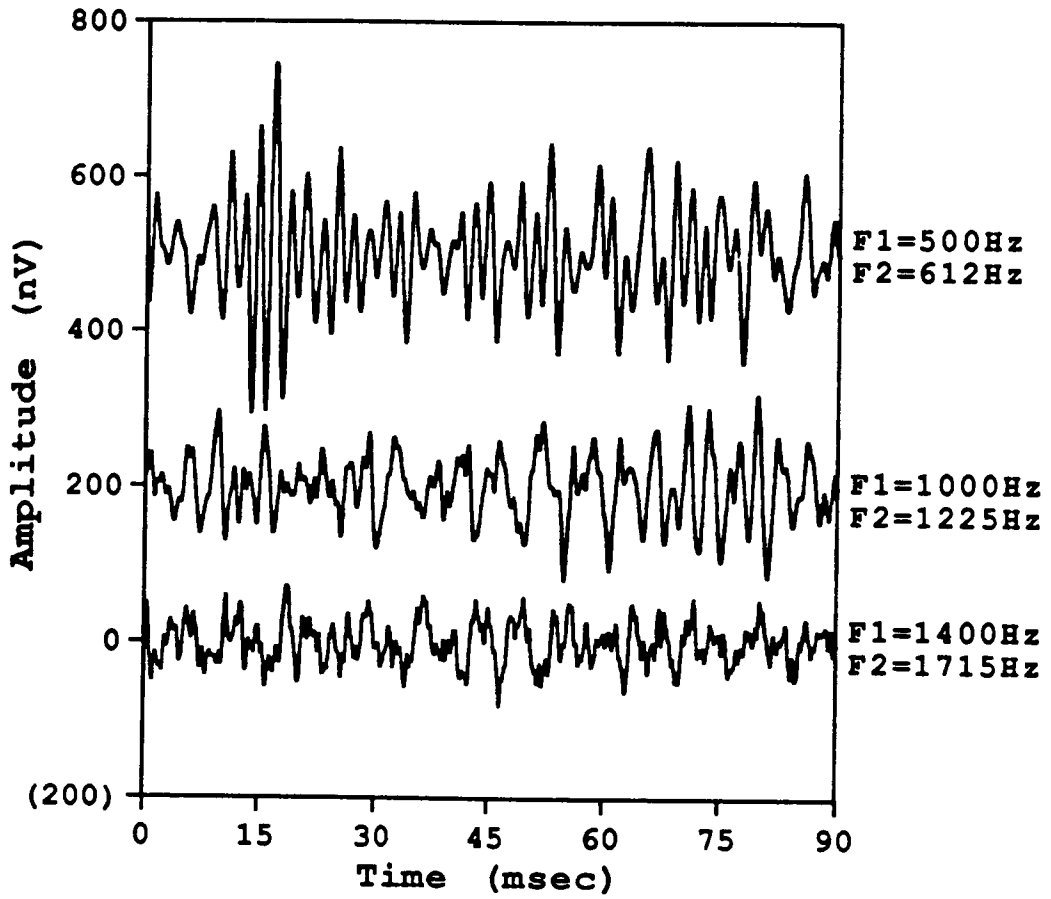

Figure 1. Derived Frequency Following Response (FFR) waveform data from one subject for the three stimulus pairs at 75 dB SPL. The frequencies of the stimulus pairs are presented to the right of each waveform.

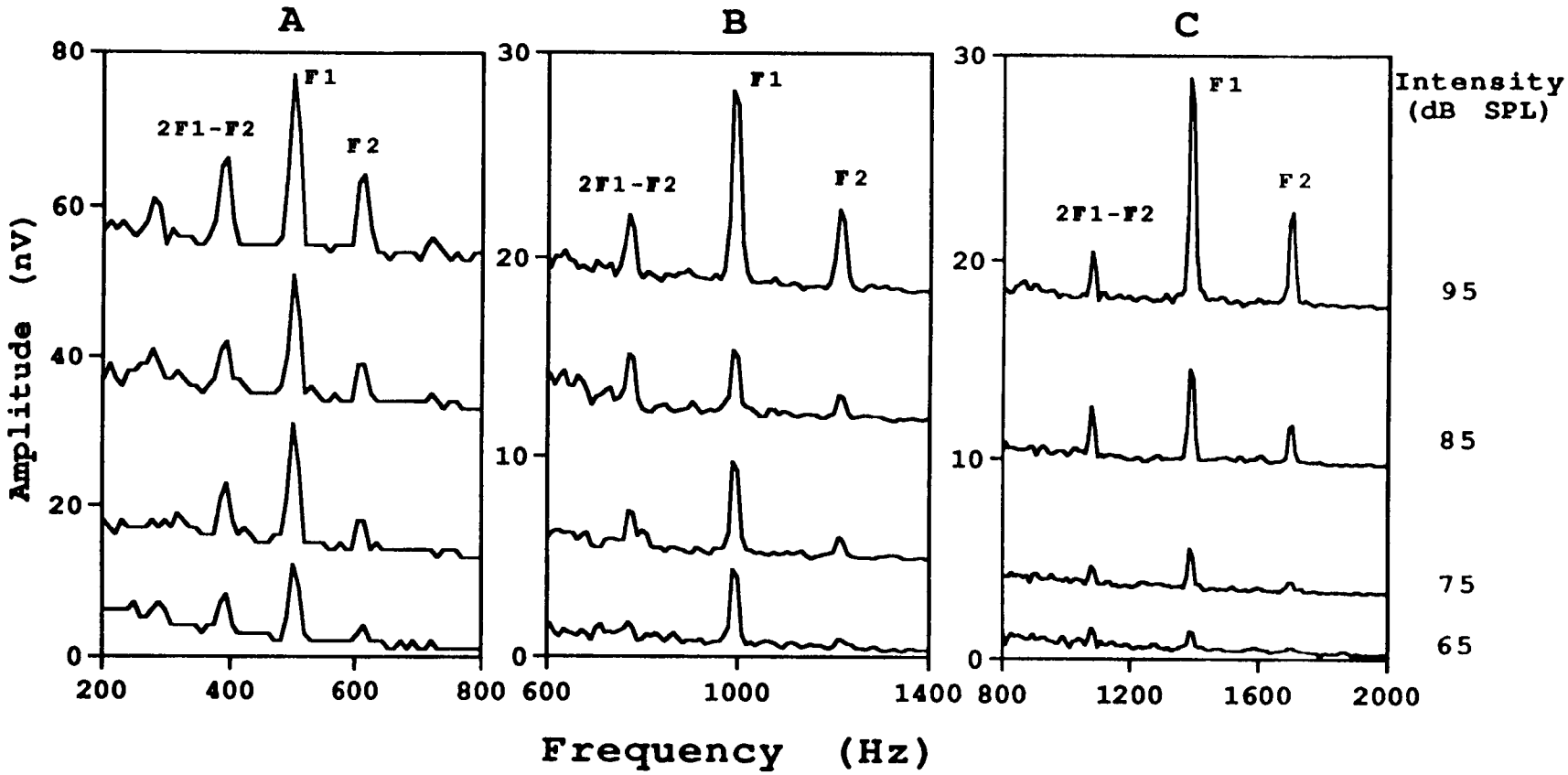

Figure 2. Mean spectrum of the derived FFRs at each level showing the response components F1, F2, and the 2F1-F2 (FFR-DP). Note the difference in the scaling of the vertical axis for Panels 2B and 2C.

each stimulus pair and across intensity, these spectral data clearly shows three robust response components identified as F1, F2, and 2F1-F2 (FFR-DP). It is clear that F1 has the largest amplitude and dominates the spectral data followed by the appreciably smaller peaks at 2F1-F2 (FFR-DP) and F2. The response peaks in general are more robust for the lowest stimulus frequency (Panel A). All the response components appear to increase in amplitude with increase in stimulus intensity. However, note that for the higher frequencies (Panels B and C) the 2F1-F2 (FFR-DP) response amplitude tends to saturate at the higher intensities. Finally, consistent with the waveform data, the amplitude of all response components tend to decrease with increasing frequency of the stimulus pair. The input-output characteristics of each response component in terms of the nature and rate of the amplitude growth with intensity and as a function of frequency is summarized in the next section.

Input-Output Functions for F1, F2, and 2F1-F2 (FFR-DP) Components

Shown in panels A, B, and C of Figure 3 are the mean amplitude of F1, F2, and 2F1-F2 (FFR-DP) plotted as a

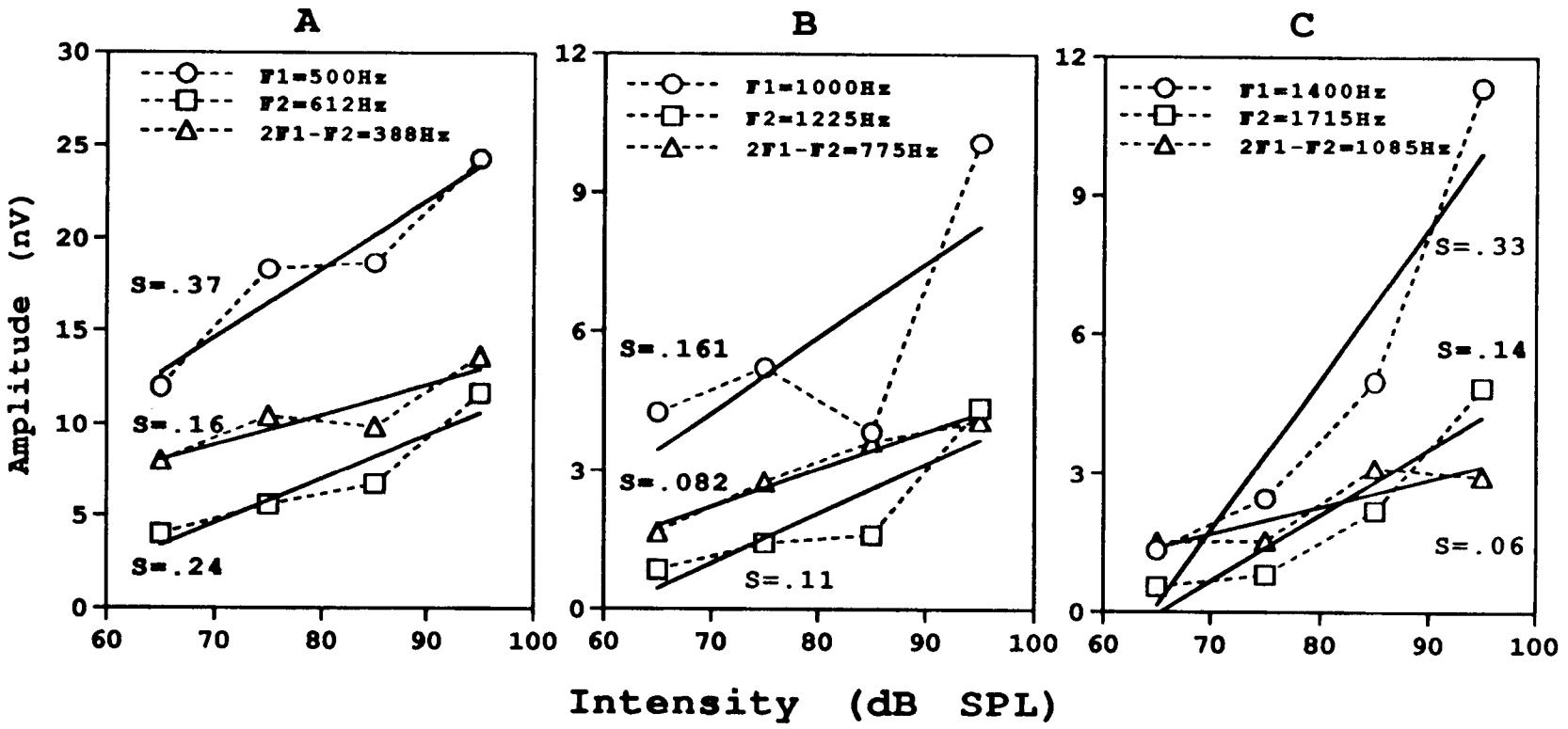

Figure 3. Mean response amplitude of F1, F2, and 2F1-F1 (FFR-DP) components for the three stimulus pairs plotted as a function of intensity. S denotes the slope of the growth function. Note the difference in the scaling of the vertical axis for Panels 3B and 3C.

function of stimulus intensity for the three stimulus pairs (i.e., the input-output functions). Consistent with the spectral data, the input-output functions for the three frequency pairs reveal that F1 has the largest amplitude across levels and stimulus pairs followed by 2F1-F2 (FFR-DP) and F2. All response components in general show amplitude increment as stimulus intensity is increased. For F1 and F2 at all frequencies and for the 2F1-F2 (FFR-DP) at the lowest frequency (Panel A) this amplitude growth is characterized by a knee-point at 85 dB SPL. The amplitude of the responses appear to grow more rapidly above the knee-point compared to the amplitude growth below the knee-point. In contrast, the growth functions of 2F1-F2 (FFR-DP) for the two higher frequencies (shown in Panels B and C) appears to saturate at the higher intensity levels.

Comparison of Slopes of the I-O Functions of F1, F2, and 2F1-F2 (FFR-DP) Across Frequency of the Stimulus Pairs

In order to compare the rate of growth of amplitude of the response components as a function of intensity, the mean data for each component was fit with a simple linear regression function of the form y= a + bx. The straight line function for each component is represented by the

darker solid line across the data points in Figure 3. The slope value in nV/dB is denoted by the letter "S". It is clear that for each stimulus pair F1 shows the steepest slope (0.37 for F1=500 Hz; 0.161 for F1=1000 Hz; and 0.33 for F1=1400 Hz) followed by appreciably less steeper slopes for F2 (0.24 for F2=612 Hz; 0.11 for F2=1225 Hz; and 0.14 for F2=1715 Hz) and 2F1-F2 (0.16 for 388 Hz; 0.082 for 775 Hz; and 0.06 for 1085 Hz). The similar slope values for F2 and 2F1-F2 (FFR-DP) is made clearer by the almost parallel regression lines for these two response components (see Panels A and B). However, note that this observation does not hold for the highest stimulus pair (Panel C) where F2 clearly shows a greater slope than the 2F1-F2 (FFR-DP).

The mean amplitude as a function of intensity is plotted in Figure 4 for the three stimulus pairs in order to specifically compare the input-output characteristics of just the 2F1-F2 (FFR-DP) as a function of frequency. It can be seen that the slope of the input-output function decreases with increasing frequency of the 2F1-F2 (FFR-DP). The earlier indicated trend for the higher frequency 2F1-F2 (FFR-DP) to saturate at higher intensities is clearer in this figure, particularly given the error bars.

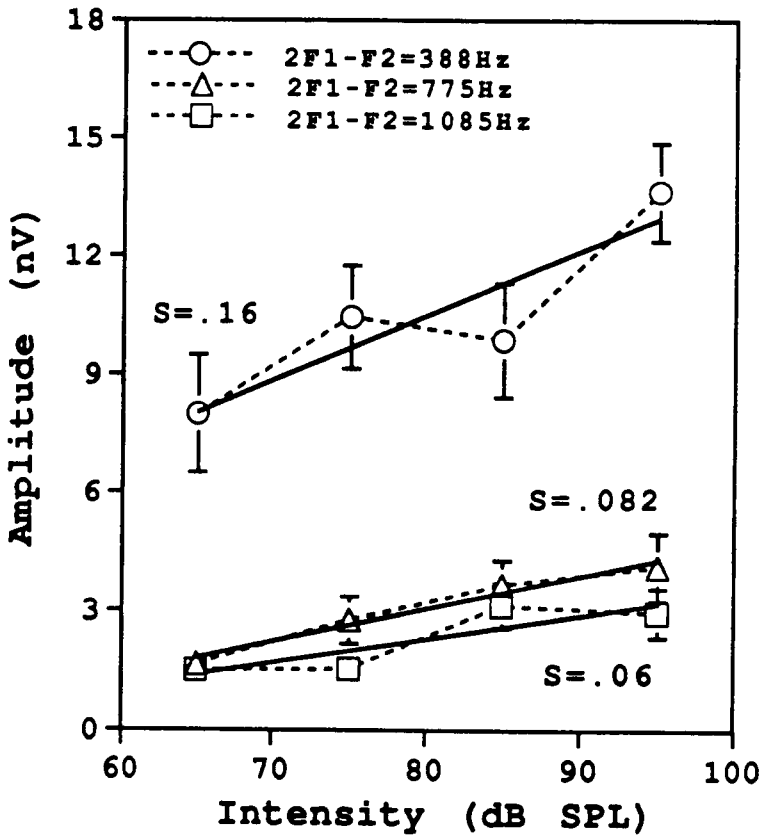

Figure 4. Mean response amplitude of the 2F1-F2 (FFR-DP) component for the three stimulus pairs plotted as a function of intensity. S denotes the slope of the growth function.

Specifically, it can be seen that the variability of the data at 85 and 95 dB SPL for the two higher frequencies seem to suggest that individual data showed amplitude saturation and/or amplitude roll-over at these levels.

Finally, closer examination of Figures 3 and 4 reveals that the amplitude of all response components decrease with increase in frequency of the stimulus pairs. This observation is clearer in Figure 5 where the amplitude of F1, F2, and 2F1-F2 (FFR-DP) is plotted as a function of frequency. Again, consistent with earlier observations for each stimulus pair, F1 component has the largest amplitude followed by 2F1-F2 (FFR-DP) with F2 showing the smallest amplitude.

Detectability of the 2F1-F2 (FFR-DP)

One other measure of interest to this investigation is to describe the ease with which the 2F1-F2 (FFR-DP) could be detected from the spectral data both as a function of intensity and frequency of the stimulus pairs. To this end, the percentage of subjects showing spectral energy at the 2F1-F2 frequencies prominent enough to be characterized as a "peak" in the FFT was calculated for each level and for each stimulus pair. The percentage detectability of the 2F1-F2

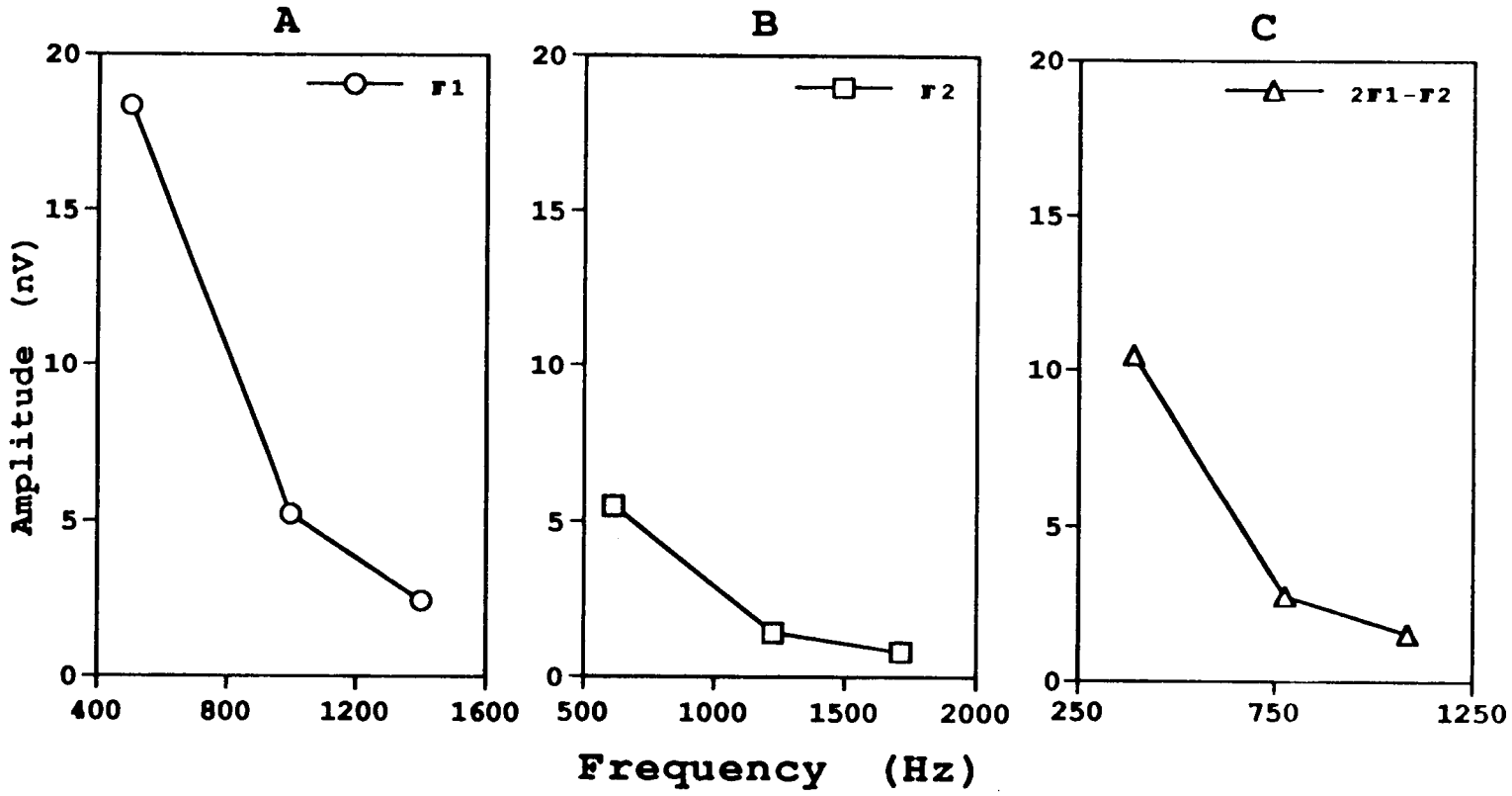

Figure 5. Mean response amplitude of F1, F2, and the 2F1-F2 (FFR-DP) components for the three frequency pairs plotted as a function of frequency at 75 dB SPL.

(FFR-DP) for each stimulus pair across the intensity range is presented in Table 1. It can be seen that the percentage detectability increases with intensity for all the stimulus pairs. The 2F1-F2 (FFR-DP) for the highest frequency stimulus pair (F1=1400 Hz, F2=1715 Hz) was the most difficult to detect above the noise floor across the levels of stimulation. In contrast, the 2F1-F2 (FFR-DP) for the two lower frequency stimulus pairs were relatively easier to detect with the lowest distortion product frequency showing the greatest percentage detectability across most stimulus levels.

EXPERIMENT TWO: 2F1-F2 (FFR-DP) DEPENDANCE ON RELATIVE LEVELS OF PRIMARIES

The mean spectral data for the lowest frequency stimulus pair (F1=500 Hz, F2=612 Hz) is plotted as a function of the level difference of the primaries (L2-L1) in Figure 6. To facilitate comparison, spectral data for the 85 dB SPL overall level (solid line) is superimposed on the 75 dB overall level (broken line) for each level difference. The level difference, L2-L1 is identified to the right of each pair of traces. As expected, it can be seen that the amplitude of most components are greater for the 85 dB SPL

TABLE 1. The percent detectability of the 2F1-F2 (FFR-DP) response from the subjects that were characterized as a "peak" in the FFT are listed.

	Level (dB SPL)			
2F1-F2 (FFR-DP)	65	75	85	95
388 Hz	66%	92.5%	100%	100%
775 Hz	60%	90%	100%	100%
1085 Hz	80%	70%	80%	100%

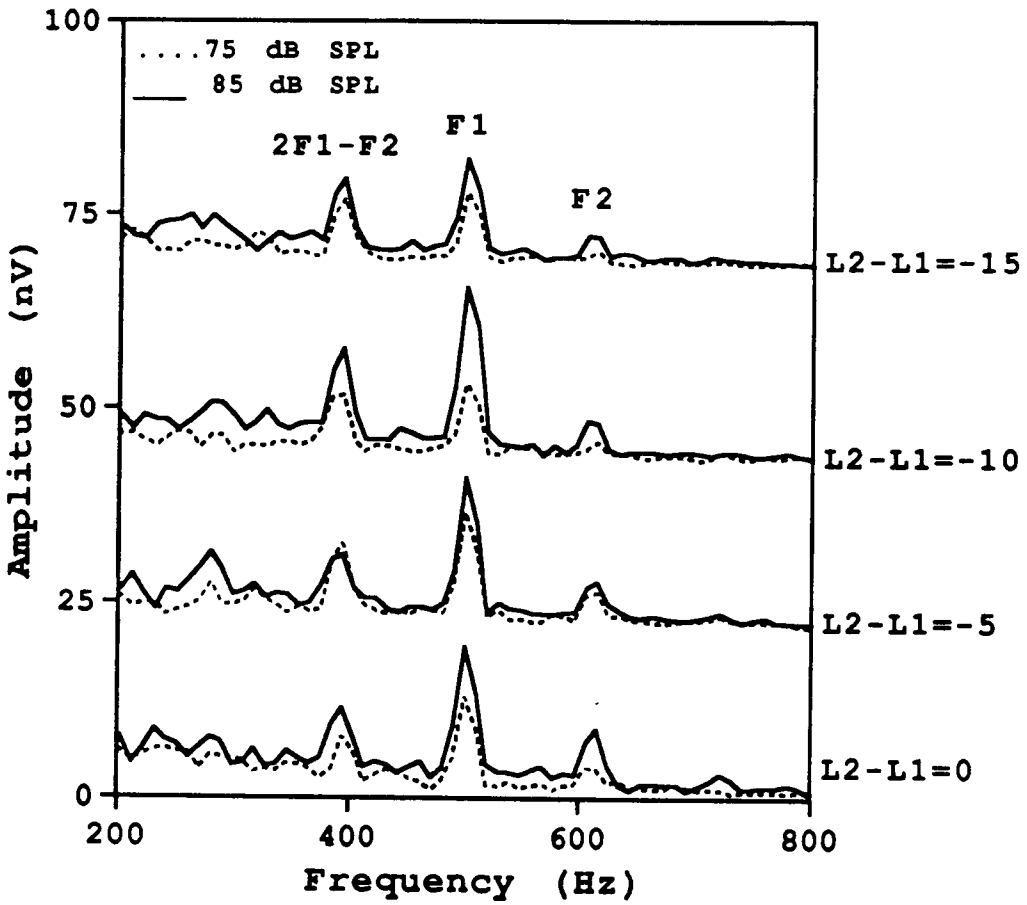

Figure 6. Mean spectrum of the derived FFRs showing the F1, F2, and the 2F1-F2 (FFR-DP) components as a function of primary tone level separation (L2-L1). The primary frequencies of the stimuli were F1=500 Hz and F2=612 Hz.

compared to the 75 dB SPL. In addition, the amplitude of F2 decreases with increasing level difference. This is not surprising, given that a greater level difference is actually brought about by decreasing the intensity of stimulus component F2 while holding the level of stimulus component F1 constant. In contrast, the FFR components at F1 and 2F1-F2 (FFR-DP) appear to show a non-monotonic amplitude increment as the level difference is increased. Furthermore, this increase in amplitude for F1 and 2F1-F2 (FFR-DP) is seen at both the overall levels. The mean amplitude change in F1, F2 and the 2F1-F2 (FFR-DP) components as a function of the level difference (L2-L1) is plotted in Figure 7. The parameter is the overall level. The curves reveal a distinct region where the separation of primary tone levels produced maximal amplitude at the distortion product frequency. For stimulation at 75 dB, the largest peak at the 2F1-F2 (FFR-DP) frequency for the mean data was found when L2 was 5 dB less than L1 for the primary pair evaluated. In contrast, stimulation at 85 dB revealed the most robust peak when L2 was 10 dB less than L1. Thus, the level differences L2-L1 generating maximal FFR-DP amplitudes depend upon L1. However, note the large

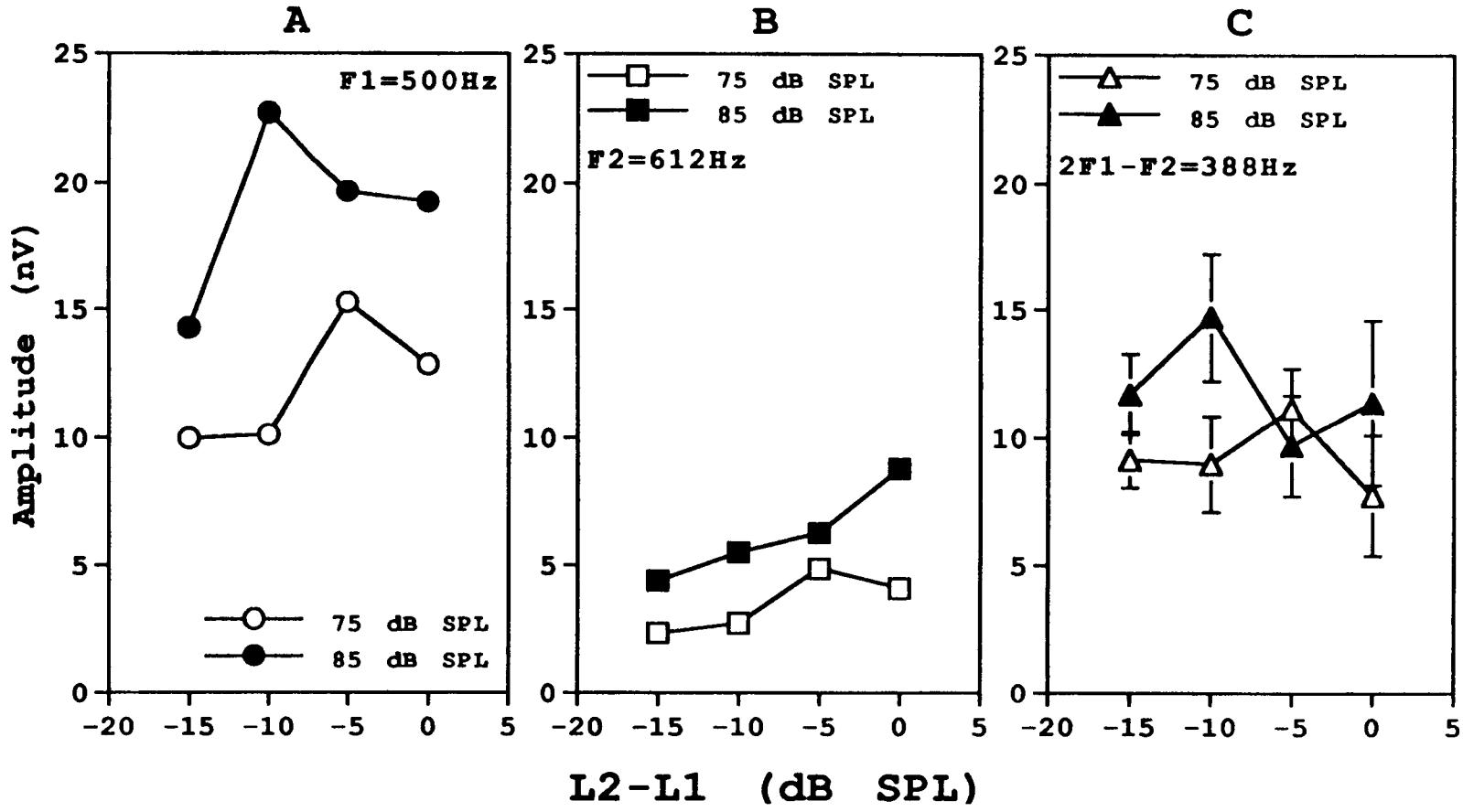

Figure 7. Mean response amplitude of F1, F2, and the 2F1-F2 (FFR-DP) plotted as a function of primary tone level variation (L2-L1).

variability of the data as indicated by the error bars representing one standard error of the mean.

EXPERIMENT THREE: FFR RESPONSE TO MONAURAL AND BINAURAL STIMULI

Superimposed spectral data comparing the mean spectrum of the monaural response (solid line) with the mean spectrum of the binaural response (broken line) for the lowest frequency stimulus pair (F1=500 Hz, F2=612 Hz) is shown in Figure 8. Recall, that for the binaural condition F1 and F2 stimulus components were presented to separate ears. Both the monaural and the binaural responses were obtained at 75 dB SPL. This figure clearly shows that the FFR components F1 and F2 are smaller in amplitude for the binaural response compared to the monaural response. More importantly, while the monaural response spectrum shows a robust 2F1-F2 (FFR-DP) component, there is no identifiable response peak at the distortion product frequency (388 Hz) in the binaural spectrum. It should be noted however, that one subject showed a prominent spectral peak and four had broad peaks at the distortion product frequency in the binaural response. Even when present, these peaks were rarely as prominent as their individual monaural response.

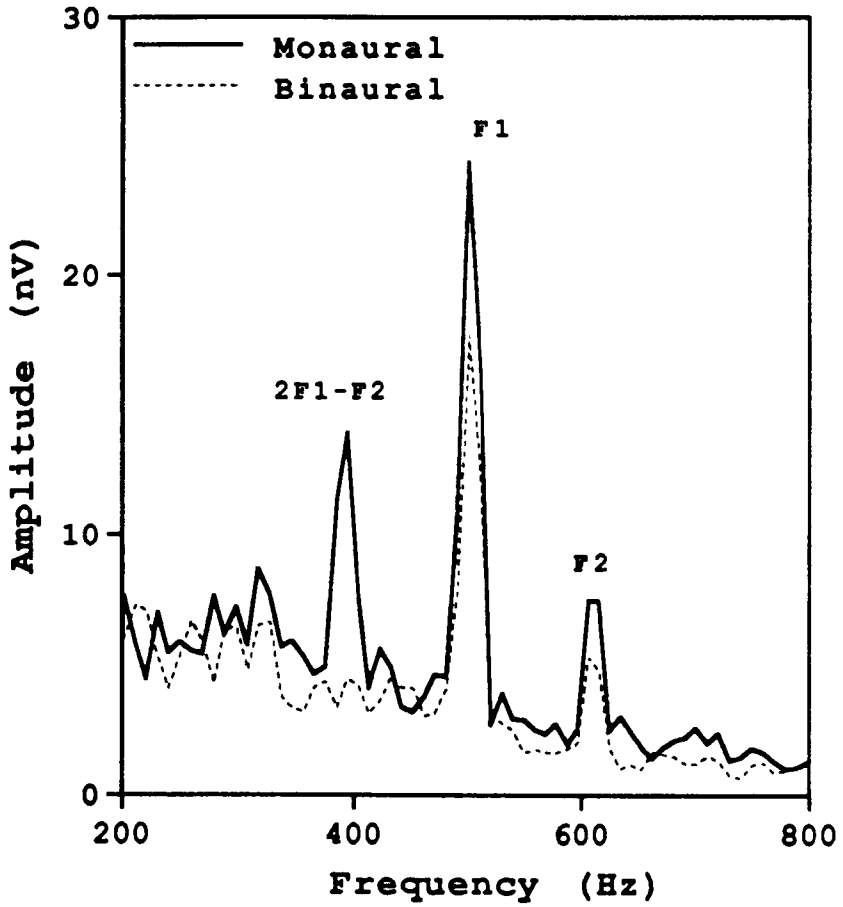

Figure 8. Mean spectrum of the derived FFRs to monaural and binaural stimulation showing the response components F1, F2, and 2F1-F2 frequencies at 75 dB SPL. The primary frequencies of the stimuli were F1=500 Hz and F2=610 Hz.

SUMMARY OF THE RESULTS

1. A trend of decreases in magnitude of F1, F2, and the 2F1-F2 components with increases in frequency.
2. A decrease in slope with increases in the distortion product frequency. The slope of F2 and 2F1-F2 components are essentially parallel for two of the stimulus pairs.
3. Percentage detectability of the 2F1-F2 FFR-DP component increases with intensity. Higher frequency distortion products were the most difficult to identify.
4. L2-L1 variations reveal a distinct region where the separation of the primary tone levels produced a maximal distortion product component at 2F1-F2. The level differences generating the maximal distortion product component depends upon L1.
5. There appears to be minimal brainstem contribution to the 2F1-F2 (FFR-DP).

CHAPTER IV

DISCUSSION

The results of this study relates specifically to four aspects of the frequency following responses to two-tone stimuli: (i) verification of the biologic nature of the 2F1-F2 (FFR-DP); (ii) characterization of the input-output behavior of the FFR components F1, F2, and 2F1-F2 (FFR-DP); (iii) evaluation of the effects of variation of the relative levels (L2-L1) of the stimulus pair on the response components F1, F2, and 2F1-F2 (FFR-DP); and (iv) determination of whether additional activity in the brainstem contributes to the generation of 2F1-F2 (FFR-DP).

VERIFICATION OF THE 2F1-F2 (FFR-DP)

In order to evaluate the 2F1-F2 (FFR-DP), it is first necessary to verify that the recorded responses are true biologic responses and not artifacts related to stimulus or the recording procedure. The existence of true biologic FFR distortion products at F2-F1 and at 2F1-F2 has been recently reported by a few studies from one laboratory (Chertoff and Hecox, 1990; Rickman, Chertoff and Hecox,1991; Chertoff and Hecox,1992). To determine if the energy in the stimulus at

the 2F1-F2 frequency generated the FFR-DP, the acoustic spectra of the three stimulus pairs derived from the averaged response of the stimulus waveform developed in a 6 cc coupler was evaluated. The level of presentation was 85 dB SPL. The acoustic spectra determined in this fashion is shown in Figure 9. For the lowest frequency stimulus pair there is no discernable component in the spectrum corresponding to the 2F1-F2 frequency. For the two higher frequency stimulus pairs there appears to be a peak at the 2F1-F2 frequency. However, this peak is almost indistinguishable from the noise floor and is 60 dB down re. F1. Given this and the higher thresholds for the FFR, it is unlikely that the neural distortion product is generated by this spectral component at 2F1-F2 in the stimulus spectrum. Thus, the 2F1-F2 (FFR-DP) recorded in this study is a true biologic response.

INPUT-OUTPUT CHARACTERISTICS OF F1 and F2 COMPONENTS

Unlike the distortion product otoacoustic emmissions, the neural activity in the brainstem generated by F1 and F2 of the stimulus can be evaluated to determine if certain aspects of the 2F1-F2 (FFR-DP) response can be predicted. Results of this study indicate that for all stimulus pairs

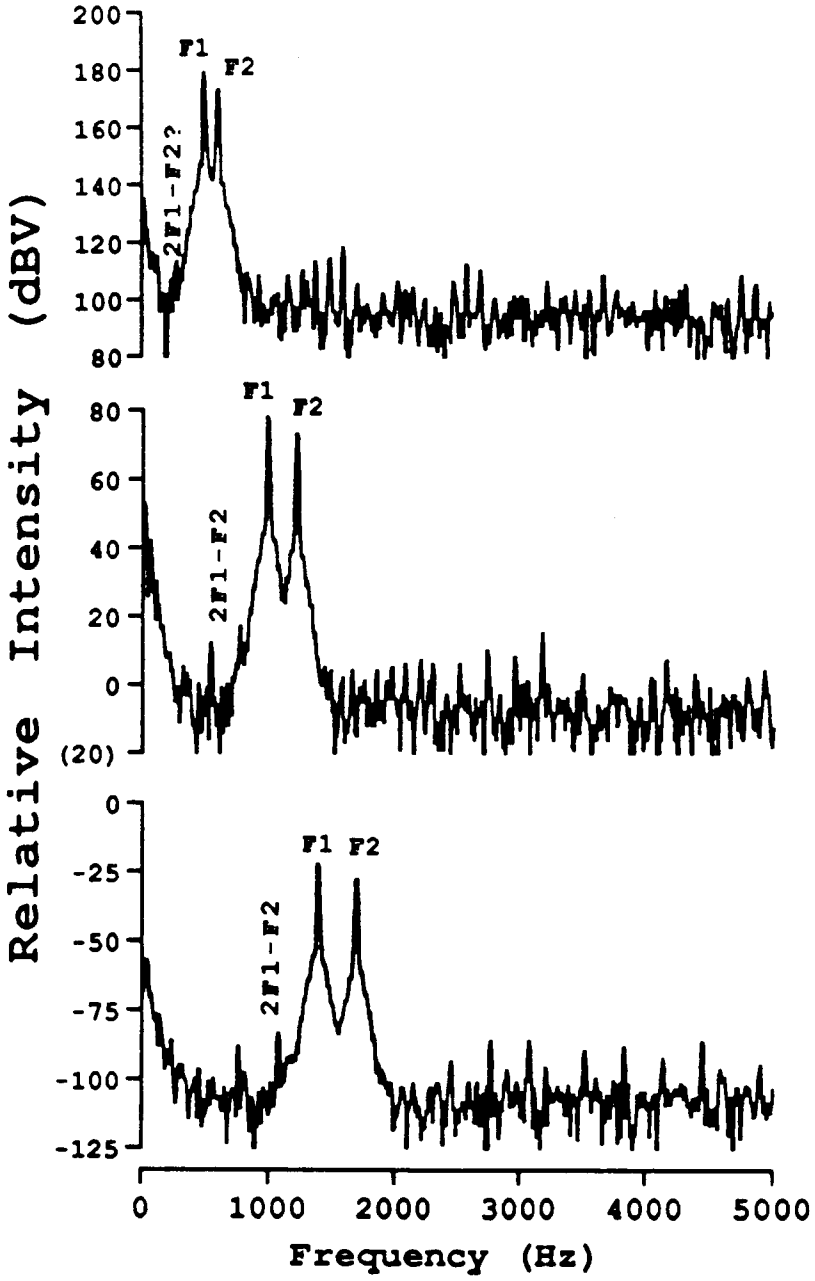

Figure 9. Acoustic spectrum of the three stimulus pairs. Spectral amplitudes at the 2F1-F2 frequencies are proximal to the noise floor (at least 50 dBV below the amplitude of the F1 component).

the input-output functions for F1 and F2 was characterized by a knee-point at 85 dB SPL. This observation is reminiscent of the characteristic input-output function for the whole-nerve action potential (Yoshie and Ohashi, 1969). These investigators interpret the change in the slope of the input-output function around 75 dB SPL to suggest a change in the intensity-encoding process.

This behavior of the input-output function may be explained by considering the nature of the single-unit tuning function. Specifically, the transition occurs because, once the stimulus intensity exceeds the low frequency thresholds of the neurons innervating the inner hair cells,the spread of excitation along the basilar membrane activates greater number of neurons. Consequently, the input-output function, which had started to saturate somewhat at moderate intensities, begins to grow again with further increase in intensity. The behavior of the FFR input-output function for components F1 and F2 in this study could very well reflect such a process.

It was also observed that the amplitude of all FFR components including the 2F1-F2 (FFR-DP) decreased with increasing frequency of the stimulus pair. This reduction

in amplitude of the FFR components as a function of frequency has been reported by Gardi et al. (1979) and more recently by Rickman and Chertoff (1991). Since the amplitude of the FFR is an index of the degree of phase-locking in the neural elements that generate the FFR, the amplitude reduction is taken to mean that the ability of the neurons to phase-lock decreases with increasing frequency. In fact, no repeatable FFRs are recorded for frequencies above about 2000 Hz (Gardi et al., 1979).

INPUT-OUTPUT CHARACTERISTICS OF 2F1-F2 (FFR-DP) COMPONENT

Although the 2F1-F2 (FFR-DP) amplitude for all the three stimulus pairs increased with intensity there were differences in the fine strucuture of their input-output functions. The 2F1-F2 (FFR-DP) at the lowest frequency (388 Hz) exhibited an input-output function very similar to the ones observed for F1 and F2. That is, an input-output function that is characterized by a gradually sloped segment at lower intensities followed by saturation or a negative slope and terminating with a rising slope at the higher intensities. Similar input-output behavior has been reported for both the DPOAE (Nelson and Kimberley, 1992) and the auditory nerve single unit studies (Goldstein and Kiang,

1967; Kim, 1980). Nelson and Kimberley (1992) utilize a model for intracochlear and ear canal distortion products proposed by Matthews and Molnar (1985) to explain their findings. Essentially this model suggests that the diphasic and/or nonmonotonic input-output functions may result from interactions between the 2F1-F2 and F2-F1 distortion products near the 2F1-F2 place. Specifically, null points in the diphasic input-output function would result from an interaction where the components (i.e. 2F1-F2 and F2-F1) are both out of phase and different in amplitude.

The 2F1-F2 (FFR-DP) at the the higher frequencies (785 Hz and 1085 Hz) exhibited input-output functions which were of the saturating/nonmonotonic type. The saturating growth curves were characterized by growth at lower levels followed by saturation at higher levels. In addition, the nonmonotonic functions were characterized by a well defined negative slope region at the highest stimulus levels. Again, these configurations were consistent with patterns observed by Nelson and Kimberley (1992) for DPOAE.

The phenomenological model they adopt to explain these growth curves was suggested by Norton et al., (1991). It presumes a passive nonlinear mechanism associated with the

basilar membrane inner hair cell subsystem and an active nonlinearity associated with the basilar membrane outer hair cell subsystem. The passive nonlinearity does not appear until moderate levels of the primaries are reached. Thus, active and passive nonlinearities subsequently may interact vectorally and account for the different functions observed in the 2F1-F2 (FFR-DP).

Slope of the 2F1-F2 (FFR-DP) Input-Output Function

Although there are inherent difficulties in direct comparison of data from the neural far-field recorded responses with DPOAE literature, the basis for drawing comparisons rests upon the fact that stimulus conditions are similar for both sets of data. However, these comparisons are only qualitative due to the differences in both dependent and independent variables between this data and the relevant DPOAE data.

The results of this study showed that the slope of the 2F1-F2 (FFR-DP) decreased as the frequency of the FFR-DP was increased. In contrast, slopes for DPOAE data, in the comparable frequency regions increased as the frequency was increased (Nelson and Kimberley, 1992). Comparable slope values close to the 388 Hz region are not available for

DPOAE. The reason for this discrepancy is not clear. It is possible that re-computation of the slopes of the 2F1-F2 (FFR-DP) using the DPOAE procedure (which excludes the steepest slope segments) would reveal a similar trend as observed for the DPOAE data. Alternatively, the differences in slope values could very well reflect fundamental differences in the neural representation of the cochlear nonlinearity at the brainstem level (FFR-DP) and the acoustical representation of presumably the same cochlear nonlinearity in the ear canal (DPOAE).

DEPENDANCE OF 2F1-F2 (FFR-DP) ON LEVEL SEPARATION

The 2F1-F2 (FFR-DP) does show sensitivity to level differences (L2-L1) in normal hearing ears. Findings in animals (Wiederhold et al., 1986) and in human ears (Hauser and Probst, 1990) for the DPOAE suggest that primary levels are most effective when L1 is 5-10 dB larger than L2. Consistent with these findings is the information obtained for the 2F1-F2 (FFR-DP) in the present study. For both levels, there appears to be a distinct region that produces a maximal distortion product at 2F1-F2. The level difference L2-L1 generating the most prominent distortion product for both methodologies appears to be dependant upon

L1. For measurements of both DPOAE and 2F1-F2 (FFR-DP), there are large intersubject differences. As with DPOAE level difference studies, optimum stimulus parameters for level differences to record the 2F1-F2 (FFR-DP) need to be investigated. It appears that from the large interindividual differences, no fixed L2-L1 is optimal for all ears. It would be expected that this level dependance may be dependant on the F2/F1 ratio as there is a complex interrelationship among these stimulus parameters.

EVALUATION OF A CENTRAL COMPONENT TO 2F1-F2 (FFR-DP)

The data recorded from monaural and binaural stimuluation reveals that much of the 2F1-F2 (FFR-DP) reflects cochlear events. There appears to be no appreciable brainstem contribution, however the presence of a broad albeit small peak at the distortion product frequency in the binaural response does not rule out the possibility of a brainstem component contributing to the generation of the 2F1-F2 (FFR-DP). However, the results of the present study suggest that the dominant generator of the neural responses at 2F1-F2 (FFR-DP) must reside within the cochlea. The specific origin of the 2F1-F2 (FFR-DP) is speculated in the next section.

Primary Generation Site of the 2F1-F2 (FFR-DP)

It is believed that there is an interaction of the primary frequencies at F1 and F2 place on the cochlear partition which generates the 2F1-F2 distortion product. This distortion product then propogagates to set up a traveling wave at its characteristic place more apically on the cochlear partition (Kim, 1980). Definite formulations concerning the cochlear place of origin of the neural 2F1-F2 (FFR-DP) cannot be made based on the results of this study. However, it is tempting to speculate that the nearly parallel slopes observed for F2 and the 2F1-F2 (FFR-DP) in the present study is suggestive of a generation site more consistent with the F2 place on cochlear partition (Kemp and Brown, 1984; Stover, Neely, and Gorga, 1994).

CLINICAL AND THEORETICAL IMPLICATIONS

This study has several important clinical and theoretical implications. One of the limitations of the DPOAE is the relative difficulty in measuring distortion products at frequencies below 1000 Hz. In contrast, the FFRs in general and the 2F1-F2 (FFR-DP) in particular, are prominent at frequencies below 1000 Hz. Thus, 2F1-F2 (FFR-DP) measures may be used to complement the DPOAE

measurements in evaluating nonlinearities of the auditory system generated from more apical regions of the cochlea. An additional advantage of the 2F1-F2 (FFR-DP) is that it will be measurable in individuals with middle ear pathology, whereas DPOAE measures are confounded by middle ear pathology. A disadvantage of the 2F1-F2 (FFR-DP) is that it would be sensitive to retrocochlear lesions involving the auditory nerve and/or brainstem structures. A final comment on clinical applications is that there is the potential for simultaneous recordings of both DPOAE and 2F1-F2 (FFR-DP).

The theoretical implications of the study include the ability to evaluate the neural response behavior to the F1 and F2 primary frequency components. Since a distortion product is the result of the interactions between F1 and F2, evaluation of the responses generated by these primaries may shed light on the generation and behavior of the distortion products. Technical difficulties in isolating the cochlear response to the primaries (F1 and F2) from the stimulus energy at these frequencies preclude analyses of the behavior of F1 and F2 responses in DPOAE measures. Finally, unlike the DPOAE measures, it is possible to evaluate both 2F1-F2 (FFR-DP) and F2-F1 (FFR-DP) from the same FFR

response due to the prominence of these components in the response spectrum. Recall that such an interaction between the 2F1-F2 and the F2-F1 place could affect the input-output function of the 2F1-F2 (FFR-DP). It is therefore possible that evaluation of this interaction can add to our understanding of the underlying mechanisms which influence the distortion product.

CONCLUSIONS

One of the basic properties of a nonlinear system is that they resist simple descriptions that are all encompassing. Thus, the characterizations for this study behave for this combination of parameters of input stimuli. As Chertoff and Hecox (1992) point out, the discrepancies between 2F1-F2 (FFR-DP) and other measures of distortion products suggest that the nonlinearity generating the neural distortion product may not be similar to the nonlinearity generating other distortion products measures. The present investigation provides data for higher primary levels to determine absolute level of the neural acoustic distortion product. It may provide an understanding of the transduction of sound into the auditory neural code. With detailed knowledge of the 2F1-F2 (FFR-DP), optimum stimulus

parameters can be chosen to generate recordable responses in normal hearing individuals. Further efforts to understand and describe the nature of this response seems warranted given the importance of nonlinear processing in the cochlea. Specifically, further investigation into the anatomic generators and properties of the 2F1-F2 (FFR-DP) may help in characterizing this response more completely. Of particular interest is whether this measure of neural distortion products will be sensitive to cochlear pathology. Additional recommendations for future studies of this response include the use of multiple channel recordings to determine the effects of electrode montage on these electrophysiological distortion products.

REFERENCES

Brown, A.M. (1987). Acoustic distortion from rodent ears: A comparison of responses from rats, guinea pigs, and gerbils. *Hearing Research*,31,25-38.

Brownell, W.E. (1990). Outer hair cell electromotility and otoacoustic emissions. *Ear and Hearing*,11,82-92.

Chertoff, M.E., Hecox, K.E., & Goldstein, R. (1992). Auditory distortion products measured with averaged auditory evoked potentials. *Journal of Speech and Hearing Research*,35,157-166.

Chertoff, M.E., & Hecox, K.E. (1990). Auditory nonlinearities measured with auditory-evoked potentials. *Journal of the Acoustical Society of America*,87,1248-1254.

Dallos, P., & Sweetman, R.H. (1969). Distribution pattern of cochlear harmonics. *Journal of the Acoustical Society of America*,45,37-46.

Gardi, J., Salamy, A., & Mendelson, T. (1979). Scalp recorded frequency following responses in neonates. *Audiology*, 18, 494-506.

Gaskill, S.A., & Brown, A.M. (1990). The behavior of the acoustic distortion product 2f1-f2 from the human ear and its relation to auditory sensitivity. *Journal of the Acoustical Society of America*,88(2),821-839.

Glaser, E.M., Suter, C.M., Dasheiff, R., & Goldberg, A. (1976). The human frequency-following response: its behavior during continuous tone and tone burst stimulation. *EEG Clinical Neurophysiology*,40,25-32.

Goldstein, J.L. (1967). Auditory nonlinearity. *Journal of the Acoustical Society of America*,41,676-689.

Goldstein, J.L., & Kiang, N.Y.S. (1968). Neural correlates of the aural combination tone 2f1-f2. *Proceedings of the IEEE*,56(6),981-992.

Greenberg, S., Marsh, J.T., Brown, W.S., & Smith, J.C. (1987). Neural temporal coding of low pitch. I. Human frequency-following responses to complex tones. *Hearing Research*,25,91-114.

Harris, F.P. (1990). Distortion-product otoacoustic emissions in humans with high frequency sensorineural hearing loss. *Journal of Speech and Hearing Research*, 33, 594-600.

Harris, F.P., Lonsbury-Martin, B.L., Stagner, B.B., Coats, A.C., & Martin, G.K. (1990). Acoustic distortion products in humans: Systematic changes in amplitude as a function of f1/f2 ratio. *Journal of the Acoustical Society of America, 85*, 220-229.

Hauser, R., & Probst, R. (1991). The influence of systematic primary-tone level variation L2-L1 on the acoustic distortion product emission 2f1-f2 in normal hearing ears. *Journal of the Acoustical Society of America*,89,280-286.

Humes, L.E. (1980). On the nature of two-tone aural nonlinearity. *Journal of the Acoustical Society of America*,67,2073-2083.

Kemp, D.T. (1978). Stimulated otoacoustic emissions from within the human auditory system. *Journal of the Acoustical Society of America*,64,1386-1391.

Kemp, D.T. (1979). Evidence of mechanical nonlinearity and frequency selective wave amplification in the cochlea. *Archives of Otorhinoloaryngology*,224,37-45.

Kemp, D.T., & Brown, A.M. (1984). Ear canal acoustic and round window electrical correlates of 2f1-f2 distortion generated in the cochlea. *Hearing Research*,13,39-46.

Khanna, S.M., Ulfendahl, M., & Flock, A. (1990). Cellular mechanical responses in the cochlea. In Grandori, I., Cianfrone, G., & Kemp, D.T., eds., *Cochlear Mechanisms and Otoacoustic Emissions*. 13-26.

Kim, D.O. (1980). Cochlear mechanics: Implications of electrophysiological and acoustical observations. *Hearing Research*,2,297-317.

Kim, D.O, Molnar, C.E., and Matthews, J.W. (1980). Cochlear mechanics: Nonlinear behavior in two-tone responses as reflected in cochlear nerve fiber responses and in ear canal sound pressure. *Journal of the Acoustical Society of America*,67,1704-1721.

Lonsbury-Martin, B.L., Harris, F.P., Stagner, B.B., Hawkins, M.D., & Martin, G. (1990). Distortion product emissions in humans. I. Basic properties in normal hearing subjects. *Annals of Otology, Rhinology, and Laryngology* (Suppl. 140), 3-14.

Lonsbury-Martin, B.L., Martin, G.K., Probst, R., & Coats, A.C. (1987). Acoustic distortion products in rabbit ear canal. I. Basic features and physiological vulnerability. *Hearing Research*,28,173-189.

Marsh, J.T., Brown, W.S., & Smith, J.C. (1975). Far-field recorded frequency following responses: Correlates of low pitch auditory perception in humans. *EEG Clinical Neurophysiology*,38,113-119.

Martin, G.K., Lonsbury-Martin, B.L., Probst, R., Scheinin, S.A., & Coats, A.C. (1987). Acoustic Distortion products in rabbit ear canal. II. Sites of origin revealed by suppression contours and pure-tone exposures.

Matthews, J.W., & Molnar, C.E. (1985). Modeling intracochlear and ear canal distortion product (2f1-f2). In J.B. Allen, J.L. Hall, A. Hubbard, S.T. Neely & A Tubis. (Eds.), *Peripheral Auditory Mechanisms*, pp.258-265.

Moushegian, G., Rupert, A.L., & Stillman, R.D. (1973). Scalp-recorded early responses in man to frequencies in the speech range. *EEG Clinical Neurophysiology*,35, 665-667.

Norton, S.J., & Rubel, E.W. (1990). Active and passive ADP components in mammalian and avian ears. In P.Dallos, C.D. Geisler, J.W. Matthews, M.A. Ruggero, and C.R. Steele (Eds.), *The Mechanics and Biophysics of Hearing*. pp. 217-227.

Probst, R., Lonsbury-Martin, B.L., and Martin, G.K. (1991). *Journal of the Acoustical Society of America*,89,2027-2067.

Rickman, M.D., Chertoff, M.E., & Hecox, K.E. (1991). Electrophysiological evidence of nonlinear distortion products to two-tone stimuli. *Journal of the Acoustical Society of America*,89,2818-2826.

Siegel, J.H., Kim, D.O., & Molnar, C.E. (1982). Effects of altering organ of Corti on cochlear distortion products f2-f1 and 2f1-f2. *Journal of Neurophysiology*,47,303-328.

Smith, J.C., Marsh, J.T., & Brown, W.S. (1975). Far-field recorded frequency-following responses: Evidence for the locus of brainstem sources. *EEG Clinical Neurophysiology*,39,465-472.

Smoorenburg, G.F. (1972a). Audibility region of combination tones. *Journal of the Acoustical Society of America*, 52,603-614.

Smoorenburg, G.F. (1972b). Combination tones and their origins. *Journal of the Acoustical Society of America*, 52,615-632.

Stover, L., Neely, S.T., & Gorga, M.P. (February, 1994). Explorations of the "filter" of distortion product otoacoustic emissions. Poster, *Association for Research in Otolaryngology Midwinter Meeting*, St. Petersburg, FL.

Wiederhold. M.L., Mahoney, J.W., & Kellogg, D.L. (1986). Acoustic overstimulation reduces 2f1-f2 cochlear emissions at all levels in the cat. *Peripheral Auditory Mechanisms*, edited by J.B. Allen, J.L. Hall, A. Hubbard, S.T. Neely, and A. Tubis (Springer, New York), pp. 322-329.

Wilson, J.P. (1980). The combination tone, 2f1-f2, in psychophysics and ear canal recording. In van den Brink, G., & Bilsen, F.A., eds., *Psychophysical, Physiological and Behavioral Studies in Hearing*,43-50.

Worden, F.G., & Marsh, J.T. (1968). Frequency-following (microphonic-like) neural responses evoked by sound. *EEG Clinical Neurophysiology*,25,45-52.

Worthington, D.W., & Dallos, P. (1971). Spatial patterns of cochlear difference tones. *Journal of the Acoustical Society of America*,49,1818-1830.

Yoshie, W, and Ohashi, T. (1969). Clinical use of cochlear nerve action potential responses in man for differential diagnosis of hearing loss. *Acta. Otolaryngol.* Suppl., 252, 71-87.

APPENDICES

APPENDIX A

INDIVIDUAL AMPLITUDE DATA (IN NANOVOLTS) FOR DERIVED MONAURAL RESPONSES EVOKED BY TWO-TONE PRIMARY SIGNALS WITH F1=500 HZ AND F2=612 HZ

SUBJECT	F1	F2	2F1-F2
	65 dB SPL		
CM	10.09	3.86	10.23
DS	3.76	3.66	9.67
HB	6.33	2.19	7.11
JM	10.70	2.55	3.53
JP	29.38	9.28	14.31
MH	6.54	4.66	5.42
MM	7.52	2.07	2.87
MS	16.88	6.26	10.43
MW	25.05	5.58	5.79
MW2	7.65	1.22	2.18
NK	10.56	1.41	16.05
SB	9.69	3.77	13.99
	75 dB SPL		
CM	19.93	5.63	12.20
DS	2.80	3.82	12.94
HB	9.41	2.62	5.53
JM	25.52	7.18	6.81
JP	26.27	10.45	5.88
MH	11.83	3.38	7.93
MM	15.18	3.86	2.84
MS	21.63	7.64	13.75
MW	49.27	13.38	21.04
MW2	9.96	5.23	10.09
NK	15.38	3.12	14.15
SB	13.27	4.71	12.52

SUBJECT	F1	F2	2F1-F2
		85 dB SPL	
CM	17.38	9.86	9.42
DS	9.57	0.95	8.84
HB	6.91	6.02	4.59
JM	39.26	7.48	6.41
JP	20.37	11.00	8.77
MH	21.88	4.15	16.92
MM	27.66	8.65	16.63
MS	15.33	7.87	6.40
MW	37.44	13.62	18.17
MW2	15.00	8.29	10.97
NK	10.93	2.65	7.09
SB	3.17	2.09	8.57
		95 dB SPL	
CM	23.95	10.15	17.78
DS	9.85	7.60	20.89
HB	19.86	11.05	8.80
JM	38.38	1.09	15.63
JP	27.74	10.86	13.57
MH	7.79	21.62	8.57
MM	63.59	36.50	21.24
MS	20.53	10.48	11.50
MW	36.30	15.82	20.34
MW2	18.83	5.35	6.36
NK	12.62	7.42	9.66
SB	12.64	5.06	15.36

APPENDIX B

INDIVIDUAL AMPLITUDE DATA (IN NANOVOLTS) FOR DERIVED MONAURAL RESPONSES EVOKED BY TWO-TONE PRIMARY SIGNALS WITH F1=1000 HZ AND F2=1225 HZ

SUBJECT	F1	F2	2F1-F2
	65 dB SPL		
CM	2.62	0.62	1.03
DS	6.01	1.26	1.44
HB	2.08	0.39	1.58
JM	5.10	1.53	2.55
JP	1.87	0.75	3.60
MH	6.01	1.02	1.35
MS	6.58	1.03	1.69
MW	5.76	1.20	3.71
MW2	4.62	1.14	1.00
NK	2.54	0.73	1.41
	75 dB SPL		
CM	3.84	0.83	4.73
DS	10.06	0.85	3.17
HB	1.84	1.63	2.27
JM	11.48	3.73	6.82
JP	2.03	1.28	1.86
MH	4.38	1.99	1.12
MS	7.68	0.95	2.71
MW	4.85	1.32	5.16
MW2	4.02	1.38	1.81
NK	3.06	1.42	1.86

SUBJECT	F1	F2	2F1-F2
	85 dB SPL		
CM	2.08	1.09	3.76
DS	9.64	0.59	7.25
HB	3.78	1.80	2.61
JM	3.64	2.15	6.98
JP	1.72	1.73	1.28
MH	2.64	0.96	3.05
MS	9.27	1.19	4.13
MW	2.78	4.84	3.62
MW2	3.60	1.66	1.71
NK	1.05	1.23	3.31
	95 dB SPL		
CM	0.97	1.28	3.33
DS	12.27	3.86	2.65
HB	19.48	4.44	5.29
JM	6.74	3.47	10.42
JP	12.94	5.73	4.16
MH	2.72	1.69	2.09
MS	18.03	2.64	2.98
MW	15.82	9.63	7.73
MW2	7.87	8.60	2.80
NK	5.62	2.71	2.61

APPENDIX C

INDIVIDUAL AMPLITUDE DATA (IN NANOVOLTS) FOR DERIVED MONAURAL RESPONSES EVOKED BY TWO-TONE PRIMARY SIGNALS WITH F1=1400 HZ AND F2=1715 HZ

SUBJECT	F1	F2	2F1-F2
	65 dB SPL		
CM	1.19	0.27	1.33
DS	4.86	1.77	1.75
HB	1.42	0.41	1.68
JM	1.48	0.37	1.61
JP	0.56	0.55	0.84
MH	1.14	0.72	0.95
MS	1.39	0.64	2.56
MW	0.88	0.60	1.91
MW2	0.74	0.49	1.90
NK	1.02	0.28	1.10
	75 dB SPL		
CM	1.44	0.70	0.46
DS	1.60	0.69	2.81
HB	1.90	1.49	1.98
JM	2.15	0.60	1.77
JP	1.23	0.79	1.53
MH	3.37	1.34	1.90
MS	2.76	0.27	1.80
MW	2.51	0.48	1.05
MW2	3.21	0.31	2.32
NK	4.77	2.08	0.62

SUBJECT	F1	F2	2F1-F2
	85 dB SPL		
CM	1.01	0.77	1.08
DS	3.57	0.51	6.48
HB	2.87	1.28	0.76
JM	6.29	3.73	3.45
JP	3.03	2.57	3.62
MH	13.25	6.00	4.38
MS	3.18	0.86	2.03
MW	9.82	3.33	3.47
MW2	4.94	2.24	4.03
NK	2.20	0.81	2.92
	95 dB SPL		
CM	2.25	1.13	2.24
DS	6.84	2.18	4.22
HB	14.42	6.66	4.80
JM	7.17	1.60	0.64
JP	13.99	8.01	1.70
MH	19.24	9.12	1.51
MS	6.83	2.08	1.96
MW	25.68	11.10	2.52
MW2	12.27	5.61	7.17
NK	4.79	1.42	2.78

APPENDIX D

INDIVIDUAL AMPLITUDE DATA (IN NANOVOLTS) FOR RELATIVE LEVEL DIFFERENCES OBTAINED MONAURALLY AT 75 dB SPL WITH F1=500 HZ AND F2=612 HZ

SUBJECT	F1	F2	2F1-F2
	L2-L1=0 AT 75 dB SPL		
CM	15.58	3.11	15.69
HB	5.19	1.14	2.98
MS	21.90	9.64	10.51
MW2	11.27	3.99	4.60
NK	10.23	2.58	4.98
	L2-L1=-5 AT 75 dB SPL		
CM	19.93	5.63	12.20
HB	9.41	2.62	5.53
MS	21.63	7.64	13.75
MW2	9.96	5.23	10.09
NK	15.38	3.12	14.15

SUBJECT	F1	F2	2F1-F2
	L2-L1=-10 AT 75 dB SPL		
CM	10.01	4.11	14.72
HB	4.03	1.19	6.89
MS	10.14	3.27	8.14
MW2	12.13	2.57	3.82
NK	14.23	2.59	11.33
	L2-L1=-15 AT 75 dB SPL		
CM	17.52	5.81	10.65
HB	4.12	1.60	11.61
MS	5.43	1.41	9.46
MW2	9.23	2.30	5.24
NK	13.51	0.75	8.76

APPENDIX E

INDIVIDUAL AMPLITUDE DATA (IN NANOVOLTS) FOR RELATIVE LEVEL DIFFERENCES OBTAINED MONAURALLY AT 85 dB SPL WITH F1=500 HZ AND F2=612 HZ

SUBJECT	F1	F2	2F1-F2
	L2-L1=0 AT 85 dB SPL		
DS	9.29	3.72	27.11
HB	3.94	3.30	2.03
JM	40.50	13.87	10.44
JP	24.99	5.09	7.30
MH	21.52	15.30	17.63
MW	31.56	16.36	15.94
SB	8.14	4.48	6.28
	L2-L1=-5 AT 85 dB SPL		
DS	9.57	0.95	8.84
HB	6.91	6.02	4.59
JM	39.26	7.48	6.41
JP	20.37	11.00	8.77
MH	21.88	4.15	16.92
MW	37.44	13.62	18.17
SB	3.17	2.09	8.57

SUBJECT	F1	F2	2F1-F2
	L2-L1=-10 AT 85 dB SPL		
DS	20.62	5.55	15.04
HB	2.99	1.52	7.50
JM	43.36	10.82	17.58
JP	29.76	3.49	9.74
MH	8.80	4.97	27.82
MW	45.05	10.60	16.39
SB	10.51	3.92	12.55
	L2-L1=-15 AT 85 dB SPL		
DS	16.25	1.98	12.92
HB	1.79	2.09	9.29
JM	19.59	10.20	8.90
JP	25.14	3.77	6.88
MH	5.99	3.07	19.51
MW	29.40	9.75	12.05
SB	4.04	2.23	13.66

APPENDIX F

INDIVIDUAL AMPLITUDE DATA (IN NANOVOLTS) FOR DERIVED BINAURAL RESPONSES OBTAINED AT 75 dB SPL WITH F1=500 HZ (RIGHT EAR) AND F2=612 HZ (LEFT EAR)

SUBJECT	F1	F2	2F1-F2
	BINAURAL AT 75 dB SPL		
CM	13.31	3.06	4.43
DS	10.86	6.98	11.46
JM	25.81	4.18	6.17
JP	29.04	4.18	3.50
MH	5.51	6.84	3.68
MS	14.18	1.30	2.45
MW	40.12	17.85	9.46
MW2	8.30	5.05	2.35
NK	13.26	1.08	3.24

VITA

Pritesh K. Pandya was born in London, England on April 15, 1973. He graduated with honors from Farragut High School in May of 1990. He immediately entered the University of Tennessee at Knoxville where in May of 1994 he received the Bachelor of Arts degree with a concentration in Audiology. Subsequently, he entered the Master's program in the Department of Audiology and Speech Pathology at the University of Tennessee at Knoxville, officially receiving the Master's degree in Audiology in May of 1996. Future plans include completing a Clinical Fellowship Year in Audiology and pursuing a doctoral degree.