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Effects of Stimulation Level and Electrode Pairing on The Binaural Interaction Component of The Electrically Evoked Auditory Brain Stem Response

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Abstract

Objectives—The purpose of this study was to investigate the effects of stimulation level and electrode pairing on the binaural interaction component (BIC) of the electrically evoked auditory brain stem response (EABR) in Nucleus cochlear implant users.

Design—Ten postlingually deafened adult cochlear implant users participated in this study. EABRs were measured using loudness balanced, biphasic current pulses presented in the left monaural, right monaural and bilateral stimulation conditions. BICs were computed based on measures of the EABR obtained for each subject by pairing the electrode 12 (out of 22 intracochlear electrodes) in the right ear with each of 11 electrodes spaced across the electrode array in the left ear. The effect of stimulation level on the amplitude of the BIC was investigated by measuring growth functions of the BIC from six subjects. The effect of electrode pairing on the amplitude of the BIC was studied at high stimulation levels in ten subjects and at low stimulation levels in seven subjects. The high stimulation level was chosen as the 90% point of the subject's dynamic range (DR) or the highest stimulation level where the electrophysiological recordings were not contaminated by muscle artifacts. The low stimulation level was chosen as a level that was 10% point of subject's DR higher than the BIC threshold for six of these seven subjects. For one subject, BIC thresholds were not available and the low stimulation level was referred to the 70% point of her DR.

Results—BICs were successfully recorded from all 11 interaural electrode pairs for a majority of subjects tested at both stimulation levels. BIC amplitudes increased with stimulation level. The effect of stimulation level on latencies of the BIC was less robust. At high stimulation levels, BIC amplitudes did not change significantly as the stimulating electrode used in the left ear was systematically varied. When low stimulation levels were used, BIC amplitude was maximal for

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interaural electrode pairs with similar intracochlear positions and decreased when the offset between interaural electrodes increased.

Conclusions—This study demonstrates that stimulation level affects amplitudes of the BIC response. It is possible to record the BIC of the EABR in bilateral CI users even from interaural electrode pairs that have large interaural offsets. This finding suggests that when high-level stimuli are used, there is a broad pattern of current spread within the two cochleae. At lower stimulation levels the spread of excitation within the cochlea is reduced making the effect of electrode pairing on the amplitude of the BIC more pronounced.

Keywords

auditory evoked potential; bilateral cochlear implantation; auditory brain stem response; electrical stimulation

INTRODUCTION

The advantage of binaural hearing over monaural hearing includes more accurate sound localization abilities (e.g. Hawley et al., 1999) and improved speech intelligibility in noise when the noise and speech sources are spatially separated (Festen and Plomp, 1986; Dillon, 2001; Cox et al., 1981; Peissig and Kollmeier, 1997; Beutelmann and Brand, 2006). Recently many individuals with severe to profound hearing losses have undergone bilateral cochlear implantation in the hope of restoring some of these binaural advantages.

Several investigators have explored the potential benefits of bilateral cochlear implants (CI) (van Hoesel and Clark, 1999; Gantz et al., 2002; Müller et al., 2002; Tyler et al., 2002a, b; van Hoesel et al., 2002; van Hoesel and Tyler, 2003; Litovsky et al., 2006; Ricketts et al., 2006; Wackym et al., 2007, Buss et al., 2008; Eapen et al., 2009). These studies have shown that some bilaterally implanted subjects obtain higher scores on speech reception/recognition tasks in conditions of spatially separated speech and noise using both implants relative to using either implant alone. Bilateral CI users, in general, also show improved sound localization/lateralization performance relative to unilateral CI users (van Hoesel and Clark, 1999; Gantz et al., 2002; Müller et al., 2002; Tyler et al., 2002a, b; van Hoesel et al., 2002; van Hoesel and Tyler 2003; Verschuur et al., 2005; Litovsky et al., 2006). While results of these studies are encouraging, the amount of binaural advantage achieved by bilateral CI users is typically less than that of normal-hearing listeners.

Early studies using listeners with normal hearing showed that matching the cochlear place of stimulation across the two ears was necessary in order to maximize binaural sensitivity (Henning, 1974; Nuetzel and Hafter, 1981). More recently, results of simulation studies have shown that mismatches between the frequency-to-electrode map in the two ears can have a negative effect on speech reception (Siciliano et al., 2006; Faulkner et al., 2005). In clinical practice, however, it is typical to use the same frequency-to-electrode map for both CIs despite possible differences in electrode insertion depth and/or differences in the pattern of neural survival in the two ears. Results of these simulation studies suggest that this practice may not always result in optimal performance. Interaural electrode pairing may be

an important factor to consider in the programming process. What is unclear, however, is the best method by which to match the electrodes between the two ears.

Several different approaches have been used to define the best-matched interaural electrode pairs for bilateral CI users. Some investigators have used CT scans in order to match electrodes based on insertion depth (Marsh et al., 1993; Skinner et al., 1994, 2003; Cohen et al., 1996; Ketten et al., 1998; Xu et al., 2000). However, a CT scan does not allow quantification of other potentially important factors like the pattern of nerve survival or the current spread within the cochlea.

Other investigators have used interaural pitch comparisons to aid in interaural electrode pairing (van Hoesel, 2004, 2007; van Hoesel and Tyler, 2003; van Hoesel and Clark, 1997; Lawson et al., 2001; Long et al., 2003). Results of these studies showed that this technique does not guarantee identification of electrode pairs with optimal interaural time difference (ITD) sensitivity. Furthermore, pitch comparison can be a challenging task even for postlingually deafened adult CI recipients and measuring pitch perception in prelingually deafened children can be impossible.

Electrophysiological methods for optimizing electrode pairing have also been explored. The binaural interaction component (BIC) of the electrically evoked brainstem response (EABR) has been recorded in adult (Pelizzone et al., 1990; Firszt et al., 2005) as well as pediatric bilateral CI users (Gordon et al., 2007). The BIC was derived in these studies by subtracting the bilaterally evoked EABR from the sum of the monaurally evoked EABR. Results showed that the electrically evoked BIC response consists of a small negative peak occurring approximately 3.6 ms after stimulus onset followed by a positive peak with a latency of approximately 4.4 ms. The peak to peak amplitude that is measured as the difference in amplitudes between the positive peak and the preceding trough is approximately 1.1 μV . Pelizzone and his colleagues hypothesized that the amplitude of the BIC should be greatest when the two implants stimulate auditory nerve fibers from comparable regions in the two cochleae. They proposed that the BIC could provide a valuable tool for positioning a cochlear implant in each ear for optimal binaural advantage. Smith and Delgutte (2007) investigated the effect of interaural electrode offset on the amplitude of the BIC of the EABR in cats. They also measured multiunit neural responses along the tonotopic axis of the inferior colliculus (IC) in order to identify the specific neural populations excited by individual stimulating electrodes. They showed that the amplitude of the BIC was maximal for the interaural electrode pair that resulted in maximal overlap between the populations of neurons at the IC stimulated by each ear individually. Results of this study also showed that the amplitude of the BIC was largest when the interaural level difference (ILD) was zero and decreased as the ILD increased. These results suggest that the BIC of the EABR could potentially serve as a tool to determine the best matched interaural electrode pairs for bilateral CI users. However, this hypothesis has not been thoroughly tested in human subjects. In addition, no previous study has systematically explored the effect of stimulation level on the BIC of the EABR. Stimulation level is known to affect the amount of spatial spread of neural excitation within the cochlea (Chatterjee and Shannon, 1998; Cohen, 2003; Abbas et al., 2004; Chatterjee et al., 2006; Hughes and Stille, 2008), which could potentially influence the effect of electrode pairing on the BIC amplitude.

The purpose of the current study is to investigate how stimulation level and electrode pairing affect the BIC of the EABR in a group of bilateral CI users. The first hypothesis is that increasing the stimulation level will result in larger BIC amplitudes and shorter latencies. The second hypothesis is that the BIC amplitude will be maximal for interaural electrode pairs with similar intracochlear positions and decrease as the separation between the two stimulating electrodes increases. Finally, we hypothesize that there will be an interaction between the effect of stimulation level and electrode pairing on BIC amplitude. Decreasing the stimulation level will make the effect of electrode pairing on BIC amplitudes more pronounced.

METHODS

Overview

Each of ten subjects participated in two psychophysical test procedures: loudness estimation and loudness balancing. Initially, loudness estimates were obtained in order to define the subject's dynamic range (DR). Next, a psychophysical loudness balancing procedure was performed for each interaural electrode pair. The stimulation levels judged by the subjects to be equally loud were used to record the EABR. For each subject, psychophysical measures of interaural pitch comparison were obtained using all 11 of interaural electrode pairs. A pair of pulse trains were presented, consisting of stimulation on electrode 12 in the right ear and one of the 11 electrodes in the left ear, with stimulation parameters described below. Each subject was then asked to indicate which stimulus was higher in pitch. In order to eliminate the possibility that subjects could use level cues, stimulus level was randomly varied among three levels within the upper portion of each subject's DR. Psychometric functions were obtained and were used to estimate chance-level performance -- the point for which the stimulus presented to the left ear was judged to be higher in pitch than the stimulus in the right ear 50% of the time. The electrode pair closest to this 50% point was defined as the "pitch matched" electrode pair. These results will be reported in a future manuscript. For a subgroup of six subjects, the loudness balancing procedure was repeated for the pitch matched electrode pair at several levels within the subjects' DR.

EABRs were recorded from a set of surface electrodes. The subjects were asked to relax or sleep while their EABRs were measured in response to both monaural and bilateral stimulation. Electrically evoked BICs were then computed offline for all interaural electrode pairs tested. The effect of stimulation level on the BIC was investigated for the "pitch matched" electrode pair in six subjects. The effect of interaural electrode pairing was investigated at a relatively high stimulation level for ten subjects and at a lower stimulation level for a subgroup of seven subjects. Details of the stimulation parameters are described below.

Subjects

Ten adult CI users (three male, seven female) with postlingual onset of bilateral, severe to profound sensorineural hearing loss participated in this study. The subjects ranged in age from 28 to 84 years, and all had received bilateral Nucleus CIs at the University of Iowa Hospitals and Clinics between 1998 and 2007. Two subjects used the Nucleus 24M CI, four

subjects used the Nucleus 24R Contour CI, and four subjects used the Nucleus 24RE CI. Full electrode insertions were achieved in both ears for all subjects. Nine out of ten subjects received their bilateral CIs in a single surgery. The tenth subject (E10) received her first implant at 46 years of age and the second implant two years later. All subjects had a minimum of six months of experience listening with two CIs before participating in this study and used both CIs on a daily basis. Demographic data for each subject are listed in Table 1. Before their participation in this study, informed consent was obtained in accordance with the University of Iowa Human Subjects Committee requirements.

Stimulation Parameters

Completion of this study required the coordination of the output of two CIs. In order to achieve this goal, two specially modified Nucleus L34 speech processors were used for both the psychophysical and electrophysiological testing (Irwin and He, 2007). Additionally, Nucleus Implant Communication (NIC) routines were used to bypass the speech processor interfaces.

The stimulus was a gated train of biphasic, charge-balanced current pulses presented at a rate of 19.9 pulses per second (pps). Each biphasic current pulse was composed of two phases that were 25 μ s in duration and separated by an 8- μ s interphase gap. For psychophysical testing, 400-ms trains of biphasic current pulses were used. For electrophysiological testing, the electrical pulse train was presented continuously.

In the Nucleus CI, the 22 intracochlear electrodes are numbered from 1 to 22 in a basal to apical direction. In this study, the letters “L” or “R” are used to indicate whether a specific electrode is in the left or right cochlea. For example, R12 refers to the electrode 12 of the right CI. Eleven different interaural electrode pairs were tested. Electrode 12 in the right side implant was always paired with one of 11 different electrodes in the left CI (R12-L6, R12-L8, R12-L9, R12-L10, R12-L11, R12-L12, R12-L13, R12-L14, R12-L15, R12-L16, and R12-L18). All electrodes were stimulated in a monopolar stimulation mode using an extracochlear return electrode (MP1).

Procedures

Psychophysical Test Procedures

Loudness Estimation: Each electrode was stimulated individually and an ascending method of adjustment procedure was used to determine the threshold and the maximum comfortable level for each electrode. The stimulation level was set initially to be inaudible. The subject was instructed to notify the experimenter when they first heard the stimulus. Once threshold was determined, the stimulation level was slowly increased and the subject was asked to indicate the stimulation level judged to be “loud but comfortable”. This procedure was performed three times for electrode R12 and each electrode in the left ear. The average of the three trials was computed and these values were used to define the DR.

Loudness Balancing: Once the subject’s DR was determined, a two interval, 2-alternative forced-choice (2I, 2AFC) paradigm was used to determine specific stimulus levels for each ear that were judged to be equally loud. The stimulus burst was presented to electrode R12

at a fixed stimulation level. The same stimulus was then presented to an electrode in the left CI. The subject was asked to indicate which of the two stimulus bursts was louder. The level of the stimulus in the left ear was varied using an adaptive staircase procedure. In the initial “lead-in” phase of this procedure, the step size was 5 clinical level (CL) units and a one up, one down rule was used to control stimulus level. After two reversals, the step size was changed to 3 CL units and testing continued until another reversal was obtained. Step size was then changed to 2 CL units and a three down, one up decision protocol was adopted. Two consecutive steps in the same direction caused step size to be changed to 1 CL unit, reverting back to 2 CL units when a reversal occurred. The test ended after a total of twelve reversals were obtained. The average of the stimulus levels over the last six reversals was defined as the balanced loudness level. The inclusion of a one down, one up “lead-in” phase has been shown to reduce the number of testing trials without affecting the accuracy of threshold estimation (Baker and Rosen, 2001).

The order in which the two ears were stimulated (i.e., right first or left first) was randomized across the trial. Each sequence started with a dialog box marked “ready” flashed to the monitor screen for 200 ms. The two ears were then stimulated sequentially. Each listening interval was marked visually for the subject on the computer screen. The time between the two listening intervals was 500 ms. After each presentation, a dialog box appeared to prompt the subjects to indicate which ear received the louder stimulus. Listeners were instructed to guess when they couldn’t tell the difference in loudness between the two stimuli. Response time was subject driven. No feedback was provided. Subjects were able to repeat the stimulus pair if they needed to hear it again before responding. For each subject, the interaural loudness balancing procedure was repeated three times for each of 11 interaural electrode pairs in order to identify the specific stimulation levels used for electrophysiological testing.

Before data collection, two practice runs (five trials for each session) were completed in order to familiarize the listener with the task and response requirements. Listeners were allowed to take frequent breaks during the test session.

Electrophysiological Test Procedures

Binaural Interaction Component Measurements: Electrophysiological testing was undertaken with subjects seated in a reclining chair. They were encouraged to sleep or to relax as much as possible during the recording session and were offered breaks as needed. EABRs were recorded differentially between electrodes positioned at Cz (positive) and a noncephalic site overlying the seventh cervical vertebra (C7). A ground electrode was placed on the forehead (Fpz). Electrode impedances were maintained below 5000 Ohms with an interelectrode impedance difference of less than 2000 Ohms. The raw EEG signal was sampled at a rate of 100 kHz using a 12 bit analog-to-digital (A/D) converter (National instruments DAQCard-6062E). An RF-shielded, ground-isolated differential amplifier (Intelligent Hearing Systems Opti-Amp 8008) with a gain of 10,000 preceded input to the averaging computer. Relatively low gain was used in order to minimize the effect of stimulus artifact in the recordings. Before sampling, the EEG activity was filtered between 1 and 5000 Hz using an analog filter (12 dB/octave). Artifact rejection with a criterion of 60

μV was used to minimize the number of trials that were contaminated by muscle artifact or excessive noise.

The EABR was measured in response to left monaural, right monaural and bilateral stimulation for each interaural electrode pair tested. The EABR was recorded in blocks of 1000 sweeps. At least three blocks of EABRs were recorded for each stimulation condition. The sequence of these recordings was pseudo-randomized on a trial-by-trial basis across electrodes and stimulation conditions.

The effect of stimulation level on the BIC was measured for six subjects. EABRs were measured at several different stimulation levels using loudness balanced stimuli presented to pitch matched electrode pairs in the left monaural, right monaural and synchronized bilateral stimulation modes. For four out of six of these subjects, the stimulation levels ranged from 0 to 90% of their DRs. For subject R87b, the BIC responses were contaminated by muscle artifact when stimulation levels were higher than 60% of his DR. Therefore, the highest stimulation level used was 60% of his DR. Similarly, for subject E23b the highest stimulation level used was 80% of her DR because the recordings obtained using higher stimulation levels was contaminated by muscle artifact.

The effect of interaural electrode pairing on the BIC was investigated by recording EABRs from all 11 interaural electrode pairs. This effect was studied at a relatively high stimulation level for all ten subjects and at a lower stimulation level in a subgroup of seven subjects. The high stimulus level was selected to equal to 90% of the subject's DR or, alternatively, the highest stimulation level that did not result in contamination of the EABR. The low stimulation level was chosen as a level that was 10% of subjects' DR higher than the BIC threshold. For example, the BIC threshold for subject E23b was 199 CL for electrode R12, which corresponded to 40% of her DR. The low stimulation level, therefore, was chosen as 206 CL for this electrode, corresponding to 50% of her DR. As described above, stimulation levels of the left ear electrodes were loudness balanced to the level of R12. The BIC threshold could not be determined for one subject (E55b) due to time constraints. For this subject, the low stimulation level was chosen to be 70% of her DR.

Data Analysis: Averaged EABRs based on 1000 sweeps were examined offline. In postprocessing, the averaged EABR traces were digitally filtered between 10 and 3000 Hz with a 31st-order FIR band-pass filter (Smith and Delgutte, 2007). Responses were filtered twice (once forward and once reversed) in order to avoid effects on latencies. Any EABR traces without a clearly identifiable wave V or with wave V that was 50% larger or smaller than the average wave V were excluded from further analysis.

The BIC was computed as the difference between the sum of monaurally and the bilaterally evoked EABR; i.e. $\text{BIC} = (\text{left monaural} + \text{right monaural}) - \text{bilateral}$ (Levine, 1981; Wrege and Starr, 1981; Jones and Van der Poel, 1990; Furst et al., 1985; Pelizzone, et al., 1990; Firszt et al., 2005). Figure 1 illustrates how the BIC was derived. A minimum of two BIC replications were obtained for each interaural electrode pair. The average of these replications was used for amplitude and latency measurements. The BIC response consists of a small negative peak near 3.3 ms followed by a positive peak near 4 ms. BIC latencies

were measured from stimulus onset to peaks of the BIC. Both peak to peak and RMS amplitudes were computed for each BIC. The peak to peak amplitude measure reflects the difference in voltage between the positive peak to the preceding trough. The RMS amplitude was defined as the square root of the arithmetic mean of the square of difference between the individual voltage measures recorded during the time window between 3 and 5.5 ms after stimulus onset and the average voltage computed over this same time window (see Figure 1). For comparison purposes, the noise floor of BIC responses, both in terms of peak to peak and RMS amplitude, was also computed. These noise floor estimates were based on the average EEG amplitudes recorded during time windows extending from 1–2.5 ms and 6.0 – 7.5 ms. The BIC threshold was defined as the lowest stimulation level that resulted in a visually detectable BIC response with an amplitude that was at least 50% larger than that of the noise floor.

RESULTS

Electrophysiological Recordings

BICs were successfully recorded from all ten subjects. The majority of subjects had measurable BICs for all 11 interaural electrode pairs. Table 2 shows mean latencies, peak to peak amplitudes and RMS amplitudes for each interaural electrode pair. Standard deviations for each measure are also shown. Peak to peak amplitudes varied from 0.31 to 0.47 μ V and RMS amplitudes ranged from 0.14 to 0.17 μ V. Figure 2 shows examples of BIC responses recorded from all subjects for a single interaural electrode pair (L12-R12) at high stimulation levels. The subject identification number is indicated for each response trace. The downward and upward triangles indicate the positive and the negative peaks used to compute BIC amplitudes.

Inspection of Figure 2 reveals a substantial amount of inter-subject variation in the general morphology of the BIC responses. Figure 3 shows examples of the BIC recordings obtained from three subjects at high stimulation levels. In all cases, the BICs shown in this figure were recorded by stimulating electrode 12 in the right ear. The left ear electrode number is indicated on each waveform. The BIC responses shown in this figure were selected because they illustrate the range of variation in response morphology that was observed. The panel on the left side of Figure 3 (subject R36b) shows that, with the exception of electrode pair L6-R12, BICs were recorded for all of interaural electrode pairs tested. This series of BICs had fairly typical morphologies (a negative peak followed by a positive peak) and latencies (around 3.3 ms for the negative peak and 3.7 ms for the positive peak). However, the recordings obtained from this subject were the smallest among the ten subjects tested. His peak to peak amplitudes ranged from 0.15 to 0.37 μ V. His RMS amplitudes ranged from 0.06 to 0.17 μ V.

The center panel of Figure 3 (subject M58b) shows BICs with typical waveform morphology resembling those obtained from R36b but with slightly longer peak latencies (approximately 3.5 ms for the negative peak and 3.9 ms for the positive peak). For this subject, peak to peak amplitudes ranged from 0.43 to 0.74 μ V and RMS amplitudes ranged from 0.14 to 0.25 μ V.

The BIC responses in the right panel of Figure 3 (subject E23b) were typical of the group data in terms of latency but the general morphology was less typical. Instead of a single positive peak, the BIC waveforms had double peaks that were quite large with peak to peak amplitudes ranging from 0.33 to 1.69 μV and RMS amplitudes ranging from 0.21 to 0.55 μV .

What is apparent from the data shown in Figure 3 is that BIC responses can be elicited not only from stimulation of closely spaced interaural electrode pairs but also from stimulation of interaural electrode pairs that are more widely separated (e.g. L6-R12).

One goal of this study was to investigate the effects of stimulation level on the BIC response. Figure 4 shows these effects for six subjects. Filled symbols indicate results of peak to peak amplitude measures and open symbols indicate latencies measured for the positive peak of the BIC response. The stimulation level in the right ear is indicated on the abscissa. The stimulation levels used in the left ear were loudness balanced to the right ear stimulation levels before data collection. These stimulation levels were chosen to represent approximately equally spaced steps that ranged from about 30 to 90% of the subject's DR. Behavioral thresholds (T-levels) and maximum comfort levels (C-levels) for each subject are also shown. Also noted on each panel is the estimated loudness level in terms of percent DR for the BIC thresholds and maximum levels tested for each subject. For all six subjects BIC threshold was recorded between 30% and 40% of the subject's DR. In general, BIC amplitudes increased with increasing stimulus levels. The straight lines on each panel of Figures 4 are the result of linear regression analyses. Two-tailed linear regression t-tests showed that slopes of the linear regression lines for the BIC amplitude growth functions were significantly different from zero for all six subjects ($p < 0.05$). The effect of stimulation level on BIC latency was less robust. Although there was a trend for the BIC latency to decrease as stimulation level increased, two-tailed linear regression t-tests indicated that the slopes of the linear regression lines were not significantly different from zero ($p > 0.05$).

The second goal of this study was to investigate how the choice of interaural electrode pair affects BIC amplitude. Figure 5 shows BIC amplitudes plotted as a function of the left ear electrode for all ten subjects (thin lines) as well as group mean average data (thick lines). The left panel shows results obtained using the peak to peak amplitude analysis method; the right panel shows the same results plotted using the RMS measures of BIC amplitude. These two amplitude measures show the same pattern of results. Regardless of the analysis method used, individual variability was considerable. Results from subject E23b were significantly larger than the other subjects. In addition, the waveform morphology was also somewhat atypical (see Figure 3). Therefore, her results were not included in the group mean average. Generally, the BIC amplitude versus electrode functions were broad and did not exhibit a clear peak.

Figure 6 shows results of peak to peak amplitude measures of BIC responses and the associated noise floors for each interaural electrode pair in all ten subjects. The BIC amplitude is indicated using filled circles and solid lines; the noise floor is indicated using open circles and dotted lines. The subject number is indicated on each graph. In general, the results showed that the majority of BIC responses were recorded at levels that exceeded the

noise floor. This was true regardless of the method used to determine BIC amplitudes (peak to peak or RMS). In addition, results of Pearson product-moment correlation tests showed that the correlations between any two replications of the BIC response recorded using the same stimulation parameters were statistically significant ($r = 0.8$, $P < 0.01$).

Figure 7 shows the series of BIC responses recorded from a subgroup of seven subjects at a lower stimulation level. While considerable individual variability is still apparent in these recordings, the general morphology of the BIC responses across subjects appears more consistent than it did for recordings obtained from the same subjects at the high stimulation level (compare Fig. 3). The largest BIC amplitudes were again obtained from subject E23b and the smallest BIC amplitudes were obtained from subject R36b. Considerable variation across subjects in BIC latencies is also apparent. The BICs recorded from subject R36b had the shortest latencies (3.61 to 3.73 ms for the positive peak) while the responses recorded from subject R87b had the longest latencies (3.78 to 4.3 ms for the positive peak), which was consistent with the results obtained at high stimulation levels.

Figure 8 shows BIC peak to peak amplitude versus electrode functions recorded from seven subjects who were tested at the low stimulation level. Also shown are the respective noise floor levels (unconnected symbols). The left and right panels show results for high and low stimulation levels, respectively. The thin lines indicate data recorded from individual subjects, and the thicker lines indicate the group mean data. The BIC responses are above noise floor for all subjects at both stimulation levels. While large interaural offsets between the two stimulating electrodes still elicit clear BIC responses (e.g. R12-L18 or R12-L6) at low stimulation levels, the effect of electrode pairing on BIC amplitude is more pronounced. Compared with the relative flat BIC amplitude versus electrode functions obtained at high stimulation levels, functions obtained at low stimulation levels generally described an inverted “V” shape for most of the subjects. These functions suggest that the BIC amplitude is maximal for the interaural electrode pair with an interaural offset of zero, one or two electrodes and decreases as the interaural offset increases. Similar trends were evident using the RMS measure of BIC amplitude.

In order to more quantitatively compare the shape of the BIC amplitude versus electrode functions at different stimulus levels, the BIC amplitudes were normalized to the maximum peak to peak or RMS amplitude for each subject. The area under the curve of the normalized BIC amplitude versus electrode function could be considered as a measure of spatial selectivity with small area indicating good selectivity. The averaged normalized BIC amplitudes, which were proportional to the area under the curve of the normalized function, were computed for each subject at high and low stimulation levels, respectively. Results of one-tailed Wilcoxon signed rank tests showed that the averaged normalized amplitudes obtained at high stimulation levels were significantly larger than those obtained at low stimulation levels for these seven subjects (peak to peak amplitude: $Z = -2.366$, $p < 0.05$; RMS amplitude: $Z = -2.028$, $p < 0.05$). This finding suggests that the BIC versus electrode functions were narrower for low than for high stimulation levels regardless of the method used to measure BIC amplitude.

Amplitudes of the BIC responses obtained from interaural electrode pairs L6-R12, L12-R12, and L18-R12 were compared using a repeated-measures ANOVA. The comparison was performed for both high and low stimulation levels. The analysis indicated no difference in BIC amplitudes for these three interaural electrode pairs at the high stimulation level (peak to peak amplitude: $F_{2,18}=2.62$, $p=0.1$; RMS amplitude $F_{2,18}=2.37$, $p=0.12$). However, BIC amplitudes measured at the low stimulation level were significantly different across these interaural electrode pairs (peak to peak amplitude: $F_{2,18}=13.25$, $p<0.05$; RMS amplitude: $F_{2,18}=7.10$, $p<0.05$). Results of within-subject contrasts indicated that electrode pair L12-R12 showed significantly larger BIC responses than electrode pair L6-R12 (peak to peak amplitude: $F_{1,6}=12.5$, $p<0.05$; RMS amplitude: $F_{1,6}=14.14$, $p<0.05$) as well as electrode pair L18-R12 (peak to peak amplitude: $F_{1,6}=21.54$, $p<0.05$; RMS amplitude: $F_{1,6}=15.70$, $p<0.05$).

Inspection of Figure 8 also revealed a weak trend for BIC amplitudes to be slightly larger when the left ear electrode was located in the apical half of the array (i.e. electrode pair L18-R12) than when it was located in the basal half of the array (i.e. L6-R12). However, results of Wilcoxon signed rank test showed that there was no significant difference between slopes of linear regression lines fitted for the data obtained from electrodes located in the basal and the apical half of the array ($Z = -0.85$, $p=0.40$).

DISCUSSION

This study investigated the effects of stimulation level and electrode pairing on the BIC responses of the EABR for bilateral Nucleus CI users. Literature on the effects of stimulus level or interaural electrode pairing on the electrically evoked BIC response is sparse. To date, only one animal study has reported effects of stimulation level on the BIC responses (Smith and Delgutte, 2007). That study showed that increasing stimulus level resulted in increased amplitudes and decreased latencies for electrically evoked BIC responses measured from acutely deafened cats. This finding is similar to that found for acoustic stimulation in normal hearing listeners (Riedel and Kollmeier, 2002a, b; Jiang and Tierney, 1996; Cone-Wesson et al., 1997). In the current study, BIC amplitude growth functions were obtained from six subjects. For most subjects, stimulation levels higher than 30% of the DR were required to evoke a BIC. Increasing the intensity of the stimulus from 30% to 90% of the DR resulted in increased BIC amplitudes but the BIC latencies did not significantly decrease (see Figure 4). These findings are consistent with similar results reported by Smith and Delgutte (2007).

Our results showed considerable individual variability in terms of BIC amplitudes and peak latencies. Despite this variation, and with the exception of the waveforms recorded at the high stimulation level from subject E23b, the responses are consistent with those reported previously using electrical stimuli in CI users (Pelizzone et al., 1990; Firszt et al., 2005; Gordon et al., 2007). They are also generally consistent with those recorded by other investigators who used acoustic stimuli and tested normal hearing listeners (Dobie and Norton, 1980; Furst et al., 1985; McPherson and Starr, 1993, 1995; Ungan et al, 1997; Riedel and Kollmeier, 2002a, b, 2006).

In the current study, maximum peak to peak amplitudes ranged from 0.37 to 1.14 μV . BIC amplitudes reported in previous studies with bilateral human CI users ranged from approximately 0.9 to 1.2 μV (Firszt et al., 2005; Pelizzone et al., 1990; Gordon et al., 2007). Smith and Delgutte (2007) reported electrically evoked BICs that ranged 1.2 to 1.5 μV in acutely deafened cats. The smaller peak to peak amplitudes in the current study may reflect the fact that in previous studies with human CI users, the stimulation levels may have been higher and/or the subjects were younger. The finding that BIC amplitudes were larger in cats (Smith and Delgutte, 2007) is not surprising given the smaller head size and presumably better neural survival that might be expected in acutely deafened cats versus humans with profound hearing loss.

In this study, BIC latencies ranged from 3.27 to 3.54 ms and 3.88 to 4.15 ms for the negative and positive peaks, respectively. This is also consistent with previous reports (Firszt et al., 2005; Pelizzone et al., 1990; Gordon et al., 2007). The BIC latencies measured from acutely deafened cats were approximately 2.6 ms and 3.11 ms for the negative and positive peaks, respectively (Smith and Delgutte, 2007), which are shorter than the BIC latencies measured in human subjects – a finding that likely reflects cross-species differences in head size.

While BICs have been measured from bilateral CI users in the past, none of those studies explored the effect of interaural electrode pairing on BIC amplitude. Smith and Delgutte (2007) tested cats and showed that BIC amplitude was largest for interaural electrode pairs with similar intracochlear locations and that the size of the BIC was reduced by approximately 50% as the interaural offset between the two stimulating electrodes exceeded approximately 1.5 mm. Our finding that BICs could be recorded even when electrodes from very different regions of the two cochleae were stimulated was, therefore, somewhat unexpected. It is possible that the relatively flat BIC amplitude versus electrode functions shown in Figure 5 were due to an excessively high noise floor. This is unlikely, however, because our results showed that most of the BIC responses were well above the noise floor (see Figure 6) and also showed robust replication. Another possibility that might account for the relatively broad nature of these functions is that, at high stimulation levels, the current spread within the cochlea might have been substantial; in turn, this could lead to excitation of interaurally matched neural channels even though the stimulated interaural electrode pairs were widely separated. In this case, reduction in the stimulus level should have resulted in less spread of current within the cochlea, making the effect of the electrode pairing more pronounced. Consistent with this possibility, our data indicated that lowering the stimulation level did in fact result in narrower functions with more easily identifiable peaks (see Figure 8). Differences between our results and those reported in cats by Smith and Delgutte (2007) may also reflect species differences or the fact that the acutely deafened cats used by Smith and Delgutte were likely to have better neural survival than our CI users. In addition, Smith and Delgutte (2007) reported introducing “cotton spears” in some animals in order to lower response thresholds. This manipulation is likely to move the electrode closer to the modiolar wall, resulting in lower stimulation levels required to achieve threshold and less current spread within the cochlea.

As noted earlier, subject inclusion criteria included full electrode insertion bilaterally. Nevertheless, it is possible that some misalignment of the electrode array may have existed

across the two ears in any particular subject because of asymmetric insertion depths. As a result, equal-numbered electrodes may have been positioned at slightly different locations within the two cochleae. Despite this, the function relating BIC amplitude to electrode number should still be expected to show a maximum; that is, a maximum should still occur for the interaural electrode pair that was most closely aligned across ears. The misalignment, however, will have an effect on which interaural electrode pair shows the biggest BIC response. Thus, it would affect the location where the peak of the BIC versus electrode function is located.

The effect of stimulation level on the pattern of spread of excitation of monaural processing has been studied using different techniques (Chatterjee and Shannon, 1998; Cohen, 2003; Abbas et al., 2004; Chatterjee et al., 2006; Hughes and Stille, 2008). These studies all used monaural stimulation and showed that there was a positive relationship between the stimulus intensity and the amount of spread of excitation across the cochlea. For example, Abbas et al. (2004) investigated the level effect on spread of neural excitation by measuring ECAP in a forward masking paradigm. They found that as the stimulation level increased, longitudinal spread of neural excitation also increased. Although these studies used monaural stimulation to investigate the effect of changes in stimulation level on spread of excitation, they suggest that the stimulation level may also have an effect for binaural processing because the pattern of spread of neural excitation available to the binaural system should be affected by that of monaural processes. Results of the current study provide evidence that there may be greater spread of neural excitation for high as opposed to low stimulation levels for binaural processing.

The spread of neural excitation may impose significant limitations on performance of cochlear implants due to the lack of across-fiber independence. If the same group of neurons is activated regardless of which electrode is stimulated, then a multichannel CI will essentially work as a single channel CI. For patients with excessive spread of neural excitation, stimulation of several adjacent electrodes may end up activating the same group of auditory neurons. As a result, the information provided by each of these stimulus channels is not independent and cannot be effectively transmitted to the central nervous system, effectively reducing the number of functional channels. In a multichannel cochlear implant, spectral information is coded through the stimulation of different electrodes along the cochlea. Therefore, CI users with wide spread of excitation will have worse spectral resolution than CI users with limited spread of excitation. Consistent with this hypothesis, Hughes (2008) found that CI users with excessive amount of spread of excitation as measured using electrically evoked compound action potentials (ECAPs) showed poor pitch discrimination. Several studies with adult, as well as pediatric, CI users have shown that electrode discrimination ability is an important factor for predicting speech perception performance (Busy et al., 1993; Busy and Clark, 2000; Collins and Throckmorton, 2000; Dawson et al., 2000; Donaldson and Nelson, 2000). Patients with good electrode discrimination abilities typically have better consonant place cues detection (Donaldson and Nelson, 2000), better speech feature discrimination (Dawson et al., 2000) and better speech perception (Busy et al., 1993). Patients with wide spread of excitation have been shown to have relatively poor consonant recognition scores (Boex et al., 2003).

However, spread of neural excitation across the cochlea may be beneficial for some bilateral CI users under some circumstances. Many bilateral CI users use speech processors that are programmed so that a single acoustic frequency band stimulates electrodes with the same number in the two ears. For some CI users, mismatches in the place of stimulation from number-matched electrode pairs could occur due to differences in the signal processing of the two devices, neural survival, electrode placement and/or other anatomic differences between the two ears. For these individuals, spread of neural excitation may provide benefit for extraction of binaural cues such as ITD. One study has shown that the ITD threshold is not affected by a difference in electrode position of four electrodes, which corresponds to a difference of 3 mm along the cochlea (van Hoesel et al., 2002). van Hoesel (2004) suggested that because interaural offsets of three or four electrodes have minimal effects on ITD sensitivity, there must be substantial spread of neural excitation that could offset the mismatches in place of stimulation across the two ears. These results, while limited due to the fact that data from only one subject are reported, suggest that spread of excitation could have a positive effect in some circumstances. This would be especially important when CI users have damaged neurons along the cochlear partition in one ear. It would allow the CI users to perceive binaural cues via excitation in the adjacent area of the cochlea.

Relatively high stimulation levels are necessary for the present study due to the relative small amplitude of the BIC responses. In addition, the stimulation used for EABR recording in the present study was at much lower rate than the stimulation rate used clinically. Thus, the amplitude of stimulation in the present study was higher than that CI users experienced with their speech processors and maps. Therefore, one caveat for interpretation of the present results is that the stimulation levels used by the speech processor are typically lower than those tested here because they use faster stimulation rates. As a result, the wide spread of neural excitation reported here may be attributable to the particular stimulation parameters of the experimental paradigm. CI users may experience much less current spread with their CI devices.

SUMMARY AND CONCLUSIONS

This study investigated the effect of stimulation level and electrode pairing on BIC responses. Measurable BICs were recorded from all ten subjects tested. The morphologies, latencies and amplitudes of BICs were consistent with previously published results. At high stimulation levels, BIC amplitude was not strongly affected by the relative position of the interaural stimulating electrodes. That is, BICs were successfully recorded not only from interaural electrode pairs with similar intracochlear locations but also for electrode pairs with large interaural offsets. The BIC amplitude versus electrode functions were very broad. When the stimulus level was reduced, the BIC amplitude versus electrode functions were narrower and maximum BIC amplitudes were obtained when electrodes near the same cochlear position were paired together. These results are consistent with the hypothesis that at high stimulation levels, there is wide spread of current within the cochlea. Reduction in the stimulation levels may have led to a more restricted spread of excitation. These results suggest that if electrophysiological measures such as the BIC of the EABR are to be used to match electrodes in bilateral cochlear implant users, testing must be performed at the lowest possible stimulation levels.

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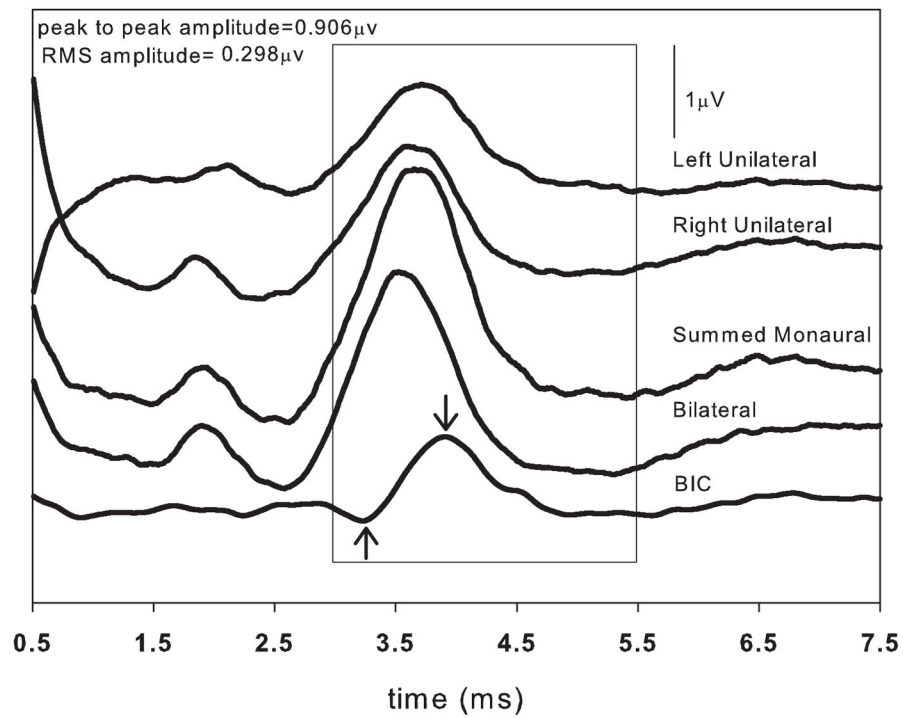


Figure 1. EABRs recorded using unilateral and bilateral stimulation are shown. Also shown are the summed unilateral responses and the derived BIC. The arrows indicate the points used to compute peak to peak amplitude of the BIC. The rectangular box indicates the time window over which the RMS amplitude is calculated. Results of peak to peak and RMS amplitude measures are indicated in the upper left corner of the graph.

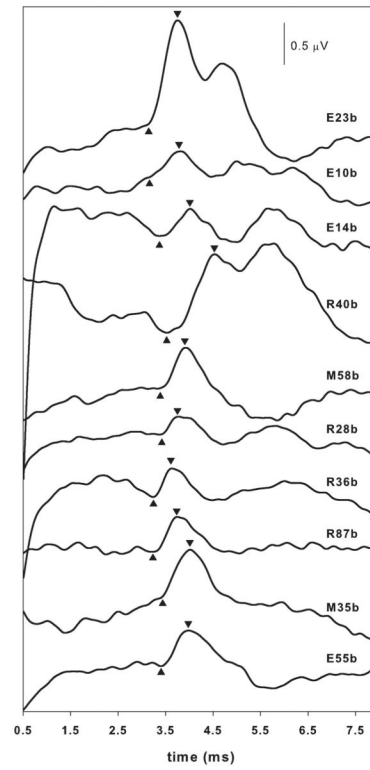


Figure 2. BIC responses recorded from interaural electrode pair L12-R12 at high stimulation levels for ten subjects. The subject's number is indicated for each BIC response. The upward and downward triangles indicate the negative and positive peaks picked for each BIC response, respectively.

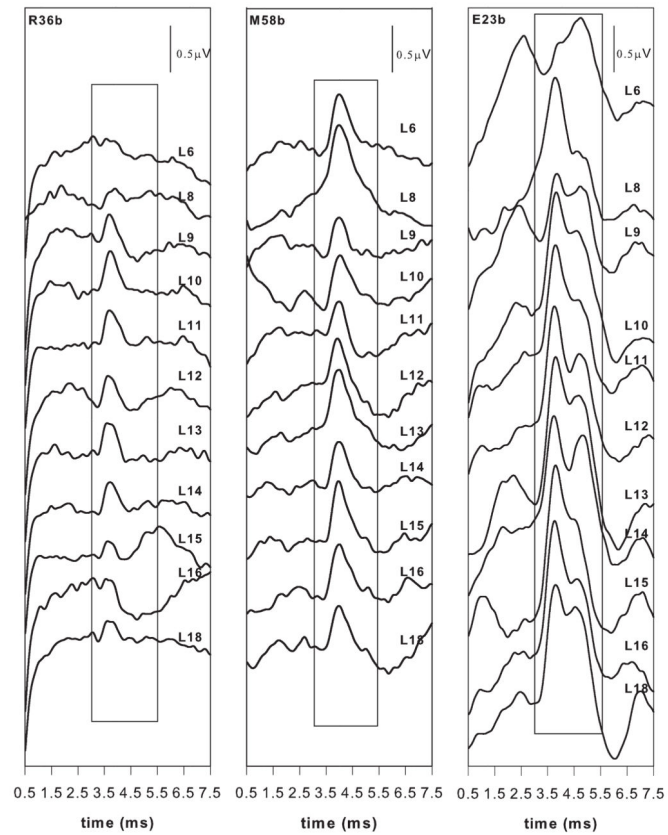


Figure 3. BICs recorded from 11 interaural electrode pairs for three subjects (R36b, M58b and E23b). The left ear electrode for each interaural electrode pair is shown. The rectangular box indicates the time window over which the RMS amplitude is calculated.

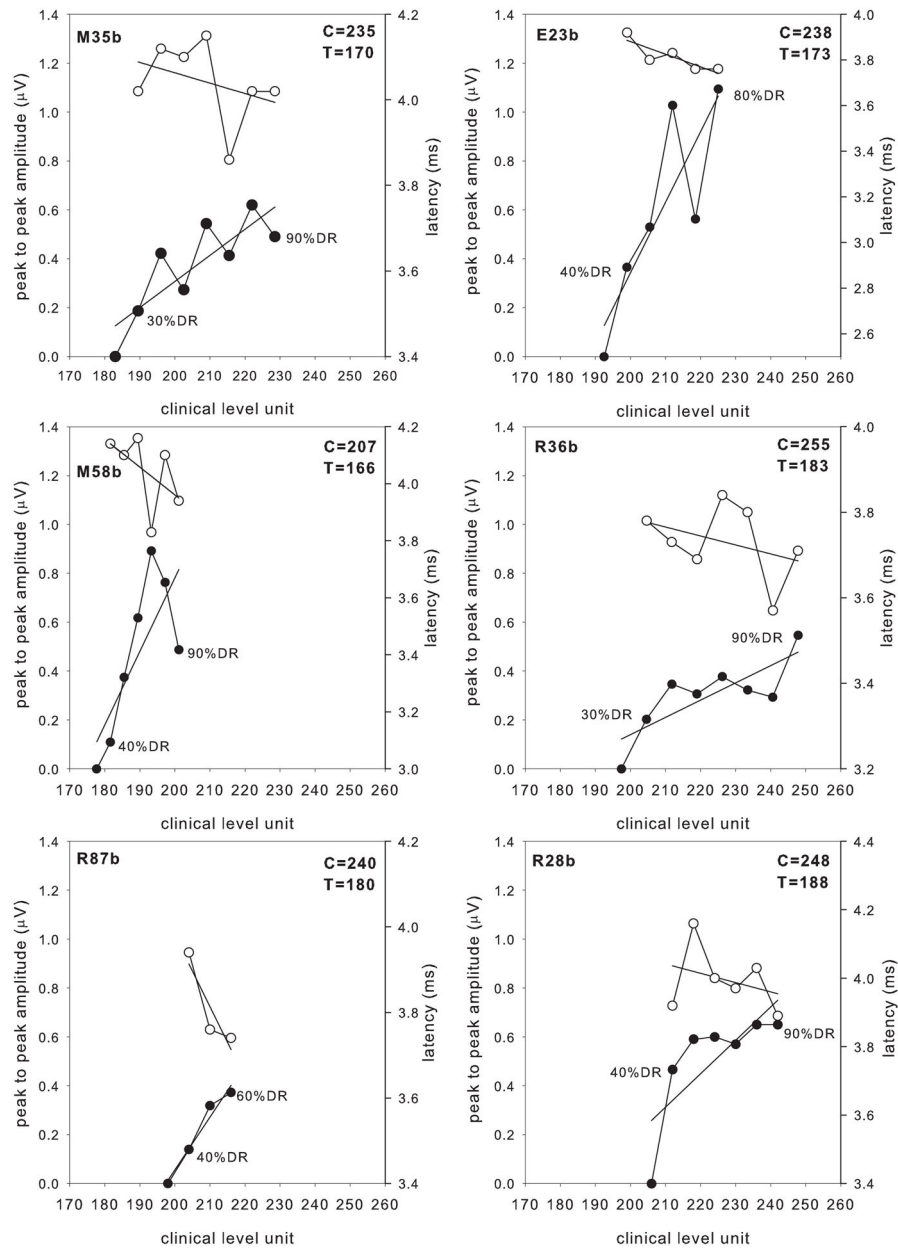


Figure 4. The peak to peak amplitudes and latencies of the BICs are plotted as a function stimulation level for six subjects. Filled symbols indicate results of peak to peak amplitude measures and open symbols indicate latencies measured for the positive peak of the BIC response. Also shown is the linear regression function fitted for each subject. C-levels and T-levels are shown in the upper right corner. The corresponding percentage of DR is indicated for the highest stimulation level tested and the BIC threshold measured for each subject.

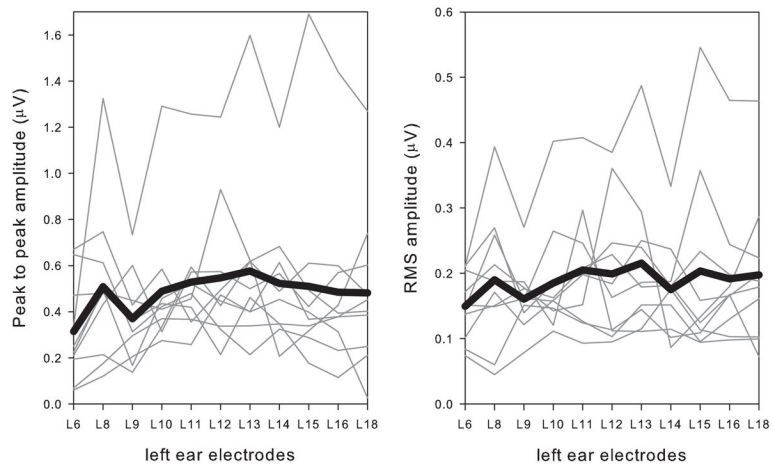


Figure 5. BIC amplitudes measured at high stimulus levels for ten subjects (thin lines) and the group mean average (thick line) plotted as a function of left ear electrode. The left and right panels show results of peak to peak and RMS amplitude measures, respectively.

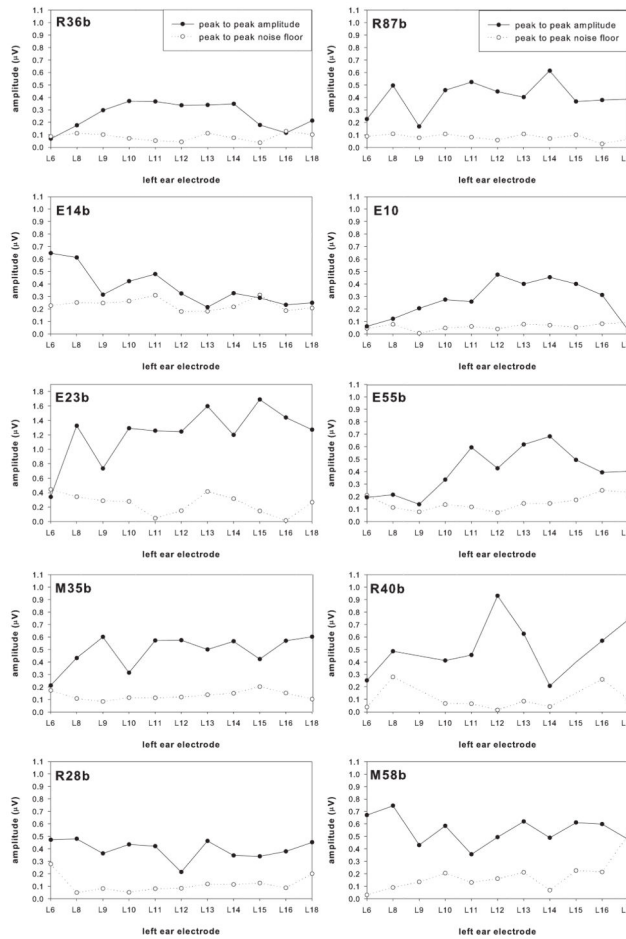
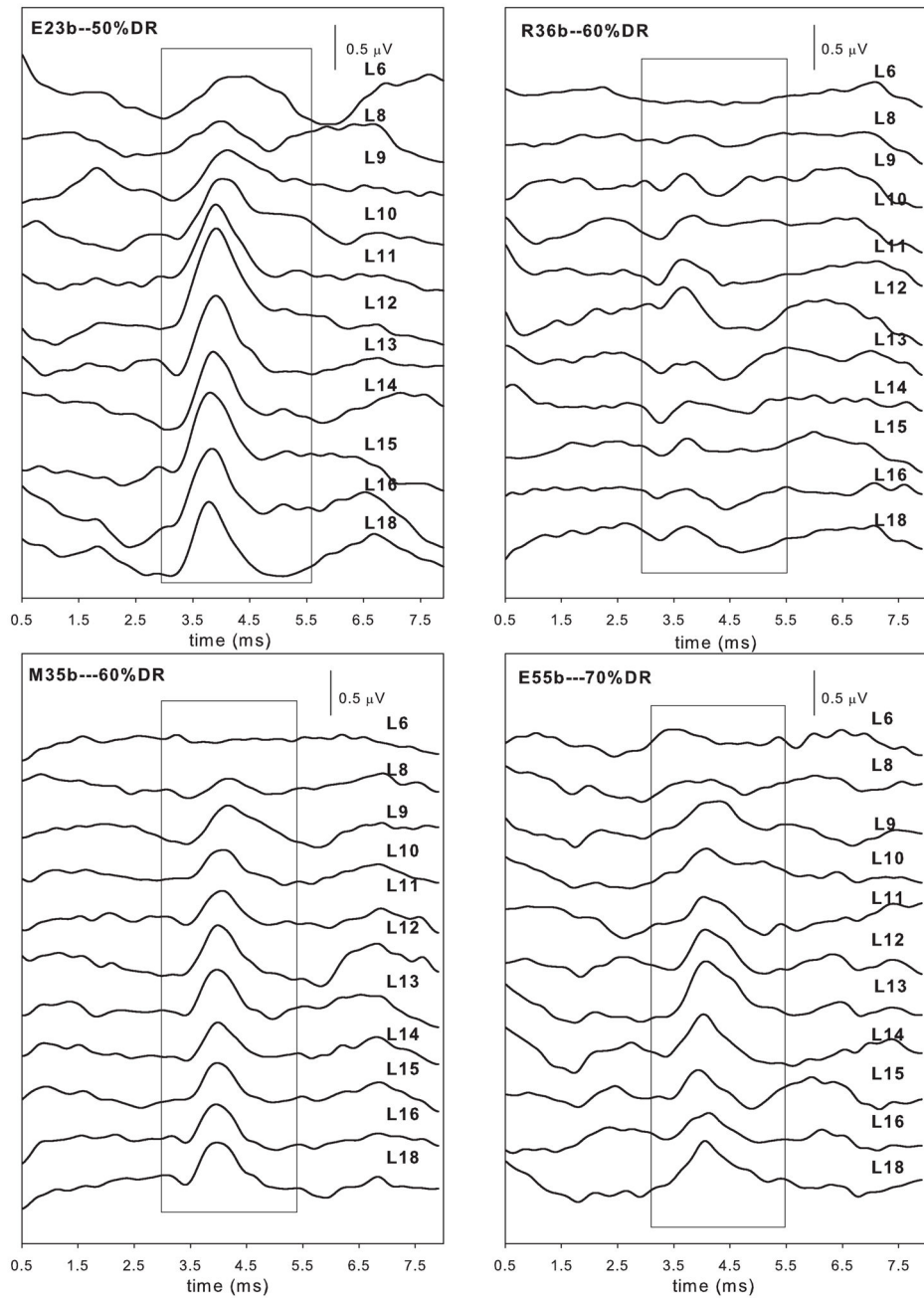


Figure 6. Peak to peak amplitudes of BIC responses (filled circles, solid lines) and noise floors (open symbols, dotted lines) measured from ten subjects at high stimulation levels for each interaural electrode pair. The subject numbers are shown in the upper right corner for each graph.



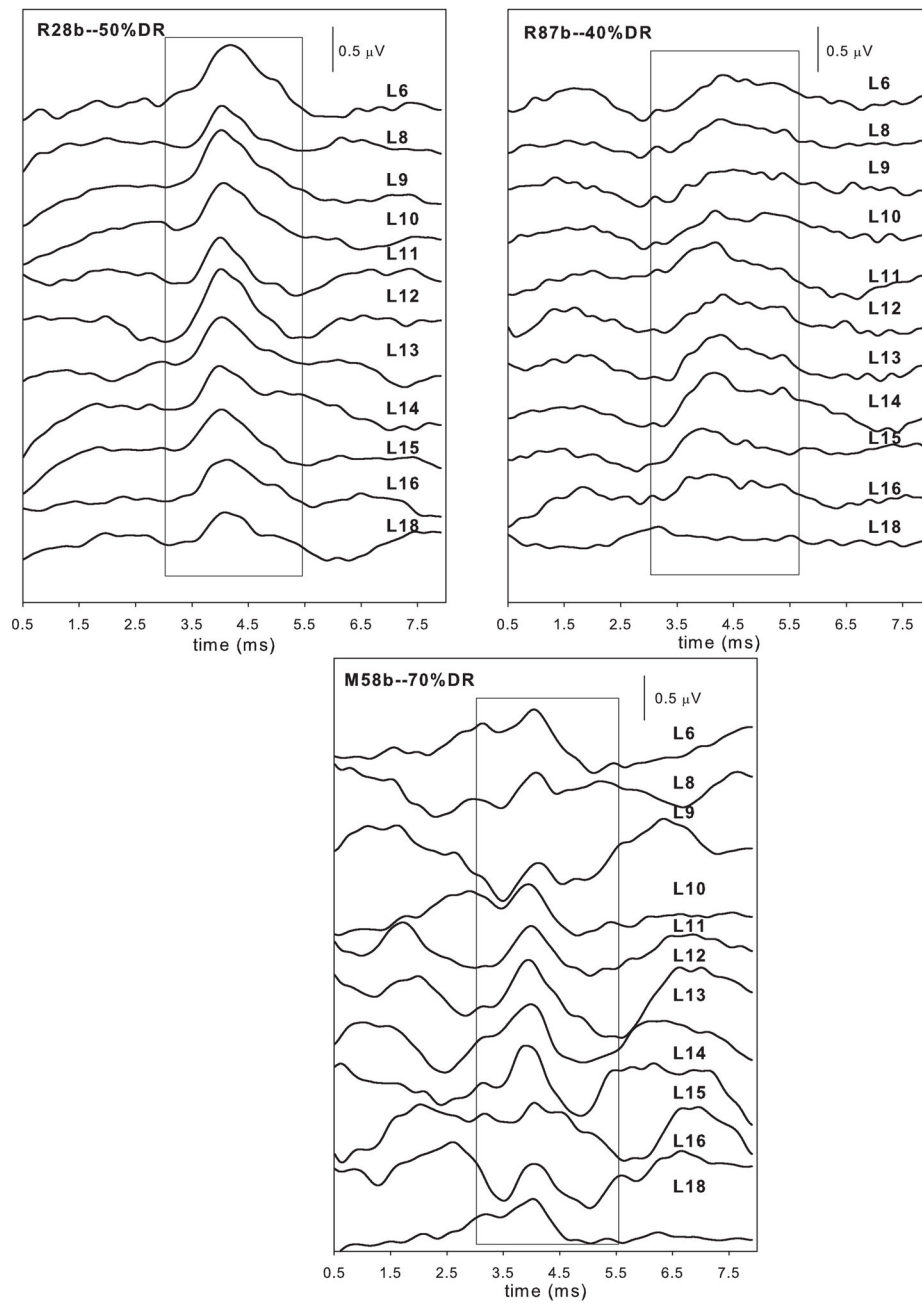


Figure 7.

BIC responses measured from seven subjects at low stimulation levels. The left ear electrode for each interaural electrode pair is shown. The subject number and the stimulation levels used for the BIC recording are shown in the upper left corner for each graph. The rectangular box indicates the time window over which the RMS amplitude is calculated.

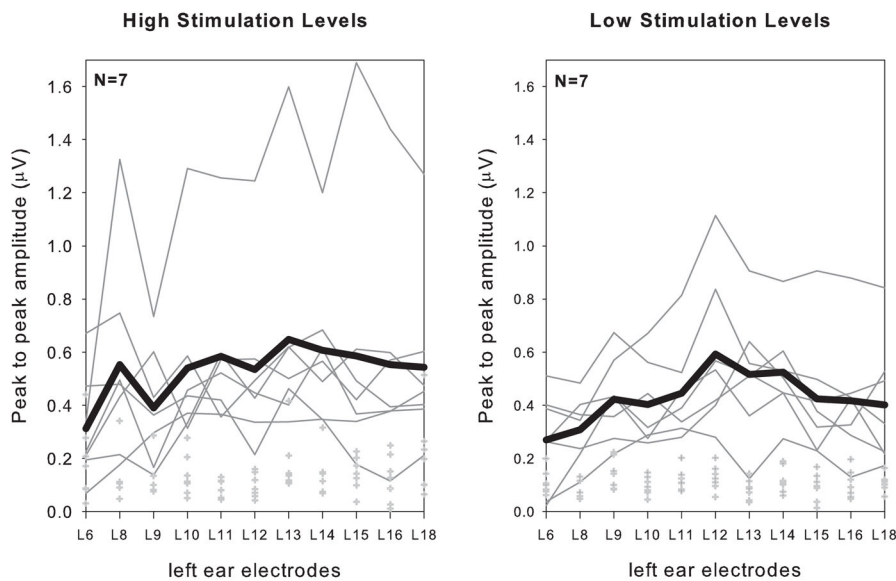


Figure 8. Peak to peak amplitudes of BIC responses (solid lines) and noise floors (unconnected symbols) recorded at high and low stimulation levels for seven subjects plotted as a function of the left ear electrode. The electrode in the right ear was fixed at electrode R12. Thin lines represent data from individual subjects; the thick line represents the averaged results across the seven subjects. The left and right panels show results obtained for high and low stimulation levels, respectively.

Table 1

General demographic information for ten subjects.

Subject number	Age	Gender	Bilateral severe or profound hearing loss (years)	Duration of bilateral implant use (months)	Etiology	Implant	Bilateral HINT (in quiet) % correct
R87b	28	M	0.6	32	Cogan's syndrome	24R (CA)	100%
R28b	59	F	1.5	62	Unknown	24R (CS)	95%
R40b	61	F	10	56	Enlarged Vestibular Aquaducts	24R (CS)	75%
R36b	53	M	28	59	Unknown	24R (CS)	100%
M58b	68	F	1	96	Meniere's disease	24M	75%
M35b	79	M	1	108	Unknown	24M	89%
E23b	84	F	5	24	Unknown	24RE (CA)	78%
E55b	59	F	3	6	Hereditary	24RE (CA)	N/A
E10	49	F	14	28	Unknown	24RE (CA)	100%
E14	73	F	10	22	Unknown	24RE (CA)	96%

Average BIC amplitude and latency values for each interaural electrode pair. Also shown are standard deviations of each measure. These results are based on data from nine subjects.

Table 2

Electrode Pairs	Peak to Peak Amplitude (μV)		RMS Amplitude (μV)		Trough latency (ms)		Peak Latency (ms)	
	Mean	STD	Mean	STD	Mean	STD	Mean	STD
L6-R12	0.31	0.23	0.14	0.05	3.54	0.31	4.15	0.29
L8-R12	0.42	0.21	0.17	0.08	3.40	0.19	4.06	0.22
L9-R12	0.31	0.15	0.15	0.03	3.41	0.11	4.00	0.15
L10-R12	0.40	0.09	0.16	0.04	3.33	0.31	4.02	0.24
L11-R12	0.45	0.11	0.18	0.06	3.38	0.24	4.01	0.21
L12-R12	0.47	0.20	0.19	0.09	3.32	0.24	3.95	0.25
L13-R12	0.46	0.14	0.16	0.06	3.30	0.25	3.95	0.26
L14-R12	0.45	0.15	0.16	0.05	3.27	0.44	3.94	0.23
L15-R12	0.39	0.13	0.16	0.09	3.30	0.11	3.88	0.16
L16-R12	0.38	0.15	0.16	0.05	3.35	0.22	3.91	0.3
L18-R12	0.39	0.21	0.17	0.07	3.27	0.27	3.94	0.26