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Auditory Brainstem Implant: Electrophysiologic Responses and Subject Perception

Barbara S. Herrmann, Ph.D.,

Massachusetts Eye and Ear Infirmary

M Christian Brown, Ph.D.,

Department of Otolaryngology Eaton Peabody Laboratories Massachusetts Eye and Ear Infirmary

Donald K Eddington, Ph.D.,

Cochlear Implant Research Laboratory/ Massachusetts Eye and Ear Infirmary Department of Otolaryngology/Harvard Medical School

Kenneth E Hancock, Ph.D., and

Eaton Peabody Laboratories Massachusetts Eye and Ear Infirmary Department of Otolaryngology and Laryngology/Harvard Medical School

Daniel L Lee, M.D.

Department of Otolaryngology Massachusetts Eye and Ear Infirmary Department of Otolaryngology and Laryngology/Harvard Medical School

Abstract

Objectives—The primary aim of this study was to compare the perceptual sensation produced by bipolar electrical stimulation of auditory brainstem implant (ABI) electrodes to the morphology of electrically-evoked responses elicited by the same bipolar stimulus in the same unanesthetized, post-surgical state. Secondary aims were to 1) examine the relationships between sensations elicited by the bipolar stimulation used for evoked potential recording and the sensations elicited by the monopolar pulse-train stimulation used by the implant processor and 2) to examine the relationships between evoked-potential morphology (elicited by bipolar stimulation) to the sensations elicited by monopolar stimulation.

Design—Electrically-evoked early latency and middle-latency responses to bipolar, biphasic low-rate pulses were recorded post-operatively in four adults with auditory brainstem implants. Prior to recording, the perceptual sensations elicited by these bipolar stimuli were obtained and categorized as: 1) Auditory sensations only, 2) Mixed sensations (both auditory and non-auditory), 3) Side Effect (non-auditory sensations) or 4) No Sensation. In addition, the sensations elicited by monopolar higher-rate pulse-train stimuli similar to that used in processor programming were also measured for all electrodes in the ABI array and classified using the same categories. Comparisons were made between evoked response morphology, bipolar stimulation sensation and monopolar stimulation sensation.

Results—Sensations were classified for 33 bipolar pairs as follows: 21 pairs were Auditory, 6 were Mixed, 5 were Side Effect and 1 was No Sensation. When these sensations were compared to the electrically-evoked response morphology for these signals, P3 of the electrically-evoked auditory brainstem response (eABR) and the presence of a middle-latency positive wave, usually between 15 and 25 ms (eMLR), were only present when the perceptual sensation had an auditory component (either Auditory or Mixed pairs). The presence of other waves in the early-latency response such as N1 or P2 or a positive wave after 4 ms did not distinguish between only auditory or only non-auditory sensations.

For monopolar stimulation, 42 were classified as Auditory, 16 were Mixed and 26 were classified as Side Effect or No Sensation. When bipolar sensations were compared to monopolar sensations for the 21 bipolar pairs categorized as Auditory, 7 pairs had monopolar sensations of Auditory for both electrodes, 9 pairs had only one electrode with a monopolar sensation of Auditory, with the remainder having neither electrode as Auditory. Of 6 bipolar pairs categorized as Mixed, 3 had monopolar auditory sensations for one of the electrodes.

When monopolar stimulation was compared to evoked potential morphology elicited by bipolar stimulation, P3 and the eMLR were more likely to be present when one or both of the electrodes in the bipolar pair elicited an Auditory or Mixed sensation with monopolar stimulation and were less likely to occur when neither of the electrodes had an auditory monopolar sensation. Again, other eABR waves did not distinguish between auditory and non-auditory sensations.

Conclusions—ABI electrodes that are associated with auditory sensations elicited by bipolar stimulation are more likely to elicit evoked responses with a P3 wave and/or a middle-latency wave. P3 of the eABR and M15-25 of the eMLR are less likely to be present if neither electrode of the bipolar pair evoked an auditory sensation with monopolar stimulation.

Introduction

The auditory brainstem implant (ABI) was developed at the House Ear Institute (Hitselberger et al., 1984) to provide auditory sensations to patients with neurofibromatosis type 2 (NF2) whose auditory nerve function was compromised during tumor removal from the VIIIth cranial nerve. The device stimulates the cochlear nucleus (CN) using an array of surface electrodes. The stimuli are controlled by an external processor programmed using processing and stimulation strategies developed for cochlear implants. During processor programming in adult patients, electrodes that elicit auditory sensations in response to monopolar stimulation are identified and included in the processor program, whereas electrodes that elicit side-effects (non-auditory sensations) are not used. Until recently, the auditory perceptual abilities of individuals using ABIs were considered to be much poorer than those obtained with cochlear implants. Better auditory perceptual abilities have been reported for individuals implanted with ABIs for reasons other than NF2 (temporal bone injury, ossification or developmental abnormalities, see Colletti et al., 2012) and in some isolated cases of NF2 (Matthies et al., 2014).

During surgery, the placement of the ABI electrode array is guided by the intraoperatively recorded electrically-evoked auditory brainstem response (eABR, Waring, 1995a; Waring et al., 1999; Nevison, 2006; O'Driscoll et al., 2011b) in order to maximize the number of

electrodes eliciting auditory sensations. This use of the response is based on the early work of Waring (1995a,b, 1996, 1998) with early versions of an ABI device. Waring found a variety of eABR waveform morphologies with two positive waves at mean latencies of 0.4 ms and 1.45 ms post-stimulus onset when the ABI electrode array was over the CN. He also reported the presence of an additional positive wave at approximately 2.2 ms in some but not all subjects. The presence of a three-wave response before 2.5 ms was thought to signal activation of the central auditory system. The 2.2 ms wave was considered to be analogous to Wave V of the acoustic auditory brainstem response. In the few subjects tested post-operatively, stimulation of electrodes which produced two- or three-wave responses were associated with the perception of sound as opposed to non-auditory sensation. Repeatable eABR waves with latencies after 4 ms were attributed to motor responses similar to those seen with eABRs from cochlear implant patients (Waring, 1995a, 1996).

O'Driscoll and colleagues (O'Driscoll et al., 2011a) analyzed intraoperative eABRs from 34 adult patients with respect to the morphology of the response and the whether electrodes elicited auditory sensation when the processor was programmed. Cluster analysis of eABR morphology identified four positive waves (P1 to P4) with mean latencies of 0.76, 1.53, 2.51 and 3.64 ms, respectively. P3 was again associated with latencies considered analogous to Wave V of the acoustic ABR. There was a trend for more electrodes with auditory percepts to be present in areas of the electrode pad that evoked eABRs with a larger number of peaks in the waveform. However, the absence of an eABR was not associated with absence of auditory sensation elicited by electrodes in the section of the array stimulated. Therefore the presence of an eABR was considered a good sign, but the absence of an eABR was not of assistance identifying non-auditory electrodes. Similar findings were found in a study of six congenitally deaf children implanted with ABIs in which eABRs were recorded intraoperatively and post-operatively (O'Driscoll et al., 2011b).

These previous reports primarily compared eABR response morphology (elicited by bipolar low-rate pulse stimulation) recorded intraoperatively in anesthetized subjects with the sensations elicited by the higher rate monopolar pulse-train stimulation used postoperatively in programming an ABI processor. There are two confounding issues with these comparisons. First, the two modes of stimulation (monopolar and bipolar) produce different current fields, even when the electrode of the ABI array stimulated monopolarly is also used as one of the electrodes stimulated in the bipolar configuration. Second, there is a difference in patient state and physical environment of the electrode array for intraoperative evoked response recording and postoperative processor programming. During evoked response recording, the patient is anesthetized deeply enough for brain surgery and responses to electric stimulation will likely be different than in the postoperative, unanesthetized state. Also, the electrode array is in an open surgical field during evoked response recording and the electric fields produced in this situation will likely differ from those produced with the surgical field closed and healed.

The primary purpose of the present study was to compare the perceptual sensation produced by electrical stimulation of ABI electrodes to the morphology of the electrically-evoked response produced using the same electric stimuli (biphasic pulses presented at 13 pps in a bipolar electrode configuration) and making both measures postoperatively without

anesthesia. The relationship between post-operative early latency (eABR) and middle-latency (eMLR) responses were recorded on the same day in four adult subjects who were awake for perceptual testing and resting quietly without medication for evoked response recording. Results indicate which eABR and eMLR waves are most likely to be associated with an “auditory” sensation, in other words, a sensation that is classified as sound.

A secondary goal was to study the relation between the electrically-evoked responses and the sensations in different stimulation modes. While responses to bipolar stimulation are typically used to guide placement of the ABI electrodes during surgery, the devices are usually programmed using monopolar stimulation of individual electrodes. This discrepancy in stimulation mode is necessary because monopolar stimulation is accompanied by large stimulus artifacts that obscure the early evoked responses when recording electrically-evoked potentials, yet monopolar stimulation requires less power/current when used in a processing strategy. We show here that there are generally strong relationships between the perceptual responses in the bipolar and monopolar stimulus configurations, but that there can be exceptions.

Materials and Methods

Subjects

Experiments were conducted under a human studies protocol approved by the Massachusetts Eye and Ear Infirmary Institutional Review Board, which conformed to the International Research Code of Ethics (1990). Subjects (Table 1) were four adults, all of whom had a diagnosis of NF2, and who had been implanted with an ABI (Nucleus 24 ABI, Cochlear Corporation) in conjunction with the surgery to remove an acoustic neuroma. All surgeries used a trans-labyrinthine surgical approach for tumor removal and ABI placement. Three subjects (#1, #3, #4) had no hearing in either ear subsequent to tumor removal and used their ABIs daily. One subject (#2) had hearing in the ear contralateral to the ABI (mild loss with 92% single-syllable word recognition score) and did not use the ABI except during her annual ABI clinical visit or during research testing. All subjects used monopolar stimulation, the SPEAK coding strategy (Cochlear Corporation) in their speech processors (SPRINT processors S1,2, and 3, Freedom processor S4) and had 8-10 electrodes active in their processor programs (MAPs). They also had all been activated for over 6 months before data collection. Speech perception ability ranged from sound detection only to some open-set monosyllable recognition.

Stimulation and Perceptual Testing

Monopolar Stimulation—Monopolar biphasic pulse trains (250 pps, 150- μ s phase duration, 8- μ s interphase gap) were generated using the manufacturer's clinical implant programming software (Custom Sound 3.2, Cochlear Corporation). Stimuli were delivered to the patient via a laboratory Freedom processor and coil and the programming pod interface. Similar to methods used in programming a subject's speech processor, psychophysical threshold (T) for each electrode in the ABI array was measured using an ascending, bracketing method starting at current levels below perception (5 clinical units (CL, Cochlear Corporation) ascending step size and 10 CL descending step size). If the

sensation evoked by stimulation of an electrode was auditory, the loudness comfort limit was measured by raising the current level from threshold until the subject reported a just uncomfortable loudness or just uncomfortable side effect (e.g., tactile, bad taste, dizzy feeling). Current was not raised above the just-uncomfortable level, whether auditory or side effect, and the upper limit of the dynamic range (C level) was set 5 CLs under the just-uncomfortable level. The upper limit of auditory and the threshold of side effect was noted as well as the type of side effect.

Bipolar Stimulation—Stimuli were generated by custom-written software using the Nucleus Implant Communicator (NIC) drivers and hardware (Cochlear Corporation). Again, stimuli were delivered to the patient via a laboratory Freedom processor and coil and the programming pod interface. Bipolar stimulation used biphasic single pulses that alternated in polarity (13 pps, 150- μ s phase duration, 8- μ s interphase gap) for both perceptual and electrophysiological measures. The phase of the biphasic pulse alternated between anodic and cathodic to provide optimal cancellation of stimulus artifact in electrophysiologic testing. Bipolar electrode pairs were selected to sample different areas of the ABI electrode pad (Nevison, 2006) as is done for intraoperative testing. Figure 1 illustrates the bipolar electrode pairs used for perceptual and electrophysiologic tests. Electrode pairs across the medial and the lateral regions of the electrode array were separated by two electrodes, for example stimulating electrode 12 and return electrode 21. Electrode pairs across the inferior and superior regions had a smaller stimulation area being separated by a single electrode. The electrode pairs selected were the same across subjects whenever possible, exceptions occurred either due to subject time constraints or the quality of the recordings. Similar to monopolar stimulation, the psychophysical threshold was measured for each bipolar electrode pair used in subsequent evoked potential recording by using an ascending, bracketing method starting at current levels below perception (5 CL ascending step size and 10 CL descending step size). The loudness comfort limit was measured for these bipolar pairs by raising the current level from threshold until the subject reported just-uncomfortable loudness or just-uncomfortable Side Effect sensations (tactile, bad taste, dizzy feeling). Current levels were not raised above the just-uncomfortable level. The C-level was designated as 5 CLs below the just uncomfortable level.

Analysis—Results of perceptual testing were used to categorize single electrodes (for monopolar stimulation) or electrode pairs (for bipolar stimulation) into four Electrode Types based on the sensations elicited over the stimulus-level range from threshold to just uncomfortable (i.e the dynamic range of stimulation):

1. *Auditory*: only auditory sensations reported,
2. *Mixed* - an auditory sensation at low current levels with the addition of side effects at higher current levels,
3. *Side Effect*: only non-auditory sensations reported (no auditory sensations)
4. *No Sensation*: no sensations, either auditory or side effects, were reported up to the current limits of the equipment.

These same four terms were used to categorize the sensations experienced at the stimulus level used for bipolar stimulation when measuring evoked potentials. In this case they are labeled Reported Sensations.

Electrical evoked response recording

Instrumentation and Response Recording—Electrical evoked potential recordings in response to bipolar stimulation were made while the subject rested quietly on a stretcher in an electrically-shielded sound treated room. Neither anesthesia nor medication was used. Electroencephalic (EEG) activity was recorded using a surface electrode montage of Cz (+) to C7 (reference) with a ground at midline on the nape (Waring, 1995a) in order to minimize stimulus artifact. Using a custom-programmed evoked-potential system, EEG activity was amplified and filtered (20K, 5-5000 Hz, TDT Bio-Amp System) then digitized (National Instruments 6251, 16-bit D/A, 20K sampling rate) for 70 ms after each biphasic pulse. Myogenic activity was eliminated by a custom artifact rejection algorithm (US Patent no 6,718,199) that was set to skip the time period of stimulus artifact. Separate buffer averages were kept for cathodic leading pulses and anodic leading pulses. The number of sweeps included in each leading phase buffer was kept equal for optimal cancellation of stimulus artifact when the two buffers were combined into one response to alternating leading phase pulses. Simultaneous acquisition of the separate averages with opposite leading phase aided in judging repeatability of the response and in determining phase-related signal artifacts. The number of sweeps per response was most commonly 4000 but ranged from 2000 to 10,000 depending upon the size of the response and repeatability of the waveform for the separate phase averages. Imperfect cancellation of the alternating pulse polarities resulted in a residual stimulus artifact which was manually blanked from each trace. Transcutaneous RF communication between the NIC hardware and the implanted receiver/stimulator created periodic transient artifacts which were removed using template subtraction and principal component analysis.

Stimulus Level—For Auditory electrode pairs, the stimulus current level for most evoked response recordings was between the most comfortable loudness and the limit of comfortable loudness. For Mixed and Side Effect electrode pairs, the current level used was limited by the presence of a side effect. If a side effect was uncomfortable, then evoked responses were recorded at a stimulus level just below the side effect threshold. In some instances, however, subjects reported that the side effect was not uncomfortable and was tolerable for the stimulation period (5-10 minutes) needed for evoked potential recording. In these instances, evoked potentials were recorded just above the threshold level of the side effect. (The only tolerable non-auditory sensations reported were tactile sensations of the head and neck.) Stimulus level was at the current limits of the instrumentation for electrode pairs that elicited No Sensation.

The sensation reported for the current level used for evoked potential recording was categorized using the same definitions as those used for Electrode Type and is referred to as Reported Sensation. Consequently, for Mixed and Side Effect Electrode Types, the Reported Sensation at the current level used for the evoked potential recording could be different than the Electrode Type (which included sensations from the threshold of sensation to the just

uncomfortable level). For example, if over an electrode pair's stimulation range, the only sensation was a side effect and the evoked potentials were recorded at a level that was below the side effect sensation because the side effect was intolerable, the Reported Sensation at the recording level was “No Sensation”. The Electrode Type, however, was “Side Effect” because at a higher current level a side effect was elicited, just not at the level used to record the evoked response. Alternatively, if the side effect was tolerable and the level for evoked potential recording was above the side-effect's threshold and both the Electrode Type and the Reported Sensation would be labeled “Side Effect.”

Analysis—Electrical evoked responses to bipolar stimulation were analyzed by identifying and measuring the latencies of replicable waves in the latency ranges associated with N1, P2, and P3 (as outlined by Waring, 1996), and also the latency ranges of P3-6 ms, N7-10 ms, P10-16 ms, M15-25 ms and M26-30 ms as illustrated in Figure 3. Since P1 was not easily distinguished from stimulus artifact, the latency of N1 was measured instead. The total number of waves present in each latency range was tabulated across subjects and the mean latency and range of latencies for each wave was calculated for each sensation category of electrode pair and the Reported Sensation for the stimulus level of the evoked response recording. Contingency analysis (Chi-square) was used to analyze the association of bipolar sensations and monopolar sensations with the presence or absence of P3 and eMLR waves.

Results

Sensations for Monopolar and Bipolar Stimulation

Figure 1 summarizes the results of the perceptual sensation categorization for both monopolar and bipolar stimulation for each subject. Sensations elicited by monopolar stimulation over the entire dynamic range of stimulation (Electrode Types) are coded by the color of each circle (electrode). Electrodes producing Auditory and Mixed sensations (green and orange circles) will be referred to as “effective” electrodes because these electrodes can be used in the processor programming. The effective electrodes were grouped together on the pad. In one case (Subject 2), this grouping extended the full medial-lateral extent of the electrode array; however in the other three subjects, the electrodes at the most medial edge were ineffective. In the other dimension (inferior/superior), three of the four subjects had groupings of effective electrodes that spanned the array, but one (Subject 4) did not. Subject 2 had the highest number of effective electrodes (19) and subject 4 the fewest (10). When totaled for all electrodes of all subjects, there were 42 electrodes (out of a total of 84 electrodes) that were Auditory; another 16 were Mixed. In all, 69% of all electrodes were effective.

Bipolar Electrode Types are coded on the ovals outside of the electrode pad in Figure 1, with the numerals indicating the two electrodes used for the bipolar pair. When totaled for all tested pairs of all subjects, there were 21 pairs (out of a total of 33 tested) that were Auditory; another 6 were Mixed. Thus, in all, 81.8% of the tested electrode pairs were effective. Of the remaining pairs, five elicited Side Effects only and one gave No Sensation up to the maximal current stimulation limit.

The relationships between the sensations for monopolar stimulation and bipolar stimulation are illustrated in Figure 2. Each bipolar pair is indicated by a horizontal line whose color represents the bipolar stimulation percept. The circles at each end of the line correspond to the monopolar percept of each electrode in the bipolar pair. For electrode pairs in which each individual monopolar electrode elicited Auditory sensation (two green circles for a pair), bipolar stimulation always elicited Auditory sensation. Each subject had at least one example of this situation and the summary of all subjects (Fig. 2, lower panel) indicates there were 7 examples in the dataset. When just one of the monopolar electrodes elicited Auditory sensation (one green circle and one non-green circle on the figure), 9 of 15 such pairs elicited sensations that were Auditory, 3 were Mixed, and 3 were Side Effect when using bipolar stimulation. These Auditory bipolar-stimulation sensations were not more likely to occur if adjacent (unstimulated) electrodes were Auditory monopolar electrodes.

Three electrodes elicited non-auditory (Side Effect) in monopolar stimulation but when paired in bipolar stimulation elicited Auditory sensations. These pairs were along the inferior edge of the array of Subject 4 (3-12 & 12-21). Subject 4 was also the least consistent in his perceptual reporting of sensation. If his sensations are not considered, then an effective bipolar pair (either Auditory or Mixed) has at least one effective monopolar (Auditory or Mixed) electrode in the pair.

Evoked Response Morphology and Subject Sensations

Figure 3 shows selected examples of evoked potentials acquired in response to bipolar stimulation. The colored ovals indicate the Electrode Type for the bipolar pair eliciting the response. The Reported Sensation (sensation experienced at the stimulus level used during recording) is given in parentheses under each oval. Each response is plotted on two time scales: 10 ms (left) to better illustrate the eABR and 70 ms (right) to better illustrate the eMLR. Responses labeled A, B and C are recorded from effective electrode pairs that elicited auditory sensations only or auditory sensations mixed with some side effects at the higher current levels. Responses D, E and F are from electrode pairs that elicited only side effects or did not elicit any sensation at the current limits of the software, i.e. non-effective electrodes.

In the eABR response A of Figure 3, the first negative wave, N1, and the first two positive waves, P2 and P3 have been identified according to the nomenclature used by Waring (1995a,b, 1996, 1998). There is also a small positive wave around 6 ms. Waves N1, P2 and P3 were often observed in recordings from electrode pairs that evoked auditory sensations and are also present in Response B. In addition, Response B has a much larger positive to negative wave after 3 ms. These two responses, A and B, were both recorded between the most comfortable and the limit of comfortable loudness and were from bipolar pairs eliciting auditory sensations over the entire dynamic range. Response C was recorded from an electrode pair with both Electrode Type and Reported Sensation classified as *Mixed*. It is unclear whether the broad positive wave after P2 contains P3 or just a later positive wave.

Examples of eABR responses from non-effective electrodes in Figure 3 are labeled as D, E and F. The amplitude of these waveforms are much smaller than Response A, B and C although the N1, P2 and a broad positive wave with a latency after 3 ms (categorized as P3.5

to 6) are present in D and E. The subject reported a side effect at the current level of evoked response recording (D) while the current level for E is below the side effect perceptual level. N1 and P2 are present in both D and E. When there is no sensation elicited by stimulation (F), no waves are present in the eABR time window.

eABRs were recorded for 30 of the 33 bipolar pairs that had been tested for perceptual sensation (responses to 3 of the bipolar pairs were not recorded due to time constraints or subject state). Twenty-four of these 30 bipolar electrode pairs were effective, 18 elicited only Auditory and 6 elicited Mixed sensations. Of these effective electrode pairs, 22 (92%) had an identifiable P3 in the eABR (Table 2A, total frequency of P3 for Auditory and Mixed Pairs). P3 was not judged to be present in any of the non-effective electrode pairs.

The right-column traces in Figure 3 contain the same responses as the left column but are plotted on 70 ms time scales to better visualize the electrical middle-latency response (eMLR.). The most frequently observed peak for effective electrodes (Responses A-C) is the one designated M15-25. In a few cases, there was a positive wave later than 25 ms. For the ineffective pairs of D-F, there are no repeatable waves in the eMLR between 15 and 25 ms or later than 25 ms. eMLR responses were available for 24 electrode pairs, 19 of which were effective pairs. MLR wave M15-25 (Table 2B) was identified in the recordings from 17 (89%, total frequency of M15-25 for Auditory and Mixed Pairs) of these 19 effective pairs.

Table 2A and 2B summarize frequency tabulations of the eABR and eMLR waves and the corresponding latency (mean and range) for each Electrode Type. The waves N1, P2 and P3 were identified following the guidelines reported by Waring (1995a,b, 1996, 1998). Repeatable waves at other latencies were grouped according to a latency range, i.e., a positive wave with a peak latency between 3.5 and 6 ms was a P3.5-6 wave. A negative wave with a latency between 7 to 10 ms was a N7-10 wave. P3 of the eABR and all three of the eMLR waves tabulated were present only for effective electrode pairs (only if an auditory sensation was reported with or without an accompanying side effect; first three columns of each table). Chi-square analysis indicated a significant association between the presence of P3 and an effective bipolar pair (RSquare=0.70, $p<0.0001$) and a significant association between the presence of an eMLR and an effective bipolar pair (RSquare=0.55, $p<0.0001$). The presence of either a P3 or an eMLR identified all of the effective bipolar pairs (RSquare = 1.0, $p<0.0001$).

eABR waves N1, P2, P3-6, and N7-10 were present for both effective and non-effective electrode pairs, i.e., for auditory sensations and for side effect sensations either singly or when mixed with auditory sensations. Interestingly, these waves were also present below the level of perceived sensation (Electrode Type: *Side Effect*; Reported Sensation: *No Sensation*). No waves were present in the recording from the one bipolar pair of: Electrode Type: *No Sensation*; Reported Sensation: *No Sensation*.

Relationship of Bipolar Evoked Potential Morphology and Monopolar Pulse Train Sensation

Table 3 combines the information from Figures 1, 2 and 3 and Table 2A and 2B to more easily evaluate the relationship between the electrically-evoked responses to bipolar

stimulation and the sensations elicited with the monopolar stimulation that is most commonly used for processor programming (higher-rate monopolar pulses). The binary categorization of effective (Auditory or Mixed) or non-effective (Side Effect or No Sensation) Electrode Types is used for the monopolar sensation evoked for each electrode in the bipolar pair. This classification is then combined with the frequency (percentage of total number of bipolar recordings) exhibiting the listed eABR and eMLR waves. P3 and the MLR are less likely to be present if neither of the electrodes in the bipolar pair evoke an auditory sensation with monopolar stimulation. This likelihood did not reach significance.

Discussion

Sensations and Patterns of Effective Electrodes

The pattern of sensations from activating individual electrodes or pairs (Figure 1) gives an indication of the alignment of the array with the underlying cochlear nucleus. In all subjects, the electrodes producing Auditory sensation for monopolar stimulation were grouped together. Electrodes producing Mixed sensation were sometimes found along the edges of this group (Subjects 3 and 4). In Subject 2, the Auditory electrodes extend to the edges of the array suggesting that the electrode array was well positioned on the CN. The other subjects had an apparent misalignment of the electrode array so that electrodes on one edge did not provide effective sensations. For instance, only Side Effect or No Sensation Electrode Types were reported for the most medial electrodes of Subjects 1 and 3 (Fig. 1). In this case, perhaps if the array had been positioned more laterally, there may have been more Auditory Electrode Types. Similarly, the most inferior electrode row for Subject 4 were Side Effect Electrode Type, consistent with the array missing the superior edge of the CN. In none of the subjects did Side Effect and No Sensation Electrode Types completely surround Auditory and Mixed Electrode Types suggesting that the “stimulatable” CN may extend beyond the limits of the electrode array. The ABI array dimensions are about 3.0 mm by 8.5 mm (O'Driscoll et al., 2011a) and this is well matched to the size of the human CN, which is about 3 mm in the rostro-caudal dimension and 10 mm in the medio-lateral dimension (Moore and Osen, 1979; Mobley et al., 1995). If surgically feasible, however, a slightly larger electrode pad might increase the probability of stimulating more of the CN.

Evoked Responses and Bipolar Stimulation Sensations

The comparison between electrically-evoked responses and perceptual sensations from an ABI presented in this report is unique in several areas: 1) the evoked responses (eABRs and eMLRs) were recorded without medication or anesthesia, 2) the evoked responses and perceptual responses used to identify associations were elicited using the same stimulus, 3) the sensations associated with bipolar stimulation were compared to the sensations elicited by the monopolar stimulation used in programming the processor. Previous reports (Waring, 1995a, 1998; Nevison, 2006; O'Driscoll et al., 2011a) compared the eABR recorded under anesthesia to the perceptual sensations reported during the monopolar stimulation used in processor programming (pulse trains), and concluded that the presence of multiple waves, often including P3, was a positive but not definitive indication of auditory sensations with monopolar stimulation. Only one previous report recorded evoked potentials in non-anesthetized subjects (O'Driscoll et al., 2011b). Similar to the previous reports, the present

study found that P3, or a positive wave around 2.0 ms was most frequently associated with auditory perceptions of the bipolar pulse stimulus and more likely to be present if one of the electrodes in the bipolar pair evoked an auditory sensation with monopolar stimulation.

The eMLR results (the first reported for the ABI), like the eABR results, also demonstrated an association with auditory perceptions elicited by bipolar and monopolar stimulation. The presence of eMLR waves was more frequently associated with reported auditory perceptions. This association is consistent with Waring's conclusion (Waring, 1998) that P3 represented transmission of stimulation up the auditory afferent pathway. Similarly, the presence of eMLR would represent continuation of this transmission. Because of the unknown influence of anesthesia on the eMLR, P3 remains the most clinically useful wave to guide intraoperative placement of the electrode with the goal of maximizing the number of electrodes eliciting auditory sensations when programming. Currently the ABI is only FDA approved for ages 12 and up in patients with NF2. However, ABIs have been implanted in children in Europe for over ten years and there are now three FDA approved clinical studies of ABIs in children without NF2 in the USA. The eMLR may be useful in post ABI implantation to evaluate and track maturation of the auditory pathway in children, as has been reported for children with cochlear implants (Sharma and Dorman, 2006).

The other waves of the eABR did not distinguish between auditory or non-auditory sensations. Of interest, was that a positive wave after 4 ms, often reported as indicating the presence of a side effect (Waring, 1996; Nevison, 2006), was frequently seen in electrode pairs that did not evoke non-auditory sensations and in pairs that evoked only non-auditory sensations. Consequently, this wave as well as N1 and P2 do not appear to be useful in identifying Auditory or Side Effect areas of the ABI electrode pad although they are associated with the elicitation of a sensation, either auditory or non-auditory. No waves were present for the one electrode pair that had no reported sensation. The absence of an evoked response for an area of the pad that did not elicit any sensation and the presence of a response for areas eliciting any type of perceptual sensation was also found by Otto (Otto et al., 2005) for measurements of the NRT (Neural Response Telemetry) from ABI electrodes who concluded that the presence of the response represented neural activation but did not discriminate the type or area of activation.

Bipolar Evoked Potential Morphology and Monopolar Pulse Train Sensation

The comparison of the bipolar single-pulse perceptual sensation to the monopolar pulse train stimulation used in processor programming resulted in the limited conclusion that P3 and the eMLR were more likely to be present for a bipolar pair if one of the electrodes in the pair elicited an auditory sensation with monopolar stimulation (Table 3). This conclusion reinforces the current clinical practice of guiding the intraoperative placement of the electrode pad using P3 and assists in identifying which areas of the electrode pad may be most useful when programming the processor. This is a much more limited use of the electrical evoked potential than is available with cochlear implant where eABR measures have been used to estimate T and C levels and the differences between bipolar single-pulse and monopolar pulse train stimulation are primarily dependent upon the stimulus rate and perceptual auditory integration of pulse trains versus single pulses (Brown et al., 1996).

Conclusions

While the conclusions of this study are limited by the small number of subjects, several interesting associations were observed. P3 of the eABR and the eMLR were associated with auditory sensations for bipolar stimulation of ABI electrodes pairs. P3 was present in 92% of the pairs that had some auditory sensation and the eMLR was present in 89% of the pairs with some auditory sensation. P3 and the eMLR were not present in electrode pairs that did not elicit auditory sensations with bipolar stimulation. With respect to sensations elicited with the monopolar stimulation used for processor programming, P3 and the MLR are less likely to be present than other eABR waves if none of the electrodes in the bipolar pair evoke an auditory sensation with monopolar stimulation.

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Figure 1.

Schematics of the ABI electrode arrays for each subject and type of stimulation. The numbered circles represent the individual electrodes in the ABI array; the color of the circle codes the percept elicited by monopolar stimulation (see key at top) over the range of currents tested. The ovals outside the ABI array represent the bipolar electrode pairs used for eABR recordings. The color of the ovals code the percept elicited by bipolar stimulation over the range of currents tested. The subject number and the orientation of the ABI array which is dependent upon the side of implantation (superior, etc.) are indicated for each subject. The cable connection of the array to the receiver stimulator is indicated by a box on the left side. (Note for Subject 3 the bipolar pairs tested were different from the other subjects because the Subject was only available for a limited time. Similarly, for Subject 4 Electrode pair 11 to 12 was not tested).

Figure 2.

Data from Figure 1 plotted to show the relationship between sensation for monopolar stimulation (x-axis, circles) and bipolar stimulation (y-axis, horizontal lines). Color conventions are the same as those used for Figure 1. Data are shown for individual subjects and for all data (bottom plot).

Figure 3.

Response waveforms from bipolar stimulation in quietly resting subjects. The stimulus began at time 0. The same responses are plotted on two time scales: in the left column, the time scale runs from 0 to 10 ms and in the right column the time scale runs from 0 to 70 ms. Shading indicates the observed range for P3 (left) or P15-25 (right). The subject's perception for stimulation of the bipolar pair for the entire dynamic range is labeled within the colored ovals; the subject's perception of sensation at the current level used for EABR recording is in parentheses under the ovals. A) Subject 1, electrode pair 11-20; B) Subject 2, electrode pair 13-22; C) Subject 1, electrode pair 12-21. D) Subject 2, electrode pair 21-20, E) Subject 2, electrode pair 4-13, and F) Subject 4, electrode pair 20-21.

Table 1

Subject characteristics and results of speech perception testing for each subject with their ABI. All subjects were assessed with The Early Speech Perception test (ESP) (Moog and Geers, 1990) and the Category level achieved is given. ESP Categories are: Category 1 - Detection, Category 2 - Pattern Perception, Category 3 - Some Word Identification, Category 4 - Consistent Word Identification. Subjects who achieved the highest category of perception, Category 4, were also tested with the Consonant-Nucleus-Consonant monosyllable (CNC) test (House Ear Institute). All speech materials were recorded.

Subject	Gender	Age at Implant	Implant Side	# Electrodes in MAP	ESP Category	CNC Score
1	Female	48	Left	10	2	-
2	Female	16	Right	10	4	10%
3	Male	31	Right	10	4	20%
4	Male	34	Left	8	1	-

*** Subject 2 does not use her ABI; she has useable hearing in her left ear

Table 2

A) Frequency and Latency of eABR waves identified for all subjects categorized according to the Electrode Type (sensations experienced over the entire dynamic range) and the Reported Sensation (sensations experienced at the current level used in the eABR recording). B) A similar tabulation of the frequency and latency of eMLR waves for the same subjects responses. Further details are in the manuscript.

Frequency and Latency of EABR Waves									
Electrode Type	Auditory		Mixed		Side Effect		No Sensation		
Reported Sensation	Auditory		Auditory		None	Side Effect	None	Side Effect	None
	(18)		(3)		(3)	(2)	(1)		
N1									
Freq	17		1	3	2	2	0		
Mean (ms)	0.80		0.84	0.83	0.94	0.89			
Range (ms)	0.68-0.96		0.00	0.80-0.86	0.88-1.00	0.88-0.90			
P2									
Freq	17		1	3	2	2	0		
Mean (ms)	1.35		1.30	1.31	1.64	1.66			
Range (ms)	1.12-1.82		0.00	1.28-1.34	1.48-1.80	1.58-1.74			
P3									
Freq	17		3	2	0	0	0		
Mean (ms)	2.55		2.22	2.82					
Range (ms)	1.82-3.40		1.86-2.86	2.74-2.90					
P3.5-6									
Freq	16		1	3	2	2	0		
Mean (ms)	4.54		5.48	3.43	4.34	3.82			
Range (ms)	3.60-5.32		0.00	3.04-4.14	3.76-4.92	3.68-3.96			
N7-10									
Freq	15		2	3	2	2			
Mean (ms)	8.38		8.85	10.23	6.12	8.54			
Range (ms)	7.52-9.16		8.50-9.20	8.80-11.98	5.04-7.20	7.80-9.28			
Frequency and Latency of EMLR Waves									
Electrode Type	Auditory		Mixed		Side Effect		No Sensation		
Reported Sensation	Auditory		Auditory		None	Side Effect	None	Side Effect	None
	(14)		(2)		(3)	(2)	(1)		

Frequency and Latency of EABR Waves									
Electrode Type	Auditory		Mixed		Side Effect		Side Effect		NoSensation
Reported Sensation	Auditory	Mixed	Auditory	Mixed	Mixed	None	Side Effect	Side Effect	None
	(18)	(3)	(3)	(3)	(3)	(3)	(2)	(2)	(1)
P10-16	Freq	4	1	0	0	0	0	0	0
	Mean (ms)	12.90	12.88						
	Range (ms)	10.80-15.20							
M15-25	Freq	12	2	3	0	0	0	0	0
	Mean (ms)	21.43	23.36	19.37					
	Range (ms)	18.24-23.92	21.92-24.80	18.72-20.56					
M>25	Freq	2	0	2	0	0	0	0	0
	Mean (ms)	26.64		26.32					
	Range (ms)	25.76-27.52		26.84-25.94					

Table 3

Percent frequency of the eABR and eMLR waves from bipolar stimulation categorized by the Electrode Type for each electrode of the bipolar pair for monopolar stimulation. Effective/Effective represents a bipolar pair for which each electrode elicits effective stimulation (Auditory or Mixed) when stimulated with monopolar pulse trains. Effective/Not Effective represents bipolar pairs for which one electrode elicits effective stimulation with monopolar stimulation but the other electrode does not. Not Effective/Not Effective indicates neither electrode in the bipolar pair elicits effective stimulation with monopolar stimulation.

Monopolar Sensations for each electrode in Bipolar Pair	(n)	eABR			eMLR		
		N1	P2	P3	P3.5.6	(n)	MLR
Effective/Effective	14	79%	79%	86%	79%	11	91%
Effective/Not Effective	11	91%	91%	82%	82%	11	64%
Not Effective/Not Effective	5	80%	80%	20%	80%	5	60%