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The Effect of Changes in Stimulus Level on Electrically Evoked Cortical Auditory Potentials

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Abstract

Objectives—The purpose of this study was to determine whether the electrically evoked acoustic change complex (EACC) could be used to assess sensitivity to changes in stimulus level in cochlear implant (CI) recipients and to investigate the relationship between EACC amplitude and rate of growth of the N1-P2 onset response with increases in stimulus level.

Design—Twelve postlingually deafened adults using Nucleus CI24 CIs participated in this study. Nucleus Implant Communicator (NIC) routines were used to bypass the speech processor and to control the stimulation of the implant directly. The stimulus consisted of an 800 msec burst of a 1000 pps biphasic pulse train. A change in the stimulus level was introduced 400 msec after stimulus onset. Band-pass filtering (1 to 100 Hz) was used to minimize stimulus artifact. Four to six recordings of 50 sweeps were obtained for each condition, and averaged responses were analyzed in the time domain using standard peak picking procedures.

Results—Cortical auditory change potentials were recorded from CI users in response to both increases and decreases in stimulation level. The amplitude of the EACC was found to be dependent on the magnitude of the stimulus change. Increases in stimulus level elicited more robust EACC responses than decreases in stimulus level. Also, EACC amplitudes were significantly correlated with the slope of the growth of the onset response.

Conclusions—This work describes the effect of change in stimulus level on electrically evoked auditory change potentials in CI users. The amplitude of the EACC was found to be related both to the magnitude of the stimulus change introduced and to the rate of growth of the N1-P2 onset response. To the extent that the EACC reflects processing of stimulus change, it could potentially be a valuable tool for assessing neural processing of the kinds of stimulation patterns produced by a CI. Further studies are needed, however, to determine the relationships between the EACC and psychophysical measures of intensity discrimination in CI recipients.

INTRODUCTION

Over the course of the last 20 years, cochlear implantation has become the treatment of choice for severe to profound sensorineural hearing loss. During this time period, not only has the age

of implantation dropped, but improvements in speech processing strategies have led to increased mean levels of performance. Despite these promising trends, variations in performance across individuals remain large. Given these facts, it seems reasonable to assume that electrophysiologic measures of the response to electrical stimulation could be useful in assessing the basis for such variations, particularly in young, difficult-to-test children.

Several studies have suggested that differences in performance across individuals with a cochlear implant (CI) may reflect differences in central auditory function (Firszt et al. 2002b; Kelly et al. 2005; Kraus et al. 1993; Micco et al. 1995). Therefore, in recent years, cortical auditory-evoked potentials have drawn considerable attention as a method of investigating central auditory function in CI users. Several different cortical potentials evoked with electrical stimulation in CI users have been reported in the literature. These measures include obligatory-evoked potentials, such as P1, N1, P2, and discriminative potentials, such as P300 and the mismatch negativity response. The focus of this study will be on the long-latency, obligatory N1-P2 response.

The N1-P2 complex is a cortically generated, auditory-evoked potential that can be recorded in a passive listening paradigm using either acoustical or electrical stimulation. In adults, the typical latency of N1 is about 100 msec. It is followed by a positive potential (P2) that has a latency of approximately 175 msec. The effect of variations in stimulus parameters on this potential in response to acoustic stimulation has been summarized in several reviews (Hyde 1997; Näätänen & Picton 1987). N1-P2 amplitudes increase with stimulus level but tend to saturate at high levels of stimulation. Latency of both N1 and P2 decreases with increasing stimulus level. N1-P2 amplitudes also increase as the length of the interstimulus interval is increased up to approximately 10 sec, suggesting adaptation or habituation has the potential to significantly affect this response. In addition, there have been several investigations describing the time course of development of this response (Eggermont & Ponton 2003; Ponton et al. 1996; Wunderlich et al. 2006).

Several investigators have also reported measuring this response in CI users. Firszt et al. (2002a) reported that response characteristics, such as latency and amplitude, of the N1-P2 that are similar to those reported for acoustic stimulation. N1-P2 amplitude tended to increase with increasing current level and was similar across stimulation electrode sites. Others have used the N1-P2 response, as recorded at suprathreshold levels, to try to understand differences in performance across CI users (Beynon et al. 2002; Firszt et al. 2002b; Groenen et al. 1996; Kelly et al. 2005; Makhdoum et al. 1998), and P1 has been used to study maturation and plasticity of cortical auditory function in children with CIs (Ponton et al. 1999; Ponton & Eggermont 2001; Sharma et al. 2002, 2005).

Although the N1-P2 response is typically recorded in response to clicks, tone bursts, or short speech tokens, this response can also be elicited by a change in an ongoing acoustic stimulus (Jerger & Jerger 1970; Martin & Boothroyd 2000; Näätänen & Picton 1987). This response has been referred to as the acoustic change complex (ACC). For example, Martin and Boothroyd (2000) measured the ACC elicited by acoustic transitions in a long-duration stimulus that included intensity, spectral envelope, and periodicity changes. They observed responses to intensity change alone for changes as low as 2 to 3 dB, similar to psychophysical discrimination thresholds for similar stimuli. Tremblay et al. (2003) used naturally produced speech stimuli to record the ACC and demonstrated that distinct ACCs were reliably evoked by speech tokens with different acoustic cues. Recently, Lister et al. (2007) used two narrowband noise bursts centered at 2000 or 1000 Hz with a temporal gap introduced into the burst to elicit the change response. They observed larger-amplitude responses for the conditions either where spectral differences were increased or where the gap duration was increased. Results of these studies suggest that the ACC may serve as an objective index of auditory

discrimination capacity (Lister et al. 2007; Martin & Boothroyd 1999, 2000; Ostroff et al. 1998; Tremblay et al. 2003).

Martin and Boothroyd (2000) recorded the ACC in response to changes in intensity of an ongoing speech stimulus. The amplitude of the ACC increased as the magnitude of the intensity change increased. Intensity increments seemed to elicit more robust ACC responses than decrements. Group mean waveforms in the normal-hearing subjects tested by these authors showed ACC responses for intensity changes as small as 2 to 3 dB. More recently, Harris et al. (2007) used the ACC recorded in response to changes in stimulation level to study age-related changes in auditory processing. Their results showed the difference between younger and older subjects in ACC intensity discrimination thresholds. In their study, the group-averaged waveforms showed that ACCs could be elicited by intensity increments as small as 1 dB for younger subjects and 2 dB for older subjects.

Friesen and Tremblay (2006) were the first to report measuring electrically evoked ACC (EACC) in CI users. They used naturally produced speech stimuli presented in the sound field and recorded a series of overlapping N1-P2 responses. Their work showed that, despite the stimulus artifact associated with electrical stimulation, it was possible to elicit the EACC using relatively long-duration speech stimuli in CI users. In 2007, Martin recorded the EACC using a stimulation paradigm similar to that used in her original studies with normal-hearing listeners. Results from a single Med El CI user were reported. The stimulus was a synthetic vowel that was 786 msec in total duration and had been modified to include a series of changes in the F2 formant frequency at approximately 386 msec. The goal of this study was to explore feasibility of recording these responses in CI recipients. The focus was on defining ways to deal with stimulus artifact contamination.

Brown et al. (2008) also used the stimulation paradigm originally described by Martin and Boothroyd (2000) to record the EACC in Nucleus CI recipients. Results from nine subjects were reported, and instead of using a speech stimulus presented in the sound field, long-duration, biphasic pulse trains were used as stimuli, and output of the CI was controlled directly rather than through the speech processor. The EACC was recorded in response to a change in the stimulating electrode. EACC amplitude was shown to be affected by the magnitude of the change in the stimulating electrode used. As the distance between the two stimulating electrodes increased, EACC amplitudes also increased. One issue that arose in the Brown et al. (2008) study was the degree to which the response to a change in stimulating electrode might be affected by a concurrent change in the overall level of stimulation.

In this article, we extend the work of Brown et al. (2008) by investigating the response to changes in the level of stimulation on one electrode. We report the result of two separate but related studies. The goal of the first study was to evaluate the effect that changes in stimulus level had on the magnitude of the electrically evoked auditory change complex (EACC). Our hypothesis was that the greater the magnitude of the change in stimulus level (either as an increment or as a decrement), the larger the amplitude of the EACC would be. In this study, the stimulus was always initially presented at 50% of the subject's dynamic range (DR), and the stimulation level was varied systematically during the second half of the pulse train.

In study 2, we attempt to relate the response recorded to a change in stimulation level to the slope of the onset response growth function. We hypothesize that the slope of the onset response input-output function is a reflection of the number of neurons stimulated for each increment in stimulation level. For instance, the rate of growth of the N1-P2 response may be more rapid for individuals with good neural survival than for individuals with more restricted neural survival. If that is the case, it would follow that a fixed increase in stimulation level that results in a large change in the amplitude of the onset response and would also elicit a large-amplitude

EACC response. In study 2, we test the hypothesis that the rate of growth of the onset response is related to the amplitude of the EACC response.

METHODS

Subjects

Electrically evoked cortical auditory potentials were recorded from 12 CI users; 10 participated in study 1 and seven participated in study 2. All were postlingually deafened adults who received a Nucleus CI24 CI at the University of Iowa hospitals and clinics between 1996 and 2003. Participants are identified in the tables and figures using a subject numbers determined by the order in which they were implanted at the University of Iowa. Each subject number begins with either an R or an M, indicating that they were implanted with the Contour (R) or straight banded (M) electrode array. Some of the subjects who participated in our studies were bilateral CI users. The R or L after the subject number indicates the implanted ear that was tested. Table 1 shows general demographic data for each study participant. All had used their CIs for a minimum of 3 months before participating in these studies. None of the study participants had a history of neurological disorders. Before testing, informed consent was obtained from all individuals.

General Procedure

A typical experimental session lasted approximately 3 hrs. Study participants were seated in a reclining chair and asked to remain awake and watch captioned videos during the recording session. Breaks were given as needed throughout the recording period. Before any electrophysiological measurements were made, detection thresholds and maximum comfort levels were obtained for the stimuli used for electrophysiologic testing.

Stimuli

All of the stimuli used for these studies were created using NIC programming routines. This software allowed us to bypass the speech processor and to control the stimulation provided by the implant directly. The stimuli were 800 msec bursts of biphasic pulses. Individual biphasic current pulses were presented at a rate of 1000 pps in a monopolar stimulation mode (MP1). Each phase of the biphasic current pulse was 25 μ sec in duration, and each biphasic pulse included an interphase gap of 8 μ sec. The interval between each 800 msec stimulus burst was 2200 msec, resulting in an overall stimulation rate of 0.3 Hz. Depending on the stimulus level, a single N1-P2 response that we refer to as the onset response was typically recorded within first 250 msec after the onset of the stimulus pulse train. To record the EACC, a change in current level was introduced 400 msec after the onset of the 800 msec pulse train. Electrode 10 was used as the stimulating electrode for all subjects except one (R22), who had short circuit between electrodes 10 and 11. For this subject (R22), the study was completed with stimulation on electrode 12.

With the Nucleus CI, stimulation level is specified as a number that ranges from 1 to 255. These current levels are used to program the speech processor of the CI. In these studies, T level (detection threshold) and C level (maximum comfort level) were measured on the experimental electrode for each subject using Nucleus Custom Sound program (version 1.3). The difference in programming units between T and C levels was defined as the DR. Initially, repeated ascending trials were used to establish C level. C level was defined for the subjects as the level where the stimulus was “loud but not uncomfortable.” The first ascending trial was performed using a step size of five current level units (CL). After the first ascending trial, step size was decreased to 2 CL and the process repeated until the same stimulation level was identified as being the C level on at least two of three trials. T level was also obtained using an ascending adaptive procedure. Stimulation was initiated at a subthreshold level and increased in steps of

5 CL. After the first positive response, the current level was then decreased by 10 CL, and ascending steps of 2 CL were used to determine threshold on at least two of three trials. Because the threshold as well as the size of the DR can vary significantly across subjects and to a lesser extent across electrodes within a subject, we elected to report stimulation levels relative to the subject's perceptual DR. This approach allowed us to compare across subjects more easily. Once the T and C levels were calculated, we computed the current levels for each subject that should correspond to 0% (T level), 25%, 50%, 75%, and 100% (C level) of the DR.

In study 1, the goal was to explore the effect of a change in stimulus level on the EACC. Because we were interested in measuring the response to both an increase and a decrease in stimulation level, the pulse train was initially presented at 50% of the subject's DR, and that level was held constant for the first 400 msec of the 800 msec stimulus burst. The stimulation level used during the second half of the stimulation period was systematically varied from as low as 0% of the DR (i.e., stimulation was decreased to T level) to 100% of the DR (i.e., stimulation was increased to C level). A control condition was also included in which no change in the stimulation level occurred during the 800-msec pulse train. The set of stimuli used in study 1 is illustrated schematically in the left panel of Figure 1. Also shown is the label we applied to each stimulus condition to describe the magnitude of the change in stimulation level from -50% to +50%. It should be noted that during data collection, the order in which these changes in stimuli were presented was randomized across subject participants.

In study 2, the goal was to assess the relationship between onset responses and the EACC. We hypothesized that because both the onset response and the EACC represent sensitivity to a change in neural activity, the slope of the onset response growth function should be related to the amplitude of the EACC. To test this hypothesis, we recorded onset response growth functions using an 800 msec burst of biphasic current pulses. The 800 msec burst was divided into two sections. The first 400 msec of the burst included biphasic current pulses presented at stimulation levels that corresponded to 25%, 50%, 75%, and 100% of the DR. The second 400 msec of the pulse train included biphasic current pulses presented at a stimulation level that corresponded to T level (0% of the DR). We opted to use a pulse train that was 800 msec (rather than 400 msec) in duration to record these onset responses to ensure that both the onset response and EACC responses were recorded using the same overall presentation rate. These stimuli are illustrated schematically in the center panel of Figure 1. We recorded the N1-P2 onset response and measured the amplitude to construct a growth function. Although offset responses were sometimes noted, they have not been included in the data presented in this study.

In the second half of this study, EACC responses were recorded in response to a 25% increment in stimulation level. To do this, an 800 msec burst of biphasic current pulses was presented. The pulses in the first half of the pulse train were fixed at level equal to 25%, 50%, or 75% of the listener's DR. At 400 msec after stimulus onset, the pulse amplitudes were increased by 25% and held constant at that higher presentation level for the second half of the 800 msec interval. That is, we measured an EACC response using stimulation levels that changed from 25 to 50%, 50 to 75%, and 75 to 100% of the DR. These stimuli are illustrated schematically in the right panel of Figure 1. In this case, the response we were interested in recording was the EACC. Although onset responses were recorded, they were not used. To compare the rate of growth of the onset response with the EACC, the effect of a 25% increase in stimulation level on the onset response was calculated and compared with the EACC amplitudes generated using a similar increment in stimulation level.

Electrophysiology

Three disposable, sterile Ag-AgCl surface recording electrodes were placed on the vertex (Cz), the forehead, and the mastoid process contralateral to the CI. Two additional electrodes were

positioned above and below the eye contralateral to the CI. The N1-P2 onset response and the EACC were recorded differentially between Cz (+) and the mastoid contralateral to the implant (-). The recording electrodes located above and below the eye were used to monitor and reject recordings that obtained muscle artifact that resulted from eye blinks. An electrode positioned on the forehead was used as ground for both recording channels.

Electrode impedance was maintained below 5000 ohms. Artifact rejection was used to minimize contamination of the EEG recordings by muscle artifact and was adjusted for each subject to ensure the recordings containing eye blinks were rejected.

Neural responses were amplified with a gain of 10,000 and sampled at 100,000 Hz. Stimulus artifact was minimized through the use of both analog and digital filtering between 1.0 Hz (high pass, 12 dB/octave) and 100 Hz (low pass, 12 dB/octave).

Four to six recordings of 50 sweeps (total, 200 to 300 sweeps) were obtained for each stimulus condition with a time window of 1000 msec. This included a prestimulus period of 200 msec and an 800 msec window during stimulation. The order of presentation of each condition was randomized across the session for each subject to avoid order effects.

Analysis Procedure

The evoked potentials recorded in this study were analyzed off-line using custom-designed (MATLAB, V.6.1) software. This software allowed replications recorded using the same stimulation parameters to be averaged together and smoothed using a 40 msec wide boxcar filter before analysis. The software also automatically picked the N1 and P2 peaks. N1 was defined as the most negative point within a latency interval ranging from 80 to 200 msec for the onset response and from 480 to 600 msec for the change potential. For both the onset and change potentials, the P2 peak was defined as the most positive voltage recorded within a time window of 120 msec duration after N1. The points identified by the software as N1 and P2 were evaluated and, in a few instances when the recordings were somewhat noisy, adjusted by the author based on visual inspection of the waveforms. This was, however, rarely necessary. Peak-to-peak amplitude of both the onset and change potentials was then determined by calculating the voltage difference between the N1 trough and the following P2 peak. We did not use baseline correction.

RESULTS

Study 1: Effects of Magnitude of Change in Stimulus Level on EACC Amplitude

The goal of the first study was to test the hypothesis that the amplitude of the EACC will be proportional to the magnitude of change in stimulation level that is introduced. That is, we would predict that EACC amplitudes should increase as the magnitude of the change in stimulus level is increased. Figure 2 provides a more detailed illustration of the stimulation paradigm that was used and shows waveforms recorded from one study participant (M66). The schematic diagrams in the left column of Figure 2 show both the control and the experimental conditions. The stimulus was an 800 msec burst of a 1000 pps biphasic pulse train that was initially presented at 50% of the subject's perceptual DR. In the control condition (top), there was no change in stimulus level. In the experimental condition (bottom), a change in stimulus level was introduced 400 msec after the onset of the pulse train. The right column of Figure 2 shows the recordings that were obtained from a single subject (M66). These averaged waveforms are the result of 200 stimulus presentations (or sweeps) and were recorded using a time window of 1000 msec including a prestimulus period of 200 msec. The waveform shown in the upper portion of the figure was elicited in response to the control stimulus and consists only of an onset N1-P2 response. The waveform shown in the lower portion of this figure was

recorded using a stimulus pulse train that increased in level from 50% of the DR to 100% of the DR at 600 msec. The thick dashed line indicates the time at which the stimulus level was changed. In the experimental condition, an N1-P2 response was elicited both at the onset of the burst as well as after the change in stimulus level. Both responses consist of a series of peaks we have labeled N1 and P2. In this report, to avoid confusion between the two evoked potentials, we will refer to the first N1-P2 response as the onset response and the second N1-P2 response as the EACC.

The subject (M66) whose data are shown in Figure 2 has particularly clear and large amplitude responses. Figure 3 shows the individual waveforms and group mean average waveforms recorded in response to a change in level from 50% of the DR to 100% of the DR for the 10 subjects who participated in study 1. The small triangles indicate the N1 peak of both the onset and the change responses. N1 latencies, P2 latencies, and the N1-P2 amplitudes measured for both the onset and the EACC responses for each subject are listed in Table 2. Latencies of the N1 and P2 peaks of the EACC are listed relative to the time the change was introduced. The mean latencies of N1 and P2 are 138.3 and 231.9 msec for the onset response and 111.1 and 196.7 msec for the EACC, respectively. Generally, the onset responses have longer latencies than the EACC. The mean amplitude of N1-P2 responses recorded at the onset of the stimulus burst was 3.67 μ V, whereas the mean peak-to-peak amplitude of the N1-P2 responses recorded in response to the change in stimulation level (the EACC) was 5.29 μ V. The latency and amplitude differences between the onset and EACC responses may reflect the different stimulus levels used (Firszt et al. 2002a). The stimulus is initially presented at only 50% of the DR and then increased to 100% of the DR. As a result, onset responses are smaller and have longer latencies than EACC responses. Some subjects show robust potentials (i.e., M66), whereas for others the onset response morphology is not as clear (i.e., R2, R46). EACC responses are recorded from all 10 subjects. We note further that because the thresholds for R2 and R46 are particularly low (see Table 2) the initial stimulation level is low (50% of the DR) in both of those subjects. The onset responses and the EACC responses show considerable variability across subjects. For a given subject, however, the EACC response has a gross morphology that is similar to the respective onset response.

Figure 4 shows the EACCs recorded from a single CI user (M66). In every case, the first 400 msec of the 800 msec burst was presented at 50% of the subject's DR. The change in stimulus level was then varied systematically in the second 400 msec of the stimulus interval, to levels ranging between 0% and 100% of the DR. These stimulation conditions are illustrated in the left panel of Figure 1. The change in stimulus level (in percent DR) is indicated in the column on the right side of Figure 4. In this figure, a change of + 50% indicates that the stimulation level was increased from 50% of the DR initially to C level or 100% of the DR. The 0% change condition is the control condition. This recording was obtained using a biphasic pulse train that was held constant at 50% of the subject's DR for the full 800 msec stimulation interval. A -50% change indicates that the stimulation level was decreased from the 50% DR point to threshold. For this subject, change potentials are evident in response to all increases in stimulation level and to decrements in stimulation level larger than 10% of the DR. The N1 peaks of the EACC are indicated with triangles. More robust EACC responses are recorded in response to increments in stimulation level than in response to decrements in stimulus level. The onset responses recorded using a stimulus level of 50% of the DR were clearly identified but tended to decrease in amplitude when the second half of the stimulus included an increase rather than a decrease in stimulus level. Even though a relatively slow stimulation rate was used, this change is suggestive of long-term or cumulative adaptation or potentially an effect of backward masking.

Figure 5 summarizes the effect that the magnitude of the stimulus change had on the N1-P2 amplitude of the EACC for the 10 subjects who participated in this study. The upper graph

shows EACC amplitudes plotted as a function of the stimulus intensity change (in percent DR) used to elicit the response. In each case, the stimulus began at a level equal to 50% of the subjects' DR. Increases in stimulus level above 50% of the DR are indicated with positive numbers, and decreases in stimulus level below 50% of the DR decrease are indicated with negative numbers. Although significant cross-subject variation in EACC amplitude is evident, all subjects had measurable responses to increases in stimulus level. Note that for some individuals, data points overlaid each other in this figure. Some subjects (4 of 10) showed little or no response after a decrease in stimulus level.

The lower panel of Figure 5 shows the mean amplitude of the EACC (± 1 SE) plotted as a function of the percent change in stimulus level used to elicit the response. As evident from the individual data, increases in stimulus level seem to elicit more robust EACC responses than decreases. The significance of these changes was evaluated using a one-factor ANOVA. Results indicated that there was a significant difference in mean EACC amplitude as a function of the percent change in DR ($F = 12.24, p < 0.0001$). Post hoc testing revealed that EACC amplitudes recorded using a 25 or 50% increase in stimulation level were significantly larger than those obtained the control conditions (0% change). Decrements in stimulation level showed a trend toward larger response amplitudes for the greater magnitude changes, but these differences were not statistically significant at the $p < 0.05$ level.

Study 2: Relationship Between Growth of the Onset Response with Increases in Stimulation Level and the EACC Amplitude

This study investigated the relationship between EACC amplitude and growth of the onset response with increases in stimulus level. We hypothesized that if a subject had a relatively steep onset response growth function compared with other subjects, a small change in stimulus level might elicit a large EACC. The purpose of this second study was to determine the extent to which EACC amplitude is related to the slope of the growth function of the onset response.

Figure 6 shows data from two (M52R, R46) of the seven subjects who participated in this study. The left graph shows how increases in stimulation level affected the peak-to-peak amplitude of the N1-P2 response recorded at the onset of the stimulus burst. For both subjects, the stimulus level was increased from 25 to 100% of their DR in increments of 25%. The right graph shows amplitude of the EACC elicited using a 25% increase in stimulus level. In this case, instead of keeping the initial stimulation level constant and varying the size of the level change used to evoke the EACC, a 25% increase in stimulation level was consistently used while the initial stimulation level varied from 25% to 75% of the DR (see Fig. 1). Thus, the magnitude of the change in stimulus level used to generate the EACC responses corresponds to the stimulus level intervals used to measure the individual onset responses. Consistent with our hypothesis, subject M52R, who has a steeper growth function than subject R46, also has larger EACC amplitudes. Additionally, the largest EACC amplitude measured for this subject (M52R) corresponded to the portion of the growth function that was steepest (50 to 75%). Subject R46 has smaller but more consistent changes in onset response amplitude with increases in stimulation level than subject M52R. Note that the EACC amplitudes recorded from subject R46 using a 25% increase in stimulation level also showed little change in amplitude with level.

Finally, Figure 7 summarizes data from all seven subjects and illustrates the relationship between slope of the onset response input output function and magnitude of the EACC response that is recorded. Rather than fitting the entire growth function with a single curve, we calculated the change in response amplitude measured for each of the adjacent points on the growth function. Three datum points are shown on the scatter plot for each of the seven study participants. Each point represents the change in amplitude of the onset response measured at one of three different stimulation levels (25 to 50%, 50 to 75%, and 75 to 100%) compared

with the corresponding EACC amplitude recorded using the same stimulus condition (see Fig. 1).

If our hypothesis relative to study 2 is correct, EACC amplitude should be correlated with the amount of change in onset response amplitude observed for each 25% change in the level of the stimulus. The solid line in Figure 7 represents the results of a linear regression analysis. The correlation between the rate of growth of the onset response with increasing stimulation level and the amplitude of the associated EACC response was found to be statistically significant ($r = 0.6105$, $p < 0.01$) and supports our hypothesis that the two measures are, in fact, related.

We further note that three points from two subjects (M56 and M11) show a negative difference between the amplitudes of the onset responses, indicating a decrease in response amplitude with increasing stimulus level. Although these may correspond to a real reduction in response, the small negative slopes may be the result of variability in response amplitude. That is, the growth of response may be small or even saturated. In each of these cases, the EACC response amplitude is relatively small.

DISCUSSION

The major finding in this study was that the EACC could be recorded from CI users in response to changes in stimulation level. These results are generally consistent with similar results reported previously for acoustic stimulation by Martin and Boothroyd (2000).

Previous research measuring the EACC in CI users has used speech or speech-like stimuli (Friesen & Tremblay 2006; Martin 2007). In our laboratory, we have used direct control of the implant to focus on the response to changing one aspect of the stimulus (Brown et al. 2008). Although such stimuli may not tap into exactly the same mechanisms used to process speech, they have the benefit of easy interpretation of response to change by separating onset and change potentials and allow the exploration of the salience of specific stimulus characteristics. Brown et al. 2008 described a technique to measure the response to changes in stimulating electrode position. They showed that the amplitude of the EACC varied with distance between stimulating electrodes. They suggested that this effect was due to nonoverlapping neural populations activated by the two electrodes and consequently could be a measure of the spatial spread of activity. An important issue in interpreting those results, however, was the extent to which relative sensitivity of each electrode might affect the EACC. As a result, this study attempted to evaluate the extent to which changes in stimulus level affected EACC amplitude for a fixed electrode.

The primary findings were that the amplitude of the EACC is dependent on the magnitude of the stimulus level change. Responses were evident to both an increase and a decrease in stimulus level for most subjects, although an increase in stimulus level generally elicited larger-amplitude response than those elicited by a decrease in stimulus level.

Our results also show significant variations in the EACC amplitude across individuals (see Fig. 5). Such variations are promising in that EACC could reflect individual variations in sensitivity to stimulus change. Recently, Harris et al. (2007) reported that ACC thresholds of response were higher for older subjects than younger subjects specifically for low-frequency stimuli. This is consistent with results for behaviorally measured intensity discrimination just noticeable differences as reported by He et al. (1998). In a future study, electrophysiological measures of level discrimination using the EACC could be compared with psychophysical measures in CI users.

A second aim of this study was to compare growth of the onset response with stimulus level to variations in the EACC to changes in stimulus level. Studies with both acoustic and electric stimulation have shown that peak-to-peak amplitude of N1-P2 responses recorded at the onset of a stimulus generally increases with stimulus level (Firszt et al. 2002a; Hyde 1997; Näätänen & Picton 1987; Picton et al. 1974). Our hypothesis was that if the growth of the N1-P2 onset response was steep for a certain electrode, then one would expect a correspondingly larger EACC response to changes in stimulation level. The data presented in Figure 7 are generally consistent with this hypothesis, although the inherent variability may be an indication that the EACC in response to a change in level is not strictly dependent on the growth of response.

The responses to changes in stimulus level (the EACC responses) that are reported here have morphologic characteristics that are similar to the N1-P2 response recorded at the onset of the stimulus burst. These responses to a change in stimulation level are also similar to EACC responses recorded in our laboratory that were evoked in response to a change in place of stimulation within the cochlea (Brown et al. 2008). These results are generally consistent with an interpretation of the EACC as a response to an increment of neural activity. If this interpretation is correct, the EACC evoked in response to an increase in the stimulus current level is essentially an N1-P2 onset response of a newly activated group of auditory neurons that respond to the stimulus in the second interval. Work by Ross et al. (2007) examining physiological responses to interaural phase differences is consistent with this interpretation in that they suggested that a common neural population likely contributes both to the onset response and to the response evoked by the introduction of a change in interaural phase. In contrast, the EACC evoked in response to a decrement in stimulus level would be considered to be an offset response from previously excited neural populations. Such offset responses have been reported previously both for acoustic and electrical stimuli (Hillyard & Picton 1978; Martin & Boothroyd 2000).

The results of study 2, specifically the significant positive correlation shown in Figure 7, also support this interpretation. The slope of the onset response growth function reflects (at least in part) the increase in the size of the active neural population. A steep slope suggests a larger increase, whereas a shallow slope may indicate that fewer neurons are available to be recruited with each increase in stimulus level. If that assumption is correct, it would follow that the amplitude of the EACC obtained in response to a specific change in stimulation level should be related to the slope of the onset response growth function. Small EACC amplitudes would be expected when changes in stimulation level result in little change in onset response amplitude (e.g., at a point where the onset response growth function is saturated). Larger EACC amplitudes would be expected for changes in stimulation level that elicit a large change in onset response amplitude. Similarly, if the rate of growth of the onset response is different on two different stimulating electrodes, one would expect that EACC amplitudes will be larger when the electrode with the steeper growth function is stimulated.

One practical implication of these results is when evaluating changes in response to one stimulus parameter, such as stimulating electrode position, one must also take into account changes in other stimulus parameters, such as level. Responses to changes in overall level are not clearly distinguishable from changes in place of stimulation on the basis of response properties. As a result, effects of stimulus level must be taken into account. The results from the second aim, however, suggest that growth functions may be an indication of the relative sensitivity of the response, so that growth functions may serve as a way to normalize the stimulus levels across electrodes.

CONCLUSION

This work describes the effect that changes in stimulus level have on the EACC response for a group of Nucleus CI users. For each listener, a single electrode was stimulated and EACC responses were recorded to both increments and decrements in stimulus level. The amplitude of the EACC was found to be dependent on the magnitude of the stimulus change. To the extent that this response reflects processing of stimulus change, it could potentially be a valuable tool for assessing neural processing in response to electrical stimulation. In addition, EACC amplitudes were also correlated with slope of the N1-P2 onset response. Subjects with steeper N1-P2 growth functions tended to have more robust EACC responses. Further studies are required to determine the impact of variation in other parameters on the EACC response and the relationship between the EACC and psychophysical measures in CI recipients.

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Fig. 1.

Schematic illustration of the stimuli used in studies 1 and 2. Each stimulus consisted of an 800 msec burst of biphasic current pulses presented at a rate of 1000 pps. The current level used for the first 400 msec of the burst can be different than the current level used in the second 400 msec interval. In each case, levels are indicated as percent of the behavioral dynamic range. The left column shows stimulus conditions used in study 1. The center and right columns show the stimulus conditions used for study 2.

Fig. 2.

The stimulation paradigm used in both the control (upper panel) and experimental (lower panel) conditions is shown schematically on the left. The waveforms on the right were recorded from a single subject (M66) in both the control (upper panel) and experimental conditions (lower panel). These recordings were obtained using a time window of 1000 msec, which included a prestimulus period of 200 msec. The thin dashed line represents the onset of the stimulus, and the thick dashed line indicates the time at which the stimulus level was changed.

Fig. 3.
The individual waveforms and group mean average waveform recorded in response to a change in level from 50% of the DR to 100% of the DR for the ten participants. Triangles indicate the N1 peaks for the onset and the EACC.

Fig. 4.

A series of waveforms recorded from a single cochlear implant recipient (M66) are shown. In each case, the stimulus was initially presented at 50% of the subject's DR. The current level used for the second 400 msec portion of the stimulation interval varied, and the percent increment or decrement in level is indicated. Dashed vertical, lines indicate onset of the stimulus and onset of stimulus level change. The small triangle indicates the point in the waveform that was identified as N1.

Fig. 5.

The individual and group mean amplitude of the EACC recorded to date from the 10 subjects. The amplitudes of the individual EACC responses are shown as a function of a change of stimulus level, ranging from 0 to 100% of the DR in upper panel. Increases in stimulus level above 50% of the DR are indicated with positive numbers, and decreases in stimulus level below 50% of the DR are indicated with negative numbers. The lower panel shows the mean EACC amplitude ($\pm$ 1 SE) plotted as a function of the percent change in stimulus level used to elicit the response.

Fig. 6.

The left panel shows how increasing the stimulus level from 25% to 100% affected the amplitude of the N1-P2 response evoked at the onset of the stimulus burst for two subjects (M52R, R46). The right panel shows amplitude of the EACC recorded from the same individuals in response to level changes for 25% to 50%, 50% to 75%, and 75% to 100% of the DR.

Fig. 7.

The relationship between EACC amplitude and slope of the N1-P2 onset response growth is shown for the seven subjects who participated in Study 2. Three datum points are plotted for each subject. Each point represents the change in amplitude of the onset response as measured between adjacent points on the growth function. These slope measures are plotted relative to the EACC amplitude obtained in response to a similar change in stimulation level. The solid line represents the results of linear regression analysis.

General demographic information on 12 study participants, including gender, age at time of testing, etiology of hearing loss (when known), ear implanted, type of implant, speech processing strategy and rate used in the subject's daily MAP, duration of deafness before cochlear implantation, and duration of CI use at the time of testing

TABLE 1

Subject	Gender	Age (yr)	Etiology	Ear implanted	Type of implant	Strategy and rate	Duration of deafness (yr)	Duration of CI use (yr)
M66	M	54	Unknown	R	CI24M	CIS 2400	2	7
M52R	F	68	Virus/fever	R	CI24M	ACE 720	0.25	8
M54L	F	60	Unknown	L	CI24M	ACE 1200	7	8
M20	M	55	Unknown	R	CI24M	ACE 1800	35	9
M56	F	83	Unknown	R	CI24M	ACE 1200	10	8
M11	F	80	Familial, progressive	L	CI24M	ACE 720	50	10
M4	M	68	Noise	L	CI24M	ACE 720	12	10
R46	M	81	Unknown	R	CI24R	ACE 900	1	4
R36R	M	51	Unknown	R	CI24R	ACE 900	28	5
R55	F	77	Unknown	R	CI24R	ACE 900	1	4
R2	F	38	Enlarged vestibular aqueduct	R	CI24R	SPEAK 250	0.1	7
R22	M	75	Familial, progressive	R	CI24R	ACE 900	0.2	5

TABLE 2

T and C levels and dynamic range obtained for stimuli are listed

	T-Level (CL)	C-Level (CL)	DR (CL)	Onset response (50% DR)			EACC (change to 100% DR)		
				N1 Latency (msec)	P2 Latency (msec)	N1-P2 Amplitude (μV)	N1 Latency (msec)	P2 Latency (msec)	N1-P2 Amplitude (μV)
M66	191	222	31	94	169	7.04	95	168	7.96
M52R	144	222	78	130	284	5.53	104	220	9.09
R46	112	184	72	183	302	2.26	141	223	2.88
M54L	146	210	64	156	240	2.43	104	187	6.12
R36R	136	214	78	129	198	2.23	109	197	5.15
M20	176	228	52	123	218	4.40	100	173	3.46
R55	116	190	74	128	230	3.86	104	217	7.07
M56	160	196	36	140	217	3.51	109	200	3.68
M11	160	228	68	122	214	3.47	90	145	3.78
R2	114	160	46	178	247	2.02	155	237	3.72
Mean				138.3	231.9	3.68	111.1	196.7	5.29
SE				8.57	12.37	0.51	6.51	9.09	0.68

T and C levels as well as dynamic range values for stimuli used in this study are listed. Also listed are the N1 and P2 latencies as well as the N1-P2 amplitude for both the onset and the EACC responses shown in Figure 2.