AN ABSTRACT OF THE THESIS OF

Pamela S. Gray for the degree of Master of Arts in Interdisciplinary Studies in the co-departments of Speech Communication, Human Development and Family Studies, and Health presented on April 16, 1987. Title: The Effects of Rise-Time and Frequency on the Auditory Brainstem Response Using High-Frequency Tone-Bursts

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The effects of rise-time and frequency on the auditory brainstem response were studied in six normal hearing adults. Stimuli were high-frequency gated tone-bursts with center frequencies of 8, 10, 12, and 14 kilohertz (kHz). Examined rise-times were .1, .25, .5, and 1.0 milliseconds (msec). Duration was maintained at 2 msec. Presentation levels were set at 60 decibels sensation level (dB SL) for each rise-time/frequency combination.

Mean absolute and inter-wave latencies for Jewett peaks I, III, and V were compared with one another as a function of treatment. The results agree with reported literature in that rise-time significantly affects latency. As rise-time is increased, absolute latencies increase. Frequency is not found to significantly affect latency. Possible underlying mechanisms responsible for this particular finding are discussed. In addition, based on initial comparisons

with the .2 msec norm for test-retest repeatability, it is discovered that slower rise-times may have a deleterious affect on latency repeatability. Further analysis and investigative needs directly related to the present study are discussed, as well as those related to rise-time in general.

It is suggested that rise-time studies should encorporate or lead to further investigations concerning the effects of rise-time on the repeatability of the evoked response. This information is needed prior to selecting or recommending an appropriate stimulus rise-time for use in frequency-specific ABR test protocols.

The Effects Of Rise-Time and Frequency on the Auditory Brainstem Response Using High-Frequency Tone-Bursts

by

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CHAPTER I.

INTRODUCTION

The auditory brainstem response (ABR) is a bioelectrical response to an abrupt auditory stimulus. It is used clinically and in research to investigate the integrity of the auditory pathway confined to the cochlea and the auditory brainstem area.

As the response is detected and measured, it is transformed into a series of identifiable waveforms. These waveforms are actually the measurement of electrical patterns emitting from the brainstem area as a result of acoustical stimulation at the ear level.

The first seven waveforms are often referred to as the seven Jewett peaks and are identified with Roman numerals I through VII. The primary wave peaks are considered to be I, III, and V.

There are a number of auditory stimulus types that have been shown to evoke an identifiable ABR. An auditory stimulus type can be defined and categorized by its characteristics. Stimulus characteristics are a result of the combination of the parameters used to create the stimulus.

Stimulus parameters have been evaluated as to their effects on the ABR. The results of these studies have been used to determine

the appropriate characteristics of an auditory stimulus.

The present investigation evaluates the effects of certain stimulus parameters on the ABR. The study is designed to explore the potential effects of rise-time and frequency, using high-frequency tone-bursts. Rise-time is described as the growth of the intensity of the auditory signal as it is turned on. Frequency is designated to be the center or "intended" frequency of the stimulus as shown by spectral analysis.

It is anticipated that the results will be used in the process of determining the appropriate characteristics of a high-frequency tone-burst. Once chosen, this stimulus type would be applied in research and clinical procedures.

A Statement Of The Problem

A review of the literature demonstrates that stimulus parameter effects are an important consideration in ABR studies. However the studies cited in the literature review utilize unfiltered clicks, or frequency-specific stimuli within the conventional range (0.5 - 4 kHz).

A stimulus type currently being considered for clinical application is a high-frequency tone-burst. Research involving High-Frequency Audiometry (HFA) is available for review (Fausti and Rappaport, 1985). However, there is a paucity of information dealing with stimulus parameter effects on the ABR in normal ears using a high-frequency tone-burst. This information is needed prior to the clinical application of this stimulus.

Assumptions

It is assumed that the final six subjects chosen for study are representative of age-matched individuals described by Schechter et al. (1986).

The measures were repeated twice. It is assumed that period one (P1) and period two (P2) conditions (i.e. electrode impedance, equipment calibration, etc.) have been closely matched and therefore have not resulted in significant differences in test results. These assumptions have been investigated previously (Fausti et al., 1979a; 1985).

Limitations

Due to the time constraints inherent in ABR testing, it was necessary to limit the number of independent variables in this study. In human studies, optimal ABR results are obtained when the test subject is relaxed. Extraneous neuronal electrical activity, resulting from muscular tension in the neck area, can interfere with the evoked responses making them less defined. This muscle artifact has been shown to increase as test length is increased (Weber, 1985).

A further time constraint is due to potentially increasing electrode impedance differences. The electrode paste hardens over time and may become less conductive. Also the subject may move his/her head disturbing the electrode paste and skin contact, as does any adjustment of the headphones. These occurrences may produce measurable differences in the impedance of each of the three

electrodes, with a potentially drastic affect on the ABR measurement. The probability of obtaining precise measurements is decreased as impedance becomes measurably different between electrodes (Hyde, 1985).

For these reasons a limit was imposed on the number of independent variables chosen for study. Although there are a number of parameters that determine the characteristics of an auditory stimulus, this study investigates the effects of two of those parameters; rise-time and frequency.

A number of investigations cited report on stimulus parameter effects on ABR wave amplitude. Some investigators recommend evaluating relative (I-V ratio) amplitude (Stockard and Stockard, 1983). It is considered to be a normal phenomenon for absolute amplitude to vary from subject to subject. Overall, peak amplitude is more susceptible to uncontrollable variables such as individual background EEG noise levels (Hyde, 1985). Therefore ABR wave amplitude was not measured.

Anticipated Contribution

The results of this study will expand the knowledge base concerned with the effects of stimulus parameters on the ABR. Specifically, by utilizing high-frequency tone-bursts, an area of the organ of Corti not previously examined under these conditions will be stimulated. The results will also be used in further investigations involving the clinical monitoring of ototoxic drug induced ABR changes as outlined in Appendix I (Fausti et al., 1985).

Hypotheses

Auditory Brainstem Response Evoked Potentials: The Null Hypotheses. Given the conditions set forth...

1) H_o there is no significant difference in mean absolute (I, III and V) latency values when comparing the responses for each rise-time condition with one another at any given test frequency.

2) H_o there is no significant difference in mean inter-wave (I-III, III-V, and I-V) latency values when comparing the responses for each rise-time condition with one another at any given test frequency.

3) H_o there is no significant difference in mean absolute (I, III and V) latency values when comparing the responses for each test frequency condition with one another at any given rise-time.

4) H_o there is no significant difference in mean inter-wave (I-III, III-V, and I-V) latency values when comparing the responses for each test frequency condition with one another at any given rise-time.

Definition Of Terms

Acoustical Analysis:

Refers to the measurement of amplitude as a function of frequency. A signal such as a tone-burst is routed to a spectrum analyzer capable of measuring amplitude at individual frequencies contained within the signal. The electrical signal (measured prior to the transformation of the electrical impulse into sound energy) and the acoustical signal (obtained at the level of the measuring microphone) are analyzed in this manner. Electrical analysis describes the output of the generating instrumentation. The acoustical analysis describes the response of the earphones. The comparison of the electrical and acoustical signal serves as a calibration tool in checking the reliability of the equipment.

Acoustic Immittance Testing:

A series of objective tests used to reveal the integrity of the tympanic membrane, ossicular chain, and stapedius muscle reflex. The basic evaluation includes tympanometry and acoustic reflex thresholds.

Audiometric Configuration:

Refers specifically to threshold measurements obtained with pure-tones. When graphed, these measurements outline the shape or configuration of the audiogram.

Acoustical Energy:

Refers to sound energy. The term is used to label the energy measured at individual frequencies with an acoustical analyzer.

Acoustical Energy Splatter:

Acoustical spread of energy away from the center frequency occurs when a stimulus is abruptly gated on and off. This spread of energy or splatter is found in the side lobes of the acoustic spectrum of a stimulus. The more abrupt the rise in intensity the greater the extent of splatter.

Auditory Brainstem Response (ABR):

An acoustically evoked bioelectrical response as opposed to spontaneous activity. The response arises from the auditory pathway as a result of cochlear stimulation at the ear level. The response is thought to be confined to the auditory nerve and brainstem area. Theoretically it is due to time-locked electrical events ocurring at synaptic junctions located within this area.

Auditory Stimulus:

An audible signal presented to the test ear, used to elicit a behavioral or electrophysiological response.

Behavioral Audiometric Testing:

Refers to the measurement of hearing sensitivity subjectively via a listening task. The test subject responds actively by indicating in some manner whether or not the stimulus is heard.

Click-Evoked Response:

An ABR obtained with an unfiltered click stimulus.

Contralateral:

Opposite the test ear.

Cross-Over Response:

A response obtained from the non-test ear. In air conduction testing an auditory stimulus will travel or cross over to the non-test ear via bone and/or intracranial conduction if loud enough. The non-test ear will perceive the stimulus and respond.

Degradation:

Refers to a diminution in the shape of the ABR waveform. Loss of peak definition, significant increases in latencies, and reduced amplitude would signify a degradation in waveform.

Derived Response:

A method used to obtain frequency-specific information from the ABR. High-pass noise with a variable high-pass cutoff frequency is utilized to mask out lower frequency regions of the basilar membrane while allowing a click stimulus to stimulate higher regions. The high-pass cutoff of the noise band is sequentially decreased, allowing lower regions to respond to the click stimulus. A "derived response" is obtained by sequential subtraction of a response in high-pass noise at one cutoff frequency from the adjacent response at the higher cutoff frequency.

Duration:

The time span measured in milliseconds from stimulus onset to offset.

EEG Electrodes:

Electroencephlagram (EEG) wires used to record electrical brain activity. These electrodes are used for EEG and Electric Response Audiometry (ERA), including ABR testing.

Electrode Impedance:

The measurement of the electrical impedance of the EEG electrode cup and the surface to which it is applied. Reducing the impedance (measured in kilohms) results in increased electrical conductance. Greater conductance and equivalent measurements at each of the active electrode

contacts allows for optimal recordings.

Far-Field Averaging Method:

Refers to the placement of recording electrodes on the outside of the skull as opposed to being in direct contact (near-field) with the nerve tissue generating the electrical activity.

Filtered Click:

A stimulus type utilized in obtaining information about the integrity of the cochlea towards the apical end. The stimulus is generated by passing a DC pulse (click) through a 1/3 octave filter.

Frequency Band:

Refers to the spectrum of a stimulus. The frequency band displays the acoustical energy present at all frequencies contained within the stimulus.

Frequency-Specific:

Relates to the loci of stimulation along the organ of Corti within the cochlea. Frequency-specific stimuli are used to determine the integrity of the cochlea at specific sites within the structure.

Gating:

The process of causing any change to occur in a signal. Turning a signal on or off, increasing intensity, etc. are all forms of gating a signal or stimulus.

Histological:

Pertaining to the study of body tissue.

Interaural:

Between ears on an individual test subject.

Interaural Attenuation:

Refers to the attenuation of sound energy as an auditory stimulus crosses over from the test ear to the contralateral (non-test) ear via bone and/or intracranial conduction.

Interstimulus Interval:

The time interval between the off-set of one signal at zero amplitude and the on-set of the next signal at zero amplitude.

Ipsilateral:

On the same side as the test ear.

Latency:

Refers to the time measurement in milliseconds (msec) between two points, peaks or waves.

Absolute Latency:

Measurement of time between the onset trigger of the signal and wave peaks. Variations of $\pm$ .2 msec between two successive runs using a click stimulus is considered to be within the normal range.

Interaural Latency:

Measurements taken of peak latencies from the right- and left-ear ABR of an individual test subject. Used primarily to determine side-of-lesion.

Inter-Wave Latency:

The measurement taken of the central conduction time (latency or time value between two waves) in the same ear. Latency measurements are taken between waves I-III, I-V and III-V on at least two stimulus runs in the same ear. A $\pm$ .2 msec difference is considered to be within a normal range.

Lesion:

A temporary or permanent pathological condition existing in body tissue.

Middle Ear Effusion:

Pertaining to the various pathological conditions affecting the middle ear space.

Modified Hughson-Westlake Technique:

A method used to obtain subjective thresholds from a test subject responding to an auditory stimulus.

Morphology:

Pertaining to the waveforms of the ABR. The morphology is the description of the shape of the ABR in its graphic form.

Non-Frequency-Specific:

Refers to an auditory stimulus having a broad frequency band such as a click. This stimulus type provides information about the general integrity of the more basal area of the cochlea but does not assess the extreme basal or apical end of the cochlea.

Objective Audiometric Testing:

A category of audiometric tests that does not depend on the subjective response of the test subject. The response is a measurable electrophysiological reaction to an audible stimulus.

On-Effect Response:

Refers to the ABR. The response is initiated by the onset of an auditory stimulus.

Organ of Corti:

That part of the cochlea responsible for transforming sound waves transmitted by the perilymphatic-endolymphatic fluid system within the cochlea into electrical impulses. The organ is directly above and connected to the basilar membrane. The first turn of the cochlea is referred to as the basal end. Here the organ is sensitive to high-frequency sounds. The final turn of the cochlea is referred to as the apical end. This area is sensitive to low-frequency sounds.

Output Characteristics:

The acoustical response of the instrumentation obtained at the level of the measuring microphone coupled to the earphone.

Peakedness:

Refers to the ABR waveform. Peakedness describes the sharpness of the individual wave peaks. Lack of peakedness is a sign of wave degradation.

Phase Presentation (Polarity):

The presenting point on the auditory stimulus sound wave that meets the tympanic membrane (eardrum). The phase of the stimulus can be triggered to begin on the condensation or rarefaction phase (positive or negative respectively) of the sound wave front. The phase can also be triggered to present on alternating phases.

Release-From-Masking:

Refers to a method used to determine the validity of a frequency-specific, behavioral response to an auditory stimulus.

Signal-To-Noise Ratio:

Refers to the auditory stimulus and the addition of ipsilateral or contralateral masking noise. The ratio of stimulus intensity to noise intensity.

Stimulus Parameters:

The components of a stimulus that combine with one another to make up the final characteristics of a stimulus. The initial parameter would be the frequency characteristics of the stimulus. Shaping the stimulus involves the addition of temporal parameters in order to create the "wave envelope". Final parameters are added that include repetition rate, phase presentation (polarity), interstimulus interval, and the output characteristics of the sound delivery system (i.e. earphones, speakers, etc.)

Temporal Stimulus Parameters:

Components used to shape a stimulus i.e. rise/fall time, duration, and intensity. These parameters combine to create the characteristic wave envelope of a stimulus.

Superimposable:

Often referred to as repeatable. Refers to the comparison of two ABR test runs. An ABR is considered to be superimposable if test runs have matching identifiable waves and can be overlayed without a significant difference in wave latencies.

Synchronized Response:

Simultaneous firing of a group of auditory nerve fibers as the electrical impulse courses through the auditory pathway.

Temporal Waveform:

A representation of an auditory stimulus as a function of intensity over time measured with an oscilloscope.

Time-Locked Response:

Refers to the simultaneous firing of a group of auditory nerve fibers. In normal ears, this synchronized response continues at each synaptic junction of the auditory pathway as the electrical signal courses through the brainstem area.

Window:

Refers to the time span during which evoked potentials are sampled by a signal averaging computer. The evoked potentials measured during the first 10 msec following the onset of an auditory stimulus are considered to be primarily

comprised of the auditory brainstem response. Therefore the "window" during which these evoked potentials are monitored is set at 10 msec.

Wave Amplitude:

Measured in microvolts, this term refers to the height of the wave peaks of the ABR in its graphic form. Absolute amplitude can be measured from the "peak" of a wave component to its negative trough. Relative amplitude is most often measured as a wave I relative to wave V ratio.

CHAPTER II

A REVIEW OF THE LITERATURE

The Auditory Brainstem Response

The auditory brainstem response (ABR) was first described by Jewett and Williston (1971) and is an electrical response to an abrupt auditory stimulus. It is a phenomenon that has allowed extensive detailed study to be carried out in both animals and humans due to its non-intrusive nature. The ABR is believed to be produced by electrical events that occur within the auditory pathway confined to the cochlea and brainstem area. It is theorized that these electrical events occur in an organized manner that correlate closely with major synaptic junctions along the auditory neural pathway (Starr and Achor, 1975).

These auditorily evoked electrical responses can be recorded from the scalp by a far-field averaging method. This method is described in detail by Davis (1976a, 1976b), and Jewett and Williston (1971). An evoked response signal averaging computer is employed to extract these time-locked responses from background electroencephalogram random activity. The responses are then displayed in graphic form. The ordinate displays amplitude in $_{u}$volts. The abscissa indicates time in milliseconds (msec). The ABR is then pictured as a series of waves often referred to as the Jewett peaks I-VII (see Figure 1).

With few exceptions it is believed that waves I-VII originate

from the following synaptic junctions: 1) I - Auditory Nerve VIII; 2) II - Cochlear Nucleus; 3) III - Superior Olivery Complex; 4) IV - Lateral Lemniscus; 5) V - Inferior colliculus; and 6) VI and VII - unknown (Buchwald and Huang, 1975).

In normal ears the wave pattern or morphology (see Figure 1) is fairly consistent in that: 1) each wave occurs within a certain time span measured as absolute latency, and can be identified by this measurement; 2) there exists an inter-wave and interaural latency relationship that can be used to evaluate wave morphology; 3) there are certain characteristics of the shape, amplitude, and latency of the waves that help to identify the response; 4) the response can be consistently repeated; and 5) the response is relatively undisturbed by attention, sleep, or non-ototoxic drugs (Davis, 1976b; Jacobson, 1985; Jewett and Williston, 1971).

There are a number of variations that are reflected in the size and shape of the waves. The most common is called a IV-V complex. There are also relative amplitude differences that may occur consistently or change from one response run to the next. Bifid waves may also be present; most commonly at wave I and wave III (Schwartz and Berry, 1985). These normal variations result in small latency differences. Chiappa and Gladstone (1979) investigated these occurrences and proposed guidelines for measuring these variations.

There are certain conditions that influence the ABR. It has been demonstrated that wave morphology is significantly influenced by the characteristics of the auditory stimulus (Jacobson, 1985). It has also been demonstrated that wave morphology exhibits change that has

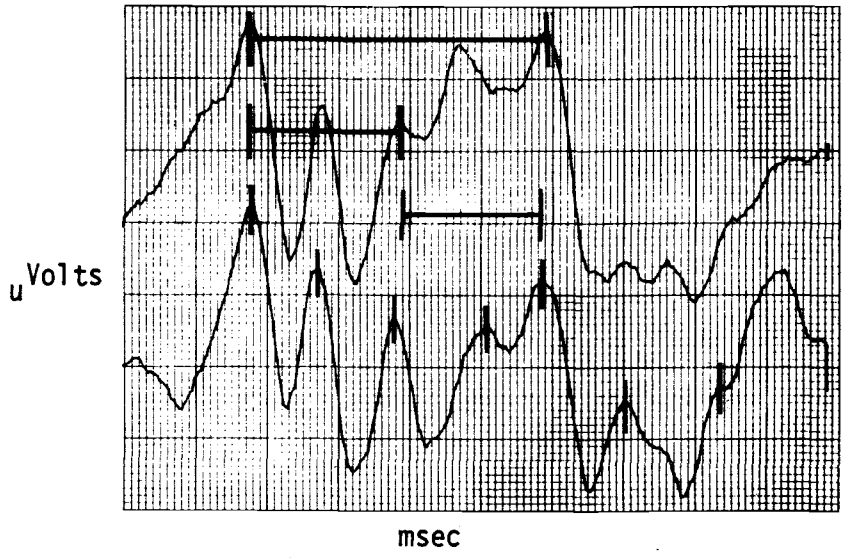

Figure 1. The graphic form of an 8 kHz tone-burst ABR, obtained from a normal female subject, depicting absolute and inter-wave latencies.

been attributed to specific pathological conditions, i.e. brainstem lesion (Starr and Achor, 1975), acoustic tumor (Clemis and Mitchell, 1977), and peripheral hearing loss (Coats and Martin, 1977; Jerger and Maudlin, 1978; Moeller and Blegvad, 1976; Schaefer et al., 1985).

The ABR and Audiological Monitoring of Drug Induced Hearing Loss.

It has been documented that audiological monitoring of patients receiving ototoxic drugs is a valuable tool in order to detect significant peripheral hearing loss secondary to ototoxic drug use. Recent studies demonstrate the advantages to be gained by including high-frequency (>8 kHz) audiological monitoring in this patient population (Fausti et al., 1984a, 1984b; Tange et al., 1985).

Numerous studies (Boheim and Bichler, 1985; Capps and Duvall, 1977; Fausti et al., 1984a, 1984b; Hawkins and Engstrom, 1964; Jacobsen et al., 1969; Schaefer et al., 1985; Tange et al., 1985; Wilson and Ramsden, 1977), demonstrate histologically and behaviorally, that ototoxic damage occurs within the organ of Corti. This organ, situated directly above the basilar membrane, stretches the entire length of the snail shaped cochlea. Generally, ototoxic damage occurs initially at the extreme basal end of the cochlea; the area believed to be responsible for high-frequency audition. Subsequent involvement occurs in a step by step fashion towards the apical end of the cochlea. Research carried out by Hawkins (1976) provides a description of histological changes and proposed mechanisms involved in drug induced cochlear damage.

A common element in reported human studies dealing with drug-

induced hearing loss is the measurement of auditory sensitivity with behavioral techniques. Many patients receiving ototoxic drugs are not candidates for these techniques because of their poor general physical condition. A technique which does not depend upon behavioral responses to monitor the auditory effects of potentially ototoxic drug agents would be highly advantageous (Fausti et al., 1985; Schaefer et al., 1985).

Recent studies have demonstrated the ability of the auditory brainstem response to reflect changes in the inner ear secondary to ototoxic drug insult (Bernard et al., 1980; Cromwell et al., 1981; Piek et al., 1985). Of those studies demonstrating the utility of the ABR to detect peripheral hearing loss, the majority deal with changes in ABR waveform using non-frequency-specific stimuli (e.g., clicks), or frequency-specific stimuli sensitive to changes occurring at frequencies below 6 kHz. However, these studies demonstrate the potential the ABR has for objectively monitoring frequency-specific auditory changes.

It has been stated above that the initial site of drug-induced cochlear change occurs primarily at the extreme basal end of the cochlea, and that hearing loss often first occurs at frequencies $>$8kHz (Fausti et al., 1984a, 1984b). The synthesis of this information has led to a proposal that by utilizing tone-bursts with center frequencies $\geq$8kHz, the ABR can be used to objectively monitor patients receiving ototoxic drugs. The advantage of this protocol would be early detection of auditory changes in patients too ill to respond appropriately to behavioral test protocols. Specifically, by utilizing high-frequency tone-bursts, it is postulated that the early

onset of cochlear damage can be detected before these changes occur in areas responsible for the reception of speech signals (Fausti et al., 1985).

The high-frequency test stimulus targeted for use in that proposed study must be characterized by two important aspects: 1) it must be frequency-specific so as to be sensitive to changes at specific sites within the organ of Corti at the extreme basal end; and 2) the stimulus must be able to produce ABR waveforms that can be easily identified and are, in the absence of drug-induced changes, repeatable. These attributes are necessary in order to readily show subsequent change or degradation as a function of drug-induced cochlear damage.

Fausti et al. (1985) has proposed a major study to investigate the utility of the ABR test protocol in monitoring the effects of ototoxicity in patients unable to respond to standard behavioral audiometric testing. In that proposed investigation, important research questions are to be evaluated (see Appendix I). The present investigation is a preliminary study dealing with question #3: Is there a most effective stimulus for eliciting the ABR to provide early detection of ototoxicity?

The Auditory Stimulus

In order to evoke a characteristic auditory brainstem response, the stimulus must be capable of causing a group of auditory nerve fibers to fire simultaneously; also referred to as a synchronized response. Evoking stimuli currently in use for such purposes can be

divided into two categories: 1) frequency-specific; and 2) non-frequency-specific.

Non-frequency-specific stimuli are referred to in the literature as unfiltered clicks and are characterized by: 1) acoustical energy throughout a wide frequency band as seen in Figure 2; 2) synchronized nerve discharge; and 3) the ability to evoke sharp ABR waveforms with latencies that are clearly measurable (Davis, 1976a; Jacobson, 1985).

Generally speaking, the unfiltered click is an acceptable stimulus for the assessment of the basal turn of the cochlea (Davis, 1976a; Don and Eggermont, 1978). The area referred to here is located along the area of the organ of Corti thought to be sensitive to frequencies from 1 to 4 kHz.

The major drawback is that this stimulus is acoustically complex and therefore does not address the need for obtaining frequency-specific information concerning the integrity of the cochlea at specific sites along the basilar membrane. To address this need frequency-specific stimuli are utilized (Davis, 1976b; Gorga et al., 1985).

Frequency-specific stimuli can be divided into four categories: 1) a tone-like stimulus from which a number of variations have been developed (Davis, 1976a, 1976b; Eggermont and Odenthal, 1972, 1974; Trenque and Gazeaud, 1978); 2) a pure-tone embedded in noise (Stapells and Picton, 1981); and 3) a filtered click (Brama and Sohmer, 1977; Kinarti and Sohmer, 1982). A fourth type of frequency-specific stimuli cannot be so easily classified. This stimulus is a combination of a broad frequency band click and ipsilateral masking

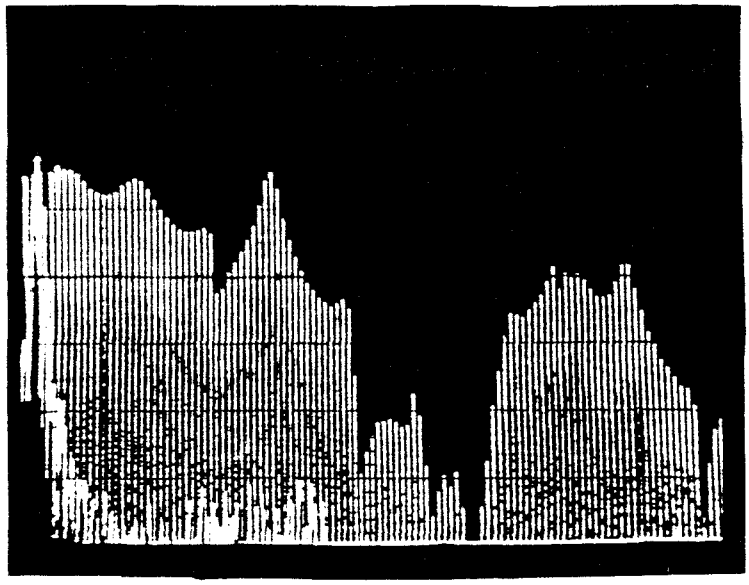

Figure 2. The spectrogram of an unfiltered click stimulus, obtained at the level of the measuring microphone. Intensity (dB SPL re 20 $_{u}$Pa), ranging from 0 to 100 SPL is measured on the ordinate, and frequency, ranging from 0 to 20 kHz is measured on the abscissa.

with a variable high-pass frequency cut-off. The frequency-specific information is the result of off-line calculations in order to obtain the response. This method is called the derived response. A complete description can be found in a study by Don and Eggermont (1978).

Several studies have investigated the validity of frequency-specific stimuli. In a published study investigating the frequency specificity of the ABR, Terkildsen et al. (1975) concluded that evoked responses to frequency-specific stimuli originated from sites within the cochlea thought to be highly correlated to the stimulus frequency. It is generally accepted that the evoked response to a frequency-specific stimulus is a valid representation of the integrity of the organ of Corti at specific sites along the basilar membrane (Kodera et al., 1983; Stapells and Picton, 1981; Weber and Folsom, 1977).

Evoked responses to brief frequency-specific auditory stimuli in the conventional range (.5 - 4 kHz) have been intensively studied (Bauch et al., 1980; Brama and Sohmer, 1977; Coats et al., 1979; Klein and Teas, 1978; Mitchell and Clemis, 1977; Suzuki et al., 1977; Terkildsen et al., 1975; Wood et al., 1979). Because of stimulus parameter differences between these studies, it would not be valid to draw specific conclusions incorporating all of the information obtained. It can be stated, however, that evoked responses using frequency-specific stimuli are generally characterized by fairly good waveforms that allow for consistent latency measurements and are superimposable (Peters and Squires, 1981; Rappaport et al., 1985).

Stimulus Parameters

Temporal stimulus parameters may be described as those components utilized to shape a stimulus. These include frequency, rise-time, intensity, and duration (Davis, 1976b; Jacobson, 1985).

There are other parameters that interact with the stimulus after it has been shaped. These include phase presentation, repetition rate, interstimulus interval, and the output characteristics of the equipment used to generate and deliver the stimulus (Davis, 1976b; Durrant, 1983; Gorga et al., 1985).

All of these components combine with one another to create the characteristics of the stimulus. One way of picturing these characteristics is by viewing the temporal waveform of the stimulus. The temporal waveform refers to the visual characteristics of the stimulus as traced by an oscilloscope. As shown in Figure 3, the outline of the stimulus (in this case, a 10 kHz tone-burst) is referred to as the wave envelope (Gorga et al., 1985).

This measurement is usually obtained at the level of the measuring microphone coupled to the earphone. When the stimulus is measured in this manner, the waveform traced by an oscilloscope "may be used as the 'signature' of the earphone" (Gorga et al., 1985). This is one way that the stability of the signal generating equipment is calibrated and checked, and is often used as a convenient screening method when checking the response of the earphone.

It is also possible to define the characteristics of a stimulus by spectral analysis (Davis et al., 1984). Stimulus parameter components combine to create a spectral picture. The acoustical

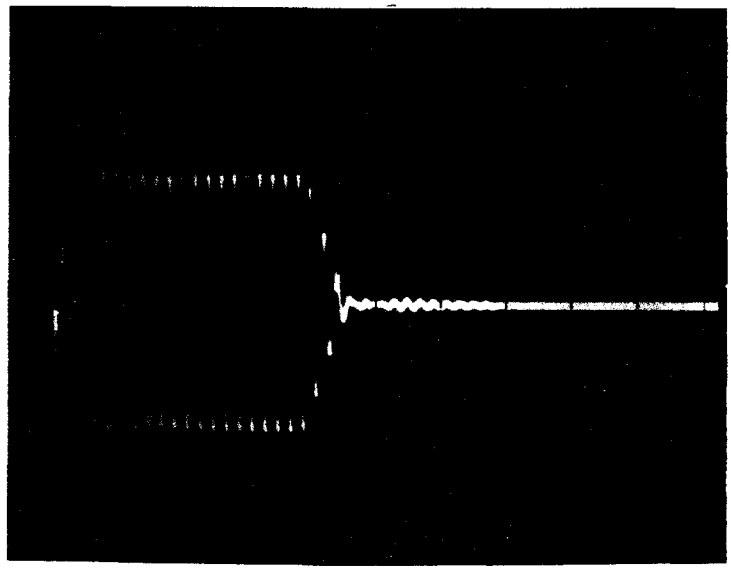

Figure 3. The temporal waveform of a 10 kHz tone-burst, obtained at the level of the measuring microphone. Intensity (dB SPL re 20 $_{u}$ Pa), beginning at 0 dB at the midline, is measured on the ordinate, and time, measured in msec is displayed on the abscissa.

energy of the stimulus is measured and displayed as a function of intensity and frequency. Intensity is measured on the ordinate and frequency on the abcissa. Stimuli are often described by the amount of acoustical energy present at individual frequencies within the stimulus. For instance the tone-burst stimulus, pictured in Figure 4, is characterized by acoustical energy concentrated near a center frequency; in this case, 10 kHz. This stimulus type is therefore referred to as a frequency-specific stimulus.

A high-frequency tone-burst stimulus is used to obtain frequency-specific information concerned with the integrity of the cochlea. The temporal waveform of a 10 kHz tone-burst with a rise-time of .1 msec has been illustrated in Figure 3. The portion of the signal referred to as rise-time can be seen as the initial broadening of height in the envelope. Because rise-time is a function of the growth of intensity over time, the temporal waveform is suited for depicting this parameter (Gorga et al., 1985).

Figure 4 is the spectral analysis of the same tone-burst. Rise-time is not measured by spectral analysis. In this illustration, the amount of acoustical energy present per frequency at a given moment in time is shown. This measuring tool is suited for depicting the effects of rise-time on the spread of acoustical energy.

It is important to note that these measuring devices do not take into account two important factors. First, the physiological make-up of the ear canal and middle ear space may change the spectral characteristics of the stimulus before it reaches the cochlea, especially at high intensity levels.

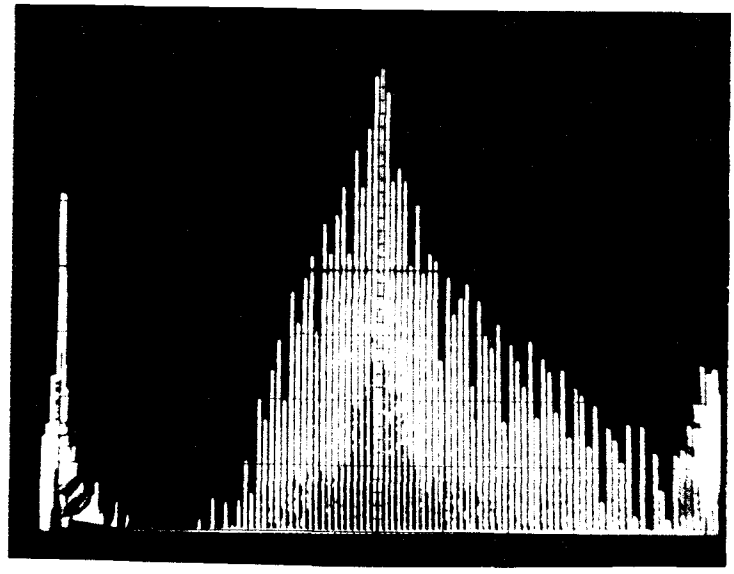

Figure 4. The spectrogram of a 10 kHz tone-burst, obtained at the level of the measuring microphone. Intensity (dB SPL re 20 $_{u}$Pa), ranging from 0 to 100 SPL is measured on the ordinate, and frequency, ranging from 0 to 20 kHz is measured on the abscissa.

Second, the ABR is primarily an on-effect response (Gorga et al., 1982). That is, as soon as the stimulus is turned on and develops sufficient intensity, a response is initiated in the auditory nerve pathway. Therefore the entire wave envelope of the stimulus holds less importance than that of the early portion (Kodera et al., 1983; Suzuki and Horiuchi, 1981).

Conclusions concerning the utility of a stimulus cannot be drawn based solely on the shape of the wave envelope and spectral analysis (Stapells and Picton, 1981). The resulting ABR must also be evaluated. The collective information should then be taken into consideration.

Stimulus parameter studies investigate the effects that parameter manipulation has on the ABR. It has been demonstrated that wave morphology is significantly influenced by the components of the auditory stimulus. Stimulus components that have been studied include rise-time (Hecox et al., 1976; Kodera et al., 1977, 1979, 1983; Stapells and Picton, 1981; Suzuki and Horiuchi, 1981; Terkildsen et al., 1975; Trenque and Gazeaud, 1978; Weber and Folsom, 1977), duration (Hecox et al., 1976), temporal waveform (Trenque and Gaziaud, 1978), stimulus intensity (Stapells and Picton, 1981; Weber and Folsom, 1977), phase presentation (Borg and Lofqvist, 1982), repetition rate (Gerling and Finitzo-Hieber, 1982; Goldstein et al., 1972; Stapells and Picton, 1981), and interstimulus interval (Davis, 1976b; Hecox et al., 1976). In each of these studies the temporal waveform and acoustic spectra of the stimulus under question are reviewed. However, it is primarily the ABR test results that are

used to form conclusions concerning these components.

The results of these studies are used to suggest appropriate choices in shaping a stimulus to be used for clinical and research purposes. Studies have shown that as certain stimulus parameters are manipulated the ABR becomes more or less like that evoked with an unfiltered click stimulus; considered to be an optimal stimulus (Jacobson, 1985; Weber and Folsom, 1977). It can therefore be said that the ABR is an appropriate test of the stimulus.

Rise-Time Defined

The ABR has been demonstrated to be an on-effect response. The parameter represented in that time period is entirely taken up by rise-time (Davis et al., 1984; Kodera et al., 1983; Stapells and Picton, 1981; Suzuki and Horiuchi, 1981; Weber and Folsom, 1977). The following discussion reviews this parameter in detail.

Generally speaking, rise-time describes the growth of the intensity of the signal as it is turned on. There are currently three definitions of the portion of the signal defined as rise-time: 1) The interval measured from the initial onset of the signal (zero amplitude) to the maximum amplitude; 2) the interval measured from 10 to 90% of the maximum amplitude; and 3) rise-time measured as a function of the frequency of the signal thus causing it to be frequency-dependent (Gorga et al., 1985).

In a published study Gorga et al. (1982) concluded that only the earliest portions of the stimulus are responsible for evoking the

auditory brainstem response. This portion is referred to as rise-time.

It is essential to evoke a synchronized, therefore time-locked, neural discharge (or response), in order for the recorded electrical activity to be differentiated from random EEG activity (Jewett and Williston, 1971). Therefore the evoking stimulus must be shaped in the early portion of the signal so as to result in this kind of response (Davis, 1976b).

Numerous investigators have commented on the difficult compromise faced when attempting to obtain frequency-specific information from the ABR (Davis, 1976a; Kodera et al., 1979, 1983; Stapells and Picton, 1981; Suzuki and Horiuchi, 1981; Terkildsen et al., 1975; Weber and Folsom, 1977). The compromise is related to the shaping of the stimulus.

The area inside the stimulus envelope represents a complex interplay between frequency and intensity. It is known that the intensity at any given frequency point and the number of freqencies present varies with the steepness of the on-slope (or rise-time). This phenomenon is known as acoustical energy splatter (Davis, 1976b). Since rise-time measurably influences this portion of the stimulus, it is a singularly important aspect of stimulus generation.

The compromise involves two opposite ends of a continuum. A pure-tone stimulus used for conventional hearing evaluations is highly frequency-specific. It is characterized by having an extremely long (200 msec or more) rise-time; a necessary component of a pure-tone. However, it is an unacceptable ABR stimulus because of the poor neural synchrony it produces. An unfiltered click is

characterized by having an instantaneous rise-time (on the order of .5 $_{u}$sec) and is an excellent ABR stimulus because of the good neural synchrony it produces. However, it is not frequency-specific.

The solution is contained in a compromise between rise-time and frequency-specificity. Rise-time must be shortened in order to produce good neural synchrony, but it must be sufficiently long enough to maintain frequency-specificity.

It has been postulated that "the exact relationship between rise-time and latency is a complex function of both the frequency and the intensity of the tone" (Stapells and Picton, 1981). Since the ABR is primarily elicited by the on-effect of the stimulus, whatever components are present in the on-slope of the stimulus will directly affect the pattern and area of stimulation within the cochlea. So far it has not been possible to differentially explain the effects frequency and intensity have on the latency function.

A frequency-specific stimulus, referred to generally as a tone pip or tone-burst, is characterized by having a concentration of acoustic energy centered on the test frequency with minimum acoustic energy spread away from the center frequency (Davis, 1976a, 1976b, Gorga, et al., 1985). This type of stimulus is the result of the manipulation of the rise-time and duration of the generated tonal signal in order to produce an abrupt, yet spectrally pure signal (Davis, 1976b; Gorga et al., 1985).

Rise-Time Effects On The ABR

Investigations concerning the effects of rise-time on the ABR are numerous. It should be noted that most studies utilize unfiltered clicks or tone-bursts with center frequencies below 6 kHz. Direct comparisons between reported studies are limited due to the highly varied configurations of the on-slope of the stimuli examined in these studies. Some utilize a linear ramp type of on-set, others calculate slope as a function of frequency, while still others use a rapid on and off, or gated procedure to produce different rise-times. These procedures all result in a varying amount of acoustical energy splatter outside the "intended frequency" of the stimulus, particularly within the area largely responsible for the initiation of the response.

It should also be stated that the complete rise-time/latency function cannot be described here. Nor has it been exhaustively dealt with in the literature. And for anatomical reasons, rise-time effects may not be projectionable to other frequency-specific tone-bursts designed to stimulate other sites within the cochlea.

At the basal end, differences in the location and number of dendritic nerve fiber endings have been documented. So to has the width and thickness of the basilar membrane. These anatomical differences seen throughout the length of the organ of Corti may cause the latency effects of rise-time and frequency to differ significantly. Therefore, direct comparisons cannot be made between studies. However, generalities may be drawn concerning overall

relationships that link these studies together.

There are two major effects that tone-burst rise-time has on the ABR: 1) as rise-time increases, the latency of wave V increases (Cobb et al., 1978; Hecox et al., 1976; Kodera et al., 1977); and 2) longer rise-times result in a decrease in wave amplitude (Kodera et al., 1979; Kodera et al., 1983). Generally speaking, these changes occur across studies.

The mechanism(s) involved in causing these effects is believed to be associated with delayed and less synchronized neural discharges. The response is initiated at the nerve endings within the cochlea as a result of a sudden presentation of a stimulus. If stimulus rise-time is slow simultaneous discharge is likely to be delayed. Further, it is hypothesized that nerve fibers fire more independently instead of as a group. This pattern perseverates as the neuronal discharge continues through the pathway. Therefore it is postulated that the time-locked response necessary to differentiate the evoked potentials from EEG activity does not occur using a slow stimulus rise-time (Davis, 1976b; Jacobson, 1985; Kodera et al., 1979).

Stapells and Picton (1981) tested eight otologically normal adults, using tone-bursts with center frequencies of .5, 1, 2, and 4 kHz. Rise-times of 1, 2, 5, and 8 msec were evaluated. They reported on latency and amplitude changes as a function of rise-time. The results reveal that wave V latencies increase with decreasing stimulus frequency and increasing rise-time. The effect appears to be most significant at .5 and 1 kHz. It was also reported that a definite decrease in amplitude is evident using longer rise-

times and results in a severe decrease using an 8 msec rise-time. The effect appears to be most significant at rise-times greater than 2.5 msec. It was concluded that rise-times of 5 msec or less were preferable.

Kodera et al. (1983), investigating the effects of rise-time reported similar results. Using rise-times of .5, 1, 2, 4 and 8 msec, evoked responses to tone pips with linear onset and offset ramps at .5, 1 and 2 kHz were evaluated in six cats. Results indicated a significant association between reduced wave amplitude and longer rise-times at each intensity level. Mean ABR latencies revealed a significant association between increased latency and longer rise-times, particularly for rise-times beyond 4 msec.

Further, other research has been done investigating these effects using stimuli quite different from a tone-burst (Kodera et al., 1979; Hecox et al., 1975). The relationship between rise-time and wave latency and amplitude is demonstrated. Decreased amplitudes and increased latencies as a function of increased rise-time are reported.

Apparently, latency reacts to rise-time more strongly than wave amplitude. Stapells and Picton (1981) reported that at shorter rise-times there may not be any changes in wave amplitude. Their results indicated that significant changes in wave amplitude occur with rise-times of 5 msec or longer. It was also evident that responses elicited with higher frequency tone-bursts showed less amplitude change than responses obtained by using lower frequency tone-bursts.

The inter-wave latency relationship, a potentially important

segment of information concerning wave latency, is not reported in the literature dealing with rise-time. It has been demonstrated that changes in external components, such as the stimulus, can affect central conduction time (Coats, 1978; Rossi et al., 1979; Stockard et al., 1979). Central conduction time is the time interval between ABR wave peaks (inter-wave latency). It has been suggested that this measurement be included in studies investigating the relationship of stimulus parameter manipulation on the ABR (Stockard and Stockard, 1983).

One final observation is the apparent association that frequency has on the effects of rise-time. Stapells and Picton (1981) reported that as frequency increases, rise-time has less of an affect on latency and amplitude. However, the above study reports on rise-time effects using tone-bursts well below the higher non-conventional frequencies. The potential relationship that exists between rise-time, high-frequency tone-bursts and ABR latencies has not been reported in the literature.

CHAPTER III

METHODOLOGY

Subjects

Data was obtained from two male and four female normal human subjects, age 25 to 33 years of age. Subject candidates reporting levels of noise exposure exceeding criterion established by Schechter et al. (1986) were excluded. Candidates reporting recent or chronic childhood middle ear effusion were excluded. All potential subjects received acoustic immittance and audiometric pure-tone threshold evaluations (see Appendix II). Those subjects demonstrating normal middle ear function and acoustic reflex sensation levels were considered for study. Potential subjects demonstrated hearing sensitivity within normal limits (≤15 dB HL re ANSI 1969) bilaterally through the conventional (.25 - 8 kHz) audiometric test frequencies. Further, potential subjects demonstrated hearing sensitivity within the normal range bilaterally for test frequencies 8 through 20 kHz according to system-specific normative data obtained previously (Schechter et al., 1986). Test subjects demonstrated an identifiable ABR to an unfiltered click stimulus according to normed data outlined by previous investigators (Jacobson, 1985; Starr and Achor, 1975). Based on the preliminary screening tests, all data was obtained from the better ear.

Potential test subjects were obtained from three sources: 1) VA Medical Center staff and employees, Portland Division, Portland,

Oregon; 2) Oregon State University; and 3) Portland State University. The subjects were informed of the nature of the study prior to their written consent to participate (see Appendix III). All potential subjects and the final six did not receive reimbursement of any kind for their participation in this study.

Instrumentation

Testing (with the exception of acoustic immittance testing) was done with the subject seated or reclining comfortably in an upholstered lounge chair placed inside an IAC model 1204M test booth.

Acoustic immittance testing was obtained using a Madsen Immittance Audiometer and chart recorder (ZO174/TP174). Hearing thresholds measured through the conventional range (.25 - 8 kHz) were obtained using a Grason-Stadler 1701 clinical audiometer and standard TDH-49 earphones.

High-frequency hearing thresholds (8 - 20 kHz) were obtained using the high-frequency component system developed by Fausti et al. (1979b). This system consists of: 1) a decade oscillator (General Radio #1312) used to generate test stimuli from 8 through 20 kHz; 2) switching, gating, and timing modules (Grason-Stadler 1200 Series) used in shaping high-frequency signals; 3) a specially fabricated amplifier-filter and tail-end attenuator added to decrease the noise floor at each test frequency and allow for greater maximum power output; and 4) utilization of a high-fidelity earphone manufactured expressly for high-frequency testing (Koss HV/1A). The stimulus output for the high-frequency pure-tone generating equipment was

monitored continuously with a frequency counter (Monsanto Counter-Timer 100C).

The equipment used in obtaining ABR data incorporates the above high-frequency component system. A duplicate decade oscillator and duplicate shaping modules have been added to generate the high-frequency tone-bursts.

The right Koss HV/1A phone was used to present the tone-burst stimulus. The left phone presented the masking stimulus. The output for the high-frequency tone-burst generating equipment was monitored continuously with a frequency counter (Hewlett-Packard, 5326A). The stimulus was routed to the external trigger input of a Nicolet 1170 evoked response signal averager.

The test stimuli consisted of gated tone-bursts having center frequencies of 8, 10, 12, and 14 kHz. Four rise-times were chosen for evaluation (.1, .25, .5, and 1.0 msec). The duration of the signal, measured from the onset to the offset remained constant at 2 msec. All stimuli were presented at 60 decibells sensation level (dB SL) with the exception of one sample obtained at 50 dB SL using a 14 kHz tone-burst.

Evoked responses were averaged and measured via the Nicolet instrumentation according to the guidelines established by Chiapa et al. (1979) and stored on its 5-1/4" floppy diskette system. All responses were charted on a Hewlett-Packard 7010B X-Y recorder.

Equipment calibration was conducted prior to each test session. A specially fabricated Koss 6 cc coupler was used to connect the high-frequency earphones to the calibrating equipment. The coupler, constructed of RTY Silicone rubber, fits snugly around a 1/2"

condenser microphone (B & K #4134). Each phone is then set into an aluminum spacer. The spacer is used to center the earphone into place on the coupler. The acoustic output, at the level of the measuring microphone, is routed to a voltmeter (Hewlett-Packard 3400A RMS) and then converted into dB SPL.

Procedures

Test subjects received preliminary testing on a day prior to data collection. Subjects received a final conventional and high-frequency pure-tone threshold evaluation on a day following data collection.

Data collection was spaced out over four, one hour sessions per subject. Each session was separated by at least four hours. Data for 8 and 10 kHz was obtained during session one. Data for 12 and 14 kHz was obtained during session two. Sessions three and four were repeats of the first two.

Each session consisted of two stages: 1) the measurment of thresholds; and 2) obtaining the ABR for each treatment. Each session was approximately 60 minutes in length.

An abrasive scrub was used to prepare the skin. Excess material was removed with rubbing alcohol. Electrode cream was applied to the skin and electrode cup followed by electrode placement: 1) positive on the vertex; 2) negative on the mastoid process on the side of the acoustically stimulated ear; and 3) ground on the contralateral mastoid process. The electrodes were held in place by absorbant rayon balls. Electrode impedance was measured before and after earphone placement. This procedure was used successfully in

obtaining electrode impedance measurements under 2 kilohms.

Using the modified Hughson-Westlake technique in 2 dB steps, thresholds for pure-tones were re-checked. Tone-burst thresholds for each frequency/rise-time combination were obtained likewise.

The ABR for each rise-time/frequency combination was obtained. Responses were recorded from the scalp by a far-field averaging method (Davis, 1976a, 1976b; Jacobson, 1985; Jewett and Williston, 1971). The rise-time/frequency treatments were randomly presented in order to negate any potential order effects. The tone-burst stimuli had a set duration (2.0 msec) and repetition rate (11.1/sec). Each combination was presented at 60 dB SL, with an alternating phase presentation. The response was sampled 1024 times each run using a 10 msec window. Two consecutive runs were obtained for each treatment and stored for later analysis.

To rule out the participation of the non-test ear under these conditions, contralateral masking was presented at +15 dB signal-to-noise ratio (Rappaport et al., 1982). Spectral analysis of this special high-pass masking signal is shown in Figure 5.

Pure-Tone and Tone-Burst Threshold and Sensation Level Data

Table 1 reveals the mean pure-tone conventional (.25 - 8 kHz) and high-frequency (8 - 20 kHz) thresholds (and standard deviations), measured in sound pressure level (SPL). Five subjects revealed pure-tone thresholds for test frequencies 8 through 14 kHz to be within one standard deviation of the age categorized mean thresholds obtained in a previous normative study (Schechter et al., 1986).

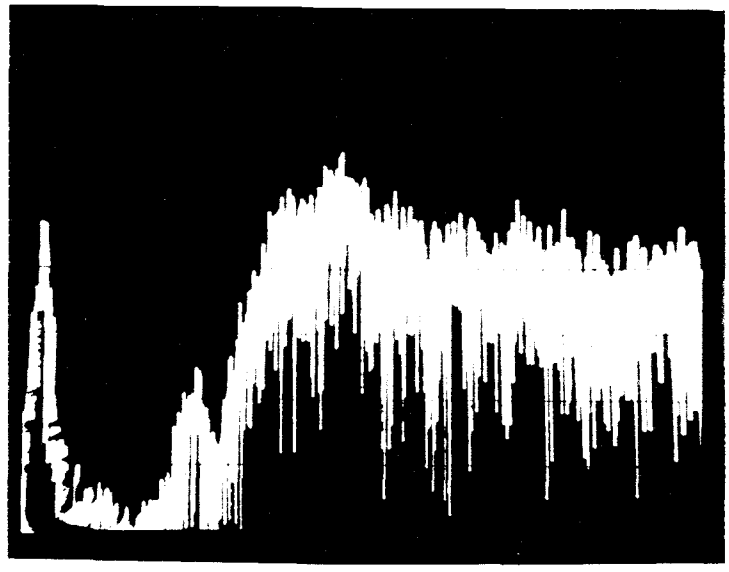

Figure 5. The spectrogram of the high-pass masking signal utilized for high-frequency ABR evaluation. Intensity (dB SPL re 20 $_{u}$Pa), ranging from 0 to 100 SPL is measured on the ordinate, and frequency, ranging from 0 to 20 kHz is measured on the abscissa.

Table 1

Mean Behavioral Thresholds and SD for Pure-Tones at All Tested Frequencies

	Frequency (kHz)												
Ear	.25	.5	1.0	2.0	4.0	8.0	8.0	10	12	14	16	18	20
R	27.67	11.17	7.17	8.17	13.50	23.17	22.00	23.83	33.67	52.83	78.00	91.67	NA
SD	2.58	4.92	3.76	6.65	4.18	5.85	3.16	6.65	6.06	19.85	9.10	2.89	NA
n=	6	6	6	6	6	6	6	6	6	6	5	3	1
L	26.00	11.17	3.83	5.67	14 17	19.50	19.83	23.00	29.00	52.50	83.00	85.75	NA
SD	3.16	3.76	2.04	7.53	7.36	9.87	4.92	3.16	9.49	19.69	9.62	2.50	NA
n=	6	6	6	6	6	6	6	6	6	6	5	4	NA

Note. n= Number of subjects responding to the tone.

R= right ear.

L= left ear.

One subject revealed like thresholds with the exception being the 14 kHz pure-tone threshold falling within two standard deviations of the mean.

Table 2 reveals mean behavioral tone-burst thresholds in SPL for all 16 treatments obtained at Period 1 (P1) and Period 2 (P2). For all treatments combined 96% (184 out of 192 cases) of the within-subject tone-burst thresholds were within ±5 dB when comparing P1 with P2. Of the 4% that were outside this range, thresholds were ±10 dB.

In connection with threshold data, all 60 dB sensation level (dB SL) measurements show similar results. Table 3 reveals mean 60 dB sensation levels measured in SPL for each treatment. For all treatments, regardless of frequency or rise-time, 96% (185 out of 192 cases) of the within-subject measurements were within ±5 dB when comparing P1 with P2. The remaining 4% were within ±10 dB. These findings indicate that the within-subject test-retest reliability for behavioral thresholds are in agreement with industry standards.

Further when evaluating within-subject tone-burst threshold change at each frequency as a function of rise-time, only 6% (3 out of 48 cases) revealed a threshold change greater than ±5 dB. These changes were no greater than 10 dB and were not repeatable from P1 to P2.

Between-subject threshold and sensation level similarities for each tone-burst treatment were not as closely matched, showing differences of 15 to 25 dB in SPL between subjects for each treatment. This is an expected finding due to the greater differences that exist in the normal population concerning high-frequency hearing acuity.

Table 2

Mean[a] Threshold and Range (dB SPL re 20 μPa) for Each Tone-Burst Treatment; Periods Combined

Rise-Time (msec)	Frequency (kHz) 8	10	12	14
.1	10.33	13.25	14.17	25.25
R	19	20	20	20
.25	11.92	13.67	15.84	21.62
R	15	20	25	25
.5	11.09	14.08	15.00	27.34
R	15	15	25	25
1.0	11.92	14.92	15.84	27.34
R	15	15	25	25

Note. R= Range from lowest reported threshold to highest reported threshold.

[a] N=12

Table 3

Mean[a] Presentation Level and Range Converted to dB SPL (re 20 μPa) for Each Tone-Burst Treatment; Periods Combined

Rise-Time (msec)	Frequency (kHz) 8	10	12	14
.1	70.25	73.67	74.17	85.33
R	20	20	20	20
.25	71.92	74.08	75.42	87.00
R	15	20	25	25
.5	71.08	74.50	75.00	87.42
R	15	15	25	25
1.0	71.92	75.33	75.83	87.42
R	15	15	25	25

Note. R= Range from lowest measured sensation level to highest in SPL.

[a] N=12

Design

This study is a fixed 3 factor, multi-level, repeated measures statistical design. The three factors are period, rise-time and frequency. Period is defined as the repeated collection of data on two separate occasions. Rise-time is evaluated at .1, .25, .5, and 1.0 msec. Frequency is evaluated at 8, 10, 12, and 14 kHz.

Statistical Analysis

Raw data in the form of absolute latencies for waves I, III, and V were categorized according to subject, treatment, wave, and period and thus entered into the computer for analysis. A number of responses at 14 kHz exhibited absent waves I and III. It is believed that the primary cause can be attributed to artifact interference from high intensity SPL's. In these particular cases only wave V could be detected in the evoked response. Due to these missing data points, the statistical analysis was completed for freqencies 8, 10, and 12 kHz only.

Data was evaluated using a computer formated Analysis of Variance with Repeated Measures. A factor for subjects was implicitly defined within the analysis format. In other words, the implicit subject factor was nested in the grouping factors and crossed with the within-subjects factors.

Further, a multiple comparison test evaluating adjacent and nonadjacent rise-time treatment means was applied to the rejected

null hypothesis for rise-time effect in order to locate significant differences. The results were used to formulate conclusions relative to the study.

CHAPTER IV

RESULTS

The purpose of this study has been to determine the existence of a significant relationship between certain acoustical characteristics of an auditory stimulus and the elicited (or evoked) auditory brainstem response (ABR). The results will be used to further evaluate the acoustical stimulus. The compilation of results will be used to determine the most appropriate stimulus for use in objective high-frequency audiological testing and monitoring procedures.

The ABR was repeatedly elicited from six normal hearing subjects (two males and four females, aged 25 to 33 years). Equipment used was specifically designed to generate and deliver high-frequency stimuli. A Nicolet 1170 evoked response signal averager was used to detect and measure the evoked responses. The unit allowed for floppy disk storage and chart recording of the responses for later analysis.

Responses were obtained using high-frequency (8, 10, 12, and 14 kHz) gated tone-bursts having rise-times of .1, .25, .5, and 1.0 milliseconds (msec) resulting in a total of sixteen different rise-time/frequency combinations. Duration was set at 2 msec. Intensity was maintained at 60 decibels (dB) above the subject's behavioral threshold (60 dB sensation level or dB SL) for each stimulus combination.

Once measured, evoked responses for waves I, III, and V were tabulated and entered into the computer for analysis. An Analysis of Variance with Repeated Measures computer program was applied to the

data. Entries were made according to period, treatment, and wave.

The program requires equal cell size. A number of responses at 14 kHz did not lend themselves well to interpretation. As there were missing data values at this frequency it was not included in the statistical analysis program.

This study was repeated twice. The analysis indicates that Period is not a significant variable. That is, the relationships illustrated, or lack thereof, are evident at P1 and P2. Period was not considered in the hypotheses statements and is therefore not included in the ANOVA Decision Tables.

Rise-Time

Tables 4, 5, and 6 reveal mean latencies and standard deviations for wave I, III, and V. Visual examination reveals a clear relationship between rise-time and latency. That is, as rise-time increases (becomes slower), latency increases (becomes longer).

Tables 7, 8, and 9 outline the statistical results for wave I, III and V absolute latencies. A significant relationship between rise-time and latency for each wave is revealed ($p < .01$).

The first hypothesis states that: there is no significant difference in mean absolute (waves I, III, and V) latency values when comparing the responses for each rise-time condition with one another at any given test frequency. Therefore in response, the null hypothesis is rejected. The relationship is that there is a significant difference in absolute latency measurements as a result of varying rise-time. As rise-time increases, latency increases

Table 4

Wave I Mean Latency and SD by Time Period for Each Treatment Combination

		Rise-Time (msec)							
		.1		.25		.50		1.0	
kHz		lat	SD	lat	SD	lat	SD	lat	SD
8	P1	2.06	.20	2.14	.19	2.22	.28	2.42	.30
	P2	2.14	.42	2.16	.20	2.25	.25	2.50	.28
10	P1	1.99	.34	1.98	.11	2.05	.26	2.30	.22
	P2	1.90	.16	1.96	.18	2.22	.19	2.34	.22
12	P1	1.98	.38	1.98	.36	2.06	.30	2.19	.20
	P2	1.82	.16	1.91	.19	2.02	.24	2.17	.23

Note. N=6.

lat= latency.

P1= period #1, P2= period #2.

Table 5

Wave III Mean Latency and SD by Time Period for Each Treatment Combination

		Rise-Time (msec)							
		.1		.25		.50		1.0	
kHz		lat	SD	lat	SD	lat	SD	lat	SD
8	P1	4.37	.33	4.34	.32	4.48	.27	4.65	.25
	P2	4.33	.26	4.39	.31	4.44	.30	4.78	.29
10	P1	4.30	.19	4.26	.31	4.40	.26	4.60	.25
	P2	4.26	.28	4.34	.23	4.48	.14	4.71	.23
12	P1	4.24	.25	4.34	.19	4.48	.26	4.60	.13
	P2	4.20	.32	4.27	.22	4.40	.26	4.51	.32

Note. N=6.

lat= latency.

P1= period #1, P2= period #2.

Table 6

Wave V Mean Latency and SD by Time Period for Each Treatment Combination

		Rise-Time (msec)							
		.1		.25		.50		1.0	
kHz		lat	SD	lat	SD	lat	SD	lat	SD
8	P1	6.16	.44	6.34	.30	6.48	.37	6.43	.45
	P2	6.29	.49	6.39	.34	6.48	.39	6.63	.38
10	P1	6.26	.43	6.24	.35	6.18	.40	6.56	.29
	P2	6.22	.34	6.39	.34	6.47	.25	6.65	.34
12	P1	6.12	.37	6.27	.38	6.47	.28	6.66	.23
	P2	6.13	.26	6.17	.37	6.36	.35	6.45	.19

Note. N=6.

lat= latency.

P1= period #1, P2= period #2.

Table 7

ANOVA Decision Table: Wave I

Source of Variation	DF	Computed F	Tabular F	Ho Decision
Rise-time	3,15	37.82	5.42**	Reject
Frequency	2,10	7.17	7.56	Retain
Interaction	6,30	0.85	3.47	Retain

Note. **$p < .01$.

Table 8

ANOVA Decision Table: Wave III

Source of Variation	DF	Computed F	Tabular F	Ho Decision
Rise-time	3,15	35.98	5.42**	Reject
Frequency	2,10	0.47	7.56	Retain
Interaction	6,30	0.72	3.47	Retain

Note. **$p < .01$.

Table 9

ANOVA Decision Table: Wave V

Source of Variation	DF	Computed F	Tabular F	Ho Decision
Rise-time	3,15	27.72	5.42**	Reject
Frequency	2,10	0.25	7.56	Retain
Interaction	6,30	1.04	3.47	Retain

Note. **$p < .01$.

across subjects.

As with any statistical analysis revealing a significant relationship involving more than two group means, further analysis is needed. Conclusions may be drawn once significant differences are located between treatment groups. The stated null hypothesis implies that a priori has been established. Therefore a multiple comparison test (see Table 16) has been used that allows evaluation between all treatment means.

Tables 10, 11, and 12 reveal mean inter-wave latencies and SD for I-III, III-V, and I-V. There does not appear to be a relationship between inter-wave latencies and rise-time. The statistical analysis, outlined in Tables 13, 14, and 15 indicate that there is an absence of any significant effect that rise-time has on this measurement.

The second hypothesis states that: there is no significant difference in mean inter-wave (I-III, III-V, I-V) latency values when comparing the responses for each rise-time condition with one another at any given test frequency. The decision has thus been made to retain this hypothesis. The conclusion is that there is no significant rise-time treatment effect on inter-wave latencies. No further analysis is necessary.

Frequency

The effect of frequency is not clearly defined by the analysis. The trend appears to be as frequency increases, latency decreases (becomes shorter). At a higher probability level this trend is

Table 10

Wave I-III Mean Latency and SD by Time Period for Each Treatment Combination

		Rise-Time (msec)							
		.1		.25		.50		1.0	
kHz		lat	SD	lat	SD	lat	SD	lat	SD
8	P1	2.31	.16	2.20	.19	2.26	.28	2.23	.29
	P2	2.19	.21	2.23	.17	2.19	.24	2.27	.20
10	P1	2.31	.27	2.27	.22	2.35	.18	2.30	.25
	P2	2.36	.26	2.38	.15	2.26	.28	2.38	.15
12	P1	2.26	.25	2.36	.24	2.42	.20	2.41	.21
	P2	2.38	.27	2.36	.24	2.37	.25	2.34	.40

Note. N=6.

lat= latency.

P1= period #1, P2= period #2.

Table 11

Wave III-V Mean Latency and SD by Time Period for Each Treatment Combination

		Rise-Time (msec)							
		.1		.25		.50		1.0	
kHz		lat	SD	lat	SD	lat	SD	lat	SD
8	P1	1.80	.26	2.00	.10	2.00	.22	1.78	.26
	P2	1.96	.28	2.00	.19	2.04	.28	1.85	.27
10	P1	1.96	.37	1.99	.07	1.78	.40	1.95	.25
	P2	1.96	.18	2.05	.22	1.99	.22	1.93	.17
12	P1	1.87	.27	1.93	.31	1.99	.25	2.06	.31
	P2	1.93	.17	1.90	.36	1.97	.23	1.94	.40

Note. N=6.

lat= latency.

P1= period #1, P2= period #2.

Table 12

Wave I-V Mean Latency and SD by Time Period for Each Treatment Combination

		Rise-Time (msec)							
		.1		.25		.50		1.0	
kHz		lat	SD	lat	SD	lat	SD	lat	SD
8	P1	4.10	.26	4.20	.13	4.26	.39	4.01	.45
	P2	4.14	.27	4.23	.17	4.23	.33	4.13	.36
10	P1	4.27	.14	4.26	.25	4.13	.47	4.26	.35
	P2	4.32	.27	4.43	.29	4.25	.27	4.31	.19
12	P1	4.13	.20	4.29	.21	4.42	.14	4.47	.19
	P2	4.31	.24	4.26	.37	4.34	.41	4.28	.21

Note. N=6.

lat= latency.

P1= period #1, P2= period #2.

Table 13

ANOVA Decision Table: Wave I-III

Source of Variation	DF	Computed F	Tabular F	Ho Decision
Rise-time	3,15	0.10	5.42	Retain
Frequency	2,10	1.69	7.56	Retain
Interaction	6,30	0.25	3.47	Retain

Note. $p < .01$

Table 14

ANOVA Decision Table: Wave III-V

Source of Variation	DF	Computed F	Tabular F	Ho Decision
Rise-time	3,15	1.41	5.42	Retain
Frequency	2,10	0.09	7.56	Retain
Interaction	6,30	1.23	3.47	Retain

Note. $p < .01$

Table 15

ANOVA Decision Table: Wave I-V

Source of Variation	DF	Computed F	Tabular F	Ho Decision
Rise-time	3,15	0.94	5.42	Retain
Frequency	2,10	2.29	7.56	Retain
Interaction	6,30	1.21	3.47	Retain

Note. $p < .01$

significant only for wave I. This pattern is not consistent for waves III and V. The statistical analysis indicates the absence of a significant relationship between frequency and latency at the .01 probability level.

The third hypothesis states: there is no significant difference in mean absolute (I, III, and V) latency values when comparing the responses for each test frequency condition with one another at any given rise-time. Therefore the null hypothesis is retained at the .01 probability level.

It should be noted that a significant relationship exists at a higher probability level but is not consistent for all major waves. It is customary to refrain from further analysis following a decision to retain a null hypothesis. However, it is apparent that frequency effects cannot be fully understood on the basis of the present study and are in need of further investigation.

The final hypothesis states: there is no significant difference in mean inter-wave (I-III, III-V, and I-V) latency values when comparing the responses for each test frequency condition with one another at any given rise-time. The statistical analysis did not reveal any relationship between inter-wave latencies and frequency. Therefore the null hypothesis is retained. The conclusion is that there is no frequency effect on inter-wave latencies. No further analysis is necessary.

Multiple Comparison Test Results

A multiple comparison test was administered in order to locate significant differences between rise-time treatments. Table 16 provides a graphic illustration of the pattern-like effect that rise-time apparently has on latencies.

The results indicate that adjacent compared rise-times do not as a whole exhibit significant differences at all wave peaks, nor at all frequencies. There is a trend however. Adjacent compared rise-times starting at .25 msec begin to reveal significant differences. The greatest occurrence of significant differences between adjacent rise-times is at the .50 - 1.0 comparison.

This "clustering" of the results continues as illustrated by the presence of significant differences at non-adjacent compared rise-times. As shown, the non-adjacent .10 - .50 comparison reveals significant differences found at all three waves but not consistently at all frequencies. However, the .25 - 1.0 non-adjacent comparison reveals significant differences in all but one instance. The most widely spaced comparison; that of .10 - 1.0; reveals significant differences at waves I, III, and V for all frequencies.

Table 16

Significant Adjacent and Non-Adjacent Comparisons Between Rise-Time Treatment Means

		Rise-Time Comparison					
Wave	kHz	Adjacent			Non-Adjacent		
		.1-.25	.25-.5	.5-1.0	.1-.5	.25-1.0	.1-1.0
I	8			X		X	X
	10			X	X	X	X
	12		X			X	X
III	8			X		X	X
	10			X		X	X
	12				X	X	X
V	8				X		X
	10			X		X	X
	12				X	X	X

Note. "X" indicates a significant difference in absolute wave latencies between two compared treatment means at a given frequency.

N=12.

$p < .01$

Chapter V

DISCUSSION

This study evaluates two components of a high-frequency gated tone-burst currently being considered for use in clinical testing and monitoring procedures. The purpose of this investigation has been to reveal the presence or absence of any effect that rise-time and frequency have on the auditory brainstem response (ABR).

Rise-Time

The results of the present study indicate that rise-time significantly affects the latencies of the three major wave components (I, III, and V) of the ABR at all test frequencies. That is, as rise-time is increased, absolute latencies increase. Inter-wave latencies were not shown to be significantly affected by rise-time.

The rise-time/latency function revealed in the present study is in general agreement with that reported in the literature. As in other studies, the rise-time/latency function described in the present study most likely resulted from a decrease in neural synchrony. It has been stated that when stimulus rise-time is increased, large group simultaneous neuronal discharge is delayed. It is postulated that two patterns develop as rise-time is increased: 1) nerve fiber discharge occurs more independently; and 2) groups of fibers discharging simultaneously are smaller. These patterns are

believed to be the primary cause of delayed peak latencies.

These changes in neuronal discharge patterns are reflected in the results obtained from the multiple comparison analysis. This pattern, clearly reflected in the table, leads to the conclusion that rise-time begins to measurably affect wave latencies between .25 and 1.0 msec and that this effect becomes greater as rise-time is increased. It would appear that the relationship is non-linear in that latency probably increases at a greater rate relative to rise-time. It has yet to be proven that at these rise-time levels the rise-time/latency function is deleterious on the evoked response using high-frequency tone-bursts.

Comparisons With Other Studies

Numerous studies investigating the rise-time/latency function have been reported. In all cases the exact parameters of the acoustic stimuli used varies significantly from the present study. Generally it is known that rise-time directly affects the acoustical energy present within the on-slope portion of a stimulus. It is also apparent that rise-time directly affects absolute peak latencies at all frequencies.

The present study discovers that rise-time significantly affects latency at higher frequencies. This relationship is not in complete agreement with that reached by Stapells and Picton (1981). They conclude that rise-time has less of an affect on latency at higher frequencies.

A direct comparison is limited due to study design differences.

The highest frequency evaluated in the Stapells and Picton (1981) study was 4 kHz. Rise-times were spaced widely apart with the fastest being 1.0 msec. Further, the stimuli were presented at 100 dB peak SPL. These differences are significant in that a separate frequency-sensitive segment of the organ of Corti was evaluated as to the effects of certain stimulus paramenters.

Frequency

Frequency effects were evaluated in the present study. The analysis did not reveal a significant relationship at the .01 probability level. A trend was seen in that a frequency effect was revealed for wave I ($p<.05$). There are a number of influential factors that may partially explain the lack of any clear frequency/latency function found in the present study.

First of all if frequency specificity is assumed, absolute latencies would shift according to frequency. That is, as the tone-burst center frequency is increased, the cochlear site of maximum displacement (or excitement) would shift closer towards the basal end. This would be reflected in shorter latency measurements. In a simple, strictly ordered system, all wave peaks would hypothetically shift accordingly.

This relationship is not clearly revealed in the present study. If the order and complexity of the human auditory pathway is considered, it may be possible to understand this result.

Wave I is thought to represent 1st order neuronal electrical activity from the cochlea to the brainstem point of entry. Subsequent

waves, such as III and V are thought to represent synaptic junctions located in higher nuclei. There is therefore a natural division of the pathway that may be reflected in the relationship seen at wave I but not at waves III and V.

First order neurons considered to be sensitive to high-frequency stimulation are shorter in length than are low frequency sensitive neurons. These frequency related length differences are present only within the VIII nerve region up to the first synaptic junction within the brainstem (Weber and Folsom, 1977). It is this VIII nerve area that the electrical activity represented by wave I is thought to arise from. From there frequency related length differences disappear. The pathway becomes very complex at this division. Some nerve fibers cross while others do not. A few even by-pass synaptic junctions and travel a straight path to a further nuclei. This complexity results in a number of nerve fiber length differences having no relation to frequency. Synaptic junctions thought responsible for the electrical activity represented by waves III and V arise from these higher level junctions.

This change from a strictly ordered, frequency related nerve fiber arrangement to a much more complex one might partially explain why a frequency/latency function is seen for wave I but not for waves III and V.

A compounding factor has to do with the anatomical arrangement of the auditory nerve fibers. The length of nerve fibers sensitive to the low and mid-frequency range differ by relatively greater amounts than those sensitive to higher frequencies. This is a direct result of the placement of nerve fibers along the organ of Corti. The

position of nerve fiber attachments corresponds to the logarithmic scale of the organ of Corti. This placement design results in progressively smaller nerve fiber length differences at the extreme basal end as higher octaves become crowded together. The high-frequency/latency function may theoretically become too small to measure between octaves using current technology.

One further comment involves subject differences. No two subjects are exactly alike. The frequency/latency function is highly dependent on the neuronal length factor. Minute subject differences may have erased the frequency/latency function. It is difficult to predict whether or not a larger sample size would weed out these small differences. Given that there is a slight trend that points to a frequency/latency function in the present study, it is worth pursuing.

Comparisons With Other Studies

Dolan and Klein (in press) have brought forth an interesting consideration dealing with acoustical stimulus envelopes. Their study indicated that at higher frequencies acoustical energy splatter may have caused a shift of the site of maximum displacement within the cochlea.

The shift was produced by decreasing the rise-time of the tone-burst stumulus thus increasing the amount of spectrum "splatter" in terms of frequency and intensity. The increase in splatter occurred in frequencies slightly below the "intended frequency" of the tone-burst. An even greater increase in the shift effect occurred when

intensity (in SPL) was increased. Intensity further increased the amount of splatter in the tone-burst spectrum. The combination of a faster rise-time and increased intensity using an 8 kHz center-frequency tone-burst was reported to produce a 2 kHz downward shift in the measurements. That is, instead of producing a maximum displacement at the 8 kHz site within the cochlea, the area sensitive to 6 kHz was thought to be stimulated. It was concluded that at faster rise-times and higher intensities, the stimulus had poorer frequency-specificity.

A problem arises when relating the effects of acoustical splatter to the evoked response. Reported studies do not state the amount of change that occurs in the spectrum of the stimulus as a result of the manipulation of rise-time and intensity. This is a direct result of the method of spectrum analysis used in that this analytical procedure does not evaluate the time domain; only intensity over frequency. What is needed is the ability to view and measure the spectra over time. Once changes in the acoustic spectra are measured, acoustical manipulation of the stimulus can be more directly related to differences in evoked responses. With this data in hand a more precise explanation of the rise-time/frequency/latency function can be proposed. However, equipment designed to quantify these changes is not widely available.

Although stimulus intensity in SPL was not controlled in the present study, it may have influenced the responses obtained. Stimulus intensity in the present study was held at 60 dB SL in order to control for differences related to SL reported in the literature. The absolute tone-burst SPL measurements between subjects varied 15

to 25 dB. This may or may not have significantly influenced the acoustic spectra of the stimulus. It does warrant further study.

Test-Retest Repeatability

One factor involving auditory evoked responses is within-subject differences. The industry standard for within-subject test-retest latency repeatability for normal ears is ±.2 msec. This standard deviation is based on evoked responses utilizing a click stimulus. A standard for frequency-specific stimuli has not yet been established.

It is known that tone-burst stimuli do not yet have the characteristics necessary to match the responses obtained with a click stimulus. Subject variability, both within and between, is expected and reported when frequency specific stimuli are used. With a small combined sample size this variability usually causes greater within- and between-subject latency differences, reflected in standard deviations greater than the ±.2 msec standard.

However, in the search for appropriate frequency-specific stimuli, the repeatability of the response in each individual must be considered. That is, the standard deviation must be held to the smallest value possible in order to insure the repeatability of the response over time for clinical use.

The present investigator proposes that the ±.2 msec industry standard for repeatability has merit when used as a comparing measurement in analytical studies. In order to determine the repeatability of the responses elicited in the present study, a mixed variable comparison was done (within session and P1+P2). All runs

were averaged and standard deviations calculated. These calculations were then tabulated according to subject, treatment, and wave. A count was made of those standard deviations less than or equal to the ±.2 msec standard across subjects for each condition, and subtracted from each total. The results were converted into percent. Waves I, III, and V exhibited very similar patterns. Therefore the scores were condensed together.

Table 17 summarizes the results. Percentages are given according to frequency and rise-time. It is apparent that a possible relationship exists between repeatability and rise-time across frequencies. Faster rise-times may elicit more stable responses. Further investigation might verify this.

Further Analysis and Investigative Needs

There are relationships revealed in the present study that are in need of further analysis. Attention should be paid to exploring the possible effects of other variables directly related to the present study. For instance, SPL differences between treatments due to subject variability may have influenced wave latencies. A three-way ANOVA incorporating SPL, rise-time, and frequency should be applied for this purpose. Further, a more detailed analysis of possible subject differences should be included.

The test-retest repeatability factor requires further study and higher level analysis. The repeatability/rise-time function might play an important role in the future when making recommendations concerning stimulus parameter choices.

Table 17

Mixed Variable[a] Percentage Score for ± .2 msec Test-Retest Repeatability for With-In Subject Absolute Latencies

	Rise-Time			
kHz	.1	.25	.5	1.0
8	94%	89%	83%	78%
10	83%	83%	67%	78%
12	89%	89%	72%	72%

Note. Percent scores for waves I, III, and V are calculated together.

[a]With-in session and P1+P2.

N=18

Further research is needed concerning stimulus parameters considered optimal for monitoring ABR wave morphology change over time. It is possible that in the desire for a cleaner acoustical spectrum exhibiting less energy splatter, the test-retest repeatability of the response may be sacrificed. Repeatability must be a considered factor in any study investigating drug treatment influences on evoked response. This concern points to the need for further study, both analytically and empirically.

Should repeatability reveal itself to be greatly influenced by rise-time, attention should be given to the proposed study outlined in Appendix I. Recent investigations question the use of extremely fast rise-times when seeking frequency-specific information. This dilemma may be solved by generating a clinical trial study.

Monitoring possible drug-induced changes in ABR wave morphology over time requires the evoking stimulus to be frequency-specific and highly repeatable. These requirements are needed in order to exhibit evoked response change as a function of drug treatment, not stimulus variability.

Therefore, it is proposed that two rise-times be evaluated: 1) a fast rise-time exhibiting good test-retest repeatability but exhibiting relatively less spectral purity; and 2) a slow rise-time characterized by a clean spectra but with relatively less test-retest repeatability. The repeatability of the stimuli using these two rise-times should be evaluated across frequencies in normal ears.

Once this data is gathered, a clinical trial can begin using matched controls and patients scheduled to receive ototoxic drug therapy. Both rise-times should be used when gathering evoked

responses over time. Following analysis of the data the conclusion might be that one or both rise-times (and their inherent characteristics) allowed early, accurate, and consistent detection of high-frequency hearing loss due to ototoxic drug use.

It is concluded that the complete rise-time/frequency/latency function has not been established for the entire length of the cochlea. Further, study differences have resulted in some confusion as to the preferred rise-time for general clinical use among investigators. Suzuki and Horiuchi (1981) stated that "there is considerable divergence of opinion among investigators as to the optimal rise-fall time for recording the ABR". The lack of agreement between studies indicates that further investigation is needed in order to come to a more succinct conclusion concerning stimulus parameter effects on ABR wave latencies. Rise-time being the most important consideration, this parameter should be given priority.

A broad study incorporating strict variable control should be proposed. A selection of frequencies should be chosen that incompasses the entire length of the cochlea. Rise-time selection should range from extremely fast to at least 6 msec. Rise-time spacing should increase in steps no greater than .25 msec.

Such a study may reveal a consistent picture of the effects of certain parameters on the evoked response. The rise-time/frequency/latency function may reveal itself to be a predictable phenomenon that may even lend itself to a theoretical equation.

A number of studies have already ventured to suggest appropriate rise-time choices for frequency-specific stimuli (Stapells and Picton, 1981; Suzuki and Horiuchi, 1981). Some are based on direct

evaluation, while others are estimates based on results at other frequencies. These choices do not always agree with one another.

Until all frequencies are evaluated under exact conditions in terms of rise-time effects on ABR wave latencies, the interactive effects of all the variables involved will remain unknown. It is therefore not practical to recommend appropriate rise-time choices for general clinical use unless directly evaluated and applied under exact conditions.

Another important factor mentioned earlier is the need for more precise acoustical measurements of the evoking stimuli. Changes in the temporal waveform and acoustic spectra of a stimulus should be quantitatively measured. These measurements can then be directly associated with resulting ABR wave latency changes. Precise measurements allow for better understanding of the effects of acoustical energy splatter regardless of the method used to generate the stimulus.

At such a time when the rise-time/frequency/latency function is better understood, broad normative studies can begin concerning standard deviations for frequency-specific test-retest repeatability. In the clinical setting, evoked responses using non-frequency-specific stimuli are compared to a normative standard deviation which has lead to the routine diagnostic use of the click-evoked ABR. It is now considered to be a valuable tool. This same documentation is needed for frequency-specific stimuli if consistent use is hoped for.

Summary

This study investigated the relationship between frequency, rise-time, and ABR wave latencies. It is concluded that there is a significant relationship between rise-time and absolute latencies for the three major Jewett peaks (I, III, and V). Further, it is concluded that frequency has a slight affect on wave I latency but not on waves III and V. Inter-wave latencies were not significantly influenced by rise-time or frequency.

The results are in agreement with other reported studies concluding that as rise-time increases, wave latency increases. There are no comparisons available at the present time concerning frequency effects in the high-frequency range. The trend seen at wave I is in agreement with reported studies in that as frequency increases, wave latency decreases.

The results of this study are not sufficient to recommend one best rise-time for the high-frequency range. It is suggested that the results of the present study be subjected to further statistical analysis in order to: 1) determine uncontrolled variable influences; and 2) determine the test-retest repeatability between rise-times.

It is proposed that further research is needed in order to: 1) determine the high-frequency tone-burst rise-time best suited for detecting auditory changes due to ototoxic drug insult; 2) better understand the over-all rise-time/frequency/latency function as it relates to stimulation site within the organ of Corti; 3) quantitatively measure and describe the effects of rise-time on the temporal wave-form and acoustic spectra of frequency-specific stimuli; and 4)

propose normative frequency-specific ABR test-retest standard deviations for wave latencies.

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APPENDICES

APPENDIX I

OVERVIEW: RESEARCH EFFORTS IN HFA AT THE VETERANS ADMINISTRATION MEDICAL CENTER AUDITORY RESEARCH LABORATORY PORTLAND DIVISION

One group of investigators has contributed a great deal of information to the field of High-Frequency Audiometry (HFA). Their first published articles dealing with HFA appeared in the Journal of Auditory Research and in the Journal of the Acoustical Society of America in 1979. However, initial research began a few years earlier.

During the 1976 annual convention of the American Speech and Hearing Association, this group of investigators headed by Steven A. Fausti reported on a study looking at the effects of Bumetanide on high-frequency hearing in humans (Fausti et al., 1978).

Although it was found that there apparently was no effect, the important highlight of the study was the development of a high-frequency test system that proved to be superior to the high-frequency audiometery available at the time. Several major improvements were developed including a greater signal-to-noise ratio, greater maximum power output, improved earphone design, and simplified calibration requirements (Fausti et al., 1979b).

As a result of these advancements a protege was developed independently by a medical instrument manufacturer based on the design created by Fausti and his associates. This high-frequency audiometer (Demlar 20k) is now being used by other investigators (Tange et al., 1985).

It has been the intent at this research center to develop equipment and methods to test high-frequency sensitivity using standardized techniques and test methods. Fausti et al., (1979a) states that "although various systems have been proposed for evaluation of high-frequencies, few utilize standard clinical procedures". Because of this concern an important preliminary study was completed that dealt with the method used to obtain behavioral pure-tone high-frequency thresholds.

The modified Hughson-Westlake technique (Carhart and Jerger, 1959) is an approved test method used extensively in clinical practice in determining hearing thresholds for frequencies in the conventional range (.25 - 8 kHz). Because of its common use, this method was chosen to undergo rigorous testing to document its validity against a scientific detection theory considered to be the best available for studies concerned with sensory events (Clarke and Bilger, 1973; Green and Swets, 1966). This theory is called the two-alternative forced choice (2AFC) procedure.

It was found that high-frequency (8 - 20 kHz) behavioral thresholds obtained with the modified Hughson-Westlake technique were not significantly different from those obtained with the 2AFC procedure. It was therefore concluded that the standard clinical test protocol used at this research center, as well as in many other settings, was a valid and feasible method to use in behavioral testing of high-frequency sensitivity (Fausti et al., 1979a).

The next series of articles generated (Erickson et al., 1980; Fausti et al., 1981a, 1981b) dealt with the effects of noise exposure upon human hearing sensitivity in the high frequencies. It has been

documented in human and animal studies, that the effects of noise exposure causes functional and histological changes, correlated to and observed at the basal turn of the cochlea (Dolan et al., 1975; Fried et al., 1975; Hawkins et al., 1976; Lipscomb 1972; Spoendlin, 1976). Because this region has been shown to be sensitive to the higher frequencies it was postulated that "high-frequency testing from 8 - 20 kHz may permit earlier detection of changes in auditory sensitivity than when lower frequencies are monitored exclusively" (Fausti et al., 1981b).

Two major findings were reported in these studies on noise induced hearing loss (Erickson et al., 1980; Fausti et al., 1981a; Fausti et al., 1981b). First was the observation that the audiometric configuration through the conventional frequencies could not reliably predict the configuration in the higher frequencies for either normal or noise exposed subjects. The second was that regardless of the type of noise exposed to (steady state or impulsive), extensive threshold shifts were observed in the higher frequencies, with the greatest shifts occurring at or above 15 kHz. Due to the unpredictable nature of pure-tone thresholds through the conventional test range, and the reduced high-frequency thresholds exhibited by the noise exposed subjects, it was concluded that HFA monitoring of noise-exposed persons "holds promise for better early detection, description, and differentiation of noise-induced hearing loss" (Fausti et al., 1981b).

As a result of the growing interest in HFA and the possible applications being suggested, it was felt that more study was needed on the technical aspects of HFA before further extensive work was

continued on the application of this test protocol. Subsequently two articles were published, one documenting the validity of high-frequency audition, and the other investigating the interaural attenuation factor for the high-frequency stimuli being used at this research center.

The validity of frequency-specific audition has been domonstrated for frequencies through the conventional range below 8 kHz (Greenwood, 1961; Scharf, 1970). It was felt that a similar study was needed for auditory perception above the conventional range, particularly since it had been demonstrated that the cochlea may be capable of producing nonlinear distortion products at high intensities in animal studies (Dallow, 1966). This discovery suggested the possibility that the perception of high-frequency stimuli may be due to some cochlear distortion artifact, particularly at high intensities, thus calling into question the validity of high-frequency audition.

"The purpose of this research was to determine the effects of narrow-band masking on high-frequency, pure-tone stimuli as the center frequency of the masker was shifted away from the pure-tone" (Fausti et al., 1982). This method used to document the validity of high-frequency audition is the same method used to document audition for frequencies below 8 kHz. It is based on the observation that when a pure-tone stimulus, perceivable in quiet, is ipsiliaterally embedded in a narrow band of noise, at a specified s/n ratio, and has a center frequency that matches the pure-tone stimulus, the behavioral threshold for that pure-tone stimulus is significantly decreased. As the center frequency of the noise band is sequentially lowered, the pure-tone threshold increases in a predicatable manner

until it matches the threshold obtained in quiet. This phenomenon is called "release-from-masking" and demonstrates that the test subject is perceiving the stimulus in question, not some cochlear distortion artifact (Dallos, 1966; Greenwood, 1961; Scharf, 1970).

The results of the high-frequency validity study established that the "release-from-masking" effect can be seen at higher frequencies in the same predicatable manner as in the conventional range. It was therefore demonstrated that the behaviorally obtained high-frequency responses were valid.

Interest in HFA generated by these and other investigators continued to increase. It was felt at that time that a study concerned with HFA equipment specifications was needed. The results could be used by other investigators for comparison purposes.

An important factor dealing with equipment specifications and design is a phenomenon known as interaural attenuation (IA). Under normal testing conditions, if a sound presented to one ear is sufficiently loud enough, the contralateral ear will perceive that sound (known as the "cross-over response"). However, the sound wave must travel a distance in order for cross-over hearing to occur. As it travels to the contralateral ear, sound energy is dissipated. When the sound wave finally reaches the contralateral ear, the sound energy of the wave will be attenuated. The amount of this attenuation is measured behaviorally and stated in decibells. The degree of attenuation depends on a number of factors, including the nature of the sound, its intensity, individual physiological differences involving tissue density and mass, and equipment design; specifically headphone transducer design (Zwislocki, 1953).

A study was therefore completed on the interaural attenuation factor for frequencies above 8 kHz using the Koss HV/1A earphone specifically designed for high-frequency testing. This earphone was chosen to be used with the high-frequency equipment designed by Fausti and his associates because of its relatively flat frequency response in the 8 - 20 kHz range. An added feature was the conventional manner in which it is coupled to the subject's head. Further, the transducer can be driven at 8 V rms, and it allows for standardized calibration methods.

The results obtained revealed that the IA factor for this headphone was much less than that commonly specified for conventional audiometric equipment. This conclusion highlighted the fact that habitual use of common clinical formulas, such as the IA factor, may not be appropriate when using equipment in which the design and/or resulting generated stimuli deviates from conventional equipment (Rappaport et al., 1982).

Following these investigations, a major study at this research center was completed designed to obtain system-specific normative data on high-frequency hearing acuity (Schechter et al., 1986). The results support the belief that there is a gradual diminution of high-frequency sensitivity associated with age and environment. It was also concluded that development of national normative threshold data should be delayed due to the lack of standard equipment and calibration procedures. Instead it was suggested that high-frequency measurements should be applied as a monitoring technique on populations at risk for developing hearing losses due to noise exposure, ototoxic drug intake, and other known causes of high-

frequency hearing loss.

A concentrated effort was initiated to apply HFA to audiometric monitoring of patients on ototoxic drug therapy regimens. Initial work utilized behavioral measuring procedures. This effort resulted in three published articles (Fausti et al., 1984a; 1984b; Rappaport et al., 1986) describing the use of the high-frequency equipment and test protocol in obtaining data on the ototoxic effects and rate of occurrence for aminoglycoside type antibiotics, and an antineoplastic agent (used in treating certain types of cancer) known as Cisplatin.

There were two major findings disclosed from these studies. The first was that auditory changes due to ototoxic drug side-effects can be detected earlier with the high-frequency test protocol then when conventional audiometric testing is used alone. The second was that if changes in high-frequency thresholds are used to determine the rate of occurrence of ototoxicity inherent in these drugs, that rate is higher then has been previously reported.

Studies are continuing to focus on high-frequency hearing loss as a result of cochlear pathology, in particular that associated with middle ear disease (otitis media) and ototoxic drug insult. A proposed co-operative study is currently under review that entails behavioral monitoring of patients on ototoxic drug regimens on a much wider scale at a number of sites in the United States.

The research in HFA at this facility is now focusing on applying HFA to the auditory brainstem response, which actually is an outgrowth of the earlier studies looking at drug-induced auditory changes as measured by high-frequency behavioral audiometry (Fausti et al., 1985). Pilot studies were presented during the 1985 American

Speech/Language and Hearing Association (ASHA) convention highlighting the work accomplished and reporting on case studies using the ABR test protocol (Rappaport et al., 1985).

An investigation is now under way to systematically apply this test protocol in a hospital setting. Along with preliminary studies dealing with stimulus generation the following research questions and objectives have been encorporated into the design (Fausti et al., 1985).

The research questions being investigated are:

1. Can a change in hearing sensitivity caused by ototoxic drugs produce concurrent change in the ABR?

2. How much change in hearing sensitivity must occur in order to observe change in the ABR?

3. Is there a most effective stimulus for eliciting the ABR to provide early detection of ototoxicity?

4. Can the ABR evoked by high-frequency tone-bursts be an effective monitoring tool that provides early detection of ototoxicity in the non-responsive patient?

The objectives of the study are:

1. During the first three years of this study, the ABR and behavioral auditory threshold data in responsive patients receiving ototoxic drugs and their controls will be documented before, during, and after treatment using established laboratory instrumentation. Changes in behavioral auditory function will be compared to various parameters of the ABR, such as absolute

latencies of Waves I, III and V, interwave latencies of Waves I, III and V, Wave V threshold, and general morphology of the ABR waveform.

2. Concurrently during the first two years, miniaturized, portable, high-frequency stimulus-generating instrumentation that incorporates stimulus parameters and testing technique used with laboratory ABR equipment to detect change in auditory function will be designed, developed, fabricated and documented on normal listeners.

3. During the third year of the study, the ABR test protocol and miniaturized instrumentation will be examined with responsive patients and their controls under laboratory conditions.

4. During the fourth year of the study, the ABR test protocol and miniaturized instrumentation will be tested on the wards with responsive patients and their controls.

5. During the final year of the study, the ABR test protocol and instrumentation will be documented with non-responsive patients and their controls on the wards.

APPENDIX II.

PRELIMINARY SCREENING PROCEDURES

Acoustic Immittance testing consisted of tymponometry and contralateral acoustic reflex thresholds at .5, 1, 2, and 4 kHz using a 226 Hz probe tone. The automated T&R mode was utilized for these tests.

Pure-tone air-conducted thresholds through the conventional (.25 - 8 kHz) range were determined using the modified Hughson-Westlake technique (Carhart and Jerger, 1959) in 5 dB steps. High-frequency thresholds (8 - 20 kHz) were likewise established in 2 dB steps (Schechter et al., 1986). All threshold levels were reported in dB SPL.

Click-evoked responses were obtained using standard procedures (Jacobson, 1985). Click-evoked responses (two runs per subject), were presented at 60 dB SL, using a 10 msec window, sampled 1024 times. Following placement of the conventional ABR earphones, a stimulus threshold for an unfiltered click with an 11.1/sec repetition rate was obtained using the modified Hughson-Westlake technique in 5 dB steps. To rule out the participation of the non-test ear contralateral masking was presented at a +20 dB signal-to-noise ratio. Each run was averaged and stored for later analysis.

APPENDIX III

INFORMATION ABOUT AND INFORMED CONSENT FOR THE RESEARCH PROJECT ENTITLED "THE EFFECTS OF RISE-TIME AND FREQUENCY ON THE AUDITORY BRAINSTEM RESPONSE"

The above named research project is under the direction of Dr. Stephen A. Fausti, Ph.D., Chief of Audiology at the Veterans Administration Medical Center, Portland, Oregon (PVAMC). This investigation has been reviewed and approved by the appropriate agencies of the PVAMC.

The purpose of the above named investigation is to obtain greater knowledge about hearing function from objective evoked responses to high-frequency stimuli. Those persons participating in this study will receive no monetary benefit from these tests.

All information obtained will be kept confidential. Anonymity will be assured by the use of code numbers. Records for this investigation will be kept in the Auditory Research Laboratory, PVAMC.

First, the investigator will look in the subject's ears with an ear light to check for wax or other substances or obvious conditions which could interfere with the tests to be conducted. Next, three silver oxide cup electrodes will be placed on the subject's head; one

on the vertex (crown), and one on each mastoid prominence (behind the ears). These electrodes will be attached to an evoked response signal averaging computer. Headphones will then be placed on the subject's ears, and subject will be asked to listen and respond to tones of differing pitches at a level of loudness where the tones can barely be heard (threshold). After thresholds are obtained, another procedure will be accomplished in which the subject will be asked simply to listen to tone-like stimuli at supra-threshold levels. For this procedure, no response is required from the subject. In fact, the subject may sleep for this procedure. Procedures utilized are the same as those used in accepted clinical practice, except to extend the frequency range of hearing tested. There are no known or expected risks involved in these hearing tests.

It is not the policy of the agency funding this research project in which you are participating to compensate or provide medical treatment for human subjects in the event the research results in physical injury. If you suffer any injury from the research project, compensation would be available only if you establish that the injury occurred through the fault of the Veterans Administration, their officers, or their employees. Eligible veterans are entitled to treatment at any VA Medical Center, and compensation (damages) may be payable under 38 U.S.C. 351, or, in some circumstances, under the Federal Tort Claims Act. Compensation for non-eligible veterans and non-veterans would be limited to situations where negligence occurred, and would be controlled by provisions of the Federal Tort Claims Act. For further information about laws, regulations, or

policies, contact Federal District Counsel at (503)221-2441.

I understand that if any significant changes in hearing function are noted as a result of these tests, I will be notified as soon as possible. I understand that it is my right to withdraw participation in this investigation at any time.

Dr. Stephen A. Fausti or his representative has offered to answer any questions about participation in this study that I may have. I have read the foregoing statements, I feel that I understand them, and they have been explained to my satisfaction. I herewith agree to participate as a subject in this study.

_____	_____
Subject's Signature	Signature of Witness
_____	_____
Subject's Address	Address of Witness
_____	_____
Signature of Investigator	Date Signed