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A COMPARISON OF FFR MEASURES OF YOUNG ADULTS WITH BIOMARK NORMATIVE VALUES

by

Kathryn Eileen Pitts

Thesis submitted in partial fulfillment
of the requirements for the degree

of

DEPARTMENTAL HONORS

in

Communicative Disorders
in the Department of Communicative Disorders & Deaf Education

Approved:

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Abstract

The BioMARK (Biological Marker of Auditory Processing) test, formerly known as BioMAP, is a measure of the frequency following response (FFR) in children to a speech stimulus. The test was designed for 8 to 12 year old children. Other tests of the auditory brainstem such as auditory brainstem responses, have normative values that are valid for listeners from age 2 to adulthood. The goal of the present study was to evaluate the speech-evoked FFR of young adult listeners to determine if a separate set of normative values is needed for this age group. FFR tests using the BioMARK with thirteen listeners aged 18 to 30 years old revealed that a majority of the adults tested fell outside the children-based normative values of the BioMARK. The most consistent differences were found in the amplitude of the FFR responses with the young adults having lower amplitudes than that of the children upon which the normative values of the BioMARK were based. The reason for these amplitude differences in not currently known but the results do support the need to collect normative data for the BioMARK specifically for young adult listeners.

Philippians 4:13

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A Comparison of FFR Measures of Young Adults with BioMARK Normative Values

Introduction

Much is still unknown about how human listeners process complex signals in the auditory neural system from the cochlea up to the cortex of the brain. The complex signal of most value to human listeners is speech; an understanding of how listeners process the information contained in the auditory speech signal could lead to many benefits, including more effective therapy for listeners with speech and hearing problems or potentially allowing people with difficulties processing the auditory speech signal to catch up to (or not fall behind) their peers in language and information processing tasks. Recent experiments using electrophysiologic measurements of the brain's response to speech sounds have been carried out to better understand how speech is processed in the auditory neural system of listeners (Kraus & Nicol 2003; Warrier, Johnson, Hayes, Nicol, & Kraus, 2003; King, Warrier, Hayes, & Kraus, 2001; Cunningham, Nicol, Zecker, Bradlow, & Kraus, 2001). The ability to measure the electrical response of the auditory neural system to speech signals is a new and exciting area of research that may advance scientific knowledge of many subtle neural processing deficits, such as auditory processing disorders and specific language impairment that appear to be either caused, or at least negatively influenced, by problems certain listeners have in processing auditory speech signals in their neural pathway (Warrier et al., 2003).

Previous research concerning the neural representation of speech in the auditory system include: comparing subcortical and cortical processes between normal learning (NL) children and children with learning problems (LP) (Wible, Nicol, & Kraus, 2004a), determining how neural speech processing is affected by background noises (Nicol & Kraus 2004), studying how speech cue enhancements can improve both encoding and perception of speech (Nicol & Kraus

2005), and analyzing training programs for learning problems that are believed to be auditory based (Nicol & Kraus 2005). Both brainstem and cortical electrophysiologic measures have been made to evaluate the functioning of the auditory neural pathway at several levels. Evaluating the brainstem provides different information from the information obtained from cortical evoked potentials because brainstem responses are believed to occur without the confounding factors of attention and other linguistic cognitive processes (Hall, 1992). Ultimately, it will be necessary to understand cortical responses to fully view the response of the auditory system to speech. However, the focus of the present work is on the response of what is considered the high or upper brainstem response called the frequency following response (FFR).

Cunningham et al. (2001) found that in some LP children, the base of their learning difficulties lay in problems with speech-sound perception. Children with speech-sound perception deficits were struggling to differentiate between similar phonemes. These issues are exaggerated in a classroom setting because of the level of almost constant background noise. In quiet environments, LP and NL children processed conversational speech at about the same rate; once background noise was added, the LP children fell behind the NL children in processing rates. These differences were found by measuring and comparing the frequency following response (FFR – brainstem recordings that originate in the upper brainstem of listeners) in the NL and LP children. 9 NL children and 9 LP (all diagnosed with a reading-based learning disability) children between the ages of 10 and 13 were presented with synthetic speech sound /da/ into the right ear. Responses of the FFR were recorded and compared between the NL and LP groups by taking the measurements and finding the average amount of time for the FFR. NL children showed to have about the same FFR time as LP children in quiet environments, but the response of the LP children did slow down in noise. This may mean that improving the FFR of

LP children in noisy environments could improve the degree of the learning disability that the child experiences.

Another study (King et al. 2001) examined the fact that a good portion of children with learning disabilities have those problems because they are not able to process auditory information as quickly as their peers. 33 NL and 54 LP children were tested to measure the FFR; all had normal IQ levels and hearing. More than one-third of the LP children showed a slower FFR than the NL children when presented with the synthetic speech sound /da/. With auditory training, the brainstem response to the sound was improved.

Kraus and Nicol (2003) pointed out in their study that speech perception is inherently automatic at the base. When some of the automatic processes do not react normally to speech sound, it may result in some type of learning disability. Synthesized speech sounds are used for testing the FFR because they are easy to keep consistent; and they can also be manipulated if the examinee wants to alter the experiment in any way or look at how simple discreet differences are detected concerning speech encoding. Lateralization of sounds occurred only with sounds that resembled speech sounds. 91 LP and 90 NL children participated in this study; synthesized speech sounds /da-ga/ and /ba-wa/ were compared. The children all had similar brainstem responses with the /ba-wa/ sound, but there were perceptual differences (the LP children fell behind) with the /da-ga/ speech sounds. The LP children had difficulty perceiving the difference in the between the stops in the /da-ga/ sounds because of the contrast. Certain contrasts are more difficult to perceive than others. The FFR was measured for the two groups and a normative time was identified with a standard deviation, and the same children that struggled with perceiving the /da-ga/ sound also had a delayed FFR. This was clinically significant because only the children with LP had a delayed FFR.

Wible et al. (2004) recorded an electrophysiologic response to speech from the brainstems of children with learning problems and children with normal language skills. These researchers found that information from the speech stimulus was transmitted at different rates from the cochlea to the auditory cortex in a significant percent of children with LP when compared to NL children. LP children processed speech sounds more slowly than NL children. Background noises made a big difference in how speech was processed. In an ideal noise situation (no background noise), LP children and NL children performed similarly; but when background noise was added, the LP children had a much more difficult time processing the signal in the brainstem as was evidenced by differences in the latency and amplitude of their brainstem electrophysiologic response the speech stimulus. This finding is clinically significant because there are constant background noises in classrooms and children with LP have been shown to struggle more than normal children in noisy environments (Cunningham et al. 2001). As part of the study, a training program was implemented for the children with LP with the intent to improve their speech processing. The program used computer-aided training where speech stimuli were presented to the children with some exaggeration of critical elements of the speech sounds. For example, cue enhancements (such as longer stop gaps and more emphasis on syllables) helped the LP children process the speech stimuli. Then, as the child showed progress in perceiving the speech stimulus accurately, the exaggerated elements of the speech sound were gradually decreased until the speech sound could be understood at a normal rate of speech. The changes in the speech processing of the children were also documented using the electrophysiologic responses to speech stimuli described above. The study of Wible et al. (2004) showed that the measurement of the FFR to speech stimuli has the potential to reveal new information about how the human auditory system processes speech.

In another similar experiment involving NL and LP children and the comparison of the FFR, Russo, Nicol, Masacchia, & Kraus (2004) explained that the use of the speech sound /da/ to determine the rate of the FFR is necessary because the stop consonant /d/ is known to be drowned out among background noise, but the vowel sound /a/ is not as likely to be drowned out because it vowels are generally sustained sounds and pronounced louder than consonants. 38 children, none of which had a learning disability, were used for this study. Subjects were tested once with and once without background noise. A normative measure for the FFR was created by combining all of the samples, which were extremely consistent. A measure of the brainstem's response to speech is clinically important because it allows professionals in the field to understand how the auditory system transmits sound from the cochlea to the brainstem, and it allows for a physical aspect in auditory processing; the clinician is able to see if the person is processing hearing at an average rate or at a slower rate, which could be the base of a learning disability.

The FFR is an evoked potential of particular interest to researchers because it represents the response of the auditory neural pathway in the subcortical region. Measuring the brainstem's representation of speech in this region is critical because once the speech signal has reached the cortex, the effects of attention, memory, and other processes make it difficult to determine the source of any speech processing difficulties. When electrodes are hooked up to a subject to measure these brainwaves, a physical representation of the FFR is seen on a computer screen. An abnormal FFR would reveal to us that the individual being tested is processing speech slowly, which could be a major contributor to various learning disabilities. Based on the results of previous testing with the FFR, it is possible to use the information gathered and target therapy to improving speech processing.

A majority of the studies of the FFR have involved children with learning problems and a control group of peers who had no known learning impairments. Based on research with children, the Biological Marker of Auditory Processing (BioMARK, formerly known as BioMAP) test was created. This test compares the onset response to a speech stimulus and the FFR and compares these brainstem responses to the responses of 8 to 12 year old children. The BioMARK was designed to show researchers when the latency (the point in time the response occurs compared to the time of the stimulus) or amplitude of a child's FFR differs from the FFR responses of the normative sample of 8 to 12 year old children. Several aspects of the brainstem response to speech have been shown to correspond to both temporal and spectral information in the speech stimulus. The creators of the BioMARK test have combined the information from both the temporal and spectral response of the brainstem into a numeric metric where a score of zero to 5 represents an overall brainstem response that is statistically similar to the normative sample of the BioMARK test. Score above 5 are considered to be statistically outside the normal range.

One important issue concerning the use of the BioMARK is the fact that the normative sample against which the response of others is compared was obtained from children from ages 8 to 12. There is evidence that evoked potentials from upper brainstem regions are different for 8 to 12 year old children than for older children and adults (Kraus, Reed, Smith, Stein, & Cartee, 1987) and that the FFR is sensitive to differences in language experience of the subjects tested (Krishnan, Xu, Grandour, & Cartani, 2005). Due to these age differences, it was believed to be useful to collect a sample of FFR responses from young adult listeners (ages 18 to 30) to determine if it is necessary to collect a larger set of data to serve as normative values for this age group. The purpose of this study was to collect these preliminary data comparing the FFR

responses of a sample of young adult listeners with normal hearing with the normative data of the BioMARK.

Methods

Participants

Normal hearing young adults, aged 18 to 30 years old, were recruited for the study through announcements made in Communicative Disorders and Deaf Education Department classes about the need for participants. Each person wanting to participate was required to read a consent form that had been approved as part of the IRB process, and those willing to sign were given a hearing screening to determine if they qualified for the study. Participants were not paid for their time. The hearing screening and the BioMARK testing took between 30 to 45 minutes to complete.

Stimuli

For each listener in the study, an auditory brainstem response (ABR) was elicited to a click stimulus in the subject's right ear. The click stimulus was a 0.001 μs click presented at 80 dB SPL through an Etymotic ER-3 insert earphone. The click was presented repeatedly at a rate of 10.7 clicks per second and had a broadband frequency response of from 10 Hz to 10000 Hz. On-line band pass filtering was accomplished using a filter from 100 Hz to 2000 Hz. The recording window for the measurement extended from 2 ms pre-stimulus to 60 ms post-stimulus with a 20 kHz sampling rate. Two thousand responses were averaged for each measurement and each measurement was repeated at least once.

The stimulus used for the elicitation of the BioMARK response was the default stimulus in the Biologic Evoked Potential system software. This stimulus was developed at the evoked potential laboratory at Northwestern University. The stimulus has been described in previous

publications as being generated using a Klatt cascade/parallel formant synthesizer (Klatt, 1980). The stimulus is a 40 ms synthetic speech syllable /da/ produced with a sampling rate of 10 KHz (Cunningham, et al., 2001). The synthetic syllable has 5 formants that have onset burst frication energy at F3, F4, and F5 during the first 10 ms that is followed by 30 ms F1 and F2 transitions. These transitions cease immediately before the steady-state portion of the synthetic /a/ vowel.

Procedure

Each participant signed a consent form on the day they come in to be tested, and filled out a questionnaire about any history of learning problems, attention problems, speech and language problems, or problems with their ears requiring surgical intervention. Before performing the electrophysiologic testing, a brief hearing screening in an audiometric suite was performed to ensure that each listener had hearing thresholds in each ear of 20 dB HL (ASHA, 1996). Next, the participant was taken to the room where the electrophysiologic testing was performed and sat in a reclining chair. The backs of their earlobes and the crown of their head (Cz) was prepared to be connected to the electrodes with a mild abrasive scrub and then electode paste was applied to cup electrodes, and the electrodes were then placed on the three prepared locations. An EAR-3 insert earphone was placed in the participant's right ear and the testing began.

A click ABR was first obtained to an 80 dB pSPL click. Two runs of 2000 quiet sweeps each were obtained and wave V of the ABR identified. Then the BioMARK test was started, which consists of presenting the synthetic /da/ speech signal through the insert phone at 80 dB pSPL repeatedly. Three waveforms that each consisted of the average of 2000 sweeps of the /da/ stimulus were collected. A weighted average of the three waveforms were then calculated by the BioMARK software and compared to the normative waveform, also contained within the

BioMARK software. The software compares the latencies of peaks in the measured waveform with the normative waveform as well as comparing the amplitude of the peaks between the two waveforms. Based on these comparisons, a number is generated to represent the extent to which the two waveforms match one another. Scores from zero to 5 are considered within normal limits, scores from 6 to 7 are considered a borderline mismatch, and scores higher than 7 are considered abnormal. After the testing, the electrodes were carefully removed and the participant was ready to depart.

Results

The latencies and amplitudes of the peaks of the electrophysiologic response to the /da/ syllable were calculated and are reported in Table 1 below. Those peaks of interest in the BioMARK response are those that are most prominent and can be identified most consistently (Russo et al., 2004). To compare this data to the normative sample upon which the BioMARK is based, the mean and standard deviation data reported by Russo et al. (2004) were the only published data available. Without the raw data, calculating a t-test or an analysis of variance test was not possible. However, a *z* test was possible if the mean and standard deviation of the 8 to 10 year old children tested for the normative sample were used as a population mean against which our sample of young adults could be compared. This allowed a calculation of the likelihood that the sample data from the thirteen young adults represented a sample of the same population as the children of the Russo et al. (2004) study. The significance level was set by convention at $p < 0.05$.

Table 1

Mean Latency in Milliseconds (ms) and Amplitude in Microvolts (μV) from the Onset Brainstem and FFR Responses of 13 Young Adult Listeners

	Mean Latency (ms)	SD	Mean Amplitude (μV)	SD
Wave V	6.74	0.28	0.09*	0.07
Wave A	7.50	0.34	-0.19*	0.07
Wave C	18.16*	0.78	-0.08*	0.05
Wave D	22.87**	0.85	-0.10**	0.07
Wave E	31.42**	1.53	-0.17**	0.05
Wave F	40.04	1.03	-0.15*	0.09
Wave O	48.19**	0.46	-0.14**	0.08

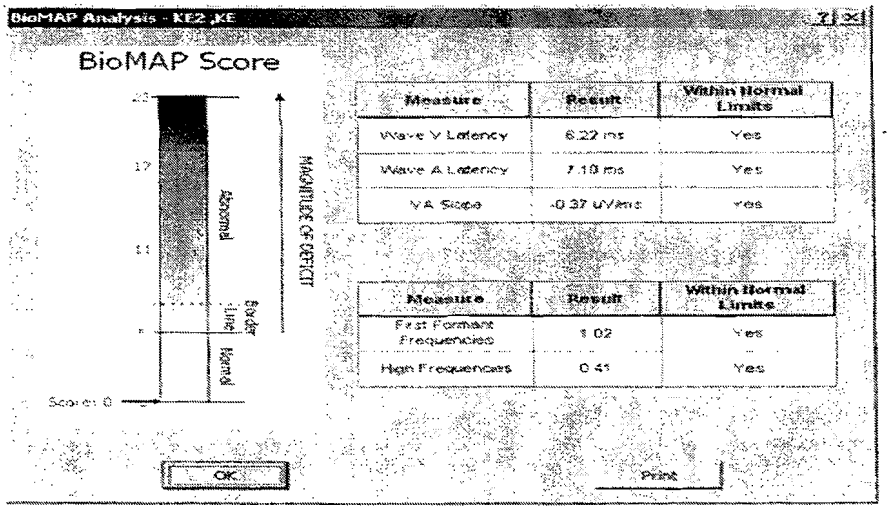
Note: These mean values that were significantly different from the Russo et al. (2004) data at the $p < 0.05$ level and have one asterisk (*) next to them. The mean values with two asterisks (**) were not able to be compared to data from the 8 to 12 year old children as no published data were found in the literature.

Overall, the data show only one statistically significant difference in the latencies of the young adults as compared to the BioMARK normative sample and that was for the waveform labeled C [$Z = 2.09$, $p = 0.0183$]. This statistically significant difference means that the likelihood that the data from the sample of thirteen young adults came from the same population as the data from the 8 to 12 year old children tests by Russo et al. (2004) was only a little less than 2%. The mean amplitudes of each of the waveforms for which data were available to compare were significantly smaller ($p < 0.05$) for the young adult participants than the mean amplitudes of the waveform peaks of the BioMARK normative data (see Table 1).

As part of the commercially available BioMARK test, a comparison is made by the software for new measures against the normative sample. A sample screen from the software

can be seen in Figure 1. The comparison consists of transforming the new measure into a positive integer score. Tests that score between 0 and 5 are considered within normal limits while scores greater than 5 are not. The precise calculation used to convert the data from new measures to this integer score is not available. However, there are five measures that are considered as part of the integer score: the latency of wave V and wave A; the slope of the waveform between wave V and wave A; the combination of the latencies and amplitudes of waves V, A and C and the slope of the waveform between V and A (which are believed to represent the electrophysiologic response to the higher frequency spectral information of the stimulus syllable /da/); and finally the spacing of the latencies of the waveforms D, E, and F along with their amplitudes, which provide information about the steady-state portion of the first formant of the vowel in the stimulus syllable /da/. In addition to the integer "BioMARK" score, the software analysis also shows whether each of these five measures falls within normal limits of the normative sample. Figure 2 shows the data graphically from the thirteen listeners of the present study for their BioMARK scores and for the five factors considered as part of the BioMARK score calculation.

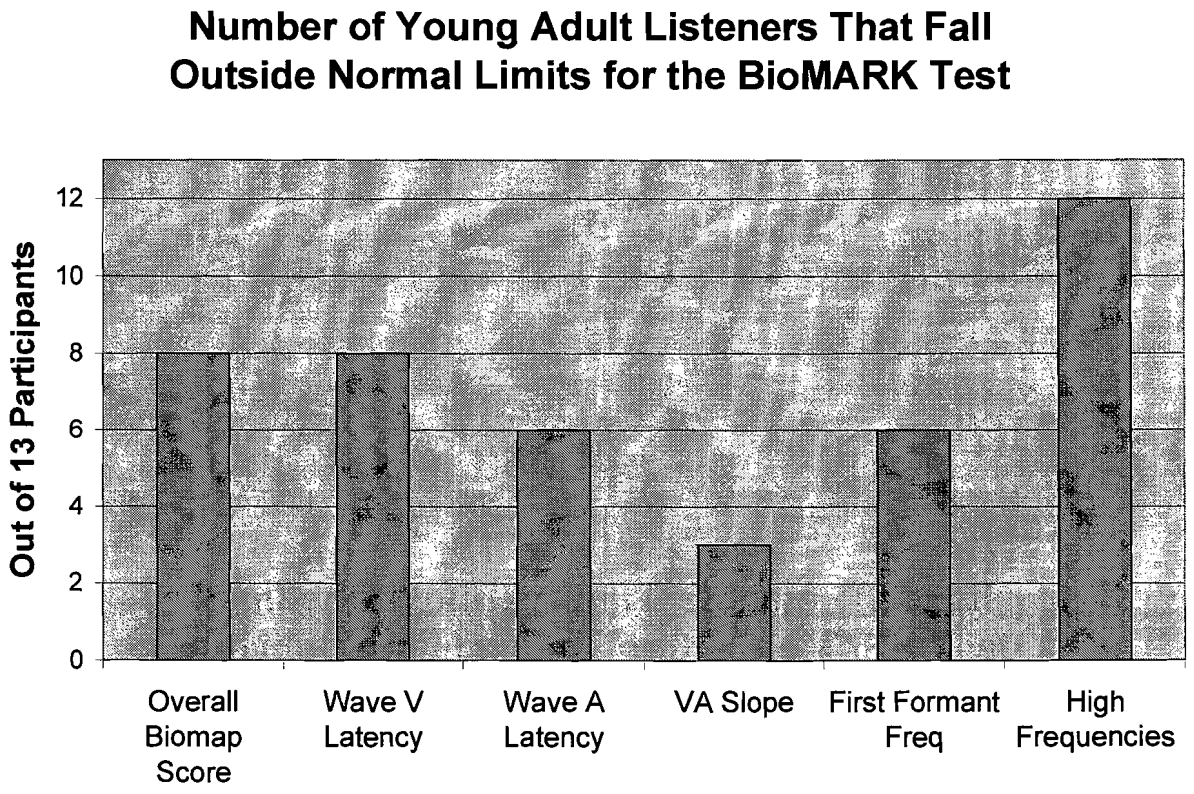
Figure 1



Component	Description
BioMAP Score	Displays a composite score derived from the 5 measures listed below and whether that value is considered within normal limits, borderline normal or abnormal and, if abnormal, where along the magnitude of deficit it falls.
Wave V Latency	Displays the latency of wave V and whether it falls within normal limits.
Wave A Latency	Displays the latency of wave A (wave V trough) and whether it falls within normal limits.
VA Slope	Displays the slope of wave V to wave A and whether it falls within normal limits. Slope Calculation: (wave V to A amplitude) (wave V to A latency).
First Formant Frequencies	Displays the average amplitude for frequencies between 456 Hz to 720 Hz and whether it falls within normal limits.
High Frequencies	Displays the average amplitude for frequencies between 721 Hz to 2000 Hz and whether it falls within normal limits.

Five of the thirteen young adult listeners in the present study obtained a BioMARK score between 0 and 5. When the additional analyses of the five parts of the electrophysiologic response were considered, twelve of the thirteen listeners had high frequency responses that were significantly different than the normative sample of the BioMARK. Eight of the young adult listeners differed significantly in their wave V latencies, six differed from the normative BioMARK values in both their first formant frequency values and in their wave A latencies. Finally, only three of the young adult listeners differed from the BioMARK normative values in the slope between their wave V response and their wave A response (see Figure 2).

Figure 2



Discussion

The purpose of the present study was to test whether or not the speech-evoked FFR of young adult listeners differed from the speech-evoked FFR data from children aged 8 to 12. Determining whether a difference exists would help to evaluate the validity of using a commercially available measure of the FFR with young adults since the commercially available test uses a normative sample obtained from 8 to 12 year old children with normal hearing. The data show that there are indeed statistically significant differences between the mean FFR data from the two groups. Therefore, the data from the present study supports the need for a separate normative sample of onset and FFR responses to speech stimuli based on listeners of the same age as the young adult listeners in the present study. This new normative sample would allow an

accurate determination of whether speech evoked FFR measures from young adult listeners truly fall within what is considered normal limits for their peers.

The primary difference between the mean FFR of a young adult and that of a child between the ages of 8 and 12 years that was observed in the present study is that the mean amplitude of the FFR is smaller for the young adults than for the children. It is not known precisely why this amplitude difference was present. Two possible explanations are explored here briefly. The first is based on data from a study of language experience differences by Krishnan et al. (2005) that showed differences in the FFR responses of young adults to Mandarin Chinese tones based on the listener's experience with Mandarin Chinese. The results of the Krishnan et al. (2005) study showed that the native Mandarin speakers exhibited smaller and broader mean phase-locked responses to the speech signals than the listeners who had learned some Mandarin as a second language. Also, the aspects of the FFR that correspond to pitch were less robust among the non-native Mandarin speakers than the native speakers. If the amplitude differences observed in the present study between the FFRs of the young adult listeners and the children were due to differences in language experience, it would have been expected that the children would have shown FFR amplitudes that were less than those of the young adult listeners. In fact, it was the young adult listeners that had lower amplitude FFRs.

A second potential explanation for the differences observed in the present study between the FFRs of the young adult listeners showed age-related differences in the ability to detect upper brainstem responses of listeners with transient clicks as the stimuli (Kraus, et al., 1987). Also, Jerger and Hall (1980) showed age-related differences in the amplitude of lower brainstem responses for listeners who ranges in age from 20 years to 79 years. These amplitude differences showed a decrease in amplitude of the response with advancing age. This is consistent with the

findings of the current study. However, due to differences between the type of stimuli used and the different comparison ages of the present study and that of Jerger and Hall (1980), the similar decrease in amplitude as subject age increased for the two studies must be viewed with caution. Jerger and Hall (1980) were not able to determine the reason for these amplitude differences. Also, Woods and Clayworth (1986) actually observed that older adults (> 70 years old) had reduced amplitude responses as compared to those of young adults. This age-amplitude difference is in the opposite direction of the present study. However, one possibility is that the amplitude differences are related to neural transmission rates which have been shown to increase into adulthood and then decrease as listeners reach advanced age (Hall, 1992). More research will be needed to determine the source of the amplitude differences between the responses of young adult listeners and children for the FFR.

The significant differences between the amplitude of the FFR responses of young adult listeners and the responses of the 8 to 12 year old children that serve as the normative sample for the BioMARK test of the current study do support the need for normative samples for FFR testing that include age as an important characteristic in determining when a measured FFR from a young adult is considered pathologic or outside what is considered normal. It is hoped that such data will help move forward our understanding of how human listeners process speech information in the auditory neural system. A better understanding of neural processing of speech will not only be helpful in determining pathological responses but also has the potential to help monitor the success or failure of therapeutic intervention with listeners of all ages.

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Author's Biography

Kathryn Pitts was raised in Ogden, Utah and graduated in 2006 as class Salutatorian from Bonneville High School. She entered Utah State University as a Presidential Scholar in 2006, majoring in Communicative Disorders in the department of Communicative Disorders and Deaf Education. Kathryn spent her undergraduate years working on a number of research projects, including projects on Cochlear Implants, Spasmodic Dysphonia, and Meniere's disease. Her interest in working with children and Deaf people led Kathryn to pursue a career as an Audiologist.

Kathryn has accepted admission into the Au.D. program at the University of Minnesota. After graduating with Honors from Utah State University in 2009, she plans to start school in the fall in the Twin Cities pursuing a degree in Clinical Audiology.