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DIGITAL FILTERING OF AUDITORY BRAIN-STEM RESPONSES (ABR) USING TONE-BURST STIMULI IN DOGS

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Michael Edward Bennett-Martin

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DIGITAL FILTERING OF AUDITORY BRAIN-STEM RESPONSES (ABR) USING TONE-BURST STIMULI IN DOGS

By

Michael Edward Bennett-Martin

A DISSERTATION

Submitted to
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DOCTOR OF PHILOSOPHY

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1993

Ernest J. Moore

ABSTRACT

DIGITAL FILTERING OF AUDITORY BRAIN-STEM RESPONSES (ABR) USING TONE-BURST STIMULI IN DOGS

By

Michael Edward Bennett-Martin

This study was designed to determine the effects of high- and low-pass digital bandpass filtering on the temporal characteristics-latency and amplitude-of the major peaks by experimenting with different tone-burst stimuli presented at suprathreshold and near-threshold intensity levels. A group of eight adult (4 females, 4 males), anesthetized mixed breed dogs were used to collect normative data and two dogs (1 male, 1 female) were included in a hearing-impaired group. High-pass (10-, 100-, 300 Hz) and low-pass (3000-, 10000 Hz) Butterworth, zero-phase shift filter setting (12 dB / octave slope) were selected, and four tone-burst frequencies (1000, 2000, 4000 and 8000 Hz) were monaurally presented at 95-, 75-, 55-, 35-, and 25 dB peak equivalent SPL with contralateral (white noise) masking at 45 dB HL.

Dependent variables of latency and amplitude were measured for the major peaks labeled I and V for the six filter settings at each intensity level across the eight subjects. Descriptive statistics were calculated and latency-intensity functions and amplitude-intensity plots were determined for both major peaks. Correlation-coefficient and least-squares regression measures were applied to the

latency-frequency and amplitude-intensity data respectively.

Mean wave-I latency measurements were found to be quite stable across the six filter conditions, although a slight decrease in peak latency was observed when the high-pass cut-off frequency was set at 300 Hz. In general, wave-V latency was unaffected by high-pass digital filtering as expected, whereas no significant differences were found ($p > 0.01$) for the 2- and 4 kHz tone burst responses elicited at high and low intensity levels. The 8-kHz tone-burst yielded a significant difference in peak latency at 95 dB SPL.

An increase in the high-pass cut-off frequency from 10 Hz to 300 Hz produced a reduction in peak-to-peak amplitude of both major peaks, and significant differences occurred for the 300-3000 Hz and 300-10000 Hz bandwidths. No significant differences emerged ($p>0.01$) between these low-pass settings when the high-pass cutoff frequency was held constant at 300 Hz.

The results of this study suggest that for routine brainstem response audiometry a digital filter bandwidth of at least 10 - 3000 Hz (with a 12 dB/octave roll-off, 3 dB down points) is feasible for ABR canine testing. No appreciable response energy appears to be present above the 3000 Hz cut-off, since peak amplitudes did not show a significant increase when the low-pass frequency was held constant at 10000 Hz.

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For, ask the animals, and they will teach you; the birds of the air, and they will tell you; or speak to the earth, and it will instruct you; even the fish of the sea will inform you! For who among these does not see that the hand of the Lord is bringing this about?

-Job 12:7-9

I feel my direct connection with all life. I thrill to the songs of the birds, and I sense the tremors of life in the earth beneath my feet. I give thanks every day for the goodness of God and for the universal bounty that is mine. I call upon inner wisdom and love to guide me in the right use of my time and talents, all to bring a greater good to life. I release this animal to the universe knowing the love and goodness she has brought me.- MEBM

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Without my strong family support, both morally and financially, this project would not have become a reality. Those persons who are responsible include my son, Trevor; my father, Richard; my aunt, Mary Pearl Walker; my beloved cousins, Sam and Rose Haynie; my faithful, loving friends, Hugh Jones and Jim Ferguson; and my spiritual friends in "high places", Octavia Christine Elkins and Gladys Edna Martin.

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CHAPTER 1

INTRODUCTION

Since the earliest description of human auditory brain-stem evoked responses (ABR) by Jewett and Williston (1971), the use of these electrophysiologic measurements has rapidly evolved into a valuable tool in the diagnosis and early detection of a wide variety of audiologic, otoneurologic and neurologic disorders. With the progressive development has come a steady increase in cross-species applicability of the ABR technique. This clinical application of this tool to veterinary medicine has introduced a powerful instrument for assessing the peripheral and central nervous system in large and small animals (Morgan, Coulter, and Marshall, 1980; Strain, Graham, and Claxton, 1989). The procedure empowers us to more accurately characterize deafness in small animals, especially the canine species where congenital and acquired sensorineural hearing loss has been reported in the Dalmatian, Border Collie, English Setter, Australian Heeler, Collie, Doberman Pincher, and the Walker American Fox Hound (Sims, 1988).

There is a paucity of investigations which have directly addressed the genetics of deafness in predisposed breeds using ABR methodology. Histopathological examination has revealed generative changes in the organ of Corti, vestibular system, and lower brain-stem regions in Dalmatians, Collies, and Terriers (Branis and Burda, 1985; Cook, Tyler, Coulter, and Chandler, 1984; Igarashi, Cohn, and Watanabe, 1972). The gene or genes appears to be recessive and sex-linked, with slightly more males than females affected, and the variance in expression of genes appears as partial and/or unilateral to complete deafness (Marshall, 1985, 1986). Further genetic studies would enhance our knowledge on the trait related to its variability, expression, and penetrance in all predisposed breeds. Yet, before genetic experiments can be pursued, more basic issues concerning methodology need to be explored in order to better understand procedural variables and their influence on the measurement, analysis and interpretation of the ABR responsivity.

Canine electrophysiology is still in its developmental stage as evidenced by the small number of published laboratory and research studies in the 1980's, as compared to the plethora of human investigations. Pioneer ABR investigations sought to determine the clinical usefulness and feasibility of the procedure in assessing peripheral and central auditory function (Whidden and Redding, 1979; Barry and Barry, 1980; Northington, 1981). Subsequent studies conducted in the next decade primarily focused on describing the ABR wave form morphology and its temporal characteristics-latency and amplitude-in groups of normal hearing and hearing-impaired dogs of mixed and pure-breeds (Kay, Palmar, and Taylor, 1984; Meyers, Redding, and Wilson, 1986; Knowles, Cash, and Blauch, 1988; Bodenhammer, Hunter, and Luttgen, 1985). The type and pattern of ABRs recorded has been consistently described as four to five major peaks (labeled after Jewett, 1971) which occur as large amplitude wave formations for the first, second, and fifth peaks, and a smaller third peak (See Figure 1). The various investigations, however, have not reported stable latency values for broad-band click stimuli. Before a clinical ABR protocol can be established to record valid and reliable assessments of auditory function in the dog, experimentation with various recording and measurement schemes in this animal model is warranted.

Statement of Problem

A comparative analysis of published research studies employing the ABR to assess canine auditory function has shown the use of different recording parameters across veterinary laboratories. In fact, there appears to be no degree of consensus with respect to which recording settings are optimal for either suprathreshold level testing used for diagnosis of retrocochlear hearing disorders or near-threshold evaluations to determine actual hearing acuity. As a result, some laboratories have reported distinctly different mean latency

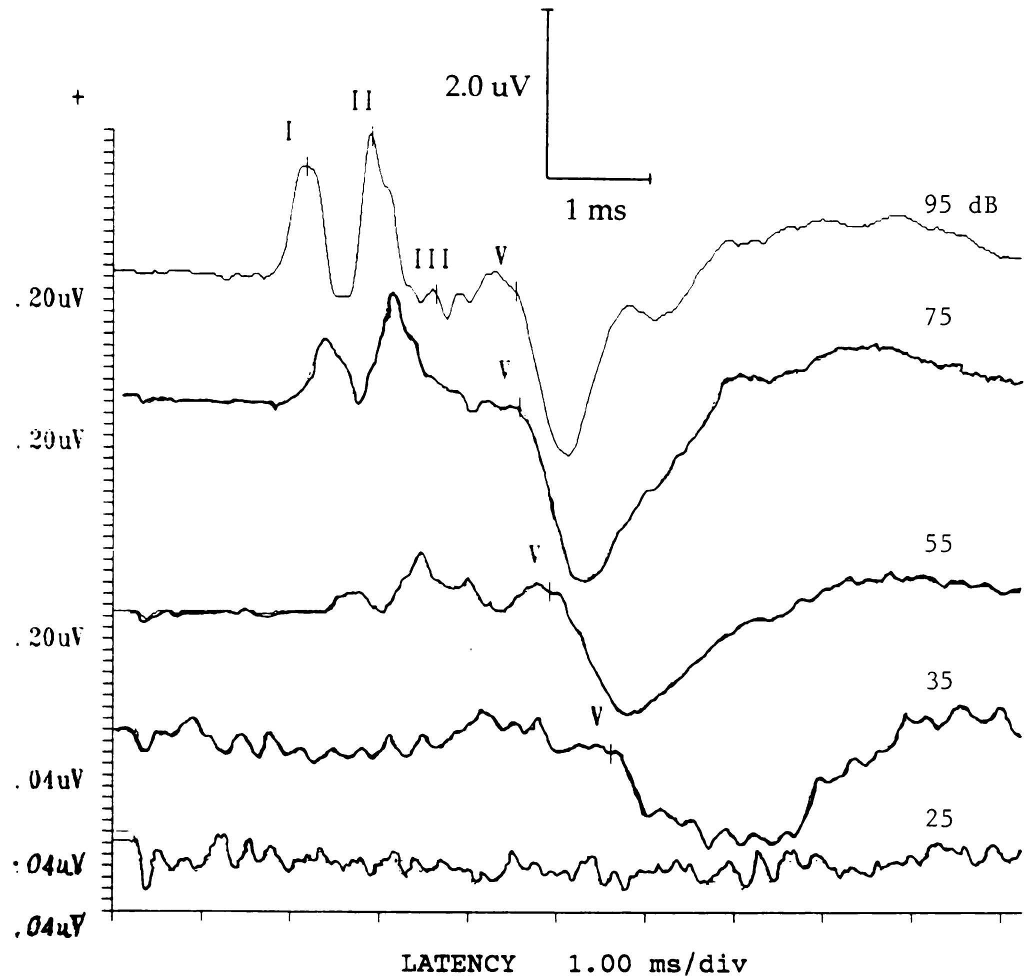


Figure 1. Typical ABR waveforms recorded from dog's right ear.

values at corresponding click stimulus intensity levels. For example, Marshall (1986) and Kay and coworkers (1984) recorded wave-I at 0.92 ms and 1.25 ms respectively for a 90 dB HL signal in neurologically normal, mixed breed dogs. Of course, inconsistencies in equipment calibration levels could also produce spurious normative data, and usually sketchy calibration information was reported by some researchers. Many laboratories (e.g. Barry and Barry, 1980; Northington, 1981) did not mention calibration procedures. On the other hand, a closer examination of these studies showed that different band-pass settings were used to record electrophysiologic activity, and the type of filtering (analog or digital) was not specified (see Table 1).

One recording parameter which quantitatively affects ABR measurements and has not received systematic research attention in small animal models is amplifier band-pass filtering. Several human studies, however, have documented how analog filtering introduces phase distortion on recorded evoked potentials and, therefore, latency and amplitude alterations emerged. A study by Boston and Ainslie (1980) concluded that increasing the lower cut-off frequency increased latency, and decreasing the higher cut-off frequency increased latency. These effects are consistent with the phase characteristics of the filter-high-pass filtration introduces phase lead and low-pass filtration introduced phase lag

Table 1. High-Pass and Low-Pass filter settings used in canine ABR published studies.

Investigators	Filter Bandpass (Hz)
Barry and Barry, 1980	3-3000
Bodenhamer *et al*., 1985	100-3000
Holliday and Selle, 1988	2-5000
Kawasaki and Inada, 1992	HP: 0.53, 1.6, 5.3, 16, 53, 160 Hz. LP: 100, 300, 1K, 3K, 10K, 30K.
Kay *et al*., 1984	100-3000
Knowles *et al*., 1984	20-20000
Marshall, 1985 and 1986	300-8000
Moore *et al*., 1990	100-3000
Morgan *et al*., 1980	30-3000
Sims and Moore, 1984	16-3200
Sims, 1988	150-3000
Strain *et al*., 1991	150-3000
Tokuriki *et al*., 1990	1.5-3000
Venker-van Haagan *et al*., 1989	100-3000

(Dawson and Doddington, 1973). Moreover, analog filtering caused a marked reduction in amplitude for the major peaks. On the other hand, zero-phase shift digital filtering did not have a significant effect on wave-V latency and caused less than a 20% reduction on overall peak-to-peak amplitude.

Domico and Kavanaugh (1986) also investigated analog and zero-phase shift digital filtering on the auditory brain-stem response wave form. They also concluded that phase distortion, as seen with analog filters, proved to be a major cause of wave form alterations including bias latency values and amplitude reduction. Several studies have documented this filtering effect (Svensson, Almqvist, and Jonsson, 1987; Doyle and Hyde, 1981; Fridman, Bergelson, Kaiser, and Baird, 1982).

The findings from these studies indicated that digital zero-phase shift filtering offers a number of advantages over the use of analog filtering at any band-pass and any slope configuration. These advantages include a cleaner, robust ABR wave form which is void of significant distortion in peak latency and amplitude, and thereby best mimics the response generated by the subject. Its use would markedly decrease accentuation and diminution of apparent peaks, intertrial variability, interlaboratory differences, and improve peak detection near threshold. Since analog filtering appeared to be commonly used in canine studies and because no systematic filter studies have been conducted in this species, the issue of appropriate amplifier band-pass filtering is unresolved. Furthermore, it has been shown that when low stimulus levels are used in threshold determination, careful high-pass (low-cut) filtering is critical to improving wave form reliability and peak identification, and that the optimal filter setting will not be the same for the two clinical applications-hearing threshold and otoneurological diagnosis (Svensson et al., 1987). Therefore, implementation of digital filtering for recording ABRs would facilitate reliable, less variable response peaks and a more accurate normative data base for pure and mixed breed dogs. By the same token, we would better understand the extent to which band-pass filtering is crucial for obtaining suprathreshold and near-threshold measurements.

Most of the canine ABR investigations have consistently employed rectangular or broad-band clicks, with acoustic energy in the 2000- to 4000 Hz frequency range, to assess auditory function and for wave-V threshold determination. What is greatly needed is frequency-specific ABR data for estimating hearing sensitivity in the 1000- to 8000 Hz region which represents the middle of the canine's audible hearing range (Heffner, 1983). Using behavioral data, Heffner concluded that 8000 Hz is the best frequency where hearing sensitivity is more acute and that threshold begins to gradually rise above and below that region that region. To date, no electrophysiologic studies have reported audiogram construction in the canine using frequency-specific stimuli.

Purpose of Study

Basic features and wave form morphology of the canine ABRs have been previously described in-depth by several investigators (Marshall, 1985, 1986; Sims and Moore, 1984; Sims, 1988). Possible generator sources of the peak waves have been postulated from intracranial recordings and transection studies conducted on the cat (Buchwald, 1982; Buchwald and Huang, 1975). Therefore, the exact origin of the peaks, especially after wave-I, have not been clearly identified and established in the dog (Sims, 1988). Ablation studies and intracranial recordings are needed to confirm origins in dog.

It is generally agreed that the generator of wave-I is the spiral ganglion and / or distal portion of the eighth cranial nerve (Buchwald and Huang, 1975). There is less agreement concerning the origins of waves-II through V, because it is more likely that the individual peaks have more than one generator and that each nucleus is likely to contribute to more than one ABR peak (Achor and Starr, 1980). As the wave IV-V combination is thought to represent activity in the upper brain-stem region -ipsilateral and contralateral lateral lemniscus (LL) to inferior colliculus (IC), neural synchronization between waves-I and V reflects brain-stem transmission time (BTT) and synaptic delays from the acoustic nerve through the cochlear nucleus and superior olive to LL and IC (Moller and Jannetta, 1982). In other words, successive peaks in the ABR originate predominately from successive levels of the auditory nervous system.

A better understanding of canine ABR behavior to tone-bursts can be achieved by systematic measurement of the larger, stable peaks labeled waves-I and V. Such information should provide valuable latency and amplitude baseline data and help to establish an interpretive algorithm for diagnostic purposes. Moreover, normative values for BTT would emerge and could be integrated into latency schemes for retrocochlear diagnosis.

This study was designed to examine the effects of zero-phase shift digital filtering on two major wave form peaks of auditory brain-stem evoked potentials in a group of neurologically normal, young adult mongrel dogs diagnosed with normal outer and middle ear function. High-pass (10, 100, 300 Hz) and low-pass (3000 and 10000 Hz) filter cut-off frequencies were manipulated, and peak latency and amplitude measurements were recorded at descending suprathreshold to near-threshold stimulus intensity levels for the four tone-burst frequencies of 1000-, 2000-, 4000-, and 8000 Hz.

A secondary goal of this investigation was to simultaneously measure the dog's mid-frequency auditory range and construct electrophysiologic audiograms and extrapolate latency-intensity functions for wave-V peak detection.

The major objectives of this experiment were established to test the following null hypotheses:

1. There are no significant differences in wave-I and wave-V peak absolute latency among three high-pass and two low-pass filter settings for each tone-burst stimulus at suprathreshold and near-threshold levels.
2. There are no significant differences in wave-I and wave-V peak absolute latency between both the high-pass and low-pass filter settings for each tone-burst stimulus at supra- and near-threshold levels.
3. There are no significant differences in wave-I and wave-V peak-to-peak amplitudes among the three high-pass and two low-pass filter settings for each tone burst stimulus at supra- and near-threshold levels.
4. There are no significant differences in wave-I and wave-V peak-to-peak amplitudes between both the high-pass and low-pass filter settings for each tone-burst stimulus at supra- and near-threshold levels.

The following questions were posed in order to investigate the assessment of auditory function and hearing

sensitivity using tone-burst stimuli:

1. What are the Latency-Intensity Functions for wave-I and wave-V peaks among the three high-pass and two low-pass filter settings for each tone-burst stimulus?
2. What are the threshold estimates (using wave-V peak amplitude and latency measures) of hearing sensitivity for the 1000-, 2000-, 4000-, and 8000 Hz tone-bursts?

CHAPTER II

REVIEW OF LITERATURE

This section presents an operational definition of digital filtering, followed by a review of major research studies which have investigated the effects of digital band-pass filtering on the ABR response, and concludes with a critique of the canine auditory brain-stem response experimentations.

Theoretical Constructs

The technical aspects and characteristics of digital filtering have been thoroughly described by several authors (Wastell, 1979; Dawson and Doddington. 1973; Doyle and Hyde, 1977; Marsh, 1988). A digital filter can be simply thought of as a mathematical operation that transforms the sampled digitized. averaged waveform in a certain way that attenuates unwanted signals amplifier and biological noise-while accentuating those frequencies of the evoked potential without introducing phase shift of the averaged response. This complicated process, based on interference or linear filtering, assumes that both signal and noise remain constant over the period of observation, and that the waveform (or spectrum) of the signal is known as well the spectrum of the noise. Essentially, linear of zero-phase filtering accentuates those frequencies of the input signal at which the desired signal is strong and the background noise is weak, and it suppresses frequency components where the desired signal is weak and the noise strong. It is assumed that a digital filter minimizes the mean square error inherent in estimations of the amount of signal in noise.

Zero-phase shift filters can also be described in the time domain by their weighting function which uses sets of weights based on the binomial coefficients associated with the expansion of $(1/2 + 1/2)^{2q}$. The filter operation is designed as a simple mathematical relationship between the weighting function and the frequency transfer function may be written as:

$$\mathcal{H}(j\omega) = M(\omega)\exp(j\phi(\omega))$$

Where M(**w**) is the filter modulus and O(**w**) us the phase at given angular frequency W. With a symmetrical weighting function the phase is given by:

$$\phi(\omega) = 0$$

i.e., no phase distortion is introduced within the frequency range within which the filters pass energy.

The frequency transfer function can also be expressed in terms of the frequency-attenuation characteristics with a nominal cut-off frequency. Thus the filter is set to pass an incoming signal in predetermined bandwidth designated as high-pass and low-pass bands. The actual amount of attenuation achieved outside the filter is a function of the slope variable. For example, a 12 dB/octave high-pass filter (-3dB down point) with a cut-off frequency of 100 Hz will only attenuate 60 Hz activity by a factor of about three, whereas a 24 dB/octave with the same cut-off will attenuate 60 Hz by a factor of about eight (Mason, 1984).

Marsh (1988) presented an exposition of some general principles of ABR recording as related to digitization and signal averaging. A summary of the review follows.

Digitizing itself is simply the electronic measurement of the waveform amplitude at intervals along the time scale. several samples of the signal which are somewhat obscured by background noise are recorded. The average contribution of the noise in the successive samples approaches zero, and the signal would be clearer. Signal averaging measures the incoming biolelectric signal at intervals 20 to 100 usec over a period of 10 to 20 usec following stimulus. When the response is averaged using repetitive stimulus, though, all components of the response will be time-locked to the stimulus and thus appear as harmonics of the frequency corresponding to the stimulus rate.

The digitized waveform is define only at the instants in time at which it was sampled, i.e., it is represented as a series of discrete points at, for example, 50 usec intervals. There is a limit with which digitizing does approximate the waveform, or Nyquist frequency. The highest frequency that can be discerned with a given sampling rate corresponds to one-second-one point every 20 usec-the Nyquist limit is 25 kHz.

Digitized filtering of the ABR involves a fast Fourier transform (FFT) of the signal, manipulating the frequency components, and reconstituting the filtered response by means of the inverse FFT. This process is an elegant computational method for spectral analysis of the digitized signals. The application of FFT to the ABR requires that the averager capture the entire interval from one stimulus to the next, and it is desirable to delay the syimulus so that the ABR of interest appears near the middle of the sweep.

Previous Filter Research Studies

Stapells and Picton (1981) investigated the effects of the slope of the filter as well as cut-off frequency on the ABR evoked by a 110 dB peak SPL 500 Hz tone. Digital High-pass settings of 10, 20, 40, 70 and 100 Hz and roll-off slopes 6, 12, 24, and 48 dB/octave were manipulated. The results of the experiment indicated that Wave V amplitude and morphology were reduced and altered respectively when the high-pass cut-off frequency was increased. Moreover, a steeper slope function (greater than 48 dB per octave) produced more distortion and marked alteration in response morphology. They concluded that Wave V-V' component of the ABR was achieved with filter settings of 20 Hz (48 dB/octave and 40 Hz (24 dB/octave).

Mason (1984) also conducted a systematic high-pass digital filter study on the detection of the auditory brain-stem response in a group (N=8) of normally hearing adults. Eight high-pass Butterworth-type filters (36 dB/octave) were investigated with cut-off frequencies at 10, 20, 30, 40, 60, 80, and 100 Hz (-3 dB points). The results of the study suggest that for routine brain-stem response audiometry employing high-frequency stimuli, a high-pass filter of 20 Hz (with a roll-off of 36 dB/octave) is optimum for detection of a response close to threshold. Filters having a shallower slope of 6 or 12 dB/octave will not produce as good a separation of the response and noise at 20 Hz; consequently, the amplitude of the response to noise ratio will be reduced. It was recommended that if shallower filters are employed, the cut-off frequency should be greater than 20 Hz in order to maintain significant attenuation of the noise at low frequencies.

Perhaps the most quoted technical study which established the superiority of digital filtering over analog filtering is an investigation by Boston and Ainslie (1980) that measured the effects of lower cutoff and upper cutoff frequencies in recording ABR's in normally hearing adults. They found that a zero-phase filter with 200-2000 Hz bandwidth provides relatively clean wave forms and does not appear to significantly affect amplitude and latency measurements. If zero-phase shift filters are used, a narrower band-pass can be tolerated than with analog filters. The authors concluded 18 that differences in filter cutoff frequencies, especially lower cutoff, are a significant source of variability in results reported by different investigators.

Doyle and Hyde (1981) employed digital high-pass and low-pass filtering in recording ABRs to monaural 70 dB nHL clicks in normally hearing adults. Butterworth and Boxcar filters with zero-phase and 4 pole (48 dB/octave) slope were considered. It was shown that both filters produced remarkable similarity of waveforms and morphology. Low-pass effects were unremarkable. High-pass filtering in the commonly used range of 20 Hz to 500 Hz produced severe waveform distortion, causing emergence of artefactual peaks, amplitude increase and decrease, absolute latency decrease and interpeak interval changes. The distortion increased with greater slopes.

Moller (1983) reported technical data on improving ABR recordings by digital or Weiner-type filtering with a 12 dB/octave slope. Empirical recordings showed that digital filters are very efficient in enhancing the signal in the background noise and make the peaks stand out clearly without displacing the peak in time. The author recommended the use of on-line or off-line zero phase shift filtering, and indicated that fewer averaged responses are needed with this process of filtering.

Auditory brain-stem response waveforms, derived from normal adults ears, were analyzed with a computer-based 19 filtering procedure as a means of systematically evaluating the effects of both analogy and digital (Butterworth) filtering in terms of phase-shift, high- and low-pass cutoff frequencies, and filter slope in a group of normally hearing adult subjects (Domico and Kavanaugh, 1986). As expected, a decrease in latency resulted form a HP cutoff frequency from 30 to 150 Hz for Wave V as compared to the unfiltered waveforms during analog filtering, The amplitudes of Waves I and V showed a continuous increase as the HP cutoff frequency was increased to 150 Hz, and then an amplitude decrease at 300 Hz. The effects of low-pass filtering was evidenced by the increase in peak latency and decrease in amplitude as the filter frequency is decreased from 3000 to 500 Hz. These effects were not seen with zero phase shift filtering. Yet, the major peak waveforms showed a amplitude decrease between the 100 and 150 Hz cutoff frequencies.

Svensson, Bengt, and Jonsson (1987) also compared analog and digital filtering in the ABRs of 20 adults with normal hearing. The results showed that the shape of ABR, especially peaks IV/V, is changed by latency and amplitude distortions. Also, it was shown that if peaks IV/V are to be identified with certainty it is necessary to raise the low-cut frequency setting. Significant differences in Wave I and Wave V latencies were found between analog and digital filtering. Therefore, zero phase-shift filtering is preferable, since it does no affect latency and can be used almost without restrictions.

The application of digital filtering combined with an automatic peak detection procedure was studied in 20 normal hearing adults (Fridman, Bergelson, Kaiser, and Baird, 1982). ABRs were recorded and exposed to analysis algorithms to identify frequency components of the peaks. Digital filtering allowed peak detection without distortion and permitted a 10-fold reduction in the sample size required to estimate ABR morphology, which may be of appreciable practical utility for an application such as on-line intraoperative monitoring of brain-stem state. The increased precision and decreased time requirements of this method also permits accurate estimation of amplitude and latency of the ABR peaks.

John, Baird, Fridman, and Bergelson (1982) also employed digital filtering and automatic peak detection to aid in the analysis of ABR component latencies. In a group of 148 children and adults subjects, ABRs were collected binaurally and monaurally and statistical analysis was performed to determine any significant differences between these test conditions. The results showed that there were no significant differences between right and left ear measures and high positive correlation among sequential peak latency values. However, binaural and overall monaural conditions were significantly different. Confidence limits for peak latencies were defined for the normative data, and a set of threshold values were developed for ABR measures to aid in subjective analysis.

A systematic investigation of filter effects on the ABR's in animals was conducted on the cat (Laukli and Mair, 1981 a, 1981 b). Employing 4000 Hz tone bursts and 24 dB/octave analog filtering, cochlear and brain-stem evoked responses were recorded from two litters (N=10). When the HP filter settings (2-, 30-, 100-, and 200 Hz) were modified by raising, the latencies of the five ABR peaks became concurrently shorter while amplitudes were variably affected. Wave I was considerable reduced in amplitudes when the responses were filtered with HP cut-off at 200 Hz. Waves II and III were also similarly affected. Wave V, however, had a consistent amplitude value for the lower HP filter settings and only decreased significantly at the 200 Hz cut-off filter. The authors concluded that the extent to which individual waves are influenced by changes in filter band-pass is closely related to their spectral composition. Furthermore, differential filter effects can be observed on the waves and their more sharply defined summits and peaks, which represent higher frequency activity. This observation was consistently made in the human and cat data presented.

Canine ABR Experiments

A small number of canine experiments, in comparison to human studies, with short latency (0-10 ms) evoked potentials have been documented. Initial investigations sought to describe the ABR waveform in terms of its temporal characteristics and to record normative data from groups of mixed-breed and purebred animals (Whidden and Redding, 1978; Northington, 1981; Barry and Barry, 1980). Descriptively, the click-evoked ABR waveform consisted of 5 to 6 peaks with similar morphology to human responses, but with larger amplitudes and slightly shorter (1.2 ms) shorter peak latencies. These responses were obtainable in unsedated as well as anesthetized animals.

The application of the ABR techniques for the purpose of determining clinical usefulness and feasibility in assessing peripheral auditory function has been investigated by several laboratories. Kay and co-workers (1984), Marshall (1985, 1986), and Venker-van Hagen (1989 reported suprathreshold and threshold click ABR data in both conscious and sedated dogs grouped as normal and hearing-impaired. The first study in this series summarized it findings as follows: (1) ABR's were recorded in all adults dogs, and the Wave V threshold responses were detectable as low as 15 dB nHL; (2) it appeared that higher thresholds were recorded for the older dogs (greater than 8 years old) and the Wave I showed a delay in latency; (3) ABRs were not detectable in two-week ago sedated pups but occurred at three weeks old; (4) between 3 and 7 weeks of age the latencies of Wave I and V and the interpeak values became shorter to resemble adult values; and (5) no brain-stem evoked potentials were detected in the four deaf dogs tested.

Marshall (1985) presented normative data comparing peak latencies (I-VI) and amplitude measures in anesthetized vs non-anesthetized adult mixed breed dogs (N=24). The whole group wad divided int subgroups according to sex and weight. Latency-intensity functions showed the expected increase in peak latencies as stimulus (clicks) level decreased. Amplitude ratios, latency, and interpeak latencies were not significantly different within or between the two subgroups. All dogs responded to click stimuli from 30 dB nHL, but only 62.5% of the dogs responded (with Wave V detection) at 5 dB nHL the mean latencies observed from all dogs were: Wave I, 1.20 ms; Wave II, 2.05 ms; Wave III, 2.7 ms; Wave IV, 3.39 ms; Wave V, 3.70 ms; and Wave VI, 5.18 ms. Larger amplitude values (greater than 1.0 uV) were measured for Waves I, II, and V.

Another ABR investigation by Marshall (1986) conducted suprathreshold searches to evaluate hearing levels and deafness in a group of Dalmatian dogs-18 adults and 28 pups. Under mild tranquilization, the adult dogs showed normal, bilateral ABRs only in five dogs (3males, 2 females). The remaining adults had normal ABR responses from one ear, and no responses, from the opposite ear. Of the 28 pups from 6 litters tested, 14 had normal responses bilaterally, 9 had monaural responses, and 5 were bilaterally deaf. Peal latencies (Wave I and V) from all ears that responded were within normal limits except that Wave V from unilaterally hearing adults had a significantly longer latency. There were no differences between male and female values, although slightly more males than females showed deafness.

Venker-van Hagen and co-workers (1989) conducted latency-intensity experiments using clicks to obtain reliable latency and amplitude peak measures in a group of neurologically normal Beagles (N=818). ABRs were recorded in both sedated and unsedated animals and compared, and stimuli were presented via insert-type and earphone-type transducers. Click thresholds were detectable as low as 20 dB nHL. The latency values at 80 dB HL or 107 dB SPL were 1.21, 1.97, 2.67, 3.12 and 3.61 ms for Waves I, II, III, IV, and V respectively. There were no significant differences in latency or amplitude values between the sedated vs. unsedated groups or earphone types. However, a longer measurement period and a greater number of averages were required for the unsedated condition.

It was concluded that using insert earphones and sedation was far more efficient than using headphones and no sedation.

A paucity of studies have investigated the relative effects of anesthetic agents and toxicity on waveform amplitude and latency measures. Tokuriki and Matsunami (1990) investigated the ABR in female mixed-breed dogs (N=4) to analyze the relationship between acoustic stimulus (click) intensities and peak latencies of each wave, and the relative effects of xylazine-atropine, xylazine-atropine-ketamine, and xylazine-atropine-pentobarbital combinations. These individual drugs and combinations have been shown to adversely affect ABR waveform latency and amplitude measures in small animals, but results have been conflicting (Cohen and Britt, 1982). Click stimulations fixed at 10/second repetition rate were delivered via headphones at intensities ranging from 10- to 110 dB SPL. In this drug study, there were no significant differences in peak latencies of major waves for about 90 minutes after xylazine-atropine-ketamine administration and for as long as 120 minutes after xylazine-atropine-pentobarbital administration, although Wave VI latency under the first combination had a tendency to slightly increase with time. It was concluded that ketamine or pentobarbital dosages used after xylazine and atropine administration may be effective for acquiring reliable ABR data at any time after drug induction. ABR recordings, however, in dogs under xylazine-atropine-ketamine anesthesia should be done within 60 minutes after drug induction because of increasing variability after that time frame.

An interest in the effects of ototoxic antibiotics on the ABR generated a study by Morgan, Coulter, and Marshall (1980) which evaluated eight anesthetized, mixed breed dogs and an equal control group (N=8). ABRs were recorded from animals intravenously administered neomycin for as long as 50 days. A control group was given as equivalent volume of isotonic saline solution IV. Latency and amplitude measurements of Wave I through V were analyzed over the days of injection. A distinct difference between the treatment and control groups was observed. Results showed that peak amplitudes, especially Wave I and II were significantly reduced after about 21 days of neomycin treatment. Similar findings were observed for latency measures, in the Wave I increased which caused latency prolongation in remaining waves. Statistical analysis of latency increase was not reported. By treatment day 28, most of the ABR activity had been extinguished. As no reversible effects were recorded and the control group remained unchanged, it was concluded that neomycin had caused a sudden loss of receptors)hair cells). Early treatment recordings of the cochlear microphonic which also later disappeared in treated dogs was another finding indicating probable loss of HCs in the organ of Corti.

Methodology and instrumentation parameters have no been vigorously investigated in small animals such as the cat and dog. Typically, the clinical studies have concentrated on recording the ABR using evaluation protocols designed for human assessment. One study by Holliday and Selle (1985) systematically researched a recording parameter, electrode placement, and provided the first published account of canine ABR electrode mapping. The effects of various electrode positions on temporal measurements were investigated. The rationale of the study was that the difference in geometry of the dog's head may preclude using recording points that were developed for other species such as the rat, cat, humans, etc. When subcutaneous recordings from sites approximating the vertex (active) with reference electrodes located at noncephalic, relatively inactive sites, ABR potentials were similar to those from humans and the cat. As reported for other species, on site on the dog's head was electrically inactive with respect to recording ABR potentials. In recordings made between the vertex and referenced ear, Wave I appeared as a large amplitude positive peak with onset latency equalling that in noncephalic recording sites. Amplitude measures for specific peaks varied as a function of the electrode site due to differing spatial locations of the peak generators and the volume conduction characteristics of the head (Plantz, Williston, and Jewett, 1974). Latency measurements remained relatively stable across the various electrodes sites, and not significant differences were obtained. As a final note, the animals (N=5) were presented at 80 dB SPL via TDH-39 earphones taped to the orifice of the external meatus.

Moore, Fisher, Gavin, and Barbee (1990) conducted an investigation to evaluate the effects of two cephalic recording electrode sites and stimulus polarity on the brain-stem auditory evoked response in a group of five healthy Beagles, with no sedation. The first montage positioned the positive electrode at the vertex and the negative one over the base of the non-stimulated ear. In the second montage, the positive electrode was placed over the base of the non-stimulated ear and the negative electrode was positioned over the base of the stimulated ear. The results indicated that various recording and stimulating methods can be used to enhance the ability to detect different components of the ABR. Wave III was best detected when using montage 2 with rarefaction clicks or montage 1 with condensation stimuli. Peak IV was absent with M2 and was most often present with M1 using rarefaction stimuli. Use of condensation clicks resulted in shorter latencies when compared to either rarefaction or alternating stimuli. The use of alternating stimuli cause the least distortion of peaks I and II.

A systematic investigation of stimulus intensity and repetition rate effects on the ABR in nonanesthetized and anesthetized, mixed-breed normal adult dogs (n=6) was reported by Sims and Moore (1984). Intravenous anesthesia-atropine and succinylcholine-was administered to one group, while the unsedated dogs were restrained in a recumbency apparatus. As expected, peak latencies increased and amplitude decreased as the stimulus intensity was decreased from 90 dB to 50 dB HL. For most intensity levels and click rates, Wave I had the largest amplitude with Wave V, II, and IV following in descending order. Wave III and IV usually formed a complex. i.e., a single wave with a latency equal to that of Wave III when it appeared alone. Peak latencies and amplitude values were not significantly decrease peak amplitudes and latencies of all peaks. This study verified the normal latency data-base reported by Kay et al (1984).

A clinical study by Bodenhammer, Hunter, and Lutten (1985) was conducted on 58 mixed-breed, sedated dogs ranging in age form 4 months to 14 years old. The purpose of the investigation was to evaluate any relationship between ABR and sex, age, head-width, and rectal temperature. A morphology of 5 to 6 major peaks were recorded using subcutaneous electrodes. The latency-intensity functions indicated the absolute latency of Waves I and II increased 0.2 to 0.3 ms for the older dogs (> 10 years) when comparison was made with younger dogs (>10 years). The remaining peaks did not significantly shift in latency with an increase in age. Interestingly, changes in rectal temperature fell below the critical 36° C (due to prolonged periods of anesthesia) increased latencies of Wave I through V appeared. Peak and interpeak latencies were found to increase more than 0.4 to 0.5 ms as rectal temperature fell below the critical point. When the rectal temperature in the same group of dogs remained between 37° to 39° C, shorter latencies of all peaks were observed. No relationship was found between gender and the ABR measurements. Also, no differences in ABR measures were seen between the three groups of head sizes. The results also suggested that the increase in peak latencies of older dogs is probably due to peripheral dysfunction, rather than a central transmission deficit. Such a conclusion would be in agreement with studies in cats Harrision and Buchwald, 1982).

Knowles and co-workers (1988) employed evoked response audiometry to study a group of mixed-breed, anesthetized dogs (N=16) for the purpose of evaluating changes in latency and amplitude in three groups: (1) "normal" hearing (N=8); (2) "reduced" hearing ability (N=4); and (3) deaf (N=5). The ABR responses in the normal and reduced groups consistently showed four major peaks, with significant latency delays and reduced amplitudes of Waves I and II in the reduced HL group. No recognizable waves were recorded from the deaf group, indication a probable lack of peripheral auditory function.

It was noted that the reduced HL and deaf groups were older (> than 10 years) than the normal group (< than 8 years) which is consistent with the common observation of auditory dysfunction in aged dogs.

Another clinical study by Barry and Barry (1980) recorded ABRs in eight mixed-breed dogs using gold-cup, surface electrodes affixed at the vertex and referenced to anterior edge of the pinna, with a ground electrode at the contralateral pinna. According to the methodology, 80 dB HL click stimuli were presented by a hand-held TDH-39 earphone. Specific instrumentation settings and the use of restraint or anesthesia were not mentioned. The reported waveforms showed five major peaks that occurred at approximately one millisecond intervals. In analyzing the recorded data, it appeared that Waves I, II and V had amplitude measures larger than 1.0 uV, while Wave III and IV revealed much smaller peaks (less than 0.5 uV). The authors, however, mislabelled the peaks by erroneously designating Wave V as Wave IV, for they were not aware that in some recordings Wave IV fuses with Wave V, and in other recordings Wave IV can be identified as a small peak having a similar amplitude to Wave III (Venker-van Hagen, 1989). Since actual latency and amplitude computations were not included in the text, it is difficult to make comparisons with other ABR studies.

Sims (1988) presented ABR data on electrodiagnostic evaluation of auditory function (early, middle, and late components) in clinically normal dogs and cats. Potentials evoked via air and bone conduction click stimuli showed Waves I, II, and V had larger amplitudes, and Waves III, IV, and VI were considerable smaller in magnitude. The same basic pattern, with slight variation, occurs in the cat, except Wave II may be larger than the dog's Wave I. In both species, Wave III and IV may fuse to form a single peak, with Wave III predomination. In some instances, Wave IV and V were observed to form a single complex with Wave V predominating. A bone conduction ABR appears to have the same basic waveform configuration as the air conduction, with some reduction overall amplitude. It was noted that peak latencies to bone conduction clicks may vary somewhat between small animals. Abnormal tracings from an adult female English Setter which showed no detectable waveforms in both ears, and from a unilaterally deaf Collie, confirmed the value of ABR as powerful diagnostic tool. The author also recommended the routine use of acoustic immittance testing to determine middle ear function prior to ABR assessment.

Postnatal development of the ABR in 13 Beagle pups of both gender from 1 to 76 days was reported by Strain, Tedford, and Jackson (1991). Responses were recorded between needle electrodes placed on the vertex and the ipsilateral ear, with ground at the interorbital line, and without sedation. Low-ground at the interorbital line, and without sedation. Low-amplitude responses to high-intensity stimuli could be recorded from animals prior to opening of the ear canals. Peak latencies did not change after day 20 for peak I, day 30 for peaks II and III, and after day 40 for peak V. As a result, the interpeak latencies between peaks I and III did not change after day 30, but continued to decrease until day 40 for peaks III-V and I-V. Peak amplitudes reached plateau values by day 20 (peak I) or day 30 (peak II, III and V). All the measured latency and amplitude values and significant regression lines of latency vs age and amplitude vs age. The brain-stem responses threshold was mature by day 20.

Yasuaki and Inada (1992) investigated the effects of analog filter frequency on ABRs in 7 non-sedated dogs. The ABRs were recorded at various low-pass (LP) and high-pass (HP) filter frequency settings using a 6 dB/octave roll-off (See Table 1). A decrease of LP filter frequency from 30 kHz to 100 Hz caused prolongation of the peak latency and reduction of the peak-to-peak and absolute amplitudes for all peaks, except the peak latency for wave-V and the absolute amplitude of wave-IV. Changes in these variables were statistically significant ($P < 0.05$) at different cut-off frequencies specific for the individual peaks. In contrast, increase of HP filter frequency from 0.53 to 160 Hz did not result in significant changes for any peaks, except for reduction in the filter frequency and negligible effects of HP filter frequency on individual peaks may be attributable to their frequency composition and/or elimination of the slow wave at higher HP filter frequency settings.

On the basis of their results, LP filter setting of 3 kHz and HP filter setting lower than 53 Hz are recommended for recording the ABR in dogs. It appears these settings sufficiently attenuate unwanted high-frequency artifacts, are adequate for recording of fast and slow waves, and have only slight effects on configurations, peak latencies, and amplitudes.

CHAPTER III

METHODOLOGY

Subjects

Acquisition of suitable canine participants was made from AALAC, an accredited supplier of conditioned animals for veterinary research. To ensure the continued health and nutritional maintenance of the dogs during the experimental period, guidelines mandated by Michigan State University Committee on Animal Use and Care (CAUC) were strictly followed. Individual animals were medically examined by a veterinarian to substantiate their general health. Medical examination criteria used for this study is outlined in Table 2. A total of ten mongrels, 5 females and 5 males, ranging in age from 19 months to 36 months (mean=23.2 months) were used in this investigation (see Table 3). Included in the physical examination were measurements of head size and body weight. Bilateral middle ear function was determined by Acoustic Immittance testing as discussed in the experimental procedures section of this chapter. Each canine had to meet the following criteria for both ears:

a. Based on visual inspection (otoscopy) of the external canals. No structural abnormalities or excessive wax accumulation.

b. Intact (no perforations) and clear tympanic membranes that reflect an otoscopic "cone of light".

c. Normal, Type-A shaped tympanometric configurations where the point of maximum compliance occurs at + 100 daPa of pressure.

Table 2. Neurological/ Medical Evaluation Summary

I. Objective Evaluation

A. Mental Status
B. posture and gait
C. muscle tone and skeletal abnormalities

II. A. Cranial Nerves: II through XII
1. N.II: Vision and response to Menance
2. NII, III: Pupil size, response to light
3. N.II: Fundus
4. N. III,IV, VI: Strabismus
5. N.V: Sensory, motor
6. N. VII
7. N. VIII: Cochlear, vestibular, nystagmus
8. N. IX,X,XI: mouth, throat, tongue
9. N. XII

B. Electrophysiologic Testing

III. Postural Reactions (Front and Hind Legs)

A. Proprioceptive positioning
B. Extensor Postural thrust
C. Hopping
D. Placing, tactile
E. Tonic neck and eye movements
F. Spinal Reflexes
G. Sensation

IV. Assessment

V. Plan

Table 3. Demographic Data on Individual Experimental Dogs

ID NUMBER	SEX	AGE	BREED	LENGTH(cm)	WEIGHT(lbs)
RDA0001	F	19 mos	Mixed	14.0	38
RDA0002	F	24 mos	Hound	17.0	50
RDA0003	F	21 mos	Beagle	15.0	29
RDA0004	F	20 mos	Beagle	15.1	27
RDA0005	M	22 mos	Beagle	15.5	25
RDA0006	M	26 mos	Mixed	16.0	33
RDA0007	M	23 mos	Mixed	13.9	21
RDA0008	F	21 mos	Mixed	14.3	35
RDA0009	F	20 mos	Mixed	14.2	38
RDA00010	M	36 mos	Mixed	18.1	55

d. Equivalent ear canal volume (Veq) measurements in the normal range (0.5 - 1.5 cm) for the dogs weight (Forsythe, 1985).

Automatic middle ear measurements (Welch-Allyn, MICROTYMP) were made 24 hours before an experimental run and again at 30 minutes before premedication was administered. The two values were compared for the purpose of confirming normal function.

Premedication and Anesthetization

Preparation of the animal for each experimental run required the elimination of food and water some 12 hours before induction. A registered veterinary technician administered pre-ops about 30 minutes prior to the insertion of the IV catheter and the induction of anesthesia. Induction of the normal dog followed a series of steps as listed below:

1. Premedication with Acepromazine IM, 0.01 mg / lb.

2. Hair clipped and area wiped around the cephalic vein of the left or right front leg with bentadine and alcohol.

3. Insertion of 20 gauge catheter and tape securely to leg. Aspirate and flush catheter with HEP saline solution.

4. Administration of Thiobarbituates - Thyamyal:
   2-4 mg/lb bouls to effect.
   Additional boluses were given until animal was deep enough to intubate.

5. Intubation of dog with a comfortable fitted endotracheal tube attached to a strip of gauze for securing the tube to the upper jaw.

6. Attachment of the CETT adapter following intubation and stimulation of the breathing circuit to promote voluntary respiration by pressing the rebreathing bag.

7. Activation of the oxygen cylinder to flow an adequate supply of O^2 (minimum 200 psi) and the anesthesia gas. The usual sequence was high flow O^2 (15 ml / lb) and 2% Halothan mixture.

8. Monitoring of respiration, pulse rate, and body temperature during the two-hour experiment. A heating pad maintained the body temperature between 37° - 39° Centrigrade.

9. Disconnection at the end of experimental run from the IV drip (5% Dextrose and Ringer, Abbott Labs) and from respiration machine (Heidbrink Compact, Model SA 3033) when it was certain that breathing was adequately maintained with an appropriate rate and tidal volume.

10. Positioning dog for recovery from anesthesia and intubation by noticing the swallow reflex and jaw tone, and other reflexes were brisk and signs of awakening were obvious.

The instrumentation and equipment arrangement for recording, sedation and respiration of the animal are illustrated in Figure 2.

Stimuli

Tone-Bursts

Recording of frequency-specific ABRs for the purpose of constructing electrophysiologic audiograms required the presentation of stimuli known to excite a narrow region along the cochlear partition, with minimal spectral spread of the signal. As human studies have reported good agreement between ABR and behavioral thresholds for tone-burst applications (Hayes and Jerger, 1982; Gorga, Kiminski, Beauchine, and Jesteadt, 1988), the use of brief tonal stimuli was appropriate. Gorga et al., (1988) concluded that on an average, tone-burst ABRs in quiet are as accurate as any other

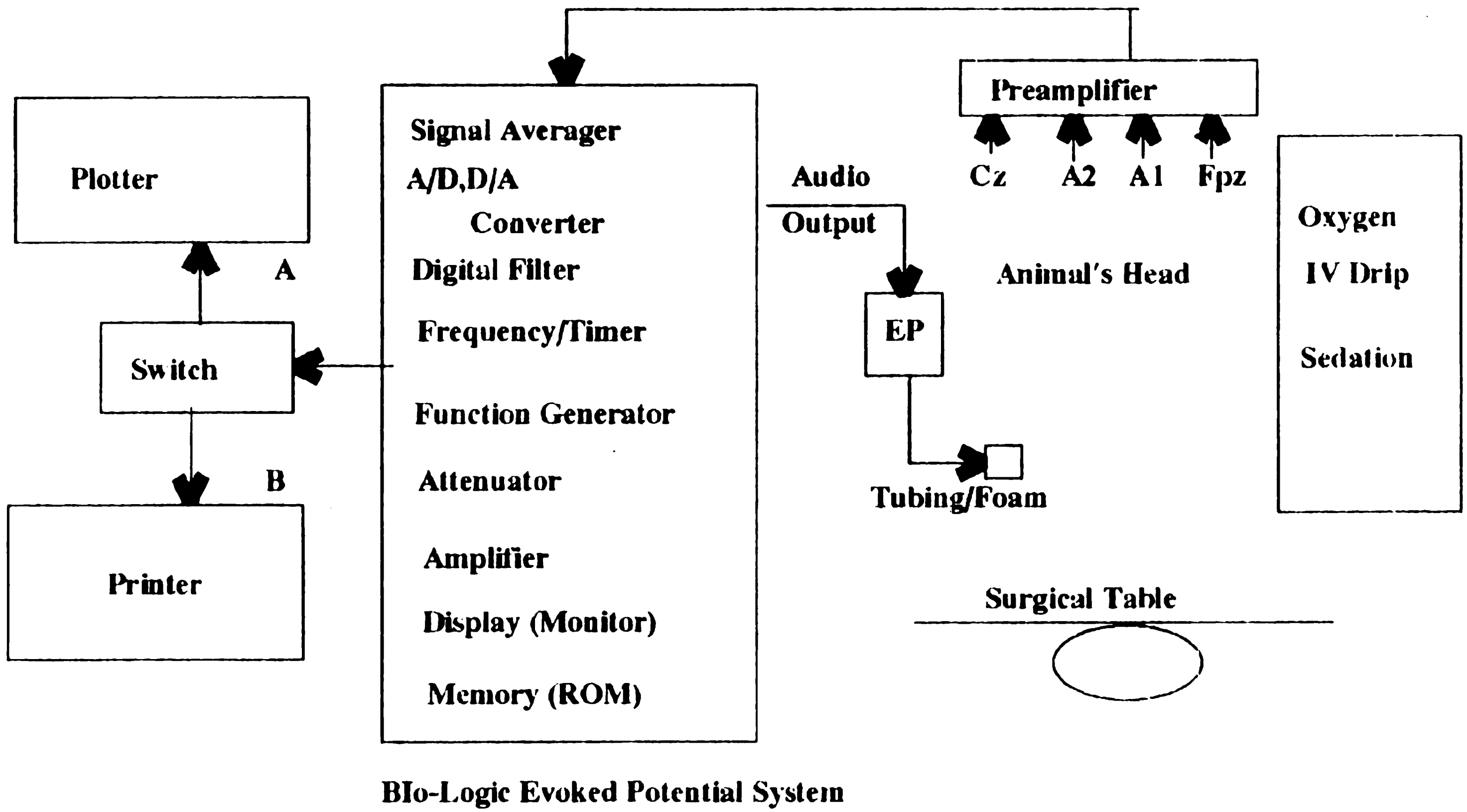


Figure 2. Instrumentation set-up for recording respiration and sedation.

techniques for estimating hearing sensitivity for octave frequencies from 500 to 4000 Hz.

Operationally defined, tone-bursts are gated sinusoids having durations in milliseconds and are electronically shaped according to its gating function-the envelop or rise / fall time by which the signal is turned on and off. Four distinct tone-bursts centered at 1000-, 2000-, 4000-, and 8000-Hz with a linear (1 ms rise / fall, 1 ms duration) function were generated from the audio output of the computer mainframe. The tapered weighting function or Hanning window of the signal transform was selected for its smooth transition from zero to the full frequency value, and thus the tone-bursts can be reproduced more efficiently as defined by the amplitude spectra which are shown in Figures 3, 4, 5, and 6 (see Appendix A). The rise / fall times and durations are depicted in Table 4. Representative electrical and acoustic spectras for the stimuli are illustrated in Figures 7, 8, 9, and 10 (see Appendix B). Transduced by insert earphones, the amplitude spectrum over the entire duration of each tone-burst has a main lobe of energy at the center frequency surrounded by side lobes at lower energy levels and second harmonics down 25 - 40 dB. The transform of the Hanning window is shown in the figure inserts.

Electrical and Acoustical Calibration

A series of measurements were made by routing the tone bursts from the auditory stimulator module to connected

Table 4. Rise/Fall times and total duration of tone bursts

Frequency (Hz)	Rise/Fall Time		Total Duration	
	msec	cycles	msec	cycles
1000	1.0	1.0	1.0	1.0
2000	1.0	1.0	1.0	2.0
4000	1.0	3.0	1.0	5.0
8000	1.0	7.0	1.0	9.0

devices capable of verifying frequency, intensity, and time characteristics of the stimuli. The essential instrumentation is diagrammed in Figure 11. Menu-driven software, which controlled signal shaping, generation, and all instrumentation parameters, directed the output of the digital tone generator to a storage oscilloscope (Tektronik, Model T912) to measure peak-to-peak voltage (mV) at a nominal attenuation setting of 80 dB HL. The input stimulus from the oscilloscope was AC coupled to a spectrum analyzer (Hewlett Packard, Model 3582A) and to a spectrum analyzer (Hewlett Packard, Model 7015B) for hard-copy. The arrangement produced the electrical spectra of the tone-bursts. Reproduction of the acoustic temporal wave forms was achieved first routing the sinusoid through insert earphones (Etymotic, ER-3A) coupled to a sound level meter (Precision, Model 83 A; Larson Labs) set to measure Root Mean Square (RMS) SPL. The stimulus repetition rate was increased to 97.0 / second so that the RMS level was stabilized to measures an impulse signal while peak-to-peak voltage was displayed by the oscilloscope. Following on-line measurement of the acoustic spectra of selected tone-bursts which were then written to the X-Y plotter.

Calibration of stimulus intensity was also conducted under the acoustical analysis procedure. In this process, the calibration files programmed on the evoked-potential software were accessed and the default peak SPL values for each tone bursts were modified to read 23 dB SPL (+ 1 dB). This SPL value set an 80 dB nominal attenuator step to produce a 95 peak SPL readout on the sound level meter (0 dB HL = 15 dB SPL). The values across the selected tone burst stimuli were equal to within + 1.0 dB.

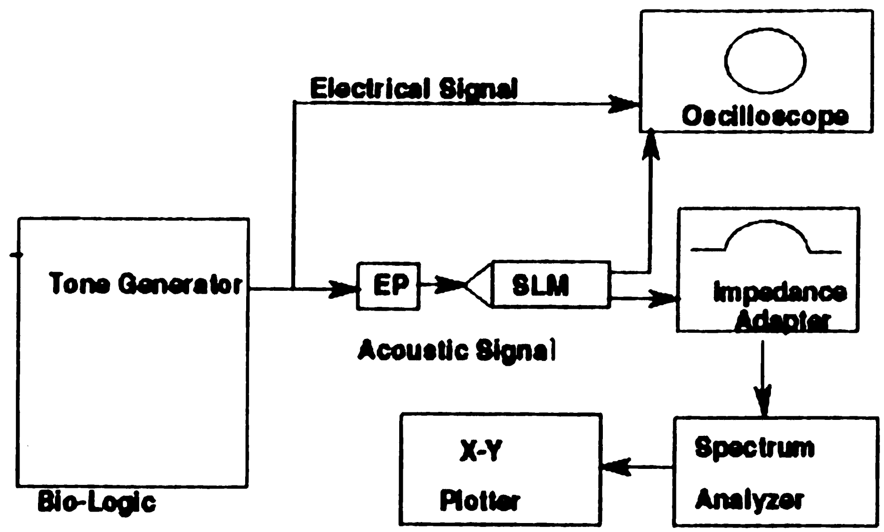
Frequency Response of Insert Earphones

This measurement provides vital information about the efficiency of the transducer output in a specified bandwidth. A diagram of the instrumentation set-up is shown in Figure 11. Briefly, the frequency response curve of the earphone was determined by routing an 80 dB white noise via the earphones coupled to the sound level meter. The noise was then AC coupled to the spectrum analyzer adjusted to a frequency bandwidth of 500-10000 Hz. The stimulus was stored and output was routed to the X-Y plotter for permanent copy. The response curve measured for the right and left earphones are shown in Figures 12 and 13 respectively.

The spectral analysis window displayed a non-linear response curve, wherein the output was relatively flat in the 1000-, 2000-, and 4000 Hz frequency region and then dropped about 20 dB at 8000 Hz and above. This means that the SPL value at this frequency was adjusted to the calibration file to read 35 dB SPL. Thus, a nominal setting of 90 dB produced a sound level meter measure of 95 dB peak SPL.

Data Acquisition and Analysis Equipment

A commercially-available evoked potential computer-averager (Bio-Logic Brain Atlas III Plus, 1988) was



Calibration Set-Up for Tone Bursts

Figure 11. Block diagram of stimulus calibration and spectral analysis.

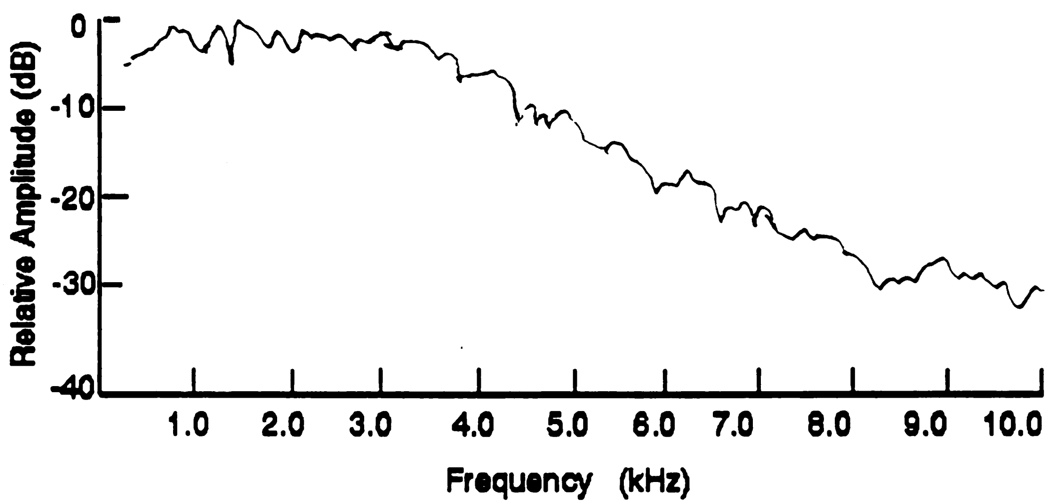


Figure 12. Frequency response of right Etymotic Insert Earphone, Type ER-3A.

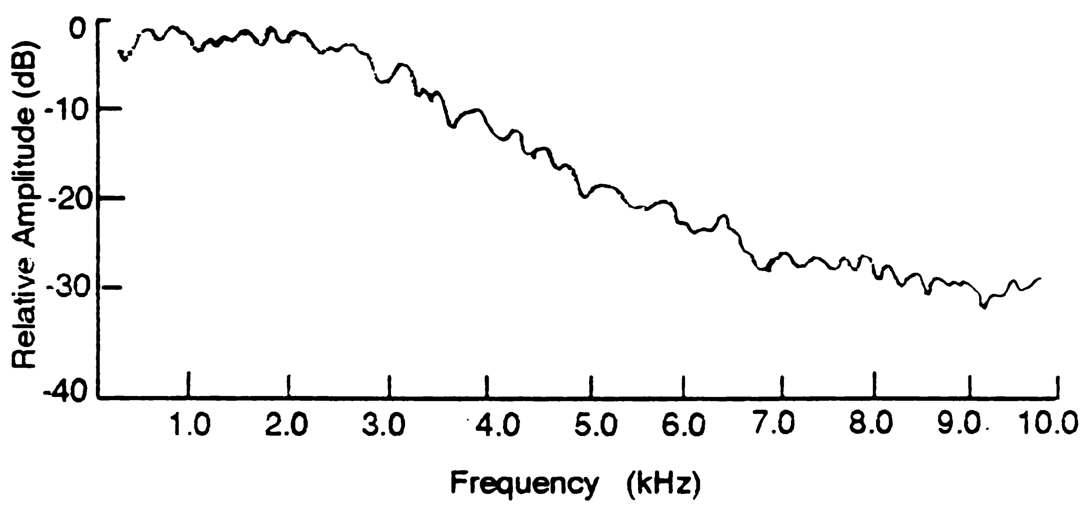


Figure 13. Frequency response of left Etymotic Insert Earphone, Type ER-3A.

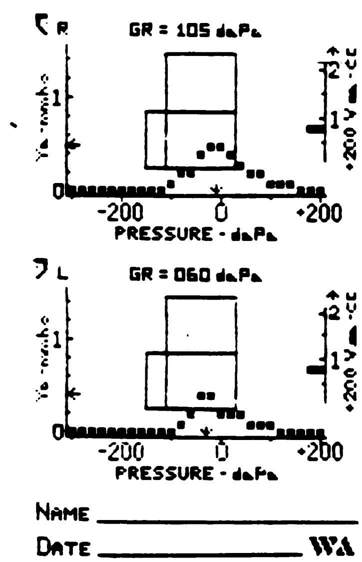


Figure 14. Acoustic Immittance templates for the dog's right and left ears.

programmed for use in the investigation. The hardware was contained in a transportable unit which housed an IBM-compatible 80286, 16-bit microprocessor. Data storage was achieved by 10 megabyte Winchester Hard-disk, 10 megabyte Bernoulli removable disks, and two 5.25" floppy disk drives. Evoked potential software (Version 4.1, 1990) controlled all phases of data collection, analysis, and graphic display. The preamplifier was connected to the rear of the mainframe at the A / D converter. Four platinum subdermal, needle electrodes (Type E2, Grass Instruments) were routed to the active (Cz), channel 1 references (A1), channel 2 reference (A2), and ground (Fpz) terminals of the pre-amplifier. The set was regularly inspected and changed if breakage, excessive bending of needle, or disfiguration occurred. As this apparatus is a potential source of electrical artifact, electrodes were braided and regularly cleaned of paste (Medi-Trace EKG Sol) and debris.

Software applications were central to the operation of the instrumentation parameters, recording, and analysis of the electrophysiologic data. Various menu-driven windows allowed for on-line analysis of averaged data which was output to either a plotter or printer (Hewlett-Packard HP Jet Laser 1800). The programmable evoked potential testing permitted multiple operations on pre- and post-stimulation activity. This activity included switch be electrode control, interactive cursors to measure latency and amplitude characters, multiple 13-point digital filtering / smoothing, built-in electrode impedance monitoring, and commonly used protocols which stored and controlled stimulus and recording parameters, as well as test sequences.

The insert earphones and tubing attachments were routinely inspected for operation efficiency and stored when not in use. Regular eartips (ER3-14A, Etymotic) were attached to 10" plastic tubing and inserted in the external canal and sealed. Biological and intensity level calibration checks were conducted before each experimental run. The peak SPL was verified by coupling the earphones to the sound level meter and reading the output at each test frequency.

The Bio-Logic equipment contained a zero-phase shift, Butterworth-type digital filter with a 12 dB / octave slope (-3 dB down) set to high-pass at 10-, 100-, and 300 Hz and to low-pass at 3000 Hz and 10000 Hz bandwidths.

Experimental Procedures

Preliminary subject screening included otoscopic examination (Welch-Allyn, Model 72A Otoscope) and acoustic immittance measurements (ANSI S3.39-1987) utilizing an automatic middle ear analyzer (Welch-Allyn, MICROTYMP). Templates for evaluating the middle ear admittance are displayed in Figure 14. Since there are no published norms for acoustic immittance values for the dog, the values obtained on this small group of experimental canines were compared with the tympanometric volume measurements reported in the dog by Forsythe (1985).

Following middle ear screening, each dog was positioned on the surgical table in a metal seternal recumbency triangle covered with disposable surgical pads. When the dog had stabilized, the needle electrodes were dipped in electrode paste (Grass Instruments) and inserted at designated scalp positions. The electrode impedance measure was adjusted to readout less than or equal to 3000 ohms. The data collection window was pre-programmed with the instrumentation settings shown in Table 5.

The data acquisition screen was stored within set-up protocols which permitted sequential recording of all the experimental conditions for each individual subject. Because this was a repeated measures designed experiment and there was a need to control for practice effects, the treatment conditions - six filter settings and four tone-bursts-were counterbalanced (Kirk, 1968). Each subject was assigned to a different presentation order for the experiment. A data matrix was constructed to consider all possible treatment conditions within and across subjects. The experimental protocol and presentation order was programmed on hard-disk and automatically recalled to initiate each experimental run. Each dog received a total of 120 treatment conditions (6 X 4 X 5) which were stored under a record number. Stimulus intensity level manipulations were fixed in the following order: 95-, 75-, 55-, 35-, and 25-dB SPL. Each experiment

Table 5. Instrumetation Parameters Pre-programmed on Bio-Logic Equipment

Parameter	Channel 1	Channel 2
Gain	150000	150000
HI Freq. Filter (Hz) 12dB/octave, -3 dB down	3000, 10000	3000, 10000
Lo Freq. Filter (Hz)	10,100,300	10,100,300
Sample Points	512	512
Analysis Window	10.24 msec	10.24 msec
Maximum Averages	512	512
Notch Filter	enabled	enabled
Electrode Montages	Cz/A1	Cz/A2
Repetition Rate	11.1/second	
Dwell Time (Digitized sampling rate): 50 kHz		
Stimulus Type: Tone Bursts, linear gating (1-1-1)		
Contralateral Masking: White Noise presented at 45 dB HL		

took approximately 120 minutes to record monaurally. Individual data files were constructed and stored on the hard-disk under a pre-selected file number description. Each file contained subject demographics and the total number of records for each experimental condition. At the conclusion of the experiment, all recorded data were transferred to floppy disk for of-line analysis of latency and amplitude of the major peaks.

When the last recording was stored, the electrodes and earphones were removed. The anesthesia IV drip was discontinued, and the dog was slowly weaned from the respiration machine and oxygen flow was gradually reduced until the animal could breath on its own. At this point, the endotracheal tube was removed and the dog was positioned on its side for recovery which took approximately 30 minutes to one-hour.

Data Reduction and Analysis

Absolute latency (ms) and peak-to-peak amplitude (uV) measurements of wave-I and wave-V peak wave forms were obtained by utilizing an off-line analysis window which controlled two interactive cursors, 13-point post-digital smoothing, and multiple wave form manipulation. Peak wave forms were recalled to the analysis screen and arranged in an order of decreasing intensity levels. Individual records were systematically analyzed.

To measure the peak of interest, cursor 1 was positioned to the apex of the wave form and the latency was determined as that value from the stimulus onset to the time of occurrence of the positive-going peak. Wave-V amplitude was measured as the difference between the positive voltage peak and the subsequent negative minimum or zero line (Glattke, 1983). Wave-I amplitude was measured from the baseline to the positive voltage peak. Both cursors were positioned on the positive and negative troughs to measure wave-V amplitude. For this study, wave-I and wave-V latency was defined as the time of occurrence of the first and fourth-fifth major peaks respectively from stimulus onset. In terms of amplitude, the value calculated from the zero baseline to the apex of the first major peak was used for wave-I, and the value between the positive and negative trough (V-V') was used for wave-V.

Data reduction forms were constructed in spreadsheet type tables that contained all levels of the independent variables. Actual latency and amplitude measures were logged for the major peaks for each subject across all treatment conditions.

Statistical Design and Analysis

The three independent variables and the interactions effects of the these factors - filters settings (A1-6), tone-bursts (B1-4), and intensity levels (C1-5)- were enumerated as individual cells in the ABC matrix spreadsheet. This constituted the initial input step to the SYSTAT statistical and graphics program (Version 5.1, SYSTAT, Inc). Four spreadsheets were constructed and saved as wave-I

latency, wave-I amplitude, wave-V latency, and wave-V amplitude. The three-way factorial design permitted ease of computation within and across subjects in a repeated measures format.

Descriptive procedures consisted of calculating the mean, standard deviation, and range of all interactive effects. Similar calculations were made to determine latency-intensity functions and amplitude-intensity values for the major peak wave forms. Pearson Product Moment Correlations and Least-Squares Regression measures were applied to the latency-frequency data and amplitude-intensity data respectively. These calculations were stored as STAT files on the hard-disk. Harvard Graphics (Version 2.3, 1989) was employed to plot all tables and statistical display of data.

In order to test the null hypotheses considered in this study, nonparametric methods were appropriate. The population frequency distribution is unknown, the dependent variable measurements were unobtainable, and a sample size was small such that assumptions of normalcy could not be met. A two-tailed, Freidman Test for Matched Pairs (Kirk, 1968) was selected to test the hypotheses of no significant differences in latency and amplitude measures among and between the filter settings. Level of significance as near as possible to $p = 0.01$ was used. Of course the raw data was changed to rank data for nonparametric analysis of variance. Of those matched pairs (filter settings) found to be significant according to the X2, further analysis of pairwise comparisons using Nemenyi's Test (Linton and Gallo, 1975) was conducted. In addition, strength of association among filter settings was tested by Kendall's Coefficient of Concordance (Downie and Heath, 1970).

The replicability of the tone-burst ABRs was assessed to the lowest intensity level tested in an effort to define ABR (wave-V) threshold as the lowest SPL that resulted in a recognizable peak having an amplitude value of 50% or greater than the random, background noise level. This latter exercise provided information for constructing electrophysiologic audiograms for the tone-burst stimuli. Extrapolation of wave-V latency and amplitude data using regression functions was conducted to predict values below the 25 dB SPL point.

Statistical outcomes expected were: (1) no significant differences in latency values of waves-I and V among and between filter settings because of the negligible effect of digital filtering; (2) significant differences in amplitude measures for waves-I and V among and between filter settings because of the low- and high-frequency composition of the ABR which is adversely affected by high-pass and low-pass digital filtration (Kawasaki and Inada, 1992).

CHAPTER IV

RESULTS

Introduction

The purpose of this study was to examine the effects of digital bandpass filtering on latency and amplitude of the auditory brain-stem responses (ABR) in a group of normal hearing, anesthetized young-adult dogs. Monaural ABRs were elicited by tone bursts with center frequencies at 1000-, 2000-, 4000-, and 8000 Hz at suprathreshold and near-threshold intensity levels. Ten neurologically normal male and female canines were pre-screened by acoustic immittance procedures as part of the selection criteria for the study, and to rule out any middle ear pathology. Two subjects (one male, one female) were eliminated from normative data collection because they failed to produce normal tympanograms and ear canal volume measures as reported in the dog (Penrod and Coulter, 1980). Thus, an equal number of male (N=4) and female (N=4) subjects participated in the normative data experiment, and the hearing-impaired subject data was collected for the conductive loss group.

Standard veterinary protocol were followed for administration of anesthesia, IV Catheter, and endotracheal insertion. Following positioning of the dog in a sternal recumbency apparatus, four platinum-tipped needle electrodes were subcutaneously inserted at designated scalp sites and impedance values were maintained below 3.5 kilohms. Etymotic insert (ER-3A) earphones were used to deliver a 95 dB peak equivalent SPL, 2000 Hz tone burst at the beginning of each experiment. Subsequent intensity levels were presented in 20 dB decrements to near-threshold levels. High and low-pass filter settings and the various tone bursts were randomly presented to each subject in a counterbalanced design, controlled by a 286 microprocessor programmed with evoked potential (EP) software.

On-line analysis of latency and amplitude values of major peaks was conducted (Jewett labeled waves I and V) using a data management evoked potential program with interactive cursors. Descriptive statistics were initially applied to transform the raw data into measures of central tendency and variability, which were plotted into histograms as a function of the six bandpass filter settings. Latency-intensity functions (LIF) for the peak waves at each tone burst were determined, along with wave-V amplitude detection at near-threshold, as an estimate of hearing sensitivity levels. The reduced data were examined to answer the following experimental questions:

1. What are the Latency-Intensity Functions for wave-I and wave-V peaks among the three high-pass and two low-pass filter settings for each tone burst stimulus?
2. Is there a statistically significant difference in wave-I and wave-V peak absolute latency among three

high-pass and two low-pass for each tone stimulus at suprathreshold and near-threshold levels?

3. Is there a statistically significant difference in wave-I or wave-V peak absolute latency between both the high-pass and low-pass filter settings for each tone burst stimulus at supra- and near-threshold levels?
4. Is there a statistically significant difference in wave-I and wave-V peak-to-peak amplitudes among the three high-pass and two low-pass settings for each tone burst stimulus at supra- and near-threshold levels?
5. Is there a statistically significant difference in wave-I or wave-V peak-to-peak amplitudes between both the high-pass and low-pass filter settings for each tone burst stimulus at supra- and near-threshold levels?
6. What are the thresholds estimates (using wave-V peak amplitude and latency measures) of hearing sensitivity for the 1000-, 2000-, 4000-, and 8000 Hz tone bursts?

Data Reduction and Analysis

The experimental questions addressed the following: (a) derived the means of latency and amplitude estimates for six digital filter settings at four nominal frequencies and five intensity levels across eight subjects; (b) quantified any significant differences in filter effects as a function of frequency and intensity; and (c) estimated hearing threshold levels for each tone burst stimulus. These statistical tasks were accomplished through the use of SYSTAT, a high resolution statistical and graphics program for analyzing raw data input to spreadsheet for multiple manipulations in a repeated measures factorial design.

Construction of a randomized block factorial design, within-subjects version, permitted manipulation of the three independent variables or treatments and treatment levels. The arrangement of the treatment conditions in such that information can be obtained about the effects of each of the independent variables considered separately, and how the variables combine jointly to influence latency and amplitude of the major peaks. Treatment effects are represented by differences within the single group of subjects serving in the repeated measures designed experiment. Given the population distributions, nonparametric statistical methods are employed to test experimental hypotheses. The raw data from alternate right and left ears are reduced to descriptive statistics across each treatment condition. Data was further grouped to high and low-pass conditions at each stimulus frequency and intensity level for latency or amplitude.

Frequency histograms across the filter conditions were formed for each response component's latency and amplitude at the highest and lowest sound pressure levels. To test the null hypotheses of significant differences in latency and amplitude of the major peaks across the filter settings, a Friedman's two-way analysis of variance (Seigel, 1956) was used, and a Wilcoxin's sign rank test was employed to detect differences between paired samples for each filter setting. A non-parametric method for multiple comparisons was also used to identify variables that were different (Conover, 1980).

Description of Results

Wave Morphology

Representative wave forms of tone-burst ABR data from the right ear in one male subject are displayed in Figures 15 to 18. The data are presented for the five intensity levels, and the individual peaks are labeled according to a classification system for the dog suggested by Moore and coworkers (1990). Typically, a reproducible wave form could be clearly identified across the frequencies at supra- or near-threshold levels, except for the 1000 Hz tone-burst which consistently generated auditory evoked activity known as (FFR) frequency-following-responses (Merzenich and Gardi, 1979). As shown in Figure 15, these responses tended to contaminate the usual wave form in that the major peaks could not be identified for reliable latency and amplitude measurements. Therefore, only 2000-, 4000-, and 8000 Hz tone-burst ABR

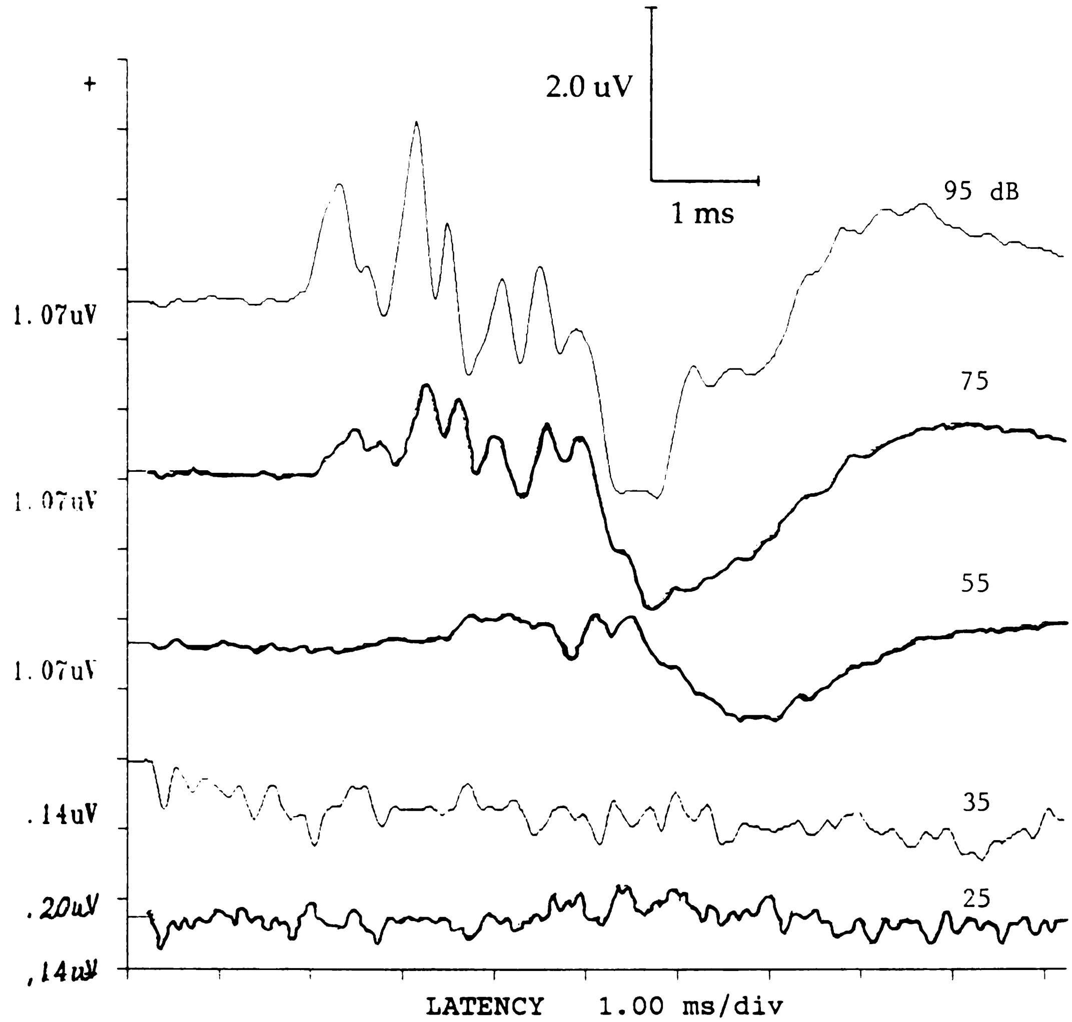


Figure 15. Representative ABR waveforms evoked by a 1,000 Hz tone burst.

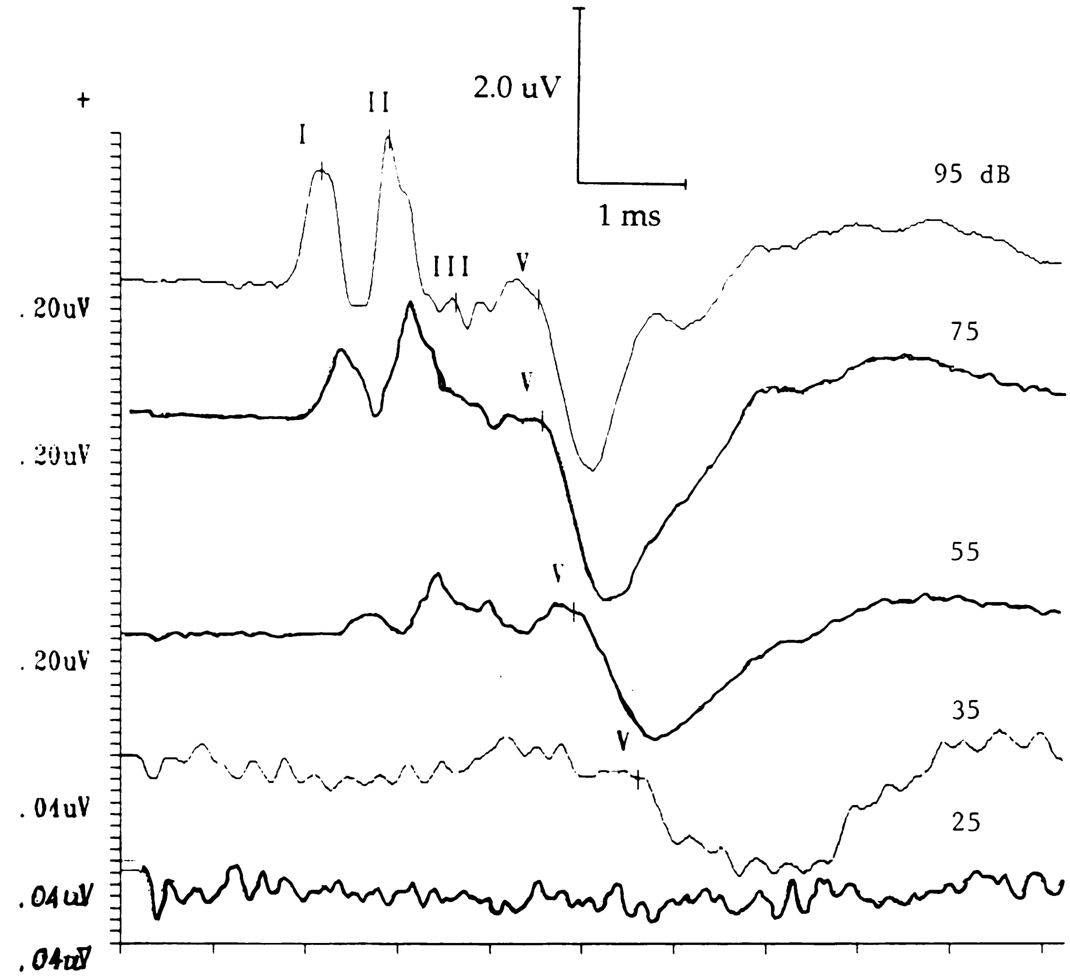


Figure 16. Representative ABR waveforms evoked by a 2,000 Hz tone burst.

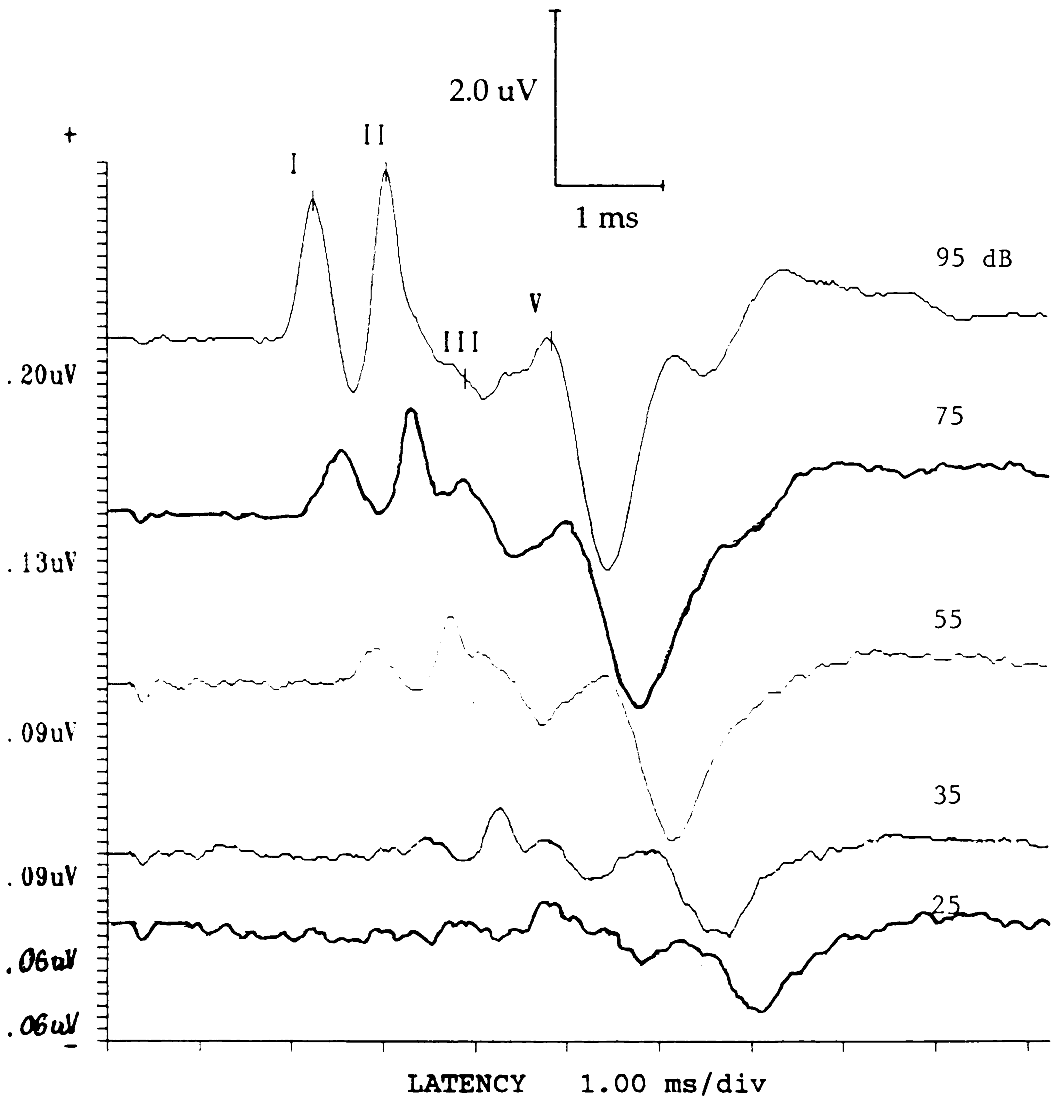


Figure 17. Representative ABR waveforms evoked by a 4,000 Hz tone burst.

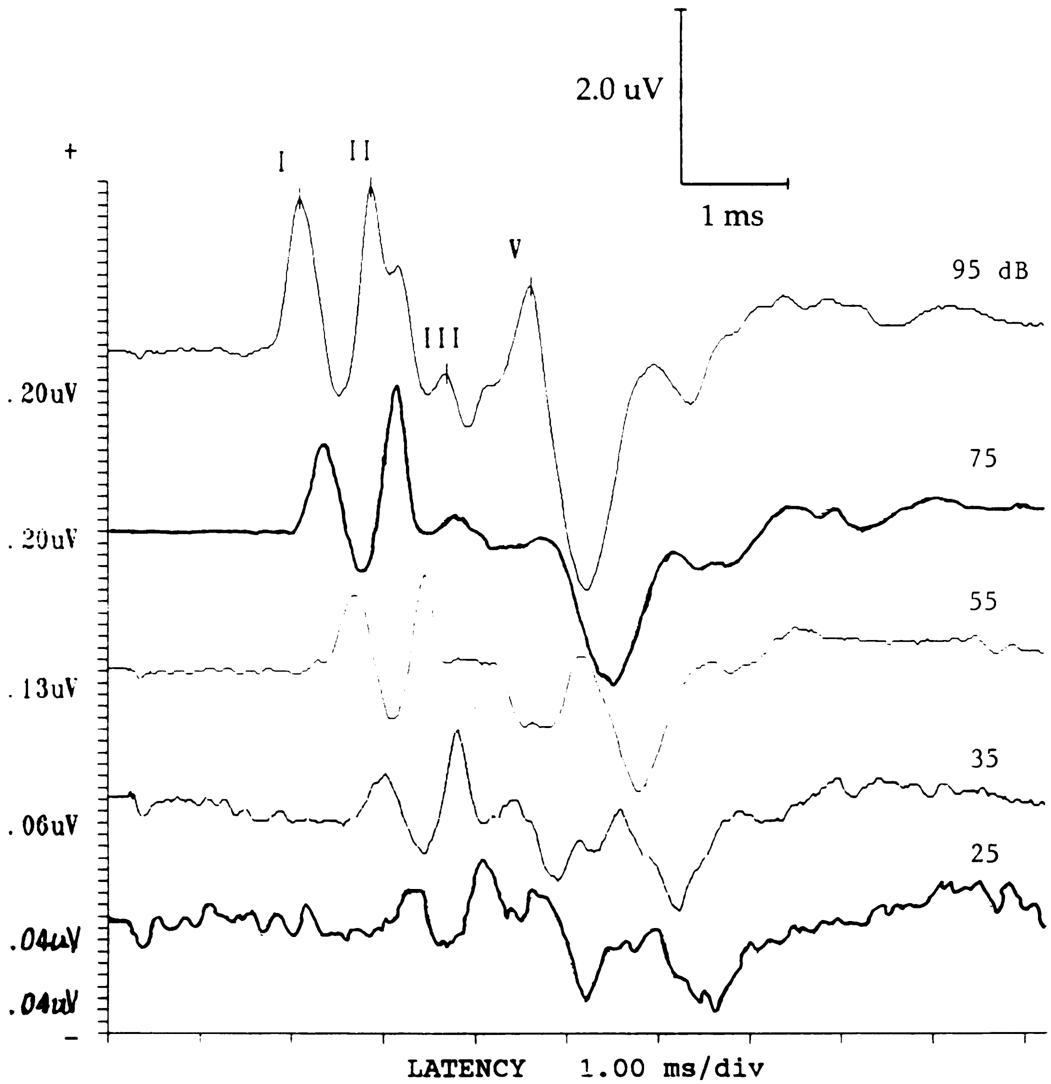


Figure 18. Representative ABR waveforms evoked by a 8,000 Hz tone burst.

normative data were analyzed in all subjects. Descriptive data for the 1000 Hz tone-burst stimuli is presented. Three general observations can be made from these data. First, canine ABRs were highly reproducible using all filter conditions, i.e., without distortion or alteration of overall wave forms. Of course, when the low-pass setting was extended to 10 kHz the data contained more high frequency noise. Thus, higher point (11 to 15) digital post-average filtering was applied to individual traces in order to better identify the major peaks recorded near-threshold levels. As observed in Figures 19 to 27 (see Appendix C), the ABR activity are equally reproducible and readily identifiable, cleaner, and well formed when the low-pass cut-off frequency is set to 3000 Hz and the high-pass setting at 10-, 100-, or 300 Hz across all stimulus frequencies.

A second general observation is that the data are quite robust at high intensity levels for any frequency, and the wave form morphology is even maintained to near-threshold levels. In fact, the major peaks were more distinct for the 8000 Hz tone burst which suggested perhaps greater synchrony of electrophysiologic activity at that frequency. In approximately 80% of the records, the ABR wave form was replicable at 25 dB for the 4000 Hz tone burst and at 35 dB for the 2000 Hz stimuli. It is apparent wave-V can be identified over a wide range of stimulus levels. The response, however, tends to become somewhat less peaked as level decreases. While among some subjects there was some variability for near-threshold data, the overall morphology of these wave forms was quite comparable across all subjects.

The third observation from these data is that within a given subject, waves-I and V latencies are highly reproducible and there is little within-subject variability at any given frequency and intensity level as noted in Tables 6 to 10 (see Appendix D). Similar invariant patterns of latencies were observed across subjects for the six filter settings (Figure 28). The largest standard deviation for latencies at any filter setting for any frequency is 0.50 dB, which was measured at near-threshold level of 35 dB SPL. Thus, it would appear that digital filtered ABR latencies are quite reproducible for individual subjects, as well as across several subjects.

In a general description of wave morphology, all records presented a series of five major peaks which were easily identifiable at suprathreshold levels. An inflection point was identified on the downward slope of peak II, and a small, sometimes biphasic peak labeled as wave-III developed as a positive-going deflection at high intensity levels in recordings of all eight subjects. Peak III was also recorded as a single, positive deflection which is substantially smaller in amplitude than the larger, adjacent peaks. At least three patterns of waves-IV and V are observed: (a) the two peaks are fused; (b) the fourth peak riding on the ascending slope of peak V; and (c) the fifth peak emerging on the descending slope of peak V. These observations have been previously reported in the dog using clicks of alternating phase and different electrode recording sites (Moore et al., 1990). These wave form configurations appeared in all subjects and across all bandpass filter settings. Thus, it would appear that tone-burst ABRs behave like rectangular click-evoked auditory brain-stem responses at suprathreshold levels as well. Thus, different filter settings do not appear to consistently alter wave form morphology or peak configurations.

Wave-I Latency

Mean wave-I latencies as a function of level are presented in Figure 29 with filter band-pass as the parameter. Data are summarized for the right and left ears for eight dogs respectively. As expected, there is a decrease in latency with increases in intensity level for all frequencies, and the higher the frequency the shorter the mean peak latency. Furthermore, there is a tendency for wave-I latencies across all filter settings to be quite stable and they superimpose at each decreasing intensity level. Mean latencies summarized for the 2000 Hz and 4000 Hz tone burst (TB), however, did not reveal the expected systematic change in latency with changes

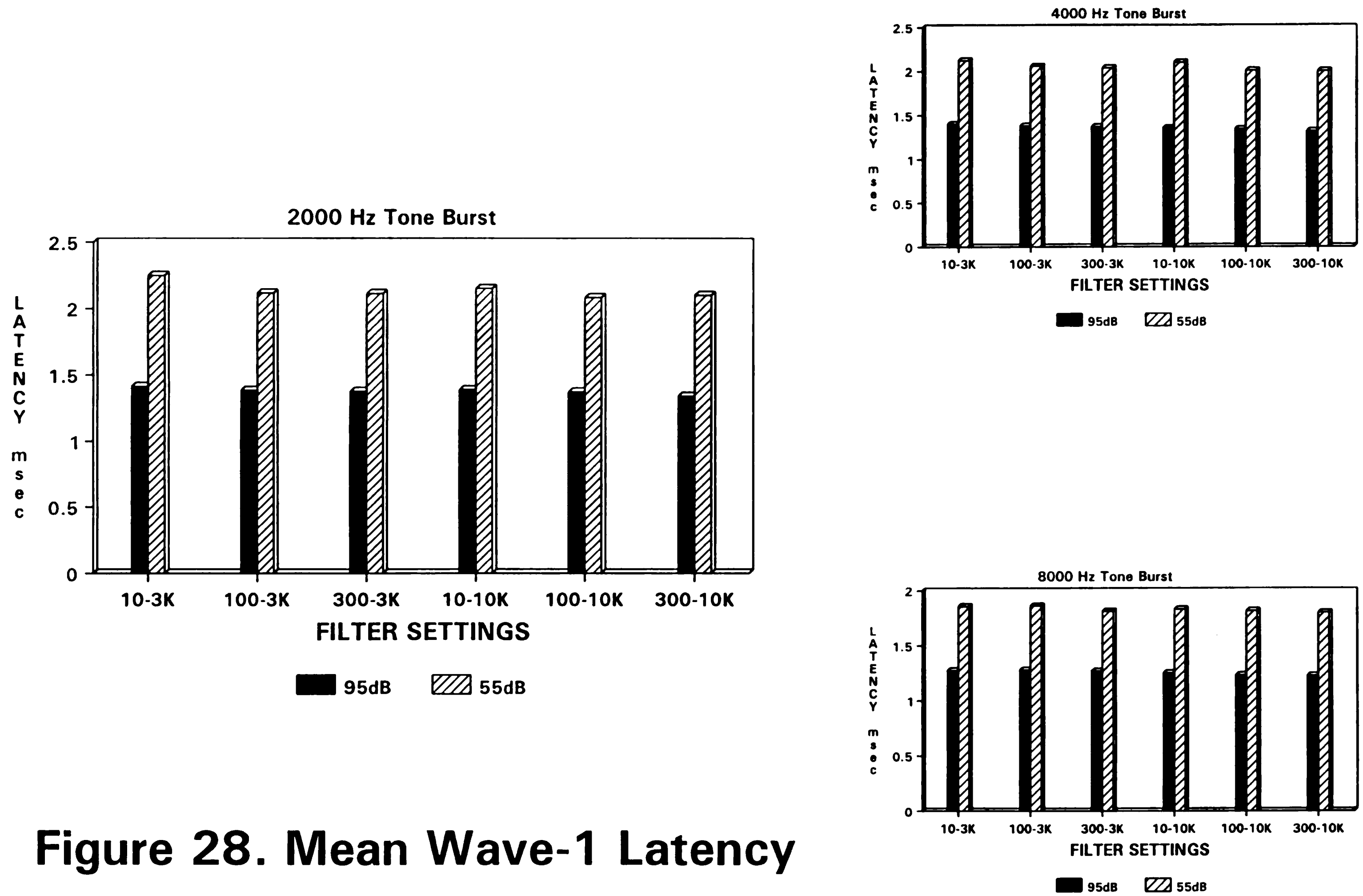


Figure 28. Mean Wave-1 Latency

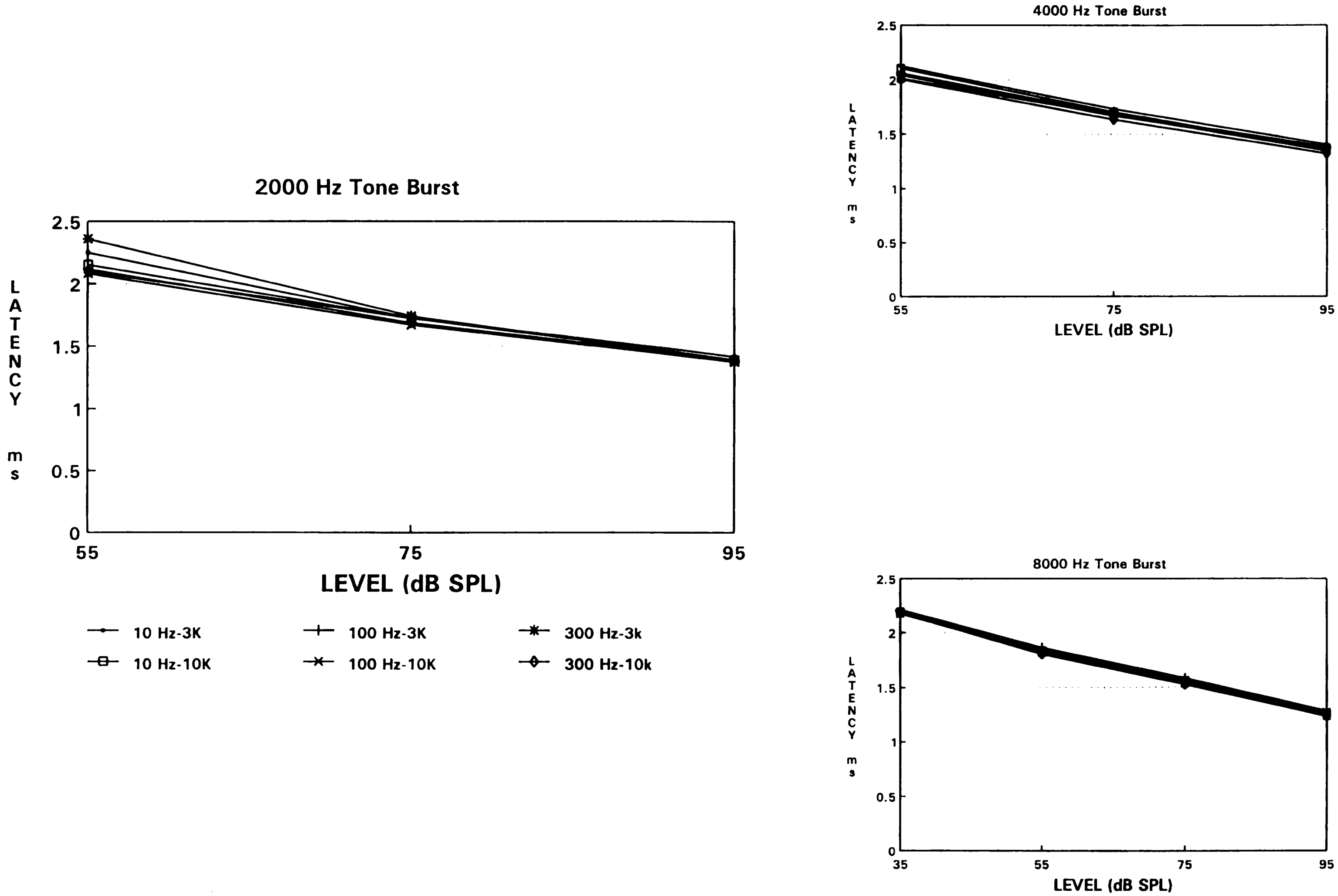


Figure 29. Wave-1 Latency-Intensity Functions

in frequency seen with human subjects (Gorga et al, 1988). In fact, the data revealed convergent latencies for both frequencies at high intensity levels which suggest that the spread of excitation along the cochlea partition for both stimuli may converge to a narrow region shifting toward the apical end of the cochlea. Mean latencies for the 8000 Hz TB were shorter across all filter settings.

In all subjects, the first peak consistently disappeared below 55 dB SPL for the 2000- and 4000 Hz TBs. Thus , wave-I latencies could only be systematically measured at the three highest supra-threshold levels. ABR recordings of four subjects showed an identifiable peak at 35 dB SPL for the 4 kHz stimuli. For the 8 kHz stimuli, wave-I was recorded at 35 dB in 100% of subject's tracings and at 25 dB in 60% of the subjects. In fact, ABR wave form morphology was still clearly identifiable at the lowest SPL tested as individual peaks were easily discerned. These suggest perhaps more acute sensitivity and/or a greater synchrony of high frequency fibers for the 8 kHz tone burst, i.e., a lower electrophysiologic threshold in this frequency region. A lower behavioral threshold for pure tones in the 8000 Hz region has been reported in the canine irrespective of breed and head size (Heffner, 1983). That is, Heffner presented hearing contour lines which indicated lower thresholds at 8 kHz and gradually elevating threshold levels above and below this frequency.

Table 6 reports descriptive mean wave-I latencies and standard deviations (+1) as a function of frequency and filter settings. These data were obtained in response to 95 dB SPL tone bursts delivered to right and left ears. Perusal of the tabled data reveals a gradual decrease in latency values as the high-pass cut-off frequency is increased. A significant Friedman's two-way analysis of variance ($p < 0.01$) statistic was utilized for the six filter settings at each tone bursts. According to Kendall's coefficient of concordance, there is a moderate degree of association between the filter conditions at all test frequencies.

To determine which filter settings were significantly different for latency at suprathreshold levels, Nemenyi's Test (Conover, 1980) allowed for multiple comparisons of high- and low-pass filter conditions. Table 11, 12, and 13 (see Appendix D) summarize the pairwise comparisons of the mean sums of ranks for 2000-, 4000-, and 8000 Hz tone bursts respectively. The latency differences are significant for the 300-10000 Hz filter bandpass which consistently measured shorter absolute peak latencies at all test frequencies. For the 4 kHz TB, significant differences were revealed for both the 100-10000 Hz and 300-10000 Hz filter conditions. These results were unexpected, as previous human ABR work with digital filtering (Doyle and Hyde, 1981) have quantified stable peak latencies

TABLE 6. Wave-1 Latencies-Mean (M) and standard deviations (SD)-at 95 dB SPL for each of six digital band pass filter settings across three tone bursts. A total of eight cases (N=8) represents the group data. The Friedman's (X^2_r) test statistic also is reported along with Kendall Coefficient of Concordance (W). ($X^2_{r\alpha}$ = 15.07)

	Band-Pass	Filters in Hz				
	10-3000 F1	100-3000 F2	300-3000 F3	10-10000 F4	100-10000 F5	300-10000 F6
2kHz TB						
M(ms)	1.413	1.383	1.375	1.388	1.370	1.338
SD	0.040	0.049	0.083	0.049	0.050	0.076
X^2_r (df=5)	>	>	> 15.71*	<	<	<
W			0.39			
4kHz TB						
M(ms)	1.403	1.383	1.373	1.360	1.345	1.320
SD	0.062	0.066	0.072	0.071	0.054	0.083
X^2_r (df=5)	>	>	> 26.44*	<	<	<
W			0.66			
8kHz TB						
M(ms)	1.275	1.280	1.270	1.255	1.233	1.230
SD	0.067	0.071	0.068	0.070	0.070	0.068
X^2_r (df=5)	>	>	> 16.62*	<	<	<
W			0.32			

* $p < 0.01$

with increasing high-pass filter cut-off frequency to 500 Hz; low-pass filter cut-off frequencies from 3000 Hz down to 1000 Hz did not affect peak latency measures. The present study did not reveal any significant latency differences when the low-pass cut-off frequency was shifted from 10000 Hz down to 3000 Hz. Our findings of shorter peak latency measures to high intensity stimuli at increasing high-pass cut-off frequencies are an exception to the general finding that zero-phase filters do not produce significant latency shifts (Elberling, 1979; Domico and Kavanaugh, 1986).

Mean latency values to 55 dB SPL tone bursts are displayed in Table 7. There were small differences in peak latencies between the filter settings, but no significant differences were found at each test frequency even at 35 dB for the 8000 Hz stimuli (see Table 8). Thus, the expected outcome of stable peak latencies under varying high-pass digital filtration was revealed for our data at lower tone burst stimulus levels. Except for 300-10000 Hz setting, there were no significant differences in wave-I peak latencies among the low-pass and high-pass filter conditions within tone bursts at suprathreshold and near-threshold intensity levels.

<u>Wave- I Amplitude</u>

Table 14 (Appendix E) displays mean wave-I amplitudes ($\pm$ 1 SD) across all filter conditions at each tone burst frequency at 95 dB SPL. These data emphasis the effects of

TABLE 7. Wave 1 Latencies-Mean (M) and standard deviations (SD)- at 55 dB SPL for each of six digital band pass filter settings across three tone bursts. A total of eight cases (N=8) represents the group data. The Friedman's (X^2_r) test statistic also is reported along with Kendall Coefficient of Concordance (W). ($X^2_{r\alpha}$ = 15.07)

	Band-Pass Filters in Hz					
	10-3000 F1	100-3000 F2	300-3000- F3	10-10000 F4	100-10000 F5	300-10000 F6
2kHz TB						
M(ms)	2.250	2.118	2.113	2.153	2.083	2.100
SD	0.203	0.261	0.196	0.102	0.186	0.214
X^2_r (df=5)	>	>	>	9.804* <	<	<
W				0.24		
4kHz TB						
M(ms)	2.125	2.063	2.043	2.105	2.013	2.005
SD	0.134	0.133	0.129	0.162	0.065	0.162
X^2_r (df=5)	>	>	>	6.268* <	<	<
W				0.16		
8kHz TB						
M(ms)	1.858	1.863	1.815	1.835	1.820	1.803
SD	0.111	0.114	0.091	0.086	0.070	0.145
X^2_r (d=5)	>	>	>	12.946* <	<	<
W				0.32		

* $p > 0.01$

TABLE 8. Mean wave-1 peak latencies across high-pass and low-pass digital filter settings at 35 dB SPL for 8000 Hz tone bursts. A two-way statistical analysis was carried out and the significance was calculated by Friedman's test.

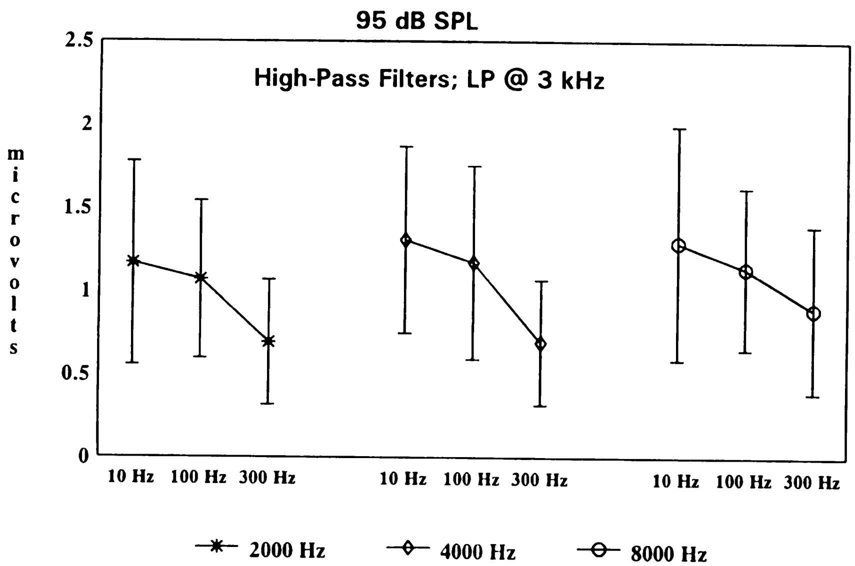
Filters......		F1	F2	F3	F4	F5	F6
8kHz TB							
	M	2.193	2.213	2.198	2.193	2.173	2.180
	STD	0.101	0.146	0.186	0.170	0.156	0.179
	X^2_r (df=5)	>	>	>	5.775*	<	< <
	W				0.18		

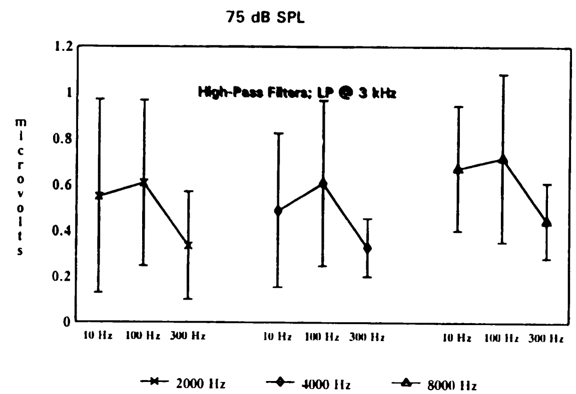
* p > 0.01

high-pass digital filtering on the ABR, i.e., a cut-off frequency at 300 Hz produced an overall reduction in response amplitude, whereas the 10- and 100 Hz settings showed similar measurements (See Figure 30). Suzuki and Horiuchi (1977) documented this reduction in ABR amplitude as the high-pass digital filter cut-off frequency was shifted from 50 Hz to 100 Hz, and then to 200 Hz.

Figures 30 and 31 present line plots of mean peak amplitude values and standard deviations obtained at high- and low-pass filters at three suprathreshold intensity levels. There is an orderly dependence of amplitude on frequency at any level and high-pass filter setting. It is also evident that 8000 Hz tone bursts consistently elicited larger peak amplitudes, followed by 4000 Hz and then 2000 Hz. Takagi, Suzuki, and Kobayashi (1985) recorded progressively increasing amplitude measures of ABR responses with increasing tone burst frequency. It appears that the more rapid rise times at higher frequencies should result in greater discharge synchrony and greater amplitude of the response relative to background noise. Additionally, the nerve-fiber density per unit distance is greater at the basal end of the cochlea as compared to high cochlea turns (Spoendlin, 1972).

The pattern of intersubject amplitude variability was not as stable as the latency measures which was expected even with digital filtration, because of the fact that amplitude





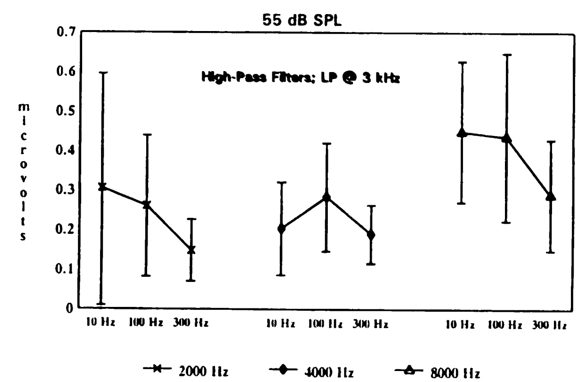
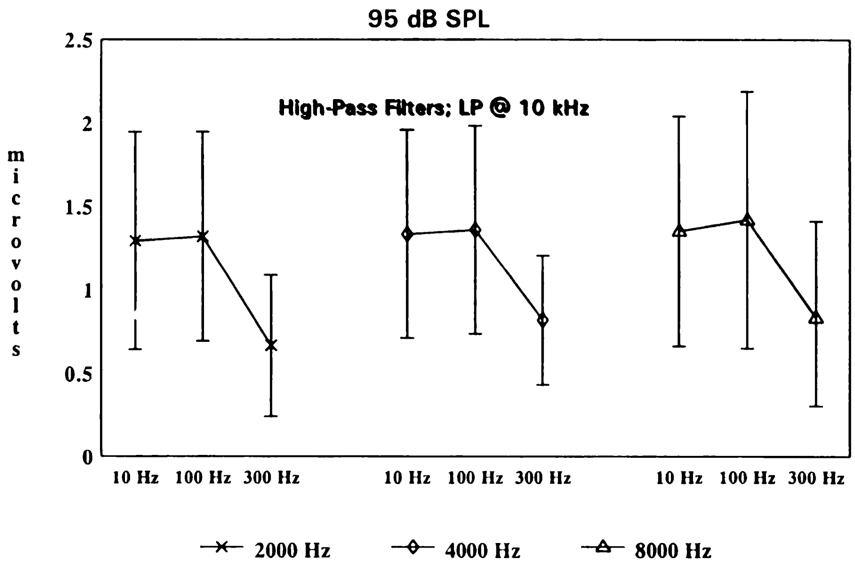
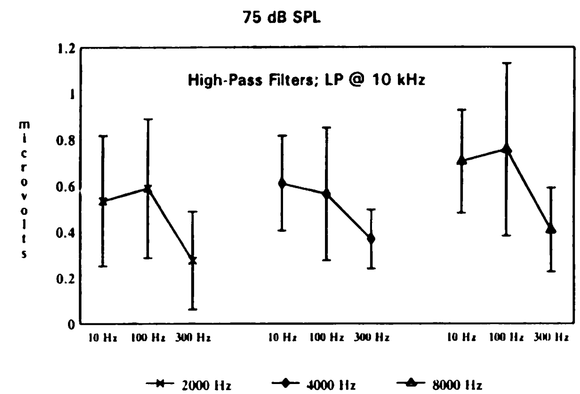


Figure 30. Wave-1 Amplitude Line Plots





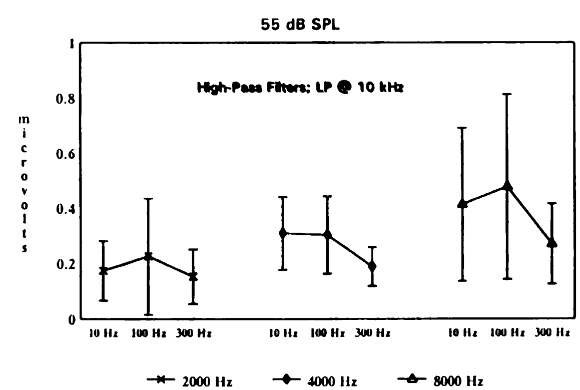


Figure 31. Wave-1 Amplitude Line Plots

measures do not appear to be normally distributed, are highly susceptible to myogenic activity and physiologic noise level, are difficult to replicate, and are easily influenced by minor alterations in recording technique (Rowe, 1981).

As noted in Tables 14, 15, and 16 (see Appendix E), significant effects of filter conditions on peak amplitude were expected in the dog given the human studies which have documented high-pass digital filtration of auditory brain-stem responses. The Friedman's test reported significant differences in mean amplitude between filter conditions at 95 -, 75-, and 55 dB SPL for each tone burst stimuli. No significant differences in peak amplitude were found at 55 and 35 dB SPL for the 2000 and 8000 Hz stimuli respectively. Overall, a moderate relationship between filter conditions was revealed by the coefficient of concordance.

To determine which filter settings were significantly different at 95 dB SPL, Nemenyi's Test allowed for multiple comparisons of high- and low-pass filter conditions. The results of these analyses are presented in Tables 17, 18, and 19 (Appendix E). Filter effects on wave-I peak amplitude were found for the 300-10K bandpass at 2000 and 4000 Hz, and the 300-3K filter was significant for 8000 Hz tone bursts . At lower stimulus levels, the Freidman's test also detected differences between high-pass filter settings for the 4-and 8 kHz stimuli, and the results are presented in Table 16. At each test frequency, the 300-10K and 300-3K bandpass settings were significantly different and tended to produce the greatest reduction in peak amplitude among the six filter conditions. These data offer further evidence that high-pass effects are remarkable at cut-off frequencies above 100 Hz. While similar trends have been observed previously in humans studies (Mason, 1984; Doyle and Hyde, 1981), the present investigation indicates that a reduction in peak amplitude at high cut-off frequencies occurs when significant amounts of low-frequency ABR activity with energy as low as 10 Hz are systematically attenuated. Because the two low-pass conditions produced similar amplitude measures and no significant differences, it seems that appreciable ABR activity and energy may not be present in the 3000 - 10000 Hz spectral range even when evoked by high frequency tone bursts.

In comparison to the present findings, Boston and Ainslie (1980) found in human subjects that a high-pass cut-off of 100 Hz did not produced significant amplitude change when implemented with zero-phase (digital) filtering. Our results produced comparable peak amplitudes at 10 - and 100 Hz cut-off frequencies, except at the 55 dB level where peak amplitudes were not superimposed but were smaller for the 2- and 4-kHz tone bursts. At the 95 dB level, a gradual decrease in amplitude with an increase in high-pass filtering was revealed with a low-pass setting of 3000 Hz.

Wave-V Latency

Mean wave-V latencies as a function of stimulus level are presented in Figure 32, with filter setting as the parameter. Data are summarized for all 8 subjects. As seen with wave-I, there is a gradual increase in latency as intensity level decreases for all frequencies, and the convergence of wave-V latencies across all filter settings was obvious at high, as well as low-intensity levels. Unexpectedly, the orderly dependence of latency on frequency at any level which has been documented in humans (Gorga et al., 1988) was not evident in these group of dogs. In fact, wave-V latency measures were very similar across filter settings and tone burst frequencies. Table 9 reports means and standard deviations ($\pm$ 1) as a function of frequency and filter settings. These data were obtained in response to 95 dB SPL tone bursts delivered to right and left ears. Perusal of the tabled data confirms the corresponding latency values, albeit shorter latency measures were recorded for the 300-10000 Hz filter with 8 kHz tone bursts only. A significant Friedman's two-way analysis of variance ($p < 0.01$) was observed at that frequency. No significant differences were found at the other test frequencies. Multiple comparisons were again made utilizing Nemenyi's Test, and significant filter effect was found at the 300-10000 Hz bandpass (Table 20, Appendix E). At near-threshold levels, no significant diferences were found

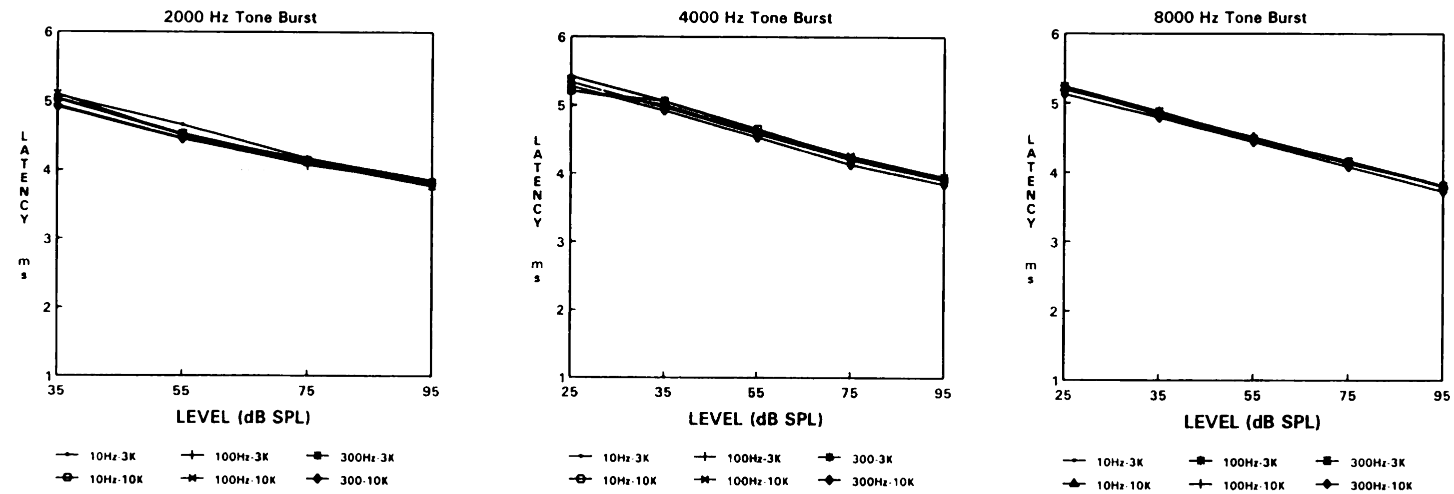


Figure 32. Wave-V Latency-Intensity Functions

TABLE 9. Mean (M) and standard deviations (SD) of wave-V latency at 95 dB SPL for each of six digital band pass filter settings across three tone bursts. A total of eight cases (N=8) represents the group data. The Friedman's (X^2_r) test statistic also is reported along with Kendall Coefficient of Concordance (W). (X^2_r = 15.07)

		Band- Pass Filters in Hz						
		10-3000 F1	100-3000 F2	300-3000 F3		10-10000 F4	100-10000 F5	300-10000 F6
2kHz	TB							
	M(ms)	3.848	3.815	3.820		3.823	3.765	3.778
	SD	0.125	0.154	0.103		0.088	0.114	0.096
	X2r(df=5)	>	>	>	9.518	<	<	<
	W				0.24			
4kHz	TB							
	M(ms)	3.928	3.900	3.913		3.908	3.950	3.843
	SD	0.140	0.150	0.163		0.165	0.160	0.164
	X^2_r(df=5)	>	>	>	14.54	<	<	<
	W				0.36			
8kHz	TB							
	M(ms)	3.815	3.815	3.913		3.803	3.795	3.728
	SD	0.087	0.106	0.163		0.076	0.078	0.092
	X2r(d=5)	>	>	>	15.27*	<	<	<
	W				0.38			

* Friedman's statistic significant at the 0.01 level.

among filter settings (see Table 10). As seen with wave-I latency, this bandpass filter greatly attenuates low-frequency ABR activity when the high-pass cut-off is set above 100 Hz (Suzuki, Sakabe, and Miyashita, 1982; Takagi, Suzuki, and Kobayashi, 1985), and it is concentrated to record high frequency components of the major peaks above the typical low-pass 3000 Hz cut-off frequency. It is possible that the higher frequency tone bursts and an extended low-pass setting are most significant for demonstrating the presence of high frequency composition of ABR activity in the dog.

Wave-V Amplitude

It is apparent that wave-V can be identified over a wide range of intensity levels as viewed in Figures 19 to 27. For the 2000 Hz tone bursts, a wave-V peak was replicated at 35 dB SPL in the recordings of five subjects and at 25 dB in three subjects. The 4000 and 8000 Hz tone bursts elicited wave-V responses at the lowest intensity level tested in all subjects and from both ears. Mean amplitude measurements were consistently larger and more robust at high intensity levels for 8 kHz tone bursts (TBs) across all filter conditions, followed by 4- and 8-kHz responses. This pattern has been reported in normal human subjects (Gorga et al., 1988). Figures 33 to 36 present line-plots of mean peak amplitude ($\pm$ 1 SD) at decreasing stimulus levels across high- and low-pass filter conditions. Characteristically, wave-V

TABLE 10. Mean wave-V peak latencies at near-threshold SPLs across six filter settings for three tone bursts. Differences were abtained from 8 dogs. A two-way statistical analysis was carried out and the significance was calculated by Freidman's (X^2_r) test.

Filters......	F1	F2	F3	F4	F5	F6
2kHz TB (35 dB)						
M	5.083	4.935	5.025	5.038	5.099	4.915
SD	0.273	0.256	0.293	0.173	0.327	0.196
X^2_r (df=5)	>	>	> 1.214*	<	<	<
W			0.030			
4kHz TB (25 dB)						
M	5.418	5.419	5.335	5.208	5.305	5.275
SD	0.284	0.354	0.315	0.585	0.465	0.172
X^2_r (df=5)	>	>	> 7.482*	<	<	<
W			0.187			
8kHz TB (25 dB)						
M	5.205	5.245	5.223	5.215	5.190	5.130
SD	0.179	0.287	0.243	0.311	0.248	0.309
X^2_r (df=5)	>	>	8.750*	<	<	<
W			0.219			

* $p > 0.01$

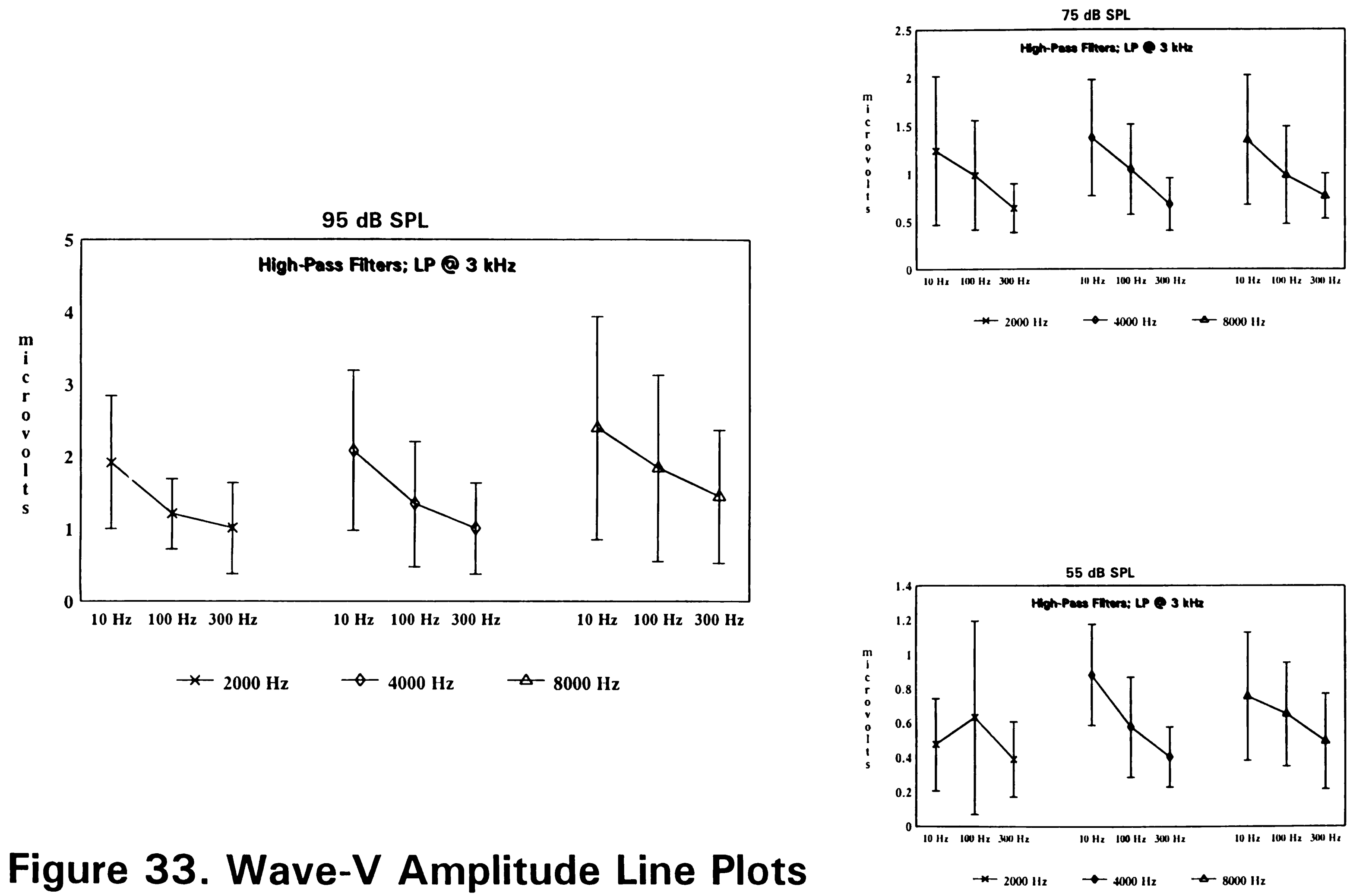
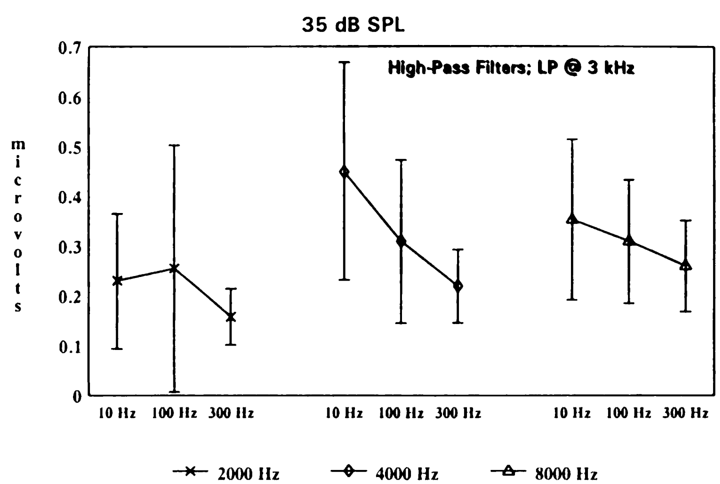


Figure 33. Wave-V Amplitude Line Plots



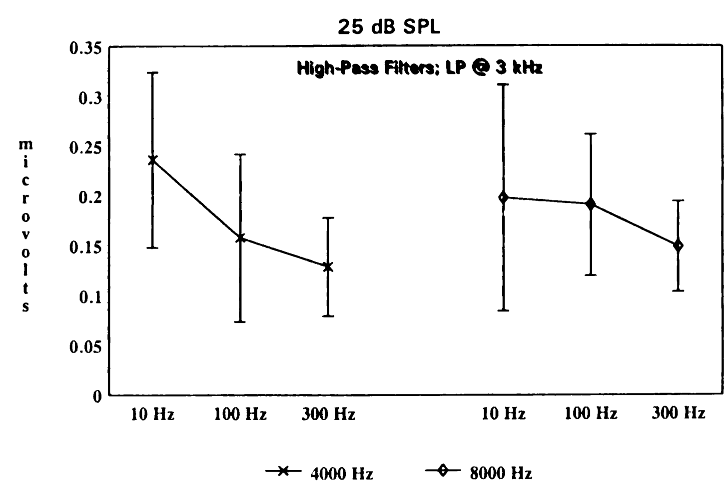
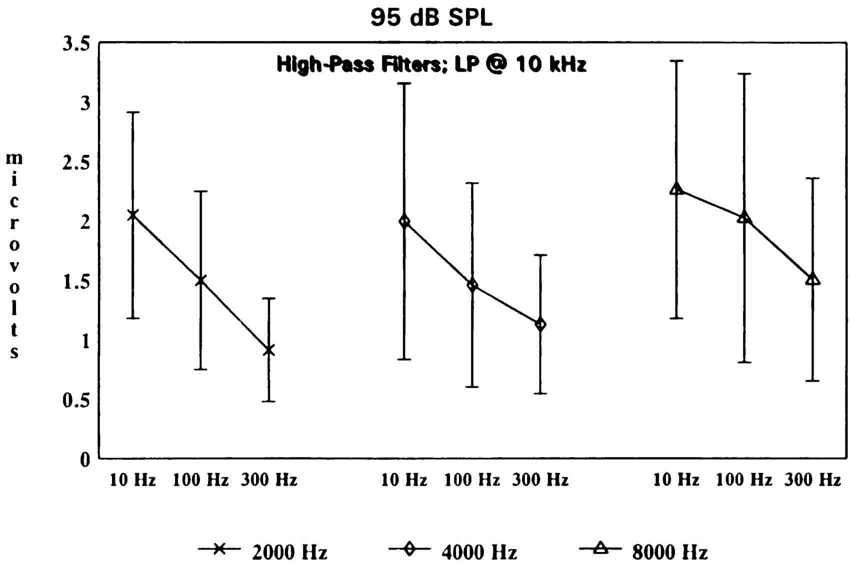
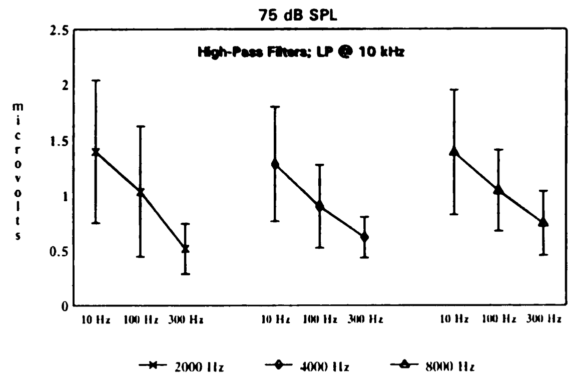


Figure 34. Wave-V Amplitude Line Plots





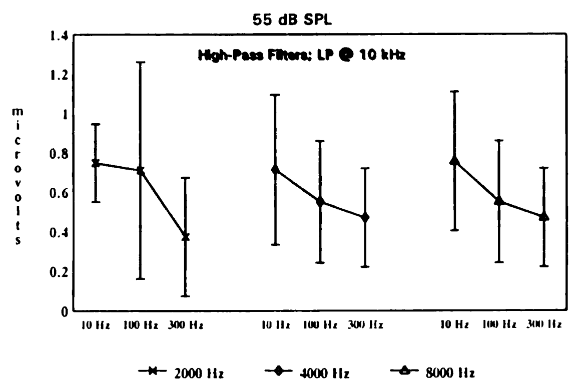
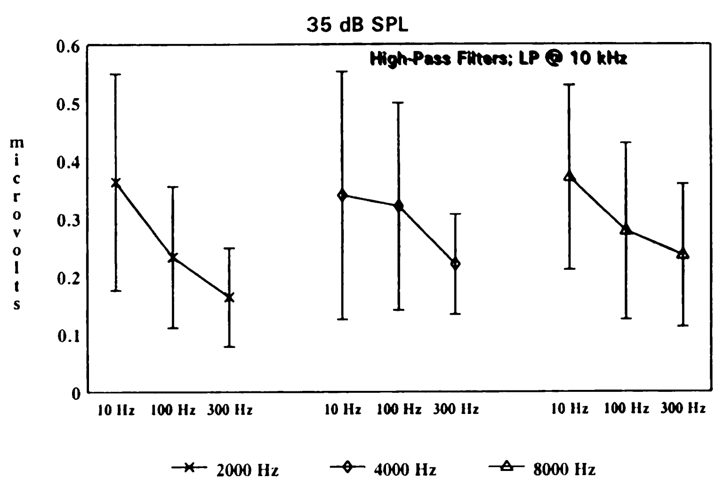


Figure 35. Wave-V Amplitude Line Plots



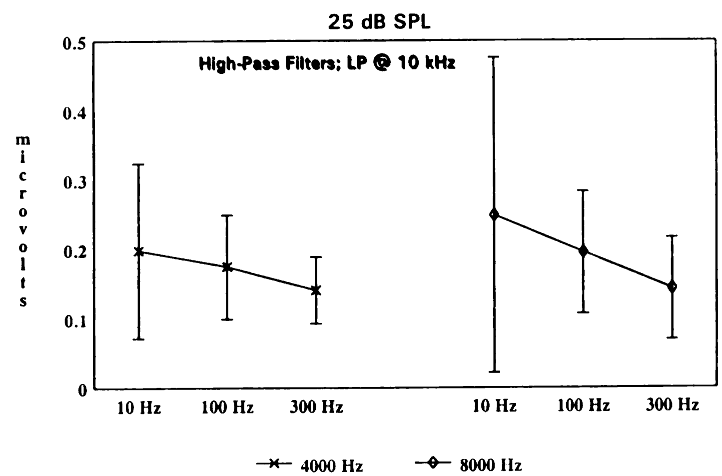


Figure 36. Wave-V Amplitude Line Plots

amplitude monotonically decreased as the cut-off frequency was shifted from 10 to 100 and then 300 Hz. That is, a marked decline in the amplitudes was observed at the 100 and 300 Hz cut-off frequencies. It was noted that the amplitude attenuation at 100 Hz was greater in response to the lower tone bursts (2 and 4 kHz) than at the higher frequency frequency stimulus (8 kHz). Similar results were also recorded in human ABR studies for lower and higher frequency tone burst stimuli (Suzuki and Horiuchi, 1977; Suzuki et al., 1982). The present investigation also confirmed that the slow positive wave-V contains a substantial amount of low-frequency energy around 100 Hz and below. Furthermore, as stimulus intensity was decreased, the monotonic pattern of amplitude reduction with increasing high-pass cut-off frequency was also observed. Several human studies have concluded that the gradual elimination of slow wave activity by high-pass filtering can cause a major reduction in response amplitude (Kavanaugh, Harker, and Tyler, 1984; Kavanaugh, Domico, Franks, and Jin-Cheng, 1988). Those studies also concluded that lowering of the mean spectral content is primarily due to the progressive loss of the high frequency components of the ABR and not to a shifting of individual response frequencies toward a lower value.

A significant Friedman's two-way analysis of variance ($p < 0.01$) statistic was observed between the six filter settings for all three tone bursts (See Table 21). In addition, Kendall's W calculations indicated a high correlation between the variables and indexed the strong relationship among the mean ranks of sums. To determine which filter settings were significantly different, Nemenyi's multiple comparison analysis (Tables 22 to 24) found that the 300-3000 Hz and 300-10000 Hz bandpass filters produced the greatest attenuation in peak amplitude which was also reported for wave-I measurements. No significant differences emerged between low-pass filter conditions at 3000 and 10000 Hz when the high-pass cut-off frequency was held constant. At near-threshold levels for the tone-bursts, no significant filter effects occured as noted in Table 25.

Larger overall mean amplitudes of wave-V elicited by 8 kHz tone bursts at lower intensity SPLs suggest a greater auditory sensitivity at this frequency for the dog. The ABR response and wave form morphology was quite clear and comparable even at near-threshold levels across subjects. This large wave form is regarded as the most useful index in the ABR for the threshold estimation of hearing. In this group of dogs electrophysiologic audiograms were constructed using wave-V elicited at the lowest SPL across four tone burst frequencies as displayed in Figure 37. For the 1000 Hz TB, wave-V activity disappeared below 55 dB , and was discernible to 35 dB for the 2000 Hz TB. A wave-V response was still

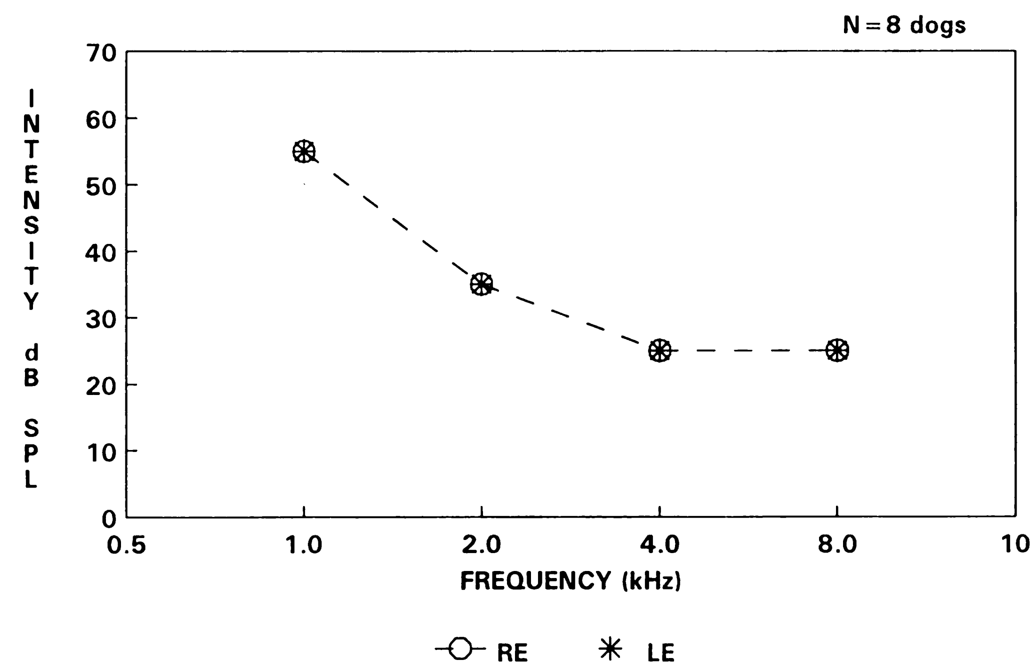


Figure 37. Audiogram of Normal-Hearing Dogs

visible and measurable at 25 dB for the 4000 and 8000 Hz stimuli, and it is apparent that a lower level threshold estimate would have been possible at these frequencies if lower SPLs had been utilized in the experiments.

Hearing-Impaired (HI) Data

From the ten original research dogs procured for this investigation, two adult canines (1 female, 1 male) did not meet the selection criteria for the normal-hearing experimental group. Otoscopic examination and acoustic immittance results are discussed in the method chapter. Both dogs manifested non-compliant middle ear systems. Thus, a conductive type hearing loss was suspected in both cases. The experimental protocol was run on the left ears in both subjects. Electrophysiologic recordings from the female (subject 1) are viewed in Figures 38 to 41 (see Appendix F), and ABR activity from the male (subject 2) are shown in Figures 42 to 45.

Visual inspection of the raw data from subject 1 revealed responses at 95 and 75 dB for 1000 and 2000 Hz tone bursts, while responses were elicited down to 55 dB for the 4000 and 8000 Hz stimulus frequencies. Recordings at 1000 Hz from subject showed showed the classic frequency-following-response (FFR), described earlier in the normal-hearing subjects at the higher stimulus levels. Evoked potentials were also measurable at 95 and 75 dB for the 2 kHz TB and at 55 dB for 4- and 8-kHz stimuli. Electrophysiologic recordings from both subjects revealed a pattern of transition from no response at a lower SPL to a larger response at the next highest SPL. Davis (1983) showed a similar transition pattern in the ABR records of his hearting-impaired subjects and concluded that this is good evidence of serious impairment of the low-intensity 'cochlear amplifier' or recruitment. Thus, it is possible that some end-organ pathology may be present in these ears, but this could not be confirmed.

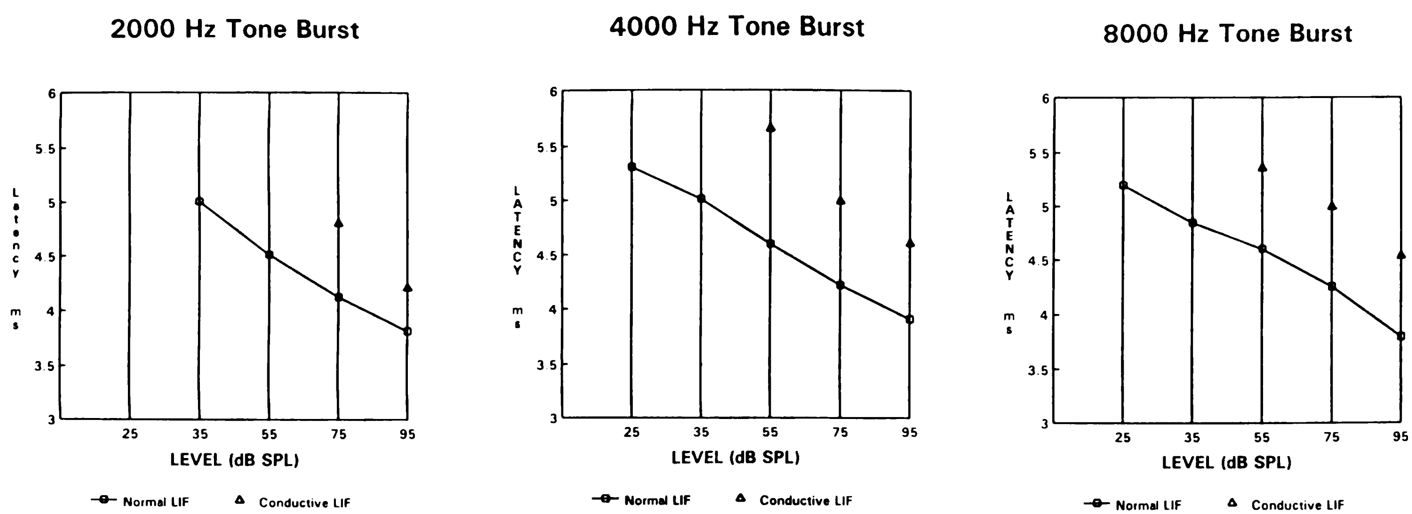
As with the normal-hearing group, HI group data was analyzed for the upper three test frequencies. The effects of filtering on latency and amplitude were not systematically studied because of the very small sample in this group. Therefore, the reported wave form calculations were collapsed across the six settings from the left ears of both dogs. Descriptive statistics of waves-I and V latency functions are displayed in Table 26. In comparison to the normative data reported in Tables 6 and 9, latency onset values for both peaks are prolonged approximately 0.4-0.6 milliseconds (ms) for each tone burst frequency. There is general consensus that conductive pathology prolongs wave component latency for unmasked air conduction stimuli (McGee and Clemis, 1982; Fria and Sabo, 1980), and that examining the wave-V latency-intensity function (LIF) is common approach to predicting the degree of the resulting hearing impairment.

TABLE 26. Waves I and V Latencies- Means (M) and standard deviations (SD)-at descending SPLs for three tone bursts. Data was collapsed across six filter settings from the left ears of two subjects (N=12).

	Wave-1			Wave-V		
(dB SPL)	95	75	55	95	75	55
2kHz TB						
M(ms)	1.857	2.383	-	4.295	4.810	-
SD(±1)	0.088	0.234	-	0.209	0.338	-
4kHz TB						
M(ms)	1.975	2.382	2.977	4.603	4.997	5.669
SD	0.046	0.038	0.156	0.100	0.137	0.181
8kHz TB						
M(ms)	1.833	2.240	2.582	4.538	5.000	5.366
SD	0.037	0.144	0.110	0.063	0.167	0.210

Figure 46 illustrates the wave-V LIF for each tone burst, with the solid lines reflecting normative values. The amount in decibels by which this function is shifted to the right of the normal function in time is considered to be predictive of the conductive loss. As displayed, the slope of the LIF in conductive impairment parallels the normal slope function ,which was first reported by Hecox and Galambos (1974) for a normal hearing, human subject and a patient with confirmed conductive pathology. In their estimation, a 1-dB intensity decrease produces a 30- to 60-us increase in latency, or a 0.3- to 0.6 ms latency increase per 10 dB of hearing loss. For our canine data, a 1-dB intensity decrease produced a 20- to 30-us latency increase per 10 dB of hearing loss. From the LIFs plotted in Figure 46, a 30- to 40-dB conductive loss (approximate) would be predicted for the test frequencies on the left ear.

When comparing ABR and audiometric findings using this technique, a predicted discrepancy less than 15 dB at 1-, 2-, and 4 kHz was reported by Fria and Sabo (1980) and McGee and Clemis (1982) in estimating conductive hearing impairment. In this regard, Eggermont (1982) has criticized this approach and stated that because a given latency value will occur for a range of intensities approximately 20 dB wide, the minimum loss detectable will be 20 dB and the inaccuracy in the amount of loss exceeding this value will also be 20 dB. Thus, mild



Bandpass: 10-10000 Hz

Figure 46. Wave-V Latency-Intensity Functions

impairments could remain unidentified and the effects of significant pathology underestimated. Furthermore, these estimates break down as the audiologic picture become complex, i.e., in cases of mixed hearing loss or primarily low-frequency impairment (Borg, Lofqvist, and Rosen, 1981). While a "normal" slope to the LIF with elevated thresholds is consistent with conductive pathology, it is not diagnostic of it. Additional research is needed before this issue is sufficiently resolved.

Summary

Digital Filter Effects on ABR Latency

This investigation applied high- and low-pass digital filtering to record auditory brain-stem responses (ABR) in a group of eight anesthetized male and female dogs. Evoked potentials were elicited by 1-, 2-, 4-, and 8 kHz tone bursts monaurally presented at decreasing sound pressure levels (SPLs). The dependent variables-latency and amplitude-were systematically measured and statistically analyzed to determine the effects of modified bandpass settings at suprathreshold and near-threshold stimulus levels.

Mean wave-I latency measurements were found to be quite stable across the six filter conditions, although a slight decrease in peak latency was observed when the high-pass cut-off frequency was shifted from 10-, to 100-, and then 300 Hz. This pattern was exhibited within each tone burst paradigm at high-intensity levels. The results of The Freidman Test for Matched Samples reported significant differences between high-pass filter settings which was unexpected given the nature of digital filtering and its accurate reproduction of the auditory brain-stem responses and related potentials, without signal distortion and delay. After each analysis of variance, Nemenyi's multiple comparison estimations determined that the 300-10000 bandpass setting was significantly different and therefore produced the shortest mean peak latency at each test frequency. Thus, the null hypothesis was rejected at the 0.01 level of confidence. At lower stimulus levels, however, no significant differences among and between filter settings were calculated at any test frequency, and only small differences in latency values were noted which was the expected outcome. The null hypothesis was therefore accepted for this research question.

In general, wave-V latency was unaffected by high-pass digital filtering as expected, whereas no significant differences were found ($p > 0.01$) for the 2- and 4 kHz tone burst responses elicited at high and low intensity levels. On the other hand, Freidman's analysis of variance revealed a significant difference in peak latency values for 8 kHz stimuli presented at the highest intensity level (95 dB). A moderate degree of association between the filter settings was measured by Kendall's Coefficient of Concordance. Pairwise comparisons using Nemenyi's Test specified the 300-10000 Hz bandpass as significantly shorter ($p < 0.01$) in latency than the other filter settings. At lower stimulus levels, a small Friedman's test statistic was calculated and latency measurements were not significant. Our data supports Moller's (1983) conclusion that high-pass digital filtering does not produce significant latency shifts on low-intensity auditory brain-stem responses.

Digital Filter Effects on ABR Amplitude

Our data corroborates previous investigations which have demonstrated major peak amplitude reductions with increasing high-pass cutoff frequency above 100 Hz. At high stimulus levels, wave-I response amplitude was reduced some 9% between the 10- and 100 Hz cutoff frequency. At the 300 Hz cutoff frequency, mean peak amplitude reduction was approximately 30% at 4- and 8 kHz ,and 50% at the 2 kHz test frequency. This trend was observed when the low-pass cutoff was held constant at either 3000- or 10000 Hz. Freidman's analysis of variance indicated significant differences ($p <0.01$) in amplitude measurements also occurred between the six filter settings at each tone burst stimuli at lower SPLs as well. Pairwise comparison calculations revealed that both the 300-3000 Hz and 300-10000 Hz bandpass filters produced the largest reduction in response amplitude and were significant at the 0.01 level of probability.

Digital filter effects on wave-V amplitude were also demonstrated in terms of magnitude reduction to increasing high-pass cutoff frequency. Average peak amplitude diminution was approximately 50% between the 10- and 100 Hz cutoff and 30% at the 300 Hz cutoff frequency for all tone burst stimuli. Significant differences ($p < 0.01$) in filter settings at high intensity levels were calculated by Friedman's Test, and a high degree of association between filter settings was revealed. Pairwise comparison analysis indicated that both the 300-3000 Hz and 300-10000 Hz filter settings produced the largest reduction in overall peak-to-peak amplitudes and were significantly different at the 0.01 level of probability, thereby rejecting the null hypothesis. No significant differences emerged ($p > 0.01$) between these low-pass settings when the high-pass cutoff frequency was held constant at 300 Hz. Our data supports Doyle and Hydes' (1981) finding that wave-V undergoes a 60% or greater amplitude decrease as the high-pass cutoff frequency changes from 10 to 100 Hz.

Conversely, digital filter effects on wave-V amplitude to low-intensity (near-threshold) levels were insignificant according to Freidman's Test results. As noted in Table 25, no substantial amplitude reduction with increasing high-pass cutoff frequency emerged for any tone burst stimuli. In fact, similar measurements were obtained across the filter settings, and in some cases the 100 Hz high-pass measurements were slightly greater in mean peak amplitude than the 10 Hz estimations. Overall, the 300-3000 Hz and 300-10000 Hz bandpass settings yielded smaller mean peak amplitude responses, while the 10-3000 Hz and 10-10000 Hz settings produced the largest amplitude measurements, and, therefore, it can be concluded from these data that the maximum amplitude of the Jewett wave-V peak for detection of a response close to threshold can be achieved with wide filter bandwidths. These settings also showed the largest mean peak-to-peak amplitudes for tone burst stimuli presented at suprathreshold levels, and the 8000 Hz stimuli consistently evoked the greater magnitude response peaks followed by 4000 and then 2000 Hz tone bursts.

CHAPTER V

DISCUSSION

Chapter IV described the results produced by 8 normal hearing, anesthetized adult dogs from investigating the use of digital filtration in recording the auditory brain-stem response (ABR) evoked by tone bursts centered at 2000, 4000, and 8000 Hz. High-pass (10, 100, 300 Hz) and low-pass (3000, 10000 Hz) Butterworth recording filters with a 12 dB /oct slope were employed in an randomized block designed experiment.

Frequency Composition of the ABR

The results of this study offer further evidence that high-pass digital filtering at 300 Hz has a large effect on waves I and V amplitude, and that as the low-cut frequency is shifted from 10 to 300 Hz peak amplitude is significantly reduced especially at high stimulus levels. The extent to which the individual waves are influenced by changes in filter band-pass is closely related to their spectral composition, and, therefore, the attenuation of peak amplitude illustrates the filtration of frequency components of the ABR. Suzuki et al., (1982) used power spectral analysis to describe the main energies of different components of high-intensity tone burst ABR which were concentrated in the following bands: 50-150 Hz for wave-V, 500-600 Hz for waves-I, III, and V, and 1000-1100 Hz for waves-I, II, III, IV, and V. According to this early nomenclature, the slow positive wave (V) contains all spectral components of the three bands. A similar experiment conducted by Kevanishvilli and Aponchenko (1979) demonstrated that the main spectral bands of wave-I (400-1000 Hz) and of wave-V (100-500 Hz) only partially overlap each other. For normal subjects, the potentials elicited by high intensity stimuli are comprised of frequencies between 50 and 1000 Hz, but , as the stimulus intensity decreases, the potentials may be composed of lower frequency components due to the progressive loss of high frequency composition (Kavanaugh et al, 1988).

The data from this study revealed only a 9% drop in wave-I amplitude between the 10 and 100 Hz settings and a 30% reduction between the 100 and 300 Hz cutoff frequencies with the low-pass slope constant at 3 kHz. That information suggests very little energy for this peak is present below 100 Hz and a modicum of energy is represented in the 100-300 Hz region. It would appear that the remaining spectral content is contained in the region above 300 Hz. Conversely, wave-V amplitude was reduced about 40% between the 10 and 100 Hz settings and some 33% between the 100 and 300 Hz high-pass filters. In this regard, the composite peak has considerable energy which is concentrated in the 10-300 Hz frequency range. Takagi et al., (1985)) performed power spectral analysis of the ABR to tone-burst stimuli and reported that two frequency components were present: 50-300 Hz which contains the frequency range for peak A band (slow activity), and 400-1500 Hz (fast activity) which encompasses the frequency range of peaks B and C bands. The present study agrees well with the above-mentioned findings of Kevanishivili and Aphonchenko (1979) as well as Takagi et al., (1985), that the ABR consist of slow and fast activity which have frequency composition above and below 300 Hz respectively.

When the low-pass filter setting was held constant at 10 kHz instead of 3 kHz, wave-I peak amplitude was not affected at high-stimulus levels, but a slight increase as the high-pass filter was shifted from 10 to 100 Hz. The 300 Hz cut-off setting produced a 43% drop in mean peak amplitude across the tone-burst stimuli which confirms our previous finding that wave-I contains energy in the region above 300 Hz. Low-pass filter conditions did not produce any significant amplitude effects and appeared to be less crucial. In contrast, wave-V peak measurements were significantly affected by both the 100 and 300 Hz high-pass cut-offs which produced 22% and 30% amplitude reductions respectively. Herewith is another confirmation that wave-V is composed of frequencies covering the slow and fast activity bands which may overlap around the 300 Hz band-pass region.

At low-stimulus levels (55 dB SPL), mean amplitude measurements of wave-I were still significantly different for either the 300-3000 Hz or 300-10000 Hz bandpass settings which produced an average 30% reduction in response magnitude. Wave-V measurements at near-threshold levels (35 and 25 dB) were similar and not significantly different between the filter settings, although amplitude attenuation at 300 Hz cut-off is greater in the response to 2 kHz stimuli than those to high frequencies. Our data indicates in Figure 32 that amplitude attenuation at the 300 Hz cut-off is greater than at the 100 Hz cut-off which appears to not significantly eliminate response energy in ABRs elicited by low-intensity stimuli. Kavanaugh et al (1988) support these findings in their ABR spectral analysis study. These results also agree closely with Elberling's (1979) conclusion which emphasized the small effect of high-pass filtering (at 100 Hz) on the low-intensity ABR recordings.

Optimal Band-pass Settings for Clinical Use

A wide range of high-pass filters has been employed in brain-stem response audiometry, as displayed in chapter 1. Many workers have used a relatively high level of filtering which removes slower components of the response (Marshall, 1985, 1986), and it is more recent that low enough cut-offs have been employed to allow these lower frequency components to be recorded (Holliday and Selle, 1988; Knowles et al, 1988). The results of this study suggest that for routine brain-stem response audiometry employing high-frequency stimuli, a high-pass filter of 10 Hz (with a a roll-off of 12 dB/octave) is preferable over 100 Hz for suprathreshold or otoneurological diagnosis in order to record slow components of the ABR which are present in the 10 to 100 Hz range. Mason (1984) concluded that a filter setting lower than 10 Hz would not be desirable since noise levels-alpha and beta activities of the EEG and myogenic background-are excessive, and he recommended that a high-pass filter of 20 Hz (36 dB/octave slope) will significantly attenuate a considerable proportion of this activity at high stimulus levels.

When using the ABR for estimating hearing thresholds, our results suggest that special care should be taken to select high-pass filtering to maximize the detection of the wave-V response close to threshold. Although no significant differences in mean peak amplitude across filter settings were calculated, the 300 Hz cut-off produced the largest reduction in response amplitude. Thus, it would appear that a high-pass filter of 10 Hz or 100 Hz (with a roll-off of 12 dB/octave) is preferable for recording close to threshold. Mason (1984) suggested that a more steeper slope, such as 48 dB/octave, be employed in order to produce as good a separation of noise and the response. It could be argued that had a steeper slope been employed in the present study, larger differences in peak amplitude between the 10 and 100 Hz cut-offs may have been observed. Low-pass filter conditions did not produce any significant amplitude effects and appeared to be less crucial for recording the wave-V response near threshold. Our data supports the findings of other reports which have clearly shown that a cut-off frequency in the range 10 to 50 Hz is necessary to record the slow components of the ABR.

Latency-Intensity Functions of the ABR

In the present study, mean wave-I and wave-V absolute latencies obtained at high-intensity levels were significantly shorter for the 300-3000 Hz and 300-10000 Hz bandpass filters. This striking result was unexpected given the evidence from investigations of digital filtering of ABRs that have demonstrated a total absence of latency change even at cut-off frequencies to 500 Hz (Boston and Ainslie, 1980; Svensson et al., 1987; Suzuki et al., 1982). This slight latency decrease at 300 Hz may result from the elimination of slow (low-frequency) ABR activity by systematic high-pass filtering and thereby emphasizing the main spectral components of fast (high-frequency) ABR activity elicited by high-intensity tone burst stimuli.

Another plausible explanation may be related to the excitation pattern of tone bursts along the basilar membrane. Eggermont, Spoor, and Odenthal (1976) used narrowband analysis of the compound action potential (CAP) to reflect the number of nerve fibers responding to the respective tone bursts at high and low-intensity levels. Their AP amplitude plot tended to cover a wide frequency band at high-intensity levels. For example, a 2-kHz tone burst excited an area from 500-10000 Hz, and as the stimulus intensity decreased, the frequency band narrowed and covered a 700 Hz to 2.6 kHz range at 35 dB HL. The increased nerve-fiber density per unit distance at the basal end of the cochlea results in a greater number of neural elements discharging synchronously for high-frequency stimuli and consequently shorter response latencies (Spoendlin, 1972; Kiang, 1975).

The interaction of frequency and level on tone-burst ABRs (waves-I and V) latency has been described in human subjects (Bausch, Rose, and Harner, 1980; Gorga et al., 1985; Gorga et al., 1988). Those studies reported an orderly dependence of latency on frequency at any level, i.e., a decrease in latency occurs with increases in level for all frequencies. A clear separation in latency between mid and high-frequency tone bursts was observed at moderate and low-intensity levels, but the convergence of' wave-I and wave-V latencies at all frequencies was evident at high levels. In the present study, waves-I and V latencies for the 2- , 4-, and 8-kHz stimuli overlapped at 95 dB SPL, and a clear, but slight separation in latency was observed at decreasing intensity levels (see Figures 29 and 32). It can be inferred from this data that the results at the highest intensity level primarily originate from relatively narrow regions of the cochlea at the most basal end, but as the stimuli are decreased, the components probably originate from a more apical region and latency is slightly increased (Elberling, 1974). At the lowest level tested (25 dB), 4- and 8-kHz latencies tended to superimpose while the latency for 2-kHz was decreased by 0.3 ms.

The frequency-specific latency-intensity patterns which have been observed previously in Figure 32 makes it possible to fit equations to the data, for there is systematic change in latency with changes in frequency. These data are replotted in Figure 47 on log-log coordinates and level as the parameter. The slight discontinuities in the data at 2000 Hz probably result from either stimulus factors such as rise time or to peripheral (cochlear) response properties. Still, for any level, there is a systematic change in latency with changes in frequency. Gorga et al., (1988) described a simple model which can be used to predict the normal latency for any frequency within the range from 250 to 8000 Hz. Latencies for each level can be fit with the equation,

$$L = 10^{a(\log f)+b}$$

where L is latency , f is the frequency, "a" is the slope and "b" is the intercept. Then the latency (L) for any frequency (f) at any level can be obtained by solving the equation.

Table 27 lists the slopes (a), intercepts (b) and measures of goodness-of-fit for each level. All of the latency values had significant (P < 0.01) linear regression lines of latency vs frequency. In all cases, the correlation coefficient was greater than 0.500 which confirms that these

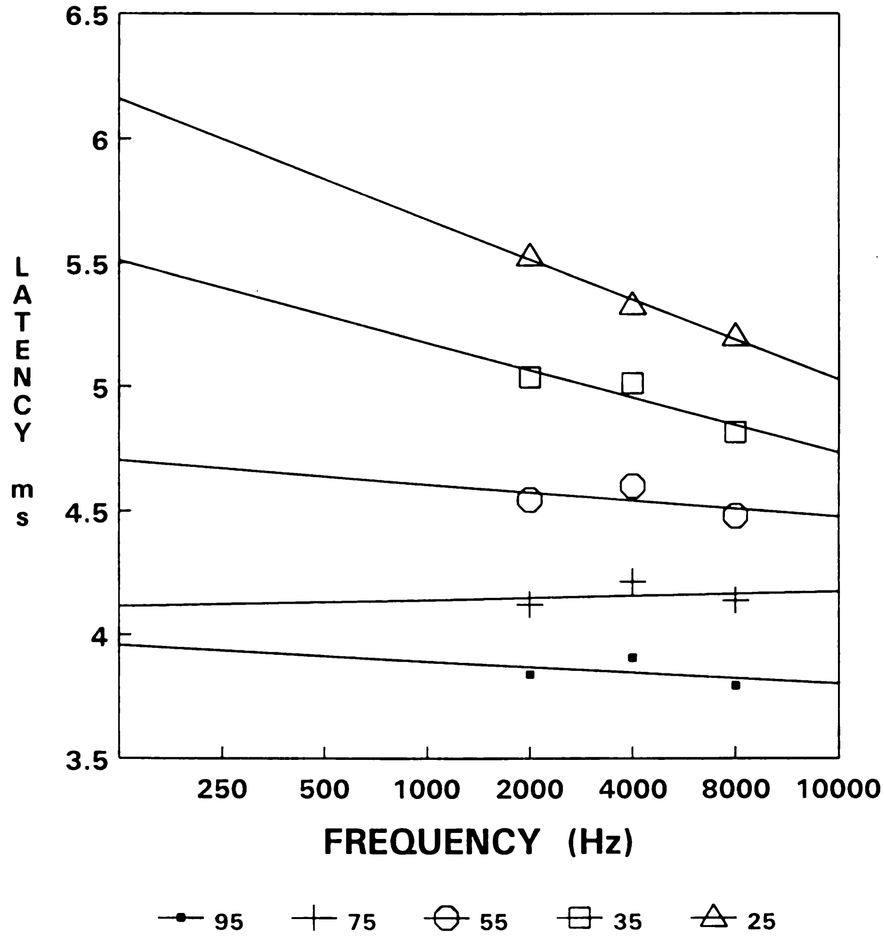


Figure 47. Wave-V Latency-Frequency Function

TABLE 27. Regression analysis* of wave-V latency vs frequency at five dB SPLs. Linear regression line = (slope x frequency) + intercept. Frequency is 2-,4-, and 8 kHz and r^2 is the slope correlation coefficient.

Measurement	Level (dB SPL)	Slope	Intercept	r^2
Latency (ms)				
	95	-0.029	5.803	0.849
	75	-0.035	5.821	0.802
2-kHz	55	-0.038	5.864	0.790
	35	-0.041	5.912	0.776
	25	-0.046	5.963	0.741
	95	-0.030	4.135	0.885
	75	-0.035	4.081	0.851
4-kHz	55	-0.039	4.150	0.794
	35	-0.042	3.935	0.776
	25	-0.046	4.011	0.752
	95	-0.027	3.061	0.924
	75	-0.033	3.101	0.892
8-kHz	55	-0.035	2.935	0.870
	35	-0.038	2.910	0.845
	25	-0.040	3.054	0.790

*Probability that the slope differs from zero is $\underline{P} < 0.01$.

functions describe the data accurately.

Wave-V Threshold Estimation

In the present study, the definition of the ABR threshold is the lowest SPL at which a response can be detected. Our data indicated that measurable peaks were recorded in 100% of the subjects at 55-, 35-, 25-, and 25 dB SPL for 1-, 2-, 4-, and 8-kHz tone-bursts respectively. These levels represent the presence of electrophysiologic activity which is likely to be higher than the subjective thresholds (Davis, Hirsch, Turpin, and Peacock, 1985; Gorga et al., 1985, 1988). In their normal hearing adult subjects, Gorga and colleagues estimated the threshold difference was 20 dB SPL at 1000 Hz and 15 dB SPL for higher frequencies. It was concluded that a correction factor, which is subtracted from the SPL values, could be applied to tone-burst ABR data to predict the pure-tone audiogram. Applying this simple method to the our data, behavioral thresholds in this group of dogs could be estimated at 35-, 20-, 10-, and 10-dB SPL at 1-, 2-, 4-, and 8-kHz respectively.

In another method, ECoG studies determined threshold by a linear function being fit to amplitude versus level functions (Eggermont, Spoor, and Odenthal, 1976; Eggermont and Odenthal, 1977). These functions were extrapolated to find behavioral threshold which was defined as the estimated level (re: behavioral threshold) resulting in a whole-nerve action

(AP) amplitude of 0.1 uV. Using tone-burst ABRs to predict behavioral thresholds has been difficult in the lower frequencies (250- and 500 Hz) and larger differences between the two measures were observed (Suzuki, Kodera and Kaga, 1982). The lower variability in higher frequencies suggest that corrections could be developed for those frequencies.

In the absence of behavioral data from our subjects, threshold determination by extrapolation of input-output curves was applied to our experimental results. Figure 48 permits a comparison and evaluation of the threshold of the test tone-bursts. As noted in the graph, for each increase in SPL at 2-, 4-, and 8 kHz peak amplitude increased 0.642 uV, 0.591 uV, and 0.672 uV respectively. The solid lines represent best fit functions for each frequency. Significant positive correlations ($P < 0.01$) between test frequencies were identified (see Table 28). From these findings it may be concluded that canine ABR behavioral threshold can be accurately determined in the 2- to 8 kHz region with tone-burst stimuli by estimating the hearing threshold from ABR latencies and amplitude measurements. The precision of the extrapolation technique is markedly increased when there are several latency values on which to base a threshold estimation (Weber, 1986).

It is important to understand that when the ABR is used to evaluate hearing status one should be aware of the

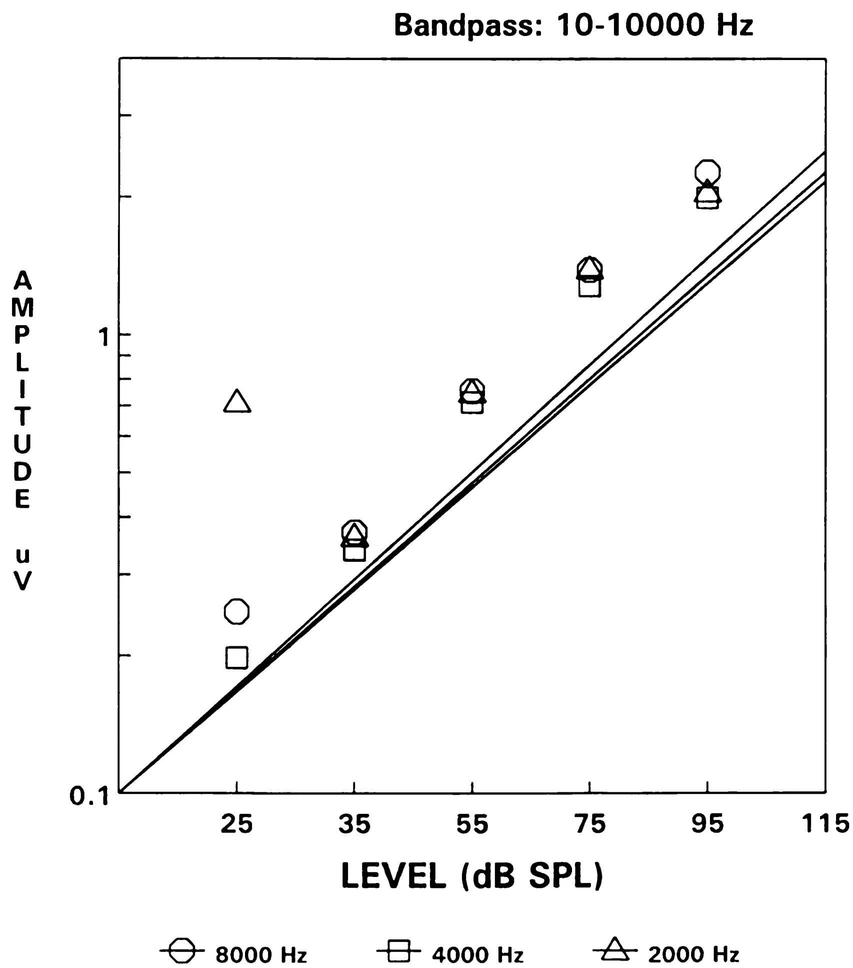


Figure 48. Wave-V Input-Output Curves

TABLE 28. Regression analysis* of wave-V amplitude vs level in dB SPL. Linear regression line = (slope x intensity) + intercept. Frequency is 2-,4-, and 8 kHz and r^2 is the slope correlation coefficient.

Measurement		Level (dB SPL)	Slope	Intercept	r^2
Amplitude (uV)					
		95	0.049	0.030	0.739
		75	0.044	0.112	0.702
	2-kHz	55	0.038	0.145	0.650
		35	0.033	0.218	0.610
		25	0.029	0.292	0.509
		95	0.048	0.210	0.772
		75	0.045	0.264	0.721
	4-kHz	55	0.039	0.325	0.674
		35	0.035	0.368	0.630
		25	0.031	0.394	0.585
		95	0.041	0.204	0.886
		75	0.037	0.262	0.842
	8-kHz	55	0.034	0.309	0.795
		35	0.031	0.386	0.754
		25	0.027	0.401	0.710

*Probability that the slope differs from zero is $\underline{P} < 0.01$.

technique's limitations and problems areas. First, behavioral audiometry and ABR testing do not tap the auditory system in the same manner and the two procedures can produce different test results, such as discrepancies in ABR and behavioral thresholds, which may be partly due to the difference in the duration of the stimuli. Second, interpretation of ABR results is highly subjective in that the examiner must look at wavy lines and make a number of very subjective decisions regarding the presence or absence of a response. With increased experience and skill, most examiners can improve their ability to interpret ambiguous ABR tracings. Third, and most importantly, no standardize recording technique for the canine presently exist and, therefore, comparison of ABR latencies with previously reported data is not possible. In this regard, standardize recording parameters and techniques must be developed to ensure validity and reliability of the ABR results.

Summary of Findings

Latency-Intensity functions for wave-I and wave-V peaks were calculated for the three high-pass and two low-pass digital filters at each tone-burst stimuli. The LIFs were observed to be superimposed within each test frequency and across intensity levels. As expected, there was a gradual increase in latency with corresponding decrease in stimulus intensity. For each 20 dB decrement , mean latency increased on an average of 0.38 ms and 0.39 ms for wave-I and wave-V respectively. The effects of frequency on the major peaks were demonstated by shorter latencies for the 8000 Hz stimuli and slightly longer latencies which overlapped for the 4000- and 2000 Hz stimuli. Although systematic measurements were not made below 95 dB SPL, the 1000 Hz stimuli produced a clear separation of peak latencies from the higher frequencies.

Significant high-pass filter effects on ABR latency were revealed at the highest intensity level (95 dB SPL) for the three tone burst stimuli. The 300-10000 Hz bandpass produced the shortest latency measures for waves I and V. At near-threshold stimulus levels, no significant differences in peak latencies were found among or between high-pass and low-pass filter settings.

Statistically significant differences in ABR peak-to-peak amplitudes were observed between the high-pass filter settings. As the high-pass cut-off frequency was shifted from 10 to 300 Hz at high stimulus levels, a gradual reduction in amplitude for both waves was revealed, with the greatest effect present at the 300-3000 Hz and 300-10000 Hz bandpass. At near-threshold stimulus levels, most peak amplitude measures were similar for the 10- and 100 Hz settings and significantly reduced at the 300 Hz cut-off frequency. No filter effects were found for the two low-pass settings at any test frequency.

The results of this study suggest that for routine brainstem response audiometry administered at either suprathreshold levels in otoneurological diagnostics or in threshold determination, careful high-pass filtering is strongly recommended. The data from this study do not permit precise selection of cut-off frequencies for ABR work. However, a high-pass filter of at least 10 Hz (with a 12 dB/octave roll-off) is feasible for ABR canine testing. In terms of low-pass filtering, no appreciable response energy appears to be present above the 3000 Hz cut-off, as the amplitude of the peaks did not show a significant increase when the cut-off frequency was held constant at 10000 Hz.

In conclusion, reproducible ABRs can be measured to tone-bursts covering a wide range of frequencies and levels in the canine. Moreover, amplifier band-pass, digital filtering must be carefully selected in order to preserved the spectral content of the ABR which covers low and high frequency components. Our data suggested a 10-3000 Hz or a 10-10000 Hz (12 dB/octave slope) bandpass limit to record either suprathreshold or near-threshold wave-V responses. A point of caution should be exercised when using the wider bandpass extended to 10 kHz, for more high frequency and electronic noise levels are averaged into the records which makes peak detection difficult at threshold levels, and more post-digital filtering is required to "clean-up" the recordings without distorting the classic brain-stem waveform morphology.

Implications for Future Research

The additional information on digital filtering presented in this document confirms the importance of selecting appropriate amplifier band-pass settings when recording ABRs in the dog. A limited number of high-pass cut-off frequencies were investigated in this study, and, therefore, a definitive statement on the optimal band-pass setting cannot be made. As previous investigations have demonstrated, a substantial amount of low-frequency energy exist in the region between 10- and 100-Hz. It is necessary to systematically investigate other high-pass settings in this region to determine any amplitude and /or latency effects. Although low-pass filter effects were less crucial in this study, high-frequency cut-offs should also be researched to identify any residual high-frequency energy that may be present in the ABR response to tone bursts above 8-kHz. Additionally, the steepness of bandpass filter slope has also been shown to effect wave form amplitude, and various combinations of filter settings and slope functions need to be investigated in this species.

In an attempt to improved the frequency specificity of ABR thresholds estimations, derived-band investigations have been introduced in animal and human studies. To data, no canine studies have been reported. Thus, a better understanding of the spectral content of the ABR to frequency specific stimuli at threshold levels would be acquired. In this regard, auditory sensitivity above 8000 Hz has not been explored because of present commercial amplifier and transducer limitations. The development and utilization of such instrumentation is germane to our recording ABR responses evoked to higher frequency stimuli in the 12 to 32-kHz region which is considered the upper audibility range of the dog. By the same token, ABRs to mid- and low-frequency stimuli in this species have not been investigated, and this information is also needed in order to develop valid hearing contour curves.

This pioneer study of frequency-specific ABRs in the dog investigated a few intensity levels to construct latency-intensity functions. Perhaps 10 dB decrements down to at least 0 dB SPL will more clearly define the functions and refine threshold estimations. Prediction of ABR threshold by latency measurement techniques used in human studies was applied to our data, and it seems reasonable that the simple model presented can reliably predict the normal latency for high frequencies to 8000 Hz. A larger sample size is needed to acquire a normative data base which could be used as a standard for veterinary electrophysiologic laboratories.

There is some suggestion in the literature (Pook and Streiss, 1991) that the interpeak latency differences remain constant as a function of frequency and level for stimuli exciting narrow frequency regions. Interpeak latency data was not reported or analyzed in this document to verify this claim. Constant interpeak latency differences would indicate that central conduction time (define as the time between the generation of waves I and V) is constant, regardless of frequency and level. This vital information if gathered on a large group of normal hearing and hearing-impaired dogs would aid in developing an otoneurologic protocol for diagnosing peripheral and central auditory dysfunction in dog breeds known the have a predisposition for sensorineural hearing loss and lower brain-stem disorders.

APPENDICES

APPENDIX A

FREQUENCY SPECTRUM OF THE TONE BURSTS

The following figures represent the power spectrums-main and side lobes-of the fixed frequency stimuli.

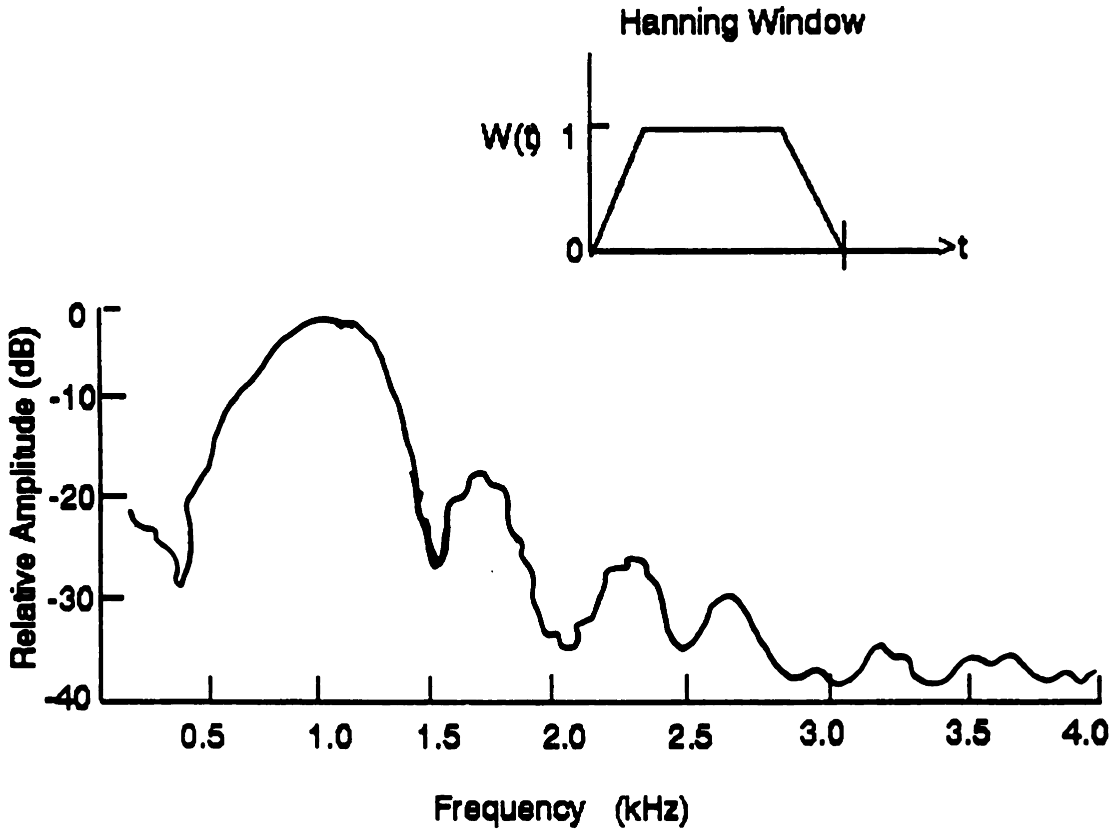


Figure 3. Frequency Power Spectrum of a 1,000 Hz tone burst.

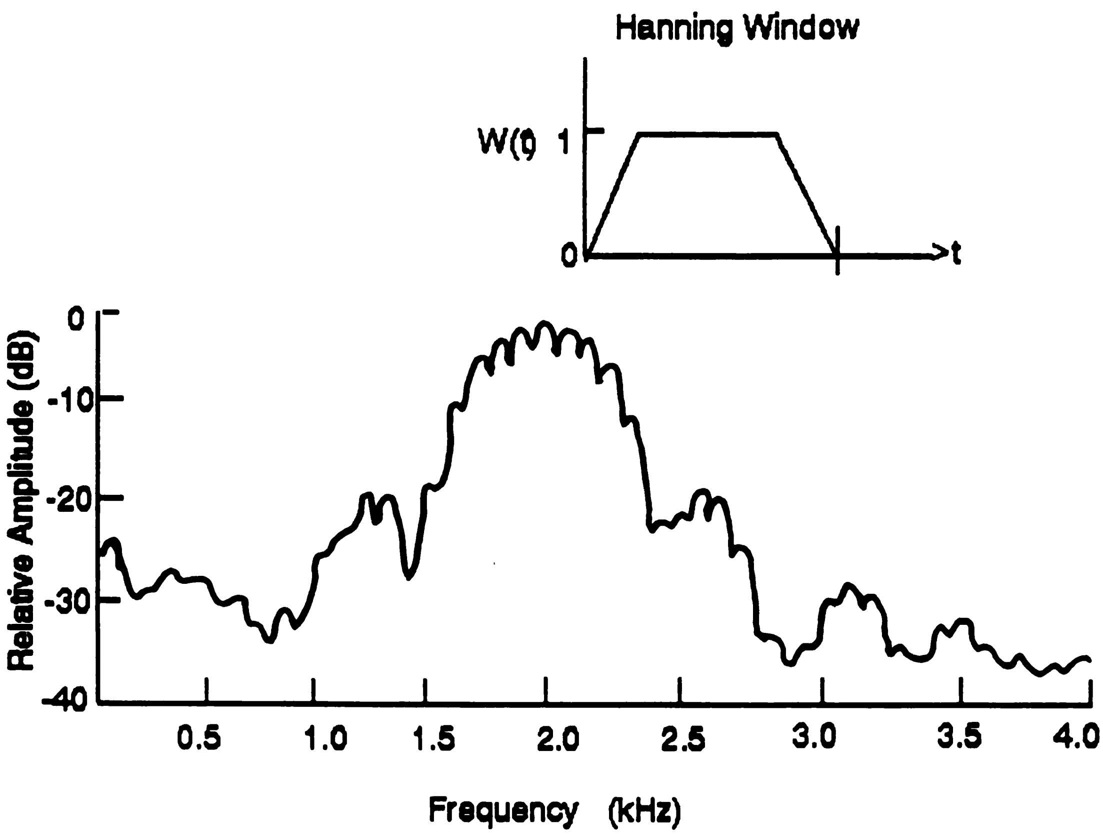


Figure 4. Frequency Power Spectrum of a 2,000 Hz tone burst.

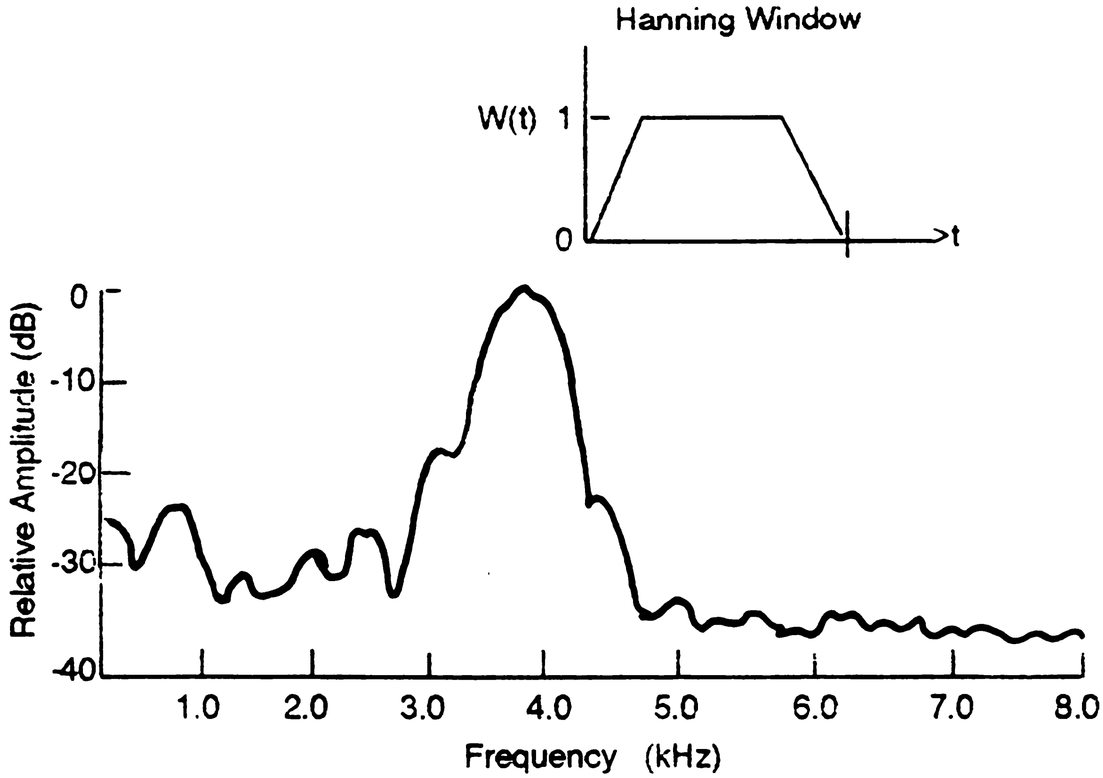


Figure 5. Frequency Power Spectrum of a 4,000 Hz tone burst.

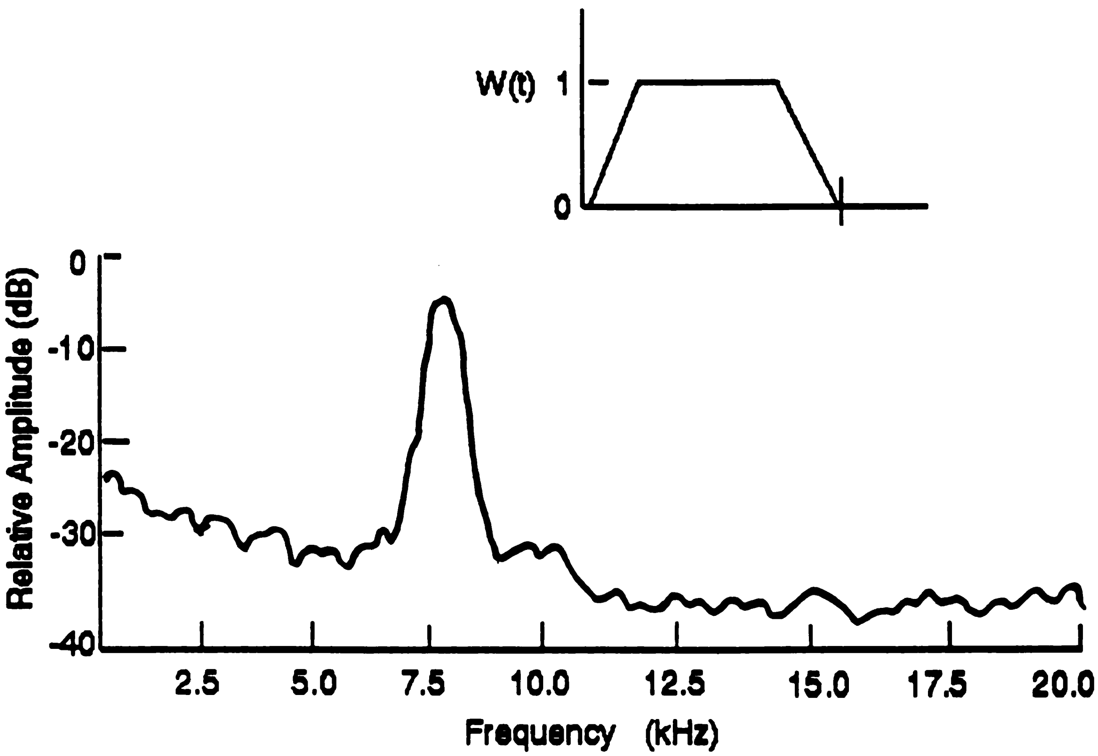


Figure 6. Frequency Power Spectrum of a 8,000 Hz tone burst.

APPENDIX B

ELECTRICAL/ACOUSTICAL TONE BURST SIGNALS

The following figures represent the input and output plots of the fixed frequency stimuli.

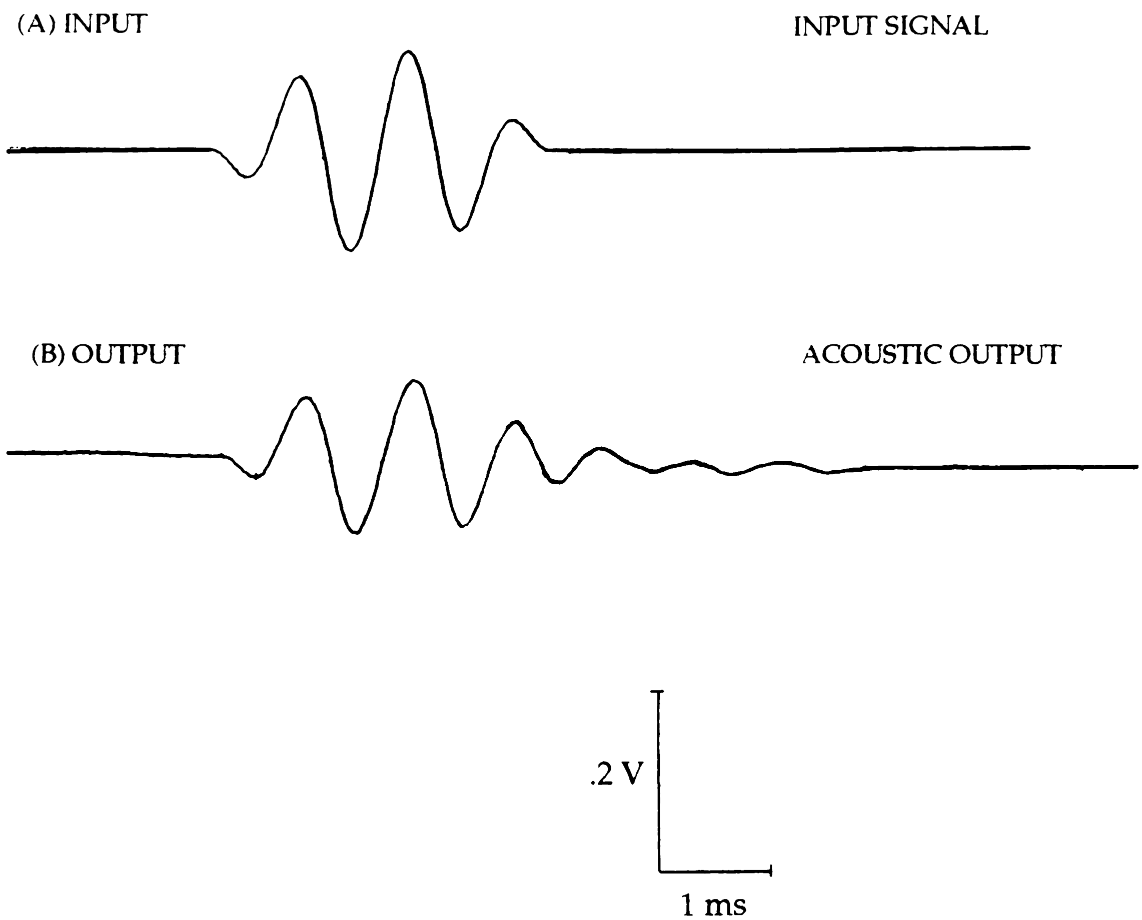


Figure 7. Electrical (A) and acoustical (B) plots of a 1,000 Hz tone burst.

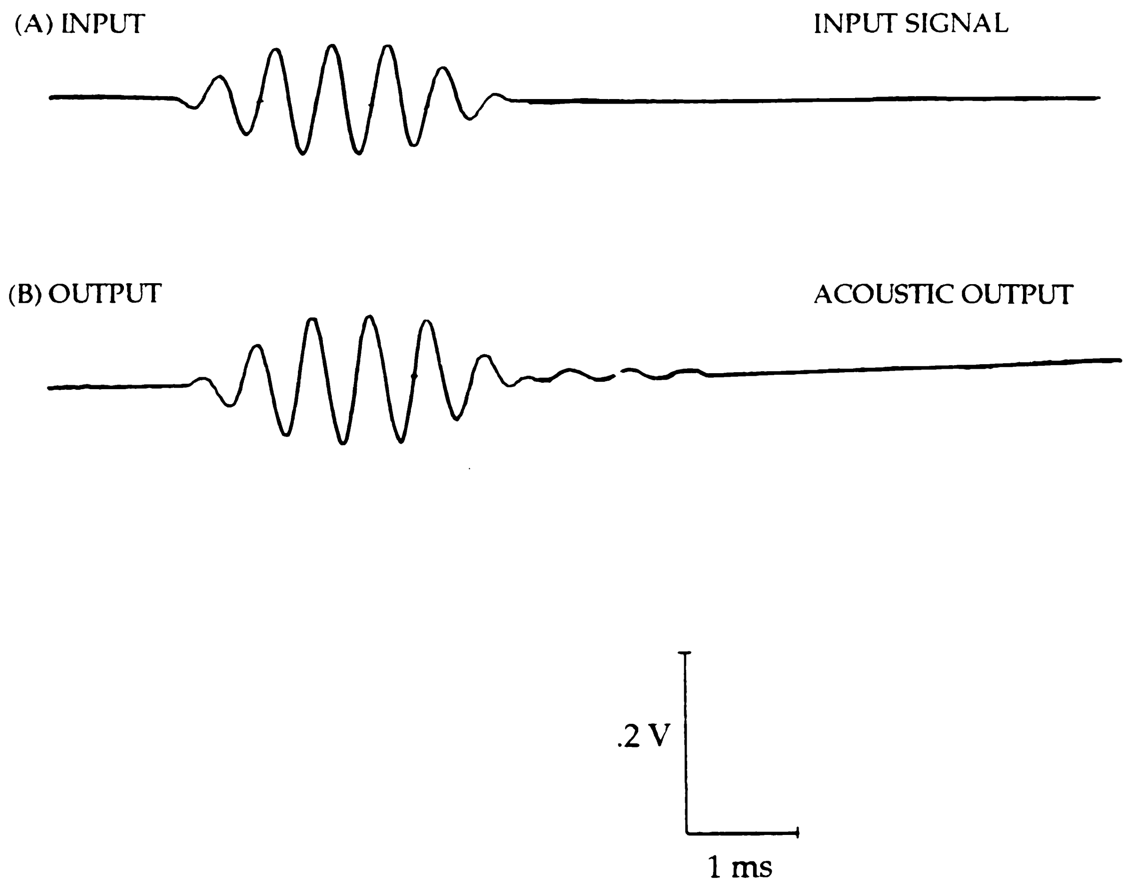


Figure 8. Electrical (A) and acoustical (B) plots of a 2,000 Hz tone burst.

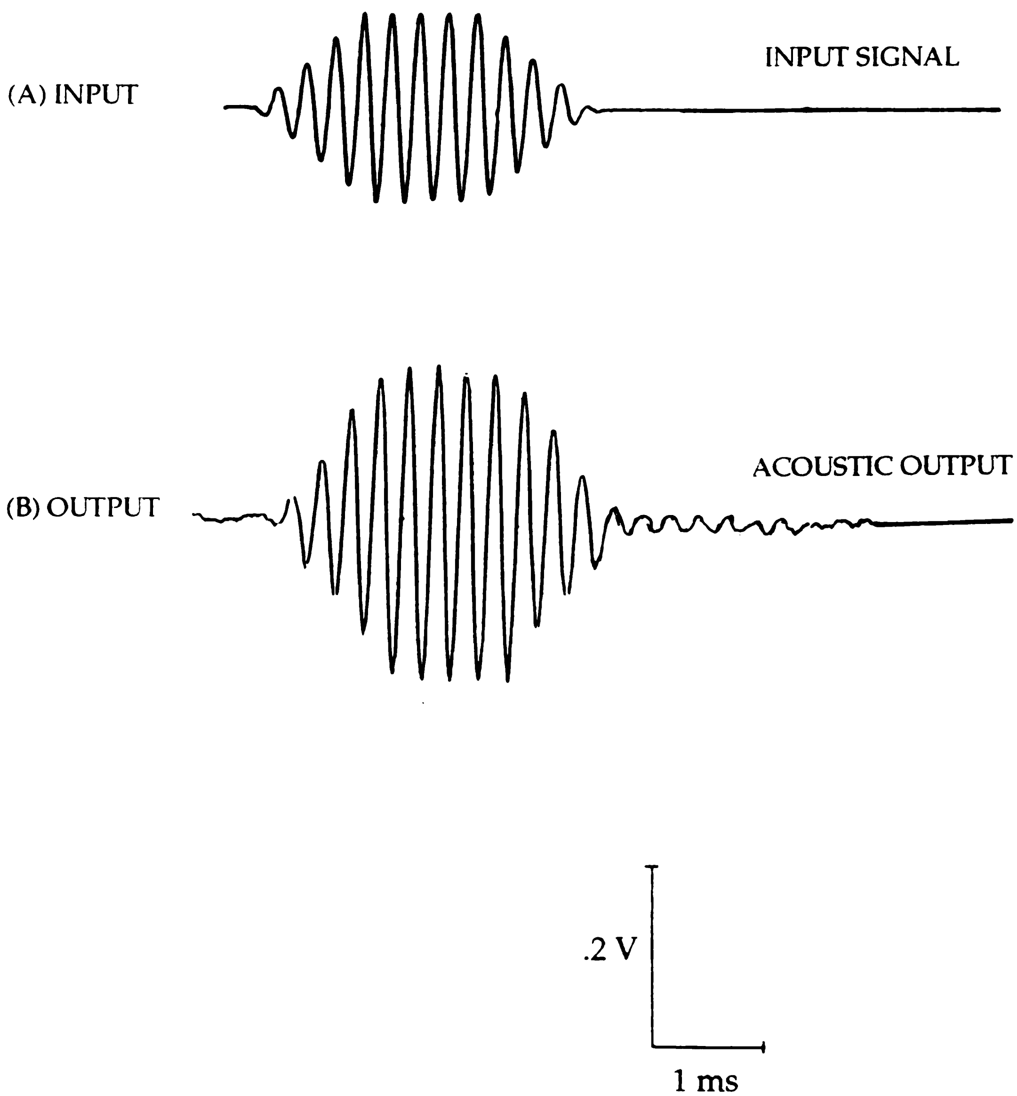


Figure 9. Electrical (A) and acoustical (B) plots of a 4,000 Hz tone burst.

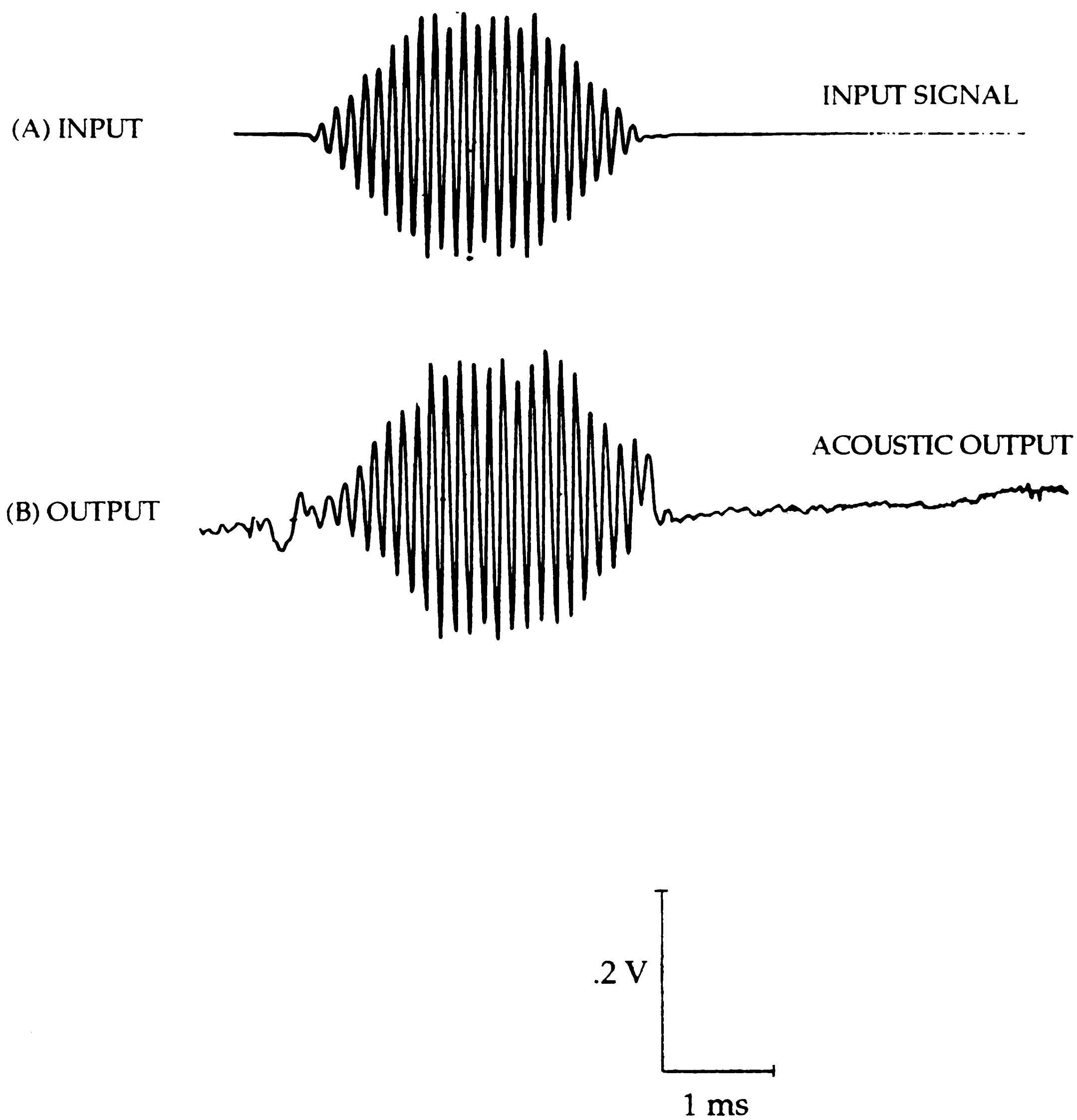


Figure 10. Electrical (A) and acoustical (B) plots of a 8,000 Hz tone burst.

APPENDIX C

AUDITORY BRAIN-STEM RESPONSES AT DIFFERENT BAND-PASS SETTINGS

The following figures display the ABRs evoked by the fixed frequency stimuli at three band-pass filter settings.

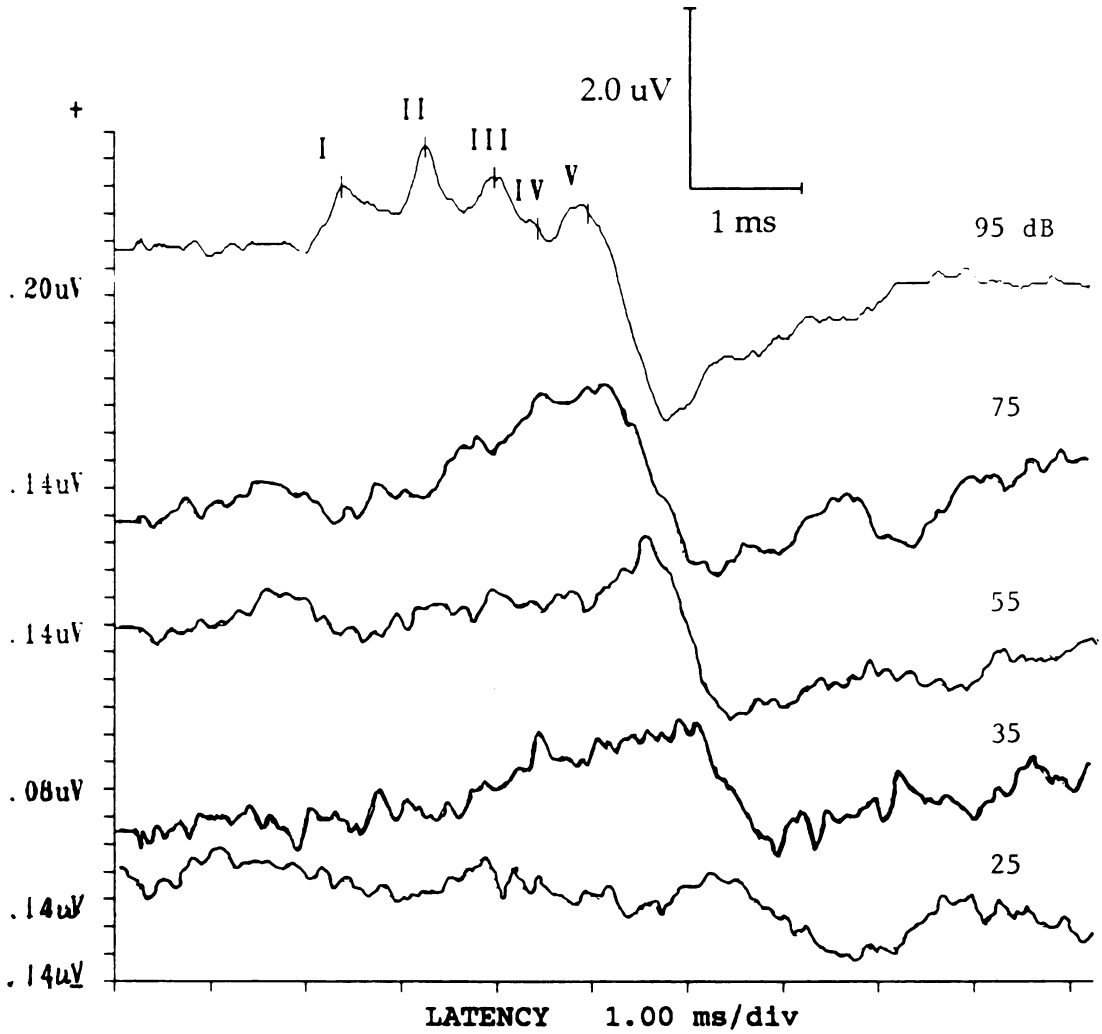


Figure 19. ABR's evoked by a 2,000 Hz TB; Bandpass 10-3,000 Hz.

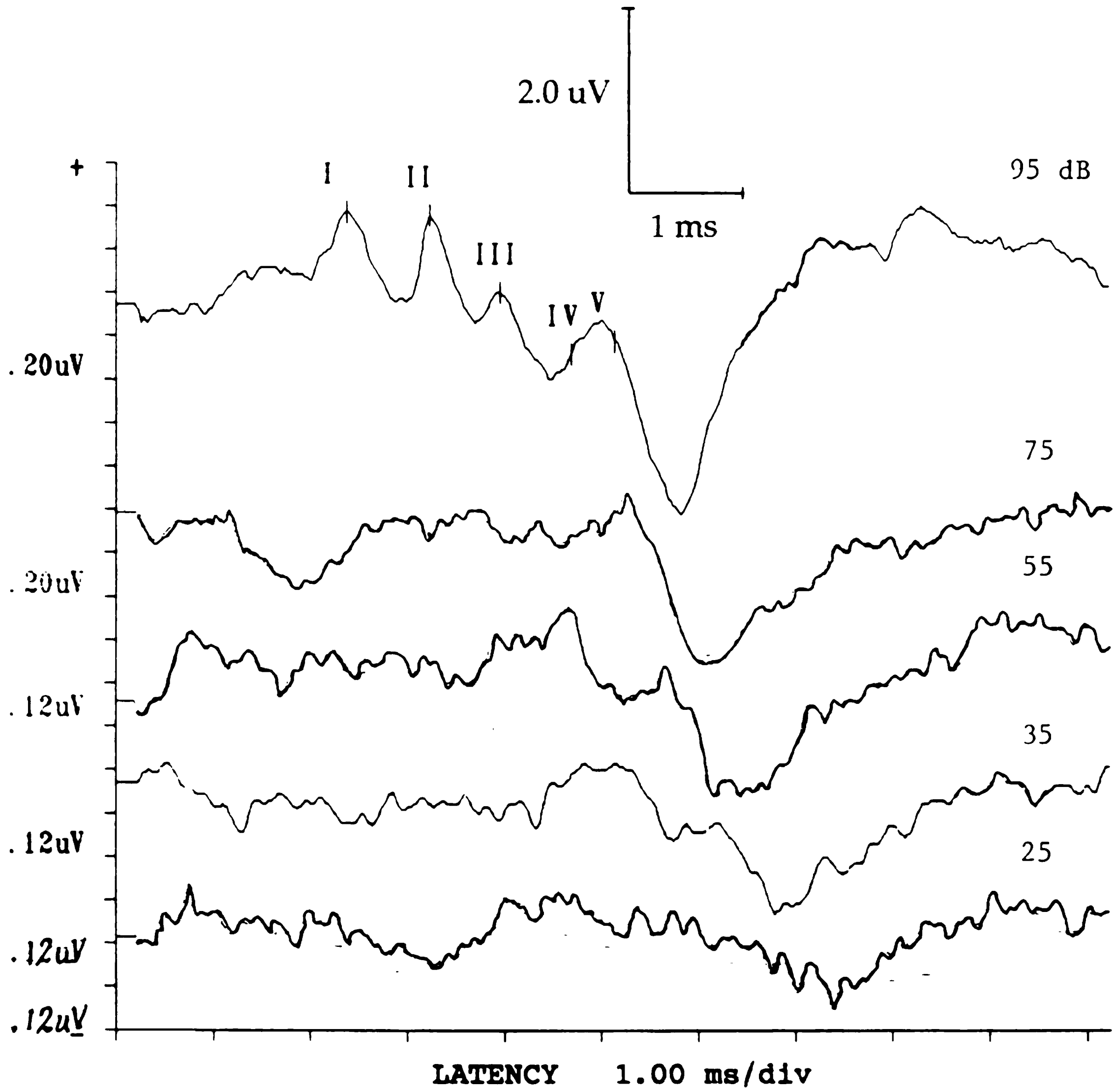


Figure 20. ABR's evoked by a 2,000 Hz TB; Bandpass 100-3,000 Hz.

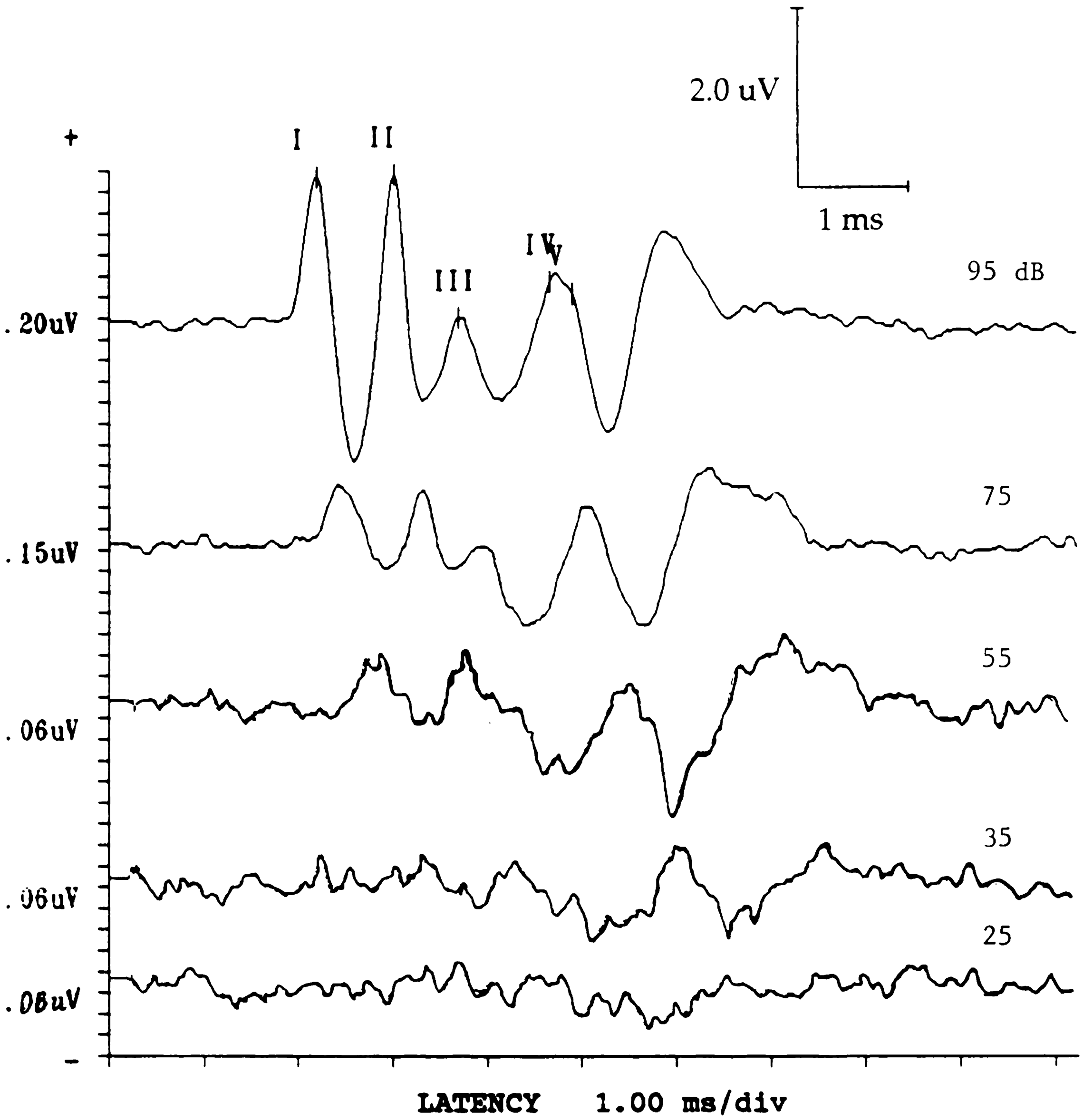


Figure 21. ABR's evoked by a 2,000 Hz TB; Bandpass 300-3,000 Hz.

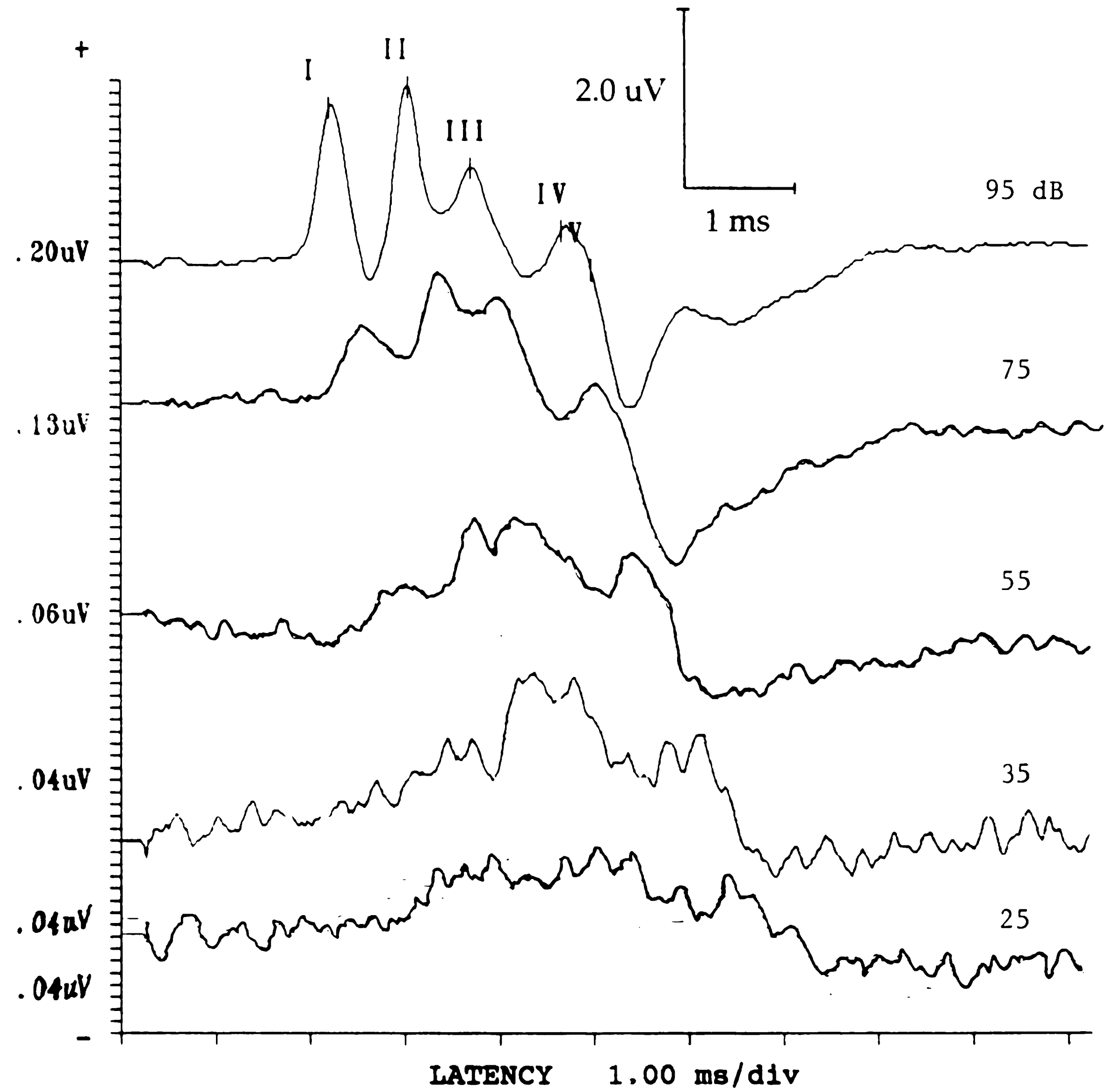


Figure 22. ABR's evoked by a 4,000 Hz TB; Bandpass 10-3,000 Hz.

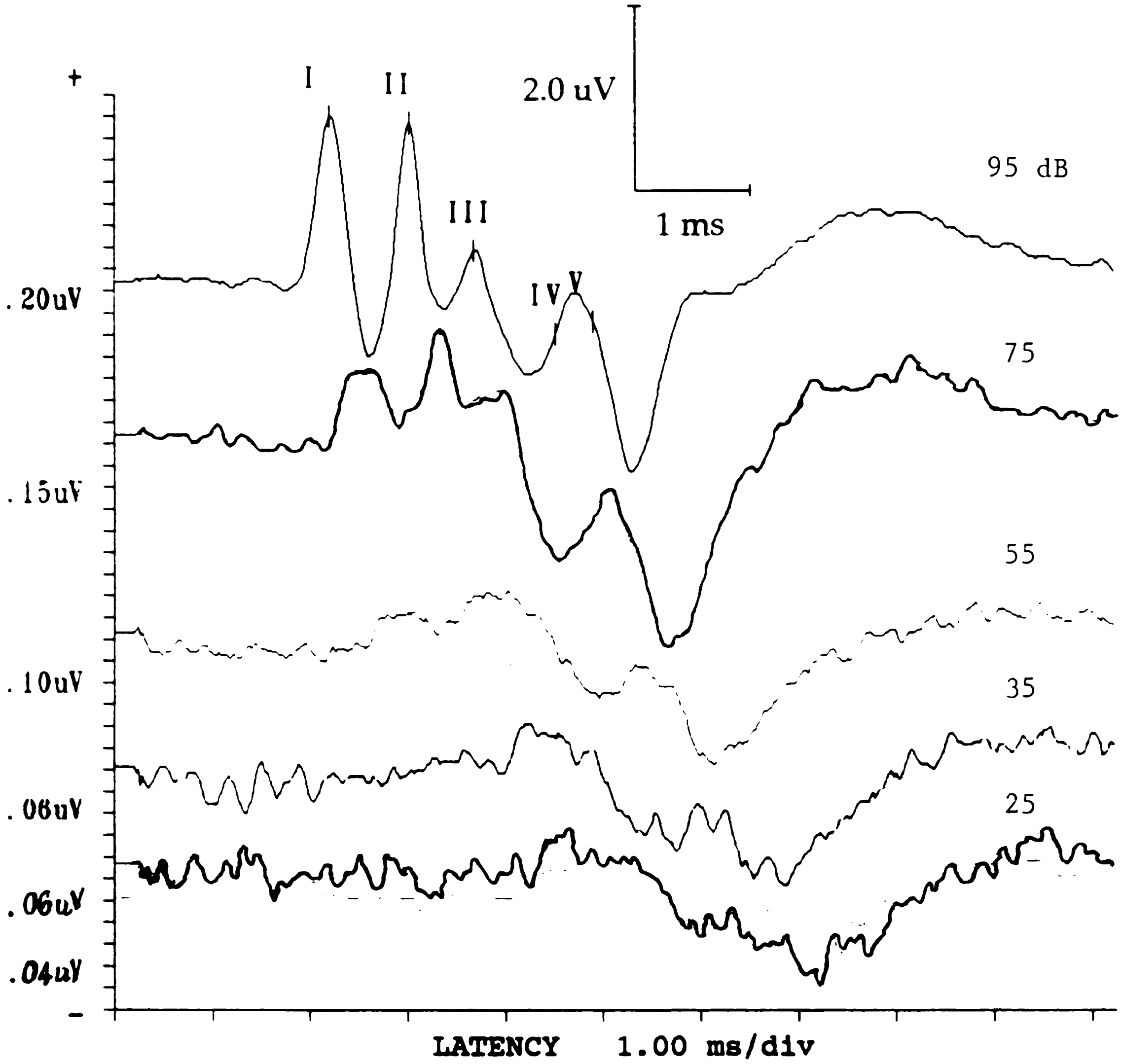


Figure 23. ABR's evoked by a 4,000 Hz TB; Bandpass 100-3,000 Hz.

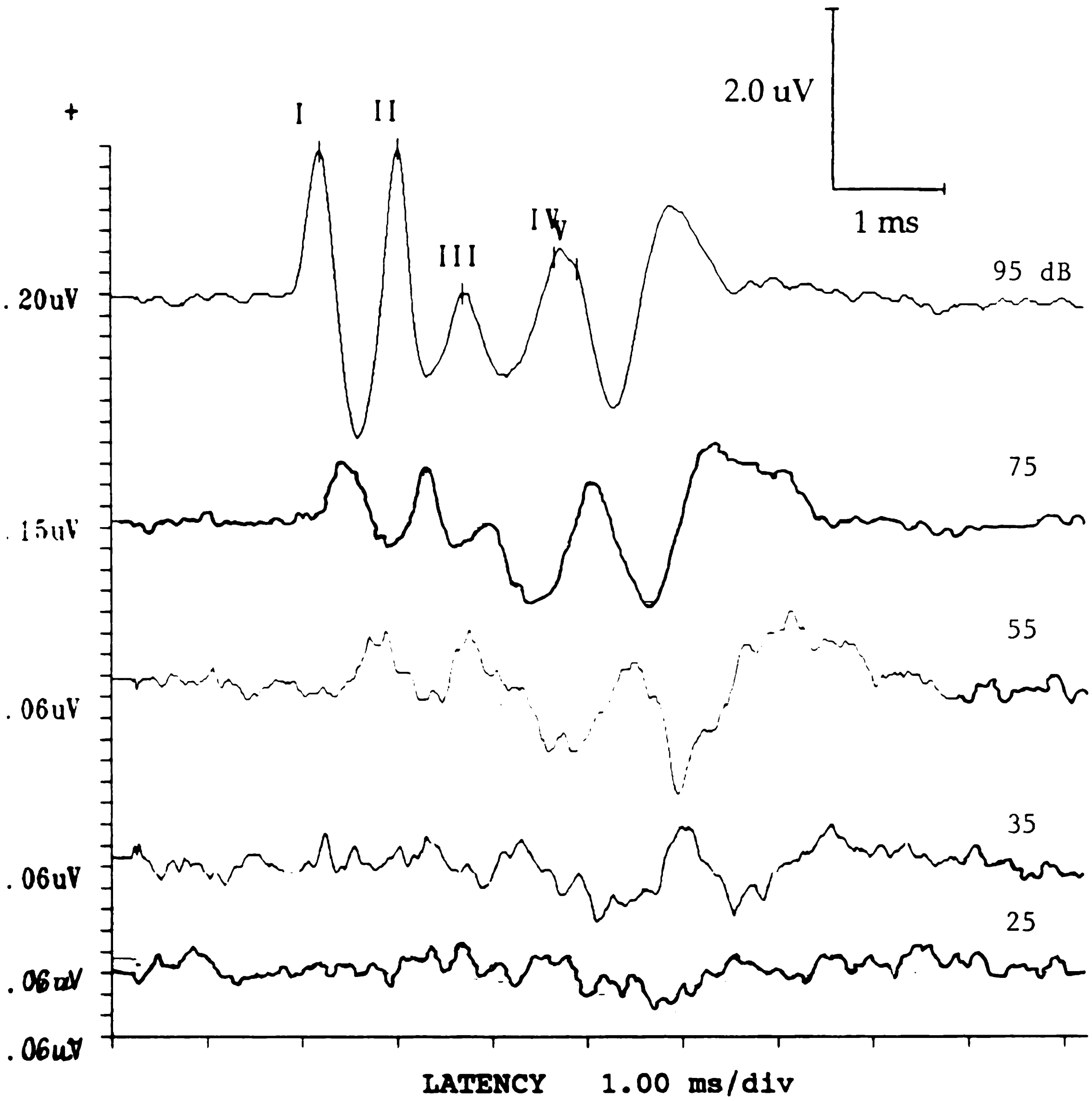


Figure 24. ABR's evoked by a 4,000 Hz TB; Bandpass 300-3,000 Hz.

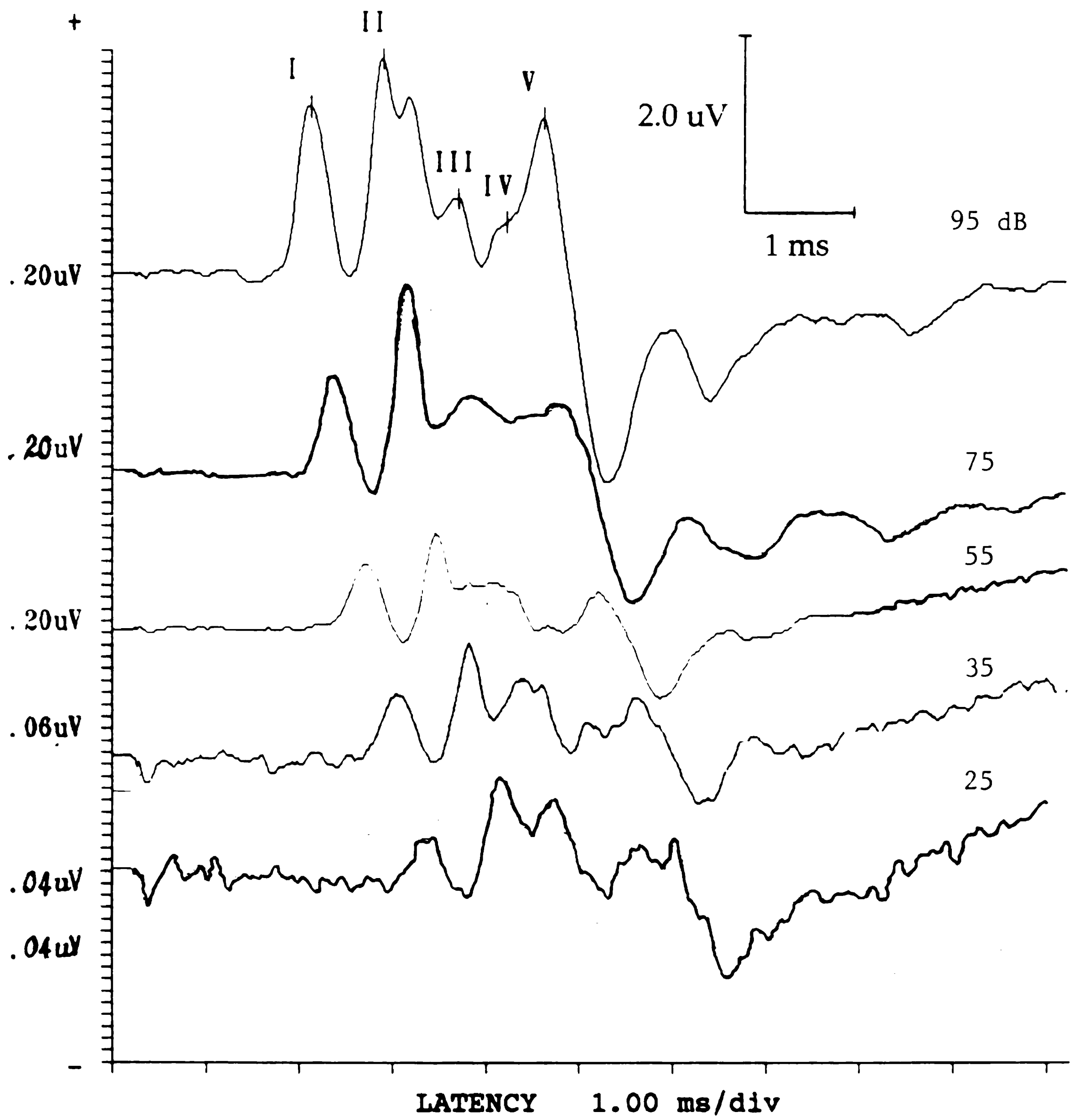


Figure 25. ABR's evoked by a 8,000 Hz TB; Bandpass 10-3,000 Hz.

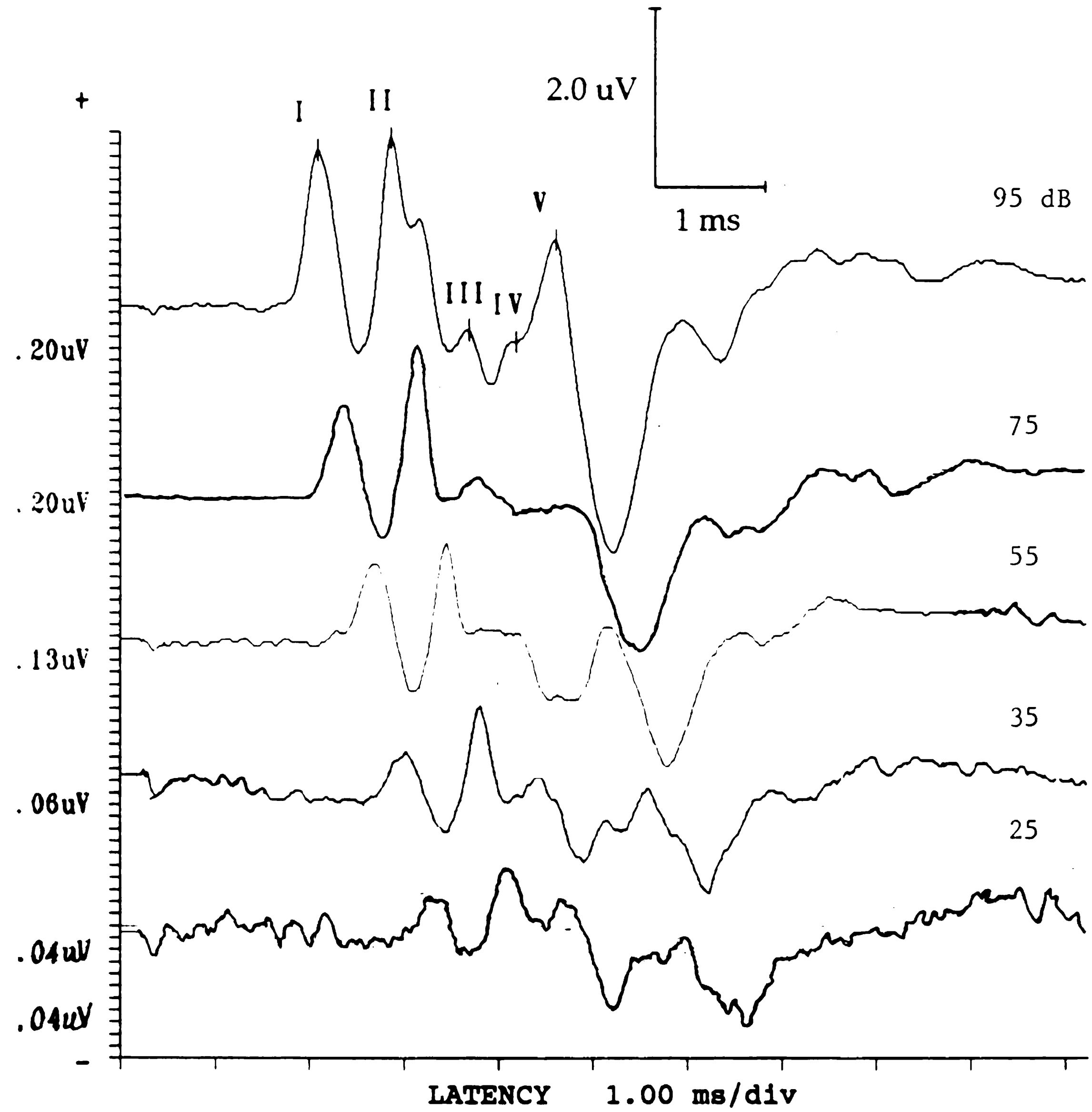


Figure 26. ABR's evoked by a 8,000 Hz TB; Bandpass 100-3,000 Hz.

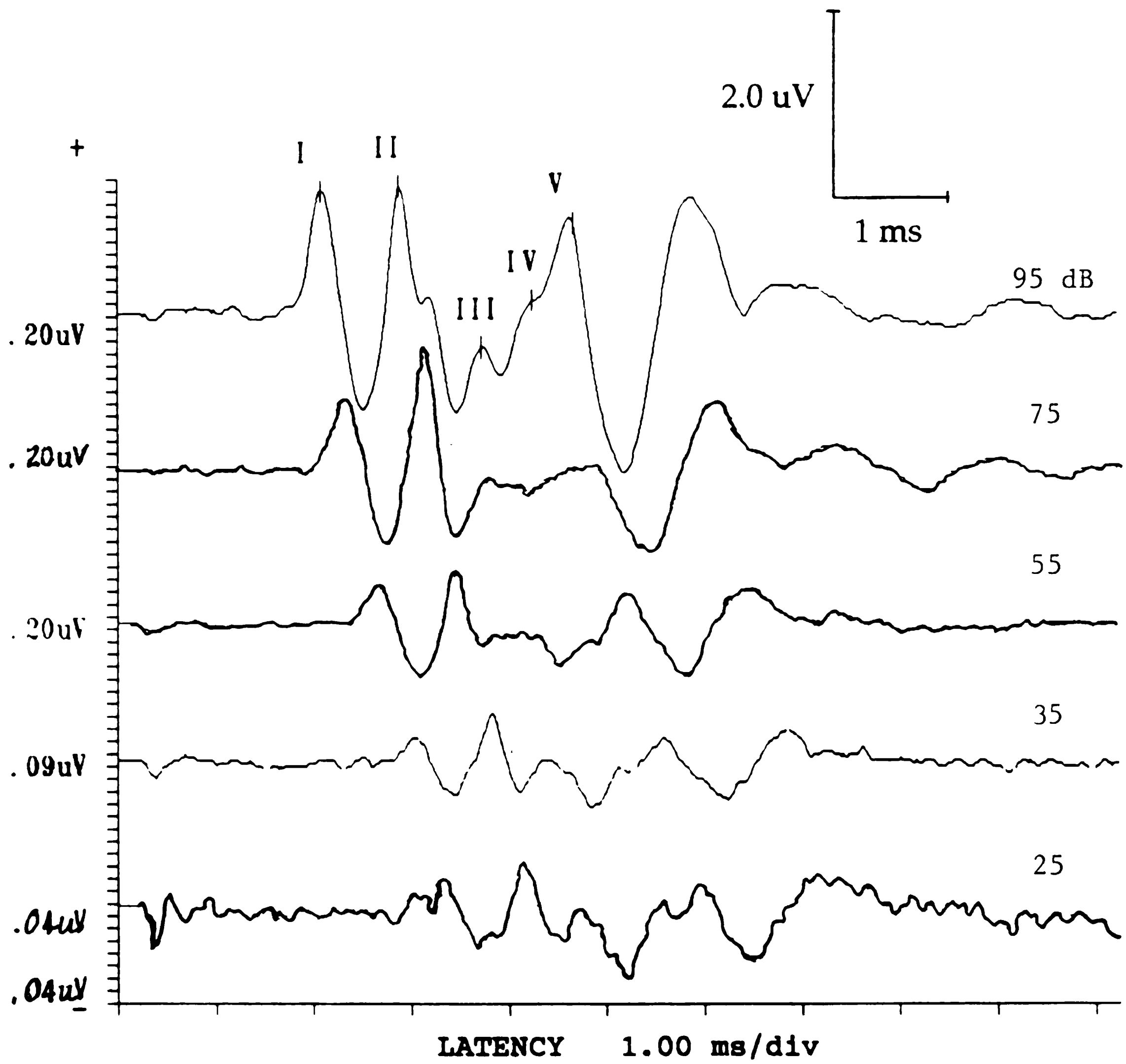


Figure 27. ABR's evoked by a 8,000 Hz TB; Bandpass 300-3,000 Hz.

APPENDIX D

STATISTICAL ANALYSIS OF WAVE-I LATENCY AND AMPLITUDE

The following tables show the non-parametric and post-hoc analyses of wave-I.

TABLE 11. Wave-1 latency paired comparisons (Nemenyi's Test, df=5) of the six filter settings for the 2000 Hz tone burst with each treatment condition arranged with the mean sums of ranks along columns and rows. $(X^2_{r\alpha} = 3.07)$

	X_{T6} 1.62	X_{T5} 3.06	X_{T3} 3.50	X_{T2} 3.56	X_{T4} 4.06	X_{T1} 5.18
X_{T6} 1.62	-	1.43	1.88	1.94	2.43	3.56*
X_{T5} 3.06	-	-	0.44	0.50	1.56	2.12
X_{T3} 3.50			-	0.06	0.56	1.68
X_{T2} 3.56			-		0.50	1.62
X_{T4} 4.06				-		1.12
X_{T1} 5.18						

*Significant at $p < .01$.

TABLE 12. Wave-1 latency paired comparisoaw (Nemawyi's Test, (df=5) of the six filter settings for the 4000 Hz tone burst with each treatment condition arranged with the mean sums of ranks along columns and rows. ($X^2_r \alpha$ =3.07)

	X_{T6} 1.50	X_{T5} 2.25	X_{T4} 3.12	X_{T3} 4.06	X_{T2} 4.37	X_{T1} 5.68
X_{T6} 1.50				-	2.80	4.18*
X_{T5} 2.25					2.12	3.43*
X_{T4} 3.12					-	2.55
X_{T3} 4.06						
X_{T2} 4.37						
X_{T1} 5.68						

*Significant at p < .01.

TABLE 13. Wave-1 latency paired comparisons (Nemenyi's Test, df=5) of the six filter settings for the 8000 Hz tone burst with each treatment condition arranged with the mean sums of ranks along columns and rows. $(X^2_{r\alpha} = 3.07)$

	X_{T6} 1.63	X_{T3} 2.06	X_{T2} 3.69	X_{T1} 3.94	X_{T4} 4.62	X_{T5} 5.06
X_{T6} 1.63		0.43	2.06	2.31	2.99	3.46*
X_{T3} 2.06				-	2.56	3.00
X_{T2} 3.69						
X_{T1} 3.94						
X_{T4} 4.62						
X_{T5} 5.06						

*Significant at $p < .01$.

TABLE 14. Means (M) and standard deviations (SD) of wave 1 amplitude at 95 dB SPL for each of six digital band pass filter settings across three tone bursts. A total of eight cases (N=8) represents the group data. The Friedman's (X^2_r) test statistic also is reported along with Kendall Coefficient of Concordance (W). ($X^2_{r\alpha}$ = 15.07)

		Band-Pass Filters in Hz					
		10-3000 F1	100-3000 F2	300-3000 F3	10-10000 F4	100-10000 F5	300-10000 F6
2kHz	TB						
	M(ms)	1.168	1.070	0.693	1.295	1.321	0.666
	SD	0.612	0.473	0.375	0.652	0.629	0.424
	X^2_r(df=5)	>	>	> 24.12*	<	<	<
	W				0.60		
4kHz	TB						
	M(ms)	1.308	1.173	0.874	1.335	1.361	0.820
	SD	0.562	0.582	0.409	0.625	0.623	0.386
	X^2_r(df=5)	>	>	22.59*	<	<	<
	W			0.56			
8kHz	TB						
	M(ms)	1.291	1.136	0.890	1.354	1.421	0.833
	SD	0.702	0.485	0.501	0.690	0.771	0.578
	X^2_r(df=5)	>	>	>	21.50* <	<	<
	W				0.544		

* Friedman's statistic significant at the 0.01 level.

TABLE 15. Means (M) and standard deviations (SD) of wave 1 amplitude at 75 dB SPL for each of six digital band pass filter settings across three tone bursts. A total of eight cases (N=8) represents the group data. The Friedman's (X^2_r) test statistic also is reported along with Kendall Coefficient of Concordance (W). ($X^2_{r\alpha}$ = 15.07)

		Band-Pass Filters in Hz					
		10- 3000 F1	100- 3000 F2	300- 3000 F3	10- 10000 F4	100- 10000 F5	300- 10000 F6
2kHz	TB						
	M(ms)	0.550	0.608	0.336	0.533	0.588	0.275
	SD	0.421	0.360	0.236	0.282	0.301	0.213
	X^2_r(df=5)	>	>	>	22.68* <	<	<
	W				0.56		
4kHz	TB						
	M(ms)	0.489	0.559	0.328	0.608	0.563	0.368
	SD	0.334	0.270	0.127	0.208	0.287	0.128
	X^2_r(df=5)	>	>	>	14.93* <	<	<
	W				0.37		
8kHz	TB						
	M(ms)	0.673	0.718	0.328	0.608	0.563	0.408
	SD	0.271	0.366	0.127	0.208	0.287	0.182
	X^2_r(df=5)	>	>	>	21.36* <	<	<
	W				0.53		

* Friedman's statistic significant at the 0.01 level.

TABLE 16. Means (M) and standard deviations (SD) of wave 1 amplitude at 55 dB SPL for each of six digital band pass filter settings across three tone bursts. A total of eight cases (N=8) represents the group data. The Friedman's (X^2_r) test statistic also is reported along with Kendall Coefficient of Concordance (W). ($X^2_{r\alpha}$ = 15.07)

	Band- Pass Filters in Hz					
	10-3000 F1	100-3000 F2	300-3000 F3	10-10000 F4	100-10000 F5	300-10000 F6
2kHz TB						
M(ms)	0.305	0.260	0.148	0.174	0.226	0.153
SD	0.294	0.178	0.078	0.107	0.209	0.098
X^2_r(df=5)	>	>	>	9.80 <	<	<
W				0.25		
4kHz TB						
M(ms)	0.203	0.283	0.189	0.309	0.303	0.189
SD	0.117	0.137	0.073	0.132	0.140	0.069
X^2_r(df=5)	>	>	>	16.41* <	<	<
W				0.41		
8kHz TB						
M(ms)	0.448	0.435	0.288	0.414	0.478	0.271
SD	0.179	0.213	0.140	0.277	0.334	0.145
X^2_r(df=5)	>	>	>	16.86* <	<	<
W				0.42		

* Friedman's statistic significant at the 0.01 level.

Table 17. Wave-I amplitude paired Comparisons (Nemenyi's Test, df=5) of the six filter settings for the 2000 Hz toneburst with each treatment condition arranged with the mean sums of ranks along columns and rows. $(X^2_r \alpha = 3.07)$

	X_{T6} 1.63	X_{T3} 1.75	X_{T2} 3.90	X_{T1} 4.13	X_{T4} 4.81	X_{T5} 4.81
X_{T6} 1.63			-	2.27	3.18*	3.18*
X_{T3} 1.75				2.38	3.06	3.06
X_{T2} 3.90				-	-	0.91
X_{T1} 4.13						
X_{T4} 4.81						
X_{T5} 4.81						

*Significant at $p < .01$.

TABLE 18. Wave-I amplitude Paired Comparisons (Nemenyi's Test, df=5) of the six filter settings for the 4000 Hz tone burst with each treatment condition arranged with the mean sums of ranks along columns and rows. ($X^2_r \alpha$ =3.07)

	X_{T6} 1.50	X_{T3} 2.25	X_{T2} 3.31	X_{T4} 4.37	X_{T1} 4.43	X_{T5} 5.13
X_{T6} 1.50			1.81	2.87	2.93	3.63*
X_{T3} 2.25				2.12	2.18	2.88
X_{T2} 3.31					-	1.82
X_{T4} 4.37						
X_{T1} 4.43						
X_{T5} 5.13						

*Significant at $p < .01$.

TABLE 19. Wave-I amplitude Paired Comparisons (Nemenyi's Test, df=5) of the six filter settings for the 8000 Hz tone burst with each treatment condition arranged with the mean sums of ranks along columns and rows. ($X^2_{r\alpha}$ =3.07)

	X_{T3} 1.62	X_{T6} 2.06	X_{T2} 3.68	X_{T5} 3.94	X_{T4} 4.62	X_{T1} 5.06
X_{T3} 1.62				2.32	3.00	3.44*
X_{T6} 2.06				-	2.56	3.00
X_{T2} 3.68				-		2.44
X_{T5} 3.94						
X_{T4} 4.62						
X_{T1} 5.06						

*Significant at $p < .01$.

APPENDIX E

STATISTICAL ANALYSIS OF WAVES-I AND V AMPLITUDE

The following tables display the non-parametric and post-hoc calculations for wave-I.

TABLE 20. Wave-V latency paired comparisons (Nemenyi's Test, df=5) of the six filter settings for the 8000 Hz tone burst with each treatment condition arranged with the mean sums of ranks along columns and rows. ($X^2_r \alpha$ =3.07)

	X_{T6} 1.25	X_{T2} 3.50	X_{T5} 3.69	X_{T4} 3.88	X_{T3} 4.25	X_{T1} 4.44
X_{T6} 1.25	-	2.25	2.44	2.63	3.00	3.19*
X_{T2} 3.50	-	-		0.38	0.75	0.94
X_{T5} 3.69					0.56	0.75
X_{T4} 3.88						0.56
X_{T3} 4.25						
				-	-	
X_{T1} 4.44						

*Significant at $p < .01$.

TABLE 21. Wave-V Amplitudes-Means (M) and standard deviations (SD) of wave V amplitude at 95 dB SPL for each of six digital band pass filter settings across three tone bursts. A total of eight cases (N=8) represents the group data. The Friedman's (X^2_r) test statistic also is reported along with Kendall Coefficient of Concordance (W). ($X^2_{r\alpha}$ = 15.07)

		Band- Pass	Filters in Hz			
	10- 3000 F1	100- 3000 F2	300- 3000 F3	10- 10000 F4	100- 10000 F5	300- 10000 F6
2kHz TB						
M(ms)	1.916	1.206	1.010	2.046	1.499	0.914
SD	0.928	0.482	0.484	0.868	0.749	0.434
X^2_r(df=5)	>	>	> 29.82*	<	<	<
W			0.74			
4kHz TB						
M(ms)	2.086	1.350	1.010	1.994	1.459	1.128
SD	1.112	0.864	0.628	1.162	0.857	0.581
X^2_r(df=5)	>	>	> 30.98*	<	<	<
W			0.77			
8kHz TB						
M(ms)	2.405	1.848	1.453	2.263	2.025	1.506
SD	1.544	1.287	0.919	1.084	1.216	0.853
X^2_r(df=5)	>	> >		27.01* <	<	<
W				0.67		

* Friedman's statistic significant at the 0.01 level.

TABLE 22. Wave-V amplitude Paired Comparisons (Nemenyi's Test, df=5) of the six filter settings for the 2000 Hz toneburst with each treatment condition arranged with the mean sums of ranks along columns and rows. ($X^2_{r\alpha}$ = 3.07)

	X_{T3} 1.25	X_{T6} 2.25	X_{T2} 3.31	X_{T5} 3.50	X_{T4} 5.12	X_{T1} 5.56
X_{T3} 1.25				2.25	3.87*	4.31*
X_{T6} 2.25					2.88	3.31*
X_{T2} 3.31					-	2.25
X_{T5} 3.50						
X_{T4} 5.12						
X_{T1} 5.56						

*Significant at $p < .01$.

TABLE 23. Wave-V amplitude Paired Comparisons (Nemenyi's Test, df=5) of the six filter settings for the 4000 Hz tone burst with each treatment condition arranged with the mean sums of ranks along columns and rows. ($\chi^2_{r\alpha}$ = 3.07)

	X_{T3} 1.25	X_{T6} 2.25	X_{T2} 3.31	X_{T5} 3.50	X_{T4} 5.12	X_{T1} 5.56
X_{T3} 1.25				2.25	3.87*	4.31*
X_{T6} 2.25					2.88	3.31*
X_{T2} 3.31						2.25
X_{T5} 3.50						
X_{T4} 5.12						
X_{T1} 5.56						

*Significant at $p < .05$.

TABLE 24. Wave-V amplitude Paired Comparisons (Nemenyi's Test, df=5) of the six filter settings for the 8000 Hz toneburst with each treatment condition arranged with the mean sums of ranks along columns and rows. ($X^2_r \alpha$ = 3.07)

	X_{T3} 1.62	X_{T6} 2.12	X_{T2} 2.75	X_{T5} 4.25	X_{T4} 5.06	X_{T1} 5.19
X_{T3} 1.62				2.63	3.44*	3.57*
X_{T6} 2.12					2.94	3.07*
X_{T2} 2.75						2.44
X_{T5} 4.25						
X_{T4} 5.06						
X_{T1} 5.19						

*Significant at $p < .01$.

TABLE 25. Wave V Amplitudes-Means (M) and standard deviations (SD)-at near-threshold SPLs for each of six digital band pass filter settings across three tonebursts. A total of eight cases (N=8) represents the group data. The Friedman's (X2r) test statistic also is reported along with Kendall Coefficient of Concordance (W). ($X^2_r\alpha$ = 15.07)

		Band-Pass	Filters in Hz			
	10-3000 F1	100-3000 F2	300-3000 F3	10-10000 F4	100-10000 F5	300-10000 F6
2kHz TB(35 dB)						
M(ms)	0.230	0.255	0.158	0.363	0.233	0.164
SD	0.135	0.248	0.056	0.187	0.122	0.085
X^2_r(df=5)	>	>	>	0.554*	< <	<
W				0.014		
4kHz TB(25 dB)						
M(ms)	0.236	0.158	0.129	0.198	0.175	0.141
SD	0.088	0.084	0.049	0.126	0.075	0.048
X^2_r(df=5)	>	>	>	10.661*	< <	<
W				0.267		
8kHz TB(25 dB)						
M(ms)	0.198	0.191	0.249	0.195	0.249	0.143
SD	0.113	0.071	0.227	0.088	0.227	0.073
X^2_r(df=5)	>	>	>	6.286*	< <	<
W				0.157		

* p > 0.01

APPENDIX F

ANALOG DATA OF HEARING-IMPAIRED DOGS

The following figures are actual waveforms recorded from two dogs diagnosed with active middle ear pathologies.

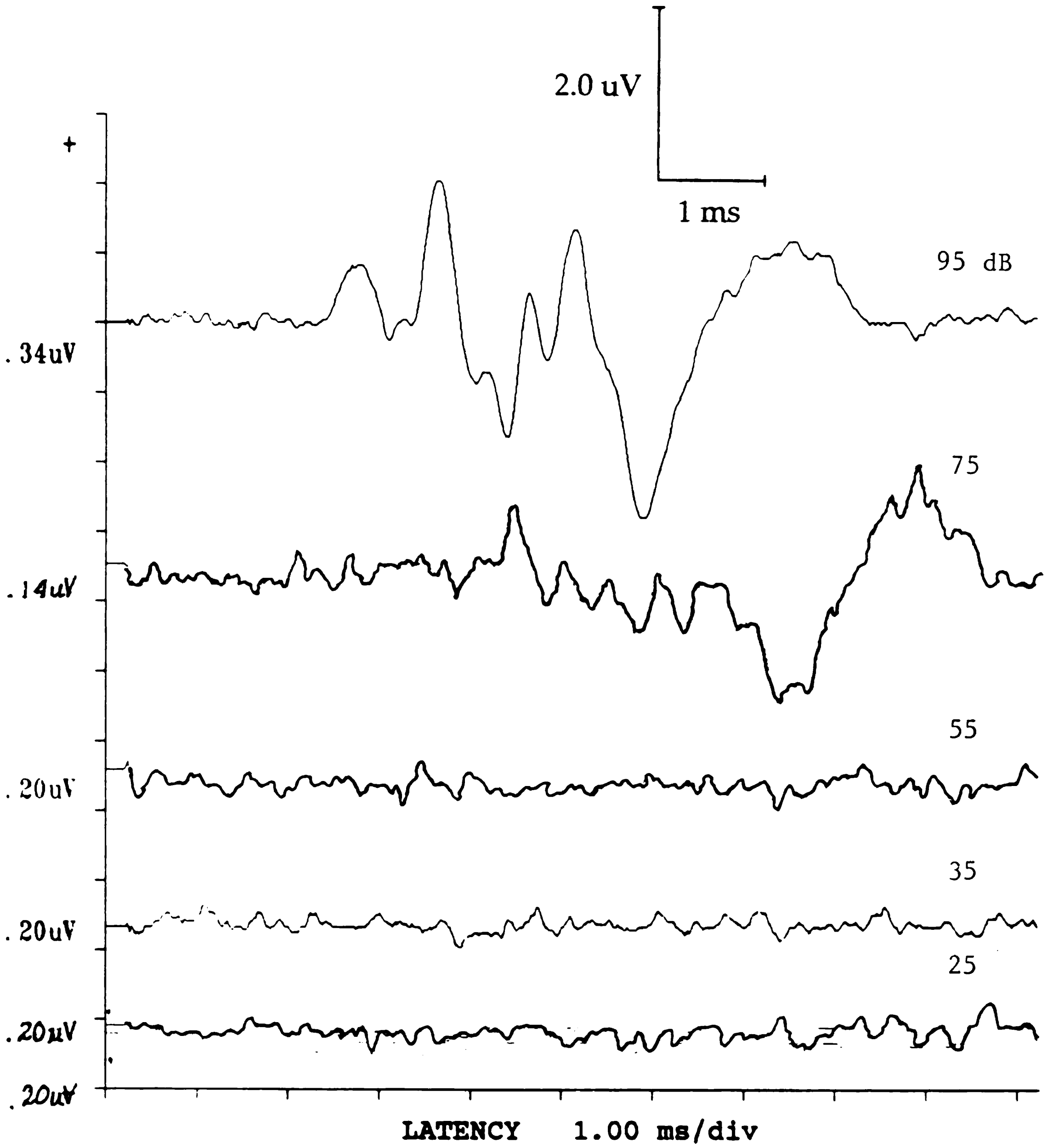


Figure 38. ABR's evoked by a 1,000 Hz TB in a female hearing-impaired dog.

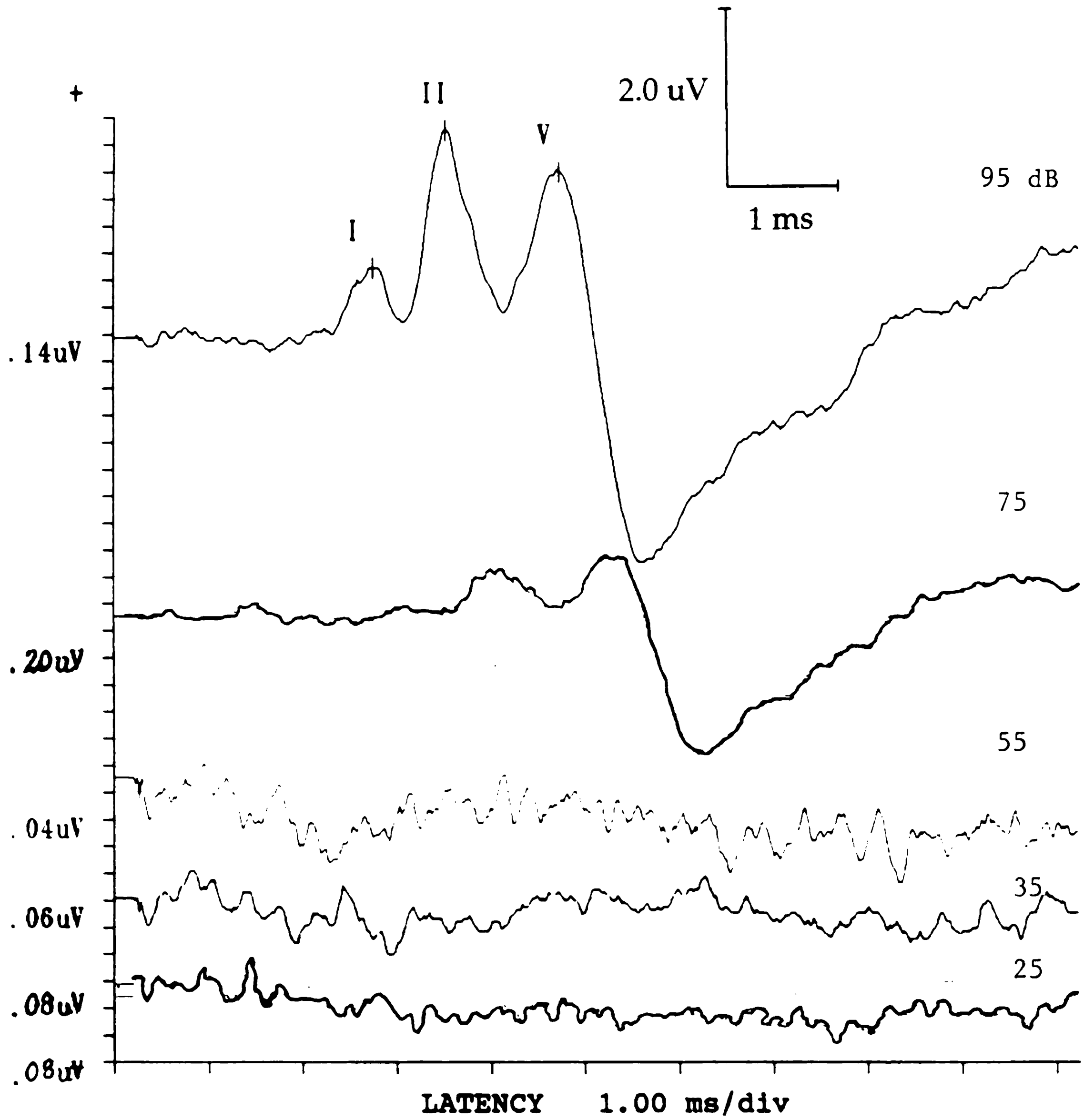


Figure 39. ABR's evoked by a 2,000 Hz TB in a female hearing-impaired dog.

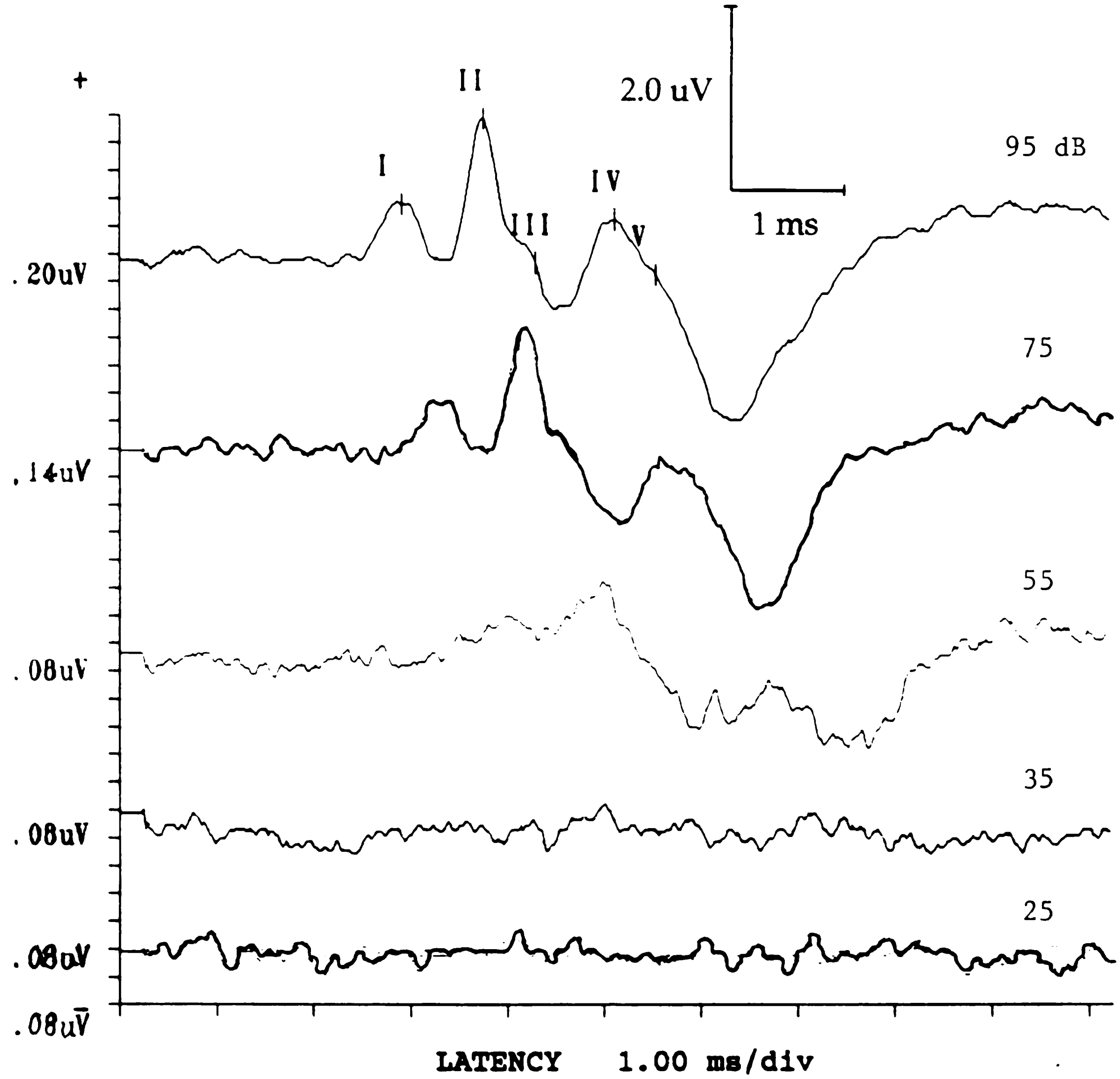


Figure 40. ABR's evoked by a 4,000 Hz TB in a female hearing-impaired dog.

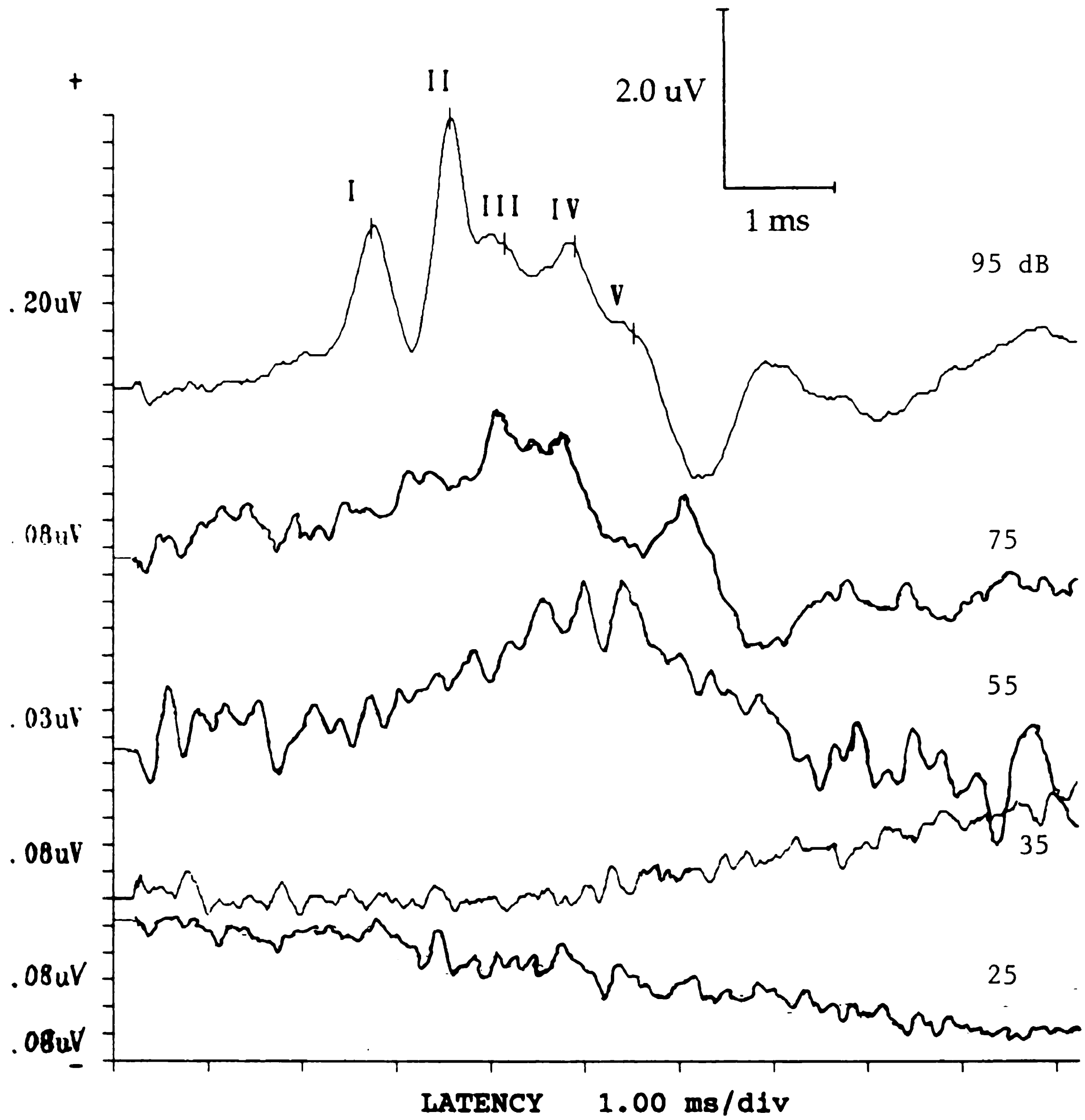


Figure 41. ABR's evoked by a 8,000 Hz TB in a female hearing-impaired dog.

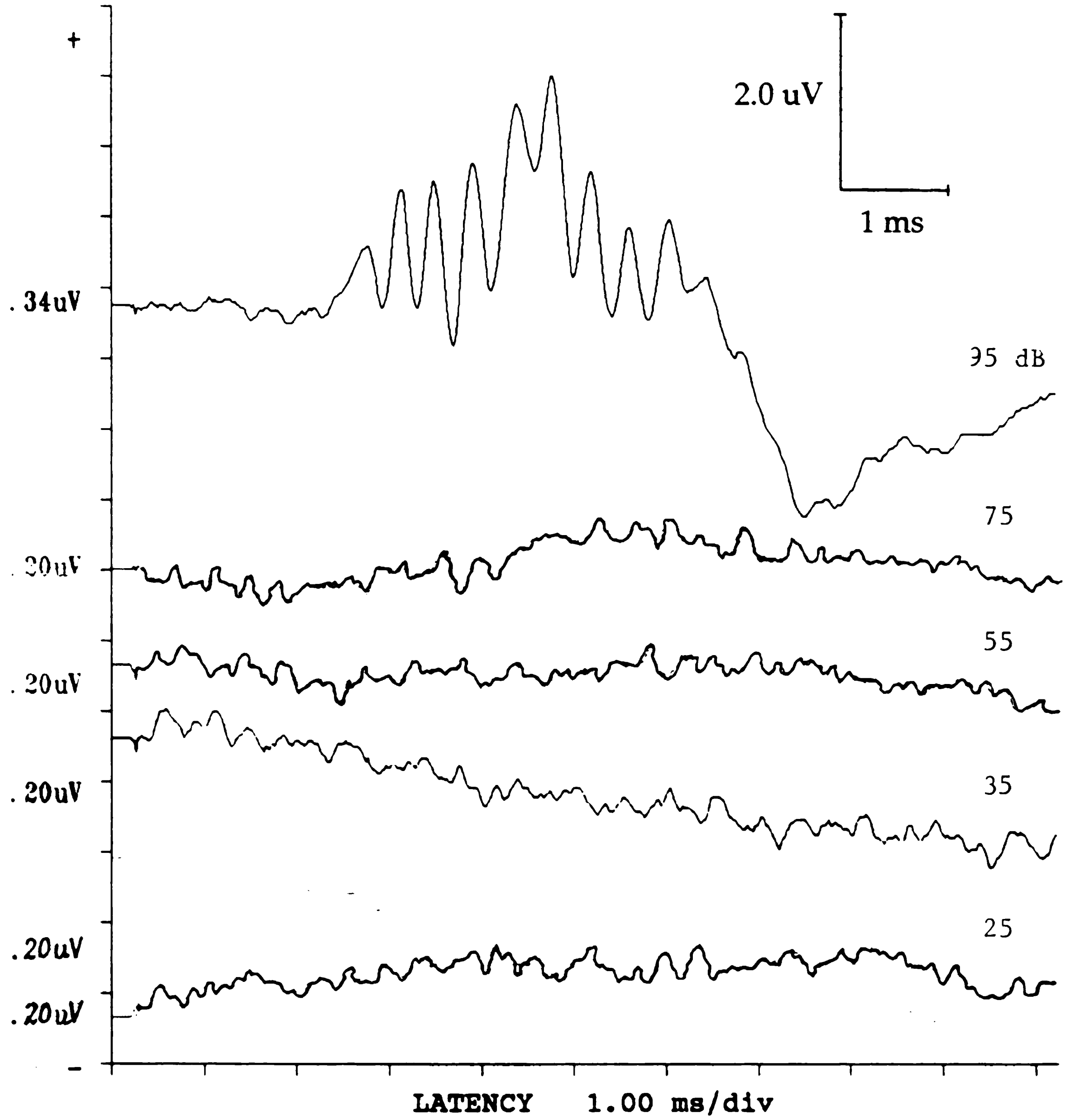


Figure 42. ABR's evoked by a 1,000 Hz TB in a male hearing-impaired dog.

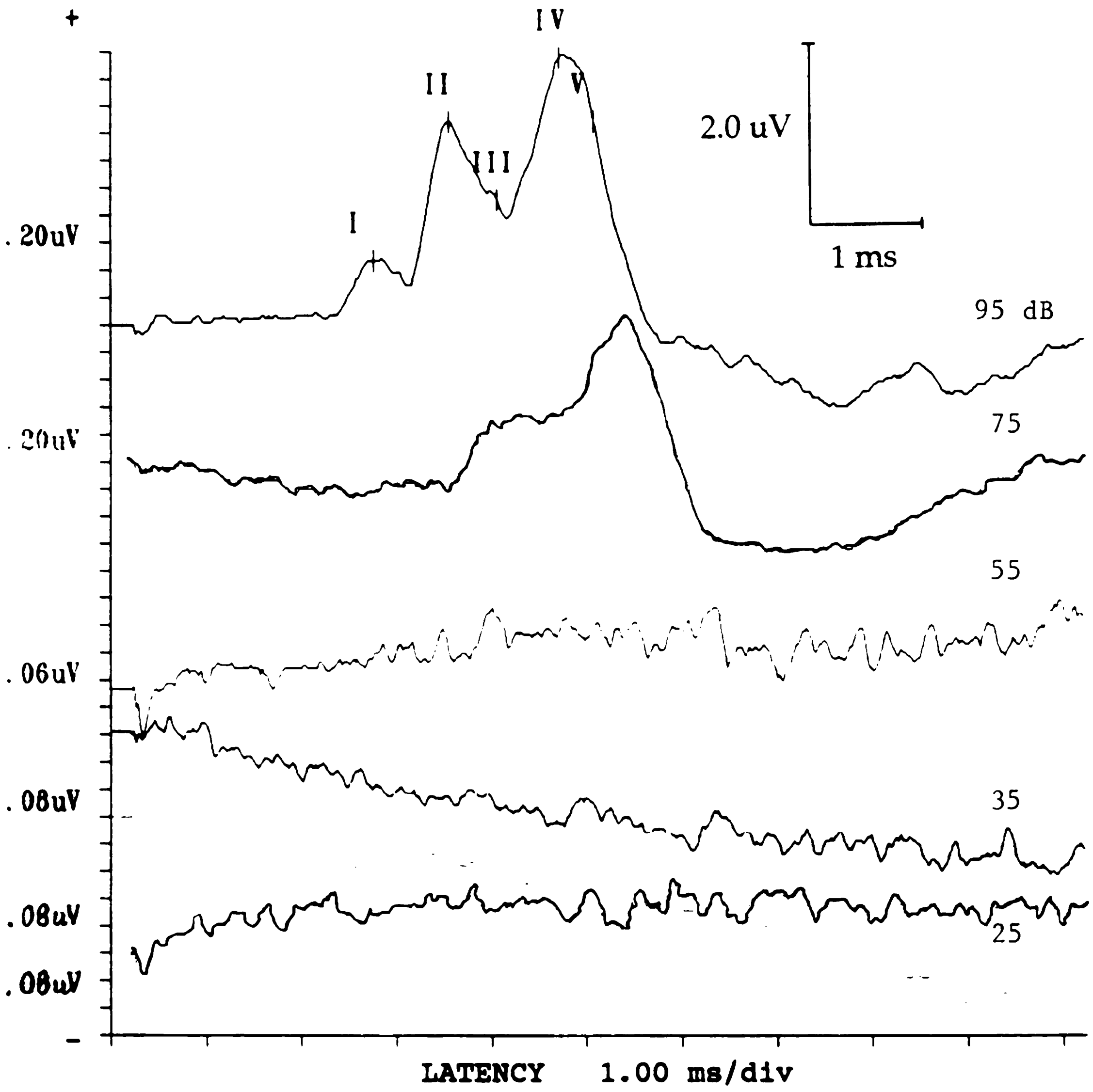


Figure 43. ABR's evoked by a 2,000 Hz TB in a male hearing-impaired dog.

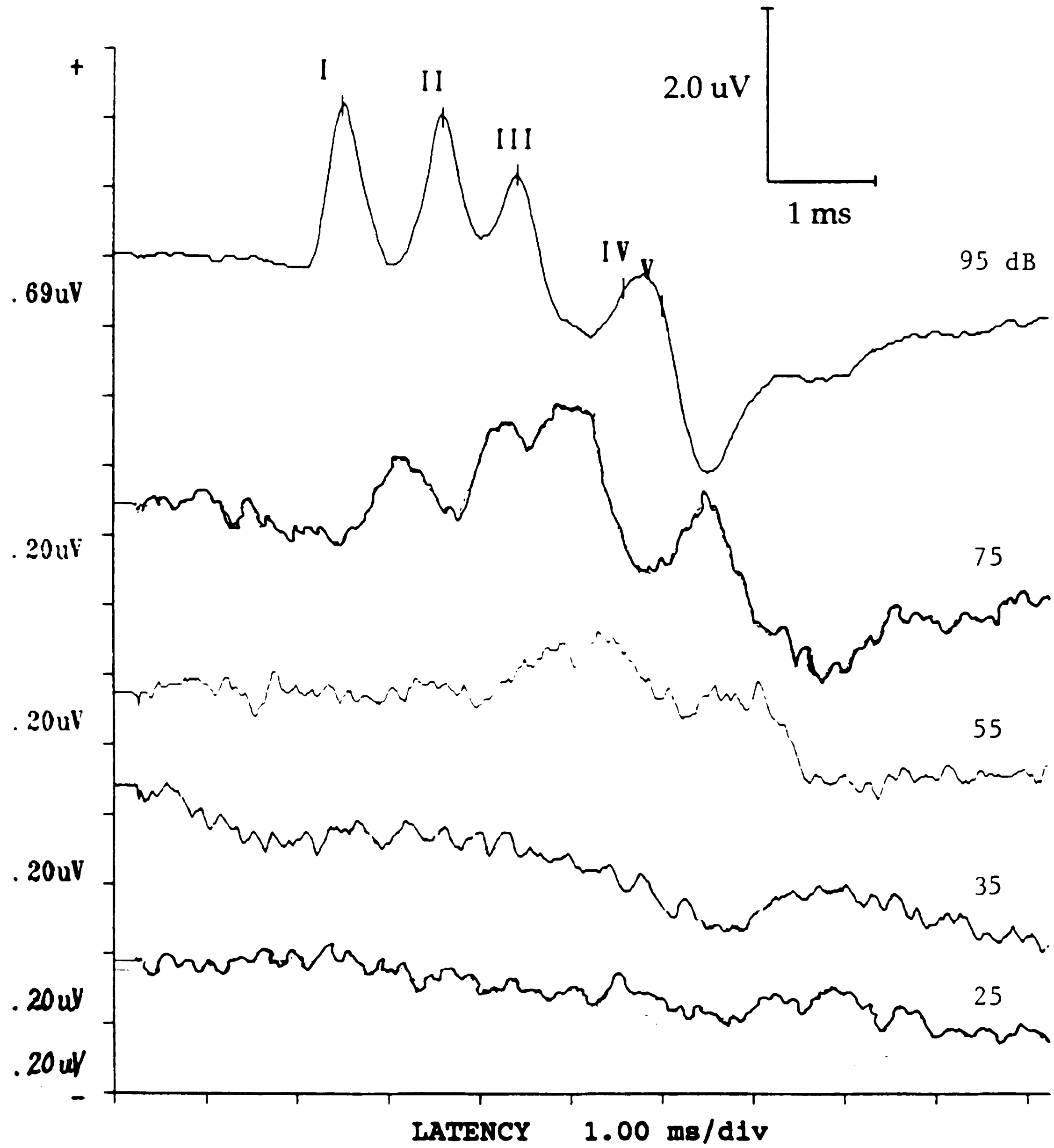


Figure 44. ABR's evoked by a 4,000 Hz TB in a male hearing-impaired dog.

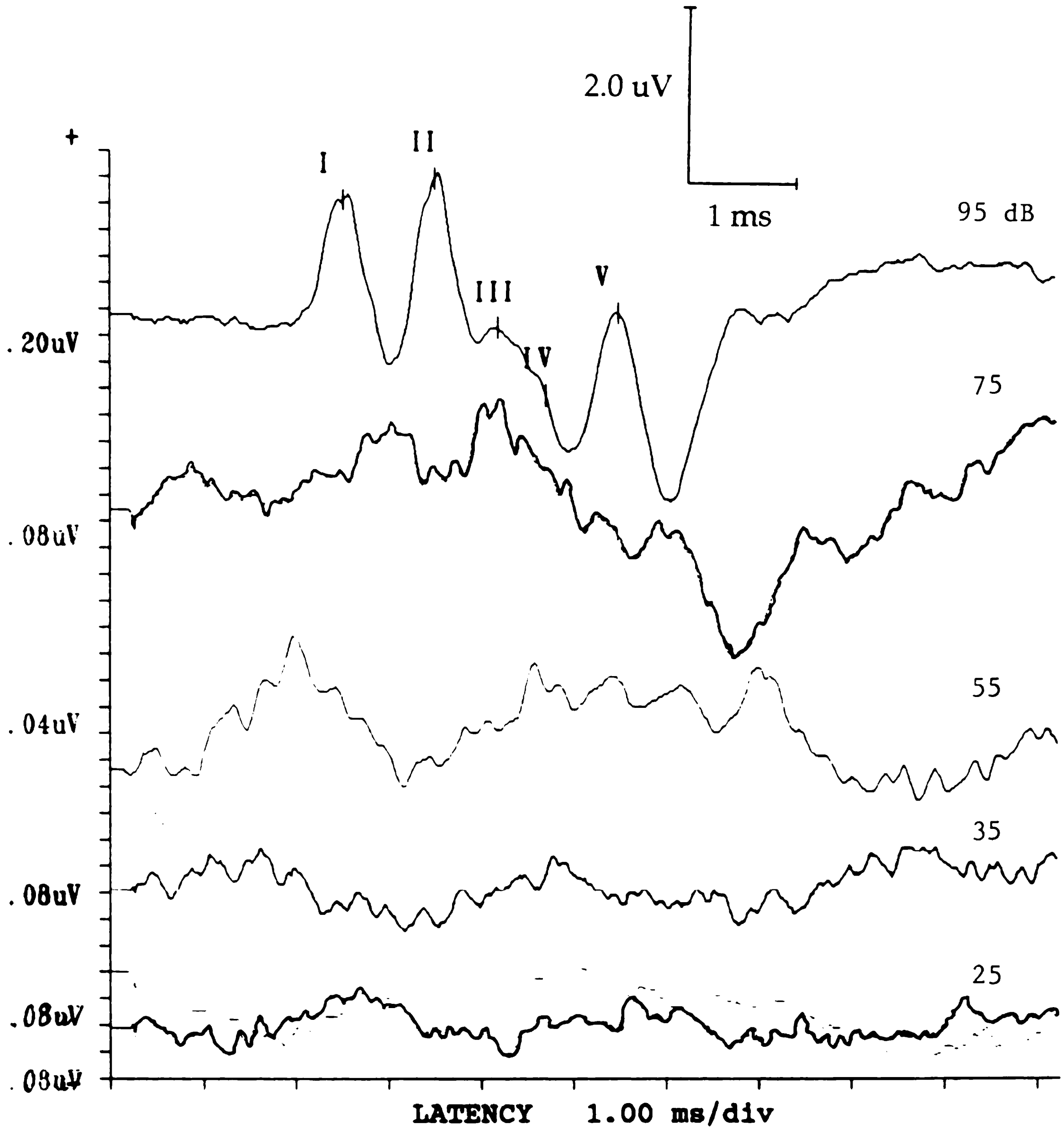


Figure 45. ABR's evoked by a 8,000 Hz TB in a male hearing-impaired dog.

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