Estimation of Hearing Sensitivity using the Auditory Brainstem and Auditory Steady State Responses

A Senior Honors Thesis

Presented in Partial Fulfillment of the Requirements for graduation
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by

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Abstract

The Auditory Brainstem Response (ABR) and the Auditory Steady State Response (ASSR) are evoked electrophysiologic responses, which are used to estimate hearing sensitivity and assess the integrity of the auditory system. The two techniques differ in the nature of their evoking stimuli and therefore potentially in the quality of the diagnostic information they yield. The ABR utilizes short duration stimuli (<5 msec) while the ASSR response is evoked with long duration (~1000 msec) stimuli modulated in amplitude, frequency, or both. The ABR has been in clinical use since the 1970s and has a substantial literature to support its efficacy, while the ASSR is a relative newcomer and comparable efficacy to the ABR has not yet been established. In particular, there is still a paucity of data demonstrating whether the ASSR is a better predictor of pure tone thresholds than the ABR.

The present study investigates this by acquiring pure-tone audiometric results, ASSR thresholds, and ABR thresholds in a sample of 9 normal-hearing young adults. Subsequent to inclusionary testing, ASSR and ABR thresholds were estimated at 1, 2, and 4 kHz using a two-channel differential recording. Blackman-windowed tonepips were utilized as the basis for both ABR and ASSR data acquisition. If both recording channels were considered and the tonepip stimuli were equated for peak-equivalent SPL, the ASSR and ABR thresholds showed no effect for frequency. However, there was no evidence of a significant correlation between the ABR and ASSR thresholds. The ABR recordings were more consistent across the two channels than the ASSR waveforms. Further, the ASSR revealed a non-monotonic relationship between the number of acquisitions and response detectability, while the wave V SNR in the ABR was essentially a monotonically increasing function of the number of acquisitions. There is no compelling evidence based on this study that the ASSR offers any clear advantage over the currently-established auditory brainstem response.

Acknowledgements

I would like to thank and acknowledge Dr. Wayne King for all of the support and guidance throughout my research study. Dr. King was an essential element and without his time and effort this endeavor would never have been successful. I would also like to acknowledge and thank Dr. Janet Weisenberger for always being available to help with any question or concerns regarding my research. I would like to extend my gratitude and appreciation to all of my subjects who volunteered their time, making it possible to conduct my research. Finally, I would like to thank my family and friends for their understanding and constant support.

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Chapter 1: Introduction and Literature Review

In order to develop normal communicative abilities, the human ear must be capable of detecting extremely low-level oscillations in the average air pressure across a 3-4 kHz bandwidth. Research has demonstrated that it is especially critical to identify hearing loss early and precisely in pediatric populations in order to avoid language delays (Yoshinaga-Itano, 1998). The earlier hearing loss is identified and the more aggressively it is remediated, the better the prognosis for the cognitive development of the child. Specificially, auditory deterioration in infants and children with early hearing loss is reduced by clinical intervention within six months after birth (Rance, 2002). To evaluate hearing sensitivity in this population, nonbehavioral measures are needed. One major class of nonbehavioral techniques is auditory evoked potential testing. Electrophysiological testing methods are also used to assess other populations that are unable to give a behavioral response, e.g. malingerers, persons with cognitive impairment. For these reasons, electrophysiologic measures have become an important part of the audiologic testing protocol.

1.1 Evoked Potentials

Activity within the auditory nervous system is elicited by stimulation with sound. Auditory evoked potentials (AEPs) are extremely small electrical potentials that originate from the brain in response to an auditory stimulus and are volume-conducted to the skin where they can be detected by an electrode array. Changes across the neuronal cell membrane are the basis for these and all other propagating electric potentials in the nervous system (Bell, 2003). The transmembrane ion movements which are a precursor of the action potential create relatively more negative and positive areas along the neuron (Bell, 2003). These current “sinks” and “sources” allow the neuron to be modeled as an electric dipole (Hall, 2007). A dipole is created by the resulting electrical field with a negative “terminal” at one end and a positive “terminal” at the other. We can associate with each dipole a vector quantity called the dipole moment. The dipole moment, P, is defined to be the product of the charge, q, and the displacement vector, r, from the negative to the positive terminal (by convention), or P=qr. The dipole moment for a system of dipoles is the sum of the individual dipole moments.

$$P=\Sigma_i q_i r_i$$

From the above, we see that if the displacement vectors are pointing in the same direction, then the magnitude of the resulting displacement vector will be the sum of the individual magnitudes. On the other hand, if the displacement vectors are not pointing in the same direction, then by the triangle inequality, the displacement vector resulting from the sum will be less than the sum of the individual dipole moments. Since each individual neuron produces a very small dipole moment, it is necessary to have a large enough resultant dipole moment to be detectable. This is especially true when doing a *far-field recording*.

Far-field recordings of neural activity are done by placing an electrode array placed on the scalp. This method of recording is overwhelmingly the method of electrophysiologic recording done in clinical audiology because it is the least invasive. However, the use of far-field recordings presents a number of limitations. The physical distance between the electrode and the evoked dipole activity is large in comparison to the dipole magnitudes. This mandates that there must be a large number of dipoles coherently aligned and synchronized to produce a net dipole moment large enough to be recordable at the scalp. Secondly, “nuisance” dipoles resulting from other neural activity within the brain not evoked by the stimulus also produce dipole moments observable at the electrodes. It must be noted that the time-varying voltage observed by a pair of electrodes represents a sum of volume-conducted activity from many dipoles. In order to overcome the aforementioned problems with far-field recording, we can average and filter the individual responses. The ability of evoked potential recordings to “lock on” to a stimulus with respect to time leads to an improvement of the signal-to-noise ratio (SNR) when large numbers of trials are averaged. The idea is that electrophysiological activity not locked to the stimulus will tend to average to zero. Similarly, a priori knowledge about the spectral characteristics of the evoked potential may allow us to enhance the SNR by filtering. The characteristic patterns of many auditory evoked potentials result in distributions in the frequency domain localized higher in frequency than the classic EEG bands. The EEG activity is larger in magnitude than the evoked response because it originates from cortical neurons closer to the recording site. Fortunately, we can high pass filter the input to lessen the impact of the EEG activity. Near-field recording is the placement of electrodes within the brain or the auditory periphery to obtain data that originates much closer to the dipoles. Near-field recording is often used with animals and can attain detailed information associated with the evoked potentials but is not generally possible in clinical populations. The rare exception is its use in intraoperative monitoring. Herdmann (2002) showed that near-field recording was much more accurate in estimating hearing threshold due to the location of electrode placement.

1.1.2 Differential Recording

The most common recording technique for auditory evoked potentials is called a *differential recording*. Voltage is electric potential and therefore is measured from one point to a reference. In electrophysiologic recordings this is often confusingly referred to as the *ground*. Differential recordings obtain the time-varying voltage between two pairs of electrodes with one of them being a common reference. Then, one of the recordings is *inverted*, or scaled by negative one and added to the 2nd recording. The resulting single waveform is the differential recording because it is the difference between what is observed at the two *channels*. The recording scaled by (-1) is referred to as the *inverting* channel while the other channels is termed *noninverting.* This method is used because real evoked activity should not have identical signal characteristics at two different electrodes. On the other hand, 60-Hz electrical noise should produce essentially the same recordings at all electrode sites since the electric field is large compared to the size of the head. The differential recording scheme should therefore facilitate a canceling of the 60-Hz artifact. This is referred to as *common mode rejection*. One assumption in the differential recording scheme is that the reference electrode is neutral with respect to the evoked activity. In practice this ideal situation is not always accomplished because of constraints on the placement of the reference electrode. This issue is discussed further in the Methods section of this paper.

1.2 Transient-evoked vs Steady State Evoked Potentials.

In evoked potential testing, there are two general methods of stimulus presentation and data acquisition. In the *transient-evoked* method, each recorded response represents the neural activity evoked by a single stimulus. This of course assumes that the stimuli are presented at a rate which allows the response to terminate before the next stimulus presentation. As an example, assume we know based on physiologic considerations that evoked activity arising from the brainstem and the auditory periphery will occur within 15 msec after the stimulus. In other words, if we present one 0.1 msec click to the ear at a sufficient level, then the dipole moments evoked specifically by that activity will occur within a 15-msec window following the presentation of the stimulus. Suppose now that 20 such clicks are presented per second. This means that there will be a 50-msec interval between each 0.1 msec click stimulus. Further, suppose that we record the electrical activity that occurs up to 15 milliseconds after the stimulus. Electrical activity that occurs in the 35-msec interval between the end of the acquisition window and the next stimulus is ignored. In Figure 1, we illustrate a transient-evoked acquisition for these parameters.

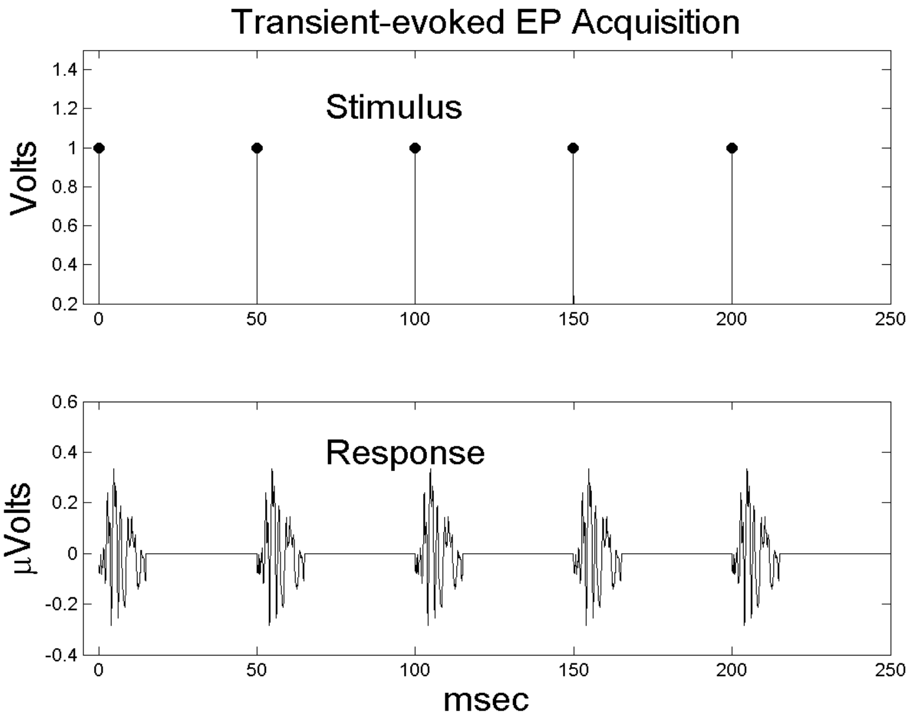

Figure 1: Top: Representation of the stimulus presentation waveform where each nonzero value denotes a 0.1 msec click stimulus presented at a rate of 20 clicks/sec. Bottom: Representation of response recordings where a 15-msec post-stimulus epoch is recorded.

To determine the final waveform, each of the individual responses are averaged. The idea is that each recording represents activity evoked by only one stimulus. This is the definition of a transient-evoked EP response: only one stimulus is presented in each acquisition window.

Steady state responses are said to occur whenever there is more than one stimulus presented in each acquisition window. According to the above scenario, if the click stimuli were presented at a rate above 66 per second, the interval between the stimuli would be less than 15 msec. In that case, a 15-msec recording window would presumably record activity evoked by more than one stimulus.

1.2.1 Auditory Brainstem Response (ABR)

The auditory brainstem response (ABR) is the most frequently used auditory evoked potential. It is an example of a transient-evoked response. The ABR consists of a series of 5-7 peaks in the time-averaged waveform to click stimuli observed in an approximately 10 msec post-stimulus recording. This response reflects auditory activity from the cochlea to the midbrain. These peaks are positive polarity peaks when the noninverting electrode is located along the midline of the top of the scalp. By convention, the waves are designated by Roman numerals. Clinically, the most significant ABR peaks are designated wave I, III, and V. In reality, waves III and V are often combinations of wave II-III and waves IV-V respectively (Stapells et al., 2005). The specific anatomical contributions to these waves remains a matter of investigation, but it stands to reason that the earlier waves are localized much more precisely than those appearing later in the recording. A typical human ABR recording is shown in Figure 2.

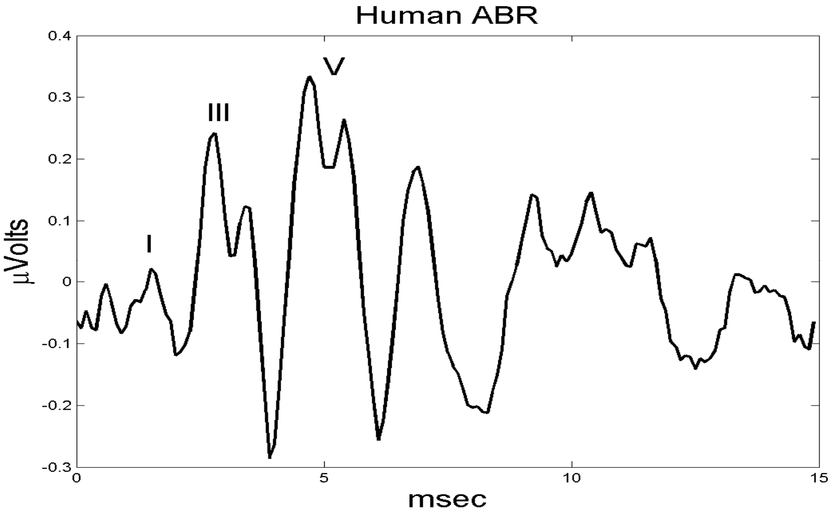

Figure 2: ABR waveform recorded in a normal-hearing adult.

The main advantage of the ABR is that it is robust with respect to the attentive state of the subject. This makes ABRs easily recordable in sleeping or sedated subjects and is not true of other evoked responses, especially cortical ones.

Identification of the ABR waves and measurements of their latencies are the two major clinically-significant measures. Latency measurements are used in neuro-otologic applications, while identification of wave V (or the IV-V complex) is used in threshold estimation procedures (Hood,1986). Wave V is the most robust ABR wave with respect to stimulus rate and intensity. Latency of wave V is not considered per se in threshold estimation procedures, but the identification of wave V is aided by the fact that latency increases as stimulus intensity decreases (Hall,2007; Hood,1986).

While the ABR is a powerful technique with a substantial literature documenting its effectiveness, it has limited frequency specificity due to the short-duration stimuli used to evoke it. The most common stimulus in ABR testing is a 0.1msec click. This stimulus has been found to stimulate enough neurons that the resulting net dipole moment is large enough to reliably record at the scalp. Further, it is thought that the human ABR is biased toward the high frequency part of the cochlea where the phase dispersion of the traveling wave patterns evoked by the click elicit the most synchronized activity. Toneburst ABRs are elicited with *windowed* tonepip stimuli that are typically five cycles of a specified sinusoid (Hall, 2007). While the frequency support of these stimuli is narrower than a click, they still contain energy spread over a more considerable range than a long-duration tone. In Figure 3, a five-cycles of a Blackman-windowed 2 kHz tonepip is shown along with its power spectrum.

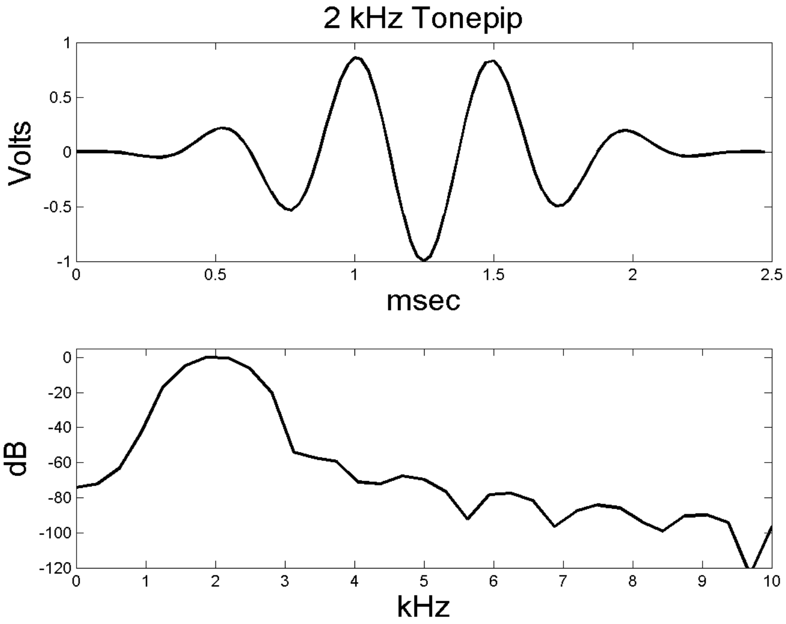

Figure 3: Top: 2 kHz tonepip (5 cycles) multiplied by a Blackman window.
Bottom: Power spectrum normalized to have the peak power equal 0 dB.

An inspection of the power spectrum shows that while the energy distribution is centered on 2 kHz, the central lobe is fairly wide. Still, several studies have advocated the use of tonepip stimuli in threshold estimation (Stapells, 2005).

1.2.2 The Auditory Steady State Response (ASSR)

When the term “steady state response” is used today in audiology, it typically refers to a steady-state response evoked by stimuli modulated in amplitude, frequency, or both (Herdman, 2002). The response is determined by detection of significant energy at the modulation frequency in the electrophysiologic waveform in the frequency domain. In most cases, these are sinusoids which are sinusoidally amplitude (SAM) or frequency modulated (Stapells et al., 1984). In the case of a SAM stimulus, the power spectrum of the stimulus does not contain energy at the modulation frequency. This is appealing because it removes a potential confound. If the stimulus contains energy at the modulation frequency, then it is possible that a “bleed over” effect from the electromagnetic transducer could be detected by the electrodes and registered as a response. Some of the earliest work on the human ASSR utilized tonepip stimuli which were repeated at a high rate. These stimuli are similar to those used in ABR, except that they are presented at a rate exceeding the transient-evoked limit of the acquisition (Picton et al., 1984). In this case, a Hilbert transform of the stimulus can be used to reveal the modulation envelope as shown in Figure 4.

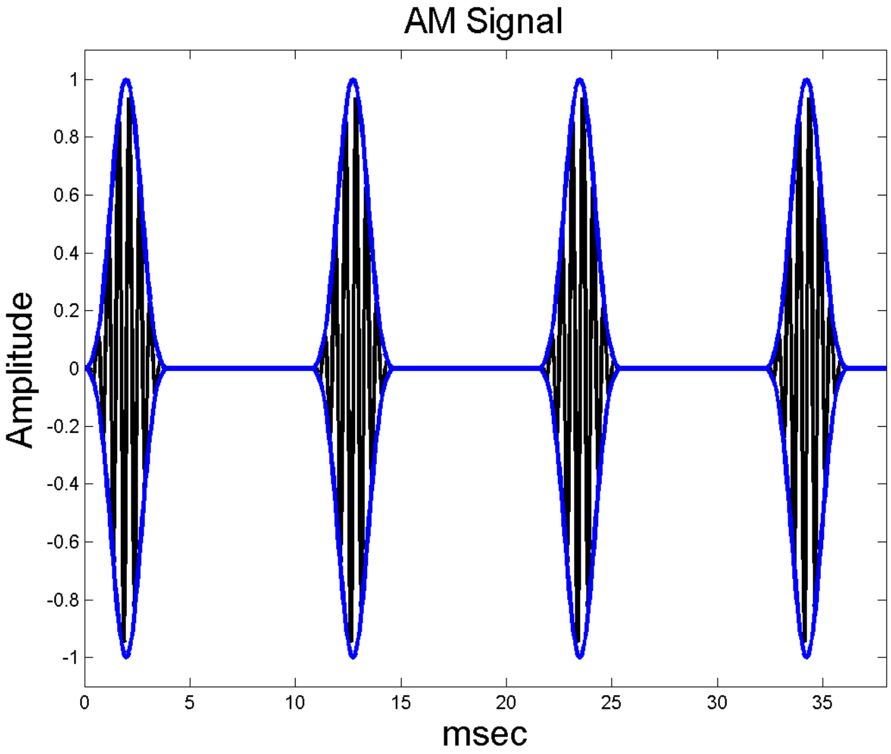

Figure 4: Blackman-windowed 2 kHz tonepips 4 msec in duration and presented at a rate of 93 per second. The envelope was extracted by taking the Hilbert transform of the signal, then taking the modulus (absolute value) of the resulting analytic signal. The detection problem would be to find 93 Hz in the electrophysiologic waveform.

In Figure 5, a power spectrum estimate of the stimulus in Figure 3 is presented.

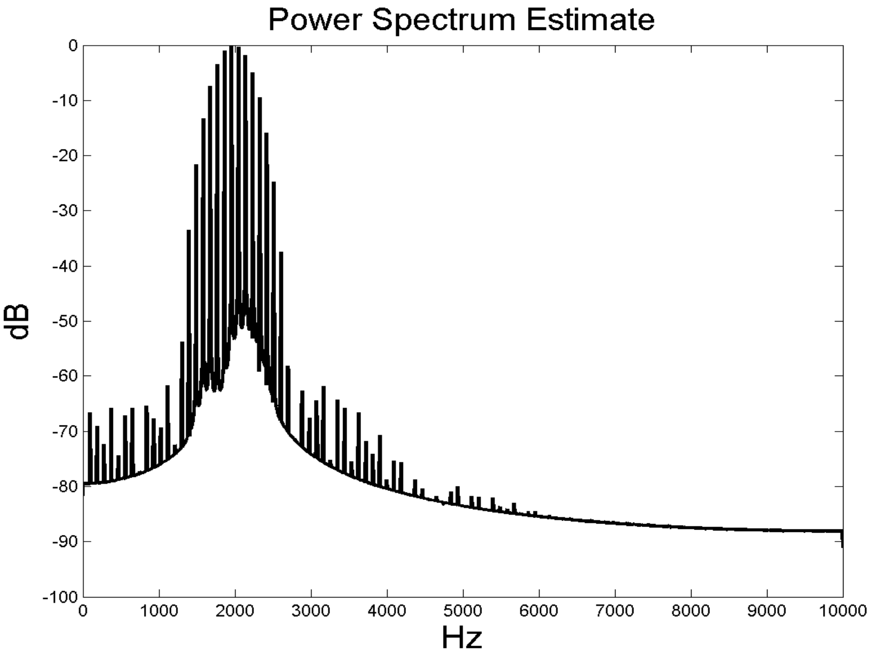

Figure 5: Power spectrum estimate of stimulus shown in Figure 3. Welch's overlapped segment averaging technique was used. Note the line components spaced at 93 Hz.

If the modulation (repetition) rates are between 70-110 Hz, the human ASSR is thought to be dominated by brainstem generators similar to the ABR. However, few studies have attempted to compare characteristics of the ASSR and ABR. There are a number of problems inherent in any such comparison. Firstly, the ABR is typically evoked with much different stimuli than the ASSR. Secondly, even if the ABR and ASSR can be placed on somewhat even footing by using tonepip stimuli, the method of signal detection is completely different. ABR waveforms are nonstationary signals and the signal detection problem of identifying a peak in the time waveform is not suited to analysis in the frequency domain. On the other hand, ASSR results in stationary signals and requires estimation of the power contained at a specific frequency. Therefore it is most naturally accomplished in the frequency domain. This analysis is most often accomplished by the use of a frequency-domain F-statistic (Craigmile & King, 2004).

Responses are detected by comparing the ratio of the estimated power at the modulation frequency to the estimated power in a specified number of frequencies above and below the “signal” frequency. Statistically, frequency-domain tests have a number of advantages over time-domain methods (like with the ABR) and this is often cited as the reason that ASSR is more “objective” than ABR.

In this study ASSR and ABR waveforms are compared in the same individuals using tonepip stimuli. The goal was to minimize the differences between ABR and ASSR acquisitions as much as possible in order to compare the two techniques in arriving at an electrophysiologic threshold in normal-hearing young adults.

Chapter 2: Methods

2.1 Participants

Nine normal-hearing young adults (5 female; 4 male) ages 20-25 served as subjects. The subjects were all students at The Ohio State University. The research was conducted with the approval of the IRB. All subjects were paid for their participation.

2.2 Inclusion Criterion

All subjects met the following inclusionary criteria. A thorough otosocpic examination was performed on the day of testing. All subjects had clearly visible and normal tympanic membranes bilaterally. Additionally, 226-Hz tympanometry was performed to ensure the subjects had peak compensated static admittance and ear canal volumes within normal limits. Pure tone air conduction thresholds at the standard audiometric frequencies were measured with a 10-dB down, 5-dB up presentation using a calibrated Interacoustics AC 33 clinical audiometer. All subjects had pure tone behavioral thresholds less than or equal to 20 dB HL on the day of testing. Transient evoked otoacoustic emission (TEOAE) testing was performed on all subjects. Subjects had to have at least a 6-dB SNR in 4 of the five frequency bands tested to be considered a pass on the TEOAE test.

2.3 Electrophysiologic Testing

All electrophysiology testing was done using the Intelligent Hearing Systems Smart EP system. Every subject was set up for a two-channel differential recording. The noninverting and reference electrodes were common to both channels. The noninverting electrode was placed on the high forehead (Fpz), and the reference electrode was placed on the C7 vertebra. C7 was chosen because it is a noncephalic site that is quiet with respect to cardiac activity. The surface of the skin was scrubbed in order to reduce the impedance between electrodes. All impedances were required to be less than 1 kOhm (the resolution of the measuring equipment). All testing was accomplished in a sound-attenuated room with the subject seated in a reclining chair. The subjects were instructed to relax and sleep if possible to reduce myogenic interference. Insert headphones (Etymotic Research ER-3) were used for stimulus presentation. Stimulus presentation was randomized for ASSR-ABR and then within ABR for the center frequency.

The tonepip stimuli were Blackman-windowed tonepips for both the ABR and ASSR recordings. An example is shown in Figure 6.

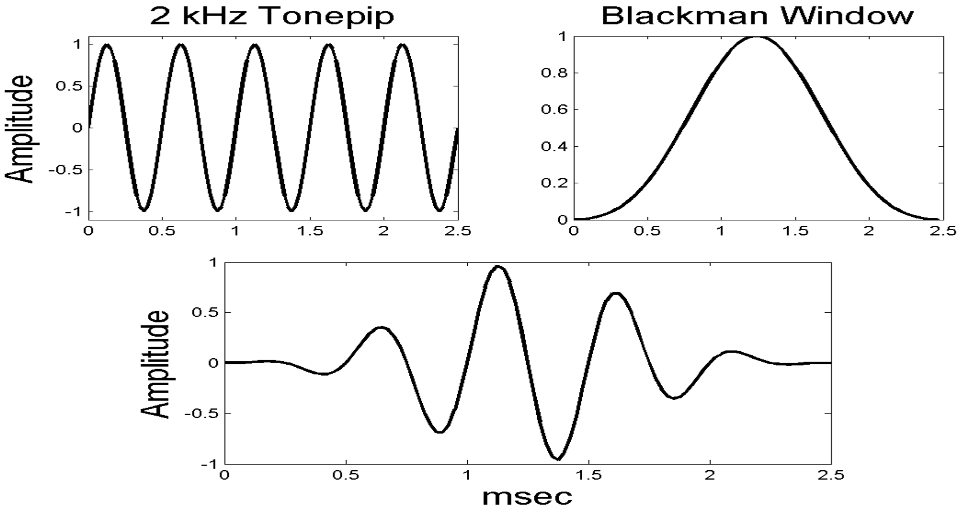

Figure 6: Top Left: 2kHz tonepip stimulus Top Right: Blackman window modulator Bottom**:** Single Blackman windowed tonepip stimulus (2kHz)

The duration of the ASSR tonepip was 4 msec in each case. This is the default stimulus for the IHS system. For the ABR, the 5-cycle convention was used so that the total duration of the stimulus was 5 cycles of the specified frequency. For the frequencies used in this study (1, 2, and 4 kHz), the ABR tonepips were 5, 2.5, and 1.3 msec respectively. All stimuli were equated for peak equivalent SPL in the following manner. The voltage waveform for an individual tonepip was captured on an oscilloscope after being routed through a sound-level meter. The peak voltage deviation (in absolute value) was matched to the voltage deviation produced by a sinusoid one second in duration. The SPL of the sine wave was measured with the sound level meter. The resulting SPL was called the peak equivalent SPL of the tonepip. Since the tonepips for the ABR and ASSR responses were of different duration, the peak equivalent SPLs were adjusted accordingly.

The ABR tonepip stimuli were presented at 35 tonepips per second. Only a single stimulus center frequency was used in each acquisition. In the ASSR acquisition, 1, 2, and 4 kHz tonepips were presented simultaneously at rates of 85, 93, and 101 Hz respectively. In the ABR acquisitions, at least two repetitions of 2,000 epochs were recorded. In the ASSR data, each epoch was 1-second in duration and 400 such epochs were recorded. ABR analysis was done by visual inspection of the resulting waveforms, both examiners had to agree on the presence of wave V. At least two replications were required. The examiners were not blind to each other’s judgements. The examiners used the fact that wave V’s latency increases as the intensity decreases. For both the ASSR and ABR data acquistions, the presentation level was reduced in 10-

dB increments until no response was obtained, then increased in 5-dB steps. A typical ABR wave V intensity series is shown in Figure 7.

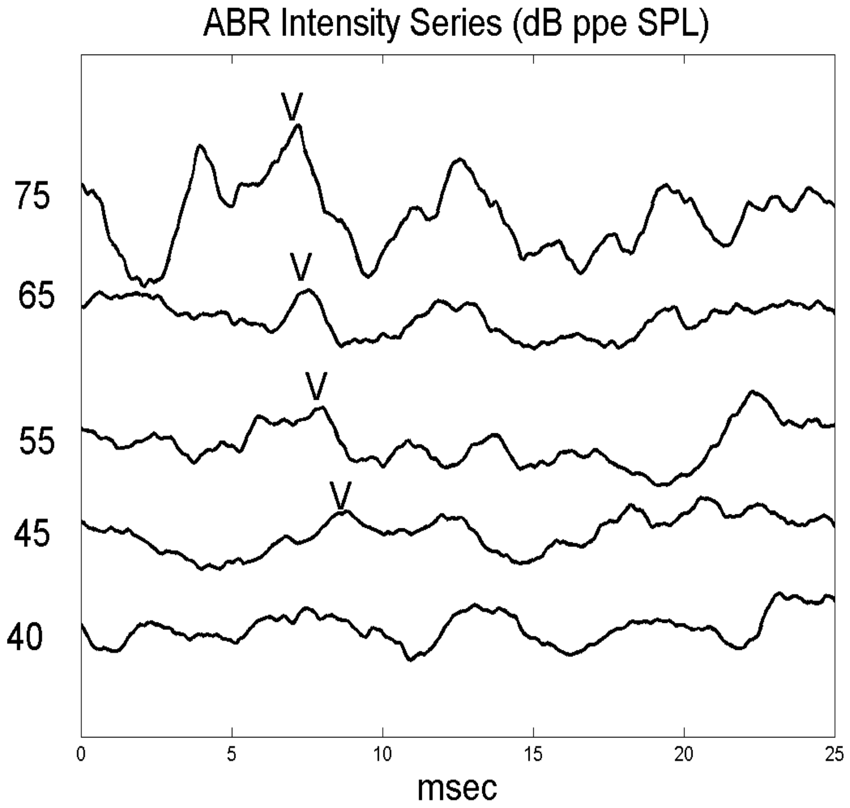

Figure 7: ABR wave V intensity series. Y-axis values are in dB peak equivalent SPL. Note that wave V increases in latency as the intensity decreases. Threshold in this case was defined to be 45 dB peak equivalent SPL.

ASSR responses were considered present if the value of the frequency domain F-statistic exceeded the criterion level to yield a test of size 0.05 (with a Bonferroni correction for the fact that three frequencies were tested simultaneously). The multitaper F-test was used in all analyses (Thomson,1982). The sampling rate for all ASSR data acquisition was 1 kHz and 1024 points were acquired. This yields a frequency resolution of 1000/1024=0.97 Hz. For the multitaper F-test the time half bandwith product was set to 3. This yields a resolution of 3(1000/1024)=2.9 Hz. This was chosen in order to prevent overlap between the modulation frequencies of 85,93, and 101 Hz. Accordingly, five Slepian tapers were used in the computation of the F-statistic (Thomson,1982; Percival & Walden, 1993). The resulting F-statistics were evaluated on the F(2,8) distribution. In Figure 8, we show an example ASSR recording and the resulting multitaper F-statistics.

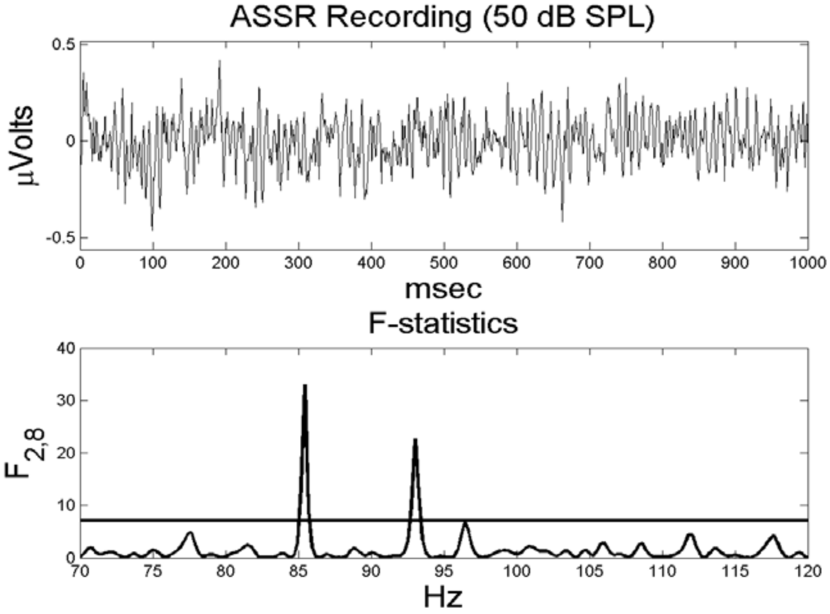

Figure 8: ASSR time data(top panel) with F-statistic showing 2 suprathreshold responses at the modulation frequencies corresponding to 1 and 2 kHz.

Chapter 3: Results

The electrophysiologic threshold results by frequency and EP type are shown in Figure 9. The data from the two hearing sensitivity measures showed no significant differences in threshold when the stimuli from both tested were equated for peak equivalent SPL.

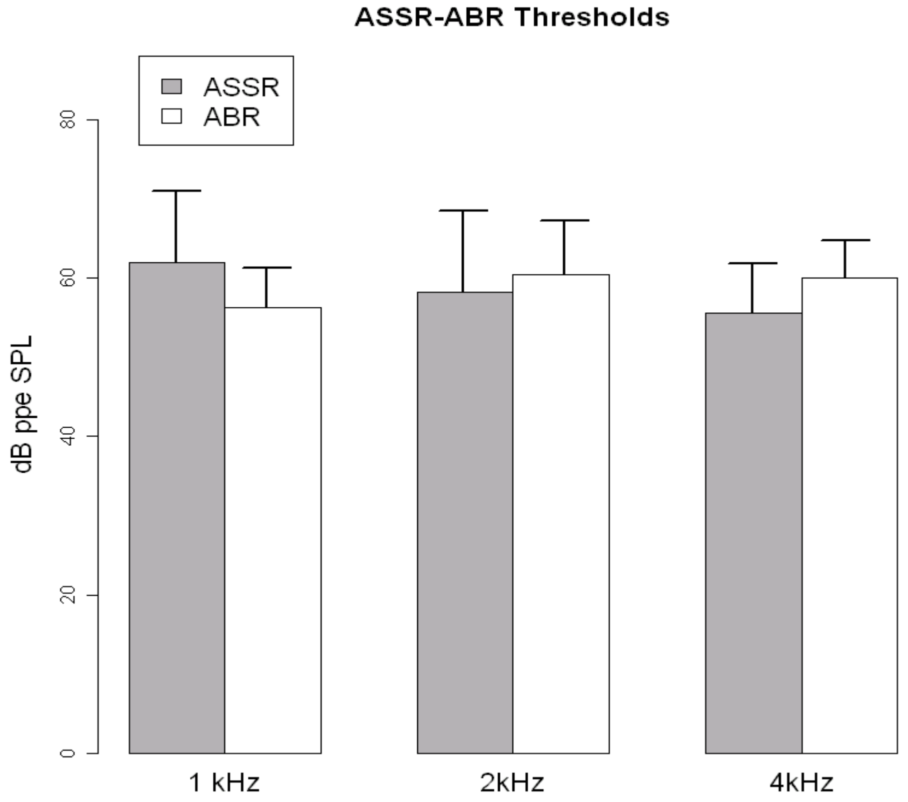

Figure 9: Mean ASSR and ABR thresholds by frequency in ppe SPL. Error bars represent one standard deviation.

No significant correlations were found between ASSR and ABR thresholds for individual subjects. This is shown in Figure 10.

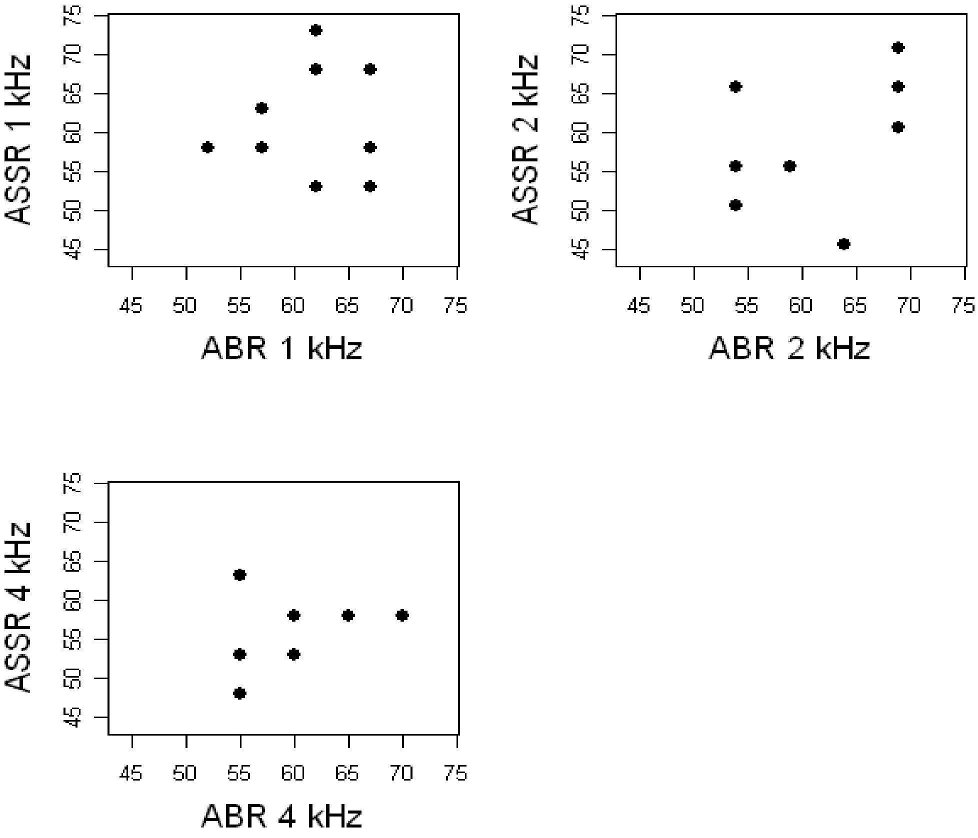

Figure 10: ABR-ASSR Thresholds for all subjects. No significant correlations were found.

While there were no significant differences in mean threshold, the lack of correlation suggests that the ASSR and ABR behaved differently across subjects. Examination of the data revealed that ASSR exhibited substantial inter-channel and inter-acquisition variability not shown in the ABR data. The present study noticed that ASSR responses absent at higher sound pressure levels could reappear at lower levels within the same subject. This is a counterintuitive situation and the examiners did not see any evidence of this issue present in the ABR testing. In Figure 12 ASSR F-statistics computed on successive aggregating blocks of 20 responses are computed for 30 dB SPL and 20 dB SPL inputs in the same subject and same testing session.

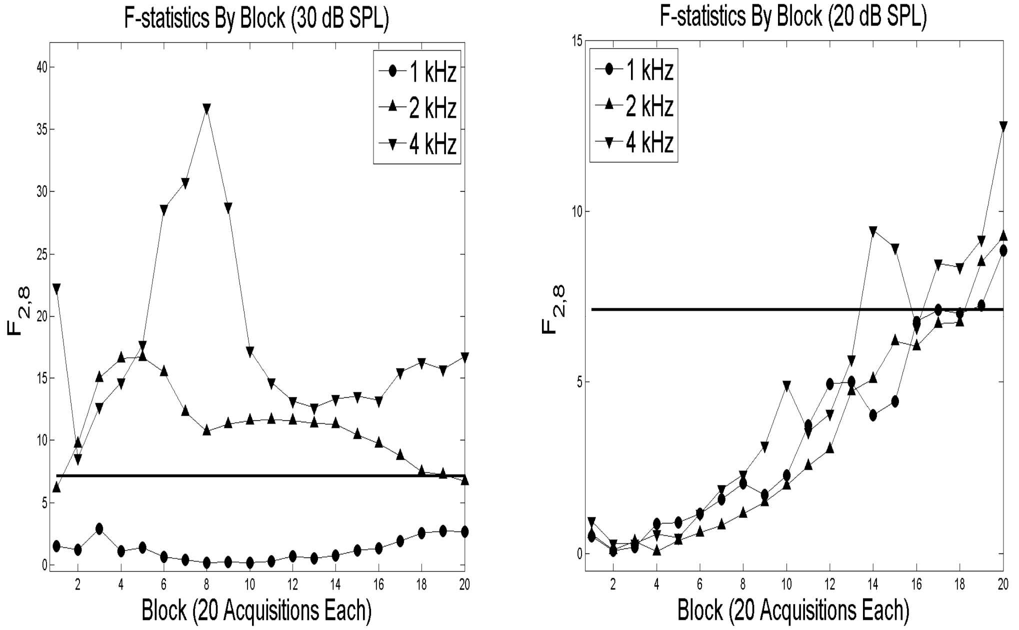

Figure 11: Left: ASSR F-statistics as a function of block for a 30 dB input. Right: ASSR F-statistics by block for a 20 dB input in the same subject.

ABR testing in wave V demonstrated the expected repeatability across the two recording channels. This was not the case with the ASSR, which often exhibited responses present in one but not the other channel. Figure 12 shows ABR repeatability across two channels in the same subject. In Figure 13, ASSR results (F-statistics by block) are shown in the same subject across the two channels.

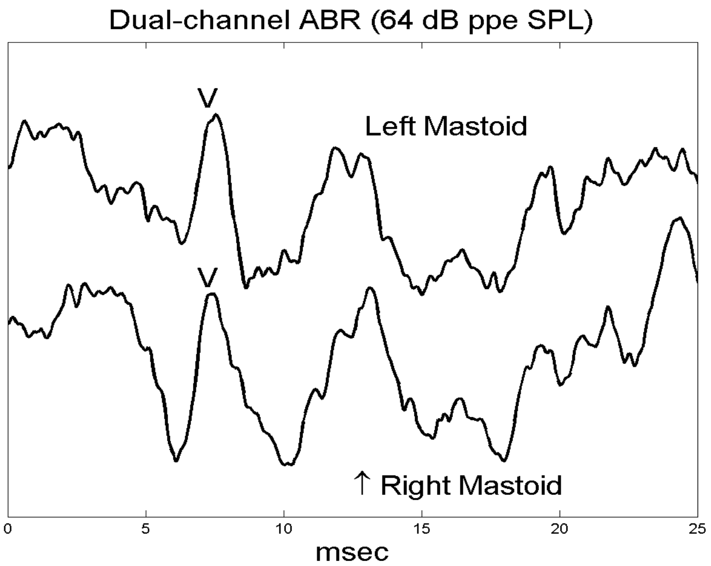

Figure 12: ABR demonstrating repeatability in both channels at 64 dB ppe SPL. Data from the same subject as in Figure 5.

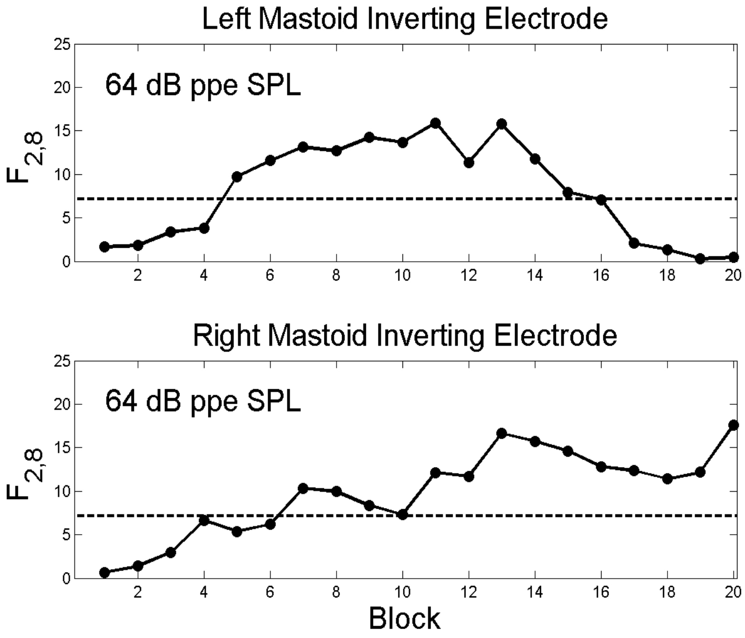

Figure 13: Top: ASSR F-statistics recorded as a function of block from left mastoid (stimulus ear) Bottom: F-statistics as a function of block as observed from the right mastoid electrode in the same subject.

In many instances the channel with a present response was not the “stimulus ear” channel. In his study, the ASSR was judged present if it occurred at any lower sound pressure level even though it did not appear at a higher level. Also, the ASSR was considered present if it occurred in one, or both of the channels.

Chapter 4: Discussion and Conclusion

In this study mean ABR and ASSR thresholds were not found to differ. However, there was no significant correlation between the ASSR and ABR thresholds for individual subjects. This lack of correlation may be attributable to the small number of subjects and the low resolution of the threshold estimation procedure.

The inconsistency the ASSR demonstrated certainly questions the push for ASSR to be an accepted method for estimating hearing sensitivity. If the ASSR is a brainstem response analogous to the ABR when using 70-110Hz modulators, the central electrode array used in this study should not have yielded appreciable inter-channel differences. The signal-to-noise ratio (SNR) of wave V in the ABR monotonically increased as a function of acquisition number, this did not occur in the ASSR testing. The inference then made is that the ASSR is not robust with respect to the point at which the data acquisition is terminated.

This study has several important limitations. While the tonepips were equated for peak equivalent SPL, there was no adjustment made for the fact that the tonepips were presented at a faster rate in the ASSR acquisition. Further, the threshold estimation procedure was too lenient in what it considered a response for the ASSR acquisition. This biased the results in favor of ASSR.

Finally, important questions were raised by this study about the variability of the ASSR. The ASSR is hailed as an objective measure because it uses a hypothesis test. However, in this study the ABR appear much more consistent in its behavior across channels and stimulus levels. Further work is planned to more systematically compare the two techniques and compare the inter-acquisition and inter-channel variability.

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