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Effect of stimulus intensity on cortical potentials in cochlear implant recipients

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EFFECT OF STIMULUS INTENSITY ON CORTICAL POTENTIALS IN COCHLEAR IMPLANT RECIPIENTS

by

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Abstract: Cortical auditory evoked potentials were recorded in cochlear implant recipients and in individuals with normal hearing using a speech stimulus. Responses were acquired over two test sessions to investigate between group differences and test repeatability. Results indicate significant differences in N1-P2 latency and amplitude measures between cochlear implant recipients and individuals with normal hearing.

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I would like to express sincere appreciation to each individual that participated in the study. Every participant truly understood the value of continued research in an ever-evolving clinical area and the potential impact of the findings on patient outcomes. Finally, I would like to thank my family for their unending support and for instilling in me a love and passion for science.

TABLE OF CONTENTS

LIST OF TABLES AND FIGURES

ABBREVIATIONS

AAI	Age at Implantation
AAO-HL	Age at Onset of Hearing Loss
AAT	Age at Test
ANOVA	Analysis of Variance
CAEP	Cortical Auditory Evoked Potential
CI	Cochlear Implant
C-Level	Comfort Level
CNC	Consonant/Nucleus/Consonant Test
Cz	Vertex
dB	Decibel
DC	Direct Current
FPz	Frontal Midline Electrode
HL	Hearing Level
Hz	Hertz
ICA	Independent Component Analysis
IDR	Input Dynamic Range
IIR	Infinite Impulse Response
ml	Milliliters
ms	Milliseconds
NH	Normal Hearing
N1	Negative Deflection of CAEP at 100 ms
P2	Positive Deflection of CAEP at 180 ms

PBK-50	Phonetically Balanced Kindergarten List
PTA	Pure Tone Average
RF	Radio Frequency
SD	Standard Deviation
SPL	Sound Pressure Level
T-Level	Threshold Level
μV	Microvolts

INTRODUCTION

Cochlear implantation is an effective treatment option in individuals with severe to profound sensorineural hearing loss. In cases of sensory hearing loss, ablation or absence of sensory hair cells within the cochlea prevents the transduction of acoustic signals to the auditory nerve. When inserted into the anomalous cochlea, the cochlear implant device converts acoustic energy into electrical impulses that directly stimulate auditory nerve fibers. Biphasic pulse trains delivered to the auditory nerve in a specific pattern model the temporal and spectral characteristics of the incoming speech signal. Although cochlear implant technology has improved dramatically over the past decade, digital processing by the implant and electrical stimulation of the auditory nerve produce a unique signal transduction pathway that is unlike that of the normal auditory system.

The peripheral, brainstem and cortical auditory regions are responsible for the detection and decoding of complex acoustic cues. To date, little is known about the cortical response to electrical stimulation by the cochlear implant. Differences in cortical processing may be in part responsible for the wide range of speech perception abilities in individuals with cochlear implants (Kelly, Purdy, & Thorne, 2005). Cortical auditory evoked potentials (CAEPs) may provide valuable information regarding speech processing at the level of the cortex, thus these cortical responses have been the focus of several recent research studies. CAEPs are measures of the brain's response to sensory stimuli that reflect synchronous neural activity along the auditory centers of the cortical pathway. Two distinct waveforms include a negative deflection at approximately 100 milliseconds (N1) followed by a positive deflection at approximately 180 milliseconds (P2) (Hall, 2007). The auditory late response has multiple generators in primary and secondary auditory cortices, including Heschl's gyrus, the planum temporale, and the superior temporal lobe (Naatanen & Picton, 1987).

The N1-P2 cortical response has been investigated in normal hearing individuals (Adler & Adler, 1989; Tremblay, Billings, Friesen, & Souza, 2006) as a means of quantifying the detection of acoustic cues. The response can be accurately and efficiently obtained using an electrode placed at the vertex (Cz) (Vaughan Jr & Ritter, 1970). Latency and amplitude characteristics of the response have been shown to differ based on stimulus parameters. Several studies have demonstrated increased N1-P2 latency and decreased amplitude with decreased stimulus intensity (Adler & Adler, 1989; Billings, Tremblay, Souza, & Binns, 2007; Rapin & Graziani, 1967). The interval between stimulus presentations has also been shown to singularly affect response amplitudes, with longer interstimulus intervals corresponding to increased response amplitudes (Friesen & Picton, 2010; Tremblay, Billings, & Rohila, 2004).

Cortical auditory evoked potentials have most frequently been elicited using tonal stimuli; although speech stimuli have been utilized recently in individuals with normal hearing (Agung, Purdy, McMahon, & Newall, 2006; Tremblay, et al., 2006; Tremblay, Friesen, Martin, & Wright, 2003) and in cochlear implant recipients (Groenen, Beynon, Snik, & van den Broek, 2001; Kelly, et al., 2005; Micco, et al., 1995). Stimuli that vary in the spectral and temporal domains best reflect natural speech and provide a realistic representation of speech processing at the cortical level. Several studies have compared cortical responses between cochlear implant users and individuals with normal hearing using a speech stimulus. Groenen et al., (2001) used /ba/ and /i/ speech stimuli presented at 70 dB SPL to evoke the late response and found prolonged N1 peak latency and reduced N1-P2 amplitudes in cochlear implant recipients, as well as a high degree of inter-subject variability among this group. Micco et al. (1995) found a similar reduction in N1-P2 amplitudes in cochlear implant recipients when presenting /di/ and

/da/ speech stimuli at 70 dB SPL, but did not observe any differences in N1-P2 latencies in the study group compared to normal hearing controls.

Besides using speech as stimuli, the aforementioned studies used a variety of presentation levels. Although each provides valuable information regarding the mechanism of cortical processing in cochlear implant recipients, few studies have examined the effect of stimulus intensity on cortical responses. Everyday conversational speech consists of acoustic signals that span a range of intensities, thus it is important to gain an understanding of how the brain interprets changes in stimulus intensity delivered via a cochlear implant. Firszt, Chambers, Kraus, & Reeder, (2002) bypassed the speech processor of the cochlear implant and presented biphasic current pulses directly to the electrode array. Pulses were presented at 25%, 50%, 75% and 100% of the participants' behavioral dynamic range. Results showed decreased latency and increased amplitude of the N1 and P2 waveforms as stimulus current level increased. Similarly, Kim, Brown, Abbas, Etler, & O'Brien, (2009) examined the magnitude of the electrically evoked cortical response in cochlear implant users through bypassing the speech processor and presenting biphasic pulse trains. Results showed increased response magnitude corresponded to increases in stimulus current.

The results of previous studies suggest that increased stimulus intensity affects cortical potentials by reducing the magnitude and increasing the latency of the response. It remains to be seen whether this phenomenon can be generalized to cochlear implant recipients. To date, studies measuring the evoked cortical response in cochlear implant users (e.g. Firszt, et al., Kim, et al.) presented electrical current directly to the electrode array and bypassed the implant processor. In bypassing the external cochlear implant device, the typical processing pathway is circumvented and any pre-processing effects of the implant (e.g. signal compression) are

eliminated. The effect of sensory devices on CAEPs has been investigated (Billings, et al., 2007; Korczak, Kurtzberg, & Stapells, 2005; Tremblay, et al., 2006) in an attempt to determine whether cortical processing of acoustic cues by device wearers differs from that of individuals with normal hearing. Tremblay et al., (2006) obtained a speech evoked cortical response in normal hearing listeners both with and without the addition of a digital hearing aid. Because previous studies have shown that increased stimulus intensity affects the evoked response, one might expect that additional stimulus intensity provided by the hearing aid gain would have similar effects on the response. In contrast, no significant effect of amplification was found for waveform latency or amplitude. These findings were further examined in a follow up study by Billings et al., (2007). The N1-P2 response was recorded in normal hearing listeners using a tonal stimulus at intensities ranging from 30 to 90 dB SPL in 10 dB increments. Evoked potentials were recorded in participants both unaided and with a digital hearing aid that provided 20 dB of gain. Similar to previously published data, as stimulus intensity increased, N1-P2 latency decreased and amplitude increased. However, a repeated measures analysis revealed no significant effect of amplification (e.g. there was no significant difference in wave latency or amplitude for a 50 dB SPL stimulus between the aided and unaided conditions.) This finding is counterintuitive, because an increase of 20 dB SPL at the eardrum due to amplification should produce a response similar to an intensity increase of 20 dB SPL. The fact that this is not the case suggests that sensory devices alter the incoming acoustic signal in a way that changes its representation in the central auditory system.

Results indicating that cortical responses may differ from expected when recorded via sensory devices (e.g., hearing aids) have provided the impetus for additional studies examining auditory evoked responses in cochlear implant users. Further understanding of cortical responses

may provide information regarding variability in patient performance after implantation. Despite increased interest in obtaining CAEPs in cochlear implant users, certain limitations brought about by implant artifact have been encountered. Noise and extraneous artifacts are common to all electrophysiologic recordings. Sources of artifact include electrical noise in the recording environment and participant movement or eye blinking. Fortunately, noise in the recording can be removed via signal averaging, and periods of excessive artifact can be removed using an artifact rejection algorithm. When recording responses in cochlear implant recipients, electrical artifact is introduced through the transmission of the radio frequency (RF) signal across the skin to the internal electrode array (Martin, 2007). The onset and offset of artifact are time locked to the stimulus, i.e. artifact begins with stimulus onset and persists throughout the duration of stimulus. The time-locked nature of the artifact may obscure the neural response and make it difficult to remove. Several methods have been utilized in an attempt to remove or reduce overlapping implant artifact in electrophysiologic recordings. One approach uses an online reference placed at a distance from the stimulated ear, typically on the nose, contralateral earlobe (Sharma, Dorman, & Kral, 2005; Sharma, Dorman, & Spahr, 2002) or contralateral mastoid. Another approach used more recently varies the interstimulus interval within a recording session and produces a difference waveform (Friesen & Picton, 2010). As previously discussed, N1-P2 amplitudes have been shown to increase with longer interstimulus interval duration. By presenting identical stimuli with different interstimulus durations, a difference waveform can be created and electrical artifact, which should, in theory, remain the same for identical stimuli, can be averaged out.

Another method under investigation for removing implant-associated artifact is independent component analysis (ICA). ICA is a mathematical algorithm that generates a series

of components that are assumed to be statistically independent of one another (Neuroscan™ Manual). Components that are statistically independent of one another are generated by separate and uncorrelated processes. Thus, cochlear implant artifact and the neural response should be separated with this method, allowing for artifact extraction. Gilley et al. (2006) were able to minimize electrical artifact, yet some residual artifact remained in the recording and partially obscured the response. The same was true of Martin (2007), who was not able to completely eliminate artifact using ICA. Individual differences introduced by the speech processor also make ICA more difficult to implement. Nonetheless, ICA is a valuable tool that shows promise for removing cochlear implant artifact.

Few studies have obtained CAEPs in cochlear implant recipients using a speech stimulus presented in the sound field. To date, no studies have quantified the relationship between stimulus intensity and the cortical response in cochlear implant users, nor have they found a fully effective method for removing implant-associated artifact. The primary goal of this study was to evaluate the effects of stimulus level on CAEPs in cochlear implant recipients when recording through the speech processor with a speech stimulus, and determine whether differences exist between this group and individuals with normal hearing.

METHODS

Study Objectives

The aims of the current study were to 1) determine the effect of stimulus intensity on the N1-P2 response in cochlear implant users and individuals with normal hearing, and 2) determine the test-retest reliability of the N1-P2 response in both groups.

Participants

The study protocol was approved by the Human Research Protection Office at Washington University School of Medicine (#08-0103). Cochlear implant users were recruited from the Adult Cochlear Implant Program at Washington University and the Cochlear Implant Program at St. Louis Children's Hospital. Individuals with normal hearing were recruited from the Washington University and Saint Louis communities. All participants were at least 18 years of age and informed consent was obtained from each individual prior to beginning the study.

Normal Hearing (NH) Participants

Nine adults (seven females and two males, ages 22-28, mean 24.4, SD 1.74) served as normal hearing controls. NH adults had pure-tone audiometric thresholds equal to or better than 25 dB HL in both ears. Auditory thresholds were obtained using a Grason Stadler GSI-61 audiometer
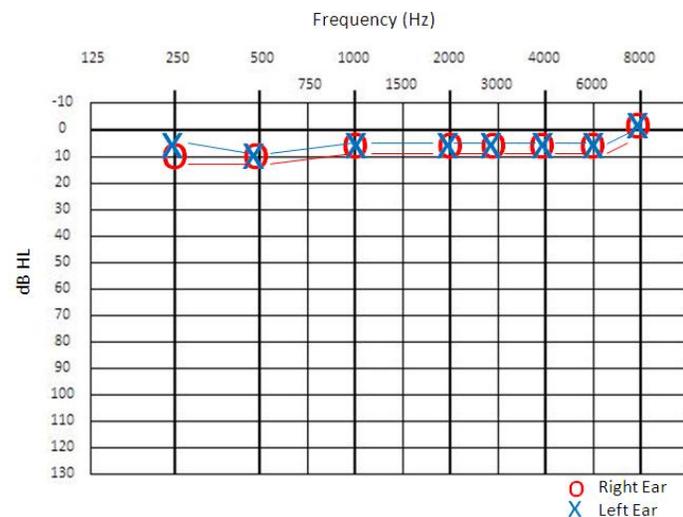

Figure 1. Audiometric thresholds for normal hearing participants.

using insert earphones. The mean pure-tone average (PTA=mean of audiometric thresholds at 500, 1000 and 2000 Hz) was 7.41 dB HL for the right ear and 7.04 dB HL for the left ear. Average audiometric thresholds for the NH participants are shown in Figure 1.

Cochlear Implant (CI) Participants

Eight adult cochlear implant recipients (four females and four males, ages 18-34, mean 24.0, SD 6.12) participated in the study. CI participants were Nucleus users who had been using their device for a period of at least six months and whose current map parameters (e.g. strategy, rate, maxima) had been stable for at least three months. Both bilateral and unilateral CI users were recruited; however, for the purposes of the current study only a monaural listening condition was employed. In cases of bilateral CI use, the individual was asked to pick their preferred implant for monaural listening. Sound field audiometric thresholds were obtained for CI participants using warble tone stimuli presented in the monaural condition to the preferred implant. Speech perception scores were obtained from each participant's most recent audiologic evaluation. Sound field audiometric thresholds and speech perception scores for CI participants are shown in Table 1.

Table 1. Sound field audiometric thresholds for cochlear implant participants using test ear.

P#	Ear Tested	250 Hz	500 Hz	1000 Hz	2000 Hz	4000 Hz	6000 Hz	Speech Perception
1	R	14	22	14	14	16	26	90% (CNC)
2	L	12	14	12	10	12	10	62% (CNC)
3	L	35	35	30	30	35	35	16% (PBK-50)
4	R	14	18	12	14	24	20	
5	R	16	14	28	16	18	18	52% (CNC)
6	L	10	16	20	10	24	14	36% (CNC)
7	R	28	28	30	26	30	32	8 % (CNC)
8	R	12	12	10	12	12	12	90% (CNC)
	Average	17.63	19.88	19.50	16.50	21.38	20.88	
	Std Dev	8.94	8.01	8.67	7.46	8.37	9.28	

Demographic information for CI participants is presented in Table 2. The sample
population consisted of individuals with pre- or peri-lingual onset of deafness, with a mean age
at onset of 1 year
(SD 1.17). The
etiology of hearing
loss also varied
among participants:
genetic (2),
meningitis (2),

Table 2. Demographic information for eight cochlear implant participants.

P#	AAO-HL	Etiology	AAI	AAT	Ear Tested
1	2	Meningitis	3	18	R
2	0	Unknown	14	19	L*
3	0	Unknown	4	20	L
4	0	Auditory Neuropathy	18	21	R
5	1	Meningitis	3	21	R
6	0	Cx26	27	28	L
7	3	Unknown	30	34	R
8	0	Hereditary Progressive	23	31	R

AAO-HL=age at onset of hearing loss (years); AAI=age at implantation (years); AAT=age at test (years)

* Tested using second sequential implant due to subjects' preference of sound quality and implant performance

auditory neuropathy (1), and unknown (3).

Study participants used a range of internal and external Nucleus devices. Internal devices
included the CI22M (2), CI24RE(CA) (4), CI24RE(CS) (1), and CI512 (1). External devices
included the ESPrit 3G (1), Freedom (6), and CP810 (1). Cochlear implant recipients were asked
to use the processor program that they most frequently utilized for everyday listening. A
summary of participant map parameters is listed in Table 3.

Table 3. Map parameters for eight cochlear implant participants.

P #	Ear Tested	Internal Device	External Device	Coding Strategy	Rate	Maxima	IDR	Active Electrodes	Stim. Mode	Volume	Sensitivity
1	R	CI22M	ESPrit 3G	SPEAK	250	8	NA	6-14; 16-22	CG	0	31.5
2	L	CI24RE(CA)	Freedom	ACE	1200	12	40	1-18; 20-22	MP1+2	9	12
3	L	CI24RE(CA)	Freedom	ACE	720	10	40	1-22	MP1+2	9	12
4	R	CI24RE (CA)	Freedom	ACE	900	12	40	1-22	MP1+2	7	12
5	R	CI22M	Freedom	SPEAK	250	8	40	14-22	CG	9	12
6	L	CI512	CP810	ACE	500	8	40	1-22	MP1+2	7	10
7	R	CI24RE(CA)	Freedom	ACE	900	7	40	4-6, 9, 13, 18, 22	MP1+2	9	12
8	R	CI24R(CS)	Freedom	ACE	1200	8	40	2-5; 7-22	MP1+2	7	12

Experimental Design

Cortical responses were obtained using a sound field speech stimulus presented from 30 to 80 dB SPL in 10 dB increments. The stimulus intensity series order was randomized for each participant. Participants underwent two test sessions to assess test-retest reliability.

Recording Apparatus

A Compumedics Neuroscan™ evoked potentials system was used for recordings. Responses were obtained using Neuroscan™ 64-channel Quik-Cap that uses the international 10-20 electrode placement with Ag/Cl electrodes. A PC based Neuroscan™ STIM program was used to time and deliver the speech stimuli. Responses were recorded and analyzed using the Neuroscan™ SCAN version 4.5 software and a Synamps2 amplifier.

Participant Preparation

Participants were instructed to refrain from using hair products on the morning of the recording session to avoid heightened impedances. Prior to cap placement, they were instructed to scratch their scalps for 1-2 minutes with a plastic comb to improve electrode impedances. After scalp preparation was performed, the appropriate cap size was selected for each participant and the cap was placed on the head.   The midline electrodes were aligned between the nasion and inion in the international 10-20 channel configuration. The reference was located directly posterior to Cz and the ground electrode was located at the high forehead directly posterior to FPz. After proper cap placement each electrode was individually filled with Electro-Cap International, Inc. Electro-Gel using a blunt 10 ml syringe. The scalp was gently abraded using the syringe before gel was injected into the electrode. Impedances of 10 kilo-ohms were

considered acceptable. If impedances of less than 10 kilo-ohms could not be achieved the electrode channel was deactivated prior to recording. Additional electrodes were also placed at the outer canthi of each eye, superior and inferior to the left eye, and on each earlobe. The skin was prepared using an alcohol wipe and a mild abrasive gel prior to electrode placement.

When filling the cap for cochlear implant participants, all electrodes directly surrounding the implant coil and cord, as well as the ipsilateral earlobe, were left unfilled in order to prevent damage to the external device. These electrodes were subsequently deactivated before recording.

Recording Environment

Recordings were obtained in a single-walled sound booth while the examiner observed the participant through a window and listened to activity within the booth using a microphone and loudspeaker. Participants were seated in a comfortable and adjustable chair and given neck and back pillows if requested. The chair was aligned such that the loudspeaker delivering stimuli was one meter away and at zero degrees azimuth. Participants watched a silent captioned DVD of their choice during recording and were asked to remain still and relaxed throughout the session.

Stimulus Parameters

A 300-millisecond duration, five formant synthetic /da/ speech stimulus was used to elicit the cortical response. Stimuli were presented in trains of 300 repetitions with a 1906 millisecond interstimulus interval. A total of 400 stimulus presentations were used on the test and retest sessions for three cochlear implant participants in an attempt to better separate the cortical response from the implant-associated artifact.

Recording Parameters

Responses in normal hearing participants were bandpass filtered online from DC to 200 Hz. All channels were amplified by a gain of 500 and converted from analog to digital at a rate of 1000 Hz. For cochlear implant participants, responses were bandpass filtered from DC to 500. Channels were amplified by a gain of 500 and an analog to digital conversion rate of 2000 Hz was utilized.

Post-Hoc Processing

Normal Hearing Participants

One continuous data file was obtained for sets of 300 trials at each discrete stimulus intensity. Continuous files were bandpass filtered from 1-30 Hz using an infinite impulse response (IIR) filter with a 6 dB per octave slope at each cutoff frequency. A linear derivation file was created for each participant to model eyeblink activity and was subsequently applied to the filtered file. Responses were then epoched from -100 to 923 ms, creating 1024 data points. A baseline correction derived from the prestimulus interval of 100 ms was then applied to the epoched file. Sweeps containing artifact exceeding +/- 50 µV were removed from analysis. In the event that this transform eliminated >100 sweeps, a less stringent artifact rejection criteria of +/- 75 µV was used. A time domain average was then created for remaining sweeps, and the averaged file was re-referenced to the earlobe corresponding to that of the participant's cochlear implant age match.

Cochlear Implant Participants

One continuous data file was obtained for each set of 300 or 400 trials at each discrete stimulus intensity from 30-80 dB SPL. Continuous files were epoched from -100 to 923.5 ms,

creating 2048 data points. Files were baseline corrected and averaged across trials. Independent

component analysis (ICA) was then performed on the averaged files as a method of removing

electrical artifact associated with the cochlear implant. The vertex electrode (Cz) was used to

carry out ICA. The entire epoch was used to model the artifact, then components one and two

were selected as the best representation of the artifact. The

file was then saved as artifact and subtracted from the

averaged response. Figure 2 demonstrates the ICA

process. The resulting response was re-referenced to the

earlobe that was contralateral to the device and bandpass

filtered from 1-30 Hz with a 6 and 12 dB per octave slope

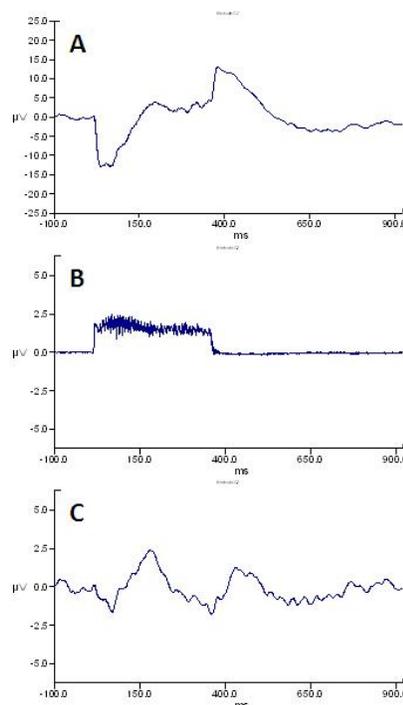on the high pass and low pass cutoff frequencies,

respectively.

Figure 2. Demonstration of independent component analysis (ICA) for the removal of artifact generated by the cochlear implant. (A) Resulting response without artifact removal. (B) Artifact model created using ICA. (C) Final result after subtraction of the artifact file, filtering and re-referencing to the contralateral earlobe.

Measurements

Waveforms were plotted and latency and amplitude

values were subsequently chosen using the Neuroscan™

Waveboard program. Absolute latency was defined as the

time in milliseconds from the onset of the stimulus to the

peak amplitude of the N1 and P2 peaks, respectively. Wave amplitude was defined as the

difference between the prestimulus baseline and the peak of the N1 and P2 waves in microvolts.

In cases where the waveform of the response exhibited jagged or double peaks, the data were

smoothed using a software transform.

RESULTS

The purpose of the present study was to examine the effect of stimulus intensity on the N1-P2 response in cochlear implant recipients and in individuals with normal hearing and to determine whether differences exist between groups. In addition, the repeatability of the response was examined in each group. Responses were analyzed from the vertex electrode (Cz). A repeated measures design was completed to examine the amplitude and latency measurements for the N1 and P2 waveforms. A mixed, between- and within-subjects analysis of variance (ANOVA) was conducted with two groups (normal hearing and cochlear implant) and across stimulus intensities (30, 40, 50, 60, 70 and 80 dB SPL).

Individual Waveforms

Figure 3 displays individual wave overlays for one NH (A) and one CI (B) participant, with stimulus intensity (dB SPL) and latency (ms) plotted on the ordinate and abscissa axes, respectively. A clear N1 trough and P2 peak can be distinguished for both the NH and CI participant. Waveform morphology was more consistent across level for the NH participant, which was a general trend for the NH group. In contrast, the waveforms for the CI participant were more variable in morphology, which was also consistent for the CI group.
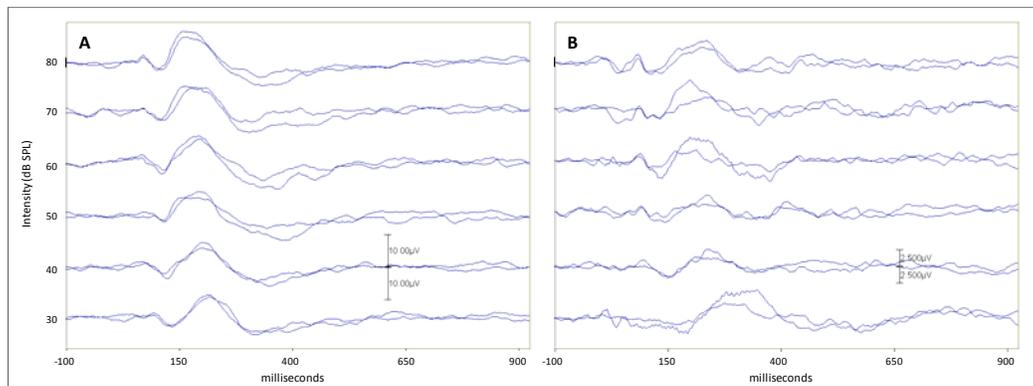

Figure 3. Test/re-test waveform overlays for one normal hearing (A) and one cochlear implant (B) participant. A general trend of high repeatability across test sessions was observed in normal hearing participants. Results obtained in cochlear implant participants suggest responses are generally repeatable across test sessions, although more variable than those of their normal hearing counterparts.

Effect of Intensity on Wave Latency

Repeated measures analysis revealed a significant main effect of stimulus level for N1 latency ($F(3,75)=34.135$, $p<0.001$) and P2 latency ($F(3,75)=22.561$, $p<0.001$) measured in the first recording session. Figure 4 displays N1 and P2 latency as a function of stimulus intensity. In addition, a significant main effect of group was found for both N1 ($F(1,15)=6.024$, $p<0.05$) and P2 ($F(1,15)=9.788$, $p<0.01$) latencies. Independent of stimulus level, N1 and P2 latencies were prolonged in CI participants compared to NH controls. A significant interaction was found between group and intensity for the N1 response ($F(3,75)=7.856$, $p=0.001$). This finding indicates the pattern of N1 latency shift as stimulus intensity increased was different between the NH and CI groups. Among NH participants, average N1 latency ranged from 135.44 ms to 110.460 ms when stimulus intensity was increased from 30 to 80 dB SPL, respectively. N1 latency among CI participants ranged from 183.55 ms to 114.15 ms across the same intensity range. Thus, at higher stimulus levels (e.g. 70 and 80 dB SPL), NH and CI participants exhibited similar N1 latencies. As stimulus level decreased, a greater shift in latency was seen in CI compared to NH participants.
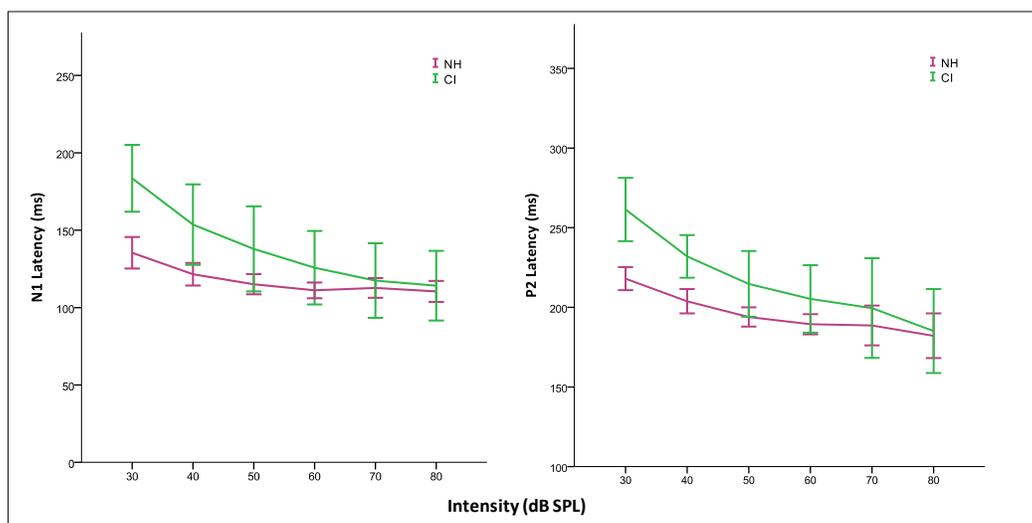

Figure 4. Latency-intensity functions for a synthetic /da/ speech stimulus presented from 30-80 dB SPL in cochlear implant and normal hearing participants. Mean values are shown +/- SEM.

A significant interaction effect between group and intensity was found for P2 latency as well ($F_{(3,75)}=2.83$, $p<0.05$). Similar to N1 latency, the pattern growth for P2 latency in response to changes in stimulus intensity was different between the NH and CI groups. Among NH participants, average P2 latency ranged from 218.02 ms to 182.17 ms when stimulus intensity was increased from 30 to 80 dB SPL, respectively. P2 latency among CI participants ranged from 261.34 ms to 185.11 ms across the same intensity range. Differences in latency shifts for P2 were similar to that of N1, with NH and CI groups exhibiting comparable latencies at the highest intensities (70 and 80 dB SPL), after which CI group latencies become prolonged compared to the NH group. For both N1 and P2 latencies, variability was greater for the CI than the NH participants, as evidenced by the standard error bars in Figure 4.

Effect of Intensity on Wave Amplitude

In contrast to latency findings, no significant main effect of intensity was noted for N1 amplitude ($F_{(5,75)}=1.344$, $p=0.255$); however, a significant main effect of group was found
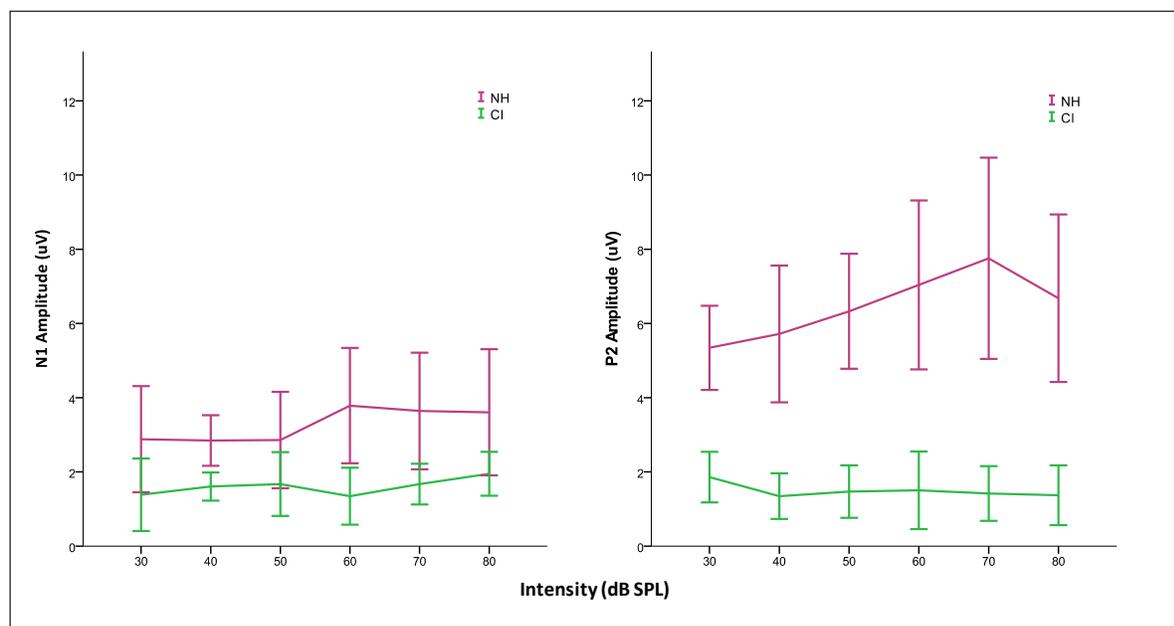

Figure 5. Amplitude-intensity functions for a synthetic /da/ speech stimulus presented from 30-80 dB SPL in cochlear implant and normal hearing participants. Mean values are shown +/- SEM.

(F(1,15)=8.327, p<0.05). N1 amplitudes were significantly greater in NH participants compared to their CI counterparts. As stimulus intensity was increased from 30 to 80 dB SPL, N1 amplitude ranged from 2.88 µV to 3.61µV in NH participants and from 1.38 µV to 1.95 µV in CI participants. Figure 5 displays N1 and P2 amplitude as a function of stimulus intensity.

No significant main effect of intensity was found for P2 amplitude (F(3,75)=2.632, p=0.06); however, a significant main effect of group was present (F(1,15)=32.260, p<0.001) as was a significant interaction between group and intensity (F(3,75)=4, p=0.016). P2 amplitude was significantly greater for the NH group compared to the CI group, with amplitudes ranging from 5.34 µV to 6.68 µV in NH participants and from 1.86 µV to 1.37 µV in CI participants as intensity was increased from 30 to 80 dB SPL. As seen in Figure 5, the slope of mean P2 amplitudes is relatively flat for CI participants, compared to the positive slope of amplitude growth seen in NH participants. For both N1 and P2 amplitudes, variability was greater for the NH than the CI participants, again evidenced by the standard error bars in Figure 5.

Test-Retest Reliability

A mixed, general linear model ANOVA was completed in order to evaluate the repeatability of the N1-P2 response across test sessions. The ANOVA analyzed measurements across three levels, including intensity (30, 40, 50, 60, 70 or 80 dB SPL), group (NH or CI) and session (one or two). Results showed no significant interaction between intensity and session for N1 latency (F(5,75)=1.249, p=0.303) or P2 latency (F(5,75)=1.137, p=0.340). Similarly, no significant interaction between intensity and session was found for N1 amplitude (F(5,75)=0.868, p=0.507) or P2 amplitude (F(5,75)=1.963, p=0.094). These results indicate that
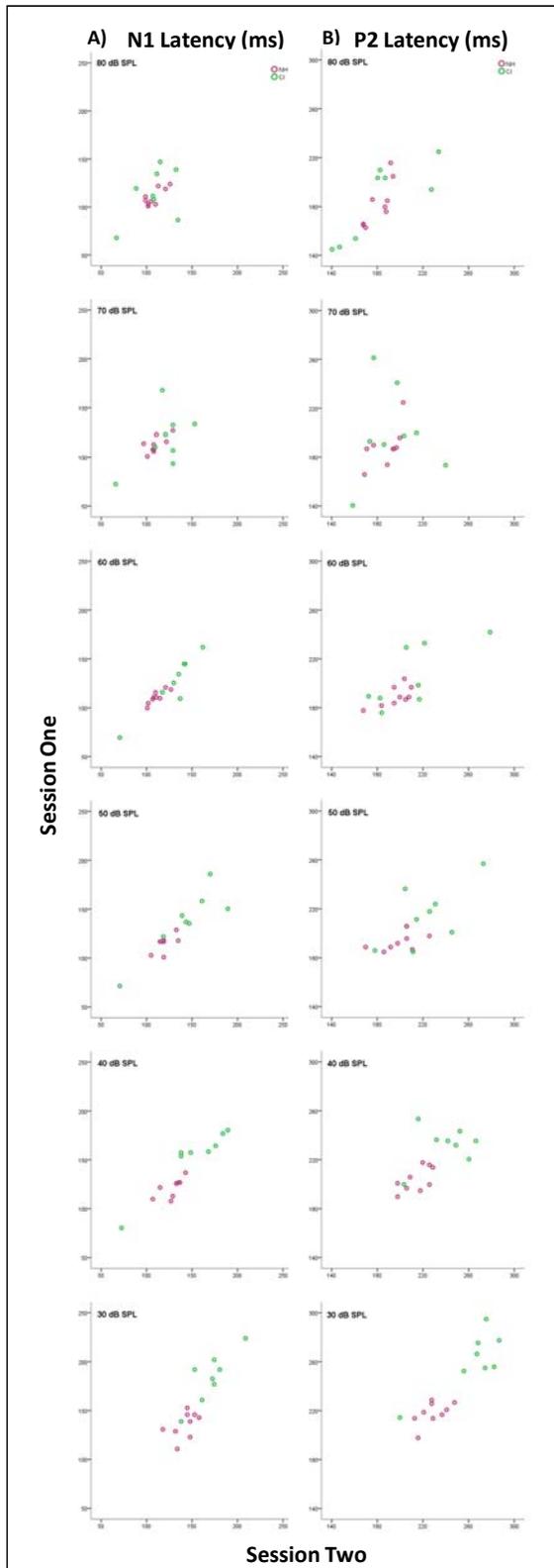
Figure 6. Scatter plots depicting N1 (A) and P2 (B) latencies for session one (ordinate) and session two (abscissa). Each data point represents the measurement from either a NH (red) or CI (green) participant.

no measureable difference was present across session one and session two for each intensity, independent of participant group.

To further examine test repeatability across sessions, scatter plots were created for latency and amplitude measures at each individual stimulus intensity. Scatter plots are displayed in Figures 6 and 7. Ordinate and abscissa axes represent session one and session two, respectively. Each individual data point represents one participant, with NH participants shown in red and CI participants shown in green. The data depicted in Figure 6 support the statistical analysis indicating good test repeatability across sessions. A trend line drawn with a one to one slope would indicate similar results for each participant across test sessions. Prolonged latencies were apparent for CI compared to NH participants, as was intra-group variability. N1 latencies for a 60 dB stimulus showed the best repeatability across sessions for both NH and CI participants. In contrast, a larger spread of data points for N1 latency was

seen at 80 and 70 dB among CI participants. Similarly, P2 latencies for a 70 and 80 dB stimulus exhibited a greater degree of spread (more so in CI participants), while data points for a 60 dB stimulus demonstrated the best repeatability.

Scatter plots created for amplitude measurements are displayed in Figure 7. Amplitudes were generally larger for NH participants compared to their CI counterparts. In contrast to latency, N1 amplitudes showed a trend of good repeatability across the range of intensities. Exceptions of this included one NH participant for the 80 dB presentation level, and NH amplitudes for the 30 dB presentation level.

P2 amplitudes were noticeably larger for NH participants compared to CI participants, the latter exhibiting amplitudes similar in magnitude to that of N1 measurements. In contrast to latency measurements, within-group amplitude variability was apparent for NH participants. In addition, a greater spread of data points existed for NH participants at the 30, 70 and 80 dB SPL presentation levels. While graphic representation of the data
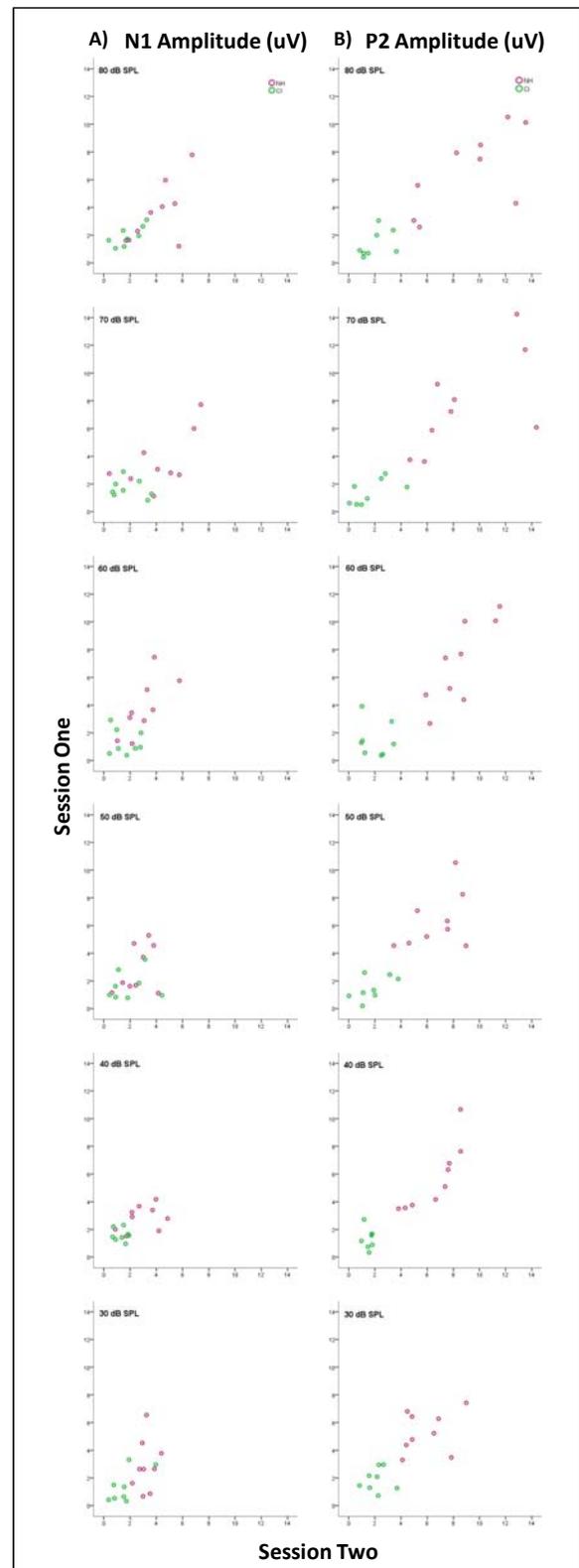

Figure 7. Scatter plots depicting N1 (A) and P2 (B) amplitudes for session one (ordinate) and session two (abscissa). Each data point represents the measurement from either a NH (red) or CI (green) participant.

points across test sessions provides a clear view of test repeatability, it is worth reiterating that a repeated-measures ANOVA did not reveal a significant interaction between intensity and test session.

Grand Average Waveforms

After repeated-measures analysis revealed no significant interaction between test session and stimulus intensity, waveforms from sessions one and two were averaged for each participant. Individual averaged waveforms were used to calculate grand average waveforms seen in Figure 8. NH and CI waves are shown in Figures 8A and 8B, respectively, at each intensity from 80 dB
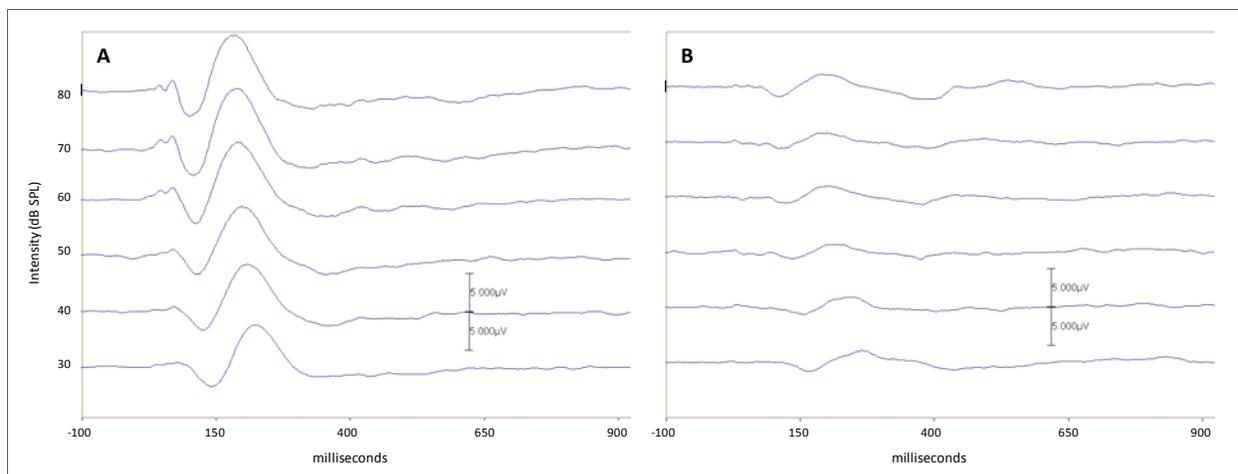
Figure 8. Grand average waveforms for 6 stimulus intensities. (A) Responses from normal hearing participants. A general decrease in amplitude and increase in latency was seen for waves N1 and P2 as stimulus intensity decreased. (B) Responses from cochlear implant participants. A general increase in the latency of waves N1 and P2 was noted as stimulus intensity decreased. Effects of intensity on amplitude of waves N1 and P2 were more variable.

SPL (top) to 30 dB SPL (bottom). Average wave amplitudes were larger for NH participants compared to CI participants, and a pattern of increased wave latency with decreased stimulus intensity was seen for both groups. Median, minimum and maximum latency and amplitude values for each group are displayed in Table 4.

Table 4: Median, minimum and maximum latency and amplitude values for normal hearing and cochlear implant participants measured at intensities from 30 to 80 dB SPL. Latencies and amplitudes are expressed in milliseconds and microvolts, respectively.

Normal Hearing							Cochlear Implant						
N1 Latency (msec)	**80**	**70**	**60**	**50**	**40**	**30**		**80**	**70**	**60**	**50**	**40**	**30**
Median	106.8	112.8	110.8	116.8	125.8	138.8	Median	115.4	116.6	129.9	140.1	157.9	187.1
Minimum	100.8	100.8	99.8	100.8	107.8	110.8	Minimum	67.9	72.4	69.4	71.4	80.4	110.8
Maximum	123.8	126.8	120.8	128.8	136.8	136.8	Maximum	146.9	167.9	161.9	185.9	180.4	152.8
N1 Amplitude (µV)													
Median	3.6	2.8	3.5	1.9	2.9	2.6	Median	1.8	1.5	0.9	1.3	1.5	1.0
Minimum	1.2	1.1	1.2	1.1	1.5	0.7	Minimum	1.1	0.8	0.4	0.8	1.0	0.3
Maximum	7.8	7.7	7.5	5.3	4.2	6.5	Maximum	3.1	2.9	2.9	3.6	2.3	3.3
P2 Latency (msec)													
Median	179.7	186.7	188.7	191.7	200.7	218.7	Median	198.6	195.1	193.9	214.6	235.3	261.1
Minimum	162.7	165.7	177.7	184.7	189.7	197.7	Minimum	144.9	140.4	175.9	184.9	199.9	214.4
Maximum	215.7	224.7	203.7	205.7	217.7	228.7	Maximum	224.8	261.3	241.8	256.8	253.3	294.8
P2 Amplitude (µV)													
Median	7.5	7.2	7.4	5.7	5.1	5.2	Median	0.9	1.4	1.2	1.2	1.4	1.8
Minimum	2.6	3.6	2.7	4.5	3.5	3.3	Minimum	0.4	0.5	0.4	0.2	0.3	0.7
Maximum	10.5	14.3	11.1	10.5	10.7	7.4	Maximum	3.1	2.7	3.9	2.6	2.7	3.0

DISCUSSION

The current study utilized a speech stimulus delivered in the sound field to elicit the N1-P2 cortical response in individuals with normal hearing (NH) and in cochlear implant (CI) recipients. Importantly, CI participants wore their speech processor, microphone and head coil while listening with their everyday processor program during recordings. Results suggest the cortical response can be reliably obtained in both groups using the present paradigm.

Effect of Stimulus Intensity on Wave Latency

Normal Hearing Participants

The effect of stimulus intensity on the N1-P2 cortical response has been studied in normal hearing individuals (Adler & Adler, 1989; Agung, et al., 2006; Billings, et al., 2007; Rapin & Graziani, 1967). Typical findings demonstrate decreased N1 and P2 latency and increased amplitude as stimulus intensity is increased. A similar pattern was seen among NH participants in the current study. Adler and Adler found N1 and P2 latencies ranging from 86 to 105 ms and 158 to 176 ms, respectively; however, the authors used a tonal stimulus delivered via headphones. The current study utilized a speech stimulus presented in the sound field, thus the fact that latencies were prolonged is not unexpected. N1 and P2 latencies found in the current study were similar to those found by Billings et al. (2007), who used a tonal stimulus but presented the stimulus in the sound field.

Cochlear Implant Participants

Previous studies examining the effect of stimulus intensity on the N1-P2 response in cochlear implant recipients have bypassed the speech processor and delivered biphasic pulse trains directly to the electrode array at a given percentage of the participant's behavioral dynamic

range (Firszt, et al., 2002; Kim, et al., 2009). One disadvantage of this approach is that

bypassing the speech processor of the cochlear implant eliminates the effect the processor has on

the incoming acoustic signal. The current study delivered a sound field stimulus to best reflect

natural signal processing. N1 and P2 latencies followed a similar overall pattern of decreased

latency with increases in stimulus intensity. In contrast to Firszt et al., the latencies obtained for

the CI group in the current study were prolonged and shifted over a greater range. The fact that

the current study delivered the sound stimulus through a loudspeaker may have contributed to

this result. The results of the current study are similar to those of Groenen et al. (2001) who

found prolonged N1 and P2 latencies in CI participants compared to NH controls when a speech

stimulus was used. In contrast, Micco et al. (1995) did not observe any statistically significant

difference in N1 and P2 latencies for CI recipients compared to NH controls when a speech

stimulus was used. Both of the previously mentioned studies used a 70 dB SPL speech stimulus

to elicit the cortical response. The findings of the current study suggest response latencies in

cochlear implant participants are more variable at higher presentation levels, e.g. 70 and 80 dB

SPL. This may contribute to the differences in the latency findings of Groenen et al. and Micco

et al.

Effect of Stimulus Intensity on Wave Amplitude

Normal Hearing Participants

Overall, N1 and P2 amplitudes were significantly larger for NH participants compared to

the CI group.   Mean N1 amplitudes were similar for the 30, 40 and 50 dB presentation levels.

Amplitudes then increased but remained similar for the 60, 70 and 80 dB presentation levels. P2

amplitudes were larger than N1 amplitudes, and the growth pattern was more gradual until 80

dB, where P2 amplitude actually decreased. The amplitude growth function obtained by Adler and Adler using similar intensities revealed increased amplitude when the stimulus was increased from 30-70 dB SPL, but stimulation from 70-90 dB SPL produced a slight decrease in N1 amplitude and slower growth for P2. The authors attribute this finding to a possible saturation effect at the highest presentation levels. A saturation effect may have caused the decrease in mean P2 amplitude seen at the 80 dB presentation level. In contrast, data presented by Billings et al. (2006) did not reveal a saturation effect for N1 and P2 amplitude as stimulus intensity was increased from 70-90 dB SPL. Within their study, mean amplitudes ranged from approximately 2 to 6 µV for N1 and from approximately 1 to 4 µV for P2. N1 amplitudes obtained in the current study were not as large in magnitude. In contrast, mean P2 amplitudes for the current study were much larger in magnitude, reaching approximately 8 µV as the maximum amplitude at 70 dB SPL.

Cochlear Implant Participants

Overall, N1 and P2 amplitudes for the CI group were smaller compared to the NH group. This difference was especially pronounced for P2 amplitudes, for which there was a large difference between NH and CI amplitudes. This discrepancy could possibly be caused by the characteristics of the speech processor. All but one of the Nucleus devices used in the current study utilized a 40 dB SPL input dynamic range (one participant used an older processor with a 30 dB input dynamic range (IDR)). Default IDR settings include a 25 dB SPL threshold level (T-level) and a 65 dB SPL comfort level (C-level) cutoff. Inputs above the 65 dB SPL C-level are infinitely compressed and mapped to the C-level. Thus, high intensity inputs in the current study (70 and 80 dB SPL) may have been compressed, altering the magnitude of the response.

Low level inputs of 30 dB may have been low enough to reach the noise floor, obscuring the magnitude of the response.

Another explanation for the small amplitudes that did not exhibit growth is the possibility that the neural response was partially obscured by electrical artifact. Independent component analysis was employed in our methodology as the main artifact removal tool. ICA was utilized for all CI participants during post-hoc processing after an average file was created. We chose to use the first two components to model the artifact and subtracted the artifact from the average file. It is likely that for some participants, the selection of additional components may have improved the removal of implant associated artifact. The problem with this approach, however is the more components that are chosen, the greater the likelihood of removing part of the neural response. Few studies have successfully used ICA as a method of removing artifact associated with the cochlear implant. Both Martin (2007) and Gilley et al. (2006) investigated the efficacy of ICA as a method of removing electrical artifact introduced by the cochlear implant. ICA proved beneficial to some degree in both studies, yet the response of interest was not wholly separated from the underlying artifact. Further investigation of ICA and other artifact removal techniques is warranted in order to accurately estimate the cortical response in cochlear implant recipients.

Test-Retest Reliability

Results of the current study suggest the N1-P2 cortical response can be repeated in normal hearing individuals and cochlear implant recipients across test sessions. No significant interaction between stimulus intensity and test session was found, indicating good repeatability of the response. This finding is similar to that of Tremblay et al. (2003), who found good

repeatability of the cortical response using a speech stimulus in normal hearing individuals. Spearman's Correlations were attempted in order to further examine the correlation between test and retest sessions, yet the small sample size prevented accurate interpretation of the results of this test. Interpretation of the scatter plots in Figures 7 and 8 suggests repeatability for each participant is the best overall at stimulus intensities of 40, 50 and 60 dB SPL. Above and below these levels, the data points for cochlear implant participants become more scattered. As previously mentioned, this could be due to compression characteristics of the cochlear implant at high input levels or the stimulus overlapping with the noise floor at lower levels. This finding may indicate that cortical responses are most reliably obtained in the mid-intensity range.

Future Directions

The current study not only generated novel findings but also created further questions for study. The study could be repeated with a larger sample size to increase the power of statistical analyses and better represent the cochlear implant population. The current study enrolled recipients with pre/peri-lingual onset of severe to profound hearing loss, therefore including those with post-lingual hearing loss would allow generalization of results to a larger recipient base. Given that postlingual patients would have had normal auditory system development prior to onset of hearing loss and then implantation, cortical responses may differ in the two populations. Future studies could expand to include individuals with different cochlear implant devices, such as Advanced Bionics™ and Med-El™, to better understand the effects of different processing strategies on cortical responses.

Another important direction for study is to find an effective method for the removal of artifact associated with the cochlear implant. This problem remains a hindrance to researchers

measuring cortical responses in cochlear implant recipients and introduces variability in the

results and interpretation of findings across studies. ICA has proven to be a promising technique

for this endeavor; yet it requires further investigation in future studies.

CONCLUSIONS

The present study showed differences in cortical processing of a speech stimulus between individuals with normal hearing and cochlear implant recipients. Differences in N1 and P2 latency and amplitude were observed between groups, and stimulus intensity was found to have a significant effect on these measurements. The N1-P2 response was reliably obtained in both groups in two separate test sessions, with no significant differences between test sessions. Future research should further investigate the efficacy of using a speech stimulus to elicit cortical responses while recipients wear their everyday speech processor programs and improve current artifact rejection techniques.

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