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Modeling the auditory brain stem response from cochlear impaired ears using high-pass masked derived band responses

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MODELING THE AUDITORY BRAIN STEM RESPONSE FROM COCHLEAR IMPAIRED EARS USING HIGH-PASS MASKED DERIVED BAND RESPONSES

by

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DISSERTATION

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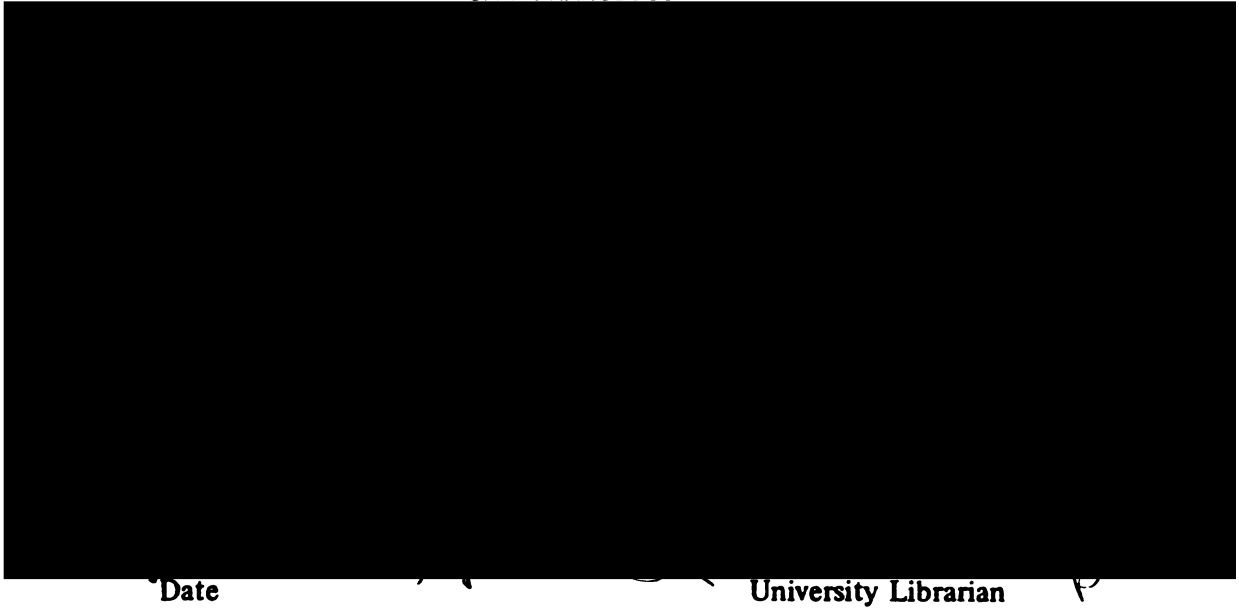

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PREFACE

Acknowledgments

Completing a research project such as this requires the cooperation and support of many people. I have been fortunate to have a large number of people on whom I could call for guidance and support. I would like to take this opportunity to acknowledge a few of them.

I would like to thank Roger Thornton who first introduced me to the derived band ABR technique and in whose lab I formulated the original idea for this study. I thank Roger for his patient teaching and encouragement while I was first discovering auditory evoked potentials.

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Manny Don, another committee member, has been most influential in the execution of this study and in my

academic career as well. Manny provided me with my first real laboratory experience and later provided a great deal of advise concerning the design of my experiment which was patterned after his hearing threshold, derived band ABR experiments. He also showed his faith in me by hiring me for a post-doctoral position (even before I was a real doc.) He is an excellent teacher from whom I shall continue to learn.

Perhaps the most influential person in my academic career, as well as in the design and execution of this study, was John Gardi. Throughout my term in San Francisco, John has instructed me in all facets of laboratory science and electrophysiology. From John I have also learned the importance of the power of positive thinking and perseverance. John provided me with the financial support, laboratory and equipment with which to perform these experiments and was always eager to help with any problems which arose. All doctoral students should have someone as supportive and encouraging as John to help them achieve their goals. I owe John a great deal of thanks for all he has done for me.

Many family members and friends have provided me with the psychological support which is so necessary during graduate school. From among many friends and fellow students, Dave Morelege and Diane Kirchner deserve special thanks for understanding and commiserating and for making feel that 'we were all in this together'. To my sister, Barbara, who

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To my husband, Lee, goes my deepest appreciation for his constant support and for understanding why I was never home. Thank you for taking over almost all the parenting of Lauren. She could not have been in better hands. Lee always helped me to focus on what was important and keep my life in perspective. He added fun and family support to what would otherwise have been the 'all work' life of a graduate student. For these things I will always be grateful to Lee.

ABSTRACT

Modeling of the Auditory Brain Stem Response from Cochlear Impaired Ears Using High-Pass Masked Derived Band Responses

Yvonne Satterblom Sininger

Several studies claim that certain relationships exist between auditory brain stem response (ABR) indices and hearing loss (secondary to cochlear pathology). The purpose of this study was to investigate the relationships between standard audiometric indices of cochlear hearing impairment and the amount of hearing loss reflected in the ABR. The latter was indicated by the intensity levels of frequency-specific, high-pass masked, derived band ABRs obtained from normal hearing subjects, used to create models of the click evoked response from subjects with cochlear impairment.

Derived band ABRs were elicited from six, normal hearing subjects in response to rarefaction clicks both unmasked and in the presence of high-pass filtered, white noise with cutoff frequencies of .5k, 1k, 2k, 4k, and 8k Hz. Derived band ABRs were created by successive waveform subtraction as described by Don et al. 1979. Responses were generated with clicks of 20 to 70 dB SL and averaged across subjects to create composite, normal, derived band responses (CNDBRs.)

Unmasked ABRs were obtained from five, hearing impaired (HI) subjects with cochlear pathology due to noise trauma or

ototoxicity. Also obtained were pure tone thresholds (PTTs), acoustic reflex thresholds (ARTs), and maximum comfort and loudness discomfort levels for pulsed, narrow-band noise stimuli.

Modeling of ABRs from HI subjects was accomplished by generating all intensity combinations of five CNDBRs. Each model was cross-correlated with unmasked HI ABRs using 1) points within a 6 to 7 ms window of the HI ABR and 2) points only within wave V. Based upon cross-correlation product and visual inspection, a best matched model (BMM) for each HI ABR was chosen.

None of the audiometric values correlated highly with the intensity levels of CNDBRs used to create BMMs for wave V only. BMMs for the entire waveform used intensity levels of CNDBRs which correlated highly only with ARTs in mid-frequency regions. It was concluded that, with the possible exception of ART, audiometric values such as PTT do not reflect amount of cochlear activity contributing to the ABR within frequency bands from HI subjects.

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INTRODUCTION

The auditory brain stem response (ABR) is considered to be the most sensitive and accurate audiometric test for detection of retrocochlear disorders, especially acoustic neuroma (Thomsen et al.,1978; Clemis & McGee,1979; Selters & Brackmann,1979; Portmann et al.,1980; Bauch et al.,1982). Selters and Brackmann (1979) claim that ABR is the "best audiometric test for acoustic tumor detection" (p. 225) and show that, in their clinic, ABR has a better false-positive and false-negative rate in detection of eighth nerve tumors than x-ray, electronystagmography or acoustic reflex testing. Clemis and McGee (1979) called ABR "the most efficient audiometric test available today in our search for tumors affecting the auditory nerve" (p. 31).

The human ABR, as first described in detail by Jewett & Williston (1971), consists of a series of five to seven, low amplitude, volume conducted waves occurring within 10 milliseconds following stimulation. These events can be measured from the scalp in response to rapid onset auditory stimuli. Obtaining an ABR in humans requires computer averaging of many individual responses in order to distinguish these sub-microvolt potentials from a background of ongoing EEG and muscle activity. Subsequent ABR waves are felt to represent far-field recordings of composite electrical events generated within the brain stem auditory pathway.

A high intensity, click-evoked, human ABR with Jewett wave nomenclature is shown in Figure 1. Wave I of the ABR is known to be the far-field reflection of activity from distal portions (at least) of the auditory nerve. Consequently, latency and amplitude of wave I will be influenced primarily by middle ear and cochlear processes. Subsequent ABR waves originate in various brain stem nuclei and/or fiber tracts. Discrete lesions at particular levels of the pathway can degrade ABR peaks which are generated at that level or higher in the auditory pathway.

The most robust of ABR peaks is wave V which is seen at lower intensities, faster click rates (Thornton & Coleman,1975) and in younger infants (Starr et al.,1977) than any other peaks. Because it generally has the largest amplitude (peak to following valley) it also is the most easily identified ABR wave. It is reasonable then, that wave V latency and/or amplitude would be involved in an index of ABR normality.

In patients with space occupying lesions which apply pressure to the eighth nerve such as acoustic neuroma, wave V, if present, usually demonstrates increased latency and many or all of the other peaks of the ABR may be obliterated (Clemis & McGee,1979; Selters & Brackmann,1979; Eggermont et al.,1980; Rosenhamer, 1977). Wave I is sometimes present in cases of acoustic neuroma (Starr & Hamilton,1976;Eggermont et al.,1980); presumably the distal end of the nerve may be

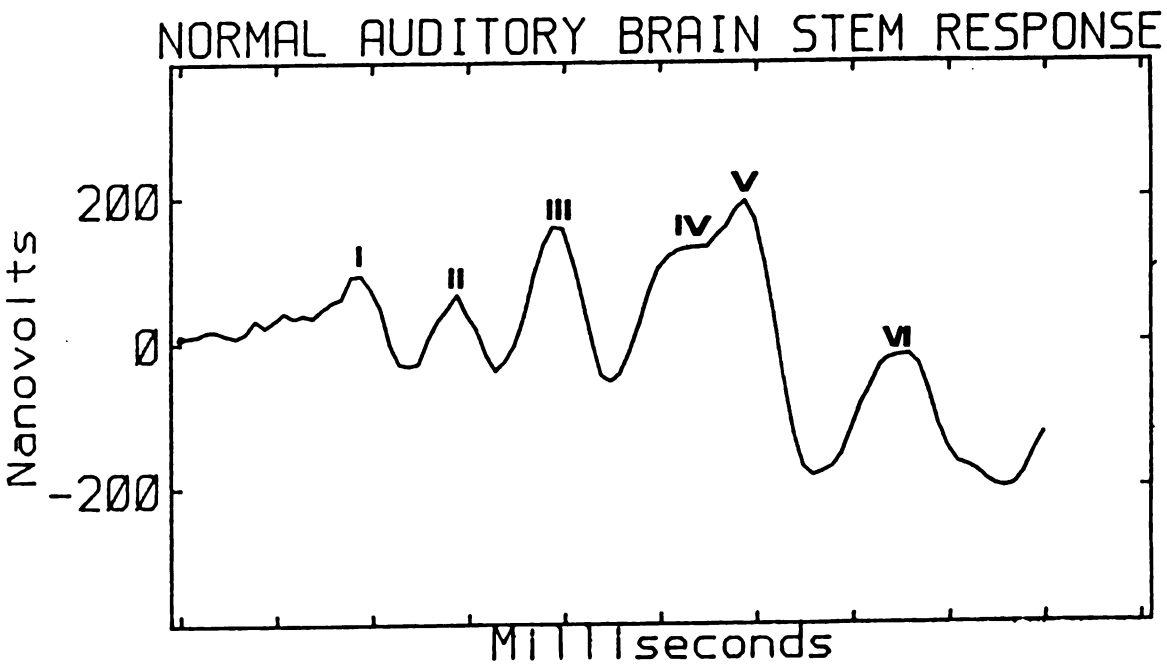


FIGURE 1. Normal, human ABR in response to high intensity (70 dB SL) rarefaction click. Response is the average of 4000 click presentations. Peaks are labeled with Jewett nomenclature (Jewett & Williston, 1971.)

unaffected by the tumor producing a normal response.

Pressure on the auditory nerve most likely affects the ABR by reducing synchrony in high frequency fibers which are outermost in the nerve trunk (Selters & Brackmann,1979; Eggermont et al.,1980). Early waves which appear to depend upon these highly synchronous, high-frequency fibers (Parker & Thornton,1978b) may be reduced or absent in response to pressure on the nerve, (Coats & Martin,1977) while wave V which appears to have less demand for synchrony may demonstrate the increased latency of lower frequency fibers which would be less affected by such pressure.

Review of Normality Indices

Some measures which have been discussed as possible indices of ABR normality or have been correlated with eighth nerve or brain stem disease include (1) absolute wave V latency (Robinson & Rudge,1975; Coats,1978; Rosenhamer,1977; Clemis & McGee,1979; Selters & Brackmann, 1979; Bauch et al.,1982), (2) overall waveform morphology (Rosenhamer,1977; Clemis & McGee, 1979; Bauch et al.,1982), (3) absolute or relative peak amplitudes (Robinson & Rudge, 1975; Rosenhamer,1977; Starr & Achor, 1975), (4) latency-intensity functions for wave V (Rosenhamer,1977; Coats, 1978), (5) interaural latency difference (ILD= wave V latency in the suspect ear - wave V latency in the normal ear) (Thomsen et al.,1978; Selters & Brackmann, 1979; Clemis & McGee, 1979; Eggermont et al.,1980; Rosenhamer et al.,1981b; Bauch et

al.,1982) and (6) inter-peak intervals especially I-III, I-V and III-V (Stockard et al., 1976; Rosenhamer, 1977; Coats & Martin,1977; Coats,1978; Portmann et al.,1980; Eggermont et al., 1980).

With the exception of absolute amplitude which demonstrates large amounts of inter-subject variability (Starr & Achor,1975) these measures generally have a high detection (hit) rate for acoustic tumors and brain stem disease. However, a high false-positive rate also has been associated with these measures and most misdiagnoses have been attributed to peripheral (cochlear) disorders which are manifested as hearing loss. Portmann et al.(1980), state that latencies of the IV-V complex are "closely dependent upon the condition of the peripheral organ and latency shifts attributable to cochlear pathologies are often undiscernible and can lead to misinterpretations" (p. 362).

Effects of Peripheral Hearing Loss on the ABR

Many studies have attempted to outline the relationship between peripheral hearing loss and the ABR. In some cases special attention has been paid to wave V latency (Møller & Blegvad,1976; Coats & Martin, 1977; Jerger & Mauldin,1978; Yamada et al.,1979b; Rosenhamer et al.,1981a & b; Shepard & Webster, 1983). These studies uniformly demonstrate that wave V latency increases with hearing threshold, especially in the 1000 to 4000 Hz region.

Møller & Blegvad (1976) studied wave V amplitude and latency from 60 patients with sensori-neural hearing losses of various configurations. They found that they could identify wave V at sensation levels closer to threshold (10 dB SL) in patients with flat losses than in those with sloping or steep, high frequency losses. They also noted that the latency of wave V from patients in the sloping or steep hearing loss groups was increased by about 1 ms over those from the flat hearing loss group.

Møller & Blegvad also noted that the ABRs from subjects with hearing impairment were of "poorer quality" than those of normal subjects. Also, ABR threshold was better correlated with 4000 Hz threshold than with PTA (pure tone average thresholds) or SRT (speech reception threshold) in this study.

Coats & Martin (1977) looked at the effects of audiogram shape on the ABR and on the ear canal recorded, auditory nerve action potential (AP) response. They evaluated 53 human subjects; 23 normals, 10 borderline normals and 20 cochlear-impaired (hearing loss) subjects by performing regression analysis on hearing thresholds and electrophysiological response parameters. They found highest correlations between AP threshold, latency and amplitude with hearing threshold at 4000 Hz. Wave V detection threshold in hearing level and wave V latency at threshold were correlated best with hearing at 4000 and 8000 Hz.

A small negative correlation (-.3) was noted for the difference between wave V and AP latency and hearing at 4000 Hz. In other words, there was a tendency for the AP-V latency to decrease with high frequency hearing loss.

Further inspection of data revealed a curvilinear relationship between AP latency and hearing threshold at 8000 Hz. There is a slight decrease in this latency with the first 20-30 dB of hearing loss which is followed by an increase in AP latency with more loss. The relationship between wave V latency and 8000 Hz threshold was best fit with a linear regression. Consequently, the AP-V interval shows a curvilinear trend when compared to 8000 Hz threshold reflecting the trend in AP latency. That is, there is an initial increase in AP-V latency interval with small amounts of hearing loss at 8000 Hz and then, with greater loss, the interval shortens.

Jerger and Mauldin (1978) also investigated the relationship between wave V latency and measures of pure tone sensitivity including pure tone threshold averages PTA_1 (.5k, 1k and 2k Hz) and PTA_2 (1k, 2k and 4k Hz) as well as 2k and 4k Hz thresholds alone. Three audiogram contour indices were also evaluated, the threshold differences between .5k and 4k Hz, 1k and 4k Hz and 2k and 4k Hz.

By means of regression analysis, these indices were evaluated from 275 ears with various degrees of hearing loss of cochlear origin. The highest correlations between wave V

latency were with hearing threshold at 4k Hz followed by contour indices. As the slope of the hearing loss between .5k and 4k Hz increased there was a dramatic increase in the predicted latency of wave V. However, the standard errors of the estimate in all cases of regression between ABR latency and audiometric data were quite high (17.2 to 25.2 dB) indicating that although trends could be seen, thresholds for individual subjects could not be predicted with accuracy from wave V latency data.

Yamada et al. (1979b) evaluated the effects of cochlear impairment on wave V latency-intensity functions in 12 hearing impaired patients with various hearing loss configurations. They found that wave V was always delayed in patients with steeply sloping high frequency losses especially those with slopes starting at 2000 to 3000 Hz. Patients with flat hearing loss showed nearly normal ABR latencies for high intensity stimuli and varying degrees of increased latency nearer to threshold. Patients with low frequency losses demonstrated nearly normal latency-intensity functions. Those with gradually sloping high frequency losses showed increased latencies especially near threshold which were predicted by the degree of loss above 2000 Hz.

Rosenhamer et al. (1981a) evaluated the relationship between ABR peak latencies and hearing threshold at 4000 Hz in 110 subjects with cochlear hearing impairment. In cases

of low frequency loss, no latency increases were noted unless the hearing at 4000 Hz exceeded 50 dB. In cases with flat losses, wave V latency increased with hearing threshold at 4000 Hz but no significant correlation between the two values was found. The interval between the surface recorded wave I and wave V did not change with hearing threshold in this group.

For subjects with high-frequency sloping losses, Rosenhamer et al., (1981a) found a significant correlation between prolongation of wave V and hearing threshold at 4000 Hz (r= .5). They noted from the regression equation that wave V was increasing approximately .1ms for every 10 dB of loss above 30 dB HL. No significant correlation between I-V latency interval and 4000 Hz threshold could be found. Also, no significant correlations could be found with hearing threshold at 1000 Hz and wave V latency.

Shepard and Webster (1983) evaluated the relationship between hearing loss and ABR waves I, III and V latency in 31 subjects with known cochlear hearing losses. These authors measured ABRs in response to clicks at 85, 75 and 65 dB nHL. With 85 dB nHL stimulation the largest correlations between latencies of both waves III and V were with 4000 Hz threshold. Wave I latency, however, correlated well with hearing thresholds at frequencies between about 3000 and 8000 Hz. Both waves III and V showed higher correlations with lower frequency thresholds (2000 Hz) when lower inten-

sities of stimulation (65 and 75 dB nHL) were used. Like Coats and Martin (1977), Shepard and Webster (1983) found a decrease in the latency interval between waves I and V with increasing high frequency hearing loss.

ABR Correction Factors for Hearing Loss

In order to increase diagnostic specificity of ABR in relation to retrocochlear disease many authors advocate correcting the specific measure of ABR normality used based on the degree or slope of hearing loss exhibited by the patient.

Table 1 outlines how the ABR has been applied to differential diagnosis of acoustic neuroma in several clinical studies. Many of these authors correct their normality index according to degree of hearing loss exhibited by the patients tested. It should be noted that some authors substitute N_1 latency measured from the promontory or ear canal for wave I latency. The most common correction factor is the one originally reported by Brackmann and Selters (1976). They add .1 ms to their normality index for every 10 dB of hearing loss over 50 dB at 4000 Hz. With the exception of Rosenhamer(1981b), where it could not be measured, the studies cited report a low false-negative rate, i.e., most of the tumors were identified by ABR. In the Rosenhamer et al. (1981b) study, none of the 45 asymmetrical cochlear disorders were misdiagnosed when the ILD measure was applied at equal sensation levels. However, since no

TABLE 1

Differential Diagnoses of Acoustic Neuroma

Study	Cases	ABR Normality Index	Hearing Loss Correction Factor	False Pos	False Neg	Stimuli
Thomsen et al. 1978	70 Cochlear 27 Neuromas	ILD (= .3ms	NONE	~12% (Fig 2)	3%	2k Hz Tone Burst 98dB PE SPL
Selters & Brackmann, 1979	266 Cochlear 142 Neuromas	ILD (= .2ms	+.1ms/10dB (over50)at4K	8%	4%	Clicks 83 dB SPL
Clemis & McGee, 1979	115 Cochlear 26 Neuromas	ILD (= .3ms	+.1ms (loss)65dB)	30%	7.4%	70-90dB HL Tone Pips
Portmann et al., 1980	26 Cochlear 14 Neuromas 9 Normals	I-V (= 4.5ms*	NONE	4%	7%	Clicks 20-90dB HL
		ILD (= .2ms	NONE	27%	NA	Clicks 90dB HL
Rosenhamer et al., 1981(b)	45 Cochlear	ILD (= .2ms	as Selters & Brackmann	9%	NA	90dB HL
		ILD=0	NONE	0%	NA	Equal SL (90 HL poor ear)
Eggermont et al., 1980	45 Neuromas	Interaural I-V (= .4ms* or ILD (= .3ms or poor morph.	NONE	NA	5%	Clicks 70dB+ HL
Bauch et al., 1982	229 Cochlear 26 Neuromas	ILD (= .2ms or poor morph.	as Selters & Brackmann	25%	4%	Clicks 80-85dB HL

TABLE 1. Summary of studies evaluating ABR measures in patients with acoustic neuroma and/or cochlear disorders. ILD is interaural latency difference for wave V. See text for details.

*Latency of N1 often substituted for wave I latency (see text.)

tumor cases were included in this study, false-negative rate cannot be evaluated. Consequently, overall efficacy of Rosenhamer's measure cannot be assessed.

Inter-aural Latency Difference (ILD)

Inter-aural latency difference (ILD) is the difference between the latencies of wave V elicited by stimulation of the right and left ears within an individual subject. It is assumed that in the absence of peripheral (middle ear or cochlear) or central (eighth nerve or brainstem) pathology, there should be no more than a small difference in the latencies of wave V (less than .2 or .3 ms) between ears. However, there are discrepancies in reported results on the use of ILD as an index of possible retrocochlear involvement. Selters and Brackmann report low false-positive and false-negative results when applying an ILD measure which has been corrected for hearing loss. However, they excluded all cases with hearing loss greater than 75 dB before reporting data. Bauch et al. (1982) employ the same criteria and correction factor and find a much higher false-positive rate of 25%. They attribute this to cases exhibiting peripheral hearing impairment even though a correction factor was applied. Bauch et al. (1982) state that "the majority of our nontumor patients with abnormal ABR results had hearing loss (sic), many of which were in the severe to profound range at 2000 and 4000 Hz" (p. 85). Unfortunately, patients who are suspect for retrocochlear lesion often

demonstrate just this sort of severe, high frequency hearing loss.

The use of the ILD as a diagnostic index for retrocochlear disorders also has some basic theoretical flaws. Any inter-aural normality index, either ILD or interaural I-V latency difference (Eggermont et al., 1980) assumes that the contralateral ABR is normal. In fact, the ABR contralateral to a space occupying lesion of any size may also be affected by displacement of the brain stem causing pressure. Rosenhamer (1977) reports that in 23 of 29 acoustic neuroma cases, contralateral ABRs were not completely normal. He assumes that this abnormality may be due to brain stem dislocation from the mass of the tumor.

ILD also disregards the possibility of bilateral acoustic neuroma. Clemis and McGee (1979) report missing the smaller of a pair of bilateral acoustic neuromas when applying ILD as a normality measure. The possibility of missing both of a pair of small but equal-size acoustic neuromas also seems possible when ILD only is used to determine ABR abnormalities.

The issue of contamination of ILD by peripheral hearing loss does not seem completely resolved by the application of Selters and Brackmann's correction factor. Their correction only considers threshold at 4000 Hz and ignores the slope of the loss which is known to influence wave V latency (Møller & Blegvad,1976; Coats & Martin,1977; Jerger & Mauldin,1978;

Yamada et al.,1979b).

I-V Interval

As shown on Table 1, Portmann et al. (1980)and Eggermont et al. (1980) report excellent diagnostic specificity for acoustic neuroma by evaluating the interval between waves I and V. Coats (1978) demonstrated that I-V interval decreases with cochlear loss and sensation level but increases with retrocochlear lesions. Consequently, this measure should be extremely well suited as an index of retrocochlear involvement. However, in these studies, wave I was not measurable in the surface recorded ABR in up to 30% of the patients tested. Elberling (1978) also noted that wave I often was not seen in the surface recorded ABR of patients with cochlear hearing loss. In these cases, latency of wave I was estimated from trans-tympanic recording of the N_1 response. While recording N_1 transtympanically greatly enhances the diagnostic ability of the ABR, it changes the test into an invasive, surgical procedure. For that reason, trans-tympanic ECoG recording capability, generally, is not available in audiological clinics.

General Comments on Normality Indices

Measures of normality that are currently applied to the ABR tend to ignore many features of the ABR except latencies of waves I and V. Overall waveform morphology, generally,

is not evaluated in any systematic way. Consequently, much of the ABR information is not utilized. Also, because peaks are sometimes difficult to identify in cases with disease or hearing loss, there is a tendency to not find or mislabel peaks. Elberling (1978), when discussing this issue in relation to patients with hearing loss, states that "in these cases the identification of the individual peaks is often uncertain" (p. 153). Consequently, either measures of normality cannot be applied or their application loses the objectivity which ABR was meant to achieve.

Statement of Need and Purpose

In order to increase the specificity of the scalp-recorded ABR as a diagnostic technique, i.e., reduce false-positive rate in the detection of retrocochlear disorders, a more accurate estimate of the effects of peripheral involvement must be taken into account.

The purpose of the following study is to investigate the potential for modeling the ABR from patients with pure cochlear impairment based on their audiometric data. This modeling will be attempted by creating a waveform made up of various intensities of normal, derived, octave band ABRs. If it is feasible to model the ABR from hearing impaired individuals in this way, such a model could be used as an individual standard by which to judge the abnormality or extent of retrocochlear involvement evidenced in the ABR.

Modeling the Abnormal ABR

Several studies have shown that portions of the ABR generated by specific frequency bands can be distinguished in the human, click-evoked ABR (Don & Eggermont,1978; Parker & Thornton, 1978a,b,d). Don et al. (1979) have used these 'derived band' responses to accurately predict hearing thresholds at specific frequencies in patients with cochlear hearing loss.

The addition of the whole frequency range of derived bands equals the non-derived, click-evoked ABR (Parker & Thornton,1978a; Don et al.(1979) in normal hearing subjects. The proposed index of retrocochlear involvement would utilize a bank of normal, frequency-specific, derived band ABRs at a wide range of intensities. Based on various audiometric information from a patient, such as pure tone hearing threshold, loudness comfort levels, loudness discomfort levels and acoustic reflex thresholds, appropriate intensities of each derived band from the bank could be added together to model the ABR of that patient. More detail and rationale for this procedure will be given after a complete discussion of the derived band technique.

High-Pass Masked Derived Band ABRs

The click-evoked ABR constitutes the composite recording of volume-conducted, neural potentials from the auditory nerve and brain stem auditory pathway. The rapid onset,

broad-band nature of the click stimulus applied to the ear initiates a rapid displacement of virtually the entire basilar membrane leading to highly synchronous firing of a large number of cochlear neurons which display a broad range of characteristic frequencies. It is this synchronous firing of cochlear nerve fibers which allows time window averaging techniques to pull the minute ABR out of its noisy background.

In contrast, the random time waveform of a white noise stimulus initiates neural responses randomly over time which tend to cancel in the averaged response. If sufficient noise is mixed with a click stimulus the averaged, whole-nerve action potential (AP) and/or the ABR will be eliminated because, as Elberling (1974) states, "the nerve fibers are unable to respond synchronously to the click, while they simultaneously are forced to respond to white noise" (p. 14).

Figure 2 (taken with permission from Don et al., 1979) illustrates the method by which the derived bands are created. R1 is an unmasked click ABR representing contributions from most of the basilar membrane. Mixing a sufficient amount of broad-band noise with the click creates the masked response, MR. In R2 the click is masked with 8k Hz high-pass noise which allows only those regions which are responsive to frequencies lower than 8k to contribute to the ABR.

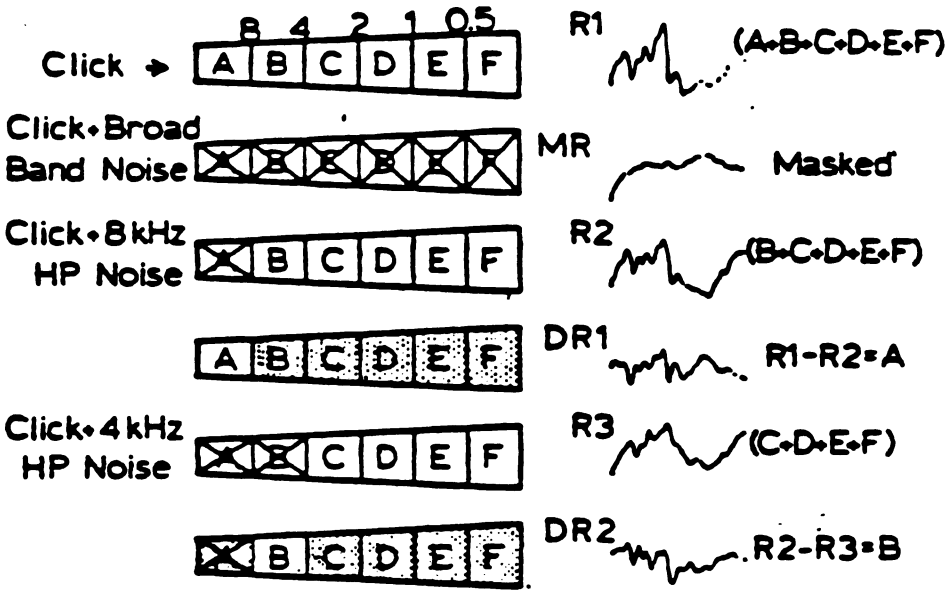


FIGURE 2. A schematic of the ABR high-pass masking technique and its application for obtaining the derived ABR. No attempt has been made in the diagram to represent the actual physical relations in terms of length, width or frequency mapping of the cochlea. Section A represents the area whose maximum sensitivity is 8k Hz and above; section B represents the region from 4 to 8k Hz; etc. (From Don et al.,1979)

Subtracting R2 from R1 reveals the derived band ABR from the region above 8k Hz (DR1). R3 is the ABR produced by clicks mixed with noise, high-pass filtered at 4k Hz. Subtracting R3 from R2 will reveal DR2, an ABR which is made up of contributions from a 4-8k Hz region. Subsequent bands are derived in the same manner.

Teas et al., (1962) applied this technique to the analysis of frequency specific components of the whole nerve AP in guinea pigs by mixing a click stimulus with band-passed or high-passed random noise. Teas et al. assumed that:

> at least as many neurons respond to the transient plus noise as respond to the transient alone, and the modal response to the transient plus noise is diminished because some of these neurons are now responding randomly to the noise. In effect, these neurons have been eliminated from synchronized response to the transient. (p. 1448)

They also felt that any additional neural response generated by addition of noise to the stimulus would be random and consequently, not contribute to the overall modal (averaged) response.

By progressively extending high-passed masking noise into lower frequencies and subtracting the resultant AP responses, Teas et al. were able to distinguish derived band AP responses. The sum of these frequency band responses closely approximated the unmasked (whole nerve) response. They concluded that the whole nerve AP is the convolution (complex product) of diphasic, single unit responses which

are sequentially activated by the traveling wave.

Elberling (1974) was the first to apply the high-pass masked, derived band technique to the analysis of the AP in humans. This allowed Elberling to evaluate the interaction of click intensity and basilar membrane generation site of the AP. The same technique was later applied by Eggermont (1976) to the evaluation and comparison of human and guinea pig AP responses. He looked at latency-intensity functions, computed basilar membrane traveling wave velocity, and made narrow band AP comparisons to single unit data. Eggermont (1979) later applied the high-pass masked derived band technique to the evaluation of his theory that AP latency shifts from intensity changes may be produced by a combination of basilar membrane travel time and the response time of the filter mechanism at the basilar membrane-hair cell transducer. He demonstrated that the shift in latency with intensity within a narrow band was greater than could be predicted by basilar membrane travel time alone. Within the derived bands, latency-intensity functions in cochlear impaired ears (known to have less sharply tuned cochlear filter characteristics with shorter impulse response delay) were found to be steeper than in normal ears. That is, Eggermont attributed these latency discrepancies to the influence of intensity on filter characteristics at the basilar membrane-hair cell transducer.

High-pass masking noise has been used by several investigators without waveform subtraction to simply enhance the frequency specificity of narrow band or pure tone stimuli in generating various auditory evoked potentials. This is done to help insure that basal portions of the cochlea are not contributing to and confounding measurements which are meant to assess more apical (low frequency) regions. Terkildsen et al. (1975) used band-pass masking in order to help define the frequency selectivity of the FFP_7 response (negativity following wave V at ~7 ms). Zerlin and Naunton (1976) combined high-pass noise with one third octave, filtered clicks when measuring human AP responses. Picton et al. (1979) used simultaneous notched noise to eliminate off-frequency responses from ABRs elicited by tone pips. Many studies of the frequency following response (FFR) have also utilized high-pass or band-pass masking in efforts to determine where, along the basilar membrane, the FFR is generated (Davis & Hirsh,1976; deBoer et al.,1977; Huis in't Veld et al.,1977; Gardi & Merzenich, 1979; and Yamada et al.,1979a).

The high-pass masked, derived band technique has been applied to the study of human ABRs to investigate effects of stimulus parameters. Eggermont & Don (1980) evaluated frequency band-specific effects of click intensity on the ABR while Hecox & Deegan, (1983) used the technique to assess the contribution of place mechanisms on the interaction of stimulus rise-fall time and ABR latencies.

Simultaneous Masking

Because the high-pass masked, derived band technique utilizes simultaneous masking, it is open to criticism on the basis of possible contamination from distortion products which would produce remote masking in frequency regions thought to be unaffected by the noise. Another possible side effect of simultaneous masking is suppression effects which would reduce the usable level of the stimulus in an unpredictable way. Any of these effects would bring into question the basic assumptions on which this technique is based.

Gorga and Abbas, (1982) addressed the issue of adverse effects of simultaneous high-pass masking on the click-evoked AP in cats. They demonstrated that thresholds of AP responses generated by tones below the cutoff frequency of steeply filtered noise (96 dB/octave) were unaffected by the presence of the masking (see Figure 3). Figure 4 (from Gorga & Abbas,1982) shows amplitude-intensity functions for 4000 Hz N_1 response in quiet and in the presence of the HP masker. Amplitudes differ significantly only for intensities of 80 dB or more. It is likely that, at these high intensities, higher frequency fibers have been recruited into the unmasked response and contribute to the rapid increase in amplitude of the response. These same high frequencies would be masked and therefore not contribute to the HP masked response. From these figures it is clear that any

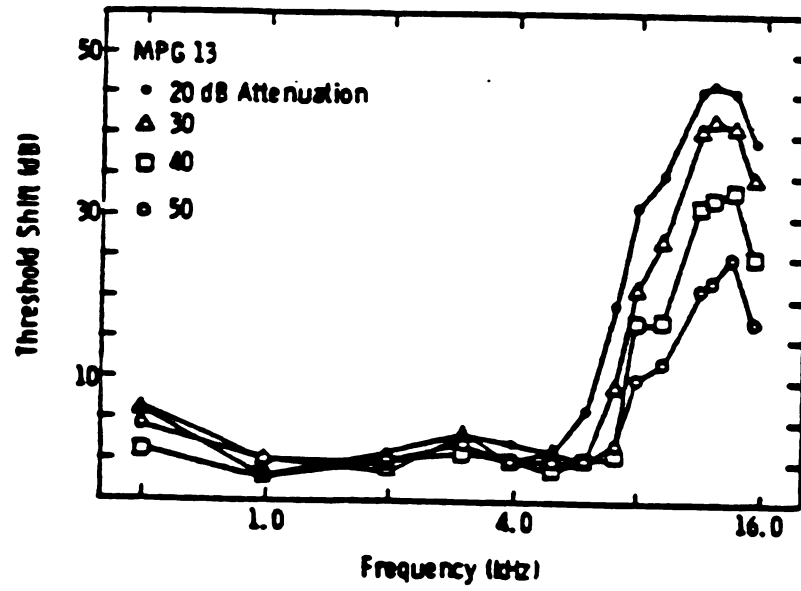


FIGURE 3. AP threshold shifts for an individual cat as a function of probe frequency. The parameter is level of the high-pass noise in dB attenuation (0 dB attenuation = 89 dB SPL). (From Gorga & Abbas, 1982.)

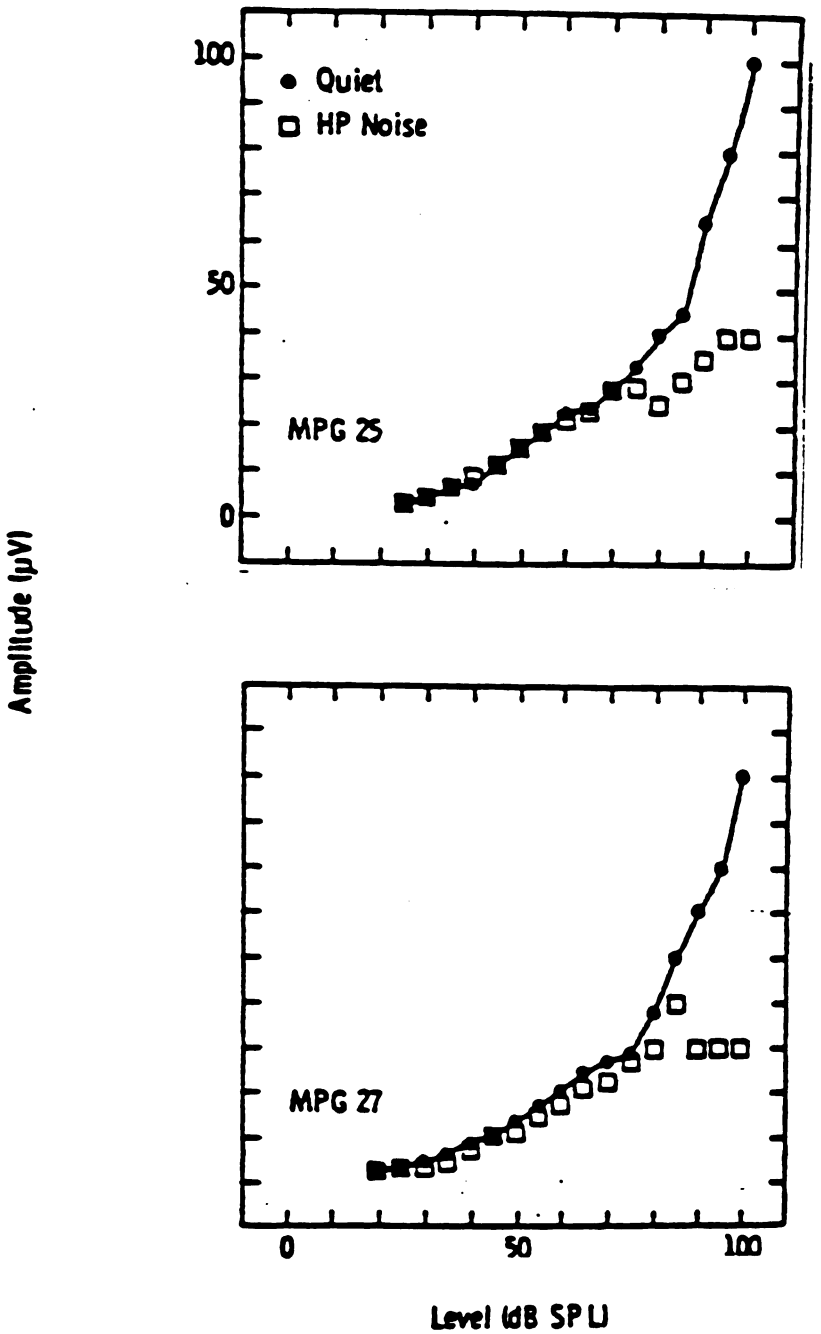


FIGURE 4. Amplitude of N1 peak as a function of 4k Hz tone burst level for two individual animals. Measurements were made in quiet and in the presence of high-pass noise. (From Gorga & Abbas, 1982)

remote masking which may exist in this situation does not seriously affect the threshold or low to mid-intensity amplitude of the AP response. Slight spread of masking into lower frequencies was observed with high intensity maskers which would caution specifying exact, derived band cutoff frequencies when intense noise is used, but would certainly not invalidate the technique.

Forward-masked, AP tuning curves were also evaluated with and without high-pass masking using probe frequencies which were just below the cutoff of the masking at two probe intensities. No change in unmasked AP tuning characteristics were observed in the presence of masking (see Figure 5 taken from Gorga & Abbas, 1982).

Evans and Elberling (1982) also evaluated the validity of the high-pass masked, derived band technique by recording AP responses from the round window as well as auditory nerve, single-unit, post-stimulus time (PST) histograms in cats with and without simultaneous, high-pass masking. Masking ratios of single fiber PST histograms were generated by integrating evoked activity over a certain time period and creating ratios with these measures in the masked and unmasked conditions. High-pass maskers with cutoff frequencies above 2k Hz showed essentially no remote masking in fibers with characteristic frequencies (CFs) below the high-pass cutoff. For high-pass maskers with cutoffs below 2k Hz some masking was noted in the lowest CF fibers (200 Hz

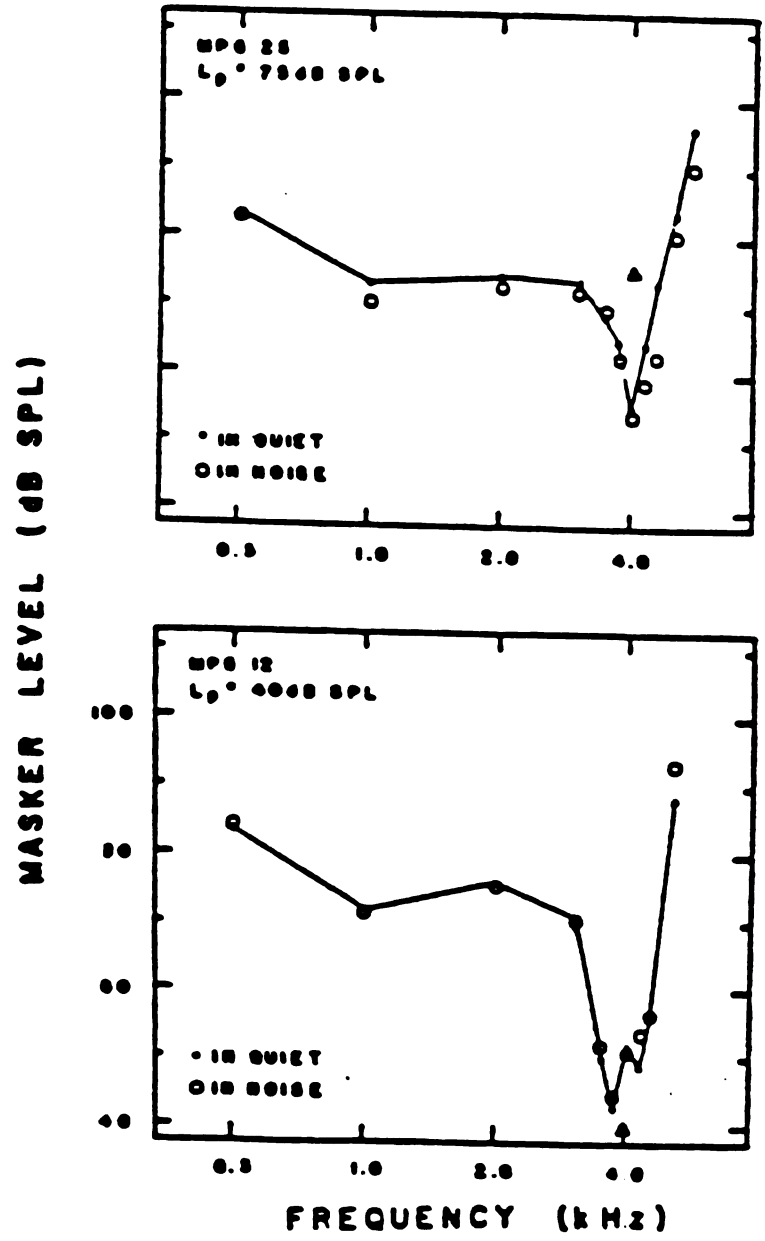


FIGURE 5. Forward masked, AP tuning curves in quiet (filled circles) and in the presence of high-pass masking (open circles). Parameter is masker level necessary for 50% reduction in probe-elicited AP response. Probe frequency and level are indicated by triangle. (From Gorga & Abbas, 1982).

and below). The 500 Hz high-pass masker caused some masking in essentially all the fibers. Similarly, high-pass masking had no effect on the latency of the PST histogram peaks except in fibers with a CF below 2000 Hz when in the presence of maskers with cutoffs of 4k or less.

Evans and Elberling noted that the latency of the first peak of the PST histogram did not correspond exactly with the latency of the compound action potential (CAP) for corresponding derived bands. The AP and the histograms, in fact, may have reflected different information since the CAP is a compound response. Eggermont (1979) found no difference in AP latency using forward compared to simultaneous masking in human ears. Forward masking will produce none of the combination tones or distortion products known to exist in simultaneous masking. If any remote masking of the AP response occured during simultaneous masking there appeared to be no effect on derived band AP latency.

Evans and Elberling concluded that their data provided "direct evidence on the validity of the high-pass masking technique for deriving frequency specific information for the gross CAP" (p 216). They cautioned only that, in the cat, some of the assumptions regarding derived band responses may be violated concerning low frequency bands. Because of differences in cat and human cochleas they felt that the high-pass masked, derived band technique may be used without reservations in humans for frequencies down to

500 to 1000 Hz.

Other direct and indirect evidence indicates that the high-pass masked, derived band technique allows for the description of specific, frequency-band contributions to the ABR. As previously noted, several studies have commented that the addition of derived bands closely resembles the unmasked, click response (Teas et al., 1962; Parker & Thornton, 1978a; Don et al.,1979). Figure 6 shows the author's comparison of the addition of five derived band responses between 500 and 20000 Hz and an unmasked ABR response from a cat. These responses were elicited by moderate intensity clicks. White noise masking levels were adjusted to just mask the averaged click response and subsequently filtered (48 dB/octave) at 8k, 4k, 2k, 1k and .5k Hz. Derived bands were obtained in the manner described by Don et al., 1979 (see Figure 2). The striking similarity of the added derived responses and the unmasked ABR lends support to the conclusions that (1) very little, if any, overlap exists between the individual derived bands and (2) distortions or remote masking do not affect the averaged, derived band ABR response. Teas et al. (1962) found the same relationship between derived bands and unmasked AP responses in guinea pigs (shown in their Figure 15) and stated that these results:

> support strongly the conclusion that the masking noise simply subtracts neurons from the population that responds to the transient stimulus. If the effect were anything more complicated, it is improb-

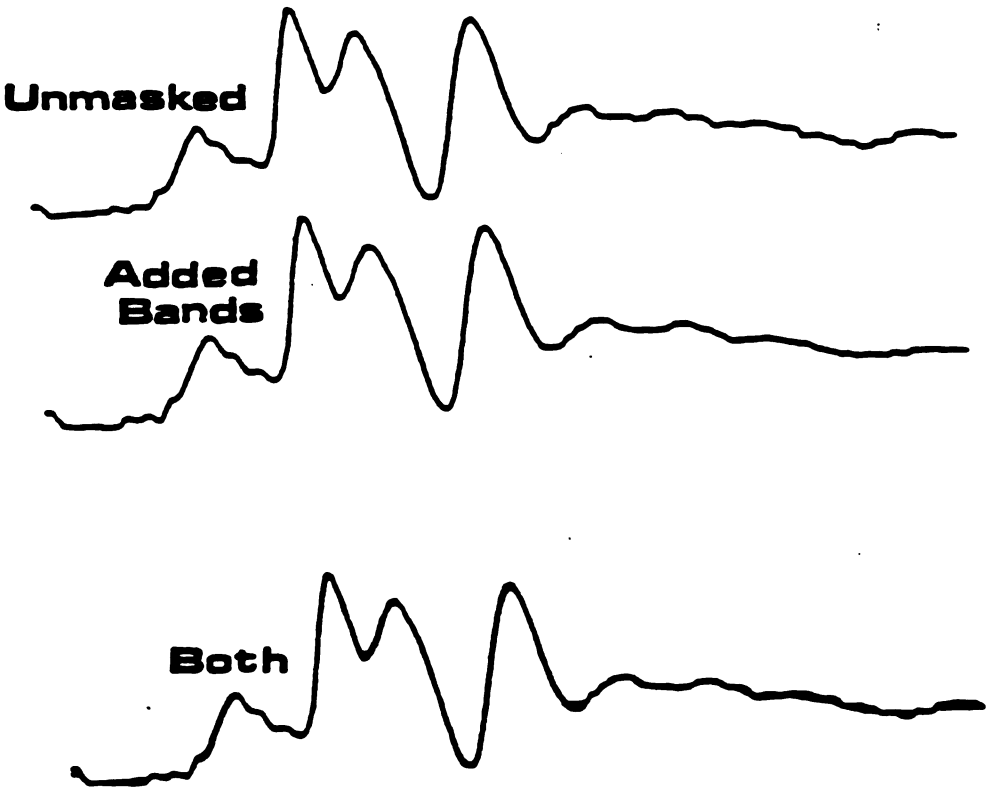


FIGURE 6. Comparison of unmasked cat ABR with the addition of all derived bands responses from the same cat (see text).

> able that the sum of the parts would so nearly equal the whole. (p. 1451)

Parker and Thornton (1978a,c,d) investigated the application of the high-pass masked, derived band technique to the auditory brain stem response. They found that subtractive and non-subtractive derived band techniques revealed indistinguishable results and concluded that waveform subtraction was a valid technique when applied to the ABR (1978a). In a subsequent publication (1978c), they showed that calculations of the velocity of the basilar membrane traveling wave based on latency shifts in ABR derived bands corresponded well with other published estimates of this velocity. Parker and Thornton (1978c) concluded that the derived band ABRs "truly represent neural activity initiated by activity at specific frequency regions along the cochlear partition" (p. 67).

Parker and Thornton (1978d) also demonstrated that band-pass maskers which were specially shaped to match the frequency characteristics of the derived bands, affected those bands only while adjacent derived bands were unaffected by their presence. This finding further supported the frequency specificity of ABR derived bands.

The final evidence of the validity of the high-pass masked, derived band technique is the fact that, in humans, Don et al. (1979) have shown that this technique can be applied to the ABR to accurately predict audiometric results

at specific frequencies in hearing impaired humans. Elberling (1974) has shown the same results using derived band AP responses.

Basic Theoretical Assumptions

As previously stated, several authors have shown a direct relationship between certain ABR measures and hearing level in cochlear pathology. Jerger and Mauldin (1978) demonstrated that wave V latency is positively correlated (r=.47 significant at .00001 level of confidence) with 4000 Hz threshold in patients with cochlear impairment. Rosenhamer et al. (1981a) found a .5 correlation (significant at .05 level of confidence) for the same measure. Jerger and Mauldin further showed that the slope of hearing loss between 1000 and 4000 Hz is correlated to wave V latency (r=.38 significant at .00001 level of confidence). Yamada et al. (1979b) showed that wave V latency-intensity functions are systematically related to slope and low-frequency cut-off of high-frequency hearing loss cases due to cochlear impairment. The goal of the current study is to predict the entire ABR waveform based on degree of hearing loss and various psychophysical results rather than to focus merely on wave V latency.

Elberling (1978) demonstrated that the generation of ABRs is clearly a product of cochlear responses filtered through a brain stem transfer function. He evaluated this transfer function in patients with pure cochlear hearing

impairment by using their eighth nerve compound action potential response as a measure of input to the brain stem. By deconvolving (inverse filtering) each patient's ABR with their AP response, Elberling could directly evaluate brain stem transfer functions for each patient. Using patients with various degrees of cochlear hearing loss in whom peripheral factors were accounted for, Elberling found brain stem transfer functions to be very consistent across subjects.

It is clear that peripheral input to the brain stem is a major influence on the ABR and if that factor can be held constant in some way, the remaining response is a reflection of brain stem integrity.

There is a direct relationship between the degree of hearing loss and the N_1 response (Coats & Martin, 1977; Elberling, 1974) or wave V of the ABR (as stated previously). Schuknecht (1974) also found a direct relationship between degree of hearing loss and percentage of damaged hair cells in cats. Therefore, it is reasonable to assume that N_1 or ABR responses reflect cochlear damage and that particular ABR waveforms and cochlear disorders are closely related.

Finally, Don et al. (1979) demonstrated that elevated thresholds in patients with cochlear hearing loss were reflected in their ABRs and could be predicted accurately at individual frequencies by utilizing derived band thresholds.

Cross Correlation Technique

Because ABRs are stored as digital amplitude values at discrete points in time, it is a simple matter to obtain a point by point, Pearson correlation (r) value for any two ABR waveforms provided they are obtained using the same analog to digital sampling rate and are the same duration and latency. The correlation values vary from +1 for a perfect correlation (exact waveforms) to -1 for two waveforms which are exactly out of phase. Correlation values near zero indicate that the two waveforms compared are very dissimilar.

Weber and Fletcher (1980) used simple waveform correlations to determine when an ABR threshold had been reached. They compared correlations between repeat ABR waveforms in response to near threshold intensities and the same responses correlated with no-stimulus control runs. Because test-retest responses should correlate highly when a response is actually present they felt that this technique improved the sensitivity of clinical threshold measures using the ABR by providing "a rapid and unbiased interpretation of test results" (p. 236).

According to Elberling (1979) "use of subjective identification of BSER peaks, or subjective description of waveforms, constitutes a severe, unsatisfactory limitation for the clinical applicability of the BSER procedure" (p. 187). To solve this problem he suggested the use of cross

correlation of clinical ABR responses with a normal template response. Elberling (1979) normalized ABR amplitudes by adjusting waveform RMS to a standard amount and consequently, reduced error which was due to large inter-subject amplitude variability. He also allowed for a relative latency shift between template and clinical ABR and plotted cross correlation values as a function of this time shift. This helped to remove small intensity differences from the analysis by allowing for determination of maximum correlation values regardless of slight phase differences. The cross correlation technique, according to Elberling, allows for "not only characteristics of specific peaks but also the complete waveform information in the individual BSER recordings to be taken into account" (p. 188-189). This technique of comparing normal template and clinical ABRs would be applied in the proposed retrocochlear index. In this way modeled ABRs could be objectively compared to individual subject's recordings.

Cochlear Pathology

In order to be certain of examining the effects of pure cochlear disorders in human subjects, these subjects must be carefully selected by history since no further confirmation of exact lesion is possible. The histopathology of both aminoglycoside ototoxicity and acoustic trauma are well documented and generally limited to sensory cell damage with excellent neuronal survival (Schuknecht,1974;

Spoendlin,1976). Spoendlin (1976) summarized anatomical results of various degrees of noise exposure in animals. Long exposures to moderately intense sound (<120 dB SPL) produced a progression of damage over time beginning with swollen nuclei in outer hair cells (OHCs), progressing to single degenerating OHCs in a scattered pattern and eventually resulting in complete degeneration of outer and inner hair cells (IHCs) without significant loss of nerve fibers.

Most aminoglycoside antibiotic and other drug-induced ototoxicity display a similar pattern of hair cell degeneration. Usually OHCs are the first to degenerate followed by IHCs while acoustic neurons are often spared although occasional secondary degeneration of ganglion cells is noted (Bergstrom & Thompson, 1976). Schuknecht (1974) found that in patients with renal failure treated with kanamycin, cochlear neurons were not damaged even in cases of profound hearing loss. Kiang et al., 1970, noted the base to apex progression of hair cell degeneration when administering kanamycin in cats but they saw equal destruction of inner and outer hair cells. Other authors working with kanamycin injections in rodents have produced outer hair cell damage in large sections of the cochlea starting at the base while sparing the inner hair cells throughout the cochlea through the use of kanamycin (Dallos & Harris, 1977).

As mentioned, it is usually the case that both ototoxic and noise-induced cochlear damage progress from base to apex

damaging high frequency sensitivity first while affecting lower frequencies only in later stages (Kiang et al., 1970; Schuknecht, 1974; Spoendlin, 1976; Dallos & Harris, 1977; Bergstrom & Thompson, 1976; Lim et al., 1982).

Conclusion

Because there is a positive correlation between cochlear damage and both psychophysical measures and ABR factors, it seems reasonable to use psychophysical information to predict ABR waveforms in patients with end-organ lesions. Such modeled waveforms could be utilized as an index of cochlear involvement or conversely, variation from the modeled response could be used as an index of retrocochlear influences. A simple example of this principle is the acoustic neuroma or brain stem tumor case with normal hearing sensitivity. The predicted ABR would be perfectly normal while the patient's ABR should show substantial abnormality and correlate poorly with the predicted one.

PURPOSE

This study was designed to answer the following questions:

(1) When modeling high intensity, click-evoked ABRs from normal subjects using the addition of high-pass masked, octave-wide, derived band ABRs, what is the distribution of cross correlation values for these modeled ABRs and those from individual normal subjects? In

other words, is it possible to accurately model ABRs from normal hearing subjects using the technique of derived band addition and how much variability exists between modeled and actual responses?

(2) Based on the distribution of cross correlation products, will the addition of composite, normal hearing, derived band ABRs be able to model the high-intensity, click-evoked ABR from subject with cochlear hearing impairment? That is, will correlations be at least as good as those found in normal hearing subjects?

(3) What psychophysical or other information from patients with cochlear hearing impairment is necessary to predict frequency specific effects upon their ABRs? Specifically, how do audiometric measures of pure tone hearing threshold, maximum comfort level, loudness discomfort level or acoustic reflex threshold from subjects with pure cochlear impairment relate to intensities of each derived band used to create a composite modeled ABR which correlates highly with the actual ABR from that subject?

(4) Are relationships in 3 (above) standard across frequency and across subjects?

METHODS

Equipment and Calibration

Stimuli

A diagram of instrumentation used for obtaining derived band ABRs is shown in Figure 7. Positive, square-wave pulses, 100 usec in duration were generated by a computer (Data General Nova III) and delivered at a rate of 20/second to a 1/3 octave band, graphic equalizer (Sundholm, model 3100). Equalizers were used in line with both click and noise stimuli to extend high frequency response through the shielded earphones. Without the use of such equalizers, the earphones produced little or no energy in response to wide band stimuli above 6k Hz. This is probably due to added mass from the shielding.

After the equalizer, click stimuli were delivered to an attenuator (Hewlett Packard, model 350D), mixed with noise and amplified (Coulbourn, model 582-24 audio mixer-amplifier) and presented to mu-metal shielded (Life-Tech) earphones.

Click stimuli, delivered through earphones, were calibrated by coupling a 6 cc coupler (Bruel and Kjaer, model 4153) to an impulse sound level meter (Bruel and Kjaer, model 2209). Maximum click intensity was found to be 103 dB Impulse SPL and attenuation was linear (within 1 dB) within

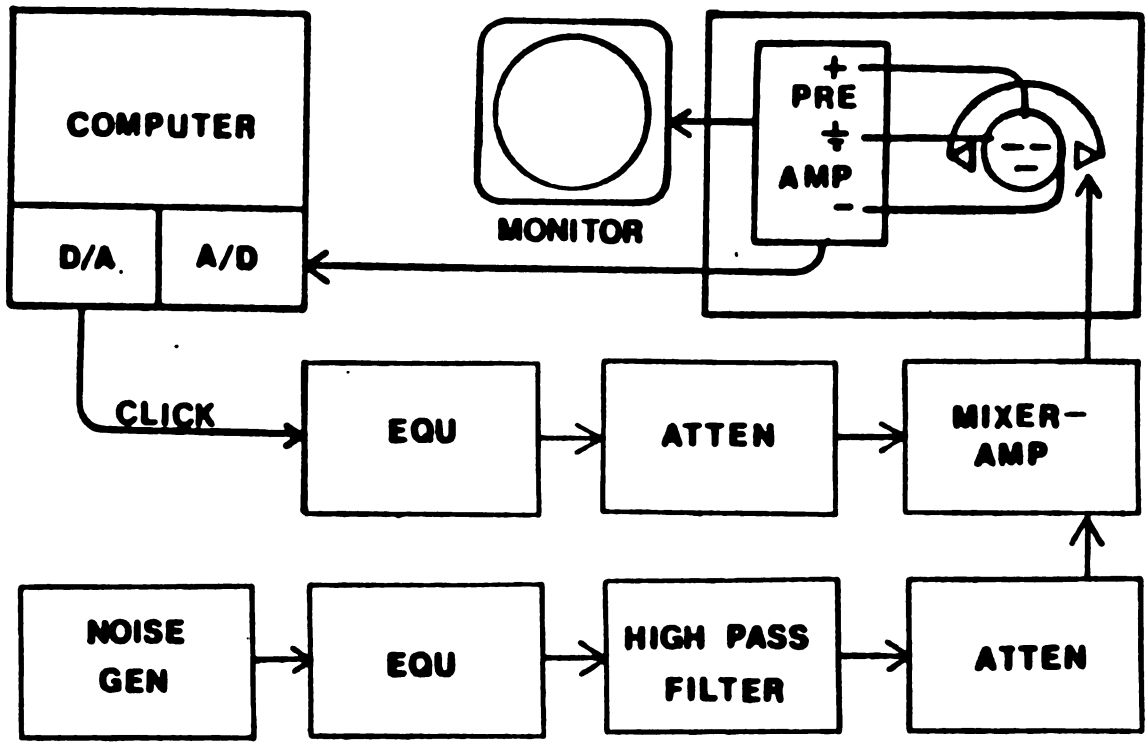


FIGURE 7. Block diagram of instrumentation used for generation of click and noise stimuli and recording of ABR data. Click stimuli were created by the computer and delivered to a graphic equalizer (EQU) and then to an attenuator before being mixed with noise and presented to mu-metal shielded earphones. White noise was also sent to a separate graphic equalizer before being high-pass filtered, attenuated and mixed with the click. Responses gathered from scalp EEG electrodes were amplified and band pass filtered before being sampled and converted to digital values and averaged by the computer. Unaveraged EEG was monitored on an oscilloscope. See text for details.

a range of 50 dB. Below this level room noise interfered with measurements.

Output of the earphone through the sound level meter monitored on an oscilloscope, demonstrated rarefaction clicks. The time-waveform of the acoustic click is seen in Figure 8. Output of the sound level meter was sent to a spectrum analyzer (Nicolet, model UA500A). While monitoring the spectrum of the click or noise, graphic equalizers were adjusted to reveal the broadest, flattest response possible. The final click spectrum can be seen in Figure 9.

Wide band noise from a noise generator (Layfayette, model 5011) was sent to a 1/3 octave band graphic equalizer (Biamp, model EQ270A). High-pass filtering of noise was accomplished by a variable frequency filter (Krohn-Hite, model 3343). Two channels of the filter, each capable of 48 dB/octave filtering, were cascaded resulting in 96 dB/octave high-pass filtering. Power spectra of the noise, unfiltered and in various filtering conditions, can be seen in Figure 10.

Filtered noise was sent to an attenuator (Hewlett-Packard, model 350D), mixed with clicks, amplified and presented to the earphones. Maximum intensity of wide band noise was determined to be 113 dB SPL and linearity of attenuation was maintained within 1 dB for at least a 50 dB range.

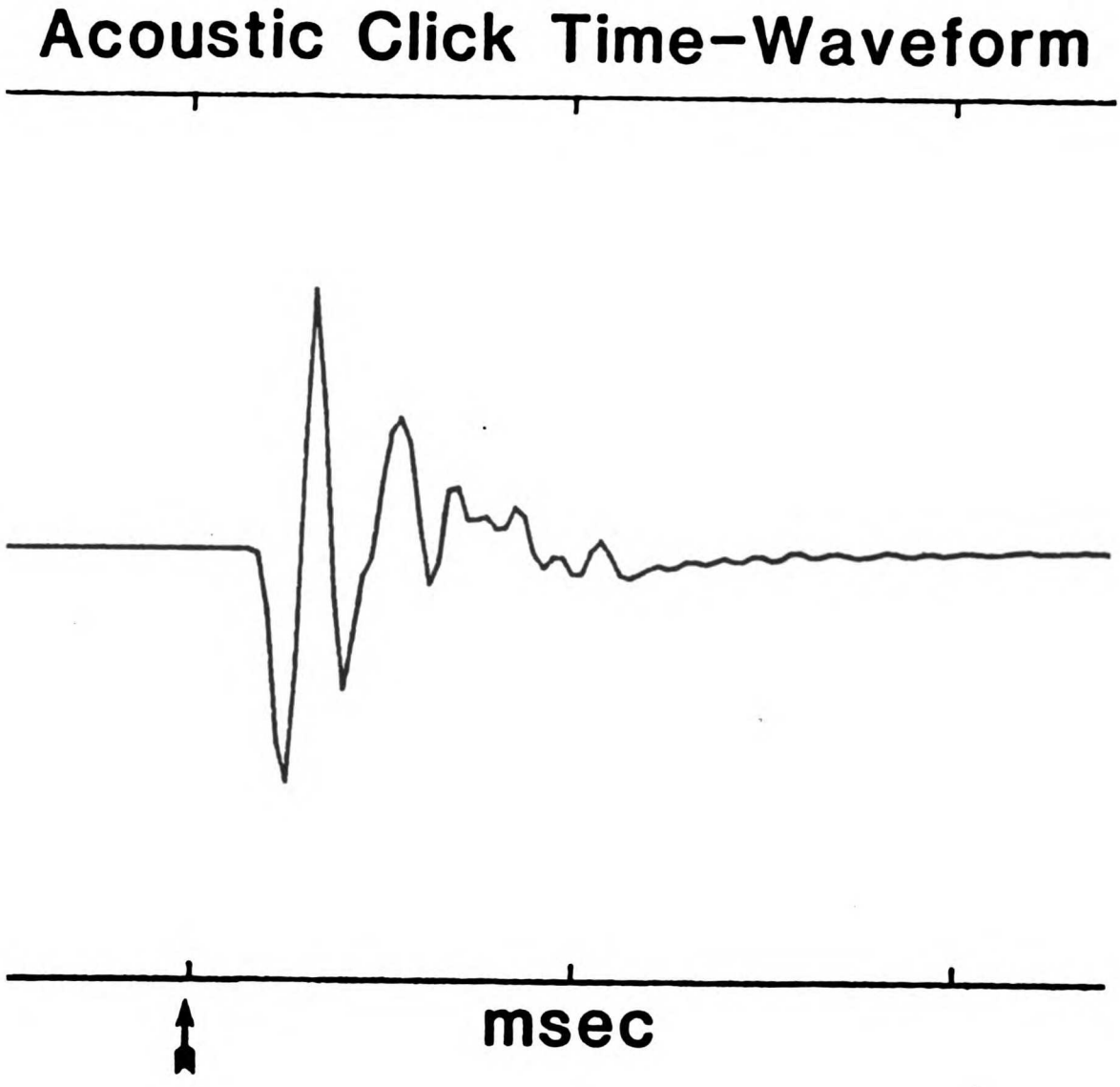


FIGURE 8. Time waveform of click stimulus through earphone. Arrow indicates stimulus onset. Spectrum of this click is seen in Figure 10.

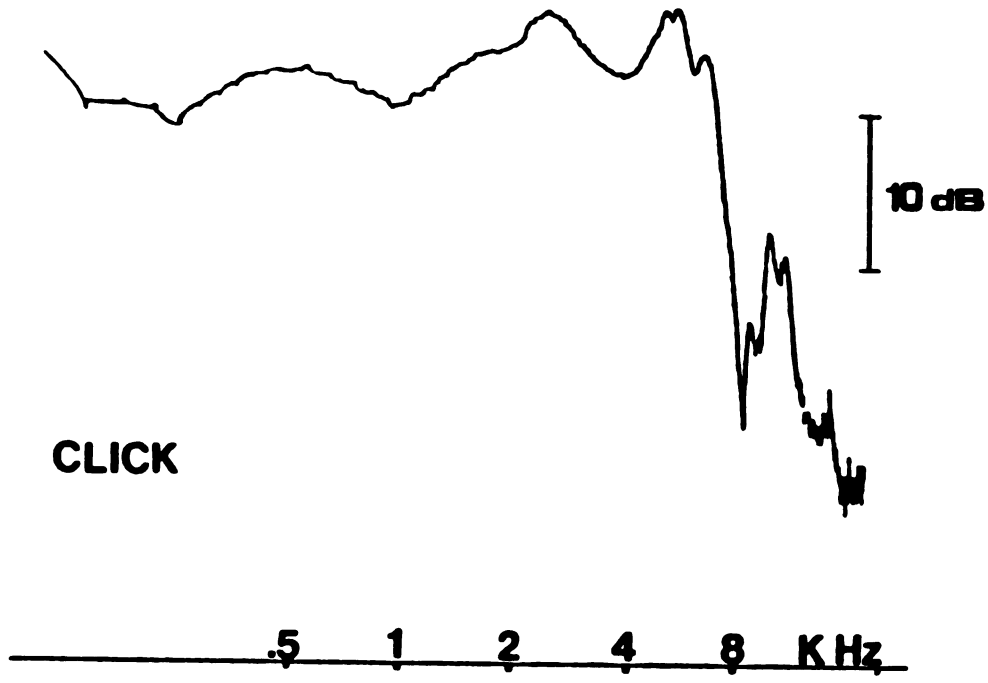


FIGURE 9. Power spectrum of click stimuli (100 us pulses) as measured by spectral analyzer (Nicolet, Model U500A). Analysis window was 20K Hz. Spectrum is the result of 256 averages.

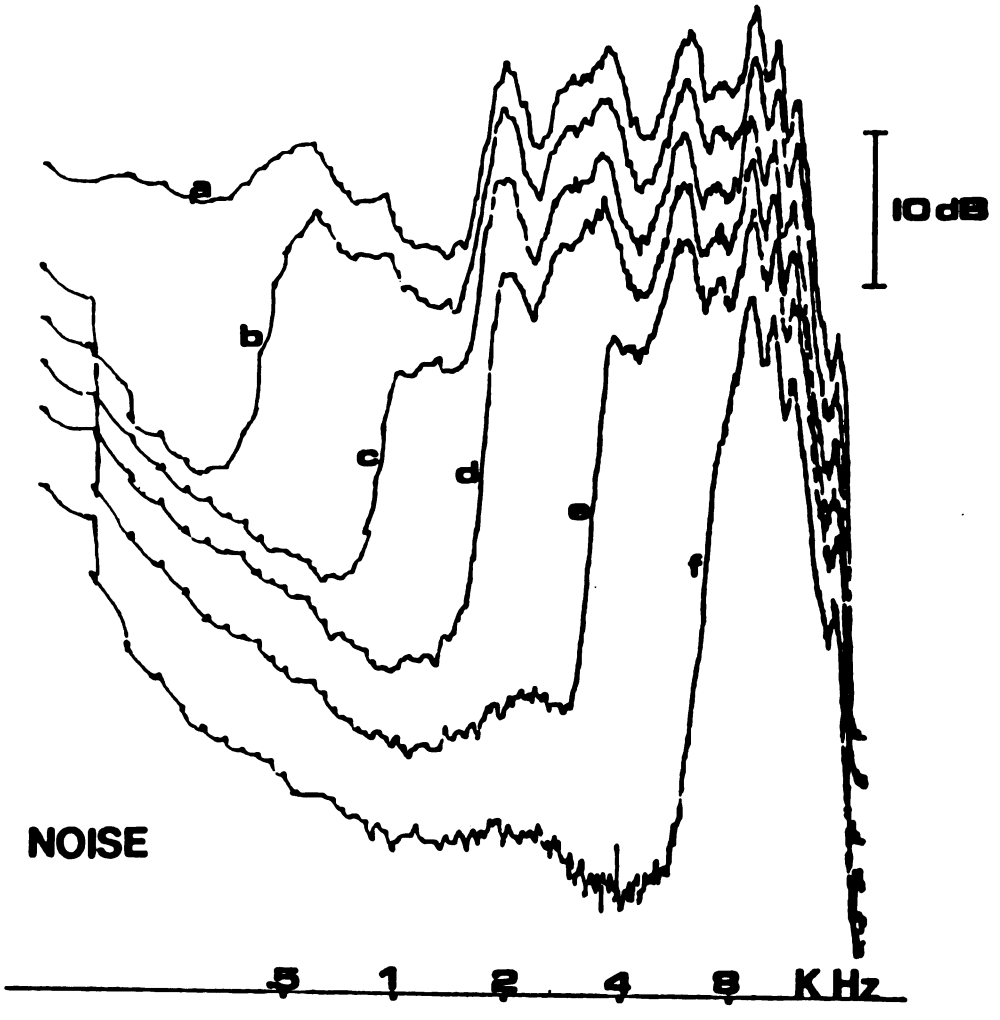


FIGURE 10. Power spectra of wide band noise (a) and the same noise high-pass filtered (96 dB/octave) at cutoff frequencies of 500 (b), 1k (c), 2k (d), 4k (e) and 8k (f) Hz. Spectra were measured in the same manner as the click spectrum.

Stimuli used to measure loudness discomfort level (LDL) and maximum comfort levels (MCL) were narrow bands of noise designed to conform with spectra of derived band ABRs and to maintain equal bandwidths relative to the width of corresponding octave bands of eventual derived band ABRs. Wide-band noise from the noise generator (Layfayette, model 5011) was band-pass filtered (48 db/octave, Krohn-Hite, model 3343) to create 5 noise bands: 600-800 Hz, 1200-1600 Hz, 2600-3400 Hz, 5200-6800 Hz and 8600-9400 Hz. These stimuli were directly recorded on 1/4" magnetic tape on a 4 channel tape recorder (Teac, model A-3440).

The output of the tape recorder was sent to an audiometer (Maico, model MA-22) where noise bands were pulsed at 1 Hz (50% duty cycle with .1 second rise and .05 second fall time), attenuated and presented to earphones (TDH-39). The output of the earphone was calibrated using a 6 cc cavity (Bruel and Kjaer, model 4153) coupled to a sound level meter (Bruel & Kjaer, model 2209). The output of the sound-level meter was recorded on a separate channel of the tape recorder and spectra of noise bands were analyzed from these recordings by a spectrum analyzer (Nicolet, model UA500A). Results of this analysis can be seen in Figure 11. Stimuli 'a' (8600-9400 Hz) and 'b' (5200-6800 Hz) show resonance effects of the 6 cc coupler.

Pure tone stimuli for threshold testing were generated by an audiometer (Maico MA-22) and calibrated as above to

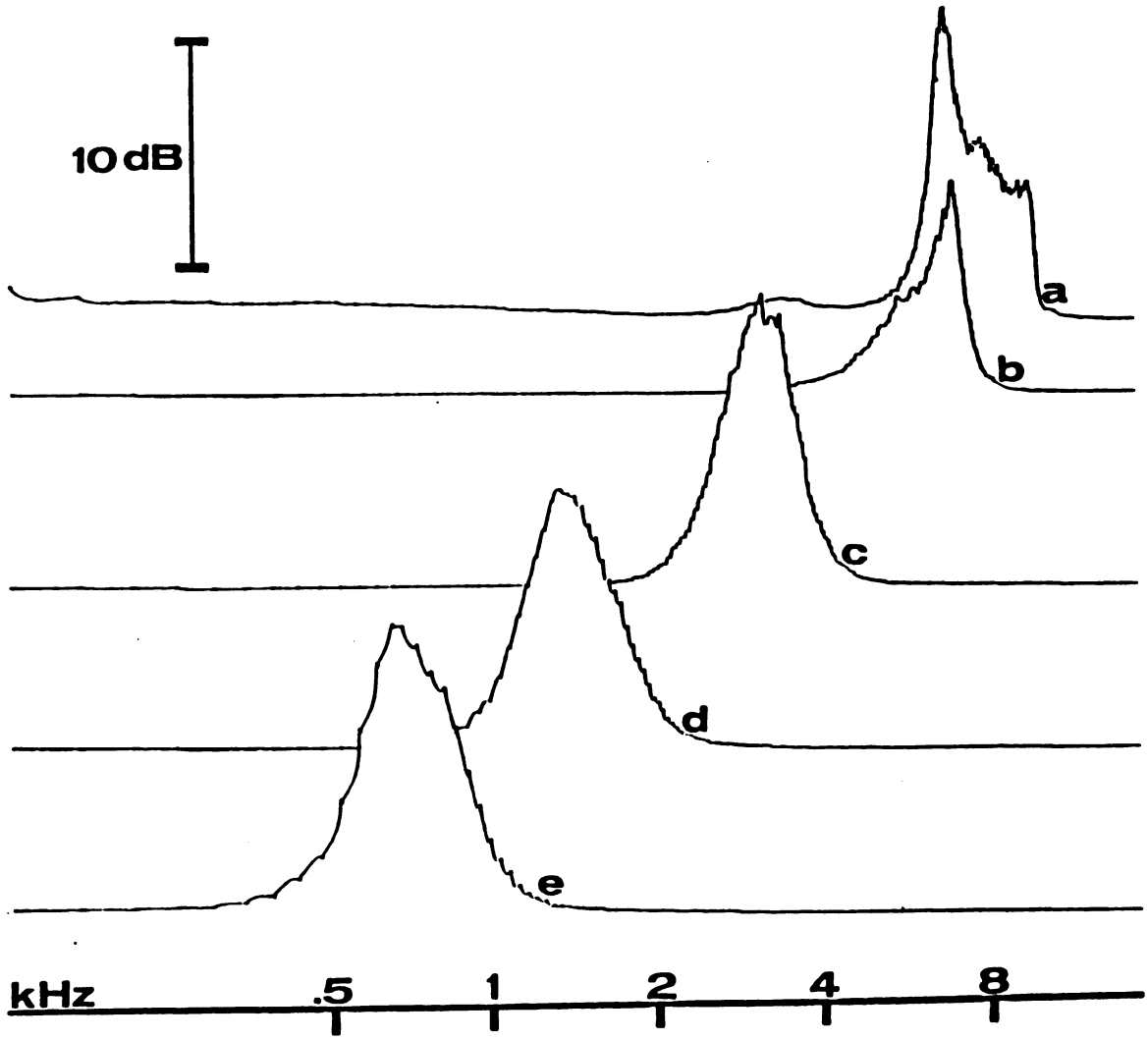


FIGURE 11. Power spectra of narrow band noise stimuli created by band-pass filtering white noise 48dB/octave from 8600-9400 Hz (a), 5200-6800 Hz (b), 2600-3400 Hz (c), 1200-1600 (d), and 600-800 Hz (e). Spectra were measured in the same manner as click and high-pass noise stimuli.

ANSI, 1969 standards. Acoustic immittance measures and acoustic reflex thresholds were obtained using an impedance bridge (Madsen, model ZS 76-1B).

Auditory Brain Stem Response

EEG activity picked up by electrodes was amplified 100,000 times and band-pass filtered 100 to 3k Hz by a preamplifier (Grass, model P511-J). Additional amplification on the A/D card gave a final gain of 200,000. Output of the A/D converter was averaged by a computer (Data General, Nova 3).

Subjects

Normal Hearing Subjects

High-pass masked and unmasked ABRs were obtained from six normal hearing subjects. All subjects had hearing thresholds of 5 dB or less (ANSI 1969) for audiometric frequencies between 500 and 8000 Hz. Normal subjects, four males and 2 females, were between 27 and 34 years of age. All demonstrated normal compliance and middle ear impedance measured in equivalent volume (range= .55 to 1.5 cc H_20) and normal acoustic reflex thresholds (75-95 dB HL) bilaterally.

Hearing Impaired Subjects

Subjects in this category had hearing thresholds greater than 50 dB HL at two or more test frequencies and demonstrated air bone gaps of no more than 10 dB at any test

frequency. Audiometric histories on hearing impaired subjects were consistent with cochlear pathology, that is, there were no clinical results indicating tone or acoustic reflex decay, or speech discrimination scores lower than expected for the degree of hearing loss.

All subjects were less than 55 years of age with histories of noise exposure or aminoglycoside ototoxicity. Descriptions of individual subjects can be found in Table 2.

Procedures

Auditory Brain Stem Response

Subjects reclined in a darkened, quiet room during testing. Gold cup electrodes were attached to vertex (+) and to the earlobe (-) ipsilateral to stimulation. A ground electrode was placed on the opposite earlobe. Electrode impedance measured on an impedance meter (Grass, model EZM1E) was between 1k and 2k Ohms measured at 30 Hz. Response amplitude was calibrated before each test session by delivering a known 10 uV square wave pulse to the preamplifier. This pulse was used by an internal calibration scheme for calibration of all further recordings.

EEG activity was digitized at 40k Hz and the computer sampled 15 ms of activity for each sweep. Stimuli were delayed 1 ms after onset of the sweep to sample prestimulus baseline activity. Ongoing EEG activity as seen by the preamplifier, was constantly monitored by the

TABLE 2

HEARING IMPAIRED SUBJECTS

Subj	Sex	Age	Hearing Loss	History
RS	M	33-2	Mild->severe, bilat. high-frequency loss.	Noise exposure-farm equipment, 8-10 years. Binaural ha user.
CM	M	54-2	Slight->severe, bilat. high-frequency loss AD>AS.	Noise exposure-iron worker, ~30 yrs. Slowly progressive, binaural ha user.
MB	M	29-10	Slight->severe, high-frequency, bilat. loss 20 dB fluct. conductive overlay AS.	Left nephrectomy, treated with tobramycin & furosemide. Rapid onset & progression (< 6 mo.)
JR	M	25-9	Slight->mild high-frequency, loss AS; slight ->moderate high frequency loss AD.	5 yrs sports car mechanic, noise exposure from tuning engines especially with right hand.
AD	M	39-7	Mild->severe, bilat. high-frequency loss.	Noise exposure: recreational hand hand guns and rock music (critic).

TABLE 2. Individual histories and statistics on hearing impaired subjects.

experimenter on an oscilloscope and responses were averaged only while background activity was quiet indicating that the subject was relaxed and not moving.

Normal Subjects

Individual ABRs from normal subjects were the average of 1000 stimulus presentations. Two responses were obtained in each condition to check for consistency and these responses were later averaged. All responses were stored on disk for later off-line analysis.

Subjective click thresholds were obtained in 1 dB steps for each normal subject. Average click threshold was determined to be 22 dB Impulse SPL and varied by 5 dB across subjects. The amount of masking needed to just mask a 70 dB SL click-evoked ABR was determined by bracketing masking level in 5 dB and finally 2 dB steps until no evidence of wave V was seen in the averaged response. This level of masking was maintained for all masking conditions with 70 dB SL clicks and attenuated in 10 dB steps in accordance with the click signal. Unmasked responses were obtained first followed by 8K, 4K, 2K, 1K and 500 Hz masking conditions for 70 through 20 dB SL clicks.

Derived band responses were obtained using successive subtraction of responses as described by Don et al. (1979). Band responses from 70 to 20 dB SL for 8k+, 4-8k, 2-4k, 1-2k and .5-1k Hz were obtained for each individual subject.

Composite derived band responses were obtained by averaging individual waveforms across subjects. In order to control for variability in peripheral conduction time, responses were adjusted in time by an amount which would equate latencies of wave I in all unmasked 70 dB SL responses before constructing the composite.

Hearing Impaired Subjects

Click thresholds were also obtained on all hearing impaired subjects. Unmasked ABRs were obtained at 70 and 80 dB nHL (92 and 102 dB Impulse SPL). Two thousand sweeps were averaged for each trace and three such responses were averaged at each intensity. These ABRs were used as the standard which derived band additions would attempt to model.

Hearing and Acoustic Immittance Measures. Hearing thresholds were obtained for each ear on all hearing impaired subjects at 250, 500, 750, 1000, 1500, 2000, 3000, 4000, 6000 and 8000 Hz by air conduction and all but 6000 and 8000 Hz by bone conduction in 5 dB steps using the modified Hughson-Westlake (1944) procedure. From these results one of the two ears was chosen for further testing based on degree and shape of hearing loss. After checking tympanograms for normal middle ear pressure and equivalent volume readings, contra-lateral acoustic reflex thresholds were obtained with pure tone stimuli at 500, 1000, 2000, 3000, 4000, 6000, and 8000 Hz presented to the test ear. Acoustic reflex thresholds were determined using an ascending, 5 dB

step procedure. Threshold was determined to be the lowest level at which a meter deflection could be detected more than 50% of the time.

LDL and MCL Responses. Loudness discomfort and maximum comfort level were determined for hearing impaired subjects with narrow band noise stimuli (seen in Figure 11) using the method of constant stimuli. Morgan et al. (1974) found this method to be the most consistent for LDL measurements.

Instructions to subjects for MCL measures were as follows:

> You will hear a series of brief pulsing sounds. Pretend these sounds are music or speech from a radio or TV. Indicate after each presentation whether the sound should be louder or softer to be at a level which would be comfortable if listening for 10 minutes or more. If the level is comfortable indicate with "OK". In other words, you tell me how to adjust the sound to make it easy to hear but not too loud.

Instructions for LDL measures were:

> You will again hear a series of brief, pulsing sounds. After each set of pulses indicate whether you could tolerate listening to that level for a few minutes by saying "YES" or, if the sound is intolerably loud respond with "NO". By intolerable I mean that you could not listen to that level for 5 minutes. At that level you should begin to feel the sounds.

Noise bands were repeatedly presented using an alternating ascending and descending technique for MCLs and an ascending technique alone for LDLs in 2 dB steps until a clear pattern emerged. Percentage of positive responses was computed for each level and MCL was designated as the level

at which the highest percentage of comfortable responses was obtained. LDL was determined to be the lowest level identified as uncomfortable more than 50% of the time. Dynamic range for noise stimuli was determined as the difference between MCL and UCL in dB.

Modeling.

In order to facilitate modeling of ABRs from hearing impaired subjects, all possible combinations (6^5 or 7776) of the five composite derived bands at each of six intensities were generated and cross-correlated against each of the 80 dB nHL ABRs from hearing impaired subjects. The cross correlation program added one intensity from each of the bands, cropped the result to a pre-determined window to avoid stimulus artifact and unwanted portions of the response and then performed correlations.

For example, the program would add the 8k+ band of 70 dB and the 4-8k Hz band of 60 dB, the 2-4k Hz band of 50 dB, the 1-2k Hz band of 50 dB and the .5-1k Hz band of 20 dB, crop the response to the appropriate window, cross correlate that template against the subject's response, record the result and begin a new addition of responses until all possible combinations of bands and intensities had been evaluated. Appropriate window length was determined individually for each subject based on the latencies of the major portions (waves I through V) of their ABR. Windows began 1 to 2 ms post stimulus and ranged from 6 to 8 ms total

RESULTS

Normal Hearing Subjects

Unmasked ABRs.

An intensity series of unmasked ABRs from one representative normal subject can be seen in Figure 12A. Means and standard deviations of peak latencies and amplitudes of 70 dB SL ABRs from six normal subjects can be found in Table 3. All amplitudes are measured from peak to following valley. Wave V mean amplitude and latency by intensity functions for the normal subjects can be found in Table 4. All of these data agree well with published ABR norms and with normative data used in the Audiology Clinic at the University of California, San Francisco.

Derived Band ABRs.

Derived band ABRs from a single subject (MR) can be seen in Figure 12B-F. Composite derived band ABRs can be seen in Figure 13B-F. The addition of all bands at each intensity is shown in Figure 13A. To allow for comparison, peak latencies and amplitudes of the 70 dB SL derived band additions, which are essentially normal templates with equal weighting of bands, are shown in Table 3 along with the unmasked data. It should be noted that before constructing composites, derived band ABRs from those subjects whose unmasked wave I was later than 1.58 ms (the earliest and

TABLE 3

MEAN NORMAL PEAK LATENCIES
& AMPLITUDES at 70dB

ABR PEAK:		I	II	III	IV	V
				UNMASKED		
Latency:	Mean	1.69	2.76	3.86	4.86	5.79
in ms.	s.d.	.13	.15	.16	.14	.17
				DERIVED BAND ADDITION		
		1.58	2.68	3.78	5.05	5.58
				UNMASKED		
Amplitude:	Mean	246.97	126.02	185.07	49.52	429.24
in nV.	s.d.	95.19	96.17	93.92	38.65	81.08
				DERIVED BAND ADDITION		
		285.88	101.39	165.61	26.06	419.23

Table 3. Mean peak data for unmasked, 70dB SL ABRs from six normal subjects and from the addition of the derived band data from all subjects at 70dB. Amplitudes were measured from peak to following valley.

TABLE 4

NORMAL LATENCY-INTENSITY AND
AMPLITUDE-INTENSITY FUNCTIONS FOR WAVE V

dB SL:		70	60	50	40	30	20
Latency: in ms.	Mean	5.79	6.02	6.38	6.78	7.12	7.58
	s.d.	.17	.20	.36	.40	.37	.43
Amplitude: in nV.	Mean	429.24	427.67	347.46	322.18	274.58	234.07
	s.d.	81.08	125.12	78.63	83.30	58.11	39.83

Table 4. Latency and amplitude as a function of intensity from unmasked ABRs of six normal subjects. Amplitude is measured from peak to following valley.

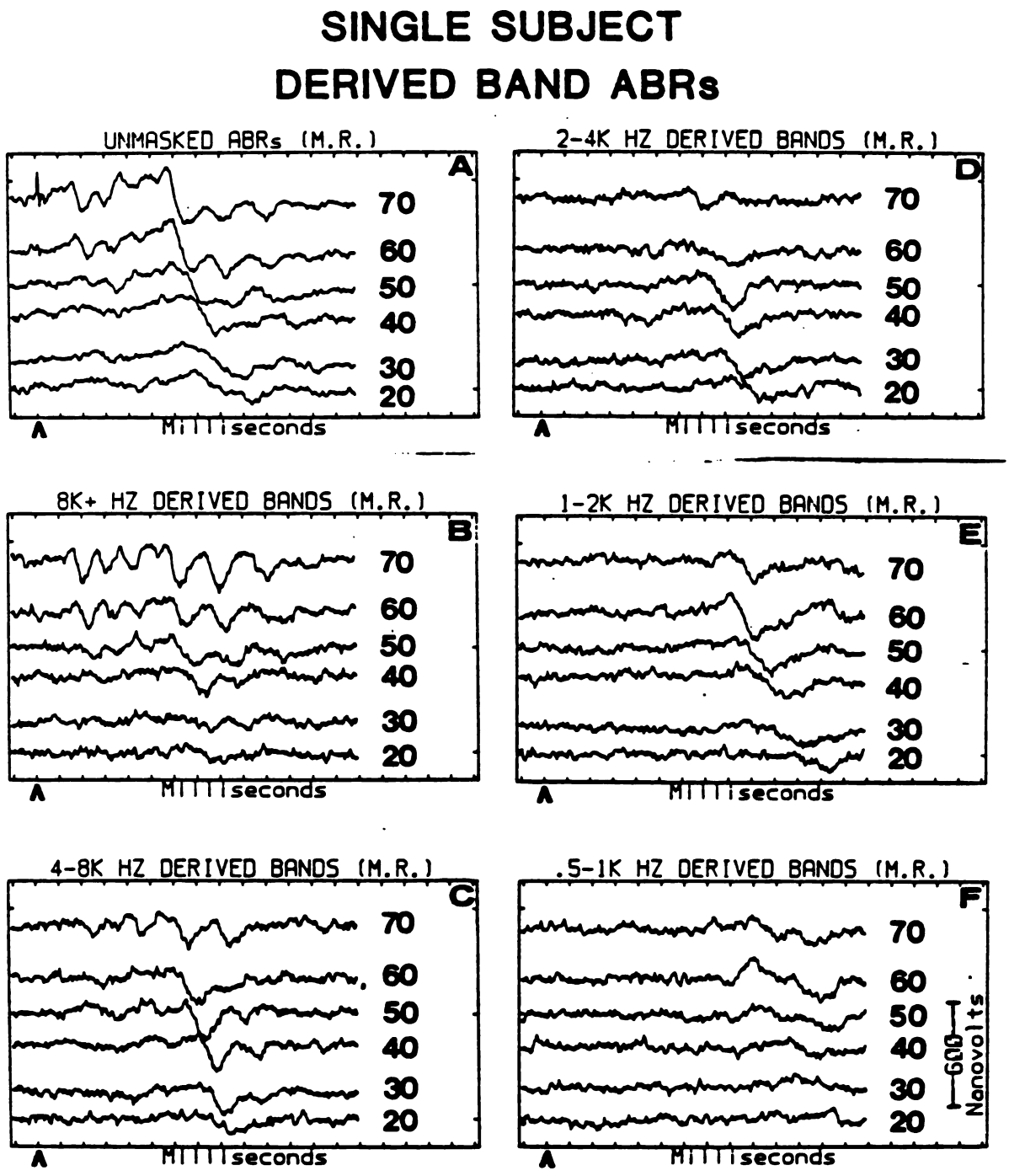


FIGURE 12. Unmasked (A) and derived band (B-F) click-evoked ABRs from subject M.R. Arrow indicates the stimulus onset. Each response is the average of two, 1000 sweep averages.

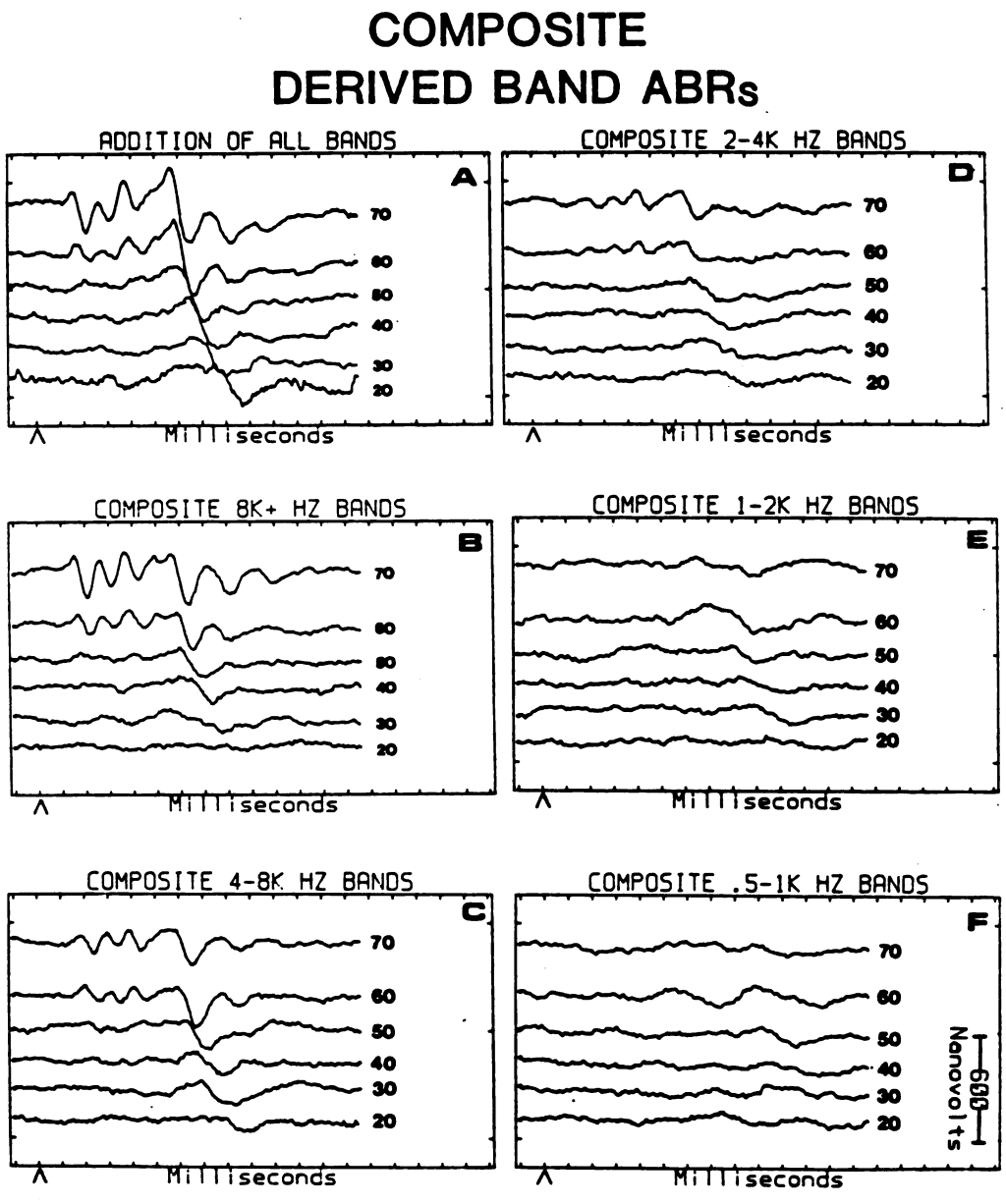


FIGURE 13. Composite derived band ABRs from six normal subjects. Responses were obtained by averaging individual waveforms, like the one shown in Figure 12, across subjects. Before averaging across subjects, responses were adjusted in time by an amount which would equate latencies of wave I in all unmasked 70 dB SL responses. Pre-stimulus baseline is approximately 1 ms. (See text for details.)

mode wave I latency) were adjusted in time, subtracting prestimulus baseline by the amount that the unmasked wave I latency exceeded 1.58 ms. Consequently, the fact that all peaks in the derived band addition response are earlier than the mean unmasked response is expected. If mean, unmasked, response latencies were adjusted to match the 1.58 ms wave I latency by subtracting .11 ms from each peak, latencies of all peaks except IV in derived and unmasked responses would not differ by more than .1 ms.

In order to further test the theory that ABRs from normal hearing subjects could be modeled using the addition of derived band components, the 70 dB SL, unmasked ABRs of each of the normal hearing subjects were cross correlated with the template produced by the addition of all 70 dB SL composite derived band responses. Results of these comparisons can be found in Figure 14. Unmasked responses were shifted in time to give a wave I latency of 1.58 ms when necessary. Cross correlations were then calculated for a latency window of .5 to 7 ms post stimulus onset. Cross correlations for these comparisons ranged from .75 to .93 with a mean of .873 and a standard deviation of .069.

Both Figures 12 and 13 demonstrate that early ABR peaks, I through III, are seen only in the highest frequency bands and then only at the highest intensities (40 dB SL or more). At intensities of 60 dB SL or less no peaks other than wave V are seen below 2k Hz. Also, wave IV is only

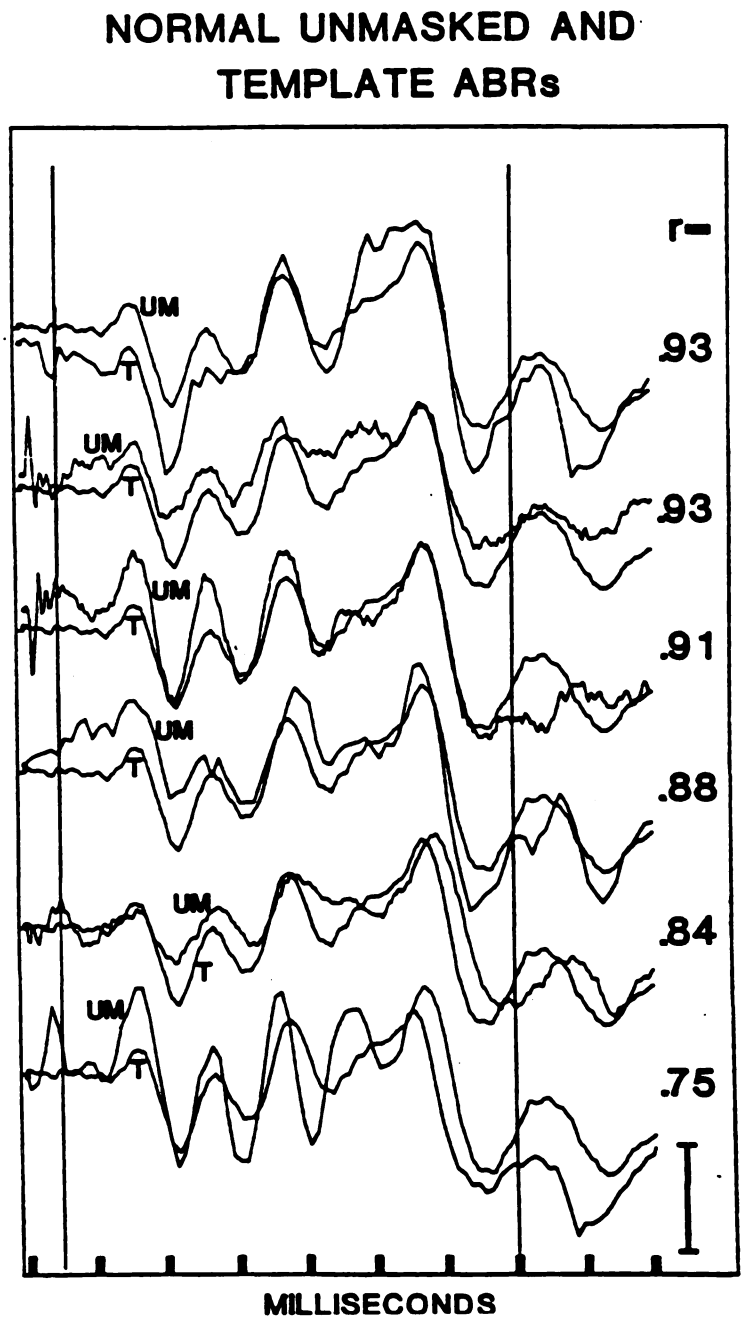


FIGURE 14. Comparison and cross-correlation products (r) of 70 dB SL derived band templates (T) and unmasked ABRs (UM) from 6 normal hearing subjects. Unmasked responses have been shifted in time to produce a 1.58 ms wave I latency when necessary (see text). Cross correlations were measured for data points between cross bars, .5 to 7 ms post stimulus. Calibration bar (lower right) indicates 200 nV amplitude.

obvious in the 8k+ Hz band at the highest intensities. It is possible that wave IV was smeared somewhat when creating the composites but most individual subjects, like the one whose responses are shown in Figure 12, demonstrated wave IV only in the higher frequency bands.

Although the signal to noise ratio in low frequency bands at low intensities is poor, a peak associated with wave V is generally identified at all intensities in all bands. The response waveforms tend to demonstrate slower activity as the frequency of the derived band decreases and the peak associated with wave V becomes less pronounced.

Amplitudes of waves I, III and V from the five composite derived bands are shown in Figure 15. At 70 dB SL all peaks show an increase in amplitude with band frequency. The 8k+ Hz band amplitudes are substantially larger than those in 4-8k Hz bands in all instances at this intensity. However, this trend does not continue at lower intensities. From Figures 13 and 15 it can be seen that the amplitude of wave V in the 8k+ Hz band at 60 dB SL is smaller than in the 4-8k Hz band at the same intensity. Waves I and III at 60 dB SL show only small increases in amplitude between 4-8k and 8k+ Hz bands. Also, from wave V data at the lowest intensities (20 and 30 dB SL) it is clear that the largest response is coming from mid-frequency (1-2 through 4-8k Hz) bands.

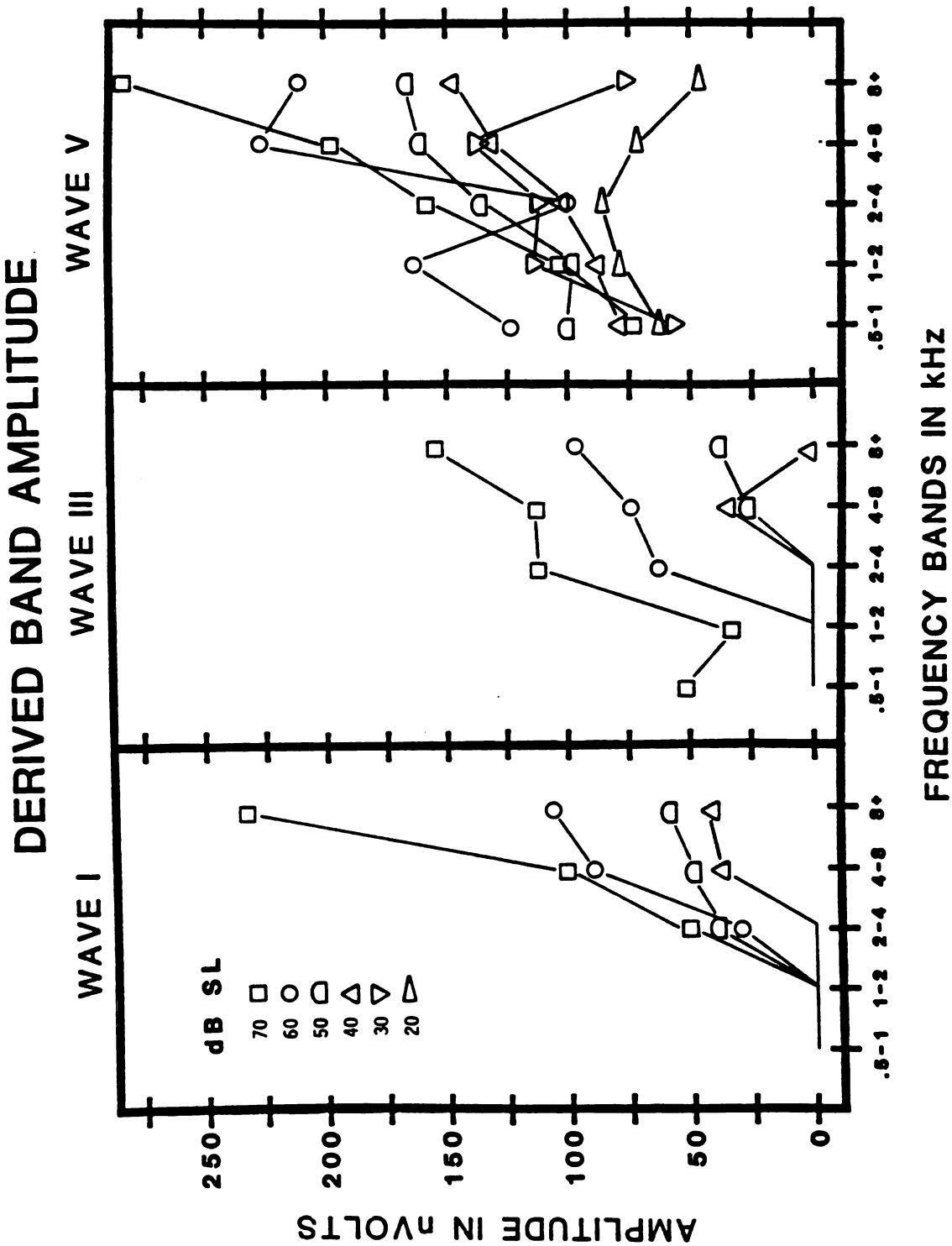


FIGURE 15. Amplitudes of major components, waves I, III, and V, from composite, normal, derived band ABRs at six intensity levels. Amplitude is measured from peak to following valley.

Latencies of major, derived band, ABR peaks at all intensities are depicted in Figure 16. It is clear, especially for data on wave V, that within each derived band, response latency decreases with intensity. Also, the amount of latency shift with intensity for wave V appears to be about equal for all bands. There is a consistent increase in peak latency of all major peaks with decreasing derived band frequency.

Hearing Impaired Subjects

Hearing and Acoustic Reflex Results

Pure tone hearing thresholds from the five subjects can be found in Table 5. All subjects demonstrated high frequency sloping losses. For purposes of comparison with derived band data, audiometric results have been averaged across those frequencies within the octave-wide derived band ABRs from the normal hearing subjects. Mean values and standard deviations for these averages across subjects are also given in Table 5. The slope of the hearing loss within each octave band was computed by subtracting the threshold in dB HL of the lowest frequency within the band from the threshold of the highest. For example, if the thresholds from an individual subject at 2k and 4k Hz were found to be 50 and 70 dB respectively, the slope of the loss within the 2k to 4k Hz band would be 20 dB. In most cases there was a positive high frequency slope to the loss while a few sub-

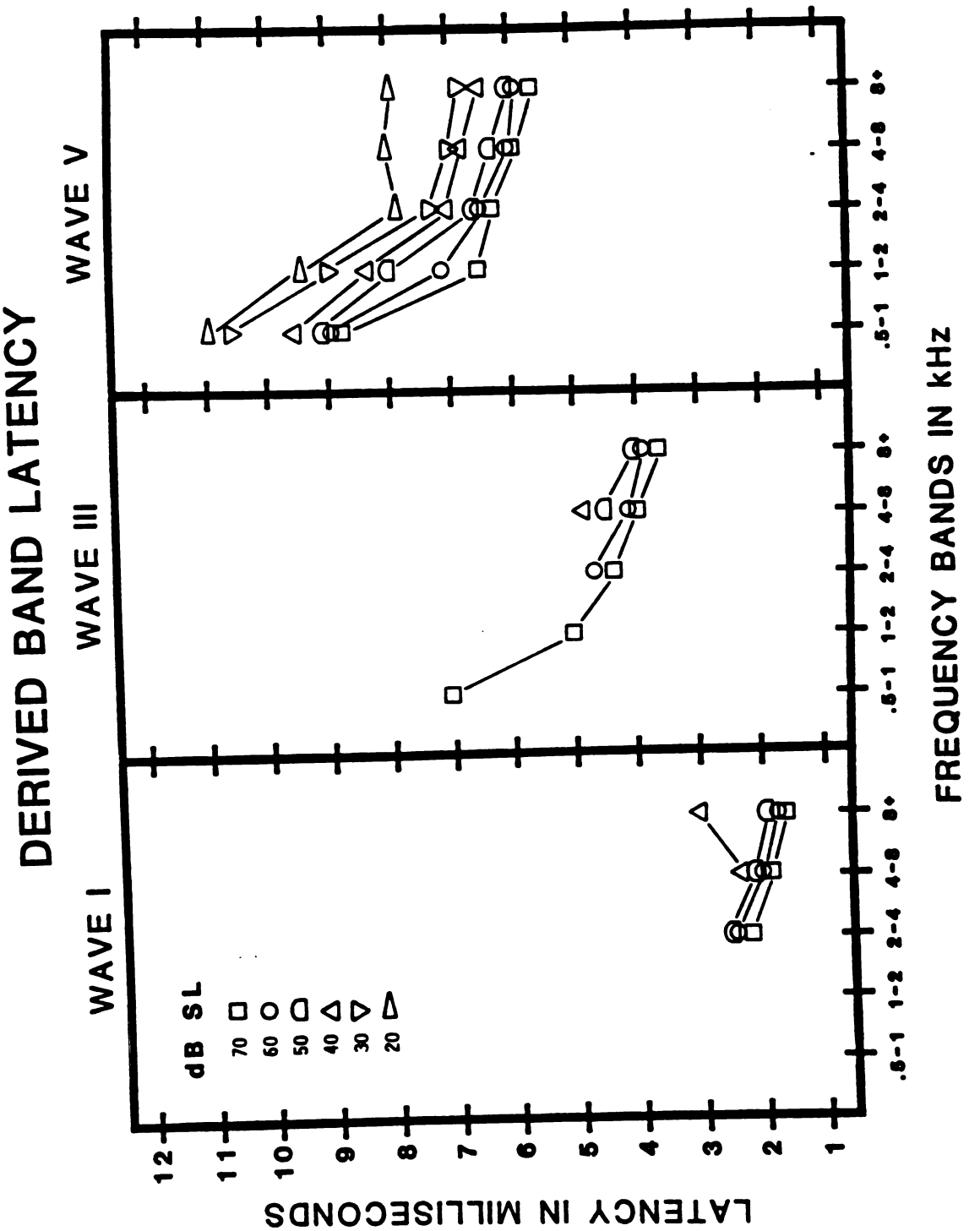


FIGURE 16. Post-stimulus latency of major peaks, waves I, III, and V, from composite, normal, derived band ABRs at six intensity levels.

TABLE 5

DATA FROM HEARING IMPAIRED SUBJECTS

	-Hearing Threshold in dB Hearing Level*-									
Subj/Hz:	250	500	750 <.5-1K>	1K	1.5K <1-2K>	2K	3K <2-4K>	4K	6K <4-8K>	8K 8K+>
RS	10	20	30	45	55	30	35	70	85	75
CM	5	10	30	40	55	60	65	70	75	80
MB	15	15	30	55	55	55	60	65	55	60
JR	15	10	20	35	70	70	70	65	65	40
AD	15	20	20	15	25	55	60	60	60	80
Mean**			<26.2>		<48>		<59>		<64.9>	67
sd			6.4		10.6		8.6		11.7	17.2

	-Hearing Loss Slope-			
RS	<25>	<-15>	<40>	<5>
CM	<30>	<20>	<10>	<10>
MB	<40>	<0>	<10>	<-5>
JR	<25>	<35>	<-5>	<-15>
AD	<-5>	<40>	<5>	<20>
Mean	23	16	12	3
sd	16.8	23.3	16.8	13.5

TABLE 5. Hearing thresholds for chosen experimental ear of each hearing impaired subject and high frequency slope of loss for thresholds within the frequencies of the normal derived bands (.5-1K, 1-2K, 2-4K, 4-8K and 8K+ Hz).

* ANSI, 1969
** Averaged <across band frequencies> and subjects.

jects demonstrated no slope to slightly negative high frequency slopes for certain bands.

Table 6 gives acoustic reflex thresholds for hearing impaired subjects. In one subject, MB, no contralateral AR threshold could be measured due to a unilateral conductive impairment. In many instances, especially at 8k Hz, acoustic reflex thresholds exceeded the limits of the impedance audiometer output or the subjects discomfort threshold. These instances are shown as + values in Table 6. Mean values for acoustic reflex threshold are given across band frequencies and subjects.

Also given in Table 6 are the expected normal values for acoustic reflex threshold (from Popelka, 1981) averaged across frequencies. In all cases the normative values given are the average of the two endpoints of the band in question. For example, normal values were quoted for 2000 and 4000 Hz which were averaged and converted from SPL to HL to created the "normal" value on the table. Subtracting these values from the band average acoustic reflex threshold gives an estimate of average amount which the acoustic reflex is elevated (above normal) in these subjects. Mean elevation values are also given in Table 6.

MCL, LDL and Dynamic Range.

Maximum comfort levels, loudness discomfort levels and derived dynamic range values (LDL minus MCL) obtained with

TABLE 6

DATA FROM HEARING IMPAIRED SUBJECTS

-Acoustic Reflex Threshold in dB HL-

Subj / Hz	500	750	1K	1.5K	2K	3K	4K	6K	8K
RS	85		85		90	105	115	115	110+
CM	80		90		110	120	120+	120+	110+
JR	90		90		100	110	100	115+	110+
AD	90		90		90	105	100	110+	110+
Mean		<87.5>		<93.1>		<104.4+>		<113.9+>	
Normal*		<83>		<83.2>		<85>		<88.3>	
Mean Elev.		<4.5>		<9.9>		<19.4+>		<25.6+>	

TABLE 6. Acoustic reflex thresholds measured contralateral to the chosen experimental ear in hearing impaired subjects. One subject (MB) had no acoustic reflex due to unilateral middle ear disease. Normal acoustic reflex thresholds are from Popelka, 1981 (see text for details.) Mean values have been computed averaging across frequencies from individual derived bands: (.5-1K, 1-2K, 2-4K, 4-8K and 8K+ Hz) and across subjects. When + values are listed, reflex thresholds were absent at the level indicated and could not be tested at higher intensities either due to limitations of equipment output levels or discomfort by the subject.

pulsed bands of noise for each hearing impaired subject are given in Table 7. There appears to be a slight tendency for mean dynamic ranges to decrease in the mid and higher frequencies although the variability across subjects was greater in the high frequencies which blurred this trend somewhat.

Unmasked ABRs

Unmasked ABRs from each of the five hearing impaired subjects can be seen in Figure 17 and the latencies and amplitudes from individual peaks can be found on Table 8. In all cases except for MB the ABRs were elicited by 80 dB nHL clicks. MB, who complained of discomfort with the 80 dB nHL click, was stimulated with a 75 dB nHL click. (Note: this subject also showed the smallest dynamic ranges for narrow band stimuli: 0dB for 2-4k and 4-8k Hz bands).

Morphology of the ABR waveforms from the hearing impaired subjects, as evidenced by Figure 17 and by large variability in latency and amplitude values on Table 8, varies greatly across subjects although the audiograms of the subjects are similar. Interpeak (I-V) latency intervals given in Table 8 also vary considerably (3.35 to 4.87 ms). across hearing impaired subjects.

Modeling of the ABR

Whole Waveform Modeling. The first attempt at modeling the abnormal ABR used an intentionally simplistic

TABLE 7

DATA FROM HEARING IMPAIRED SUBJECTS
NARROW BAND NOISE

Subj/kHz:	.5-1	1-2	2-4	4-8	8+
			-Maximum Comfort Levels- dB SPL		
RS	102	101	104.5	110.5	99.5
CM	91	104	114	113.5	103.5
MB	97	100	103.5	99.5	95.5
JR	95	98	102.5	104.5	99.5
AD	92	92	96.5	92.5	87.5
			-Loudness Discomfort Levels- dB SPL		
RS	126	122	116.5	120.5	110.5
CM	114	118	124.5	128.5+	118.5
MB	100	100	103.5	108.5	102.5
JR	104	109	110.5	116.5	111.5
AD	104	104	102.5	102.5	98.5
			-Dynamic Range in dB- (LDL minus MCL)		
RS	24	21	12	10	11
CM	23	14	10.5	15+	15
MB	3	0	0	9	7
JR	9	11	8	12	12
AD	12	12	6	10	11
Mean	14.2	11.6	7.3	11.2+	11.2
sd	9.1	7.6	4.7	2.4+	2.9

TABLE 7. Maximum comfort levels, loudness discomfort levels and dynamic ranges (UCL - MCL) for narrow band stimuli in hearing impaired subjects (see text for details.)

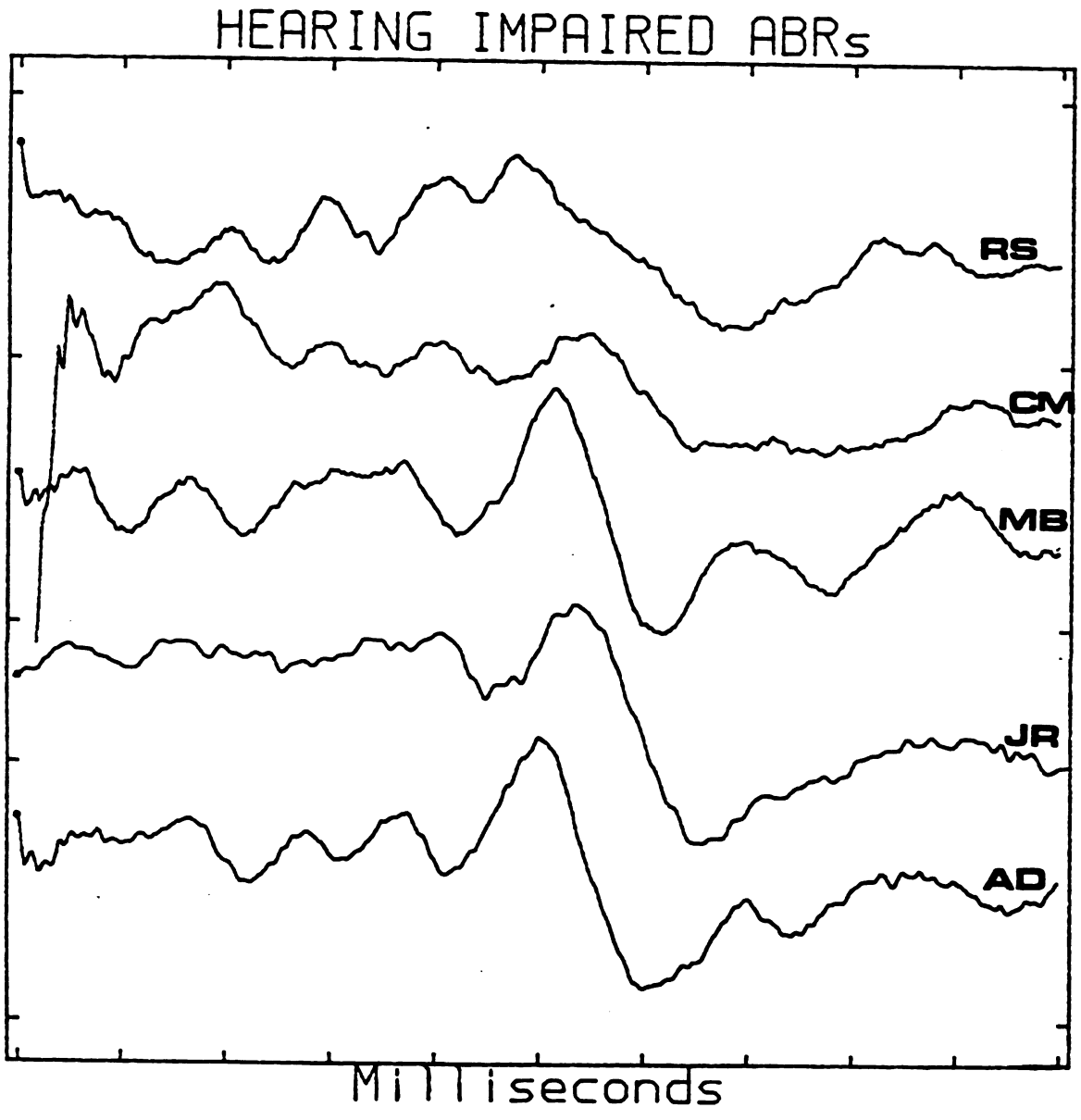


FIGURE 17. Unmasked ABRs from hearing impaired subjects in response to high intensity (80 dB nHL except MB who was stimulated at 75 dB nHL) rarefaction clicks. Each response is the average of 8000 click presentations.

TABLE 8

HEARING IMPAIRED SUBJECTS
AUDITORY BRAIN STEM RESPONSE

Subj/ABR Peak	Latency (ms) I	II	III	IV	V	I-V
RS	1.85	3.05	3.9	5.1	5.75	3.90
CM	2.95	4.0	5.05		6.48	3.53
MB	1.53	2.55	4.35		6.13	4.60
JR	1.48				6.53	4.87
AD	2.65	3.78	4.75		6.00	3.35
	Amplitude (nV)					
RS	133	89	145	63	456	
CM	187	74	92		257	
MB	221	130	168		753	
JR	81				749	
AD	122	53	117		478	

TABLE 8. ABR peak latency and amplitude measures from hearing impaired subjects in response to unmasked, rarefaction click stimuli at 80 dB nHL (75 dB nHL for MB). Amplitudes were measured from peak to following valley. Missing values represent no identifiable peak.

hypothesis. The level of each derived band added into the model for a given subject was determined by the amount of that subject's hearing loss within each band. For example, subject RS has an average loss for the .5-1k Hz band of 31.66 dB (see Table 5). This value was subtracted from the click level used to elicit the ABR (80 dB) and the result was rounded to the nearest 10 dB (50 dB). The 50 dB composite .5-1k Hz derived band was then used in the first attempt modeling of RS's ABR along with other bands whose levels were selected in the same manner. If the level needed to model a certain band was less than 20 dB (the lowest intensity of composite normal derived bands) no band was added in that frequency region, assuming that very little was being contributed by that region.

This technique revealed very poor cross correlation values when models were compared to actual ABRs in four subjects (r= -.20, .31. -.02, and .24) and a borderline value (.70) in one subject, JR.

The purpose of the previous modeling strategy was to demonstrate that a simplistic modeling strategy which assumed a straight reduction in ABR input based on reduction of hearing sensitivity, could not work. However, no more sophisticated strategy was readily apparent. In order to determine if modeling of the ABR from subjects with cochlear impairment could be accomplished, all possible combinations of derived bands were generated and each modeled response

was cross correlated with actual click-evoked ABRs from the hearing impaired subjects. Then, modeled responses which generated correlations greater than .8 were visually inspected. In general, the matches with the highest correlations were judged by the experimenter to be best matched to the abnormal ABR. One of the top two or three matches, based on cross correlation value, was always chosen as the "best" match for the abnormal ABR. Visual decision was based on a combination of factors including overall, peak latency matching and resolution of early (I-V) peaks.

The "best match" modeled waveforms superimposed upon the hearing impaired ABRs can be seen in Figure 18. These traces have been cropped to show only those sections of the response used to compute the cross correlation product. In all cases a modeled response could be generated which produced cross correlation products with hearing impaired ABRs in an acceptable range i.e., within the range of those found in the normal modeling experiment. The poorest match of modeled response to abnormal ABR reveals a cross correlation product of .83 with is better than the poorest match of normal responses to normal templates which was .75.

Intensity levels of composite normal derived band ABRs added to produce the best matched model was subtracted from the click stimulus level used to elicit the unmasked ABRs in the modeled subject. This was done for each subject and results are given on the top of Table 9. Theoretically,

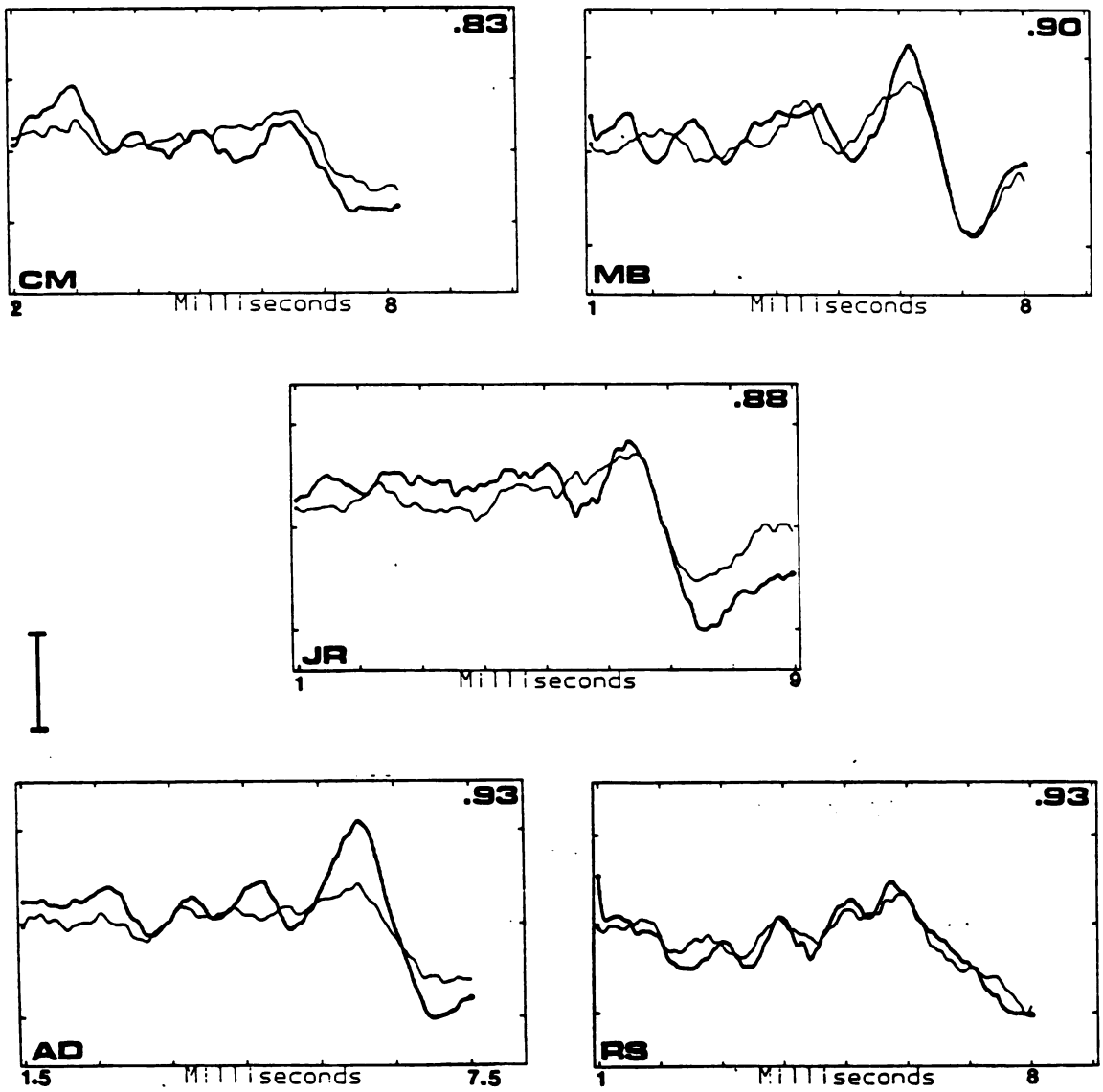


FIGURE 18. Best matched modeled ABR (thin trace) superimposed upon actual ABRs (wide trace) from five hearing impaired subjects. Responses are windowed to show only those points which were involved in the actual cross correlations. Post-stimulus time is given on the abscissa and an amplitude calibration indicating 600 nV is shown middle left. Cross correlation values for each match are indicated in the upper right corners.

TABLE 9

BEST MATCHED MODELED ABR BASED ON WHOLE WAVEFORM

	Level* in dB				
Subj/Band	.5-1	1-2	2-4	4-8	8+ KHz
RS	10	10	30	30	20
CM	30	50	40	40	40
MB	5	5	5	45	25
JR	20	10	20	40	40
AD	20	10	10	40	20
Mean	17	17	21	39	29
sd	9.8	18.6	14.3	5.5	10.3

Correlation with Other Parameters

Parameter:					
Threshold	-.61	.14	-.05	-.75	-.45
Slope	-.31	.14	.31	-.05	-
AR Elev.	.00	.83	.99	-.11	-
Dyn. Range	.35	.16	.41	-.43	.48

TABLE 9. Values shown are based on the intesities in nHL of individual derived bands which made up the waveform which best matched the unmasked ABR from hearing impaired subjects. Values at the top* represent the stimulus level used to elicit the ABR from the hearing impaired subject (75 or 80 dB nHL) minus the level used for the band addition. For example, subject AD's ABR was elicited with an 80 dB click and, the level of the 2-4K Hz band added into the composite which best matched that ABR, was 70 dB. The 10 dB shown on the table represents the modeled decrease in intensity for that band theoretically imposed by that subject's hearing loss. The second half of the table shows correlation coeficients for those values from the top and other measured parameters whose values are given in Tables 5,6 and 7.

these values represent the amount of hearing loss reflected in each derived band frequency range in the abnormal ABR. For example, in subject AD, the click was delivered at 80 dB nHL but the best matched ABR contained a 60 dB nHL band at 8k+ Hz. Theoretically, the impaired ABR is reflecting a 20 dB reduction of response in this band, and that value appears on the table.

Correlation coefficients between these values and the following parameters were then computed: pure tone hearing thresholds (average threshold within the corresponding derived band, for example 1000, 1500 and 2000 Hz for the 1-2k Hz band), slope of hearing thresholds within each band (see Table 5), acoustic reflex elevation from normal (see Table 6) and dynamic range (see Table 7). These correlations were computed for each band of frequencies across subjects. Those values are also given in Table 9.

The amount of hearing loss reflected in the modeled abnormal ABR has a high negative correlation with actual threshold elevation for the .5-1, 4-8 and 8k+ Hz bands. This trend is opposite the direction predicted. The within band slope of the hearing loss does not correlate well with the modeled loss but acoustic reflex elevation shows very high positive correlations with modeled ABR loss at 1-2k and 2-4k Hz (r=.83 and .99 respectively). Dynamic range shows no high correlations although all but the 4-8k Hz band show positive values indicating a trend to correlate more loss in

the modeled waveform with greater dynamic range.

Wave V Modeling Because high correlations were not found it was hypothesized that the masking paradigm used may have over-masked the early components of the ABR (A.R.D. Thornton, personal communication). A second attempt at modeling the response was made which windowed the correlations only around wave V of the abnormal ABR. Results of that modeling can be found in Figure 19. Again heavy lines represent the unmasked response and the thin line is the modeled response. The window for cross correlation was chosen based on the morphology of each individual abnormal ABR to incorporate the entire positivity and following negativity of wave V. The resulting correlations are very high, .96 to .99. Although wave V is well matched the early components in these templates do not match well with the abnormal ABRs.

The levels of derived bands used to model wave V in the abnormal responses subtracted from the unmasked ABR click intensity can be found on the top of Table 10. The bottom of Table 10 gives the correlations of these values with the other parameters as was described previously for the whole waveform matching. Only in the case of dynamic range are there any high correlations and even in that case the lowest frequency band shows a negative rather than positive correlation.

WAVE V-TEMPLATE MATCHES

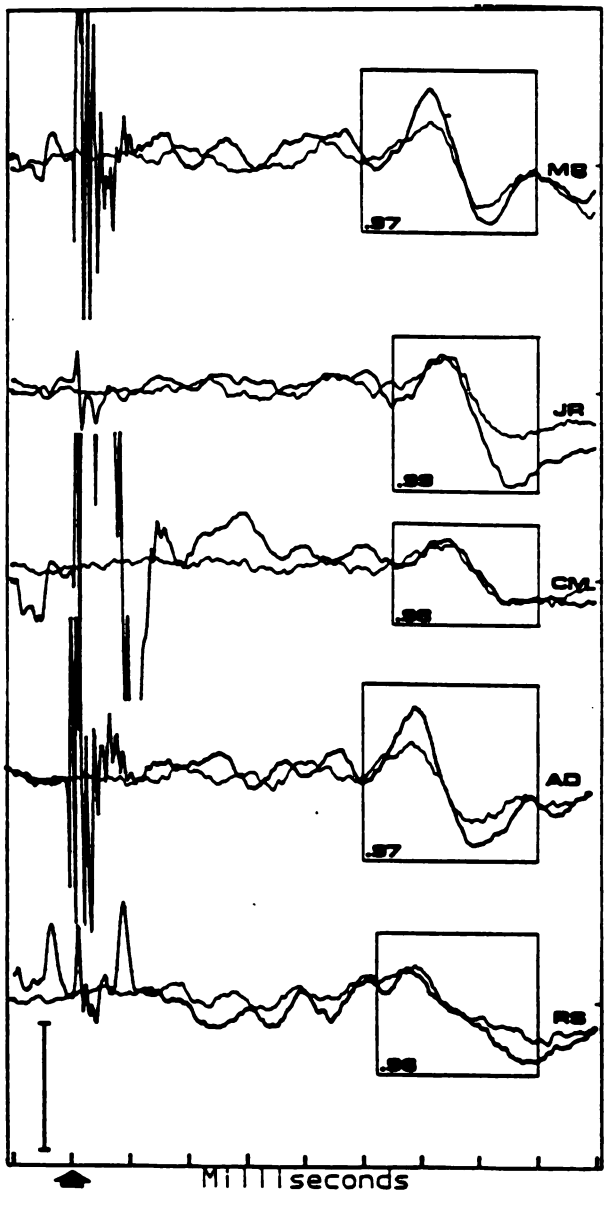


FIGURE 19. Best matched modeled ABR (thin trace) superimposed upon actual ABRs (wide trace) from five hearing impaired subjects. Response areas within boxes indicate those points which were involved in these cross correlations. Time is given on the abscissa with stimulus onset indicated by the arrow and an amplitude calibration indicating 600 nV is shown lower left.

TABLE 10

BEST MATCHED ABR BASED ON WAVE V

	Level* in dB				
Subj/Band	.5-1	1-2	2-4	4-8	8+ KHz
RS	20	30	30	20	20
CM	50	50	20	50	40
MB	55	15	5	25	25
JR	40	10	20	40	40
AD	50	60	20	20	40
Mean	43	33	19	31	33
sd	14	21.7	8.9	13.4	9.8

Correlation with Other Parameters

Parameter:					
Threshold	-.23	-.79	-.50	.08	-.08
Slope	.01	.33	.43	-.19	**
AR Elev.	.41	.02	-.18	-.27	**
Dyn. Range	-.56	.24	.85	.57	.57

TABLE 10. Values shown are based on the intesities in nHL of individual derived bands which made up the waveform which best matched the unmasked ABR from hearing impaired subjects windowed to include only wave V. Values (*) are computed as in Table 9. See text for detail. ** values cannot be computed.

It appears that the original modeling of the entire waveform, by virtue of the acoustic reflex correlations, was the better of the two procedures in terms of actual predictions of intensities that contribute to the ABR from specific frequency regions. Figure 20 shows audiograms from the five hearing impaired patients with modeled 'hearing loss' from the ABR in the whole waveform match and wave V match situations. The acoustic reflex thresholds and dynamic ranges for narrow band stimuli are also indicated. From these representations, it appears, with the exception of the acoustic reflex threshold and the whole waveform hearing loss prediction, that no systematic relationships exist between the parameters.

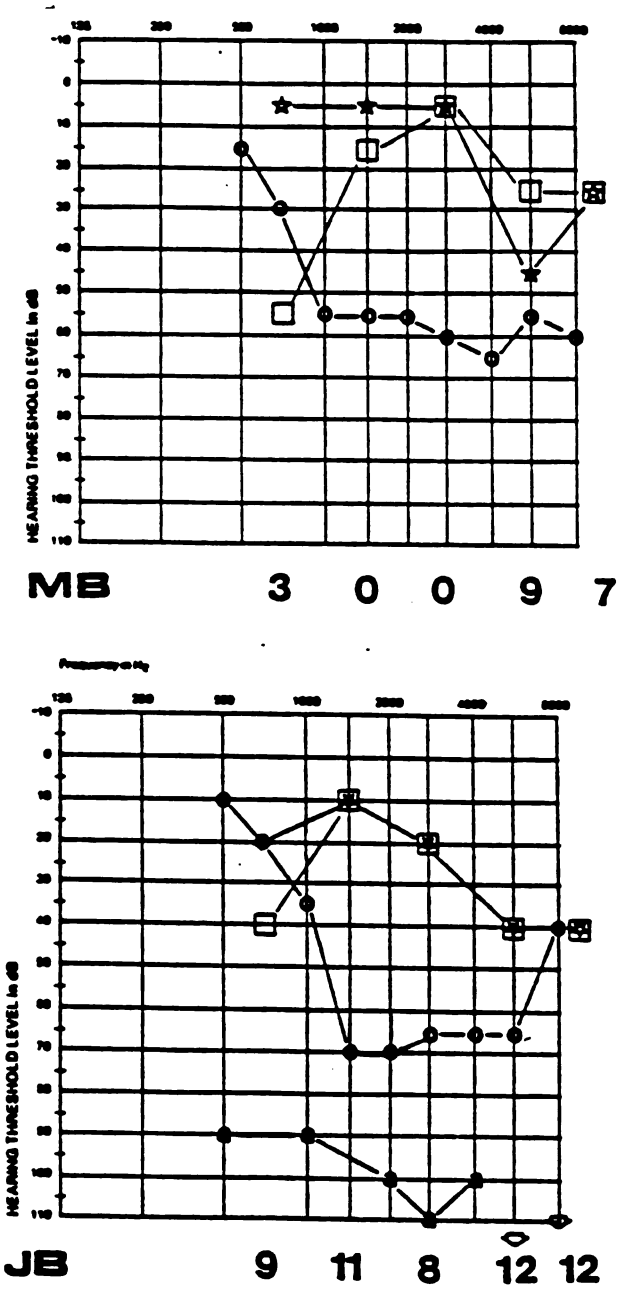
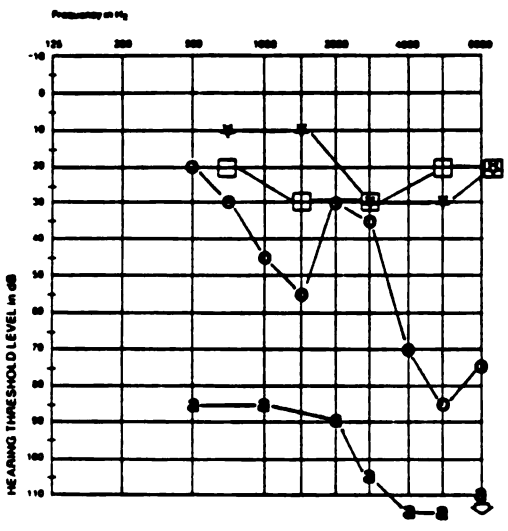
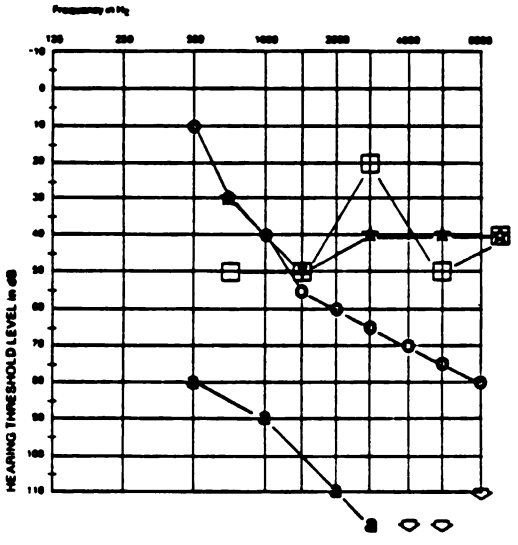


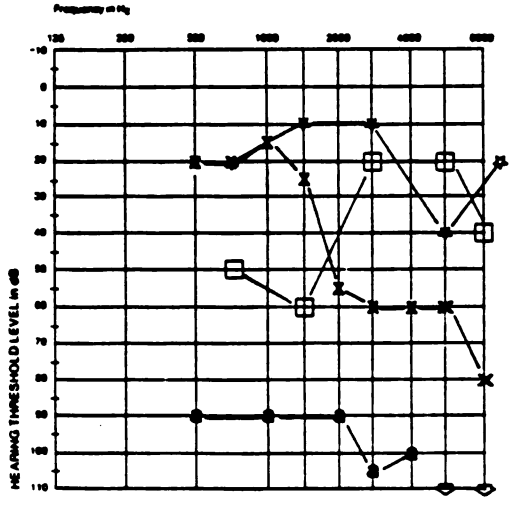
FIGURE 20a. Graphic depiction of hearing levels for correlated parameters from two of five hearing impaired subjects. X or O indicates pure tone thresholds from left or right experimental ear, stars are the assumed hearing loss from the whole wave ABR modeling (see Table 9) and open squares are the same values obtained from the wave V modeling (see Table 10). Acoustic reflex thresholds are indicated by an a with an arrow indicating no response at maximum level. Numbers along the bottom of each audiogram indicate dynamic range (see Table 7). Cross correlation values for each match are indicated.



RS 24 21 12 10 11



CM 23 4 10 15+ 15



AD 12 12 6 1 11

FIGURE 20b. Remaining three subjects. See 20a for legend.

DISCUSSION

Normal Derived Band ABRs

Modeling of high intensity ABRs from normal hearing subjects using the addition of derived bands responses worked well as evidenced by high correlations between templates and actual responses (see Figure 14). Only in one normal subject, who demonstrated an early wave V, was the correlation lower than .84. It appears that, for normal hearing subjects, modeling of ABRs using derived band ABR techniques neither adds significant amounts of unwanted noise nor removes any vital portions of the ABR. From these results it was reasonable to assume, as a first approximation, that this same technique might be used to model ABRs generated by abnormal cochleas.

Analysis of normal derived band ABR responses indicates that the majority of the 4 to 5 peaked, scalp recorded ABRs to high intensity click stimuli originate from portions of the cochlea which are sensitive to high frequency stimulation since the early peaks (I through IV) are seen only in the high frequency derived bands. Similar results have been reported by Don & Eggermont (1978) and Parker & Thornton (1979b). This result may explain why the early peaks are often missing in the scalp recorded ABRs of patients with high frequency hearing loss (Elberling, 1978; Eggermont et al., 1980; Portmann et al., 1980). In contrast, sensory units responsive to low frequency stimuli (1k Hz and below)

demonstrate activity (usually a single slight positivity followed by a more pronounced negativity) with latencies of 8 ms post stimulation or longer. Phase differences in this activity with changes in frequency region in the cochlea which initiate them, may cause this late activity to cancel or lose amplitude in the unmasked, click-evoked ABR. In fact, these low frequency sensory units (below about 1k Hz), by virtue of the latency of their response, contribute little or nothing to high intensity, click-evoked wave V of the ABR. This would explain why the unmasked response more closely resembles the response from the higher frequency derived band ABRs (see Figure 12).

Amplitude data from Figure 15 indicate a shift in the relative contribution to the overall response of individual bands from high to mid frequencies with a decrease in intensity of stimulation. The same shift toward more apical influence near threshold was seen in the AP response by Elberling (1974) and in the ABR by Eggermont & Don, 1980. This finding explains why ABR thresholds generally agree most closely with auditory sensitivity in the 1-4k Hz range (Møller & Blegvad, 1976; Coats & Martin, 1977; Jerger & Mauldin; 1978; Shepard and Webster, 1983). Peak latency shifts in the ABR with decreased click intensity can also be explained in part by this shift in the major frequency contribution to the response.

Figure 15 shows a clear increase in response amplitude with derived band frequency for 60 and 70 dB SL responses. This result is in contrast to that of Don & Eggermont (1978) who noted that peak amplitude, especially of wave V, did not decrease, but in many instances increased, with decreasing derived band frequency. This discrepancy may be due, at least in part, to differences in click spectra. Don & Eggermont's 170 us click has a spectrum which shows decreased energy (~20 dB dips) at 6k and 8k Hz. The spectra of the click used in this study was relatively flat to 8k Hz. The added high frequency energy of this click above 4k Hz may explain the greater response amplitudes in derived band ABRs containing these frequencies.

Figure 16 demonstrates shifts in peak latency with decreasing derived band frequency previously noted by Teas et al. (1962), Elberling (1974), Eggermont (1976), Don & Eggermont (1978), Parker & Thornton (1978c), Hecox & Deegan (1983) and others. This finding certainly reflects travel time along the basilar membrane and possibly also response delay imposed by the (second?) filter mechanism in the cochlea (Eggermont, 1979).

Modeling

While this study demonstrated that models of normal ABRs could be adequately built using derived band responses averaged across normal hearing subjects, it failed to find clear correspondence between audiometric data and amount of

hearing loss reflected in the ABR. One possible exception to this conclusion is the relationship between elevation of acoustic reflex thresholds and intensity of derived band used to model the whole waveform ABR in cochlear impairment. Even that relationship was demonstrated only for 1-2k and 2-4k Hz bands. However, it was often noted that the acoustic reflex could not be elicited in the high frequencies. Of the four subjects in whom an acoustic reflex could be expected (one subject displayed a unilateral conductive impairment), one subject had no reflex at the equipment output limits at 4k Hz, three had no reflex at 6k Hz and no subject showed an acoustic reflex at 8k Hz. Values of the output limits at each frequency were substituted in the no response situation in order to compute a statistic. However, it is not surprising that no clear relationship was seen between acoustic reflex threshold elevation and hearing loss reflected in the ABR at 4-8k or 8k+ Hz because of the limitation of this ceiling effect.

The reason why no relationship between derived band ABR level in the modeled response and acoustic reflex was demonstrated at .5-1k Hz is less clear but several possibilities exist. As previously stated, sensory units stimulated by lower frequencies contribute to the click-evoked ABR with activity later than 8 ms. Consequently, when the focus of ABR modeling is on only those portions of the ABR up to and including the click-evoked wave V, the lower frequency con-

frequency contributions are excluded from consideration. In fact, ABR modeling stopped by at least 9 ms post stimulus in all cases and by 8 ms in all but one. Because this time window excluded ABR activity originating from low frequency sensitive units, it is understandable that no clear correspondence is found between low frequency audiometric indices and intensities of low frequency bands (especially .5-1k Hz) used to model the ABR.

There may also be limitations inherent in the creation of derived band ABRs in the low frequencies due to contamination from lateral suppression or remote masking. Evans and Elberling (1982) in fact found spread of masking effects in recording from single eighth nerve fibers with central frequencies below about 2k Hz in cats and concluded that derived band responses in humans may be contaminated by this sort of spread below 500 to 1000 Hz. Don et al., 1979 found their .5-1k Hz derived band to be about 20 dB higher (less sensitive) in threshold than mid frequency bands. In general, low frequency derived band ABRs (below 1k Hz) may be less frequency specific and be more susceptible to contamination from the simultaneous masking condition.

Derived Band Technique

There are several possible explanations why the amount of loss predicted in the ABR did not relate to psychophysical hearing data in subjects with cochlear impairments. The first general set of explanations has to do with problems

related to the derived band ABR technique itself. As stated previously, the low frequency band may be contaminated by spread of masking and lack of frequency specificity. Additionally, responses obtained via derived band techniques may be inherently noisy as compared to unmasked responses in that all derived bands are the result of a waveform subtraction. According to Picton et al.,1981, each addition or subtraction of different averaged waveforms has the potential of increasing the noise in the result by the square root of the number of responses added or subtracted. Even after allowing for noise reduction from averaging across 6 subjects, an overall increase in noise is possible in the modeled ABR as compared to the unmasked response. The addition of such noise may have complicated the modeling and cross correlation process somewhat, although it did not appear to do so for the normal hearing subjects.

Another problem arose because the filter slopes used to high-pass the masking stimulus were 96dB/octave rather than infinite. Consequently, there will be some shift in the derived bands frequency endpoints with intensity. The problem which could arise in modeling is that, unless all derived bands used have the same intensity, as they do in the modeling of normal responses, there may be overlaps or gaps in the frequency regions represented by the modeling.

Experimental Design

Other potential problems have to do with the design of this study. It is certainly possible that the steps of 10 dB used in obtaining normal derived bands were too large especially when compared to hearing thresholds which were measured in 5 dB steps. The potential for plus or minus 15 dB error in comparing these parameters may be too large to allow for adequate correlations with derived band intensities when considering the compacted intensity range of cochlear impaired ears. In other words, testing error was much larger than the normal variability of the hearing thresholds.

It is also possible that the derived bands may not have been narrow enough in frequency (one octave) to follow rapid changes in the physiology of these impaired cochleas along the frequency domain. The width of these derived bands may be such that attempts would be made, in some cases, to model normal and abnormal cochlear regions in the hearing impaired subjects by a single derived band. One of the main assumptions in this case, that cochlear lesions would produce different input-output functions as compared to normal cochleas could not be adequately modeled.

Other than problems with experimental design, there are potential difficulties with the application of the modeling technique. It was assumed that averaging across normal hearing subjects to create composite normal derived bands

would reduce the noise and potential for individual spurious responses. It is also possible, however, that individual differences across normal subjects, when averaged, simply smeared response parameters, i.e., altered amplitude or latencies of composite responses in a way that did not reflect normal data.

Other difficulties which arose throughout the study included the fact that no correction for peripheral conduction time (differences in wave I latency) were made in the hearing impaired ABRs because of the influence which the hearing loss has on that parameter. It was impossible to determine how much of wave I latency was due to peripheral factors such as ear canal volume or middle ear transfer etc. and how much was due to high frequency hearing loss. Consequently, no latency corrections could be applied before cross correlating the impaired ABRs with potential models.

One important assumption made in this study was that the contribution to the ABR from certain frequency regions of an impaired cochlea could be mimicked by the response from a normal system elicited by a signal of less intensity. This may not be the case as evidenced by the fact that certain relationships between the ABR and hearing loss are not similarly reflected in intensity changes of derived band ABRs. For example, Coats and Martin, 1977, show that with hearing loss at 8000 Hz up to about 60 dB, there is an initial decrease in wave I latency followed by an increase in

latency with more loss. This trend was not reflected in latency changes with intensity seen in the 8k+ or 4-8k Hz bands of the composite normal responses shown on Figure 16. In the normal responses there were only increases in latency of peaks with decreased intensity. This discrepancy may help to explain why early peaks of abnormal ABRs were not well modeled (see Figure 18).

Eggermont (1979), compared derived band AP responses in normal and recruiting ears and found smaller latency increases with decreasing intensity in the recruiting ears than in normals. This also points out that simple linear transformations may not exist between normal and hearing impaired ABR functions. However, in this case, it would have been possible for the present study to handle a non-linearity like a compressed intensity scale. The example from Eggermont's study merely points out that simple reduction in intensity will not be adequate in modeling the effects of cochlear hearing loss on the ABR.

The above problems relate to the ability of the technique used to actually create an adequate model of an ABR from an ear with cochlear impairment. However, the fact that acoustic reflex elevation correlated so highly, at least in the mid frequencies, with derived band levels used to model the ABR from hearing impaired subjects lends some validity to the modeling procedure for the ABR and to the resultant intensity levels used to characterize the cochlear

activity within each band. It is assumed, that the acoustic reflex and ABR may reflect cochlear processes in a similar way and, in fact, in a way that is different from audiometric thresholds or other psychophysical responses.

Although little nas been done to compare the acoustic reflex and ABR it seems reasonable that these two measures would give similar reflections of cochlear processing. Both the ABR from this study and the acoustic reflex are elicited with high intensity stimuli which may reflect similar amounts of neural synchrony required in both. Both are mediated within the brain stem and are not subject to contamination from higher level processing. Other interesting parallels exist between the ABR and the acoustic reflex findings in patients with cochlear and retrocochlear hearing loss. Latency corrections for wave V generally occur when cochlear hearing loss is greater than 50 dB (Selters & Brackmann,1979) and acoustic reflex thresholds tend to be unchanged with cochlear hearing loss up to about 40 dB (Popelka, 1981). Both of these relationships become invalid in situations with retrocochlear disorders where wave V latency and acoustic reflex thresholds can be significantly altered even with small amounts of hearing loss or normal hearing.

The close relationships between the acoustic reflex and the ABR might indicate that acoustic reflex data could be used to predict the waveform of the ABR based on the addi-

tion of normal derived ABRs. Unfortunately, high frequency acoustic reflexes are often absent or not measurable at equipment output limits in cases of hearing loss. Clinically, the reflex is not measured at 8000 Hz because a significant percentage of the normal population does not have a response at this frequency. Consequently, the acoustic reflex alone is not a viable tool in the modeling of ABRs from hearing impaired patients.

Audiometrics and the ABR

Assuming that the modeling procedure used gave accurate representations of the amount of activity in each frequency band that was contributing to the unmasked ABR, it remains to be shown why these values correlate so poorly with hearing level or dynamic range. In fact, it is very likely that derived band ABRs and audiometric thresholds give two very different characterizations of underlying physiology in hearing impaired (or even normal) subjects. The derived band technique, by its design, is meant to give frequency specific responses even at high intensities as explained in the introduction. Pure tone threshold measurements, on the other hand, make no attempt to control for spread of activation within the cochlea. It has been clearly shown that the tails of single, eighth nerve fiber, frequency tuning curves (FTCs) at least in animals, become much broader especially toward the low frequencies in the presence of outer hair cell damage accompanied by moderate hearing loss (Dallos &

Harris, 1977). Difficulties in estimating actual frequency specific thresholds in the subjects used for this study because of such spread of activation may be minimized by the fact that all subjects had high frequency sloping hearing loss. The effect of increasing the low frequency tail of tuning curves would be to underestimate low frequency hearing loss rather than high. However, if any broadening of the tuning curves occurs on the high frequency slope, it is possible that the amount of loss in the high frequencies of the hearing impaired subjects indicated by the pure tone audiogram might actually be reflecting sensitivity from lower frequency regions. The effect of increasing stimulus intensity on the tuning of the single fiber FTC is also to broaden the tails especially on the low frequency slope. Because the actual stimulus intensity used to elicit threshold is elevated in the hearing impaired subjects, pure tone stimuli will be less specific in terms of the area of the cochlea stimulated. The combination of high intensity stimuli used to elicit thresholds and effects of cochlear damage in the hearing impaired subjects used may make pure tone audiometric thresholds suspect for lack of true frequency specificity despite the use of pure tone stimuli. This would be in contrast to derived band data which has been shown to be extraordinarily frequency specific (see introduction).

It is possible that neural requirements for eliciting a pure tone threshold and an ABR are very different. It is not known how much damage can occur within the cochlea before pure tone threshold is affected but it is conceivable that threshold determination requires less than a full compliment of neurons from any particular region of the cochlea. Certainly, threshold determination does not have the stringent requirements for neural synchrony known to exist with the ABR. In this way the two may give different representations of cochlear damage. On the other hand, threshold determination requires a considerable amount of high level (cognitive and motor) processing not required by the ABR. In fact, Dallos et al.(1977) found tuning in psychophysical tuning curves and single unit FTC from both normal and Kanamycin treated chinchillas to be very different (have different values of Q_{10}). This was attributed to additional neural processing required for psychophysical measures and/or differences in the number of neurons needed for responses in each case.

Several possible explanations exist as to why the dynamic range measures from this study did not correlate well with derived band ABR levels used to model the hearing loss. Again, no attempt was made to control for spread of activation in the frequency domain for these stimuli other than to use narrow band stimuli for the task. Certainly, the intensities at which these stimuli were delivered would

cause significant amounts of frequency spread within the cochlea. The other complicating factor in comparing these dynamic range measures with ABR measures has to do with the difficulty of the task of finding loudness discomfort and especially maximum comfort levels for these stimuli. Subjects complained that they had difficulty determining comfort levels for a stimulus that was so foreign to them.

Finally, it was assumed that the relationships between cochlear hearing loss and parameters of the ABR could be applied to a case by case modeling procedure for the abnormal ABR. Closer inspection of the results of studies which compared audiometric and ABR data indicates that the dispersion of the data makes a case by case predictive procedure seem doubtful. Jerger and Mauldin, 1978, make this same conclusion when trying to predict hearing level from a high intensity ABR stating that:

> The precision with which prediction can be made is limited by a SD if about 15 dB. Thus if, for example, a 50-dB level is predicted, the probability is 0.67 that the actual level is between 35 and 65 dB, and about 0.95 that the actual level is between 20 and 80 dB. (pg 459).

Coats and Martin (1977) also found significant trends in ABR data when related to hearing loss but noted large amounts of variability across subjects.

It remains to be proven that the modeling procedure used in this study revealed accurate estimates of the amount of activity contributing to the ABR in various frequency

bands. It is clear, however, that the levels used to create models of the ABR from subjects with cochlear impairment cannot easily be predicted from readily available audiometric procedures. Whether or not they can be predicted from more sophisticated measures remains to be shown.

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