October 2016

The Auditory Brainstem Response and Envelope Following Response: Investigating Within-Subject Variation to Stimulus Polarity

Rebekah Taggart
The University of Western Ontario

Supervisor
Dr. David Purcell
The University of Western Ontario

Graduate Program in Health and Rehabilitation Sciences

A thesis submitted in partial fulfillment of the requirements for the degree in Master of Science

© Rebekah Taggart 2016

Follow this and additional works at: https://ir.lib.uwo.ca/etd
Part of the Speech and Hearing Science Commons

Recommended Citation
https://ir.lib.uwo.ca/etd/4122

This Dissertation/Thesis is brought to you for free and open access by Scholarship@Western. It has been accepted for inclusion in Electronic Thesis and Dissertation Repository by an authorized administrator of Scholarship@Western. For more information, please contact tadam@uwo.ca, wlswadmin@uwo.ca.
Abstract

Though the envelope following response (EFR) has potential to become an effective tool for hearing aid validation, studies have observed a considerable degree of within-subject variation with stimulus polarity that could affect its clinical usefulness. This study investigated whether a relationship exists between the polarity-sensitive variation observed in EFR amplitude and that observed in the latencies of a related neural response, the auditory brainstem response (ABR). Low frequency masked clicks and the dual-$f_0$ stimulus /susəfi/ were used to evoke alternating polarity ABRs and EFRs, respectively, in 31 normal hearing adults. Maximum and median differences between polarity conditions were calculated. A significant correlation was found between median absolute differences in EFR amplitude and ABR latency, indicating the polarity-sensitive variation may arise from common sources in the auditory pathway when low frequency stimuli are used. Future studies should employ imaging techniques to further explore the relationship between the EFR and ABR.

Keywords

auditory brainstem response (ABR), envelope following response (EFR), normal hearing, adults, within-subject variation, polarity, auditory pathway
Acknowledgments

First and foremost, I would like to express my sincere gratitude to my research supervisor Dr. David Purcell: thank you for advocating for me, for helping me create stimuli, for writing code for me, for editing endless drafts of the manuscript and above all, for believing that I could actually pull this off in a year. To say I couldn’t have done this without you would be an understatement. It has been an absolute pleasure working under your supervision.

I am also indebted to my advisory committee Dr. Ingrid Johnsrude and Dr. Susan Scollie for their encouragement and invaluable suggestions with regard to the analysis, as well as Dr. Robert Burkard for his insight into the best ABR stimuli for this project. Also, I would like to thank Dr. Andrew Dimitrijevic whose inquiry about the relationship between polarity-sensitive variation observed in the EFR and ABR inspired this project.

Thank you to my lab mates Linh Vaccarello, Takashi Mitsuya and Emma Bridgwater for the countless laughs and memories accrued over the past year and for the continuous supply of moral support. Also, thanks for agreeing to be my guinea pigs for every pilot experiment and artifact check.

Thank you to Kathryn Toner for her help in recruitment and to all of my participants who willingly gave up their time to contribute to this project.

Lastly, I am eternally grateful to my loving family and my incredible husband Wes for their unfailing support every step of the way.

Funding for this project was provided by Western University and the Natural Sciences and Engineering Research Council of Canada.
# Table of Contents

Abstract ................................................................................................................................. ii
Acknowledgments ................................................................................................................ iii
Table of Contents ................................................................................................................ iv
List of Figures ....................................................................................................................... vi
List of Appendices ................................................................................................................ viii
List of Abbreviations .......................................................................................................... ix
Chapter 1 .............................................................................................................................. 1
  1 Introduction .................................................................................................................... 1
    1.1 Objective aided validation measures ................................................................. 1
    1.2 The effect of stimulus polarity on the EFR ..................................................... 3
    1.3 The effect of stimulus polarity on the ABR ..................................................... 6
    1.4 Neural generators of the ABR and EFR ......................................................... 11
    1.5 Purpose of this thesis ......................................................................................... 13
Chapter 2 ............................................................................................................................ 14
  2 Methods ......................................................................................................................... 14
    2.1 Participants ......................................................................................................... 14
    2.2 Stimuli ................................................................................................................. 14
    2.3 Stimulus presentation ......................................................................................... 18
      2.3.1 EFR condition ............................................................................................. 21
      2.3.2 ABR condition ............................................................................................. 21
        2.3.2.1 ABR preparation phase ...................................................................... 21
        2.3.2.2 ABR preparation phase ...................................................................... 213
    2.4 Response recording ............................................................................................. 233
    2.5 Response analysis and detection ....................................................................... 255
2.6 Stimulus artifact checks

2.7 Statistical analyses

Chapter 3

3 Results

3.1 Effect of polarity on the EFR

3.2 Effect of polarity on the ABR

3.3 Correlation of polarity-sensitive variation in the EFR and ABR

Chapter 4

4 Discussion

Chapter 5

5 Summary and Conclusions

References

Appendices

Curriculum Vitae
List of Figures

Figure 1: Diagram of the brainstem showing the locations of the main nuclei and fibre tracks of the ascending auditory system .................................................................12

Figure 2: Amplitude-time waveform of /susaʃi/ stimulus .............................................16

Figure 3: Spectrum of the electrical signal of the low frequency click .........................17

Figure 4: Spectrum of the electrical signal of the pink noise high-pass filtered at 1 kHz .19

Figure 5: Spectrum of the electrical signal of the standard 100 µs click .......................20

Figure 6: Diagram depicting the experimental protocol of the ABR condition ..............22

Figure 7: Effect of increasing level of high-pass filtered pink noise on wave V latency ..24

Figure 8: Mean EFR amplitudes across vowel stimuli for the F1 band .........................32

Figure 9: Mean EFR amplitudes across vowel stimuli for the F2+ band .......................34

Figure 10: Comparison of EFR amplitude differences between polarities for /u/ with and without h1 in the F1 band .........................................................................................35

Figure 11: Comparison of EFR amplitude differences between polarities for /a/ with and without h1 in the F1 band .........................................................................................36

Figure 12: Comparison of EFR amplitude differences between polarities for /i/ with and without h1 in the F1 band .........................................................................................37

Figure 13: Histogram of EFR amplitude differences between polarities across vowels in the F2+ band .................................................................................................38

Figure 14: Correlation of EFR amplitude differences between polarities for the vowels /i/ and /u/ in the F1 band .................................................................................................40
Figure 15: Correlation of EFR amplitude differences between polarities for the vowels /a/ and /u/ in the F1 band........................................................................................................41

Figure 16: Correlation of EFR amplitude differences between polarities for the vowels /a/ and /i/ in the F1 band ........................................................................................................42

Figure 17: Correlation of EFR amplitude differences between polarities for the vowels /u/ and /i/ in the F2+ band ........................................................................................................43

Figure 18: Mean ABR latencies across waves.................................................................................45

Figure 19: Mean ABR amplitudes across waves ..............................................................................46

Figure 20: Histogram of ABR latency differences between polarities across waves .......47

Figure 21: Histogram of ABR amplitude differences between polarities across waves....48

Figure 22: Correlation of median absolute differences in ABR latency and EFR amplitude in F1 carrier vowels without h1 .................................................................................................50

Figure 23: Correlation of maximum absolute differences in ABR latency and EFR amplitude in F1 carrier vowels with h1 .................................................................................................51
List of Appendices

Appendix A: Ethics approval notice .................................................................66

Appendix B: Sample letter of information and consent .....................................68
List of Abbreviations

µs  Microseconds
A1  Electrode site on the left earlobe
ABR  Auditory brainstem response
C  Condensation phase
Cz  Electrode site on the vertex
dB  Decibel
EEG  Electroencephalography
EFR  Envelope following response
f0  Fundamental frequency
F1  First formant
F2  Second formant
F2+  Region of the second formant and above
FDR  False discovery rate
FFR  Frequency following response
h1  First harmonic, same frequency as f0
HL  Hearing level
Hz  Hertz
kHz  Kilohertz
LEAQ  LittLEARS Auditory Questionnaire
<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>MEG</td>
<td>Magnetic encephalography</td>
</tr>
<tr>
<td>min</td>
<td>Minutes</td>
</tr>
<tr>
<td>ms</td>
<td>Milliseconds</td>
</tr>
<tr>
<td>nHL</td>
<td>Normal hearing level</td>
</tr>
<tr>
<td>nV</td>
<td>Nanovolt</td>
</tr>
<tr>
<td>p.-p.e.</td>
<td>Peak-to-peak equivalent</td>
</tr>
<tr>
<td>R</td>
<td>Rarefaction phase</td>
</tr>
<tr>
<td>RM-ANOVA</td>
<td>Repeated measures analysis of variance</td>
</tr>
<tr>
<td>s</td>
<td>Seconds</td>
</tr>
<tr>
<td>SD</td>
<td>Standard deviation</td>
</tr>
<tr>
<td>SL</td>
<td>Sensation level</td>
</tr>
<tr>
<td>SPL</td>
<td>Sound pressure level</td>
</tr>
</tbody>
</table>
Chapter 1

1 Introduction

1.1 Objective aided validation measures

Hearing loss is one of the most common congenital disorders, affecting over 1,100 infants born in Canada every year (Hyde, 2005). Newborn hearing screening programs have been implemented in many countries across the world to identify hearing loss early in life, as research has shown that an undetected hearing impairment can have detrimental long-term effects on cognitive and language development (Hyde, 2005; Joint Committee on Infant Hearing & American Academy of Pediatrics, 2007). In Ontario, the majority of newborns are screened within their first month of life and referred to an audiologist for a full hearing assessment in the case of an abnormal result (Speech-Language & Audiology Canada, 2010). One frequently used component of the hearing assessment is an electrophysiological measurement known as the auditory brainstem response (ABR), which involves presenting a series of click or tone burst stimuli at various rates and intensities to the child and evaluating if a reliable neural response is present via electrodes placed on the scalp (Joint Committee on Infant Hearing & American Academy of Pediatrics, 2007). Information from this test can provide the clinician with the best estimate of the child’s pure-tone hearing thresholds and, if amplification is the recommended intervention, may be used to develop prescriptive targets for hearing aids by the time the child is six months old.

However, a gap exists between the time the child is fitted with hearing aids and the time the prescribed gain and output level can be confidently validated. In the meantime, it is possible that certain acoustic features of speech (e.g., the fricatives /s/, /z/ or /əs/ at the end of words to designate plurality) could be missed if they are not amplified to an adequate level. While audiometric and speech testing are typically employed to validate hearing aids in adults, these methods are inappropriate for young children who are unable to produce a reliable behavioural response. In their place, subjective methods such as the LittlEARS Auditory Questionnaire (LEAQ) are used to evaluate auditory performance
based on observation in clinical and everyday listening environments for the first two years (Bagatto et al., 2011). Though this is an effective and validated tool, it requires several months of observation before conclusions can be drawn about the appropriateness of the hearing aid output. For this reason, it would be beneficial to have an objective electrophysiological tool that could provide information about device effectiveness soon after they have been fitted. This data would nicely augment that collected from the LEAQ and allow the clinician to ensure the child is getting the best intervention as quickly as possible.

Ideally, natural speech stimuli should be used to evoke a neural response as it would yield a better indication of hearing aid performance in everyday listening conditions. Signal-processing algorithms in the device circuitry are designed to enhance speech while providing less gain to non-speech sounds; therefore, they may not run in their normal mode if other types of stimuli are used (Scollie & Seewald, 2002; Easwar, Purcell, & Scollie, 2012). Unfortunately, using artificial stimuli such as clicks, tone bursts and modulated tones or noise is more practical as they are steady and will generally elicit a response that is easier to analyse (Choi, Purcell, Coyne, & Aiken, 2013). This is because, despite a considerable degree of neural synchronization in response to an auditory stimulus, the magnitude of the EFR signal is negligible compared to that of the accompanying myogenic and electroencephalographic noise; thus, many sweeps evoked by an identical, fixed stimulus must be averaged to attenuate the noise and improve detection (Jewett & Williston, 1971). Unlike artificial stimuli, natural speech—even individual phonemes—vary in level, frequency, bandwidth and spectral shape over time and therefore must often be modified in order to obtain a synchronized neural response in a reasonable recording time (Scollie & Seeward, 2002; Choi et al., 2013).

The envelope following response (EFR), a steady-state measure that can be evoked by modified speech stimuli, is of particular interest as a clinical validation measure. The EFR arises from neurons phase-locked to the stimulus amplitude envelope and can be elicited by an amplitude modulated tone or a voice’s fundamental frequency \( f_0 \) when producing vowel sounds (Aiken & Picton, 2006; see the “neural generators of the ABR and EFR” section for more detail). This electrophysiological measure is particularly
advantageous because it can be evoked by running speech stimuli with similar acoustic characteristics to normal, conversational speech (Aiken & Picton 2006; Choi et al., 2013). Additionally, the EFR is an objective measure of temporal acuity, the perceptual ability to discriminate changes in frequency, rhythm and amplitude at suprathreshold levels, which is crucial for speech comprehension (Purcell, John, Schneider, & Picton, 2004). For these reasons, the EFR provides an ecologically valid measure of how hearing aids contribute to natural speech processing, though it has yet to play a significant role in standardized clinical practice.

1.2 The effect of stimulus polarity on the EFR

In addition to collecting a large number of neural responses to the same stimulus and averaging across them to attenuate noise, signal detection is routinely improved by recording responses evoked by opposing polarity stimuli. In the EFR protocol, the original stimulus waveform (in polarity A) is multiplied by the factor -1 to produce the opposite polarity waveform (polarity B); the responses are then averaged post hoc (the ‘+ –’ average, see Aiken & Picton, 2008). This protocol is based on evidence that certain components concomitant with the EFR are highly sensitive to an inversion of stimulus polarity, and thus contamination from these sources can be reduced (Small & Stapells, 2004, 2005; Aiken & Picton, 2008). These sources include the spectral frequency following response (FFR), a steady-state response phase-locked to the stimulus fine structure, the cochlear microphonic, a potential generated by outer hair cells that mirrors the waveform of the stimulus, and stimulus artifact (Small & Stapells, 2004; Aiken & Picton, 2008). Meanwhile, the EFR signal is enhanced as the stimulus envelope is generally unaffected by an inversion of polarity (Krishnan, 2002; Small & Stapells, 2004; Aiken & Picton, 2008). Though polarity-sensitive differences in EFR amplitude have been noted in a few studies, these differences tend to be small or non-significant when averaged across participants (Small & Stapells, 2005; Aiken & Purcell, 2013; Krishnan, 2002).

However, despite studies showing only negligible differences at a group level, there is a notable degree of individual variation across adult listeners as stimulus polarity is varied. A small study using synthetic vowel stimuli to evoke the FFR found that the EFR was not
fully cancelled when response waveforms to opposite polarities were subtracted and that this residual EFR varied across the three participants and vowel stimuli (Greenberg, 1980, chapter 7). In a more recent study, Aiken and Purcell (2013) further investigated the polarity sensitivity of the EFR by analyzing the responses evoked by the $f_0$ of natural vowel tokens /i/ and /a/. Each vowel token was presented twice in the original polarity and a third time in the inverted polarity. Absolute values of response amplitude change across conditions were analyzed for each subject, revealing that the magnitude of change was significantly greater across opposite polarity conditions than across repeated measures of the same polarity. Similar to Greenberg’s study, the effect of polarity varied considerably across participants and vowel tokens, with amplitude changes ranging from near zero to a maximum of 72 nV (Aiken & Purcell, 2013). Yet, when response amplitude changes were averaged across the nine participants, the data showed that the ‘+ –’ average was not significantly different from the average across repeated measures of the same polarity. These findings were further demonstrated in Easwar et al. (2015), where nearly 30% of the 24 normal hearing participants who had a significant EFR detection to the stimulus /hεd/ exhibited polarity-sensitive amplitude differences greater than 39 nV, including one participant who exhibited a difference of 100 nV. Since test-retest variation in EFR amplitude and fluctuations in electrophysiological noise could only logically explain differences up to 39 nV, the magnitude of the differences observed in these subjects indicated a polarity effect (Easwar et al., 2015). However, because the magnitude and direction of change varied from person to person (e.g., some subjects exhibited a larger amplitude in response to polarity A than polarity B, whereas others had the opposite response), the effect of polarity became non-significant when the responses were averaged across the group.

Though at a group level it may be sufficient to conclude that polarity has only a minor effect on EFR amplitude, the large degree of polarity-sensitive differences across individuals has clinical implications if the method is to be adopted into the validation regimen for hearing aid fittings. Of the 24 participants who had a significant EFR detection in Easwar et al. (2015), 11 had the significant response in either polarity A or B, but not both. Furthermore, two participants who exhibited a response in one of the polarities did not have a significant detection in the ‘+ –’ average. Therefore, for those
individuals who are particularly sensitive to shifts in stimulus polarity, averaging responses in accordance with the recommended protocol may attenuate response amplitudes and possibly lead to false negative results (Easwar et al., 2015). Though the simple solution would be to conduct multiple trials of the EFR in both polarity conditions, this is not necessarily feasible in a clinical setting due to time constraints, particularly when testing young children.

An underlying factor that may be contributing to the polarity sensitivity of the EFR is the degree of envelope asymmetry in speech stimuli. The aforementioned EFR protocol was originally developed using modulated tone stimuli, which have symmetrical envelopes around the baseline (Aiken & Picton, 2008). Therefore, though the fine structure would be inverted in the opposite polarity waveforms, the envelopes would theoretically remain unchanged and elicit the same neural response. Unfortunately, in the case of natural speech stimuli, the voice’s first harmonic (h1; same frequency as f0) and other factors tend to produce varying degrees of envelope asymmetry that may attenuate response amplitude in the ‘+ –’ average (Skoe & Kraus, 2010; Easwar et al., 2015). Additionally, h1 may elicit a polarity-sensitive FFR close enough in frequency to the f0 that it could interfere with the EFR, although studies suggest that this effect is likely minor (Aiken & Picton, 2006; Aiken & Picton, 2008; Easwar et al., 2015). To account for this potential confound, Easwar et al. (2015) developed a second experiment that investigated the effect of h1 on the polarity-sensitive variability of EFR amplitude. Each vowel of the stimulus /susaʃi/ was high-pass filtered at 150 Hz to remove h1, minimizing envelope asymmetry and eliminating any contribution from the h1 FFR. Responses elicited by this stimulus in both polarities were then compared to those elicited by the same stimulus with h1 present in 20 normal hearing adults. Though results showed that 64.5% of response amplitude variation due to polarity could be explained by envelope asymmetry, the remaining variation suggests that there are other factors contributing to the individual differences in EFR amplitude. Easwar et al. (2015) speculated that this polarity-sensitive variation not related to envelope asymmetry was most likely arising at some point in the peripheral auditory system or brainstem.
In addition to removing h1, Easwar et al. (2015) made another modification to the /susaʃi/ stimulus that allowed them to simultaneously record EFRs from two separate frequency bands: one from the region of the first formant (F1) where the harmonics are lower in frequency and spectrally resolved in the cochlea and the other from the region of the second formant and above (F2+) where the harmonics are higher in frequency and spectrally unresolved. The purpose of this modification was to investigate whether the frequency of the carrier and the type of harmonics in the stimulus influenced the variation in EFR amplitude. Results from the experiment showed that significant amplitude differences within participants due to polarity were more commonly found in EFRs evoked by the F1 carrier, even when h1 (which was only present in the F1 carrier) was removed. Therefore, it would appear that lower frequency stimuli tend to elicit larger polarity effects.

1.3 The effect of stimulus polarity on the ABR

The ABR is another evoked response generated in the vestibulocochlear nerve and brainstem in response to a transient stimulus, such as a click or brief tone burst. The responses from different parts of this track add together to form a characteristic waveform with five peaks labeled I to V (see “Neural generators of the ABR and EFR” section for more detail). Even minute latency differences in waves I, III and V can indicate cochlear pathology, auditory neuropathy or the presence of an acoustic neuroma (Schwartz et al. 1990). Similar to EFR protocol, ABR stimuli are often presented in opposing polarities in an alternating fashion so that polarity-sensitive contaminants such as the cochlear microphonic and stimulus artifact may be attenuated, though ABR click stimuli differ in that they are a transient pulse of either rarefied or condensed pressure. Many researchers have investigated the effect of stimulus polarity on wave latencies and amplitudes, yielding widely inconsistent results. For example, regarding the latency of wave V, studies have found shorter latencies to rarefaction phase (R) than condensation phase (C) stimuli (Ornitz & Walter, 1975; Borg & Lofqvist, 1981; Maurer, Schäfer, & Leitner, 1980); shorter latencies to C than R stimuli (Pijl, 1987; Hughes, Fino, & Gagnon, 1981); and others have revealed no significant latency differences at all (Kumar, Bhat, D’Costa, Srivastava, & Kalaiah, 2013; Rosenhamer, Lindstrom, & Lundborg, 1978;
Beattie & Boyd, 1984; Tietze & Pantev, 1986). In a comprehensive study by Swartz et al. (1990), 92 participants with normal hearing and 78 participants with mild to severe cochlear hearing loss (N = 340 ears) were tested with the click-evoked ABR in order to better quantify the individual variation observed in previous studies. Corresponding with the results of Rosenhamer et al. (1978), Beattie and Boyd (1984) and others, there were no significant R-C latency differences when the data was averaged across all participant ears. However, when absolute R-C latency differences were examined—arguably a more appropriate method for assessing clinical significance since the magnitude of individual differences are not obscured by measures of central tendency—there was a surprising degree of variation. Setting the criterion for a clinically significant R-C latency difference at ±0.15 ms, a more conservative cutoff value than used in other studies (Borg & Lofqvist, 1982; Tietze & Pantev, 1986; Beattie, 1988; Edwards, Buchwald, Tanguay, & Schwafel, 1982), they found that 41%, 46%, and 29% of participant ears exhibited clinically significant R-C latency differences in waves I, II, and V, respectively. Furthermore, 27% of participant ears exhibited wave III latency differences as large as ±0.30 ms. Interestingly, though the majority of participants who exhibited this differential response tended to have shorter wave I and V latencies to clicks presented in R phase, 12% and 7% of participants exhibited the opposite response, with shorter latencies to clicks presented in C phase. This finding has been replicated in many studies (Schoonhoven, 1992; Borg & Lofqvist, 1982; Orlando & Folsom, 1995; Coats & Martin, 1977) and is remarkably similar to the variation found in EFR studies. Cats and gerbils also exhibit a substantial degree of individual variability in response to varying stimulus polarity (Tvete & Haugsten, 1981; Burkard & Voigt, 1989). Furthermore, when Stockard, Stockard, Westmoreland and Corfits (1979) and Orlando and Folsom (1995) tested a few of their subjects with the most distinctive responses six months later, they exhibited the same latency patterns, indicating that the majority of the individual variation is originating from physiologic factors and remains relatively stable over time.

Curiously, the pattern of variation appears to be highly irregular across different stimulus parameters. An experiment conducted on anesthetized cats showed that as the stimulus level was increased from 0 to 80 dB above the minimal level required to obtain a reproducible ABR, mean latency differences between responses evoked by R and C
clicks increased in four of the five cats (Tvete & Haugsten, 1981). Stockard et al. (1979) also found that latency differences are minimal at lower stimulus levels (30 and 40 dB SL) and greater at higher levels (50 to 70 dB SL). However, when Beattie (1988) varied the click level between 60, 75 and 90 dB nHL and Orlando and Folsom (1995) varied the level of single-cycle sinusoids between 40 and 60 dB nHL, neither study found a consistent trend of variation related to stimulus intensity in normal hearing adults.

Ballanchanda, Moushegian and Stillman (1992) also failed to find a significant effect of intensity on latency in regards to polarity differences, though they did find a small effect on peak amplitudes. Looking at responses from the auditory nerve recorded from the round window of the cochlea, Peake and Kiang (1962) found the most striking polarity differences in latency and morphology at moderate stimulus intensities. A study by Rawool and Zerlin (1988) found that when click level was increased from 35 to 95 dB SPL in 10 dB steps, all six participants exhibited a shift from shorter latencies to C clicks to shorter latencies to R clicks, though the level at which this occurred varied considerably. Orlando and Folsom (1995) also saw this shift in their data, but with more variability—some participants exhibited shorter latencies to R stimuli at low levels and longer latencies at high levels, whereas others showed the opposite response or exhibited no change at all. In summary, individual variability to stimulus polarity makes it difficult to identify a consistent trend of intensity, though in general it would appear that variation is greatest when stimuli are presented at moderate to high intensities (50 or 60 dB nHL and higher).

Many researchers have also investigated the effect of stimulus frequency on the polarity-sensitive variation of the ABR. Using single-cycle sinusoids at octave frequencies from 250 to 2000 Hz, Gorga, Kaminski and Beauchaine (1991) found that R-C latency differences in wave V increased as the stimulus frequency was decreased, particularly when the stimulus intensity exceeded 50 dB peak equivalent SPL. These findings were replicated by Orlando and Folsom (1995), who found that a 300 Hz single-cycle sinusoid consistently elicited greater R-C latency differences in waves I, III and V than a 3000 Hz single-cycle sinusoid. When longer and more frequency-specific tone pips of 500, 1000, 2000 and 4000 Hz were presented to 10 normal hearing women, only the two lowest frequency tone pips elicited significant R-C latency differences (Fowler, 1992). This
effect of stimulus frequency on polarity-sensitive ABR variation was further confirmed by Schoonhoven (1992) in a derived band paradigm, where alternating polarity clicks were presented with high-pass noise at various cut-off frequencies. Results showed that the greatest differences in wave III and V latency due to polarity occurred when the cutoff frequency was 1.6 kHz and lower (Schoonhoven, 1992). Other studies demonstrating this effect include Salt and Thornton (1984) and Coats (1978). Interestingly, these results correspond closely with the findings from the Easwar et al. (2015) EFR study, where the degree of polarity-sensitive variation was larger when elicited by the lower frequency carrier.

The effect of low frequency energy in the stimulus on polarity-sensitive variation may be one of the underlying factors explaining why those with high frequency hearing loss tend to show even greater R-C latency differences than those with normal hearing. In their large subset of hearing impaired participants, Schwartz et al. (1990) found a clear trend of greater R-C latency differences in waves I, III and V as the average degree of high frequency hearing pure tone sensitivity loss at 2000, 3000 and 4000 Hz increased. Borg and Lofqvist (1982) also found greater wave V R-C latency differences in 29 ears with steep high frequency hearing loss, whereas Coats and Martin (1977) only found significant differences in waves II to IV. Polarity-sensitive variation also appears to be greater in those with diseases affecting the brainstem and auditory nerve, such as multiple sclerosis and acoustic neuromas (Maurer, 1985; Emerson, Brooks, Parker, & Chiappa, 1982).

To an extent, the increased polarity sensitivity elicited by lower frequency stimuli can be explained physiologically. In the simplest model, the initial phase of a R stimulus causes the diaphragm of an earphone to move inwards, creating a wave of rarefied pressure that propagates down the ear canal and induces an outward movement of the tympanic membrane (Møller, 1994). Next, the vibration of the ossicles in the middle ear causes the stapes to move outwards and sets the cochlear fluid into motion, deflecting the basilar membrane towards the scala vestibuli and displacing the stereocilia of the inner hair cells towards the stria vascularis (Møller, 1994). This action depolarizes the sensory hair cells and leads to increased neural firing of the auditory nerve (Peake & Kiang, 1962; Møller,
In the case of C stimuli, the diaphragm of the earphone moves outwards leading to deflection of the basilar membrane towards the scala tympani and displacement of the inner hair cells away from the stria vascularis, thereby hyperpolarizing the cells and inhibiting neural firing of the auditory nerve (Peake & Kiang, 1962; Möller, 1994). After a half-cycle delay, the excitatory phase following the initial C peak depolarizes the sensory cells and increases auditory nerve firing; therefore, if the neural response to the stimulus is being measured at the brainstem, C waves should theoretically lag behind R waves by this half-cycle period (Peake & Kiang, 1962; Don, Vermiglio, Ponton, Eggermont, & Masuda, 1996). In a high frequency stimulus, the half-cycle is almost negligible; however, the half-cycle of a low frequency stimulus (e.g. 1 ms for a 500 Hz stimulus) is considerably longer and should have a notable effect on wave latencies (Don et al., 1996). However, a review of ABR latency data would suggest that this model is too simplistic—not only do latency differences frequently deviate from the expected half-cycle delay, but many individuals actually exhibit shorter wave latencies to C than to R stimuli, as previously mentioned. Experiments conducted on cats and chinchillas have found that, depending on the stimulus frequency and intensity, hair cells can become excited by basilar membrane deflection in both directions and so are capable of depolarizing to an initial peak of either phase (Sokolich, 1980; Ruggero & Rich, 1983; Antoli-Candela & Kiang, 1978; Kiang, Watanabe, Thomas, & Clark, 1965). Additionally, fluid velocity and tectorial membrane displacement appear to interact with hair cell depolarization in a complex manner that is poorly understood (Ruggero & Rich, 1983).

Salt and Thornton (1984) and Debruyne (1984) postulated that there are two components that contribute to the click-evoked ABR: one that is insensitive to polarity and originates from basal regions of the cochlea and another that is phase-locked to the stimulus and originates from apical cochlear regions. It is known that differences in cochlear travel time and synchronization contribute to the variability seen in wave V amplitude (Don, Ponton, Eggermont & Masuda, 1994); therefore, it is possible that those who show the greatest polarity differences have larger contributions from individual phase-locking units or better neural synchronization of the apical regions in response to stimuli (Orlando & Folsom, 1995). Furthermore, this response pattern would vary from person to person, but remain consistent over repeated presentations of the stimulus (Orlando & Folsom, 1995;
Don et al., 1996). Alternatively, phase-locking neurons throughout the brainstem may also show a pattern of excitation and synchronization unique to the individual (Debruyne, 1994).

### 1.4 Neural generators of the ABR and EFR

The similarities between the polarity-sensitive variation seen in the EFR and ABR suggest that the variation could arise from a common source (or sources). Therefore, it may be helpful to compare what is known about the neural generators of the ABR and EFR (see Figure 1 for diagram of brainstem anatomy). The ABR is generated by neurons throughout the brainstem and peripheral auditory system that are evoked by the onset of a transient stimulus, such as a click or brief tone burst. The recorded response takes the shape of a characteristic waveform with a series of normative peaks representing synchronized responses from sequential sites in the neural pathway (Jewett & Williston, 1971). The earliest components of the waveform, waves I and II, are generated by the distal and proximal portions of the vestibulocochlear nerve, respectively (Møller, Jannetta, & Møller, 1981; Møller, Jannetta, & Sekhar, 1988; Møller, 1994). At this point, the ascending auditory system diverges into several parallel pathways, making it difficult to pinpoint the exact structures in the brainstem that are generating the next three waves. Intracranial studies suggest that wave III is generated primarily by the cochlear nucleus (Møller & Jannetta, 1982; Møller, 1994), wave IV by third-order neurons in the superior olivary complex (Møller & Jannetta, 1982; Møller, 1994), and wave V by the termination of the lateral lemniscus on the contralateral side of the inferior colliculus (Møller & Jannetta, 1982; Møller, 1994). However, these studies also show that waves III, IV, and V are highly complex and likely have contributions from more than one brainstem structure (Møller, 1994).

Less is known about the neural generators of the EFR, particularly those located in subcortical regions. Studies employing magnetic encephalography (MEG) and scalp-recorded electroencephalography (EEG) technology have shown that neurons throughout the entire auditory pathway have the capacity to follow a modulated stimulus envelope, though evaluation of response latencies and dipole source analysis point to two dominant generators: one in the brainstem with an approximate latency of 7.3 ms and another in
Figure 1: Diagram of the brainstem showing the locations of the main nuclei and fibre tracks of the ascending auditory system.

Cochlear nucleus (CN), superior olivary complex (SOC), lateral lemniscus (LL), inferior colliculus (IC), medial geniculate (MG). Reproduced from Møller et al., 1988.
the cortex with an approximate latency of 29 ms (Frisina, 2001; Herdman et al., 2002; Kuwada et al., 2002; Purcell et al., 2004). It is generally accepted in the literature that cortical sources of envelope following responses respond best to lower modulation rates (< 50 Hz), whereas subcortical components contribute a growing amount as modulation rate increases (Herdman et al., 2002; Kuwada et al., 2002; Purcell et al., 2004), though new evidence has emerged suggesting that the human auditory cortex contributes more at higher modulation rates than previously thought (Coffey, Herholz, Chepesiuk, Baillet, & Zatorre, 2016). In the case of speech stimuli where harmonics are amplitude modulated at the $f_0$ (between 88 Hz and 100 Hz in this present study), the neural response contains large contributions from subcortical structures (Herdman et al., 2002; Aiken & Picton, 2006). Intracellular recordings in rabbits and gerbils have identified peak amplitude responses at the level of the cochlear nucleus and inferior colliculus at frequencies comparable to the $f_0$ of speech (Frisina, Smith, & Chamberlain, 1990; Kuwada et al., 2002). Coffey et al. (2016) also identified the cochlear nucleus and inferior colliculus, as well as the medial geniculate and auditory cortex, as dominant generators when using MEG to record responses to the speech stimulus /da/ in 22 young adults.

1.5 Purpose of this thesis

In conclusion, a review of the literature on the ABR and EFR reveals that there is a wide degree of within-subject variation in response to varying stimulus polarity that cannot currently be explained. This polarity-sensitive variation poses significant clinical implications, particularly in the EFR where large differences in amplitude between polarity conditions could potentially lead to false negative results. Expanding what is known in the normal hearing adult population, this thesis project will investigate whether a relationship exists between the variation observed in both measures by correlating the prevalence and degree of polarity-sensitive variation in EFR amplitude and ABR latency. If significant correlations are found, future studies may be able to draw from the vast body of ABR literature to better understand polarity-sensitive variability of the EFR at the peripheral level, which cannot be explained by stimulus envelope asymmetry.
Chapter 2

2 Methods

2.1 Participants

Thirty-one adults (26 females, 5 males) between the ages of 22 and 34 (mean age 24.8 years; standard deviation 2.88 years) were recruited from the Western University community in London, Ontario to participate in the study. All participants reported English as their first language and reported no hearing, speech, language or neurological impairments. Using a 10 dB-down, 5 dB-up bracketing technique, audiometric thresholds were obtained at octave and inter-octave frequencies between 250 and 4000 Hz with a Madsen Itera audiometer and TDH-39 headphones. The upper testing level of 4000 Hz was chosen because vowels have most of their energy below 4000 Hz. All participants had thresholds below 20 dB HL across test frequencies. Routine otoscopy revealed no occluding wax, discharge, or foreign objects that may have negatively impacted results. Participants provided informed consent and were compensated for their time. The study was approved by the Health Sciences Research Ethics Board of Western University.

2.2 Stimuli

EFRs were evoked by the vowels /u/ (as in ‘hoot’), /a/ (as in ‘pot’) and /i/ (as in ‘heat’) in the stimulus token /susəfi/, previously developed and used by Easwar et al. (2015). The vowels, representing a range of F1 and F2 frequencies, were produced by a 42 year old male talker from Southwestern Ontario and were individually edited using the software Praat (Boersma, 2001) to elicit two separate EFRs—one arising from the lower frequency F1 region and the other from the higher frequency F2+ region (see Easwar et al., 2015 for more detail). In brief, the F1 and F2+ bands were isolated by filtering each vowel at a cutoff frequency approximating the midpoint between F1 and F2. The $f_0$ of the F1 band was then lowered by 8 Hz and recombined with the F2+ band to form dual-$f_0$ vowels. Once reassembled as /susəfi/, the stimulus waveform (in polarity A) was multiplied by the factor -1 to produce the opposite polarity waveform (polarity B). It should be noted that both polarity waveforms produce both rarefied and condensed pressure, as they contain positive and negative numeric values.
An additional modification was made to a copy of the dual-f0 /susaʃi/ stimulus in each polarity to account for the influence of stimulus envelope asymmetry on EFR polarity sensitivity. Easwar et al. (2015) high-pass filtered each vowel at 150 Hz in Praat in order to remove the first harmonic, h1, from the F1 band, significantly reducing the envelope asymmetry of each vowel. A pilot study of 8 participants established that the vowel category was perceived to be the same after the removal of h1. The modified stimulus token was then concatenated with the original dual-f0 token of the same polarity. Therefore, the full EFR stimulus sequence comprised four tokens of /susaʃi/: two were presented in polarity A with and without h1, then two were presented in polarity B with and without h1. Each sweep was 8.2 s and was presented 300 times for a total duration of 41 min. See Figure 2 for the amplitude-time waveform of the /susaʃi/ stimulus.

ABRs were evoked by a series of stimuli developed in Praat. Using the ‘Create new sound from formula’ function, a 1 ms R click (formula = -0.05) was created and concatenated with 20 ms of preceding silence and 54 ms of following silence (formula = 0) to produce a single 75 ms R click stimulus at a sampling rate of 32000 Hz. This stimulus was then copied and strung together many times to produce a train of 2000 R clicks with a total duration of 150 s and a presentation rate of 13.3 clicks per second. This relatively slow presentation rate was chosen to obtain the clearest ABR waveforms possible. A second click train of the same duration and presentation rate was made with clicks alternating between R and C phase. A single 75 ms C click was created in the same fashion as the R click, but with a positive rather than a negative amplitude (formula = 0.05). Beginning with the R stimulus, the stimuli were then concatenated many times until an alternating click train of 1000 clicks of each polarity was obtained. Longer in duration than the standard 100 µs click stimulus used in clinical practice, these R and C click stimuli contained significant acoustic energy around 300 Hz with a null at 1 kHz. The decision to use a click stimulus with a greater proportion of low frequency energy was based on evidence in the ABR literature suggesting that lower frequency stimuli elicit greater polarity differences (Coats, 1978; Gorga, Kaminski, & Beauchaine, 1991; Orlando & Folsom, 1995; Salt & Thornton, 1984; Schoonhoven, 1992). See Figure 3 for the spectrum of the electrical signal.
**Figure 2: Amplitude-time waveform of /susaf/ stimulus.**

Though the F1 and F2+ carriers are illustrated separately here, they are presented simultaneously during EFR recording. Reproduced from Easwar et al., 2015.
Figure 3: Spectrum of the electrical signal of the low frequency click.
The click trains were also presented with ipsilateral masking noise to ensure that the ABRs were generated from the low frequency apical region of the cochlea and not the high frequency base through spread of the traveling wave. Using the ‘Create new sound from formula’ function in Praat, 720 s of white noise (formula = randomGauss [0,0.1]) was created at a sampling rate of 32000 Hz, then modified into pink noise which contains equal energy in each octave (formula = if $x > 100$ then self*sqrt[100/$x$] else 0 fi, with $x$ representing frequency). This stimulus, henceforth referred to as full band pink noise, was used during the preparation phase of the ABR condition to determine the minimum level of masking noise required to generate an ABR from the apical region of the cochlea. A copy of the full band pink noise stimulus was high-pass filtered at the cutoff frequency 1 kHz (see Figure 4). This stimulus, henceforth referred to as high-pass filtered pink noise, was used during the data collection phase of the ABR condition. Both the high-pass filtered and full band pink noise stimuli were trimmed to 150 s, the same duration as the R and alternating polarity click trains.

To evoke a standard ABR for comparison, a final 150 s click train with classic 100 µs clicks was developed. Similar to the creation of the low frequency click train, 100 µs clicks (R = -0.05; C = 0.05) were created in Praat and concatenated with 20 ms and 54.9 ms of silence to produce individual 75 ms click stimuli, then strung together into a train of 2000 alternating polarity clicks beginning with R phase. These standard clicks had a flat acoustic spectrum to about 6 kHz, after which acoustic energy began to decline (see Figure 5).

2.3 Stimulus presentation

Stimulus presentation and data acquisition were controlled by software developed using LabVIEW (version 8.5; National Instruments, Austin, TX, USA). A National Instruments PCI-6289 M-series acquisition card was used to convert the stimuli from digital data to analog signals, as well as to convert the EEG input from analog to digital. All stimuli were presented at a 32000 Hz sample rate with 16-bit resolution, with EFRs recorded at 8000 samples per second and ABRs recorded at 32000 samples per second with 18-bit resolution. Stimuli levels were controlled by a Tucker-Davis Technologies PA5 attenuator and SA1 power amplifier.
Figure 4: Spectrum of the electrical signal of the pink noise high-pass filtered at 1 kHz.

Due to physical characteristics of the Etymotic ER-2 stimulus transducer, the relative sound pressure level of the acoustic spectrum decreased more rapidly with frequency above 10 kHz.
Figure 5: Spectrum of the electrical signal of the standard 100 µs click.
Due to physical characteristics of the Etymotic ER-2 stimulus transducer, the relative sound pressure level of the acoustic spectrum decreased more rapidly with frequency above 10 kHz. There was a pressure node closer to 11 kHz than exactly 10 kHz due to the sampling rate of 32000 Hz.
The order of the EFR and ABR conditions was counterbalanced. Though the majority of participants completed both conditions in a single session, three participants chose to complete the EFR and ABR in two separate sessions within a week apart.

2.3.1 EFR condition

In the EFR condition, the /susəʃi/ stimulus was presented at 65 dB SPL for 300 sweeps, which required 41 min. Stimulus level was calibrated using a Brüel and Kjær Type 2250 sound level meter in flat-weighted L\text{eq} mode as the stimulus played for 60 s into a Type 4157 ear simulator.

2.3.2 ABR condition

The ABR condition required multiple measurements that were shorter in duration than the EFR condition (see Figure 6 for a diagram of the condition’s experimental protocol). First, 2000 of the low frequency (1 ms in duration) clicks in R phase were presented at 95 dB peak-to-peak equivalent (p.-p.e.) SPL to obtain a baseline ABR waveform. This level was calibrated using the sound level meter in flat-weighted mode and observing the waveforms on an oscilloscope where the peak-to-peak amplitude of a 300 Hz tone was matched to the stimulus waveform. This level also corresponded to 59 dB nHL, established by obtaining the minimum average hearing threshold for each of the ABR click stimuli from nine normal hearing adults prior to the study.

2.3.2.1 ABR preparation phase

Once the baseline ABR waveform was obtained, the next objective was to find the minimum level of ipsilateral masking noise needed to ensure that the apical region of the cochlea was generating the ABR. This was accomplished in a two-step preparation phase. First, the minimum level of full band pink noise required to eliminate wave V in the ABR was found. During successive presentations of 2000 low frequency R clicks, the level of full band pink noise was varied in 5 dB steps between 43 and 53 dB nHL (68 and 78 dB SPL; calibrated in slow flat-weighted mode) depending on the individual. On average, the minimum level of pink noise needed to significantly attenuate wave V was 50 dB nHL (75 dB SPL). Second, high-pass filtered pink noise was presented with 2000 low
Figure 6: Diagram depicting the experimental protocol of the ABR condition.
frequency R clicks to confirm that the minimum noise level determined in the previous step would adequately shift the latency of wave V. A low frequency ABR should have a 1 to 2 ms shift in wave V latency from the baseline waveform, as it takes longer for mechanical energy introduced by the stapes at the cochlear window to reach the apical region of the cochlea than the basal region (Don & Eggermont, 1978; Burkard & Hecox, 1983). Figure 7 illustrates the shift in wave V latency in one participant with increasing level of high-pass filtered pink noise.

### 2.3.2.2 ABR data collection phase

Next was the data collection phase, where the ABRs for use in the analysis were recorded. A run of 4000 low frequency alternating polarity clicks was presented at 95 dB p.-p.e. SPL (59 dB nHL) with the previously selected level of high-pass filtered pink noise. Though the actual click train stimulus was only 2000 clicks and 150 s in duration, the LabVIEW program seamlessly repeated the click train and pink noise so that the responses to 2000 clicks of each polarity could be obtained in a single run. The measurement was repeated another two times for a total of three runs of 4000 low frequency alternating clicks. The last step of the ABR condition was to record three runs of 4000 standard (100 µs in duration) alternating polarity clicks for comparison. The clicks were presented at 93 dB p.-p.e. SPL (55 dB nHL) without ipsilateral masking noise. The total duration of the ABR condition ranged from 45 to 50 min.

### 2.4 Response recording

To record the EEG, four disposable Medi-Trace Ag/AgCl electrodes were applied to the skin using Grass Technologies EC2 electrode cream. The inverting electrode for the EFR was placed on the posterior midline of the neck below the hairline, whereas the inverting electrode for the ABR was placed on the left earlobe (A1). The last two electrodes were placed on the vertex (Cz) and collarbone and acted as the non-inverting and ground electrodes, respectively, for both the EFR and ABR. Each electrode site was gently cleaned with NuPrep skin gel and an alcohol wipe to ensure that all electrode impedances were less than 5 kΩ and within 2 kΩ of each other, as measured with an F-EZM5 Grass impedance meter at 30 Hz.
Figure 7: Effect of increasing level of high-pass filtered pink noise on wave V latency.

ABR waveforms from one participant evoked by low frequency clicks with varying levels of high-pass filtered noise. Wave V is marked with a crosshair cursor in each panel. a) No noise, b) noise level at 28 dB nHL (53 dB SPL), c) noise level at 38 dB nHL (63 dB SPL), d) noise level at 48 dB nHL (73 dB SPL), e) noise level at 53 dB nHL (78 dB SPL)
After electrode placement, participants were seated in an electromagnetically shielded sound booth and reclined into a relaxed position, with a blanket provided for comfort. A rolled towel was placed behind their neck to support the head and reduce muscle artifact. An Etymotic ER-2 mu-metal shielded insert earphone (shielded by Intelligent Hearing Systems) with an appropriately sized foam tip was placed into the left ear canal. For the EFR condition, the non-inverting, ground, and posterior neck inverting electrode recording leads were plugged into a Grass LP511 EEG amplifier set to bandpass filter between 3 and 3000 Hz. For the ABR condition, the posterior neck inverting electrode lead was switched out for the earlobe inverting electrode lead and the lower filter setting of the amplifier was changed to 100 Hz. In both conditions, the amplifier applied a gain of 50000 to the input EEG, which was further increased by two to 100000 by the PCI-6289 card. Electrode recording leads were carefully separated from the ER-2 transducer to reduce stimulus artifact. Lastly, the booth lights were switched off and participants were encouraged to close their eyes and sleep in order to minimize muscle noise.

2.5 Response analysis and detection

Though the EEG waveforms and spectra were displayed during EFR and ABR data collection, the analysis was conducted offline. EFR analysis was performed using MATLAB (version 7.11.0 [R2010b]; MathWorks, Natick, MA, USA) in a similar method as Easwar, et al. (2015). First, each 8.2 s sweep was divided into 8 epochs and a noise metric of the averaged EEG amplitude between 80 and 120 Hz was calculated. This noise metric included all muscle and brain activity, including the EFR signal. Any epoch with a noise metric that exceeded two standard deviations above the mean noise metric was rejected from the analysis, as it was assumed to be dominated by muscle artifact. Epochs that passed this noise rejection were used to calculate a synchronous average sweep. Next, a Fourier analyser was used to compare the average sweep to a reference signal over time to estimate the EFR. Sine and cosine sinusoids were generated from the instantaneous $f_0$ frequency to act as the reference signal. After correcting for an estimated brainstem processing delay of 10 ms as in previous related studies (Aiken & Picton, 2006; Choi et al., 2013; Easwar et al., 2015; Purcell et al., 2004), the EEG was multiplied by the reference sinusoids to produce real and imaginary components of the EFR. An
estimate of EFR amplitude and phase was obtained by averaging these components across the duration of the vowel into a single complex number, then corrected for possible overestimation from noise (Easwar et al., 2015; Picton, Dimitrijevic, Perez-Abalo, & Van Roon, 2005). This was repeated for the three vowels with and without h1, in both F1 and F2+ carriers and in both polarities, for a total of 24 EFR estimates.

In addition to computing the EFR amplitude and phase of a vowel, the Fourier analyser used six frequency tracks below and eight frequency tracks above the f0 response track to estimate the background EEG noise. The separation in Hz of the frequency tracks was different for each vowel as it varied with analyser bandwidth, which is the reciprocal of the vowel duration. Certain tracks, such as the one containing 60 Hz or those that overlapped with the other response track (for F1 or F2+), were excluded. The EEG noise from all 14 frequency tracks was averaged to produce a single noise estimate used in comparison to the EFR amplitude estimate in an F-test. If the ratio of EFR amplitude to average background noise exceeded the critical F-ratio (2, 28 degrees of freedom) of 1.82 at an $\alpha$ of 0.05, then an EFR was considered to be detected for that condition.

There were many occasions where a participant would exhibit a significant EFR detection to a vowel stimulus in one polarity, but not the other. Easwar et al. (2015) also noted this in their experiments, speculating that the discrepancy may be due to an effect of polarity sensitivity. To account for this potential effect, Easwar et al. (2015) included the participant’s data for that vowel if a significant detection was found in at least one of the polarity conditions. This ‘either polarity’ rule was based on the assumption that the response estimate in the polarity condition considered non-significant represented a small amplitude EFR that could not be statistically distinguished from the noise floor. A Bonferroni correction (critical $p$ value = 0.025) was applied to increase the stringency of EFR detections and account for multiple comparison bias. Applying this ‘either polarity’ rule increased the number of significant EFR detections in their sample; however, they still found that a considerable number of subjects had a non-significant EFR detection in at least one vowel condition (20% of subjects in the F1 band and 30% of subjects in the F2+ band).
Initially, the present study emulated the methods of Easwar et al. (2015) and employed the same ‘either polarity’ rule. Unfortunately, an even greater number of subjects were found to have at least one non-significant EFR detection after the rule had been applied (26% of subjects in the F1 band and 42% of subjects in the F2+ band). Since all of the data from these participants would need to be excluded in order to complete the repeated measures analysis of variance (RM-ANOVA) portion of the analysis, employing the ‘either polarity’ rule was appropriate for this present study, as it would not accurately represent the true portrait of polarity sensitivity in the population. Instead, all EFR data was included in the analysis regardless of significant detection. To reduce the impact of noise on EFR estimates as much as possible while still maintaining a maximum sample size, the noise estimates computed for each vowel condition in MATLAB were averaged across all participants and conditions (mean = 28.84 nV, $SD = 10.59$ nV). EFR data from subjects with noise values that exceeded 2 SDs of the mean (50.01 nV) in over 10% of conditions were excluded from the analyses (3 subjects), as their values were likely to be highly influenced by muscle artifact.

ABR analysis was performed using software developed with LabVIEW. Each run was individually loaded into the program and a noise metric was calculated for the averaged EEG amplitude between 100 and 500 Hz for each 10-click (0.75 s) epoch. Like in the EFR analysis, any epoch that exceeded the mean noise metric by two standard deviations was rejected. Once a run was processed, two waveform traces were displayed on a separate panel of the LabVIEW program so that responses to odd number clicks were grouped together into one average waveform and responses to even number clicks into another. In the case of the run of low frequency R clicks without noise, both of the resulting traces were average responses to R clicks and therefore were combined into a grand average waveform. Each run of alternating polarity clicks, however, produced one trace that was the average response to R clicks and another that was the average response to C clicks. The three runs of standard alternating polarity clicks were loaded into the program and the R and C traces were combined into a grand average R waveform and a grand average C waveform. This process was repeated for the three runs of low frequency masked clicks.
The latencies and amplitudes of waves I, III, and V were marked by an evaluator on each of the five grand average waveforms. Latency was marked at the peak for waves I and III, and on the shoulder for wave V. Amplitude was determined by marking the peak amplitude and the amplitude of the following valley, then finding the difference. Unfortunately, masking the low frequency click train with ipsilateral high pass pink noise, though necessary for obtaining an ABR from the apical region of the cochlea, inevitably reduced the robustness of the response and attenuated peak amplitudes. As a result, many of the R and C waveforms became significantly degraded despite using the minimum noise level. Waveforms that were particularly difficult to interpret were marked by a second independent evaluator and results were compared; however, in some cases only wave V could be confidently identified. Two participants with significantly degraded waveforms returned for an additional three to four runs of the alternating low frequency click train at lower noise levels. Much less ambiguous, these waveforms were used for comparison when marking the original R and C grand average waveforms. Another participant with significantly degraded waveforms was unable to return for additional ABR measurements and was therefore excluded from all ABR analyses.

2.6 Stimulus artifact checks

To check for stimulus artifacts in the ABR condition which may be caused by electromagnetic leakage, an individual was fitted with three electrodes in the ABR montage and situated in the sound booth as usual. Instead of inserting the foam tip of the transducer into the individual’s ear canal, the tip was placed inside a Zwislocki coupler (an ear simulator) resting beside the individual. Each stimulus was presented for its full duration and the responses were analysed offline in the LabVIEW program in the same fashion as the main experiment. No stimulus artifacts were observed. The total recording time was 20 min.

To check for stimulus artifacts in the EFR condition, 15 individuals were fitted with three electrodes in the EFR montage and situated in the sound booth as usual. As in the ABR artifact check, the /susəʃi/ stimulus was routed to the Zwislocki coupler resting beside the individual. The total recording time per participant was 41 min. Afterwards, the EFR data was analysed offline in MATLAB in the same fashion as the main experiment. Any
significant EFR detections found were labeled as false positives. Across the 15 individuals, the false positive rate was 4.4% for polarity A and 6.7% for polarity B. Since the difference between the two polarity conditions was marginal and close to the expected $\alpha$ of 0.05 for type I error, it is unlikely that false positives had a significant impact on the polarity-sensitive amplitude differences observed in the EFR.

### 2.7 Statistical analyses

EFR and ABR statistical analyses were completed using SPSS (version 24; IBM, Armonk, NY, USA). Emulating the analysis from Easwar et al. (2015), a three-way RM-ANOVA was completed with EFR data in the F1 band to compare the effects of polarity across vowel stimuli. The three within-subject factors were polarity (A or B), vowel (/u/, /a/ or /i/) and h1 (present or absent). A RM-ANOVA was also completed for EFR data in the F2+ band, however, because h1 was only present in the F1 band the data set was collapsed into two levels, polarity and vowel, thereby doubling the sample size to 56. Significant interactions between within-subject variables, interpreted at an $\alpha$ of 0.05, were analysed post-hoc using Sidak-corrected pairwise comparisons.

To evaluate the effect of polarity on ABR wave latencies and amplitudes, multiple paired $t$-tests were completed for waves I, III and V. Results were evaluated using critical $p$ values determined by the False Discovery Rate (FDR) method (Benjamini & Hochberg, 1995) for multiple comparisons.

Polarity-sensitive differences in EFR data were compared to those found in ABR data using correlational analyses. Latency and amplitude differences were calculated by subtracting polarity A from polarity B for the EFR and subtracting C from R for the ABR. Absolute differences were also calculated. To obtain a more global picture of an individual’s polarity sensitivity, maximum and median amplitude differences were identified across F1 carrier vowels with h1, F1 carrier vowels without h1 and all F2+ carrier vowels, as well as latency differences across ABR waves. This approach was selected to avoid computing correlations for every possible relationship, as there would be 144 to consider (eg F1 /u/ with h1 amplitude difference vs. wave I latency difference, F2+ /i/ without h1 absolute amplitude difference vs. wave V absolute latency difference,
etc.), and to increase the sample size and power of each test. Results were interpreted using FDR-corrected critical $p$ values for multiple comparisons.
Chapter 3

3 Results

3.1 Effect of polarity on the EFR

A three-way RM-ANOVA was completed to examine the effects of polarity, h1 and vowel on EFR amplitude in the F1 band. Twenty-eight of the 31 adults who participated in the study were included in the analysis, as three subjects were removed due to excessive noise. Prior to the comparison of within-subject effects, a Mauchly’s test for sphericity was computed for each within-subject factor to determine if the variances of the differences between all possible pairs of groups were significantly different. The test indicated that the assumption of sphericity had not been violated for the three-way interaction of polarity, h1 and vowel, $\chi^2(2) = 0.799, p = 0.671$; therefore, it was unnecessary to correct the degrees of freedom. The RM-ANOVA revealed a significant three-way interaction between the effects of polarity, h1 and vowel on EFR amplitude, $F(2, 54) = 3.184, p = 0.049, \eta^2_{\text{partial}} = 0.105$. Post-hoc tests using the Sidak correction for multiple comparisons were completed to further investigate this interaction. For the vowel /u/ with h1, polarity A amplitude (140.11 ± 11.56 nV) was significantly greater than polarity B amplitude (117.59 ± 8.81 nV) by a mean of 22.52 nV, $p = 0.011, 95\% \text{ CI } [5.49, 39.55]$. For the vowel /u/ without h1 the trend was reversed: polarity A amplitude (108.72 ± 9.13 nV) was significantly lower than that of polarity B (138.26 ± 11.01 nV) by a mean of 29.54 nV, $p < 0.001, 95\% \text{ CI } [14.54, 44.54]$. The amplitude of polarity A was also significantly greater than that of polarity B for the vowel /a/ with h1 (128.18 ± 11.11 nV and 103.49 ± 9.27 nV, respectively) by a mean of 24.69 nV, $p = 0.002, 95\% \text{ CI } [10.10, 39.28]$. The mean amplitude difference between polarity A and B approached significance for the vowel /i/ without h1, $p = 0.072$. There were no significant differences between polarity conditions for /a/ without h1 and /i/ with h1. EFR amplitude differences across conditions, as well as the average electrophysiological noise estimate for each are illustrated in Figure 8.

A two-way RM-ANOVA was conducted to examine the effects of polarity and vowel on EFR amplitude in the F2+ carrier band. EFR data from the same 28 adults as in the F1
Figure 8: Mean EFR amplitudes across vowel stimuli for the F1 band.
Error bars represent ±1 SD ($N = 28$). * indicates a significant difference at $p < 0.05$.
Grey bars represent the mean noise estimate in each condition.
analysis were included. Since h1 would have no bearing on EFR amplitudes in the F2+ band, EFRs with and without h1 were combined under each vowel category, thereby doubling the sample size (N = 56). Mauchly’s tests computed for each within-subject variable indicated that sphericity had not been violated for the main effect of vowel or for the interaction of polarity and vowel, $\chi^2(2) = 1.038$, $p = 0.595$ and $\chi^2(2) = 1.069$, $p = 0.586$, respectively. Only vowel was found to have a significant main effect on EFR amplitude, $F(2, 110) = 30.04$, $p < 0.001$, $\eta^2_{\text{partial}} = 0.35$. Pairwise comparisons with Sidak correction completed post-hoc revealed that the amplitude of /a/ ($113.73 \pm 4.37$ nV) was significantly greater than that of /u/ ($83.71 \pm 5.16$ nV) by a mean difference of 30.02 nV, $p < 0.001$, 95% CI [18.40, 41.65]. The amplitude of /a/ was also significantly greater than that of /i/ ($83.38 \pm 4.91$ nV) by a mean difference of 30.36 nV, $p < 0.001$, 95% CI [19.12, 41.59]. The amplitudes of /u/ and /i/ were not significantly different from each other. A main effect of polarity on EFR amplitude approached significance, $F(1, 55) = 30.04$, $p = 0.069$, $\eta^2_{\text{partial}} = 0.059$. EFR amplitude differences across conditions in the F2+ carrier are illustrated in Figure 9.

In agreement with the findings of Easwar et al. (2015), the degree of polarity sensitivity of EFR amplitude varied considerably across individuals. Histograms were constructed to compare individual amplitude differences between polarities across vowel, h1 and carrier conditions. Figures 10 through 13 illustrate the directionality of amplitude changes by plotting the differences of polarity A amplitude minus polarity B amplitude. Positive differences indicate a greater amplitude in the polarity A condition than the polarity B condition, whereas negative differences indicate the reverse. Though the majority of subjects exhibited small amplitude differences less than 30 nV, seven individuals exhibited differences greater than 100 nV in at least one condition.

Furthermore, it would appear that, in general, those who exhibit large differences in one vowel condition tend to have similarly large differences in the other two vowel conditions as well. Amplitude difference data was grouped into the three vowel categories for each F1 and F2+ band and correlated using Pearson’s correlation
Figure 9: Mean EFR amplitudes across vowel stimuli for the F2+ band.
Error bars represent ±1 $SD$ ($N = 56$). Grey bars represent the mean noise estimate in each condition.
Figure 10: Comparison of EFR amplitude differences between polarities for /u/ with and without h1 in the F1 band.

The vertical dashed line marks the bin containing zero difference in response amplitude between the two polarities.
Figure 11: Comparison of EFR amplitude differences between polarities for /a/ with and without h1 in the F1 band.

The vertical dashed line marks the bin containing zero difference in response amplitude between the two polarities.
Figure 12: Comparison of EFR amplitude differences between polarities for /i/ with and without h1 in the F1 band.

The vertical dashed line marks the bin containing zero difference in response amplitude between the two polarities.
Figure 13: Histogram of EFR amplitude differences between polarities across vowels in the F2+ band.

The vertical dashed line marks the bin containing zero difference in response amplitude between the two polarities.
coefficient. A positive, moderate-strength correlation was found between /u/ and /i/ in the F1 band, indicating that as the degree of polarity sensitivity increased in one vowel it also increased in the other, \( r = 0.462, N = 56, p < 0.001, \) critical \( p \) value = 0.008 (see Figure 14). There were also positive correlations between /u/ and /a/ (\( r = 0.272, N = 56, p = 0.042, \) critical \( p \) value = 0.033) and /a/ and /i/ (\( r = 0.283, N = 56, p = 0.035, \) critical \( p \) value = 0.025) in the F1 band, though these relationships were not as strong and failed to reach significance (see Figures 15 and 16). In the F2+ band, a moderate-strength, inverse correlation between /u/ and /i/ approached significance, \( r = -0.307, N = 56, p = 0.021, \) critical \( p \) value = 0.017 (see Figure 17).

It is possible that fluctuations in noise between polarity A and polarity B conditions could be contributing to EFR amplitude differences. To account for this potential confound, correlation analyses were completed comparing the absolute differences in noise estimates to those in EFR amplitude between the polarity conditions. Spearman’s rho was used to analyse the correlations due to the highly right-skewed nature of the absolute difference distributions. The correlations indicated no significant relationships between the variables in the F1 (\( r = 0.104, N = 168, p = 0.179 \)) and F2+ bands (\( r = 0.026, N = 168, p = 0.738 \)). Therefore, as Easwar et al. (2015) also concluded, it is unlikely that variations in noise are significantly contributing to the EFR amplitude differences observed between polarity conditions.

### 3.2 Effect of polarity on the ABR

Multiple paired t-tests were completed to examine polarity sensitive differences in the latency and amplitude of waves I, III and V. Of the 31 participants, 20 had an identifiable wave I, 23 had an identifiable wave III and 30 had an identifiable wave V in both R and C conditions. R latency (\( M = 3.04 \text{ ms}, SD = 0.68 \text{ ms} \)) was found to be significantly longer than C latency (\( M = 2.71 \text{ ms}, SD = 0.46 \text{ ms} \)) for wave I after FDR correction by a mean difference of 0.33 ms, \( t(19) = 2.74, p = 0.031, \) critical \( p \) value = 0.033, 95% CI = [0.03, 0.62]. R latency was also numerically longer than C latency for wave V, though this difference failed to reach significance after FDR correction (\( p = 0.020, \) critical \( p \) value = 0.017). There were no significant differences between polarity conditions for wave III.
Figure 14: Correlation of EFR amplitude differences between polarities for the vowels /i/ and /u/ in the F1 band.

$r = 0.462$, *$p < 0.001$, critical $p$ value = 0.008, $N = 56$. Amplitude differences were calculated by the subtracting polarity B amplitude from polarity A amplitude. Equation of trend line is $y = 0.5944x - 6.8817$. 
Figure 15: Correlation of EFR amplitude differences between polarities for the vowels /a/ and /u/ in the F1 band.

$r = 0.272$, $p = 0.042$, critical $p$ value = 0.033, $N = 56$. Amplitude differences were calculated by subtracting polarity B amplitude from polarity A amplitude. Equation of trend line is $y = 0.2001x + 14.537$. 
Figure 16: Correlation of EFR amplitude differences between polarities for the vowels /a/ and /i/ in the F1 band.

$r = 0.283, p = 0.035$, critical $p$ value = 0.025, $N = 56$. Amplitude differences were calculated by subtracting polarity B amplitude from polarity A amplitude. Equation of trend line is $y = 0.4945x - 15.809$. 
Figure 17: Correlation of EFR amplitude differences between polarities for the vowels /u/ and /i/ in the F2+ band.

$r = -0.307$, $p = 0.021$, critical $p$ value = 0.017, $N = 56$. Amplitude differences were calculated by subtracting polarity B amplitude from polarity A amplitude. Equation of trend line is $y = -0.2611x - 0.8855$. 
latency and the amplitudes of all waves. ABR latency and amplitude differences are illustrated in Figures 18 and 19, respectively. Similar to the EFR, there was a considerable degree of individual variability in polarity sensitive latency and amplitude differences across participants. Figure 20 depicts the histogram of ABR latency differences when C latency is subtracted from R latency. Though differences varied greatly across all waves, the bulk of the histogram lay to the right of the bin of zero differences, indicating that more subjects tended to exhibit longer latencies to R stimuli. ABR amplitudes were extremely variable across participants as shown by the histogram of amplitude differences (Figure 21) and the large standard deviations in Figure 19. Unlike the variation seen in the latency data, which has been shown in previous studies (Stockard et al., 1979; Orlando & Folsom, 1995) to remain stable over time and likely originate from physiologic factors, the variation in amplitude data was more likely a result of residual noise left in the average. As discussed in Elberling and Don (1984), residual noise is not controlled for in most ABR studies since ABRs are typically obtained through repeated runs of the same number of sweeps. Changes in patient state and other factors cause noise to vary from one run to another; therefore, obtaining the same signal-to-noise ratio across all runs can only be achieved by varying the number of sweeps until the target residual noise level is reached (Elberling & Don, 1984). When Elberling and Don (1984) used this adaptive method to collect multiple runs of ABR data, they found that the variability in wave amplitudes typically observed in ABR studies was considerably reduced. In the case of this present study, using an adaptive method for collecting ABR data was not appropriate as the total measurement time would be unknown for an experiment that was already long. For this reason, ABR amplitudes were not included in the correlational analyses with EFR amplitudes.
Figure 18: Mean ABR latencies across waves.

Error bars represent ±1 SD. N of wave I = 20, N of wave III = 23, N of wave V = 30.
Figure 19: Mean ABR amplitudes across waves.

Error bars represent ±1 SD. N of wave I = 20, N of wave III = 23, N of wave V = 30.
Figure 20: Histogram of ABR latency differences between polarities across waves.
The vertical dashed line marks the bin containing zero difference in response latency between the two polarities.
Figure 21: Histogram of ABR amplitude differences between polarities across waves.
The vertical dashed line marks the bin containing zero difference in response amplitude between the two polarities.
3.3 Correlation of polarity-sensitive variation in the EFR and ABR

Multiple correlations were computed to compare polarity differences in EFR amplitude to those in ABR latency. Latency and amplitude differences were calculated by subtracting polarity A from polarity B for the EFR and subtracting C from R for the ABR. To obtain a more global picture of an individual’s polarity sensitivity and to avoid computing correlations for every possible relationship (144 in total), maximum and median amplitude differences were identified across F1 carrier vowels with h1, F1 carrier vowels without h1 and all F2+ carrier vowels, as well as latency differences across waves. Three correlations comparing maximum EFR and ABR polarity differences and three correlations comparing median EFR and ABR polarity differences were computed with Pearson’s correlation coefficient. There were no significant relationships between variables after FDR correction for multiple comparisons. These six correlations were repeated using absolute ABR latency and EFR amplitude differences. Spearman’s rho was used to analyse the correlations due to the right-skewed nature of the absolute difference distributions. A strong, positive correlation between median absolute ABR latency differences and median absolute EFR amplitude differences across F1 carrier vowels without h1 was found to be statistically significant, $r = 0.693$, $N = 27$, $p < 0.001$, critical $p$ value = 0.004 (see Figure 22). Another positive correlation of moderate strength was found between maximum absolute ABR latency differences and maximum absolute EFR amplitude differences across F1 carrier vowels with h1, though it failed to reach significance after FDR correction, $r = 0.448$, $N = 27$, $p = 0.019$, critical $p$ value = 0.008 (see Figure 23). No other absolute difference correlations were significant.
Figure 22: Correlation of median absolute differences in ABR latency and EFR amplitude in F1 carrier vowels without h1.

$r = 0.693$, $^*p < 0.001$, critical $p$ value = 0.004, $N = 27$. 
Figure 23: Correlation of maximum absolute differences in ABR latency and EFR amplitude in F1 carrier vowels with h1.

$r = 0.448, p = 0.019$, critical $p$ value $= 0.008, N = 27$. 
Chapter 4

4 Discussion

The speech-evoked EFR has the potential to become a valuable objective resource for validating hearing aids in young children. However, the relatively large degree of polarity-sensitive variation observed in studies of normal hearing adults continues to challenge our complete understanding of the clinical usefulness of the measure. The present study also found large polarity differences in the EFR, with a quarter of subjects exhibiting differences greater than 100 nV in at least one vowel condition. Statistically significant differences in amplitude were found between polarity conditions for the vowel /a/ in the F1 band and the vowel /u/ in both F1 and F2+ bands. This was an even greater effect of polarity than observed by Easwar et al. (2015) in a previous experiment using the same /susajj/ stimulus. In their sample of 16 adults, a statistically significant difference in amplitude was only found between polarity conditions for the vowel /u/ in the F1 band. Furthermore, this difference was primarily caused by asymmetry in the stimulus envelope, as removing h1 eliminated the significant difference in amplitude observed between the polarity conditions (Easwar et al., 2015).

While this present study also found an effect of h1 on polarity-sensitive amplitude differences in vowels in the F1 band, most notably in /a/, a considerable amount of variation remained that could not be explained by envelope asymmetry. Interestingly, removing h1 from the vowel /u/ did not eliminate the significant difference as expected, but instead reversed the direction of the difference by producing a statistically greater mean amplitude in the polarity B condition than the polarity A condition. Removing h1 also had only a minor effect on the degree of variability in /i/. Though there were no significant differences between polarity conditions for /i/ at a group level, the large spread of differences shown by the histogram of /i/ without h1 was not appreciably narrower than that of /i/ with h1 (see Figure 12). Perhaps the greater sample size of this study compared to Easwar et al. (2015) provided a more representative view of polarity-sensitive variation in the adult population that is not related to stimulus envelope asymmetry (28 subjects vs. 16 subjects).
In the F2+ band, only vowel was found to have a significant main effect on EFR amplitude. Response amplitude of the vowel /a/ with both polarity conditions combined was over 30 nV greater than the amplitudes of the other two vowels. This main effect was also observed by Easwar et al. (2015), though the amplitude differences were smaller (~18 nV) and a statistically significant difference was only observed between /a/ and /i/. The researchers pointed to differences in the RMS levels of the vowel stimuli as a possible explanation for this effect (Easwar et al., 2015). Though the /susəʃi/ stimulus sweep was presented at 65 dB SPL, the exact levels of the vowels naturally varied due to formant characteristics and other factors. When Easwar et al. (2015) compared the levels of F2+ carrier vowels in an ear simulator, the RMS level of /a/ was about 9 dB higher relative to /i/ and /u/. Since a higher level stimulus produces a greater spread of activation in the basilar membrane and increases the prospect of neurons firing due to greater depolarization, it is not surprising that /a/ evoked a larger amplitude response than /u/ or /i/ (Easwar et al., 2015). As for the main effect of polarity on EFR amplitude in the F2+ band, the amplitude of the polarity B condition was numerically larger than the amplitude of the polarity A condition for all vowels, though the difference failed to reach significance ($p = 0.069$). Furthermore, the histogram of amplitude differences between polarity conditions depicted in Figure 13 indicates that the vast majority of subjects exhibited amplitude differences within 30 nV. Though there were some large polarity-sensitive differences in amplitude observed across vowels in the F2+ band, these tended to be less frequent and to a smaller degree than those observed in the F1 band (compare the histograms in Figure 13 to those without h1 in Figures 10 to 12). This evidence is consistent with our expectation that lower frequency stimuli tend to elicit greater polarity effects in the EFR.

The fact that the vowel /u/, and to a lesser extent /i/, evoke the greatest degree of polarity-sensitive variation in the F1 band not related to envelope asymmetry is also consistent with our expectation that polarity sensitivity in EFR amplitude is the greatest when elicited by lower frequency stimuli. /u/ and /i/ contain the greatest proportion of low frequency energy, with their F1 frequencies for this talker at 266 Hz and 277 Hz, respectively. In contrast, the F1 frequency of /a/ for this talker is over an octave higher at 684 Hz. The similarity in F1 frequency between /u/ and /i/ may explain why an individual
exhibits a comparable degree of polarity-sensitive variation to these vowels, but not to /a/. Figure 14 illustrates the positive, moderate-strength correlation (r = 0.462, p < 0.001) between an individual’s difference in amplitude between polarity conditions for /u/ and /i/, indicating that those who exhibit large or small amplitude differences in one vowel tend to exhibit a comparable amplitude difference in the other. This relationship was found between F1 carrier vowels /u/ and /i/, however; only weaker and non-significant correlations were found between /u/ and /a/, /i/ and /a/, and between all vowels in the F2+ band. Therefore, it would appear that the EFRs of certain individuals are more sensitive to a shift in polarity when produced by stimuli of a certain frequency range. This is consistent with the findings of Aiken and Purcell (2013), who found that some subjects exhibited highly differential responses to polarity depending on the vowel. Avoiding the use of low frequency stimuli in the clinical application of the EFR could effectively eliminate some of the variation in amplitude between polarity conditions in those who are particularly sensitive. However, doing so would necessarily reduce the ecological validity of the measure as responses to certain acoustic features of speech may not be accurately assessed.

Polarity-sensitive variability was also observed in ABR wave latencies in accordance with previous ABR polarity studies. To an extent, differences in latency between polarity conditions are expected and can be explained physiologically. In the simplest model of the peripheral auditory system, the initial phase of a R stimulus induces depolarization of sensory hair cells and increased firing of the auditory nerve, whereas the initial phase of a C stimulus induces hyperpolarization and decreased firing (Peake & Kiang, 1962; Møller, 1994). Therefore, a half-cycle delay (which for a 500 Hz stimulus would be about 1 ms) should theoretically exist between wave latencies evoked by R and C stimuli. Yet, results from this present study augment the already overwhelming evidence from previous ABR studies that suggest this model is too simplistic. Though some individuals exhibited differences in latency around the theoretical half-cycle delay point, others exhibited differences that were negligible (eg. 0.03 ms) or much larger (eg. 1.75 ms), with a mean absolute difference of 0.59 ms (SD = 0.45). This polarity-sensitive variability in wave latencies is consistent with that observed in previous studies using similar low frequency stimuli (Schoonhoven, 1992; Salt & Thornton, 1984; Coats, 1978) and supports the
recommendation that low frequency stimuli should be presented only in a single polarity when obtaining clinical ABRs (Orlando & Folsom, 1995). Furthermore, the majority of subjects exhibited shorter latencies to C stimuli than R stimuli, suggesting that nerve fibres of a particular characteristic frequency may be depolarized by C stimuli or an initial peak of either phase (Sokolich, 1980; Ruggero & Rich, 1983; Antoli-Candela & Kiang, 1978; Kiang et al., 1965).

Though most ABR polarity studies have observed some subjects who exhibit shorter latencies to C stimuli, only two out of many studies have found that the majority of their subjects exhibit this response (Pijl, 1987; Hughes et al., 1981). Therefore, it was unexpected to observe shorter mean latencies to C stimuli across all waves in this study. While this finding could be a product of random sampling, it may also be a natural outcome from using this particular stimulus and presentation level. As previously discussed, evidence from Rawool and Zerlin (1988) and Orlando and Folsom (1995) suggest that stimulus frequency and intensity can interact with polarity to produce unpredictable and differential effects on wave latencies. Furthermore, as the low frequency click stimulus used is unique to this study, it may have interacted differently with polarity than the standard clicks and tone bursts typically employed by ABR studies.

The aim of this study was to investigate whether a relationship exists between polarity-sensitive variation observed in the ABR and in the EFR that cannot be explained by stimulus envelope asymmetry. Maximum differences and median differences (as well as absolute differences for both categories) were calculated for EFR amplitude differences across F1 carrier vowels with h1, F1 carrier vowels without h1, all F2+ carrier vowels, and latency differences across ABR waves. Adopting this approach allowed for the computation of a fraction of the total possible correlations (12 vs. 144 correlations) and provided a more global picture of an individual’s sensitivity to varying stimulus polarity. Since both the EFR and ABR represent an overall summation of neural activity throughout the auditory pathway when recorded at the scalp (albeit certain sources contributing more than others), it is not necessarily expected that EFR amplitude would correspond with a specific ABR wave. However, it is useful to compare if those
individuals who tend to be more sensitive to varying stimulus polarity in the EFR tend to also be more sensitive to varying stimulus polarity in the ABR.

The strong, significant correlation found between median absolute ABR latency difference and median absolute EFR amplitude difference across F1 carrier vowels without h1 (see Figure 22) supports the hypothesis that a portion of the variation in both measures arises from a common source (or sources) in the auditory system. Source localization studies reviewed in the introduction have pointed to the cochlear nucleus and inferior colliculus as the primary subcortical generators of EFRs elicited by the f0 of speech, as well as the dominant generators of ABR waves III and V, respectively. Therefore, it is possible that the polarity-sensitive variation shared by both neural responses arises from one or both of these sources in the auditory pathway. Future studies could use imaging techniques to further investigate these neural sources and deepen our understanding of the shared variation and the underlying mechanisms.

The fact that no significant correlation existed between the maximum differences and median differences of ABR latency and EFR amplitude among F2+ carrier vowels is consistent with the expectation that certain individuals are more sensitive to shifts in polarity when produced by low frequency stimuli. The ABR stimulus and F1 carrier vowels (particularly /u/ and /i/) have considerable energy around 300 Hz, therefore it is reasonable that individuals would exhibit a similar degree of polarity sensitivity to these stimuli. However, it is interesting to note that a significant relationship was not found between the maximum absolute differences of these same variables. It may be that median differences provide a better indication of the person’s natural propensity towards polarity sensitivity than maximum differences since median differences are less affected by extreme values. Also, since a significant correlation was only found between absolute differences, it would appear that greater amplitudes in one polarity condition of the EFR do not necessarily correlate with greater latencies in a specific polarity condition in the ABR. This is rational, as there is technically no reason why a specific polarity of EFR stimulus envelope would correspond with a specific ABR phase since EFR stimuli of a given polarity contain more balanced contributions of both R and C phase than the acoustics of a transient click stimulus where either R or C phase is dominant. Though the
effect of polarity is being compared in both measures, the actual definition of polarity is different: in the ABR stimulus, polarity is designated by the initial phase of either rarefied or condensed pressure, whereas in the much more complex EFR stimulus (which contains both rarefied and condensed pressure), polarity is determined by the stimulus envelope. Therefore, it would appear that those who exhibit large polarity differences in F1 carrier vowels without h1, regardless of which polarity condition elicits the greater amplitude, tend to also exhibit large polarity differences in the ABR.

The existence of ‘polarity-sensitive’ individuals has clinical implications if the method is to be adopted as a standardized hearing aid validation tool. When Easwar et al. (2015) computed polarity AB averages for each of their 20 subjects across vowel conditions, they found that two subjects had non-significant detections in at least one vowel condition despite having a significant detection in one polarity when polarities were analysed separately. These findings suggest that following the recommended EFR protocol of averaging responses to opposite polarity conditions could significantly attenuate response amplitudes and lead to false negative results in those who are particularly sensitive to varying polarity stimuli. However, at this point it would be premature to draw conclusions about the frequency and degree to which polarity sensitivity could detrimentally affect the clinical usefulness of the EFR as all available data has been collected from normal hearing young adults. Future studies should focus their attention on exploring the prevalence of polarity-sensitive amplitude differences in more clinically relevant populations such as hearing-impaired adults or normal hearing infants.
Chapter 5

5 Summary and Conclusions

In accordance with previous EFR and ABR studies, this present study found a large degree of polarity-sensitive variation across normal hearing adults in both measures. Though removing h1 from F1 carrier vowels eliminated some of the EFR amplitude differences between polarity conditions, a considerable degree of variation remained that could not be explained by asymmetry in the stimulus envelope, particularly in responses evoked by the lowest frequency vowel /u/. Using maximum differences and median differences to obtain a more global picture of an individual’s polarity sensitivity, a strong, significant correlation was found between median absolute ABR latency difference and median absolute EFR amplitude difference across F1 carrier vowels without h1. This finding supports the hypothesis that individuals who are more sensitive to varying stimulus polarity in the EFR tend to also be more sensitive to varying stimulus polarity in the ABR when low frequency stimuli (significant energy around 300 Hz) are used. Furthermore, the evidence suggests that polarity-sensitive variation in both measures may arise from a common source (or sources) in the auditory system. In future studies, researchers may be able to draw from the vast body of ABR literature and combine ABR and EFR measurements to better understand and control polarity-sensitive variation in the EFR, with the ultimate goal of improving its clinical application.
References
_Audiol Neurotol, 11_(4), 213–232. doi: 10.1159/000092589
responses to vowel sounds. _Hearing Research_, 245(1), 35–47. doi: 
10.1016/j.heares.2008.08.004
frequency-following responses (3aPP31). In _Proceedings of Meetings on Acoustics Vol.19_ (pp. 1–5). New York, NY: Acoustical Society of America. doi: 
10.1121/1.4800244
In: R.F. Naunton and c. Fernandez (Eds.). Evoked Electrical Activity in the 
critical review of audiological outcome measures for infants and children. _Trends in 
Amplification_ , 15(1), 23–33. doi: 10.1177/1084713811412056
brainstem response: Effects of click intensity, polarity, and position. _Journal of the 
the auditory brainstem response. _Scandinavian Audiology_ , 17(2), 99-109. doi: 
10.3109/010503988809070698
evoked response. _Journal of Speech, Language, and Hearing Research_. 27(1), 70-
76. doi: 10.1044/jshr.2701.70
5(9-10), 341-345.


Appendices

Appendix A: Ethics approval notice

ROMEO - Researcher Portal

General Info

FileNo: 102557
Title: Aided Auditory Evoked Potentials
Start Date: 05/07/2012
End Date: 05/07/2017
Keywords:

Project Members

Principal Investigator
Prefix: Dr.
Last Name: Scollie
First Name: Susan
Affiliation: Health Sciences\Communication Sciences & Disorders
Rank:
Gender: Unspecified
Email:
Phone1:
Phone2:
Fax:
Mailing Address:
Institution: Western University
Country: Canada
Comments:

Others

<table>
<thead>
<tr>
<th>Rank</th>
<th>Last Name</th>
<th>First Name</th>
<th>Affiliation</th>
<th>Role in Project</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Folkheard</td>
<td>Paula</td>
<td>Health Sciences\Communication Sciences &amp; Disorders</td>
<td>Co-Investigator</td>
</tr>
<tr>
<td>Postdoctoral</td>
<td>Holmes</td>
<td>Emma</td>
<td>Social Science\Psychology</td>
<td>Co-Investigator</td>
</tr>
<tr>
<td>Fellow</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Professor</td>
<td>Johnsrude</td>
<td>Ingrid</td>
<td>Social Science\Psychology</td>
<td>Co-Investigator</td>
</tr>
<tr>
<td>Name</td>
<td>Title</td>
<td>Department</td>
<td>Status</td>
<td></td>
</tr>
<tr>
<td>------------------</td>
<td>---------------------------------</td>
<td>-----------------------------</td>
<td>--------------</td>
<td></td>
</tr>
<tr>
<td>Bagatto</td>
<td></td>
<td>Health Sciences/Audiology</td>
<td>Support Staff</td>
<td></td>
</tr>
<tr>
<td>Purcell</td>
<td></td>
<td>Health Sciences/Communication Sciences &amp; Disorders</td>
<td>Other</td>
<td></td>
</tr>
<tr>
<td>Marlene</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>David</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

## Attachments

<table>
<thead>
<tr>
<th>Description</th>
<th>File Name</th>
<th>Version Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Notice (FYI)</td>
<td>DOC040913-04092013153606-0001.pdf</td>
<td>09/04/2013</td>
</tr>
<tr>
<td>Approval Notice (revision)</td>
<td>DOC060713-06072013113138-0002.pdf</td>
<td>07/06/2013</td>
</tr>
<tr>
<td>Approval Notice (study team)</td>
<td>DOC072313-07232013150736-0008.pdf</td>
<td>23/07/2013</td>
</tr>
<tr>
<td>Approval Notice (study team)</td>
<td>DOC101713-10172013133434-0002.pdf</td>
<td>16/10/2013</td>
</tr>
<tr>
<td>Approval Notice (study team)</td>
<td>DOC122313-12232013133023-0003.pdf</td>
<td>23/12/2013</td>
</tr>
<tr>
<td>2015/07/15 - CER</td>
<td>DOC073015-07302015103053-0005.pdf</td>
<td>30/07/2015</td>
</tr>
<tr>
<td>Tracked Letter of information and consent</td>
<td>Revised letter of information EEG tracked.doc</td>
<td>26/01/2016</td>
</tr>
<tr>
<td>2F002 102557- tracked</td>
<td>2F002 EEG revision 26_Jan_2016 tracked.doc</td>
<td>26/01/2016</td>
</tr>
<tr>
<td></td>
<td>Revised letter of information EEG clean.doc</td>
<td>26/01/2016</td>
</tr>
<tr>
<td></td>
<td>2F002 EEG revision 26_Jan_2016 clean.doc</td>
<td>26/01/2016</td>
</tr>
<tr>
<td>2016/01/26 - Amendment</td>
<td>DOC030216-03022016150044-0004.pdf</td>
<td>02/03/2016</td>
</tr>
<tr>
<td>2016/06/29 - CER</td>
<td>DOC070516-0008.pdf</td>
<td>05/07/2016</td>
</tr>
</tbody>
</table>
Appendix B: Sample letter of information and consent

Letter of Information
Aided Auditory Evoked Potentials

Principal Investigator: Susan Scollie, Ph.D.
Project Coordinator: Vijayalakshmi Easwar, M.Sc. (Ph.D. student under the supervision of Susan Scollie)
Location: Child Amplification Laboratory/ Speech, Auditory Feedback and Evoked Responses, The University of Western Ontario

Dear Study Participants,

The pronouns ‘you’ and ‘your’ should be read as referring to the participant who is signing the consent form.

You are invited to participate in a research study that involves recording brain potentials and relating that to your sound detection tasks. The aim of the study is to explore the relationship between brain potentials recorded and one’s ability to perform in detection tasks. This study will help us learn about how we can use these brain potentials to gauge detection ability in children. Normally hearing participants in the study will act as “controls”. This means that the performance of listeners with hearing impairment will be compared to those participants with normal hearing to help determine if the results are considered within normal limits.

It is your choice whether to be in the study. Please take your time to make a decision. The purpose of this letter is to tell you about the study so that you can decide. It is important that you understand why the study is being done and what it will involve. Please read this letter carefully and ask any questions you have.

If you wish to participate in this study, the tests will be carried out in a maximum of 4 sessions of 2-3 hours per session depending upon your comfort and scheduling convenience. While recording the auditory evoked potentials, you will

Adults: Normal hearing group
listen to speech sounds while you may stay awake or asleep. This is to examine how your brain responds to certain speech sounds. This will be done by placing sponge pads on your scalp. The pads will measure your brain responding to sounds by picking up currents (electrical energy) from your brain. These pads will not cause you any discomfort.

There are no known risks to participating in this study. Findings from this study will contribute to the development of hearing aid benefit assessments tools of benefit to society in the long term. Participation in this study is voluntary. You may refuse to participate, refuse to answer any questions, or withdraw from the study at any time with no effect on your future care. If you would like to be invited for future studies, you are required to sign the required consent.

The information obtained in this study will be used for scientific purposes and may be included in scientific reports. Your name will not appear in any publication. Your confidentiality will be protected by assigning you an identification number. All data obtained in this study will be stored in a network drive specific to the Child Amplification Laboratory that can only be accessed by authorized personnel. Hard copy records will be stored in a locked cabinet in a secure place. Research data collected will be retained indefinitely. All data retained will correspond to numerical identifiers only.

If you wish to obtain additional information regarding this project please contact Rebekah Taggart at or by email at or Dr. Susan Scollie at or by email at . If you have any questions about the conduct of this study or your rights as a research subject you may contact the Office of Research Ethics at or by email at . This letter is for you to keep.

Sincerely,

Susan Scollie, Ph.D.                  Rebekah Taggart, B.Sc.
Principal Investigator              M.Sc. (candidate)

Adults: Normal hearing group
Consent Form

Aided Auditory Evoked Potentials

I have read the accompanying letter of information, have had the nature of the study explained to me and I agree to participate. All questions have been answered to my satisfaction.

Study Participant:

Name (print)       Signature       Date

Person Obtaining Consent:

Name (print)       Signature       Date

Adults: Normal hearing group
### Curriculum Vitae

**Name:** Rebekah Taggart  

**Post-secondary Education and Degrees:**  
Western University  
London, ON, Canada  
2011-2015, B.Sc.  
Western University  
London, ON, Canada  
2015-2016, M.Sc.  

**Honours and Awards:**  
Undergraduate Student Research Award, Natural Sciences and Engineering Research Council of Canada (NSERC)  
2015  
Province of Ontario Graduate Scholarship  
2016-2017  

**Related Work Experience:**  
Graduate Teaching Assistant  
Western University  
2015-2016