TOWSON UNIVERSITY
COLLEGE OF GRADUATE STUDIES AND RESEARCH

THE AUDITORY BRAINSTEM RESPONSE (ABR):

A NORMATIVE STUDY USING THE INTELLIGENT HEARING SYSTEM'S

SMART EVOKED POTENTIAL SYSTEM

by

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AUDIOLOGY DOCTORAL THESIS APPROVAL PAGE

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ABSTRACT

The Auditory Brainstem Response (ABR): A Normative Study Using the Intelligent Hearing System's Smart Evoked Potential System

Rachelle Webster

An otoneurologic Auditory Brainstem Response (ABR) was recorded on 20 normal hearing adult subjects to determine equipment specific normative data using the Intelligent Hearing System's (IHS) Smart Evoked Potential System. Results revealed an increase in the mean latencies of wave's I, III, and V as stimulus intensity decreased. Interpeak latency was consistent across all stimulus intensities. In addition, all interaural latency differences were below 0.2 ms. Peak-to-peak amplitude measurements of waves I-I' and V-V' were used to calculate the wave V/I amplitude ratio. These ratio values revealed a mean ratio greater than 0.5 μV at all stimulus intensities. The stimulus rate effects showed a 0.39 ms shift in wave V when the stimulus rate was increased. These results were compared to previous data collected and Towson University and published normative data. Excellent agreement was seen across all results obtained in the current study as seen in the mean normative data and the variability represented by the standard deviation.

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Chapter 1

Introduction

An auditory evoked potential (AEP) is a general term for electrical responses generated along the peripheral and/or central auditory pathway, when auditory stimuli are presented (Picton, 2011). These potentials are categorized based on timing, location of the response, as well as their underlying neural generators. The specific AEP being investigated in the present study is the Auditory Brainstem Response (ABR). The ABR is an electrophysiologic test that looks specifically at the electrical response occurring between the VIII nerve and the brainstem (Burkard & McNerney, 2009). It has two main clinical purposes including otoneurologic testing as well as the estimation of pure tone threshold as a function of stimulus frequency.

In the current study, we are studying the ABR to for otoneurologic purposes to assess the integrity of the auditory pathway from the VIII nerve to the auditory brainstem. In this study, the ABR was recorded to click stimuli presented at several moderate to high stimulus intensities (i.e. 70-90 dBnHL). The purpose of this study is to collect normative data for the ABR recorded on the Intelligent Hearing System (IHS) SmartEP System. This normative data has been collected on young normal hearing adults who have no significant otologic history. Equipment specific normative data is needed due to differences in stimulus and recording parameters across equipment, as well as different acoustical environments in which ABR's are recorded. An often overlooked area related to collecting appropriate ABR response measurements is ensuring that the AEP equipment is properly calibrated according to dBnHL units. Prior to data collection in the

present study, a thorough calibration of the equipment was conducted including a linearity and stimulus polarity check.

For otoneurologic purposes, various latency and peak-to-peak amplitude measurements were taken on the ABR's recorded at 70, 80, and 90 dBnHL. Latency measurements include the absolute latencies of waves I, III, and V, interpeak latencies of waves I-III, III-V, and I-V, and the interaural latencies of waves I and I-V. Amplitude measurements included the peak-to-peak amplitudes of waves I-I' and V-V' which were used to calculate the wave V/I amplitude ratio at these stimulus intensities. Lastly, the stimulus rate was increased from 19.1 clicks/sec to 61.1 clicks/sec to evaluate the effect of stress on the auditory system. The absolute latency of wave V at each of these stimulus rates was calculated.

The results from the current study were compared to normative data previously collected at Towson University on the IHS SmartEP System as well as published normative data from Hood (1998). Descriptive statistics including mean and standard deviation were calculated on each type of response measurement. The mean latency and amplitude data in the current study are in excellent agreement with this previous normative data.

In the current study, the investigators also judged the overall morphology and replicability of the response as well as the effect of stimulus polarity on the ABR. The majority of responses showed excellent waveform morphology and replicability. No reversal of the neural responses was seen in the waveform of any participants when the polarity of the click stimulus was changed from rarefaction to condensation.

Audiologists should not solely depend on published normative data or data provided by the equipment manufacturer. Instead, audiologist's need to initially ensure that their AEP equipment is properly calibrated according to dBnHL units. Secondly, specific normative data should be collected and then compared to published norms to ensure that their ABR measurements are being accurately judged.

Chapter 2

Literature Review

Auditory Evoked Potentials

Auditory evoked potentials (AEPs) are electrical responses generated in the peripheral and/or central auditory nervous systems which occur when an auditory stimulus is presented. Auditory evoked potentials are time-locked waveforms represented by a series of positive peaks and negative troughs following the presentation of the stimulus. The electrical activity seen in AEPs is recorded from surface electrodes placed at various locations on the scalp. This electrical activity is generated by a variety of locations within the entire auditory pathway including the cochlea, auditory nerve, auditory brainstem, medial geniculate body and auditory cortex (Burkard & McNerney, 2009). There are several different types of AEPs that can be recorded based on the timing and location of the underlying electrical activity. Some of these AEPs include the Auditory Brainstem Response (ABR), the Middle Latency Response (MLR), and the Late Auditory Evoked Potential (LAEP) (Burkard & McNerney, 2009). Picton (1990) suggested four classification schemes to categorize these AEP's. These schemes will be briefly discussed below.

The first classification scheme is based on the latency of the response. The latency of an AEP is defined as the time in milliseconds (ms) following the onset of an auditory stimulus in which an electrical response is seen (Gelfand, 2009). The earliest latency responses are classified as "first" and occur between 0-5 ms post-stimulus onset. Examples of first responses include the VIII Nerve Compound Action Potential (CAP) and waves I and II of the ABR. The next latency responses occur between 2-20 ms and

are classified as “fast” AEPs. Fast AEP responses include waves III, IV, and V of the ABR. These first two latency classifications are often grouped together as “early responses” (Picton, 1990). Following the early responses is the MLR, which occurs between 10-100 ms. The MLR consists primarily of waves Na, Pa, and Nb. The final two latency categories are slow (50-300 ms) and late (150-1000 ms) responses. They are often collectively referred to as the Late AEPs. The slow response consists of the slow vertex potential waves P1, N1, P2 and N2. The late response consists of the Mismatch Negativity and waves N2b, P3b and N4.

The second major classification scheme described by Picton (1990) was the relationship of the response to the stimulus. This classification is broken into three types of responses: transient, sustained, and steady-state (Picton, 2011). Transient EPs occur after a change in the stimulus, such as the onset or offset. The ABR, MLR and Slow Cortical Response are all examples of transient responses. In contrast, a sustained EP occurs after a continuous stimulus (Hood, 1998). An example of a sustained response is the Frequency Following Response (FFR). Lastly, steady state responses occur in response to continual repetition of stimuli presented at rapid rates of stimulation. Generally, these steady state responses are recorded at stimulus rates greater than 40 per second. At these higher rates, the response to the second stimulus begins to overlap with the response to the first stimulus (Hall, 2007). An example of a steady state response is the Auditory Steady-State Response (ASSR).

A third classification scheme of AEPs proposed by Picton (1990) is to categorize responses according to their underlying neural generators. Many generator studies have been completed first in animals and later in humans in an attempt to understand from

where these responses are coming. The early AEPs discussed above have been mapped to receive contributions from the VIII nerve auditory pathway and the brainstem (Don & Kwong, 2009). In contrast, McGee and Krause (1996) reported that the primary neural generator for the MLR is the auditory cortex with some sub-cortical contributions as well. The late AEPs are also generated in the auditory cortex with input from areas located near the Sylvian Fissure (Hall, 2007; Jacobson, 1985).

The final classification scheme used to describe AEPs is the processing relationship to the stimulus. In this category, AEPs are described as either Sensory EPs or as Processing-Contingent Potentials (PCPs). Sensory EPs, or exogenous potentials, are obligatory responses to a stimulus. These responses are largely independent of the subject but rather are dependent on the stimulus itself (Hall, 2007). For example, if the intensity of the stimulus is decreased, this will cause a reduction in the amplitude and an increase in the latency of the AEP. In contrast, the PCP's, or endogenous potentials, are potentials which require additional brain processing of the stimulus. The P300 is an example of a PCP. In this response, the subject is asked to not only detect the auditory stimulus but also to discriminate between different acoustic stimuli (i.e. 1000 vs 2000 Hz tones) (Picton, 2011).

Since the ABR is the primary focus of this study, the remainder of the literature review will focus on this response. According to the classification schemes discussed above the ABR is an early/fast transient response. The neural generators of the ABR occur between the VIII nerve and the brainstem, thus giving name to this response. Finally, it is a sensory or exogenous response which is dependent upon the stimulus

characteristics. Since the ABR is commonly used in a clinical setting, it is important to understand how this response was first discovered.

History of the Auditory Brainstem Response

The auditory brainstem response is comprised of a series of 5-7 positive peaks and negative troughs which are recorded to an auditory stimulus from surface electrodes placed at several locations along the scalp (i.e. the vertex, earlobes or mastoids and forehead). This electrophysiologic response is typically seen within the first 15 ms after the onset of the stimulus (Don, Ponton, Eggermont, & Kwong, 1998). Generally, the ABR is recorded to brief transient stimuli, such as a broadband click or a toneburst stimulus. Jewett and Williston (1971) were among the first researchers to study this response and to label each of the peaks.

In 1970, Jewett completed a study of electric potentials recorded to high intensity click stimuli in eighteen cats. Surface electrodes were placed on various far field locations along the cat's body and needle electrodes were placed along the auditory pathway for comparison of these two responses. Jewett reported that a series of four positive peaks were recorded which he labeled peaks P1-P4. He reported that these surface peaks closely correlated to the timing of the peaks recorded along the auditory pathway (Jewett, 1970).

To further understand this response in the human auditory system, Jewett and Williston (1971) completed a similar study on 12 normal hearing individuals with no significant aural history. Surface electrodes were placed on the subjects' vertex and right ear lobes. The ABR was recorded to a click stimulus presented at 60-75 dB above the

subject's subjective threshold. Jewett reported that a series of distinct waves were recorded in each subject. He labeled these waves using roman numerals I through VII (Jewett, 1970). Several interesting characteristics of the ABR were demonstrated, as seen in figure 1 below. First, the waveform morphology of the ABR was similar in all 12 subjects. The first six positive peaks were detectable in all the subjects and the timing or latency of these peaks was essentially the same in these various subjects. Since this ground breaking study, numerous investigators have replicated these findings and described similar characteristics of the ABR.

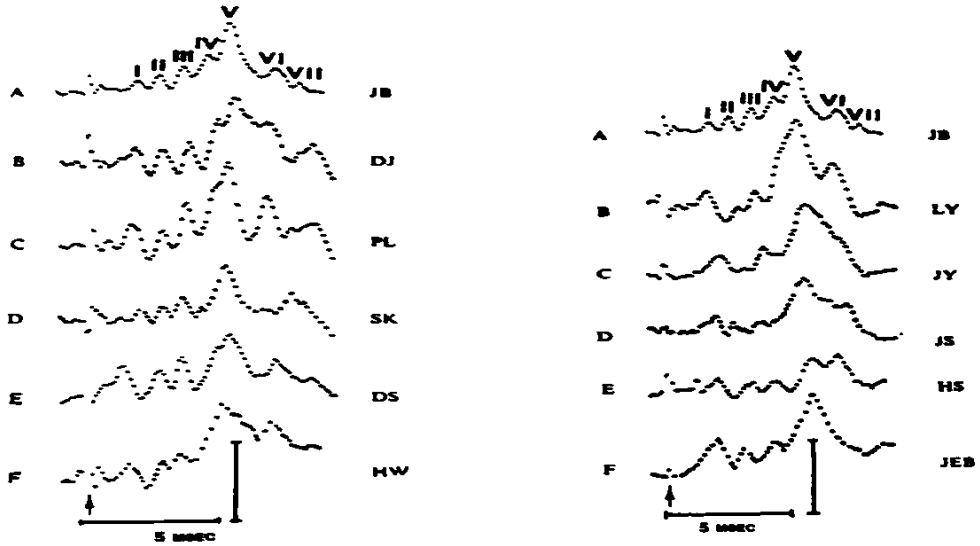

Figure 1. Far-field responses recorded from 12 normal hearing individuals to a high-intensity click stimulus. Associated waves labeled I through VII. (Jewett & Williston, 1971)

Description of the Response Characteristics of the ABR

The ABR has several important response characteristics which are used as diagnostic criteria for judging the integrity of the VIII nerve and auditory brainstem pathways. These include several latency and amplitude measurements as well as the

overall morphology of the response. An ABR recorded to a high intensity click stimulus in a normal hearing adult is shown in figure 2 below.

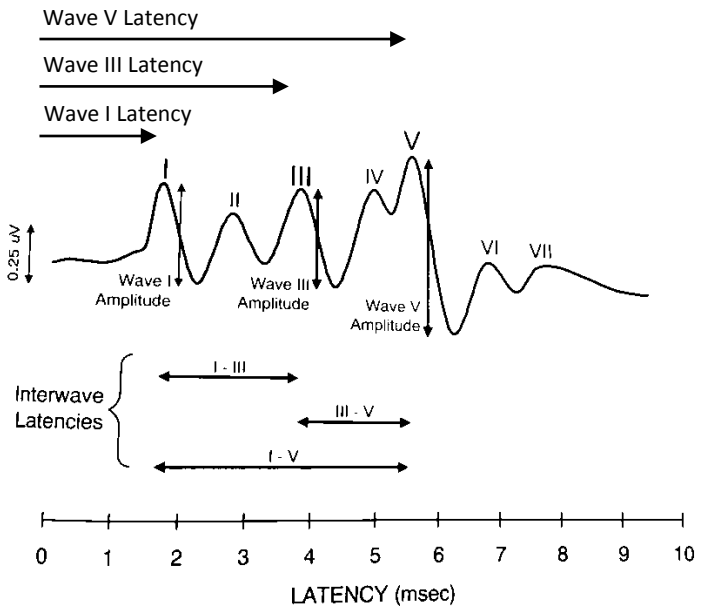

Figure 2. An ABR recorded to a high-intensity click stimulus in a normal hearing adult. Waves I through VII are labeled. Also pictured are the absolute latencies of waves I, III and V, the peak-to-peak amplitudes of waves I, III and V, and the interpeak latencies of I-III, III-V, and I-V (Gelfand, 2009).

As previously mentioned, several latency measurements are calculated on the ABR to determine the integrity of the VIII nerve and brainstem neural pathways. These measurements include absolute latency values of the various peaks, the interpeak latency (IPL) values, and interaural latency differences. Absolute latency is the time in milliseconds (ms) between the onset of a stimulus and when a peak in the waveform is seen (Hood, 1998). We typically measure the absolute latencies for waves I, III, and V. These are the primary waves used for otoneurologic applications of the ABR. Figure 2 above displays the absolute latencies of waves I, III, and V, which are approximately 1.5, 3.8 and 5.5 ms, respectively. A second important latency measure is interpeak latencies. This refers to the difference in ms between various peaks recorded along the ABR. The

important IPL's measured include waves I-III, III-V, and I-V. These IPL measures provide information regarding central conduction time and are influenced by the synchronicity of the auditory pathway (Hood, 1998). The final latency measure employed for otoneurologic purposes is the interaural latency difference of wave V, known as IT5. This measurement compares the absolute latency values of wave V between the responses from the right and left ears to the same stimulus presented at identical stimulus intensities. Assuming the ears have similar behavioral audiometric thresholds, it can be assumed that they should also have similar wave V latencies and thus the IT5 difference should be minimal (≤ 0.2 ms) (Don & Kwong, 2009).

The peak-to-peak amplitude of wave I and wave V are also used to assess the otoneurologic ABR. Response amplitudes are generally measured as the peak to peak difference in microvolts (μV) between the positive peak of the response (wave V) and the negative trough immediately following it (wave V') (Hood, 1998). Generally, peak to peak amplitude measurements are taken on waves I and V. Another important amplitude measurement that is calculated is the Wave V to Wave I amplitude ratio. Wave V/I amplitude ratio values in a normal functioning systems typically are >0.5 μV. If the amplitude ratio is <0.5 μV this suggests a possible retrocochlear pathology (Hall, 2007).

Lastly, audiologists assess the morphology of the response in an otoneurologic ABR. The morphology of the ABR is a recognizable waveform which consists of characteristic peaks and troughs. The morphology or shape of the ABR can vary across individuals and yet still be considered a normal response (Hall, 2007). One component of the ABR that tends to vary amongst individuals with normal functioning auditory systems is the shape of the wave IV-V complex, as seen in figure 3 below. Some individuals have

larger amplitudes for wave V versus wave IV, as seen in tracing A. Whereas others display the opposite pattern, as seen in tracing C. Some individuals may also present with a bifid pattern, where the amplitude of waves IV and V are equal (seen in tracing D). It is important for audiologists to be familiar with the various morphologies of the ABR that they may encounter in their clinical practice.

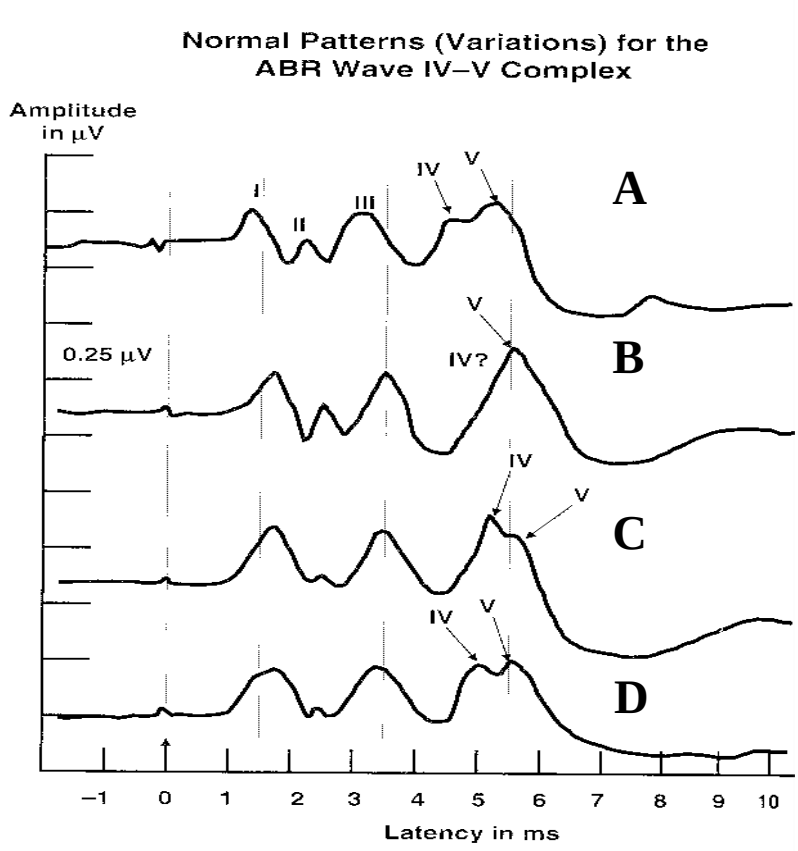

Figure 3. Normal variations of the wave IV-V complex, seen in the ABR response of normal hearing individuals (Hall, 2007).

Clinical Applications of the ABR

There are three primary clinical applications of the ABR. These applications include: differential diagnosis of retrocochlear pathologies; audiometric threshold prediction; and intraoperative monitoring. Otoneurologic ABRs are used clinically for

differential diagnosis of retrocochlear pathologies, such as VIII nerve tumors (Hood, 1998). For this purpose, various latency and amplitude measurements described above are calculated on waves I, III, and V of the patient's response. These response measurements are then compared to normative data to determine the integrity of the VIII nerve and brainstem pathways. The otoneurologic application of the ABR is the primary focus of the current study and thus will be discussed in greater detail later in this literature review.

Audiologic threshold prediction of the ABR has become common practice in pediatric and difficult- to- test populations. In these populations, it is not always possible to obtain accurate behavioral thresholds and alternative measures are needed to accurately predict these thresholds (Burkard & McNerney, 2009). Threshold prediction of the ABR focuses on wave V and the response is recorded to toneburst stimuli in order to provide the best estimate of the patient's pure tone thresholds. In these recordings, the intensity of the stimulus is lowered until there is no longer a replicable response of wave V (Gelfand, 2009). The ABR thresholds obtained in this approach have been shown to be quite accurate in predicting behavioral thresholds to within 10 dB (Hood, 1998).

The final application of the ABR is intraoperative monitoring. Intraoperative monitoring primarily focuses on the preservation of the auditory nerve for hearing but is also used to prevent brain and brainstem ischemia as well as trauma during various surgery procedures (Burkard & McNerney). In order to fully understand these various applications of the ABR, it is imperative for audiologists to understand the underlying neural generators of this response.

Neural Generators of the ABR

Researchers have primarily used two techniques to investigate the neural generators of the ABR. The first technique involved placing intracranial needle electrodes at various locations along the VIII nerve and brainstem and then comparing the latencies of these responses obtained at these locations to the latencies obtained from surface electrodes (Jewett, 1970; Moller & Janetta, 1982a). Secondly, several researchers have used patients with radiologically confirmed brainstem lesion studies and compared their ABR results to normal controls. In general, these neural generator studies have been completed on both animal and human participants, with the exception of intracranial recordings, which have only been completed in humans. In this section of the literature review, the evidence from generator studies conducted in animals will be reviewed first, followed by evidence from human studies.

Buchwald and Huang (1975) were among the first investigators to study the origins of the ABR in 10 adult cats. These investigators chose to study cats as the anatomy of their auditory systems is closely aligned with humans. These investigators made specific lesions in the cats at the levels of the inferior colliculus, cochlear nucleus, and acoustic nerve. ABRs were recorded in these cats to determine what specific peaks in the response had been affected. Buchwald and Huang (1975) reported that potentials I and II originated from the acoustic nerve and cochlear nucleus respectively. Potential III originated from the medial superior olivary complex, relying heavily on the crossed pathways. Potential IV required input from the ventral nucleus of the lateral lemniscus and preolivary complex with equal reliance on the crossed and uncrossed pathways.

Lastly, potential V originated in the inferior colliculus, also relying most on the crossed projections (Buchwald & Huang, 1975).

While this study proved fruitful information on the neural generators of ABRs in cats, these investigators were interested in studying the specific neural generators in the human ABR. During the 1980's, Dr. Moller and colleagues conducted a series of studies to investigate the origin of waves I, III, and V in the human ABR (Moller, Janetta, & Moller, 1981; Moller, Janetta, & Sekhar, 1988; Moller & Janetta, 1982a; Moller, Janetta, Bennett, & Moller, 1981). In these studies, the patients' ABRs were recorded pre- and post-operatively. These patients were receiving surgical procedures for cranial nerve dysfunction. The ABR was recorded to a 2000 Hz toneburst and the surface electrodes were placed at various locations on the scalp and mastoid. During the surgery, the VIII nerve was exposed and needle electrodes were placed directly on the VIII nerve and various nuclei in the brainstem including the cochlear nucleus, superior olivary complex, lateral lemniscus and inferior colliculus. Moller and colleagues compared the latencies of responses from the scalp recording to the latencies of the response from the direct recording on the VIII nerve and brainstem structures.

From these latency measurements Moller and colleagues determined that wave I of the ABR is coming from the distal portion of the VIII nerve. Waves III and V both showed aspects of originating within the auditory brainstem. Specifically, it was determined that wave III stemmed from the cochlear nucleus and superior olivary complex at the level of the pons (Moller & Janetta, 1981, 1982a). Lastly, Moller and colleagues determined that wave V had its origin in the lateral lemniscus and inferior colliculus (Moller & Janetta, 1982a, 1982b).

Hashimoto and colleagues, using a similar method, recorded AEP's from surface electrodes placed on the VIII nerve, medulla, pons, midbrain and cortex of neurosurgical patients. They reported a P3 component at the level of the pons, similar in latency and amplitude to the wave III component found in the scalp recordings. Hashimoto et al. (1981) also reported a P5 component with similar latency and amplitude to the wave V response of the ABR coming from the inferior colliculus (Hashimoto, Ishiyama, Yoshimoto, & Nemoto, 1981). The results from this study support the results reported by Moller and colleagues on the origins of waves III and V.

Collectively, the evidence from animal and human studies suggest that the neural origin of wave I is the distal portion of the VIII nerve. Wave III receives contributions from the cochlear nucleus and superior olivary complex. Lastly, wave V originates from the lateral lemniscus and inferior colliculus. It is generally agreed that there is overlap between all of the neural generators in the ABR, except for perhaps the VIII nerve (Burkard & McNerney, 2009). It has been speculated that there is no clear start and stop point for each peak, but rather a correspondence and overlay between each of the primary generating sites (Burkard & McNerney, 2009). Since the neural generators of the ABR have been identified, researchers also began to investigate how the technical parameters of the ABR shape the response.

Technical Parameters of the Auditory Brainstem Response

The technical parameters of the ABR encompass the stimulus, recording and subject parameters necessary to optimally record an ABR. Each of these parameters will be discussed further in regards to their effects on the otoneurologic ABR.

Stimulus-related effects on the auditory brainstem response.

There are numerous stimulus-related parameters that affect the recording of an otoneurologic ABR in a normal-hearing adult. These factors include: stimulus type, stimulus intensity, stimulus rate, and stimulus polarity. Each of these stimulus factors and their effects on the ABR will be discussed briefly below.

Effects of stimulus type.

The two most common types of stimuli used to record an ABR include clicks or brief tonebursts. A click stimulus is a brief pulse, which is typically 100 μs in duration, with a broad spectrum of energy located between 100-10,000 Hz, as seen in the left hand side of figure 4 (Gorga & Thornton, 1989; Picton, Stapells, & Campbell, 1981). As can be seen in this figure, this broad spectrum of energy is not dependent upon the polarity of the stimulus.

When this click stimulus is presented at a high intensity (i.e. 80-90 dBnHL) through a supra-aural and/or ER3A insert earphone, this stimulus has the capability of activating the majority of the length of the basilar membrane (Picton et al., 1981). This occurs due, in part, to the broad range of frequencies present in the stimulus. In an intact neural system, the presentation of a high intensity click elicits a high level of neural synchrony, which results in robust peak-to-peak amplitudes for waves I, III, and V. Therefore, a high intensity click stimulus is an optimal choice for otoneurologic purposes because it elicits robust ABR peaks and allows audiologists to assess the central conduction time from the VIII nerve to the level of the inferior colliculus.

In contrast, a toneburst stimulus has a concentration of energy around a target frequency with side lobes of energy located above and below the target frequency, as seen in the right side of figure 4 (Gorga & Thornton, 1989). This creates a stimulus with its energy concentrated at the target frequency. This toneburst stimulus is thus more frequency specific in comparison to a non-masked click stimulus. A tonal stimulus is the optimal choice of stimuli for estimating audiometric behavioral thresholds in individuals who cannot be reliably tested using conventional behavioral techniques. Since the aim of the current study is to collect normative data for otoneurologic ABRs, a click stimulus will be employed.

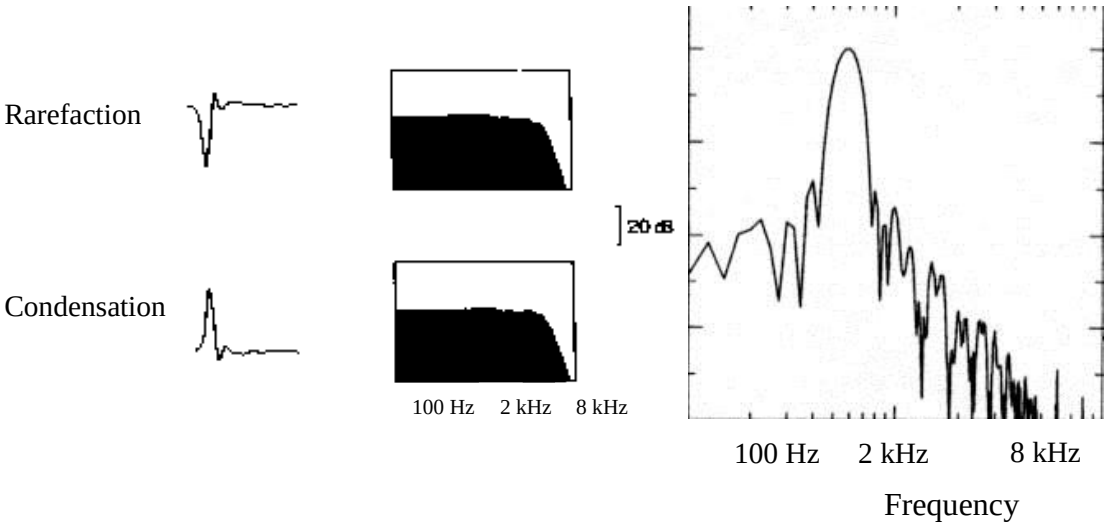

Figure 4. The left side of this figure depicts the spectrum of energy present in a rarefaction click stimulus on the top and in a condensation click stimulus on the bottom presented through a TDH-49 supra-aural earphone. This spectrum of energy is widely distributed from approximately 100 to 10,000 Hz for both types of click stimuli. In contrast, the right side of this figure depicts the spectrum of energy present in a 2000 Hz toneburst stimulus. The primary energy in this toneburst is centralized around the target frequency with side lobes of energy on either side of the peak energy (Stapells, Picton, & Smith, 1982).

Effects of stimulus intensity.

Changing the intensity of a click stimulus has been shown to change the latency, amplitude and morphology of the ABR (Hood, 1998; Picton et al., 1981). Specifically, a decrease in the intensity of the click stimulus results in an increase in the absolute latencies and a decrease in peak-to-peak amplitudes of the various peaks in the response, as seen in figure 5 below.

Picton et al. (1981) specifically examined the effects of decreasing the intensity of the click stimulus from 80 dBnHL to 10 dBnHL on the response measurements and overall morphology of the ABR. These investigators reported that when stimulus intensity was 80 dBnHL, wave V had an average latency of ~5.6 ms. However, when the intensity of the click was decreased to 10 dBnHL wave V latency increased to ~8.2 ms. While this study mainly focused on the latency and amplitude of wave V for threshold seeking purposes, it was noted that waves I and III typically have a larger latency shift in comparison to wave V. This also affects the wave the IPL between waves I and V that are ~4.02 at 70 dB SL, down to ~3.68 at 30 dB SL (Picton et al., 1981).

Similarly, when stimulus intensity was decreased from 80 dBnHL to 30 dBnHL, a 40% reduction in amplitude of wave V (from 0.6 μV to 0.35 μV) was reported, and an even larger reduction occurred in the amplitudes of waves I and III (Picton et al., 1981). Typically waves I and III are not able to be clearly identified and/or measured below 50 dBnHL. Wave V is the most robust response seen close to threshold levels.

As can be seen in figure 5 below, the morphology of the ABR in normal-hearing adults begins to drastically change below 50 dBnHL. Wave V is often the only replicable

peak seen at these low stimulus intensities. It has a much broader shape/morphology, often referred to as a "saucer shape", in comparison to a well defined wave V peak which occurs at the higher levels.

When the ABR is being recorded for otoneurologic application, audiologists are trying to obtain robust waves I, III, and V. Therefore, a high intensity click stimulus is needed. A stimulus intensity between 70-90 dBnHL is typically used to ensure a robust response, especially for wave I (Gerling, 1989; Hall 2007; Hood, 1998; Burkard & McNerney, 2009). Generally, these 70-90 dBnHL levels are well above the behavioral audiometric thresholds for adults with normal hearing sensitivity and below their uncomfortable levels. In the proposed study, the ABR will be recorded to a click stimulus presented at levels between 70-90 dBnHL in order to obtain normative data for an otoneurologic ABR in a group of young normal hearing adults.

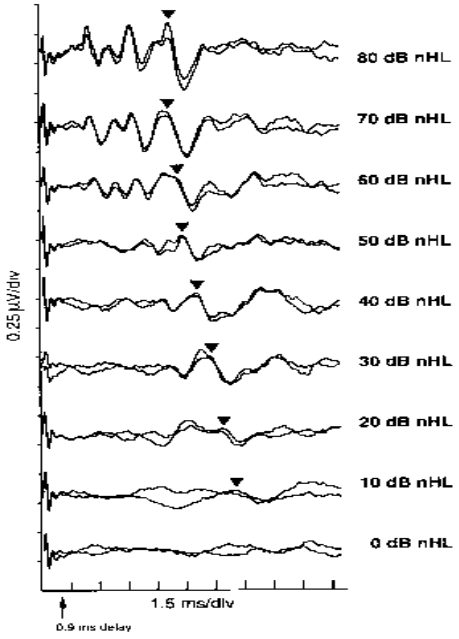

Figure 5. Effects of stimulus intensity on the latency, amplitude and morphology of the otoneurologic ABR (Hood, 1998).

Effects of stimulus rate.

Similar to stimulus intensity, there are latency, amplitude and morphology changes in the click-evoked ABR which occur as a function of stimulus rate. As the stimulus rate is increased, there is an increase in latency and a reduction in amplitude of the response which is different for the various ABR waveform components (Lasky, 1997). When the stimulus rate was increased from 10 to 80 clicks per second, the latency of wave I increased by ~0.14 ms, whereas the latency of wave V increased by ~0.39 ms across the same change in rate (Picton et al., 1981). This finding suggests that stimulus rate has an increased effect on more central parts of the auditory system.

In contrast, changes in amplitude as a function of stimulus rate have a larger effect on the peak-to-peak amplitudes of waves I and III, and smaller effect on the amplitude of wave V. When stimulus rate is increased above 20 clicks per second, there is a 50% reduction in the amplitudes of waves I and III. In contrast, only small (10-15%) reductions in the amplitude of wave V are seen when stimulus rate is increased to 80 clicks per second (Picton et al., 1981). For example, when a click stimulus is presented between 10-60 clicks per second, wave V has an average peak-to-peak amplitude of ~0.6 μV. At rates above 60 clicks per second, the amplitude begins to decrease to an average of 0.5 μV.

Increasing stimulus rate above 20/sec can also have a dramatic effect on the morphology of waves I and III. In most cases, these early peaks cannot be accurately identified and/or measured at click rates above 20 clicks per second. This can be seen in the extensive morphology change between 20 and 40 clicks per second in figure 6 below.

Since waves I and III are necessary in obtaining an otoneurologic ABR in order to assess central conduction time at various levels within the brainstem, rates of less than 20 click per second are recommended (Hood, 1998; Picton et al., 1981).

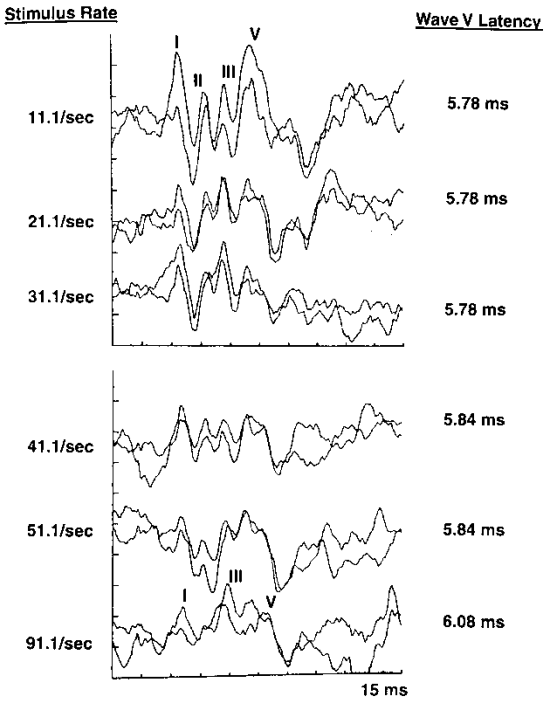

Figure 6. Effects of increasing the stimulus rate on the ABR to a 70 dBnHL click. (Hall, 2007).

Employing higher click rates, such as 61.1 clicks per second, have also been suggested when conducting an otoneurologic ABR because it places stress on the auditory system and is sensitive to neurological deficits (Ackley, Herzberger-Kimball, Burns, & Balew, 2006; Hall, 2007; Pratt, Ben-David, Peled, Podoshin, & Scharf, 1981). Pratt and colleagues collected data from 10 children and 10 adults with normal hearing to identify normal ABR changes when the stimulus rate is increased. They presented each individual with a high intensity click stimulus at a rate of 10 and 50 clicks per second. A

significant shift in latency (0.35 ms) was seen specifically for wave V in both the adult and pediatric populations (Pratt et al., 1981).

Daly and colleagues have reported that abnormal shifts in wave V latency or the disappearance of wave V due to an elevated stimulus rate may indicate a retrocochlear pathology (Daly, Roeser, Aung, & Daly, 1977). These investigators reported that when click stimuli are presented at a high stimulus rate, audiologists should expect to see both an increase in wave V latency and a decrease in peak-to-peak amplitude of this wave. Specifically, Daly and colleagues reported that for every increase of 10 clicks per second, there is an expected wave V latency shift of approximately 0.1 ms. Therefore, when the rate of the click stimulus is increased from 19.1 clicks per second to 61.1 clicks per second, there should be an approximate 0.4 ms shift in the latency of wave V seen in the response.

In the proposed study, both a 19.1 and a 61.1 clicks per second rate will be employed to obtain robust waves I, III and V and to determine the normal variability in latency and amplitude values for wave V which occurs at slower versus faster stimulus rates.

Effects of stimulus polarity.

The stimulus polarity choices for an ABR are either a rarefaction or a condensation click stimulus, or a click stimulus which alternates between rarefaction and condensation. A rarefaction click stimulus leads with a negative electrical pulse, which produces an outward movement of the diaphragm of the earphone. This results in an initial outward movement of the tympanic membrane and stapes footplate at the oval

window and an upward movement of the basilar membrane (Hood, 1998; Burkard & McNerney, 2009). These effects can be seen in the upper portion of Figure 7 below. On the other hand, a condensation stimulus leads with a positive electrical pulse which results in an initial inward push of the diaphragm of the earphone as seen in the lower portion of figure 7. This leads to an inward movement of the tympanic membrane and stapes footplate at the oval window as well as a downward movement of the basal end of the basilar membrane. An upward motion, or rarefaction stimulus, causes an initial excitation of the hair cells. In contrast, the downward motion of the condensation stimulus causes in initial depolarization of the hair cells (Hood, 1998; Burkard & McNerney, 2009).

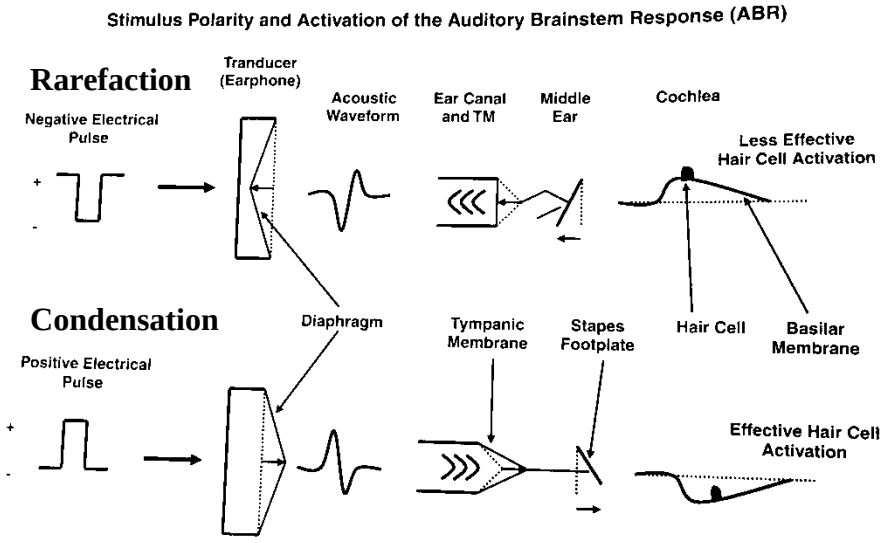

Figure 7. Depicts the movement of the auditory system to a rarefaction and condensation stimulus (Hood, 1998).

Several studies have been demonstrated that recording an ABR to a rarefaction stimulus usually results in slightly shorter latencies and larger amplitudes of waves I and V in comparison to condensation clicks (Borg & Lofqvist, 1981; Stockard, Stockard,

Westmorelant, & Corfits, 1979). In 1979, Stockard and colleagues investigated the effect of stimulus polarity on the latencies and amplitudes of ABR wave I in 64 normal hearing adults between 18-75 years of age (Stockard et al., 1979). These investigators reported that when the ABR was recorded to a rarefaction click stimulus at 70 dB SL, shorter wave I latency values were consistently seen in all participants compared to a wave I latencies for condensation click presented at the same intensity. Specifically, the mean latency for wave I was 1.62 ms with a rarefaction click and 1.69 ms with a condensation click. Stockard et al. also reported that wave I amplitude was larger in 80% of individuals when using a rarefaction versus a condensation click stimulus. Since a robust wave I is an imperative part of the otoneurologic response, a rarefaction click will be used in the proposed study.

Borg and Lofqvist (1981), also investigated the effects of stimulus polarity on the absolute latency of wave V recorded to a 2000 Hz toneburst. Participants with normal hearing as well as with varying degrees of hearing loss participated in the study. These investigators reported that a shorter wave V latency was consistently seen in response to rarefaction stimuli in participants with normal hearing as well as participants with hearing loss. The largest latency difference between rarefaction and condensation stimuli was seen in participants with high frequency hearing loss (Borg & Lofqvist, 1981). Therefore, it has been suggested that differences in latency and amplitude measurements are smaller in individuals with normal hearing in comparison to individuals with a high frequency hearing loss (Borg & Lofqvist, 1981).

In an otoneurologic ABR, the responses to a rarefaction and a condensation click are recorded separately in order to investigate whether there is any evidence of auditory

neuropathy synchrony disorder (ANSD). In an adult with a normal functioning peripheral and central auditory system, when their ABR recordings to both stimulus polarities are compared, the ABR waves should display the same polarity for both types of stimuli. In contrast, the polarity of their cochlear microphonic (CM) response should be inverted, because this response mimics the properties of the stimulus. Therefore, when the ABRs to rarefaction and a condensation stimuli are summed in an individual with a normal functioning system, the CM is cancelled out and robust waves I, III and V of ABR remain. These effects are shown in the left side of Figure 8 below. The cochlear microphonic, seen at a latency of ~ 0.8-1.0 ms, represents the integrity of the outer hair cells (Burkard & McNerney, 2009).

In contrast, in the case of ANSD, the ABRs to the rarefaction and condensation stimuli will be inverted or absent (Berlin, Hood, Morlet, Rose & Brashears, 2003). Therefore, when the rarefaction and condensation waveforms are summed, there is essentially a flat response. These effects are shown in right side of Figure 8 below. Generally, an individual with ANSD will have properly functioning outer hair cells represented by the cochlear microphonic, but a disorder of the auditory nerve (Berlin et al., 2003; Hood, 1998; Burkard & McNerney, 2009). The pathology of the nerve will result in the change in morphology seen in the ABR. For the purposes of this study, an ABR will be recorded to rarefaction and condensation click stimuli to rule out ANSD.

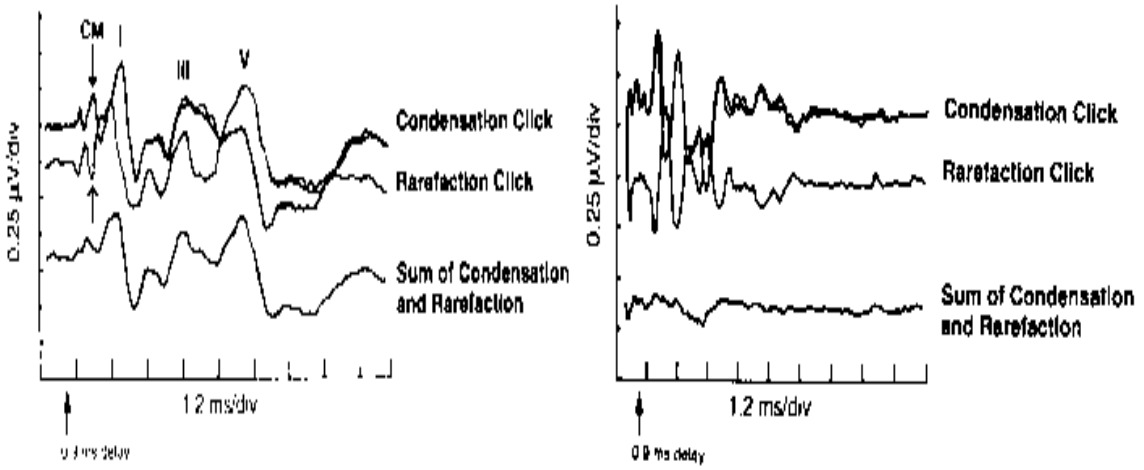

Figure 8. On the left hand side of the figure, ABRs were recorded separately to a high intensity click stimulus with a rarefaction polarity and a condensation polarity in an individual with normal hearing. The final waveform represents the sum of the condensation and rarefaction waveforms. On the right hand side of the figure, the same conditions were presented to an individual with ANSD, resulting in a reversal in ABR waveforms (Hood, 1998).

Auditory brainstem response recording parameters.

There are a number of recording parameters that can affect the ABR. These include: EEG bandpass filter settings, artifact rejection rate, length of post-stimulus analysis window, number of trials, and electrode montage. Each of the recording parameters will be briefly discussed below in regards to their effects on the otoneurologic ABR.

Effects of EEG bandpass filter settings on the ABR.

The goal of employing an analog bandpass filter when recording the ABR is to capture all of the energy present in the response and remove background energy components that are not related to the response (Don & Elberling, 1994). Therefore, choosing the correct EEG bandpass filter settings are critical to obtaining an ABR.

In 1982, Suzuki and colleagues, conducted a study to investigate the primary frequencies of energy present in an ABR (Suzuki, Sakabe, & Miyashita, 1982). In this study, the ABR was recorded to tonal stimuli presented at 1000, 2000, and 4000 Hz in three adults with normal hearing sensitivity. The stimuli at each frequency were presented at both 40 and 80 dB SL. A spectral analysis was conducted using Fast Fourier Transform (FFT) to determine where the primary peaks of energy existed in this response. Three dominant peaks of energy were found in the ABR to the 80 dB SL stimuli. These peaks occurred at 50-150 Hz, 500-600 Hz, and 1000-1100 Hz, as seen on the left hand side of figure 9 below (Suzuki et al., 1982). The largest contributor of energy to the ABR at this stimulus intensity was the lowest peak, which contained energy below 250 Hz.

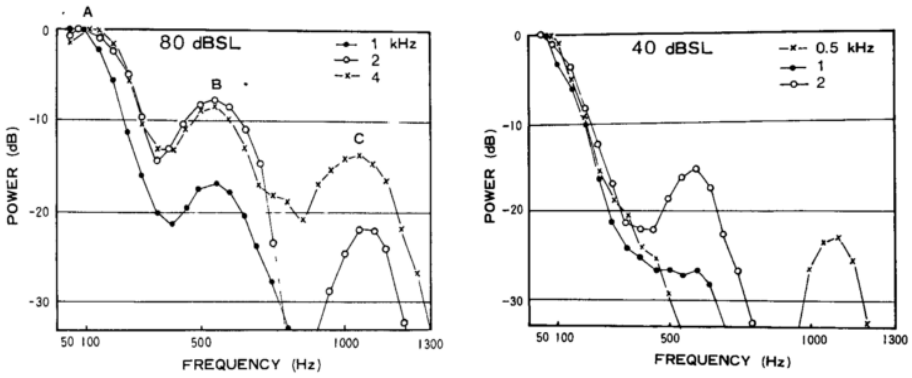

Figure 9. Spectral energy present in a 1000, 2000 and 4000 Hz tone of recorded ABRs to an 80 dB SL and 40 dB SL stimulus (Suzuki et al., 1982).

Suzuki and colleagues (1982) also demonstrated that as the intensity of the stimulus decreased, the energy present in the response shifted to even lower frequency regions. This can be seen on the right hand side of figure 9. At this lower stimulus intensity, the contributions of the peaks at 500-600 Hz and 1000-1100 Hz to the ABR are substantially less than for the higher intensity (80 dB SL) stimulus (Suzuki et al., 1982).

Since the otoneurologic ABRs are typically conducted using high intensity click stimuli, a recommended bandpass filter setting of 100-3000 Hz should be used to properly capture the energy present in this response.

Furthermore, the slope of the filter can also alter the outcome of the response. Elton, Scherg and Von Cramon (1984) investigated the effects of EEG filter slope on the ABR. These investigators progressively increased the slope of the filter from 6 dB/octave to 24 dB/octave in 6 dB steps, when recording the ABR to click stimuli in 20 normal hearing participants. Their results suggested that filter slopes less than or equal to 12 dB/octave produce the least amount of distortion in the ABR. In contrast, when filter slopes are greater than 12 dB/octave, distortion occurs in the response which in turn produces significant reductions in the amplitudes and increases in the absolute latencies of waves I, III and V. Based on these findings, Elton and colleagues have recommended using filter slopes less than or equal to 12 dB/octave when recording the ABR in order to reduce distortion in the morphology of the response. In the proposed study, the analog bandpass EEG filter will be set to 100-3000 Hz and will have a 12 dB/octave filter slope.

Effects of artifact rejection rate on the ABR.

The goal of artifact rejection is to reduce any excess noise from contributing to the desired neural response. When a signal or noise surpasses a pre-determined amplitude level, such as +/- 25 μV, set by the artifact rejection, any potential contributors to the response which are larger or smaller than this level are automatically rejected from the averaged response (Sanchez & Gans, 2006).

Varying the artifact rejection rate can affect both the morphology of the response and the number of trials necessary to complete ABR. When the artifact rejection rate is set to a stringent rejection level, such as +/- 25 μV, fewer sweeps or trials will be accepted to create an average response. This in turn will increase the number of trials necessary to complete a significant response, increasing total test time. In general, most ABR studies have successfully employed +/- 25 μV artifact rejection criteria as an aid in the reduction of background noise without significantly increasing test time (Don & Elberling, 1994). In the proposed study we will also employ a +/- 25 μV artifact rejection criteria.

Effect of length of post-stimulus analysis window.

The length of the post-stimulus window (in milliseconds) should be set to encompass all the ABR components present in the response. At high stimulus intensities, wave V to a click stimulus typically occurs between 5-6 ms post-stimulus onset and at 8-9 ms post-stimulus onset as the stimulus intensity decreases (Chalak, Kale, Deshpande, & Biswas, 2013; Lolas and Hoeppner, 1977; Picton et al., 1981). In infants, the response is typically at least 1 ms delayed than that of an adult, resulting in the need for a longer post-stimulus analysis window (Hood, 1998). Most click-evoked ABR studies have typically used a post-stimulus time window of ~12 ms to successfully record waves I, III, and V in normal hearing adults and children (Picton et al., 1981; Chalak et al., 2013). Since this study will be recording ABRs to high intensity click stimuli in young adults with normal hearing sensitivity, the length of the post-stimulus analysis window will be set to 0 -12.8 ms, which should be sufficient in capturing the entire response in our young normal hearing adults.

Effect of the number of trials.

The ABR to an auditory signal, such as a click, is too small to recognize in the presence of other background electrical activity, such as EEG and myogenic/muscle activity. In order to enhance the low amplitude desired neural signal from the high amplitude of the residual background noise, a series of time-locked responses are averaged together. The principles of this averaging technique are based on the assumption that the ABR signal is constant in time and the background noise is random (Picton et al., 1983). Therefore, as the number of trials increases, the amplitude of the desired neural response will remain constant, while the amplitude of the residual noise will decrease. This results in an improved signal-to-noise ratio (SNR), such that the amplitude of the desired neural response, in the numerator, will be larger than the amplitude of the residual background noise, in the denominator. Several researchers have suggested that a SNR of at least 2:1 is typically required to achieve a replicable ABR (Picton, Linden, Hamel, & Maru, 1983; Stapells, 1989). Increasing the SNR of the ABR can be accomplished by increasing the number of trials averaged together and increasing the number of replications. Picton and colleagues (1983) recommend a total of at least 1600 trials to obtain a SNR of 2:1.

Another way to enhance the signal to noise ratio is to replicate the response 2 or more times (Hood, 1998). The number of trials is the amount of stimuli presented for one averaged waveform and the number of replications is the number of times an averaged waveform is completed (Stapells & Oates, 1997). In the proposed study, each trial will have a total of 1,024 trials. Each run will have at least 2 replications, for a total of 2,048 trials per test condition.

Effect of electrode montage and number of recording channels.

The ABR can be recorded from various locations on the scalp using surface electrodes. To create a more standard method of electrode placement, Jasper (1958) created a standardized system of electrode placement on the scalp and a universal designation of these various electrode sites. This helped to ensure that placement sites were similar between patients with different size and shape skulls. This standardized system is referred to as the 10-20 electrode system (Jasper, 1958).

According to this system, electrode sites were named based both on their location on the head as well as the anatomical positioning of the electrode over the brain. Electrodes placed on the left side of the scalp are referred to with odd numbers, electrodes placed on the right side of the scalp are referred to as even numbers, and a lower case "z" was used to indicate electrode placement along the midline between the anterior and posterior portion of the skull. A letter system is also used to indicate the anatomical positioning of the electrodes over the brain (Klem, Luders, Jasper, & Elger, 1999). For example, an uppercase "F" refers to the frontal lobe; an upper case "C" refers to the coronal line (midway between the anterior and posterior portion of the skull); an upper case "P" refers to the parietal lobe, and an uppercase A or M refers to the ear or mastoid, respectively. When an electrode is placed in the midline position in the coronal area, it would have the designation Cz, which is a typical electrode location for the active or non-inverting electrode when recording the ABR.

The typical electrode montage used to record an otoneurologic ABR involves 4 electrode sites using a two channel recording. This allows the audiologist to record both

the ipsilateral and contralateral responses to the click stimuli simultaneously. The advantage of using a simultaneous 2 channel recording technique is that it provides the audiologist with more information in order to accurately identify and measure the various ABR waves. For example, wave I is often as a robust wave seen in the ipsilateral channel and is typically not seen in the contralateral waveform. The contralateral channel allows better definition and separation of waves IV and V. These distinctions can be seen in the top and bottom waveforms in figure 10 below.

In the proposed study, the electrode placement for the ipsilateral and contralateral recording channels will be as follows: a non-inverting or active lead is placed above the Sylvian fissure at Cz. This placement results in the most robust amplitude of wave V (Beattie & Lipp, 1990; Beattie & Taggart, 1989; Hall, 2007; Terkildsen & Osterhammel, 1981). The inverting or reference electrode leads will be placed on the test earlobe for the ipsilateral recording and on the opposite earlobe for the contralateral recording. A final electrode will be placed on the forehead at Fpz, which will serve as the ground.

An example of this electrode montage and the accompanying 2-channel recording can be seen in figure 10 below. This will be the electrode montage used in this study to ensure standardization and a maximum response from each participant.

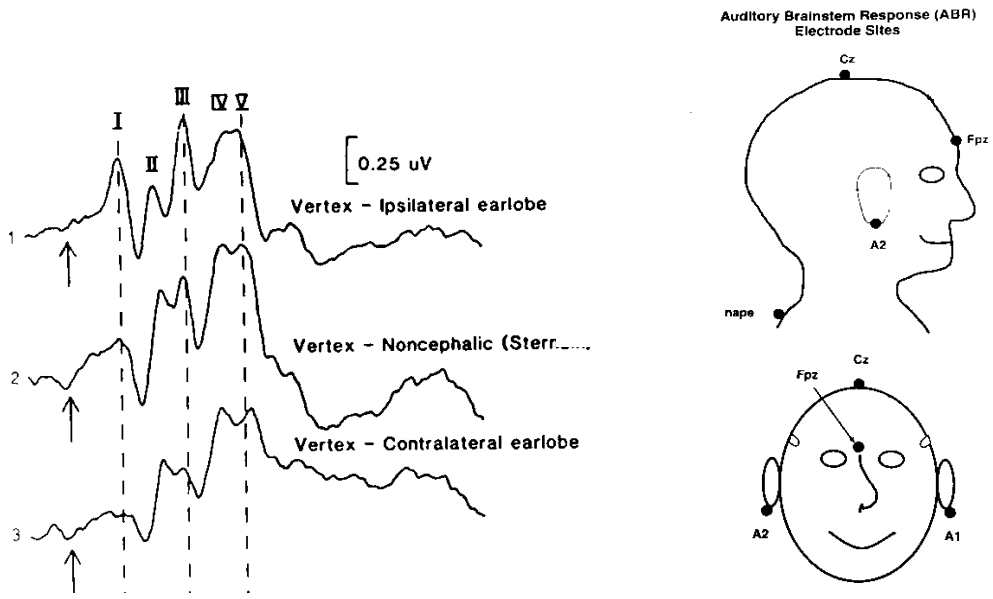

Figure 10. Electrode montage and accompanying ipsilateral and contralateral waveforms used for the purposes of otoneurologic ABR. Figure modified from Hall, 2007.

Two important considerations related to electrodes are the actual impedance value in ohms measured at each electrode site as well as the difference in impedance values across electrode sites. An impedance level of less than 5000 Ohms at each electrode site is suggested to reduce the level of electrical noise present in the response (Hall, 2007; Burkard & McNerney, 2009). It is also suggested that there be less than a 2000 Ohm difference between electrode sites. This helps to ensure that the electrode sites are properly able to reduce electrical noise in the recording and increase the effectiveness of common mode rejection (Hall, 2007; Burkard & McNerney, 2009). In the proposed study, all electrodes will have impedance values <5000 Ohms and the inter-impedance value will be <2000 Ohms.

Subject factors affecting the ABR.

There are numerous subject factors that influence the ABR. These include age, gender, and subject state. Each of these factors will be briefly discussed below.

Effects of patient age on the ABR.

The age of the subject can have an impact on the latency and amplitude measures of the ABR. This impact is first seen in infants and then again in the aging population. A study completed in 1974 compared the ABR of infants between 3 weeks and 3 years of age to that of adults (Hecox & Galambos, 1974). These investigators reported an increase in the latency of wave V seen in the infants until they reach between 12-18 months of age. At this time, their waveform begins to resemble an adult ABR (Hecox & Galambos, 1974). These findings are still consistent with more recent studies completed by Konrad-Martin et al. (2012) and Marcoux (2011).

Several studies have also looked at the difference in ABR waveforms between younger adults versus older adults (Kjaer, 1979; Konrad-Martin et al., 2012). Konrad-Martin and colleagues (2012) examined age effects in 131 individuals between the ages of 26 and 71 years. ABRs were recorded to a click stimulus which was presented to participants through insert earphones and recorded from disk electrodes placed on the vertex and mastoid. The click stimulus was recorded at a slow (11/sec), medium (51/sec), and fast (71/sec) click rates comparing age differences at each rate. Results from this study showed an increased latency and diminished amplitude for waves I, III, and V as the age of participants increased. This aging effect was most predominant at the slowest click rate of 11/sec. However, there was similar latency shifts between younger and older

participants as rate increased providing no evidence that showed an enhanced effect of aging on rate. To control for any effects of aging on the ABR in the proposed study, adults with normal hearing between the ages of 18-25 years will be recruited for this study.

Effects of subject gender on the ABR.

It has been demonstrated that there are significant differences in the amplitudes, latencies and interpeak latencies of the ABR between genders (Jerger & Hall, 1980; Kjaer, 1979; Stockard et al., 1979). Specifically, these studies have shown that females typically have larger amplitudes, shorter latencies, and shorter interpeak latencies in comparison to men (Jerger & Hall, 1980; Kjaer, 1979; Stockard et al., 1979).

Kjaer (1979) completed a study using 21 female and 19 male normal hearing participants between the ages of 13-48 years. He recorded the ABR to a click stimulus presented at 75 dB HL in each participant. Kjaer measured the latency and amplitudes of waves I-VII in each participant. He reported that the absolute latency values for all the ABR waves were longer in males compared to females. This gender difference was more pronounced for the later waves, specifically IV-VII. For example, the average latency difference between genders for wave I was 0.025 ms and was 0.208 for wave V. Kjaer also reported that female participants had significantly larger amplitude values for waves I, III and V in comparison to the male participants. The gender-related differences in amplitude values for waves I, III, and V were 0.15, 0.15, and 0.12 respectively.

There have been several reasons speculated for these gender differences in the ABR response measurements. These reasons include differences in head size between

genders and differences in core body temperatures between men and women. Dempsey, Censoprano, and Mazor (1986) compared the latencies and amplitudes of ABR wave V across genders. These investigators reported that even when men and women were matched for head size, women still demonstrated shorter wave V latencies and larger amplitudes in comparison to men. Therefore, Dempsey and colleagues concluded that as head size increases, so does absolute latency, regardless of gender.

Body temperature was also seen as a potential rationale for differences between male and female ABR components since males have a higher average core temperature by ~0.3 degrees Celsius (Hall, 2007). However, Hall (2007) reported that this relatively small difference in body temperature is not enough to produce the latency differences seen between males and females. Extreme body temperature changes, such as hypo- or hyperthermia, are more likely to cause differences in latency and amplitude and should be monitored in patients at risk for such exposure (Hall, 2007).

Don, Ponton, Eggermont and Masuda (1994) conducted a study to investigate what might be possible physiological reasons for these reported gender difference in the ABR response measures. These investigators speculated that the shortened latencies in females may be due to shorter cochlear response times. Don et al. (1994) demonstrated that the cochlear response times in females are 13% shorter than that of males. They also reported a steeper gradient in the female cochlea, which also contribute to these shorter latencies.

To control for gender effects on the ABR response measurements in the proposed study, an approximately equal number of males and females will be recruited to participate.

Effects of subject state on the ABR.

Osterhammel, Shallop, & Terkildsen (1985) conducted a study to determine the effects of natural sleep on the ABR and MLR. Osterhammel and colleagues recorded the ABR and MLR responses to 60 and 30 dBnHL click stimuli in 4 adults. These recordings were obtained throughout the subjects' entire night's sleep. This allowed researchers to evaluate changes in the response throughout all four stages of sleep and compare them to their response obtained while awake. These researchers reported that there were no significant differences in the amplitude or latencies in the various peaks of the ABR as a function of sleep stage, as seen in top portion of Figure 11 below. In contrast, the MLR showed an overall reduction in amplitude and an increase in latency in stages 3 and 4 of sleep.

Pharmacologically induced sleep was another concern reported among investigators. Since otoneurologic and threshold ABRs are often completed under sedation in difficult to test populations, many of these sleep inducing anesthetics were investigated for possible latency or amplitude changes. Several studies have demonstrated that many of the most commonly used pharmacological agents, such as barbiturate and nitrous oxide/halothane anesthesia, fortunately have no significant effect on latency or amplitude of the ABR (Picton, 1981; Sanders, Duncan, McCullough, 1979).

Since sleep state has been shown to have no significant alterations to the response properties and/or morphology of the ABR, participants in the proposed study will be encouraged to relax and sleep if possible throughout testing. No pharmacological agents will be given to any participants in this study.

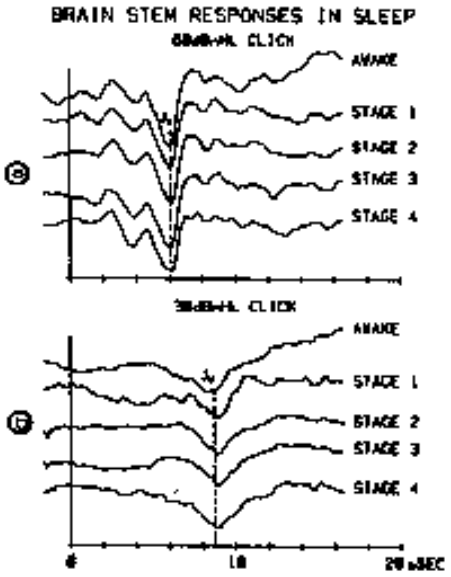

Figure 11. The ABR recorded to a 60 dBnHL and 30 dBnHL click while awake and throughout the four stages of sleep (Osterhammel et al., 1985).

Calibration

Calibration of the ABR equipment is a key factor in obtaining an accurate response. There are two primary procedures that are used to properly calibrate the click stimulus. Each will be briefly described below and calibrated using a sound level meter.

The first procedure is referred to as the peak-to-peak measure. To obtain an accurate reading it is necessary to have an oscilloscope, a 2 cc coupler and a sound level meter or SLM (Beattie & Rochverger, 2001; Burkard & McNerney, 2009). First, a click stimulus is played through the ABR equipment. In this procedure, the transducer from the

evoked potential equipment, for example the ER3A insert receiver, is fed into the 2 cc couple on the SLM. An output cable then takes the AC output from the SLM and then delivers it to the oscilloscope. Once the equipment is set up, a 70 dBnHL click stimulus is played through the ABR equipment. The magnitude of the output from this click stimulus is then read on the oscilloscope. This process is now repeated using a continuous 1000 Hz pure tone stimulus from the audiometer coupled to the sound level meter, using the same transducer and same settings on the SLM. The intensity of the sine wave stimulus from the audiometer is then adjusted to match the peak-to-peak measurement of the ABR stimulus on the oscilloscope. The measurement is then read on the SLM to ensure the expected output in dB SPL (Beattie & Rochverger, 2001; Burkard & McNerney, 2009).

The second procedure for calibrating ABR stimulus is called the peak-hold measure. The peak-hold calibration technique has been described as a more accurate and consistent technique among calibration of ABR stimuli (Beattie & Rochverger, 2001). This type of calibration procedure requires the use of a SLM that has a very sensitive time constant and is able to capture brief signals, such as a 100 microsecond click stimulus, with a peak-hold feature. An example is the B&K SLM 1620 and 1-inch microphone. The click stimulus is directed from the ABR equipment through the ER3A insert earphone transducer to the 2-cc coupler on the SLM. This peak-hold feature would be able to capture the stimulus at its loudest point or peak values. The level of energy at the peak is then displayed on the SLM.

It is important to note which of these methods is used when explaining the calibration of the equipment. When using the peak hold method, the SLM is capturing the energy at the peak of the signal; whereas when using the peak-to-peak method, it is

capturing the 3 dB down point from the peak. Due to the measurement difference between the peak-to-peak and baseline to peak, there is a 3 dB difference between the two calibration measures with the peak-to-peak measure being 3 dB less than the peak measure. For example, the baseline to peak measurement could read 77 dB SPL on the SLM, while the peak-to-peak measurement could read 74 dB SPL for a 1000 Hz tone. Both measurements are considered within the normal range for calibration.

For the purpose of the proposed study, we will be using a SLM with a peak hold function to ensure the proper calibration of the stimulus.

Sensitivity and Specificity of Otoneurologic ABR Response Measures

As discussed earlier in the literature review, there are various response measurements that are calculated on a click-evoked otoneurologic ABR to determine whether the patient's response is within the normal limits or is an abnormal response. These measurements include: the absolute latency of waves I, III and V; the interpeak latency (IPL) values for waves I-III, III-V and I-V; interaural latency differences for waves V and the I-V interval; and the wave V to wave I amplitude ratio.

One of the main aims of conducting an otoneurologic ABR is to detect a tumor or obstruction located along the VIII nerve or the auditory brainstem pathways. Determining how well each of these response measurements is able to detect an acoustic neuroma can be assessed by looking at the sensitivity and specificity of the measurement. Sensitivity reflects the true-positive rate and specificity reflects the true-negative rate (Don & Kwong, 2009). In terms of the ABR, sensitivity is the amount of tumor cases that are

correctly identified by that response measurement. In contrast, specificity is defined as the amount of non-tumor cases that are properly identified by that response measure.

Several studies have investigated the sensitivity and specificity of individual latency and response measurements in accurately detecting the presence of an acoustic neuroma (Bauch, Olsen, & Pool, 1996; Bockenheimer, Schmidt, & Zollner, 1984). The results of these studies will be discussed below.

Bauch, Olsen, and Pool (1996) examined the sensitivity of individual ABR response measurements and their ability to accurately detect tumors of various sizes. Their study was completed on 75 patients with surgically confirmed VIII nerve tumors and 342 individuals who radiologically showed no tumors. The participants with a present VIII nerve tumor were divided into a three groups based on tumor size; 1.0 cm or less (n=22), 1.1-2.0 cm (n=30), and 2.0 cm or larger (n=23). The latency measurements evaluated were the absolute latencies of waves I, III, and V, the interpeak I-III, III-V and I-V latencies and the interaural latency difference (ILD) of wave V. Abnormal criteria was based on normative measures found on their equipment and an ILD of greater than 0.4 ms (Bauch et al., 1996).

Bauch et al. reported that the most sensitive measurements were consistently found in patients with large tumors (>2.0 cm). Specifically, the absolute latencies of waves III and V, the IPL of III-V and I-V and the ILD of wave V all had sensitivity rates above 96% (Bauch et al., 1996). For participants with medium sized tumors (1-2 cm), there was a slight decrease in the sensitivity rate across all measurements. The most sensitive measurements for this group were the absolute latency of wave V and the ILD

of wave V, both of which had sensitivity rates of 93%. Lastly, in the group of subjects with small tumors, the sensitivity rate continued to decrease. Specifically, the sensitivity rate for wave V latency was 83% and the sensitivity of ILD V dropped to 68% in this group (Bauch et al., 1996). Based on this data, Bauch and colleagues concluded that the sensitivity of the ABR response measurements are dependent, in part, on the size of the tumor. These investigators speculated that the greater the number of nerve fibers affected by the tumor, the greater the likelihood of having an abnormal latency and/or amplitude measurement.

Bauch et al. (1996) also investigated the false-negative rate among non-tumor patients. These investigators found an overall false-positive rate as high as 37%, meaning a specificity of only 63% in non-tumor patients. These investigators speculated that the lower specificity rates were likely due to the presentation level of the stimulus and the variability among individuals even when matched for hearing loss. Bauch and colleagues reported that the highest combination in both sensitivity (92%) and specificity (88%) rates occurred for the absolute latency of wave V, interpeak latency of wave I-V and interaural difference of wave V. For this reason, Bauch et al. (1996) stressed the importance of looking at multiple response measures of each individual to properly assess the presence of a tumor.

Other studies have reported similar findings to those of Bauch et al. (1996) with sensitivity rates as high as 100% for tumors larger than 1 cm (Dornhoffer, Helms, & Hoehmann, 1994). These studies also reported a rapid decrease in sensitivity, as low as 63%, and increase in false positive findings, as high as 37%, when obtaining ABR measurements on individuals with small tumors (Dornhoffer et al., 1994, Schmidt et al.,

2001). This analysis was completed through a retrospective study of 70 patients with confirmed acoustic nerve tumors (Dornhoffer et al., 1994).

Currently the MRI is able to detect tumors as small as 3mm and has a sensitivity of 99% in detecting VIII nerve tumors (Chandrasekhar, Brackmann, & Devgan, 1995). While the otoneurologic ABR is not as sensitive as an MRI in detecting small tumors, it is still a valuable tool in the diagnosis of VIII nerve tumors and other clinical applications of the otoneurologic ABR. This is especially true in larger rural areas where the access to MRI technology is not readily available and the cost of imaging is high.

Another alternative option to increase the sensitivity of the ABR in detecting small tumors is the stacked ABR method. As stated earlier, the standard otoneurologic ABR measurements are impacted by the amount of neural fibers affected by any retrocochlear pathology. In the case of tumors < 1 cm, there is a greater possibility of obtaining normal latencies and amplitude measurements since less neural fibers are being interrupted. This section will briefly describe the stacked ABR technique in comparison the standard otoneurologic ABR, advantages of this technique, and current limitations in practice.

The goal in obtaining a stacked ABR is to measure the neural activity or contributions from the entire cochlea and not obtain a response dominated by contribution from the high frequency regions of the cochlea (Don, Masuda, Nelson, & Brackmann, 1997). This is achieved by stimulating the auditory pathway with a 60-65 dBnHL click stimulus, which is presented simultaneously with a high-pass filtered noised delivered to the same ear. The purpose of the high-pass noise is to mask certain areas of

the cochlea that are able to respond to the click stimulus and therefore contribute to the ABR response. During the stacked ABR recording, the ABR is initially recorded to the non-masked click. Then the cut-off frequency of the high-pass filter is lowered in 1-octave steps in order to limit the frequency regions of the cochlea that are capable of contributing to the response. Once all the high-pass filter conditions have been run, derived band responses are calculated. A derived band is calculated by subtracting the high-pass noise response at one cut off frequency from the high-pass noise response at the next highest cut-off frequency (Don et al., 1997). For example, the response obtained with a high-pass noise filter of 2000 Hz is subtracted from the response obtained with a high-pass noise filter of 4000 Hz. This subtraction results in a derived band waveform comprised of the energy coming from 2000-4000 Hz frequency region of the cochlea. To construct the stacked ABR, each derived band response is temporally aligned such that the latency of wave V in each derived band occurs at the same point in time. The peak-to-peak amplitude of all derived bands are summed to create the stacked ABR wave V. The amplitude of wave V-V' is then measured and compared to normative data. Any reduction in amplitude of the stacked ABR from any or all of the derived responses is suggestive of a tumor affecting the VIII nerve (Don et al., 1997).

To assess the reliability of sensitivity and specificity of the stacked ABR technique, Don et al. (1997) studied a series of case studies involving 25 confirmed acoustic neuromas. In this study, they compared the sensitivity of the standard otoneurologic ABR measures (i.e. IT5 and the interaural I-V interpeak latency) to the sensitivity of the stacked ABR. In this group of patients, the standard ABR measures missed a total of five small (<1 cm) tumors. In contrast, using the stacked ABR method

applied to the same case population, successfully detected all 25 tumors. An additional 30 small (<1 cm) tumor cases were calculated using the stacked ABR method and revealed a 100% sensitivity and 90% specificity rate in a control group. Don et al. (1997) concluded with these results that the stacked ABR was more sensitive in detecting the presence of small tumors than standard otoneurologic ABR's.

Limitations of the stacked ABR technique include the intensity level of the click stimulus. Typically, an intensity level of 60-65 dBnHL is used to elicit a response. This level can not be increased due to the level of masking noise needed for the high-pass noise test conditions. This limitation means that any patients with hearing loss greater than 60 dB HL can not be tested using stacked ABR measures. However, most patients reporting with small tumors do not present with a hearing loss above 60 dBnHL (Don et al., 1997).

Statement of Purpose

The purpose of this current study is to obtain normative data for various response measurements of the ABR for otoneurologic purposes. This normative data will be collected on our new Intelligent Hearing System Smart Evoked Potential System. Adults with normal hearing will participate in this study to accurately reflect a normal functioning auditory system and control for effects of aging and hearing loss. This study will specifically look at otoneurologic measurements including absolute latency of waves I, III and V; interpeak latency (IPL) values for waves I-III, III-V and I-V; interaural latency differences for waves V and I-V; wave V/I amplitude ratio; rate differences (19.1

vs 61.1 per second) and the comparison of the response to rarefaction and condensation stimuli to rule-out for ANSD.

Chapter 3

Materials and Methods

Subjects

Twenty normal hearing volunteers between the ages of 18-25 years participated in this study. An equal number of male and female participants were recruited (10 male, 10 female). Criteria for inclusion in the study was: (1) hearing thresholds that are ≤15 dB HL between 250-8000 Hz bilaterally, (2) normal middle ear function in each ear defined by middle ear pressure ranging from +50 to -150 daPa and static compliance values ranging from 0.2-1.6 ml (Shanks & Shohet, 2009), and (3) present contralateral acoustic reflexes within the 90th percentile at 500 Hz, 1000 Hz, and 2000 Hz in each ear (Gelfand, Schwander, & Silman, 1990). Participants also had no self-reported significant otologic history as indicated by the case history form completed prior to testing. An example of the case history form and the informed consent form are located in the appendix. Participants were recruited via word of mouth and fliers posted on campus.

Procedures

All testing took place at Towson University in a double-walled sound treated booth made by Industrial Acoustics Company. Testing took place in one session lasting approximately one to two hours. This session included behavioral audiometry to ensure qualification for participation followed by otoneurologic ABR testing.

Prior to this visit, participants were sent an otologic/neurologic case history form for them to complete. The case history form was reviewed by the investigator and if no significant case history was reported, an otoscopic examination, tympanometry and acoustic reflex testing were completed. Next, behavioral air-conduction thresholds were

screened for 250-8000 Hz at 15 dB HL bilaterally. If all inclusion criteria were met, the participant moved on to otoneurologic testing bilaterally. All 20 subjects met this criterion and were able to participate in the study.

Pure-Tone Behavioral Test Protocol

All behavioral air-conduction was completed using a GSI-61 audiometer. Air conduction thresholds were screened at 15 dB HL according to the modified Hughson-Westlake procedure using pulsed pure-tone stimuli in one-octave intervals between 250-8000 Hz. Participants were instructed according to ANSI S3.21-2004: "(1) Indicate the purpose of the test, to find the faintest tone that can be heard. (2) Indicate the need to respond whenever the tone is heard, no matter how faint it may be. (3) Indicate the need to respond overtly as soon as the tone comes on and to respond overtly immediately when the tone goes off. (4) Indicate that each ear is to be tested separately" (p. 4). Testing was completed using TDH-49 Supra Aural headphones.

ABR Test Protocol

Testing was completed on the Intelligent Hearing System (IHS) SmartEP system. Participants were instructed to relax/sleep in a reclined chair within the double-walled booth. Standard EEG disk electrodes were attached to the following locations using Ten20 conductive paste; Fpz (ground), Cz, (non-inverting), A1 and A2 (inverting for ipsilateral and contralateral ear). These areas were prepped using an alcohol wipe and a Nuprep skin prep gel to effectively reduce inter-electrode impedance values. Impedance values at each electrode site were monitored to remain less than 5000 Ohms with an inter-impedance value less than 2000 Ohms. These impedance values were monitored

throughout testing to ensure consistent values. An ipsilateral and contralateral channel were employed simultaneously for a 2-channel recording system using channels C and D of the IHS equipment.

A click stimulus, 100 μs in duration, was delivered via ER3A insert earphones. A rarefaction click stimulus presented at 19.1 clicks per second was delivered at 70, 80, and 90 dB HL. A condensation click was also delivered at 19.1 clicks per second at an intensity of 90 dB HL to rule out ANSD. Finally, a rarefaction click stimulus was run at 61.1 clicks per second at 90 dB nHL to stress the auditory system. Both the right and left ears were tested under these conditions. The starting ear was alternated across subjects.

An EEG analog bandpass filter was employed between 100-3000 Hz. The ABR was recorded with a post-stimulus window of 0-12.8 ms and an artifact rejection rate of +/-25 mV. Each trial of the ABR contained 1024 sweeps with at least two replicable trials for each recording parameter.

Once two replications of a response were obtained, both responses were summed. The following response measures were taken on the summed response: (1) absolute latencies of waves I, III, and V (2) interpeak latencies of I-III, III-V, and I-V (3) interaural wave V and wave I-V differences (4) wave V latency at 61.1/second and (5) wave V/I amplitude ratio. To ensure consistency among latency values, the latency of waves I and III were taken on the peak of the wave. The latency of wave V was taken on the shoulder of wave V unless a clear separation of wave IV and wave V were seen.

Calibration

The IHS system was calibrated for intensity, linearity, and stimulus polarity prior to any data collection. This was completed using a Larson Davis model 824 sound level meter and Larson Davis model 2575 one-inch microphone. Using the IHS system, a calibration factor of 0 dB nHL = 32 dB SPL was employed. According to these criteria all calibration data collected was within normal limits for the piece of equipment being used for data collection, as seen in table 1 below. Linearity was also within normal limits and a reversal in polarity was recorded during calibration.

Table 1. *Calibration Intensity Levels*

dB nHL	Right dB SPL	Left dB SPL
70	101.8	101.6
80	112.1	112.0
90	122.4	122.3

Statistical Analysis

Descriptive statistics were completed separately for each response measurement obtained from the participants. These descriptive statistics included the mean and standard deviation. A series of independent t-tests were conducted to determine if there were any significant differences any of in the response measure between ears. These t-tests were run separately for each response measurement at each stimulus intensity. An alpha level of $p < .05$ was originally employed to determine statistical significance. Since multiple t-tests were completed, there was an increase in the chance of a type I error. To correct for this, a Bonferroni correction factor was calculated by dividing the original p

value (.05) by the number of t-tests completed (33). This resulted in a corrected alpha level of $p < .001$ which was then applied to determine statistical significance between ears. If no significant differences were found, then data across ears was combined for those test conditions. A two-way repeated measures ANOVA was also completed to examine the effects of stimulus rate and ear on the absolute latency of wave V. An alpha level of $p < .05$ was used to indicate significance for the two-way repeated measures ANOVA.

Chapter 4

Results

The ABR's from the participants in this study were analyzed in terms of five primary characteristics of the response. These characteristics include: the latency measurements of the various waves; the peak-to-peak amplitude values of waves I-I' and V-V'; the effect of a slower versus faster stimulus rate on the absolute latency of wave V; the overall morphology and replicability of the response; and the effect of stimulus polarity on the response. Each of these characteristics will be discussed separately below.

In this study, the ABR was recorded to click stimuli presented at 70, 80, and 90 dBnHL in both the right and left ears of each subject. A total of 20 subjects participated in the study. A series of independent t-tests were run to determine if there was any significant difference in the ABR latency and amplitude response measurements between ears. Each latency and amplitude parameter was evaluated separately. Similarly, responses at each stimulus intensity were evaluated separately. The results of these series of t-tests revealed there were no significant differences between ears for any of the latency and amplitude response measurements. Therefore, the data was collapsed across ears for the various latency and amplitude measurements. The descriptive statistics (mean and standard deviation) calculated on this collapsed data is therefore based on a total of 40 ears. The specific results of these t-tests are reported in each section below.

Latency Results as a Function of Stimulus Intensity

For the purposes of this study, multiple ABR latency measures were taken on each subject's data. These include: the absolute latencies of waves I, III, and V; interpeak

latencies of waves I-III, III-V, and I-V; and the interaural differences for wave V latency and the I-V interpeak latency. Each of these results will be discussed separately in the sub-sections below.

Absolute latency values of waves I, III, and V.

As expected, the mean latency values of waves I, III, and V increased as stimulus intensity decreased from 90 to 70 dBnHL. These mean latency values and associated SD values are shown in table 2 below. The variability in these absolute latency values, reflected in the SD measures, was quite small, ranging between 0.095 to 0.173 across all waves.

Table 2. *Descriptive Statistic Values for the Absolute Latency of Waves I, III, and V in ms at Three Stimulus Intensities (n=40)*

Click Intensity		Wave I	Wave III	Wave V
90 dBnHL	**Mean**	**1.57**	**3.81**	**5.57**
	SD	0.097	0.137	0.095
80 dBnHL	**Mean**	**1.66**	**3.87**	**5.68**
	SD	0.101	0.146	0.119
70 dBnHL	**Mean**	**1.80**	**3.97**	**5.82**
	SD	0.111	0.166	0.173

The effects of stimulus intensity on the mean absolute latencies of waves I, III, and V are graphically displayed in figures 12, 13, and 14 respectively. As expected, the largest shift in latency as a function of stimulus intensity occurred for wave V, which was a 0.25 ms increase. This was followed by a 0.23 ms shift of wave I and finally a 0.16 ms shift of wave III.

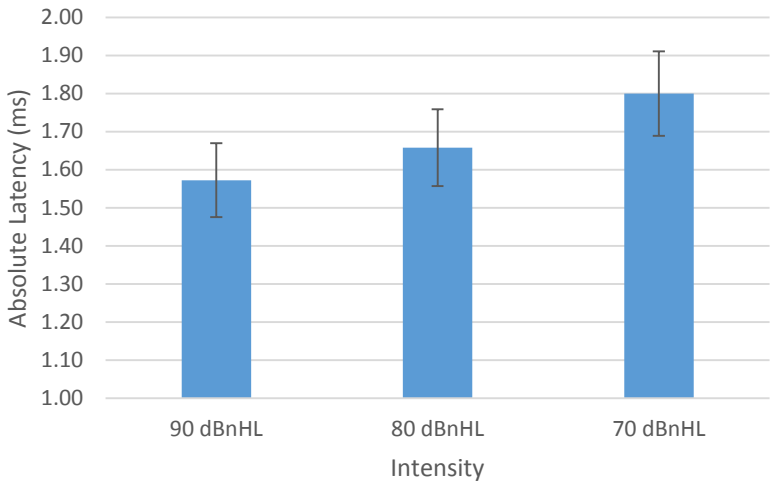

Figure 12. Mean absolute latency values (in ms) of wave I at the three stimulus intensities (n=40).

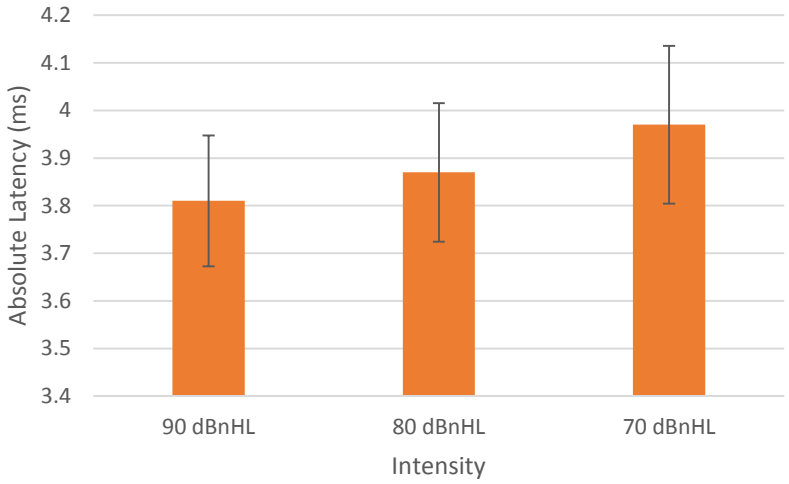

Figure 13. Mean absolute latency values (in ms) of wave III at the three stimulus intensities (n=40).

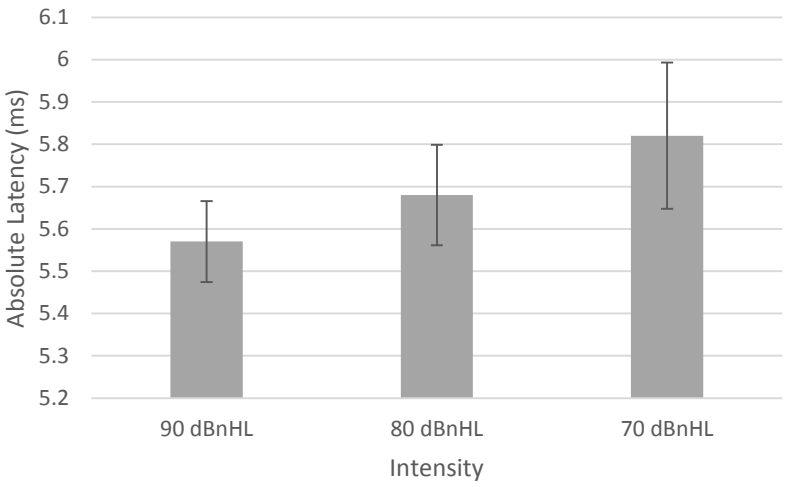

Figure 14. Mean absolute latency values (in ms) of wave V at the three stimulus intensities (n=40).

As previously mentioned, a series of independent t-tests were run to compare the absolute latencies of waves I, III, and V at 90, 80, and 70 dBnHL in the right ear and the left ear of each individual. No significant differences were found in any of these test conditions with p-values ranging from .207 to .976 and therefore the latency data at each stimulus intensity was collapsed across ears. Individual data for the absolute latency values for waves I, III, and V from the 40 ears can be found in Appendix C.

Interpeak latency values.

The interpeak latencies were measured for waves I-III, III-V, and I-V and descriptive statistics calculated on these values are displayed in table 3 below. The interpeak latency values for waves I-III ranged between 2.17 ms at 70 dBnHL to 2.24 ms at 90 dBnHL. Similarly, the interpeak latency of waves III-V ranged from 1.76 ms at 90 dBnHL to 1.85 ms at 70 dBnHL. The I-V interpeak latency had a consistent value of approximately 4.0 at each of these 3 stimulus intensities, as seen in figure 15. The

variability in these interpeak latency values, reflected in the SD values, was again quite small, ranging between 0.105 and 0.176 across all measurements.

Table 3. *Descriptive Statistic Values for the Interpeak Latencies in ms of Waves I-III, III-V, and I-V at Three Intensity Levels (n=40)*

Click Intensity		I-III	III-V	I-V
90 dBnHL	**Mean**	**2.24**	**1.76**	**4.00**
	SD	0.152	0.111	0.131
80 dBnHL	**Mean**	**2.21**	**1.81**	**4.02**
	SD	0.142	0.105	0.131
70 dBnHL	**Mean**	**2.17**	**1.85**	**4.02**
	SD	0.163	0.144	0.176

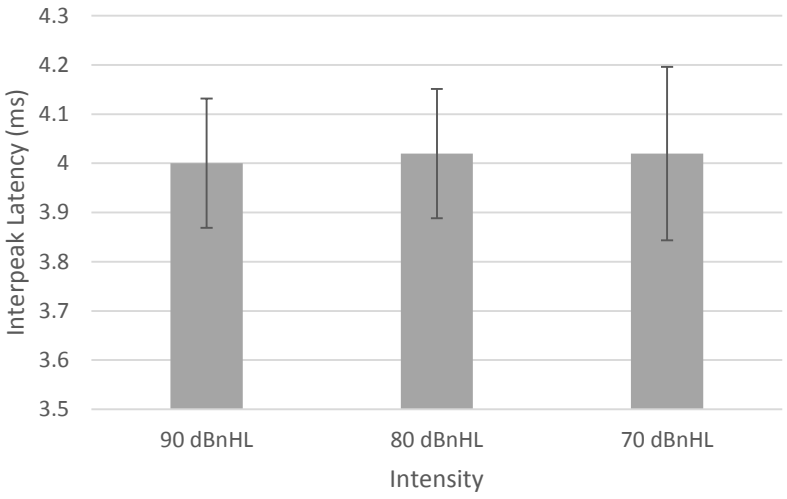

Figure 15. Mean interpeak latencies (in ms) of waves I-V at three stimulus intensities (n=40).

The results of the independent t-tests revealed there were no significant differences in any interpeak latency difference between ears with p-values ranging from .073 to .965. Individual data for the interpeak latency values for waves I-III, III-V, and I-V of 40 individual ears can be found in Appendix D.

Interaural latency differences.

The interaural latency differences were calculated for wave V and for the I-V interpeak interval at each stimulus intensity. The mean interaural difference values for wave V ranged from 0.05 ms to 0.09 ms across the three stimulus intensities, as seen in table 4 below. Similarly, the interaural latency values for the I-V interpeak latency ranged from 0.06 ms to 0.12 ms. Variability in this data, represented by SD measures, was quite low across all interaural measures, ranging between 0.028 and 0.094. Individual data for the interaural latency values for the 20 participants can be found in Appendix E.

Table 4. *Descriptive Statistics Values for Interaural Difference of Wave V and Wave I-V Interpeak Latency in ms at Three Intensity Levels (n=20)*

Click Intensity		Wave V	Wave I-V
90 dBnHL	**Mean**	**0.05**	**0.09**
	SD	0.028	0.053
80 dBnHL	**Mean**	**0.06**	**0.06**
	SD	0.038	0.053
70 dBnHL	**Mean**	**0.09**	**0.12**
	SD	0.094	0.078

Figure 16 below displays the mean interaural latency difference for wave V (solid) and the I-V interpeak interval (stripes) as a function of stimulus intensity. The maximum acceptable interaural difference for wave V and the I-V interaural difference is 0.2 ms (Don & Kwong, 2009) which is represented by the black line in this figure. Both mean interaural latency differences for wave V and the I-V interpeak interval are well below this line at all three stimulus intensities. There is a small increase (0.04 ms) in interaural differences for wave V as stimulus intensity decreased. No pattern was seen in the interaural differences of the wave I-V interpeak latency.

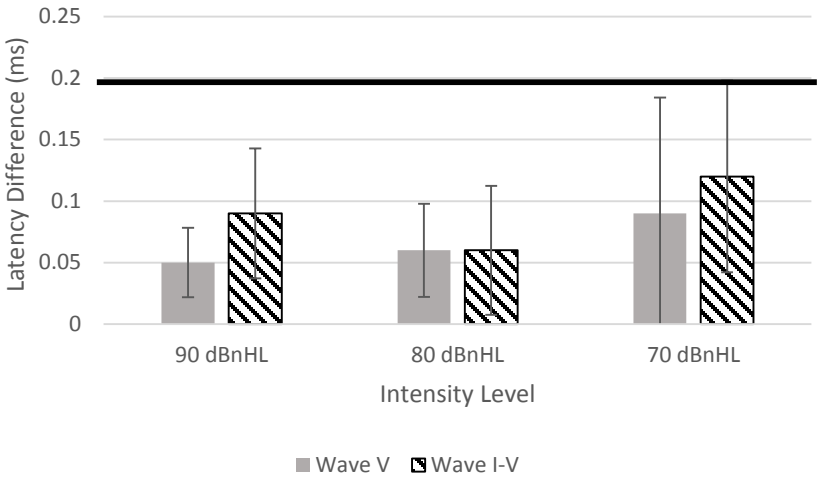

Figure 16. Mean interaural latency difference for wave V and wave I-V interpeak interval at the three stimulus intensities (n=20).

Peak-to-Peak Amplitudes as a Function of Stimulus Intensity

The peak-to-peak amplitude measurements of wave I-I' and V-V' were taken on a total of 40 ears. The data from both of these measurements was used to calculate the wave V/I amplitude ratio of each ear. As expected, the mean amplitudes of waves I-I' and V-V' both showed a decrease as stimulus intensity decreased, as seen in table 5 below. The variability in actual amplitude values for waves I-I' and V-V', as seen in SD values, ranged from 0.138 to 0.237 which is somewhat greater than that seen for the absolute latency measurements. The variability seen for the wave V/I amplitude ratio was fairly consistent at approximately 0.56-0.603 across stimulus intensities.

Table 5. *Descriptive Statistic Values for Amplitude Values in μV of Wave I and V and the V/I Ratio (n=40)*

Click Intensity		Wave I	Wave V	V/I Ratio
90 dBnHL	**Mean**	**0.45**	**0.64**	**1.48**
	SD	0.146	0.237	0.560
80 dBnHL	**Mean**	**0.41**	**0.52**	**1.38**
	SD	0.140	0.203	0.575
70 dBnHL	**Mean**	**0.29**	**0.41**	**1.59**
	SD	0.138	0.151	0.603

The mean wave V/I amplitude ratios ranged from 1.38 μV (80 dBnHL) to 1.59 μV (70 dBnHL). The AEP literature has shown that V/I amplitude ratios in normal hearing adults with negative neurologic histories should fall above 0.5 μV (Hall, 2007). In this study, the mean wave V/I amplitude ratios were well above this 0.5 μV minimum ratio criteria at all stimulus intensities, which is represented by the black line in figure 17. The individual peak-to-peak amplitude data for waves I-I' and V-V' and the V/I amplitude ratio are provided in Appendix F.

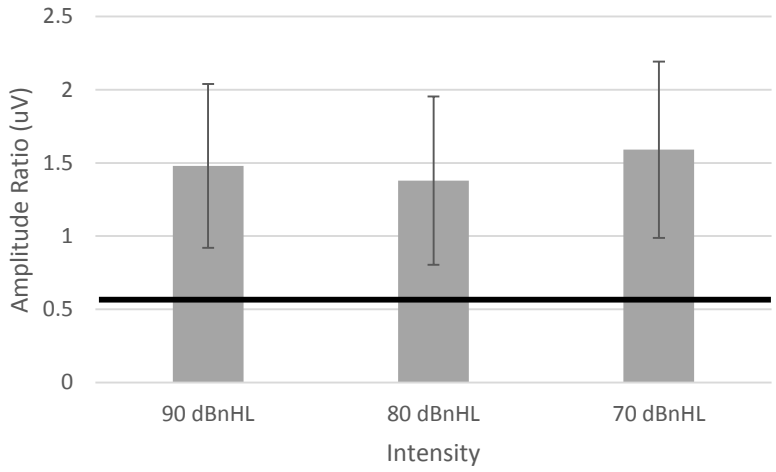

Figure 17. Mean wave V/I amplitude ratio (n=40).

No statistically significant difference between ears was found for the peak-to-peak amplitudes of waves I-I' and V-V' or for the wave V/I amplitude ratio in this series of

independent t-tests. The p-values in this series ranged from .196 to .932. Therefore, the amplitude data was collapsed across ears to provide the group averages of 40 ears as seen in the data above.

Effect of Stimulus Rate

As previously mentioned in the methods section, the ABR was recorded to a click stimulus presented at a slow (19.1 clicks/second) and a fast (61.1 clicks/second) rate at a fixed stimulus intensity level of 90 dBnHL. The latency shift of wave V as a function of rate was then calculated in the responses to both ears of 20 participants. Independent t-tests were calculated to determine if there was any significant difference in the wave V latency between ears. No significant difference was revealed and thus the shift in wave V latency data was collapsed across ears. Results of these analysis are reported at the end of this section.

The mean absolute latency of wave V at the slow click rate was 5.57 ms. The mean absolute wave V latency at the faster click rate was 5.96 ms. This resulted in a mean wave V latency shift of 0.39 ms, as seen in table 6 and figure 18 below. The variability in this data was quite small across all three latency measurements, indicated by the SD values ranging from 0.064 to 0.120. The individual latency data for subject's responses at the slower versus faster rates for all 40 ears can be found in Appendix G.

Table 6. *Descriptive Statistic Values for Absolute Latency in ms of Wave V at a Slow and a Fast Click Rate (n=40)*

		19.1 c/s	61.1 c/s	Rate Shift
90 dBnHL	**Mean**	**5.57**	**5.96**	**0.39**
	SD	0.095	0.120	0.064

Note. c/s = clicks per second

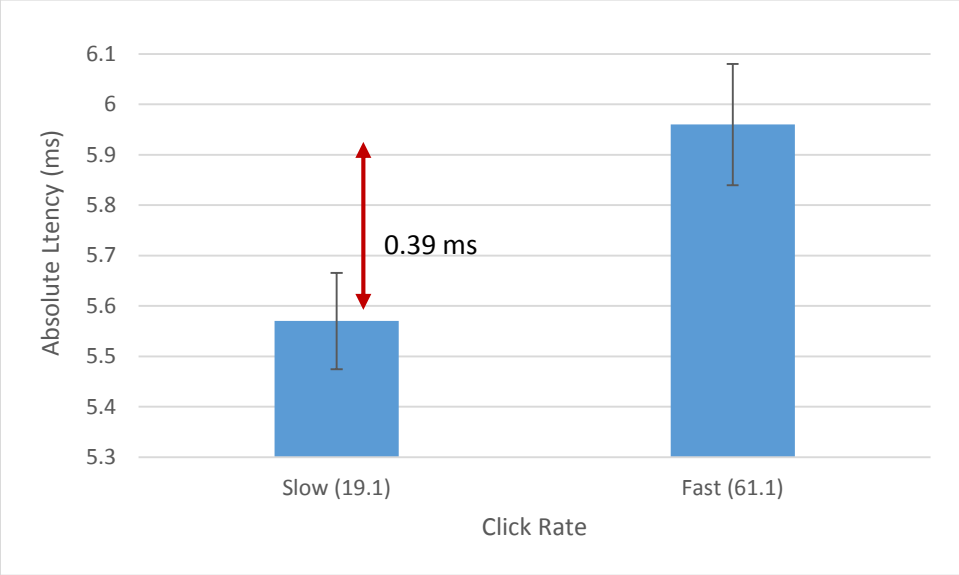

Figure 18. Mean absolute latency of wave V at a slow (19.1) and fast (61.1) click rate (n=40).

A two-way ANOVA was also conducted to examine the effect of stimulus rate and ear on wave V absolute latency. The two factors in this ANOVA were rate (19.1 versus 61.1 clicks/second) and stimulus ear (right versus left). The results of this two-factor analysis of variance showed a significant main effect for rate [$F(1,76) = 297.9$, $p = .000$], such that the mean wave V for the faster rate condition was significantly longer than the mean V latency for the slower rate condition. However, there was no significant main effect for ear [$F(1,76) = 3.893$, $p = .052$] and the interaction between rate and ear did not reach statistical significance [$F(1,76) = 0.369$, $p = .546$].

Overall Morphology and Replicability of the Response

The morphology and replicability of the click-evoked ABR was observed for each individual participant. The vast majority of subjects in this study had overall good morphology and replicable ABR responses at all stimulus intensities. For the few subjects who had noisier responses, additional trials were conducted to ensure that their ABR waves were replicable. Below are examples of two subjects ABR's with varying waveform morphology. One displays overall good waveform morphology and replicability, while the second displays a replicable but noisier ABR.

Figure 19 below displays an example of an ABR with good waveform morphology and replicability. This response was elicited from a 90 dBnHL rarefaction click stimulus. Only two replications were needed in order to obtain a replicable response for both the ipsilateral and contralateral tracings.

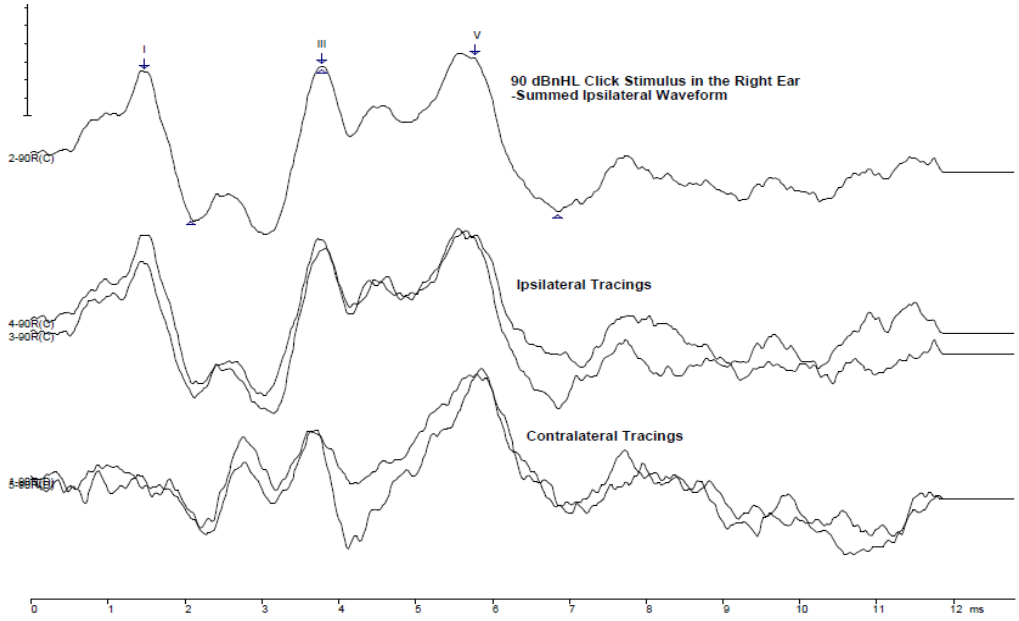

Figure 19. Waveforms obtained to a 90 dBnHL rarefaction click stimulus. Waveforms include a summed ipsilateral response, separate ipsilateral tracings, and separate contralateral tracings. ABR waves I, III and V are labeled in the summed response.

In contrast, the ABR seen in figure 20 has a poorer overall waveform morphology. This response was elicited to a 70 dBnHL rarefaction click stimulus. The response is considerably noisier in both the ipsilateral and contralateral tracings. A total of four replications were run in order to obtain an appropriate replicable response for ipsilateral and contralateral tracings. The two most replicable responses can be seen in the figure below. Even though this was a somewhat noisier ABR response, waves I, III, and V are identifiable in the summed response.

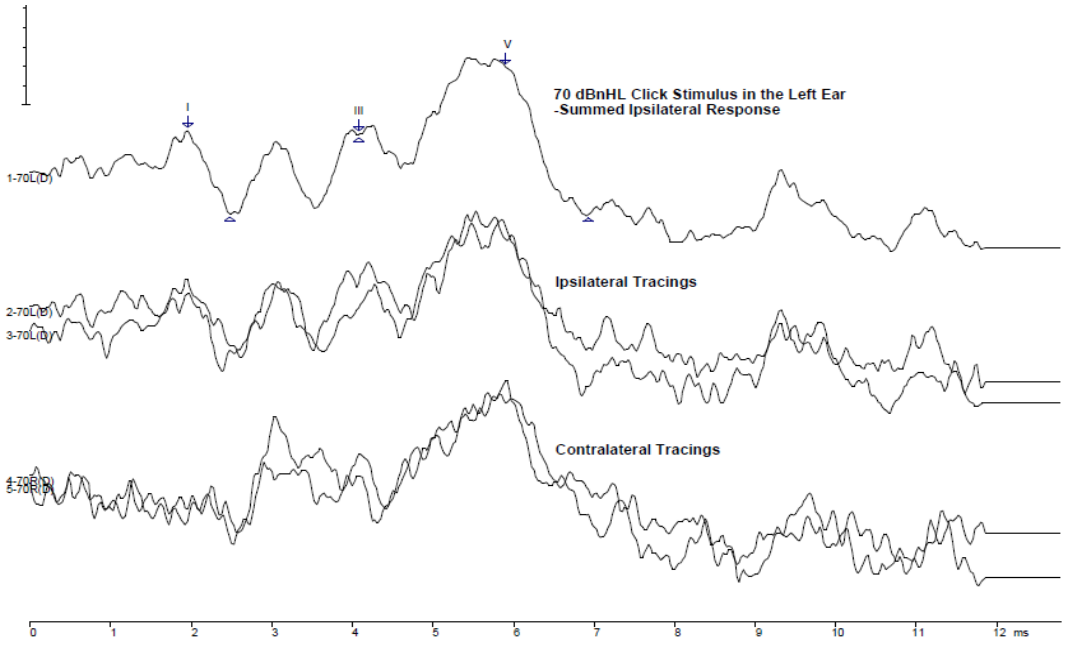

Figure 20. Waveforms obtained to a 70 dBnHL rarefaction click stimulus. Waveforms include a summed ipsilateral response, separate ipsilateral tracings, and separate contralateral tracings. ABR waves I, III and V are labeled in the summed response.

Effects of Stimulus Polarity on the Response

An otoneurologic ABR is typically recorded separately to a rarefaction and a condensation click stimulus in order to investigate evidence of ANSD. In a normal functioning auditory system, there should not be any reversal in the polarity of waves I, III, and V when recorded to a rarefaction and condensation click separately. In contrast,

in cases of ANSD often waves I, III, and V invert in polarity when the click polarity is reversed.

In the present study, we examined the ABR responses to see if there was any evidence of inversion of the ABR waves with a change in stimulus polarity. For all 20 participants, there was no evidence of inversion in the neural response as a function of stimulus polarity in either ear. An example of both a rarefaction and condensation waveform are represented in figure 21 below. As expected, waves I, III, and V all occur at similar latencies to both stimulus polarities and show no indication of reversal in polarity.

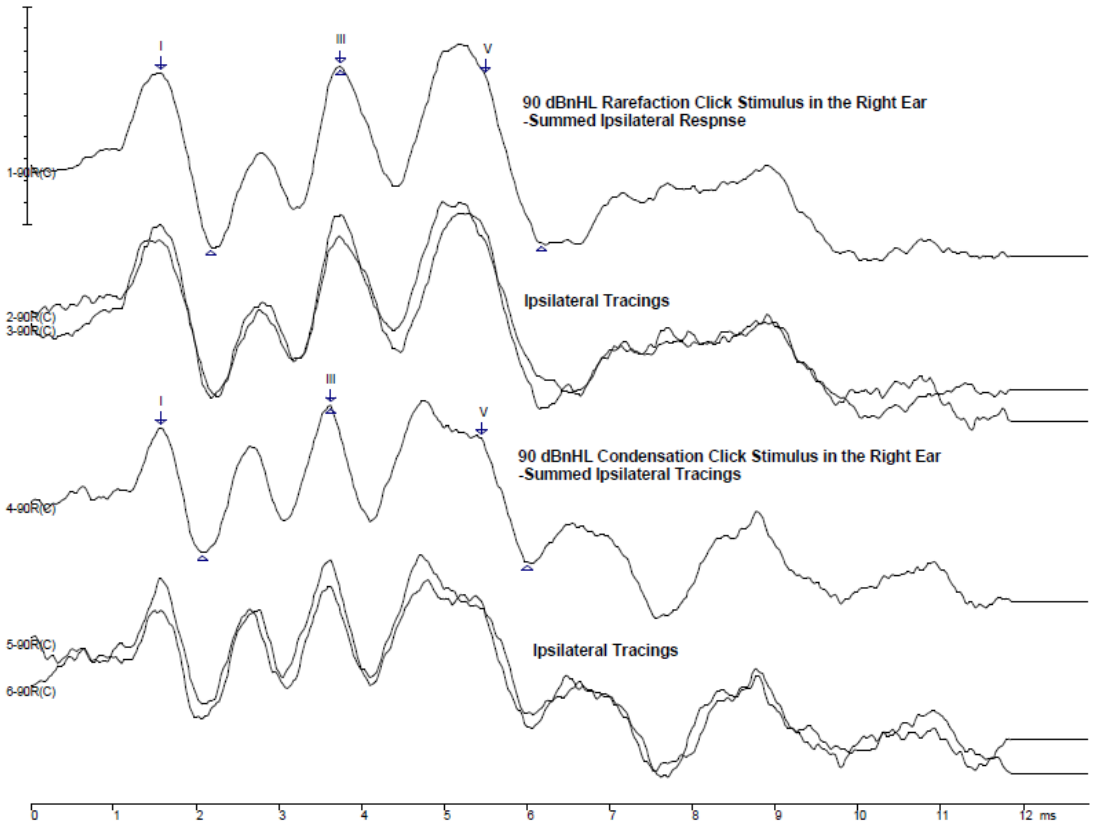

Figure 21. Waveform responses in response to a rarefaction and condensation 90 dBnHL click stimulus in the same participant. Both the replications and summed response of each stimulus polarity are represented. ABR waves I, III and V are labeled in the summed response for each stimulus polarity.

Clinical Normative Data

The results of the data reported above will be used in a clinical setting at Towson University. This normative data includes mean and standard deviation values for the various latency and amplitude response measurements discussed above. The standard deviation ranges typically used for otoneurologic normative data fall between two and three standard deviations of the mean value. For the purposes of our clinic at Towson University we employ a criterion of the mean ± 2.5 SD to determine the acceptable range of latency values in ms for our normative otoneurologic ABR data. The mean values and acceptable range of latency values for absolute latency, interpeak latencies, and rate differences for the Intelligent Hearing System (IHS) Smart EP system are seen on the clinic sheet attached in Appendix H.

Chapter 5

Discussion

This chapter will follow the same organization as the previous results section. This includes discussion of the latency measurements, amplitude measurements, effects of stimulus rate, overall morphology and replicability of the ABR, and finally the effects of stimulus polarity on the response. Each of these sections and their relevance to obtaining clinical normative data will be briefly discussed below.

Latency Measurements

In the present study, the click evoked ABRs were recorded at several stimulus intensities (90, 80, and 70 dBnHL). Our normative data revealed that the mean absolute latencies of waves I, III, and V increased as stimulus intensity decreased. Specifically, in the present study, we had a 0.25 ms increase in wave V as stimulus intensity changed from 90 dBnHL to 70 dBnHL. These changes in latency as a function of stimulus intensity were expected according to a number of studies completed on the effects of stimulus intensity on the absolute latencies of the various ABR waves (Gerling, 1989; Hood, 1998; Picton et al., 1981). Picton et al. (1981) reported that the mean absolute latencies of all three ABR waves increased as stimulus intensity decreased from 80 dBnHL to 30 dBnHL. A similar 20 dBnHL decrease displayed a ~0.3 ms in wave V from ~5.6 ms at 80 dBnHL to ~5.9 ms at 60 dBnHL.

When mean absolute latency results of the current study were compared to previous data, such as normative data previously collected at Towson University on the IHS SmartEP System as well as normative data from Hood (1998), similar mean absolute

latencies for waves I, III, and V were found across all three studies. The variability on the normative data, reflected in SD values, for the present study as well as these two other sources of normative data were quite similar for all three waves across stimulus intensities. These mean absolute latency comparisons and SD values are summarized in table 7 below.

Table 7. *Normative Data Comparing Absolute Latencies in the Current Study, Previous Towson University Data, and Published Normative Latencies by Linda Hood (1998).*

		Wave I			Wave III			Wave V		
		Current	Towson	Hood	Current	Towson	Hood	Current	Towson	Hood
90 dBnHL	**Mean**	**1.57**	**1.51**	**1.53**	**3.81**	**3.80**	**3.58**	**5.57**	**5.59**	**5.37**
	SD	0.10	0.08	0.11	0.14	0.13	0.09	0.10	0.16	0.12
80 dBnHL	**Mean**	**1.66**	**1.61**	**1.62**	**3.87**	**3.86**	**3.68**	**5.68**	**5.65**	**5.47**
	SD	0.10	0.12	0.12	0.15	0.15	0.08	0.12	0.16	0.12
70 dBnHL	**Mean**	**1.80**		**1.82**	**3.97**		**3.85**	**5.82**		**5.64**
	SD	0.11		0.17	0.17		0.13	0.17		0.16

Note. The previous data collected at Towson University also used the IHS SmartEP system on ~20 young adults with normal hearing and the same click stimulus and recording parameters used in the present study. Data published by Hood (1998) had an *n* of 14 females and used similar stimulus and recording parameters for click evoked ABRs.

Similarly, normative data was collected on the mean interpeak latencies of waves I-III, III-V, and I-V at these three stimulus intensities. As expected, these interpeak latency values remained essentially stable across all intensities. This is especially true for the wave I-V interpeak latency which was ~4.0 ms at all intensities. These results are in good agreement with Picton et al. (1981) who reported no substantial shifts in these three interpeak latencies at moderate to high stimulus intensities (70 and 80 dBnHL). He reported a wave I-V interpeak latency of ~4.02 at both 70 and 80 dBnHL. Again, mean values and SD values of the interpeak latencies obtained in the present study were in good agreement with data previously collected at Towson University on the IHS SmartEP System as well as published normative data from Hood (1998). The variability of the

normative data, reflected in SD values, for the present study as well as these two other sources of normative data were quite similar for all three interpeak latencies across stimulus intensities. In table 8 below, we compare the mean interpeak latencies and SD values in the present study with those previously collected at Towson University and Hood (1998).

Table 8. *Normative Data Comparing Interpeak Latencies in the Current Study, Previous Towson University Data, and Published Normative Latencies by Linda Hood (1998).*

		Wave I-III			Wave III-V			Wave I-V		
		Current	Towson	Hood	Current	Towson	Hood	Current	Towson	Hood
90 dBnHL	**Mean**	**2.24**	**2.28**	**2.05**	**1.76**	**1.79**	**1.79**	**4.00**	**4.08**	**3.84**
	SD	0.152	0.14	0.14	0.111	0.15	0.14	0.131	0.16	0.16
80 dBnHL	**Mean**	**2.21**	**2.25**	**2.06**	**1.81**	**1.79**	**1.79**	**4.02**	**4.04**	**3.85**
	SD	0.142	0.17	0.11	0.105	0.15	0.09	0.131	0.16	0.14
70 dBnHL	**Mean**	**2.17**		**2.03**	**1.85**		**1.79**	**4.02**		**3.82**
	SD	0.163		0.11	0.144		0.12	0.176		0.11

Note. The previous data collected at Towson University also used the IHS SmartEP system on ~20 young adults with normal hearing and the same click stimulus and recording parameters used in the present study. Data published by Hood (1998) had an *n* of 14 females and used similar stimulus and recording parameters for click evoked ABRs.

The previous research conducted on interaural latencies values for wave V and I-V have generally established a criteria for the maximum acceptable interaural difference for these two response measures (Don & Kwong, 2009). The investigators stated that the rationale for this criteria is that if the peripheral and central auditory nervous systems are working properly and there are similar behavioral pure tone thresholds across frequencies, there should not be any substantial difference in latency values between the two ears. In the present study, we applied a strict criteria of <0.2 ms as our maximum acceptable interaural difference for the absolute latency of wave V and interpeak latency of wave I-V. A few other studies have used various interaural latency criteria ranging from 0.2-0.4 ms to indicate a significant difference between ears (Don & Kwong, 2009).

As expected, the majority of participants in the present study displayed interaural latency differences of wave V and wave I-V interpeak latency below the permissible 0.2 ms interaural latency difference.

Amplitude Measurements

The effects of stimulus intensity on the peak-to-peak amplitude of waves I-I' and V-V' displayed an overall decrease in amplitude with a decrease in stimulus intensity. Again, this was the expected result according to previous studies on the effects of stimulus intensity on the peak-to-peak amplitude of waves I-I' and V-V' (Gerling, 1989; Hood, 1998; Picton et al., 1981). The V/I amplitude ratio was calculated from the peak-to-peak amplitude values for these two waves. In the current study, we employed a cut-off value for the V/I amplitude ratio of >0.5 μV indicating a normal functioning system. Our criteria were based on the Don and Kwong (2009) statement that any wave V/I amplitude ratio value below this <0.5 μV cut-off value is considered to be abnormal and indicative of a retrocochlear pathology (Don & Kwong, 2009).

Musiek and colleagues (1984) also investigated whether certain V/I amplitude ratio criteria could be used to differentiate between cochlear and retrocochlear pathologies. In this study, the participants included 25 normal control subjects, as well as 25 individuals with cochlear hearing loss and 25 individuals with confirmed retrocochlear pathologies. These investigators reported that all subjects with normal hearing and cochlear hearing loss had wave V/I ratios >1.0 μV. However, 44% of participants with a confirmed retrocochlear pathologies displayed wave V/I ratios <1.0 μV. As expected, all the participants in the present study had V/I amplitude ratios that are consistently greater

than the 0.5 μV criteria with mean amplitude ratios ranging from 1.38-1.59 μV across these three stimulus intensities, which are in excellent agreement with previous literature.

Stimulus Rate

The next otoneurologic measurement obtained for normative data included the effects of stimulus rate on the absolute latency of wave V. It has been suggested in the ABR literature that clinicians compare the wave V latency obtained to a click stimulus at both a faster and a slower stimulus rate (Ackley et al., 2006; Daly et al., 1977). Specifically, Ackley and colleagues (2006) explained that the rationale for using a faster click rate is that it places additional stress on the auditory system. For every increase of 10 in clicks per second (e.g. going from 20 clicks/sec to 30 clicks/sec), there is an expected latency shift of ~0.1 ms in wave V (Ackley et al., 2006).

The current study employed a slow rate of 19.1 clicks per second and a fast rate of 61.1 clicks per second. This approximate increase of 40 clicks per second would indicate an expected 0.4 ms shift in wave V latency. The results from this study showed a mean latency shift in wave V of 0.39 ms agreeing with the expected results reported in the literature (Daley et al., 1977).

It has been suggested that if clinicians encounter a problem of getting a clear and repeatable wave I when recording the ABR to a click stimulus presented at ~20 clicks/second, then lowering the stimulus rate to either 11.1 or 7.1 clicks/sec may be a way to elicit a more robust wave I. However, if any changes in stimulus rate are used while testing, then this needs to be indicated on the report as normative data has been collected at the rate of 19.1 clicks/second.

Morphology and Replicability of the ABR

The overall morphology and replicability of the ABR was observed in each individual. The morphology can vary greatly between participants and still be considered a normal response, particularly the wave IV/V complex (Hood, 1998). At high stimulus intensities such as 70, 80, and 90 dBnHL, each response should have an identifiable wave I, III, and V in normal hearing individuals. This variability in the morphology of the response is another reason why it is important to obtain at least two replications of each response to ensure that it is a repeatable measure. All responses in this study were obtained using at least two trials at each test condition. If the response was not repeatable within two trials, more trials were completed until a replicable response was obtained. The summed waveform represented the sum of the two most replicable responses. All latency and amplitude measures were taken on the summed response.

In the present study, the vast majority of the subjects ABRs were recorded using two trials at each stimulus intensity. Their overall waveform morphology was judged to be very good. A common error that is made in conducting ABR's is that not enough replications are completed to judge a valid and replicable response. This can occur in otoneurologic ABR evaluations as well as threshold ABR evaluations. These replications become increasingly important in threshold ABR's where the response is occurring at low intensities with very small amplitudes.

Stimulus Polarity of the Response

For an otoneurologic purpose, the ABR is typically recorded separately to both a rarefaction and a condensation click stimulus. The purpose of reversing the polarity of the

stimulus is to identify patients with ANSD. A key characteristic of patients diagnosed with ANSD is an inversion of waves I, III, and V when the polarity of the stimulus is changed (Berlin et al., 2003). This is due to a response from the outer hair cells instead of a proper response from the VIII nerve and auditory brainstem. To ensure that ANSD was not present in any participants, separate tracings of rarefaction and condensation were completed on all subjects.

In the present study, no reversal in waves I, III, and V were seen among the 20 normal hearing participants when the polarity of the stimulus was changed. This was the expected result since no participants reported any other otologic symptoms.

Important Considerations for Clinical Application

All of these characteristics of the response together make up the normative data collected for the otoneurologic ABR. It is imperative that normative data be obtained on any ABR system that is used in that clinical environment to ensure an accurate interpretation of the response is obtained. It is important for clinicians to not rely on the normative data that may come with the equipment or published normative data as their only source. Instead, clinicians should be collecting their own equipment specific normative data and then comparing it to the published normative data. The normative data for the AEP unit employed in their current clinical setting could be affected by a number of outside factors. These include influences such as environmental noise, the location of the equipment and the test subject, as well as specific stimulus and recording parameters. The normative data collected for the purpose of this study showed excellent

agreement in latency, amplitude, and rate measurements when compared to previous data collections completed at Towson University and in the literature.

An often overlooked yet critical component of obtaining accurate otoneurologic and threshold ABR's is accurate calibration of the equipment. Prior to collecting any normative data on an AEP system the clinician needs to ensure that equipment is appropriately calibrated in dBnHL units. This calibration protocol needs to include a check on the linearity of the stimuli across a broad range of stimulus intensities and a check on the polarity of the stimulus (Burkard & McNerney, 2009). Running normative data in a clinical environment is a relatively straight-forward process and should be the gold standard for collecting accurate otoneurologic ABR's.

APPENDIX A

Subject #_____ **Date: _____**

Otologic Case History Form

Please answer the following questions. If your answer is yes to any of the questions below, please explain in the comments section.

QUESTIONS	YES	NO
1. Are you currently experiencing any ear pain?		
2. Are you currently experiencing any fullness of your ear(s)?		
3. Do you have any problems with dizziness or vertigo?		
4. Do you have a history of ear infections?		
5. Are you currently or have you ever experienced draining of your ear(s)?		
6. Do you have any known pathologies of your ear(s)?		
7. Have you ever had any surgical procedures completed in or around the ear?		
8. Have you ever been diagnosed with a hearing loss?		
9. Do you have any known syndromes/diagnoses associated with hearing loss?		
10. Are you currently or have you ever experienced chronic ringing, buzzing, or humming in your ears?		
11. Have you ever experienced a traumatic head/brain injury?		
12. Do you experience migraines?		
13. Do you have any known neurological disorders?		

Comments:_____
_____
_____

APPENDIX B

TOWSON UNIVERSITY

Department of Audiology, Speech-Language Pathology, and Deaf Studies

Informed Consent and Disclosure Agreement

Project Title:

The Auditory Brainstem Response (ABR): A Normative Study Using the Intelligent Hearing System's Smart Evoked Potential System

Principal Investigator: Rachelle Webster, B.S. **Phone:** 410-236-6027

Purpose of the Study:

This study is designed to obtain normative Auditory Brainstem Response data for otoneurologic testing in adults. This data is being specifically obtained for the Intelligent Hearing Systems electrophysiology equipment. A critical step to obtain further data is to first establish normative results specific to the piece of equipment being used.

Procedures:

Participants will be asked to complete an otologic case history questionnaire prior to any testing. A screening of middle ear function and hearing will be performed. If results are within normal limits, the participant may choose to complete the auditory brainstem response testing. Test time will take approximately 2 hours in total.

Risks/Discomfort:

There are minimal risks to the individuals participating in this study. The Auditory Brainstem response is routinely used in clinical practice for adults and children. This is a non-invasive procedure using intensity levels that will be calibrated and below any levels that may be harmful to the participant.

Benefits:

It is hoped that the results of this study will provide a normative baseline for otoneurolgic ABR results. This information will be able to be used in the determination of abnormal otoneurolgic ABR results and used in future studies moving forward. Each participant will receive a free hearing screening and ABR for participating in this study.

Alternatives to Participation:

Participation in this study is voluntary. You are free to withdraw or discontinue participation at any time. Refusal to participate in this study will in no way affect any future services provided by the Towson University Speech-Language and Hearing Center or affect your ability to participate in any future studies.

Cost Compensation:

Participation in this study will involve no costs or payments to you.

Confidentiality:

All information collected during the study period will be kept strictly confidential. You will be identified through identification numbers. No publications or reports from this project will include identifying information on any participant. If you agree to join this study, please sign your name below.

_____ I have read and understood the information on this form.

_____ I have had the information on this form explained to me.

_____ _____
Subject's Signature Date

_____ _____
Witness to Consent Procedures Date

_____ _____
Principal Investigator Date

If you have any questions regarding this study please contact Dr. Smyth of the Hoffer Clinic at (301) 468-5924 or the Institutional Review Board Chairperson, Dr. Debi Gartland, Office of University Research Services, 8000 York Road, Towson University, Towson, Maryland 21252; phone (410) 704-2236.

THIS PROJECT HAS BEEN REVIEWED BY THE INSTITUTIONAL REVIEW BOARD FOR THE PROTECTION OF HUMAN PARTICIPANTS AT TOWSON UNIVERSITY.
**If investigator is not the person who will witness participant's signature, then the person administering the informed consent should write his/her name and title on the "witness" line.

APPENDIX C

Table 1. *Absolute Latency of Waves I, III, and V at Three Intensity Levels (n=40)*

	70 dBnHL			80 dBnHL			90 dBnHL		
Ear	Wave I	Wave III	Wave V	Wave I	Wave III	Wave V	Wave I	Wave III	Wave V
1	1.60	4.10	5.88	1.53	4.03	5.75	1.50	3.80	5.68
2	1.70	4.08	5.93	1.60	4.00	5.72	1.53	3.80	5.65
3	1.88	4.03	5.88	1.75	3.85	5.75	1.70	3.80	5.47
4	1.93	4.08	5.98	1.83	4.03	5.80	1.70	4.03	5.65
5	1.73	3.98	6.00	1.60	3.95	5.83	1.48	3.93	5.58
6	1.73	3.93	5.72	1.65	3.80	5.72	1.60	3.73	5.65
7	1.85	4.10	5.78	1.73	4.03	5.72	1.73	3.93	5.65
8	1.70	3.90	5.93	1.65	3.80	5.70	1.60	3.75	5.58
9	1.70	4.10	5.93	1.60	4.03	5.75	1.50	3.98	5.68
10	1.70	3.83	5.85	1.60	3.73	5.75	1.53	3.78	5.63
11	1.80	3.80	5.53	1.65	3.75	5.43	1.53	3.70	5.38
12	1.80	3.85	5.72	1.70	3.80	5.58	1.60	3.78	5.47
13	2.05	4.05	6.05	1.90	4.00	5.72	1.78	3.98	5.63
14	1.80	3.83	5.68	1.58	3.75	5.58	1.53	3.60	5.50
15	1.78	3.95	5.53	1.60	3.75	5.47	1.48	3.80	5.40
16	1.68	3.70	5.70	1.58	3.70	5.63	1.53	3.75	5.53
17	1.75	3.60	5.60	1.48	3.63	5.53	1.43	3.63	5.43
18	1.93	3.83	5.70	1.75	3.75	5.58	1.68	3.75	5.43
19	1.85	3.90	5.72	1.63	3.68	5.68	1.55	3.65	5.50
20	1.83	3.90	5.70	1.70	3.70	5.53	1.68	3.60	5.50
21	1.70	4.00	5.88	1.60	3.83	5.85	1.55	3.73	5.63
22	1.78	4.20	5.85	1.60	4.10	5.75	1.43	3.98	5.68
23	1.98	4.10	5.83	1.73	3.85	5.65	1.68	3.83	5.55
24	1.95	4.35	6.35	1.83	4.20	5.83	1.65	4.10	5.60
25	1.85	4.03	6.20	1.63	3.98	5.85	1.50	3.93	5.58
26	1.68	4.05	5.75	1.60	3.90	5.63	1.45	3.83	5.63
27	1.85	4.38	5.88	1.73	4.22	5.83	1.63	4.10	5.72
28	1.80	3.98	5.88	1.68	3.95	5.72	1.55	3.85	5.65
29	1.73	4.13	5.95	1.68	4.08	5.80	1.50	4.03	5.70
30	1.75	3.88	5.80	1.58	3.85	5.78	1.53	3.85	5.58
31	1.73	3.78	5.55	1.55	3.75	5.45	1.48	3.68	5.43
32	1.75	3.95	5.75	1.63	3.83	5.60	1.50	3.78	5.53
33	2.03	4.08	5.93	1.88	3.95	5.83	1.70	3.93	5.70
34	1.68	3.85	5.83	1.50	3.80	5.68	1.48	3.55	5.58
35	1.85	3.98	5.55	1.63	3.70	5.45	1.60	3.68	5.38
36	1.65	3.75	5.72	1.65	3.73	5.55	1.63	3.70	5.53
37	1.70	3.63	5.65	1.50	3.78	5.58	1.38	3.83	5.50
38	2.00	4.00	5.95	1.83	3.85	5.63	1.73	3.85	5.47
39	1.88	4.00	5.85	1.65	3.83	5.70	1.58	3.75	5.60
40	1.93	3.98	5.68	1.73	3.80	5.65	1.68	3.68	5.58

Note. All values measured in milliseconds (ms).

APPENDIX D

Table 2. *Interaural Latency Differences of Waves I-III, III-V and I-V at Three Intensity Levels (n=40)*

	70 dBnHL			80 dBnHL			90 dBnHL		
Ear	I-III	III-V	I-V	I-III	III-V	I-V	I-III	III-V	I-V
1	2.50	1.78	4.28	2.50	1.72	4.22	2.30	1.88	4.18
2	2.38	1.85	4.22	2.40	1.72	4.13	2.28	1.85	4.13
3	2.15	1.85	4.00	2.10	1.90	4.00	2.10	1.67	3.77
4	2.15	1.90	4.05	2.20	1.77	3.97	2.33	1.63	3.95
5	2.25	2.03	4.28	2.35	1.88	4.22	2.45	1.65	4.10
6	2.20	1.80	4.00	2.15	1.92	4.07	2.13	1.93	4.05
7	2.25	1.68	3.93	2.30	1.70	4.00	2.20	1.73	3.93
8	2.20	2.03	4.22	2.15	1.90	4.05	2.15	1.83	3.98
9	2.40	1.83	4.22	2.43	1.72	4.15	2.48	1.70	4.18
10	2.13	2.02	4.15	2.13	2.03	4.15	2.25	1.85	4.10
11	2.00	1.73	3.73	2.10	1.67	3.78	2.18	1.67	3.85
12	2.05	1.87	3.93	2.10	1.78	3.88	2.17	1.70	3.87
13	2.00	2.00	4.00	2.10	1.72	3.83	2.20	1.65	3.85
14	2.03	1.85	3.88	2.17	1.83	4.00	2.08	1.90	3.98
15	2.18	1.58	3.75	2.15	1.72	3.87	2.32	1.60	3.93
16	2.03	2.00	4.03	2.13	1.92	4.05	2.23	1.78	4.00
17	1.85	2.00	3.85	2.15	1.90	4.05	2.20	1.80	4.00
18	1.90	1.88	3.78	2.00	1.83	3.83	2.08	1.67	3.75
19	2.05	1.82	3.87	2.05	2.00	4.05	2.10	1.85	3.95
20	2.08	1.80	3.88	2.00	1.83	3.83	1.93	1.90	3.83
21	2.30	1.88	4.18	2.23	2.02	4.25	2.17	1.90	4.08
22	2.43	1.65	4.07	2.50	1.65	4.15	2.55	1.70	4.25
23	2.12	1.73	3.85	2.13	1.80	3.93	2.15	1.72	3.88
24	2.40	2.00	4.40	2.38	1.63	4.00	2.45	1.50	3.95
25	2.18	2.17	4.35	2.35	1.87	4.22	2.42	1.65	4.08
26	2.38	1.70	4.08	2.30	1.73	4.03	2.38	1.80	4.18
27	2.53	1.50	4.03	2.50	1.60	4.10	2.47	1.63	4.10
28	2.17	1.90	4.08	2.28	1.77	4.05	2.30	1.80	4.10
29	2.40	1.83	4.22	2.40	1.72	4.13	2.53	1.67	4.20
30	2.13	1.92	4.05	2.28	1.93	4.20	2.33	1.73	4.05
31	2.05	1.78	3.83	2.20	1.70	3.90	2.20	1.75	3.95
32	2.20	1.80	4.00	2.20	1.77	3.97	2.28	1.75	4.03
33	2.05	1.85	3.90	2.08	1.88	3.95	2.22	1.78	4.00
34	2.17	1.98	4.15	2.30	1.88	4.18	2.07	2.03	4.10
35	2.13	1.57	3.70	2.08	1.75	3.83	2.07	1.70	3.78
36	2.10	1.97	4.07	2.08	1.82	3.90	2.08	1.83	3.90
37	1.93	2.03	3.95	2.28	1.80	4.08	2.45	1.67	4.13
38	2.00	1.95	3.95	2.03	1.78	3.80	2.13	1.62	3.75
39	2.13	1.85	3.97	2.18	1.88	4.05	2.17	1.85	4.02
40	2.05	1.70	3.75	2.07	1.85	3.93	2.00	1.90	3.90

Note. All values measured in milliseconds (ms).

APPENDIX E

Table 5. *Interaural Difference of Wave I, V and I-V Interpeak Latency at Three Intensity Levels (n=20)*

	70 dBnHL		80 dBnHL		90 dBnHL	
Participant	Wave V	Wave I-V	Wave V	Wave I-V	Wave V	Wave I-V
1	0.00	0.10	0.10	0.03	0.05	0.10
2	0.08	0.15	0.03	0.02	0.03	0.12
3	0.05	0.15	0.10	0.07	0.08	0.11
4	0.37	0.35	0.03	0.03	0.05	0.00
5	0.20	0.07	0.02	0.00	0.00	0.02
6	0.03	0.08	0.09	0.04	0.02	0.13
7	0.10	0.10	0.11	0.10	0.07	0.17
8	0.05	0.14	0.02	0.00	0.07	0.12
9	0.02	0.00	0.05	0.02	0.02	0.02
10	0.05	0.10	0.03	0.05	0.05	0.05
11	0.02	0.10	0.02	0.12	0.05	0.10
12	0.03	0.07	0.02	0.09	0.06	0.16
13	0.12	0.10	0.11	0.12	0.07	0.15
14	0.15	0.27	0.10	0.18	0.08	0.12
15	0.02	0.05	0.02	0.04	0.02	0.15
16	0.02	0.04	0.08	0.15	0.00	0.10
17	0.05	0.10	0.05	0.03	0.07	0.13
18	0.25	0.17	0.05	0.03	0.04	0.00
19	0.13	0.10	0.02	0.00	0.10	0.07
20	0.02	0.13	0.12	0.10	0.08	0.07

Note. All values measured in milliseconds (ms).

APPENDIX F

Table 3. *Amplitude and Amplitude Ratios of Waves I and V at Three Intensity Levels (n=40)*

	70 dBnHL			80 dBnHL			90 dBnHL		
Ear	Wave I	Wave V	V/I Ratio	Wave I	Wave V	I/V Ratio	Wave I	Wave V	V/I Ratio
1	0.58	0.32	0.56	0.56	0.73	1.32	0.70	0.75	1.07
2	0.27	0.31	1.16	0.52	0.57	1.10	0.39	0.74	1.90
3	0.21	0.38	1.82	0.32	0.35	1.11	0.39	0.55	1.40
4	0.25	0.22	0.86	0.32	0.25	0.78	0.33	0.33	1.01
5	0.13	0.16	1.19	0.38	0.21	0.56	0.47	0.24	0.50
6	0.25	0.42	1.68	0.30	0.61	2.02	0.33	0.57	1.76
7	0.31	0.56	1.79	0.42	0.72	1.71	0.48	0.61	1.27
8	0.17	0.25	1.46	0.23	0.45	1.94	0.27	0.55	2.07
9	0.30	0.51	1.82	0.43	0.71	1.69	0.23	0.43	1.64
10	0.23	0.28	1.25	0.49	0.41	0.84	0.38	0.78	2.04
11	0.23	0.32	1.40	0.42	0.46	1.09	0.50	0.64	1.29
12	0.38	0.50	1.33	0.66	0.61	0.93	0.82	0.81	0.99
13	0.24	0.27	1.11	0.39	0.35	0.89	0.38	0.35	0.94
14	0.20	0.47	2.41	0.31	0.68	2.19	0.27	0.71	2.66
15	0.30	0.31	1.03	0.47	0.44	0.92	0.56	0.59	1.05
16	0.46	0.49	1.06	0.46	0.72	1.57	0.52	0.90	1.73
17	0.12	0.25	2.04	0.20	0.27	1.34	0.22	0.32	1.44
18	0.11	0.36	3.37	0.37	0.59	1.57	0.49	0.68	1.39
19	0.22	0.44	2.05	0.27	0.58	2.11	0.36	0.46	1.28
20	0.43	0.76	1.75	0.56	0.25	2.25	0.56	1.25	2.22
21	0.77	0.47	0.61	0.67	0.45	0.67	0.70	0.86	1.24
22	0.31	0.52	1.70	0.58	0.79	1.38	0.50	0.86	1.73
23	0.19	0.35	1.86	0.34	0.44	1.30	0.39	0.48	1.24
24	0.10	0.17	1.82	0.28	0.36	1.30	0.51	0.45	0.88
25	0.20	0.17	0.87	0.31	0.20	0.63	0.40	0.42	0.53
26	0.38	0.59	1.58	0.22	0.74	3.33	0.28	0.65	2.30
27	0.29	0.57	1.93	0.57	0.69	1.22	0.70	0.66	0.94
28	0.19	0.42	2.20	0.21	0.49	2.39	0.35	0.57	1.64
29	0.38	0.32	0.84	0.41	0.43	1.06	0.47	0.71	1.51
30	0.32	0.60	1.85	0.38	0.46	1.19	0.56	1.12	2.01
31	0.19	0.44	2.28	0.44	0.42	0.94	0.51	0.54	1.07
32	0.38	0.42	1.09	0.74	0.60	0.82	0.75	0.64	0.86
33	0.32	0.36	1.48	0.18	0.27	1.12	0.30	0.49	1.62
34	0.37	0.48	1.30	0.44	0.54	1.23	0.37	0.83	2.20
35	0.33	0.41	1.23	0.36	0.50	1.40	0.46	0.38	0.84
36	0.55	0.47	0.85	0.63	0.78	1.24	0.55	0.90	1.63
37	0.15	0.28	1.80	0.23	0.28	1.22	0.22	0.53	2.44
38	0.15	0.43	2.83	0.39	0.40	1.03	0.52	0.48	0.93
39	0.21	0.51	2.43	0.37	0.59	1.59	0.51	0.59	1.17
40	0.43	0.87	2.04	0.53	1.21	2.30	0.48	1.30	2.72

Note. All values measured in microvolts (μV).

APPENDIX G

Table 4. *Wave V Latencies Between a Slow (19.1) and Fast (61.1) Click Rate (n=40)*

	90 dBnHL		
Ear	19.1	61.1	Difference
1	5.68	6.13	0.45
2	5.65	6.00	0.35
3	5.47	5.85	0.38
4	5.65	6.00	0.35
5	5.58	6.03	0.45
6	5.65	5.93	0.28
7	5.65	6.03	0.38
8	5.58	5.95	0.37
9	5.68	6.03	0.35
10	5.63	5.98	0.35
11	5.38	5.72	0.34
12	5.47	5.85	0.38
13	5.63	6.05	0.42
14	5.50	5.83	0.33
15	5.40	5.78	0.38
16	5.53	5.90	0.37
17	5.43	5.75	0.32
18	5.43	5.85	0.42
19	5.50	5.98	0.48
20	5.50	5.83	0.33
21	5.63	6.15	0.52
22	5.68	5.98	0.3
23	5.55	6.00	0.45
24	5.60	6.10	0.5
25	5.58	6.00	0.42
26	5.63	6.00	0.37
27	5.72	6.13	0.41
28	5.65	6.00	0.35
29	5.70	6.18	0.48
30	5.58	5.88	0.3
31	5.43	5.72	0.29
32	5.53	5.93	0.4
33	5.70	6.20	0.5
34	5.58	5.98	0.4
35	5.38	5.83	0.45
36	5.53	5.95	0.42
37	5.50	5.85	0.35
38	5.47	6.00	0.53
39	5.60	6.03	0.43
40	5.58	5.95	0.37

Note. All values measured in milliseconds (ms).

APPENDIX H

Towson University, Van Bokkelen 109C – IHS SmartEP System
Towson University - 8000 York Road, Towson, MD 21252
Normative Data Collected in 2016

Name: DOB:

Tester: Age:

Date of Evaluation: Phone:

Absolute Latency Differences – Rate 19.1/second

	90 dBnHL		80 dBnHL		70 dBnHL	
Absolute Latency	Mean	+/- 2.5 SD	Mean	+/- 2.5 SD	Mean	+/- 2.5 SD
Wave I	1.57	1.33-1.81	1.66	1.41-1.91	1.80	1.52-2.08
Wave III	3.81	3.47-4.15	3.87	3.51-4.24	3.97	3.56-4.39
Wave V	5.57	5.33-5.81	5.68	5.38-5.98	5.82	5.39-6.25
Interpeak Latency	Mean	+/- 2.5 SD	Mean	+/- 2.5 SD	Mean	+/- 2.5 SD
I-III	2.24	1.86-2.62	2.21	1.86-2.57	2.17	1.76-2.58
III-V	1.76	1.48-2.04	1.81	1.55-2.07	1.85	1.49-2.21
I-V	4.00	3.67-4.33	4.02	3.69-4.35	4.02	3.58-4.46

	Right Ear			Left Ear		
Absolute Latency	dBnHL	dBnHL	dBnHL	dBnHL	dBnHL	dBnHL
Wave I						
Wave III						
Wave V						
Interpeak Latency	dBnHL	dBnHL	dBnHL	dBnHL	dBnHL	dBnHL
I-III						
III-V						
I-V						

Interaural Latency Differences – Rate 19.1/second

Latency	90 dBnHL	80 dBnHL	70 dBnHL
Wave V			
I-V			

***Differences greater than 0.2 ms are considered abnormal*

Amplitude Ratio for Wave V/I

	Right Ear	Left Ear
90 dBnHL		
80 dBnHL		
70 dBnHL		

***Amplitude ratios less than 0.5 μV are considered suspect of auditory dysfunction*

Rate Differences – *Mean rate shift of 0.39 ms (+/- 2.5 SD = 0.23-0.55)*

90dBnHL	Right Ear			Left Ear		
	19.1/sec	61.1/sec	Difference	19.1/sec	61.1/sec	Difference
Wave V						

Reversal in polarity seen between Rarefaction and Condensation Stimuli – *Circle Answer*

Right Ear	Yes	No
Left Ear	Yes	No

APPENDIX I

TOWSON UNIVERSITY

APPROVAL NUMBER: 16-A038

To: Rachelle Webster
2505 Philadelphia Rd
Edgewood MD 21040

From: Institutional Review Board for the Proctection of Human Subjects Debi Gartland,Chair

Date: Monday, October 19, 2015

RE: Application for Approval of Research Involving the Use of Human Participants

Office of Sponsored Programs & Research

Towson University
8000 York Road
Towson, MD 21252-0001

t. 410 704-2236
f. 410 704-4494
www.towson.edu/ospr

Thank you for submitting an Application for Approval of Research Involving the Use of Human Participants to the Institutional Review Board for the Protection of Human Participants (IRB) at Towson University. The IRB hereby approves your proposal titled:

The Auditory Brainstem Response (ABR): A Normative Study Using the Intelligent Hearing System's Smart Evoked Potential System

If you should encounter any new risks, reactions, or injuries while conducting your research, please notify the IRB. Should your research extend beyond one year in duration, or should there be substantive changes in your research protocol, you will need to submit another application for approval at that time.
We wish you every success in your research project. If you have any questions, please call me at (410) 704-2236.

CC: Peggy Korczak
File

TOWSON UNIVERSITY

Date: Monday, October 19, 2015

NOTICE OF APPROVAL

TO: Rachelle Webster **DEPT:** ASLD

PROJECT TITLE: *The Auditory Brainstem Response (ABR): A Normative Study Using the Intelligent Hearing System's Smart Evoked Potential System*

SPONSORING AGENCY: None

APPROVAL NUMBER: 16-A038

The Institutional Review Board for the Protection of Human Participants has approved the project described above. Approval was based on the descriptive material and procedures you submitted for review. Should any changes be made in your procedures, or if you should encounter any new risks, reactions, injuries, or deaths of persons as participants, you must notify the Board.

A consent form: [✓] is [ ] is not required of each participant

Assent: [ ] is [✓] is not required of each participant

This protocol was first approved on: 19-Oct-2015
This research will be reviewed every year from the date of first approval.

Amy L Taylor for

Debi Gartland,Chair
Towson University Institutional Review Board

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B.S. in Speech Language Pathology and Audiology Graduated May 2013
Towson University, Towson, Maryland
GPA: 3.78

RESEARCH EXPERIENCE

Doctoral Thesis
Spring 2015 – Spring 2016

- The Auditory Brainstem Response (ABR): A Normative Study Using the Intelligent Hearing System's Smart Evoked Potential System
- Advisor: Dr. Peggy Oates-Korczak, Towson University

CLINICAL EXPERIENCE

Ear, Nose & Throat, Asthma and Allergy Specialty Group (ENTAA Care) – Columbia, MD
Audiology Intern – August 2015-Present

- Comprehensive adult and pediatric hearing evaluations
- Adult and pediatric hearing aid fitting, orientation, and follow up
- Adult and pediatric amplification services
  - Assistive listening device fitting and orientation
  - Hearing aid repairs
- Auditory Brainstem Response (ABR)
- Electronystagmography (ENG) and Videonystagmography (VNG) assessment
- ECochG and VEMP assessment
- Assisted with cochlear implant evaluations and mapping

Nemours/Alfred I. DuPont Hospital for Children – Wilmington, DE
Audiology Intern – May 2015-July 2015

- Comprehensive pediatric hearing evaluations
  - Standard, visual reinforcement, and conditioned play audiometry
- Pediatric hearing aid fitting, orientation, and follow-up
- Pediatric amplification services
  - FM fitting
  - Hearing aid repairs
- Otoacoustic emissions (OAE) testing
- Auditory Brainstem Response (ABR) testing
  - Otoneurologic ABR
  - Air- and Bone- conduction ABR for threshold determination

- Participation in cleft-palate and ear anomaly team meetings
- Performed 2-part newborn hearing screenings: aABR and OAE
- Complete patient reports and updates using a hospital wide medical database

A&E Audiology and Hearing Aid Center – Lititz, PA
Audiology Intern – January 2015-May 2015

- Comprehensive adult hearing evaluations
- Adult hearing aid fitting, orientation, and follow-up
    - Real Ear Measurements and electroacoustic analysis
- Adult amplification services
    - Hearing aid accessory fitting and orientation
    - Hearing aid repairs
- Otoacoustic emissions (OAE) testing
- Cerumen Management
- Participation in community outreach and seminars
- Participation in audiology team meetings
- Submit patient reports and updates using a healthcare medical database

Towson University Hearing and Balance Center – Towson, MD
Student Clinician – August 2013-December 2014

- Comprehensive adult and pediatric hearing evaluations
- Adult and pediatric hearing aid fitting, orientation, and follow-up
- Diagnostic Auditory Brainstem Response (ABR) testing
- Videonystagmography (VNG)
- Rotary Chair testing

RELATED WORK EXPERIENCE

The Goddard School for Early Childhood Development - Bel Air, MD
Teacher/Operational Office Administrator – January 2007-Present

- Care for children of various ages; often servicing those with special needs.
- Classroom management.
- Participation in community outreach.
- Quality assurance; ensure all classrooms meet quality and safety standards.
- Office Management; communication with current and prospective clients.
- Control of daily opening and closing procedures.

STUDENT RELATED SERVICES

Vice President of Towson Student Academy of Audiology	May 2014 - May 2015
Audiology Volunteer at Special Olympics - Towson, MD	Summer 2014, 2015
Volunteer at Maryland Academy of Audiology Conference	Fall 2014, 2015
Hearing Conservation Volunteer at Towson University Events	Fall 2014 - 2015
National Student Academy of Audiology	Fall 2013 - Present
Undergraduate Student Mentor	Fall 2013 - Present
Volunteer at Camp Koski for Children with Autism	Summer 2012, 2013

References available upon request.