Neural Response Telemetry and Auditory/Nonauditory Sensations in 15 Recipients of Auditory Brainstem Implants

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Abstract

Auditory brainstem implants (ABIs) provide a means of restoring some hearing sensations to individuals with neurofibromatosis type 2 (NF2) who are deaf after vestibular schwannoma removal. In this study, neural response telemetry (NRT) was used to record electrically evoked neuronal activity near the ABI electrode array in 15 such subjects. Our interest was to investigate whether NRT recordings from the brainstem might be useful in implanting or programming ABIs. We therefore sought relationships between postoperative NRT recordings and the sensations reported by the subjects in response to the test stimuli. However, no clear relationships among these variables were found, and it was not possible to differentiate recordings associated with auditory versus nonauditory sensations. The findings suggest that the categorization of NRT recordings used in this study is inappropriate for assisting with placement of an ABI electrode array intra-operatively or for programming the sound processor postoperatively.

Key Words: Auditory brainstem implant, neural response telemetry, neurofibromatosis type 2

Abbreviations: ABI = auditory brainstem implant; CI = cochlear implant; MP1 = remote ball electrode; MP2 = remote plate electrode; NF2 = neurofibromatosis type 2; NRT = neural response telemetry

Sumario

Los implantes auditivos del tallo cerebral (ABI) ofrecen la posibilidad de restaurar ciertas sensaciones auditivas a individuos con neurofibromatosis tipo 2 (NF2) quienes han quedado sordos después de la remoción de un schwannoma vestibular. En este estudio, se utilizó la telemetría de respuesta neural (NRT) para registrar, en 15 sujetos, la actividad neuronal eléctricamente evocada cerca de los electrodos de un ABI. Nuestro interés fue investigar si los registros de la NRT del tallo cerebral serían útiles para implantar o programar los ABIs. Por lo tanto, buscamos relaciones entre los registros de la NRT post-operatoria y las sensaciones reportadas por los sujetos en respuesta a los estímulos de la prueba. Sin embargo, no se encontró una relación clara entre estas variables, y no fue posible diferenciar los registros asociados con sensaciones auditivas versus no auditivas. Los hallazgos sugieren que la categorización de los registros de la NRT utilizada en este estudio es inapropiada para ayudar en la colocación intra-operatoria de un arreglo de electrodos para ABI, o para la programación post-operatoria del procesador de sonido.
Auditory brainstem implants (ABIs) provide a means to restore partial hearing in individuals having neurofibromatosis type 2 (NF2) who are deaf after vestibular schwannoma removal. More than 170 patients have received an ABI at House Ear Institute since 1979 when the first ABI was implanted. During this time, the device was upgraded to a multichannel system (Laszig et al, 1996; Otto et al, 1998), and in October 2000 the Nucleus multichannel ABI (Cochlear Limited, Australia) was formally approved by the U.S. Food and Drug Administration. Details regarding the ABI and its use have been reported elsewhere (e.g., Otto et al, 2002a, 2002b).

The latest model of the Nucleus auditory brainstem implant (ABI24M) has the same receiver/stimulator as the CI24M cochlear implant (CI). A feature of these devices is a technique, neural response telemetry (NRT), for recording near-field neuronal activity evoked by the electrical stimuli (Carter et al, 1995; Abbas et al, 1999; Lai and Dillier, 2000). NRT utilizes a modified version of the forward-masking artifact subtraction paradigms described by Charlet de Sauvage et al (1983) and Brown et al (1990) to recover the electrically evoked compound action potential. The technique has been used in fitting young children with cochlear implants (Hughes et al, 2001).

The NRT capability of the ABI24M offers an opportunity to measure neuronal activity elicited by electrical stimulation of the human cochlear nucleus, but interpretation of the recordings could be problematic. The NRT technique has been successfully used to record auditory neural responses with cochlear implants because usually the only neurons that can be stimulated from within the cochlea are the spiral ganglion cells. Thus, it is quite likely that a compound action potential recorded by NRT in the cochlea will be generated by auditory neurons and associated with auditory sensations.

Action potential generation is not specific to auditory neurons, however. All neurons that generate action potentials when electrically stimulated undergo similar electrochemical processes in their cell membranes and thus will produce qualitatively similar compound action potentials. Consequently, in the brainstem, where there are many different groups of neurons, it may not be clear which neurons contribute to a given compound response. Even in the immediate vicinity of the auditory neurons of the cochlear nucleus, there are also nonauditory neurons, as evidenced by the relatively common nonauditory sensations reported by ABI patients, often simultaneously with hearing sensations (Shannon et al, 1993; Otto et al, 1998; Ebinger et al, 2000; Nevison et al, 2002; Otto et al, 2002a). This could complicate or confound interpretation of NRT recordings made with an ABI.

In this study, an indication about the modality of each recorded neural response was obtained by asking the ABI recipients to report the nature of any sensations, nonauditory as well as auditory, experienced during postoperative NRT testing. We then sought relationships between the NRT recordings and the reported sensations, to determine whether auditory NRT recordings could be distinguished from nonauditory NRT recordings. This study was intended to address the questions of whether the NRT procedure might be useful intra-operatively for accurately placing the ABI electrode array, or postoperatively for programming the sound processor.
METHODS

Fifteen ABI subjects with NF2 (age range 15–54 years; 7 males, 8 females) were tested after vestibular schwannoma removal and ABI implantation. The duration of deafness at the time of initial ABI stimulation was less than one year for the majority of subjects, but one subject had been deaf for three years. The data reported in this study were collected during a test session that occurred 2–6 months postoperatively for 14 subjects and 12 months postoperatively for 1 subject. All subjects were postlingually deafened recipients of the most recent Nucleus ABI (ABI24M), which incorporates the NRT feature. Otherwise, subjects were not selected or excluded for any special characteristics.

The ABI24M has a 21-electrode array (Figure 1) that is surgically placed on the surface of the cochlear nucleus in the brainstem. Accurate placement is assisted by monitoring the electrically evoked auditory brainstem response recorded via scalp electrodes (Waring, 1995a, 1995b, 1996, 1998). To sample the electrode array for postoperative NRT testing, six stimulating electrodes were used (3, 8, 9, 14, 15, 20). The electrodes used for recording were located two electrodes away from each stimulating electrode, and in the same row (9, 2, 15, 8, 21, 14, respectively). The remote ball electrode (MP1) was used as the return for stimulation, and the remote plate electrode (MP2) as the reference for recording.

The focus of the present study was to try to relate NRT waveform morphology to the subject’s perceptual experience. Prior to an NRT run, the stimulus level typically was increased to achieve a maximum comfort level auditory sensation or, in the case of nonauditory sensations, a level that was tolerable for the short duration of the test run. When no sensations were elicited by stimulation via an electrode, the maximum stimulus level available from the software was used. The NRT run (a descending series) was then initiated, the subject reported immediately in their own words what they heard and/or felt in response to the NRT stimulation, and the experimenter recorded these observations. One experimenter (SO) was responsible for all the testing. Other details of the NRT test procedures have been described elsewhere (Lai, 1999). About half of the recordings were made with the NRT version 2.04 software, the remainder with NRT version 3.0. Data acquisition is the same with both versions.

In pilot work for this study, a variety of NRT test parameters were evaluated.

Figure 1. The electrode array of the multichannel auditory brainstem implant (ABI) showing the electrodes used for neural response telemetry (NRT) testing. See text for details.
Effective parameters for ABI testing were found that are generally similar to those used with cochlear implant recipients: probe pulse duration = 50 µsec/phase, amplifier gain = 60 dB, measurement delay = 50 µsec, stimulus rate = 80 Hz, masker advance = 500 µsec, masker offset = 10, masker pulse duration = 50 µsec/phase, and average = 200 sweeps. The NRT data were collected in high-resolution mode and analyzed using the standard A-(B-[C-D]) subtraction paradigm available in the NRT software (A = probe-alone response, B = masker + probe response, C = masker-alone response, D = amplifier switch-on artifact; Lai, 1999).

Subsequent to the data collection sessions, the NRT recordings were reviewed and classified independently by two of the authors (SO, MW) who then collaborated and came to agreement on each assignment. Although the primary author (SO) had access to the subjects’ perceptual outcomes and therefore was not totally blinded during his initial classification, the second author (MW) was blinded to the perceptual outcomes and served as a control. Classification was based on both a comparison of the low-resolution components and an examination of trends in the high-resolution series displayed with the Linear Regression correction. Specifically, for a neural response to be considered present, the two low-resolution components had to exhibit similar waveforms (i.e., be “parallel”) and grow together with stimulus level. Although the HiRes (high resolution) Smoothing correction available in NRT version 3.0 was used for making illustrations, it was not used during classification in order to avoid obscuring any significant details, especially in the many low-amplitude waveforms (on the order of 100 µV or less).

The NRT recordings were classified into three categories based on waveform. Those that showed evidence of a negative-positive biphasic neural response waveform like that typical of recordings from cochlear implant subjects were called “CI-like.” Waveforms that were essentially flat were considered “no response.” The remaining waveforms were called “questionable responses” because noise or a long declining ramp prevented determination of the presence or absence of a response.

RESULTS

Fourteen of the 15 ABI subjects were tested on all six stimulating electrodes, but due to time constraints, one subject was tested on only four electrodes. This resulted in a total of 88 postoperative NRT runs consisting of the NRT recordings and the subject reports of auditory and/or nonauditory sensations experienced during each run. The subjects did not have difficulty describing their perceptions.

The NRT recordings were subsequently classified into three categories based on waveform (see “Methods” section). Of the total, 56% were classified as “CI-like,” 15% as “questionable response,” and 29% as “no

Figure 2. Pairs of stimulating and recording electrodes (Stim Elec, Rec Elec) used for NRT testing and the percentage of NRT recordings obtained with each pair that occurred in each waveform category.
response.” Figure 2 shows the percentage of the recordings obtained with each stimulating-recording electrode pair that occurred in each category. The frequency of occurrence of CI-like responses was approximately the same across electrodes. The distributions for the other two categories were not as uniform, perhaps partly due to the smaller numbers of recordings in each of those categories. Nevertheless, it appeared that roughly similar results were obtained with each tested electrode pair in the array, so results can be pooled across electrodes.

Figure 3 shows the percentage of NRT recordings in each waveform category for which concomitant auditory sensations were reported by the subjects. Eighty-four percent of all CI-like NRT responses were associated with auditory percepts (whether alone or in combination with nonauditory side effects). However, 16% of the CI-like responses were not associated with hearing sensations. Furthermore, auditory sensations also occurred with the other NRT waveform categories. Hearing was associated with 62% of the “questionable responses” and with 35% of the “no response” recordings. Thus, auditory sensations were not exclusively linked to the presence of a CI-like response in the NRT recording.

Nonauditory sensations (e.g., mild tingling, dizziness, visual jittering) likewise occurred with all NRT waveform categories. Figure 4 shows the percentage of NRT recordings in each category for which concomitant nonauditory sensations were reported by the subjects (whether alone or in combination with auditory sensations).
recordings in each category for which concomitant nonauditory sensations were reported by the subjects. Nonauditory side effects (whether alone or in combination with auditory sensations) occurred in about 50% of the cases in the CI-like and “questionable response” categories, and about half as frequently in the “no response” category. Thus, nonauditory sensations were not exclusively linked to any one NRT waveform category. It should be noted that the data presented in Figures 3 and 4 are not mutually exclusive, since stimulation often evoked both auditory and nonauditory sensations simultaneously.

The difficulty relating ABI NRT responses to reported perceptual outcomes is further illustrated in Figure 5, which shows NRT responses recorded from two subjects with four different perceptual outcomes: auditory sensations alone (5A), nonauditory sensations alone (5B), combined auditory and nonauditory sensations (5C), and no sensations at all (5D). Note that all four outcomes yielded CI-like responses. This suggests that all neural sources can generate similar NRT response waveforms. Therefore, the presence of a CI-like response in an NRT recording does not indicate the presence of hearing.

A similar observation was made in the case of the only subject in this study with bilateral implants. This subject received hearing from only one electrode with her first ABI. Therefore, when she required second-side tumor removal, she was implanted with a second ABI, which provided excellent results. NRT testing using selected electrodes on both sides resulted in similar CI-like NRT response waveforms even though the stimulation on the first side caused only side effects or no sensation while that on the second side elicited only hearing sensations. This is further evidence that with ABI
recipients the presence (or absence) of a CI-like neural response is not associated with a specific perceptual outcome.

Although the CI-like NRT responses obtained in this study were associated with various sensations, the waveforms of these responses generally had similar temporal properties. Table 1 shows that the distributions of the positive peak latencies associated with hearing alone, with side effects alone, and with combined hearing and side effects, were essentially the same. Thus, it did not appear that the CI-like neural responses associated with different sensations could be distinguished based on latency.

**DISCUSSION**

The classification of the “CI-like” ABI NRT recordings was based on a qualitative similarity of the waveforms to those typical of cochlear implant recordings, regardless of latency. NRT recordings from CI subjects commonly contain a biphasic neural response waveform having a negative peak (N1) at a latency of 300–400 µsec followed by a positive peak (P1) at a latency of 600–700 µsec (Lai and Dillier, 2000). Only two of the present ABI NRT recordings exhibited waveforms with latencies comparable to these ranges for CI recordings. All the rest of the CI-like records had the appearance of a similar biphasic waveform shifted to shorter latencies, with the assumed negative peak occurring before the onset of sampling at 170 µsec. The positive peak in the ABI recordings usually occurred in the range 400–550 µsec but was most commonly at 400 µsec (Table 1). Thus, the latencies of the peaks in the ABI NRT recordings were typically much shorter than those in CI recordings. Evidently the neural generators of the compound action potentials recorded near the cochlear nucleus have different properties from those in the cochlea.

A possible clue about the difference comes from the large study by Lai and Dillier (2000) in which a small percentage (<10%) of CI NRT waveforms was found to have two positive peaks, often only at higher stimulation levels. In addition to the usual one at 600–700 µsec, there was an earlier positive peak at 400–500 µsec. When this occurred, the negative peak often was so early that it was not visible in the NRT sweep. The explanation considered most likely for such double-peaked waveforms involved the idea proposed by Stypulkowski and van den Honert (1984) that there are two sites of action potential initiation: a lower-threshold site that produces the later response and a higher-threshold site that produces the earlier response. In the bipolar cells of the cochlea, the site that produces the later response ordinarily dominates. The latencies of the present ABI NRT responses are essentially the same as those of the earlier CI responses observed by Lai and Dillier (2000). This suggests that action potentials may be initiated mainly at a different site in the brainstem neurons generating the ABI NRT responses.

The present study sought to determine relationships among three categories of NRT recordings and the concomitant sensations (auditory and nonauditory) reported by the ABI subjects during postoperative testing. However, no clear relationships were found. The lack of any definitive relationship presents two obstacles to using the NRT technique for assisting with positioning the ABI electrode array during surgical implantation. The first obstacle is that hearing sensations were not restricted to CI-like responses but were associated with all

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*Note:* For each type of associated sensation, the number of CI-like NRT recordings having the positive peak at the indicated latency is given.
waveform categories. In particular, 44% of the postoperative NRT records obtained in this study were not CI-like in morphology, being categorized as either “no response” or “questionable response.” Nevertheless, almost half of these non-CI-like waveforms were associated with hearing sensations. This would create a dilemma regarding whether to reposition the ABI electrode array intraoperatively if the NRT waveform showed no clear response. Doing so might result in displacing the array from a location where stimulation actually provided the desired hearing outcome.

It is possible that this obstacle could have been partially reduced by optimizing the recording conditions. Some of the present recordings in the “questionable response” category probably could have been replaced by CI-like records if the measurement delay had been increased from the standard 50 µsec used here. Thus, those recordings in which the later low resolution component shows a neural response waveform but the earlier component exhibits a long declining ramp suggest that a greater delay was needed to avoid saturating the amplifier. Perhaps some of the “no response” records also could have been replaced by CI-like records, if different recording electrodes had been used. The ABI electrode array is not a single row of electrodes as in cochlear implants, so more variation is possible in the recording location relative to the stimulating electrode. Of course, the process of optimizing the recording conditions in an individual case would entail additional time intra-operatively to make more runs and the loss of more of the response waveform if the delay were increased.

The second obstacle is that the CI-like responses were not uniquely associated with hearing sensations. Among the 56% of NRT waveforms classified as CI-like, some were associated with auditory sensations alone, but others were associated only with nonauditory sensations, or with combined auditory and nonauditory sensations, or even with no sensations at all. This is probably because all neurons that generate action potentials when electrically stimulated produce qualitatively similar compound action potential waveforms. Since the identity of the neurons generating an NRT neural response is not apparent from a CI-like response waveform, it would be unclear whether to accept a location or seek another during intra-operative placement of the ABI electrode array.

Perhaps some quantitative property of an NRT neural response could be found that would identify the nature of the response. The easiest to obtain would be temporal properties of the waveform. It has already been mentioned that a clear negative peak was rarely present, so only the positive peak is available for latency measurement. Unfortunately, it appeared that the distributions of the positive peak latencies associated with hearing alone, with side effects alone, and with combined hearing and side effects, were essentially the same (Table 1). Thus, it did not appear that the modality of the associated sensation could be determined from the latency of the positive peak. Other properties of neural responses might be explored for possible use, but the measurement of physiological properties such as refractory periods would require considerably more recording time, which may not be practical in a surgical setting.

The lack of any clear relationship between the NRT recordings and the corresponding sensations reported by the ABI subjects also has implications for another possible application of the NRT technique. Inability to identify the perceptual modalities of ABI NRT responses would present obstacles to using NRT recordings to assist with programming the sound processor for very young patients or others who are limited in their ability to communicate their percepts in response to stimulation. It would not be known whether the stimuli were being set to optimize auditory or nonauditory sensations.

CONCLUSIONS

This study sought to relate NRT recordings to the sensations reported by ABI recipients with NF2 during postoperative NRT testing. It was found that (1) hearing could be present whether or not a CI-like neural response was seen in the NRT recording, and (2) CI-like neural responses were associated with nonauditory as well as auditory sensations. The inability to distinguish auditory NRT recordings from nonauditory NRT recordings indicates that the utility of NRT with auditory brainstem implants requires further study. Although optimizing the stimulating and recording parameters might increase the percentage of NRT tests yielding CI-like responses, to
provide a useful technique there is a fundamental need to find a way to distinguish the neural responses associated with auditory versus nonauditory sensations. Our findings suggest that simply recording CI-like neural responses with NRT is inappropriate for assisting with placement of an ABI electrode array intra-operatively or for programming the sound processor postoperatively.

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