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# Electrically Evoked Auditory Event-Related Responses in Patients with Auditory Brainstem Implants: Morphological Characteristics, Test-Retest Reliability, Effects of Stimulation Level and Association with Auditory Detection

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## Abstract

**Objective—**This study aimed to 1) characterize morphological characteristics of the electrically-evoked cortical auditory event-related potentials (eERP) and explore the potential association between onset eERP morphology and auditory vs non-auditory stimulation; 2) assess test-retest reliability of onset eERPs; 3) investigate effects of stimulation level on onset eERPs; and 4) explore the feasibility of using the onset eERP to estimate the lowest stimulation level that can be detected for individual stimulating electrodes in patients with auditory brainstem implants (ABIs).

**Design—**Study participants included five children (S1-S5) and two adults (S6-S7) with unilateral Cochlear Nucleus 24M ABIs. Pediatric ABI recipients ranged in age from 2.6 to 10.2 years (mean: 5.2 years) at the time of testing. S6 and S7 were 21.2 and 24.6 years of age at the time of testing, respectively. S6 and S7 were diagnosed with neurofibromatosis II (NF2) and implanted with an ABI after a surgical removal of the tumors. All pediatric subjects received ABIs after being diagnosed with cochlear nerve deficiency. The lowest stimulation level that could be detected (behavioral T level) and the estimated maximum comfortable level (C level) was measured for individual electrodes using clinical procedures. For electrophysiological measures, the stimulus was a 100-ms biphasic pulse train that was delivered to individual electrodes in a monopolar-coupled stimulation mode at stimulation levels ranging from sub-threshold to C levels. Electrophysiological recordings of the onset eERP were obtained in all subjects. For studies evaluating the test-retest reliability of the onset eERP, responses were measured using the same set

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of parameters in two test sessions. The time interval between test sessions ranged from two to six months. The lowest stimulation level that could evoke the onset eERP was defined as the objective T level.

**Results—**Onset eERPs were recorded in all subjects tested in this study. Inter- and intra-subject variations in morphological characteristics of onset eERPs were observed. Onset eERPs with complex waveforms were recorded for electrodes that evoked non-auditory sensations, based on feedback from subjects, as well as for electrodes without any indications of non-auditory stimulations. Onset eERPs in patients with ABIs demonstrated good test-retest reliability. Increasing stimulation levels resulted in increased eERP amplitudes but showed inconsistent effects on response latencies in patients with ABIs. Objective and behavioral T levels were correlated.

**Conclusions—**eERPs could be recorded in both non-NF2 and NF2 patients with ABIs. eERPs in both ABI patient groups show inter- and intra-subject variations in morphological characteristics. However, onset eERPs measured within the same subject in this study tended to be stable across study sessions. The onset eERP can potentially be used to estimate behavioral T levels in patients with ABIs. Further studies with more adult ABI recipients are warranted to investigate whether the onset eERP can be used to identify electrodes with non-auditory stimulations.

### Keywords

Auditory brainstem implant; electrically-evoked cortical auditory event-related potentials; auditory detection threshold

## INTRODUCTION

The auditory brainstem implant (ABI) bypasses the cochlea and the auditory nerve and directly stimulates the cochlear nucleus (CN) in the auditory brainstem. It was initially used to partially restore hearing in patients with neurofibromatosis II (NF2) who lost their hearing due to the surgical removal of a tumor. Most recently, it has been used to establish auditory sensation in patients who have either absent or abnormally small auditory nerves (e.g. Choi et al., 2011; Colletti et al., 2009; Colletti & Shannon, 2005; Nevison et al., 2002; Sennaroglu et al., 2011).

Many aspects of the programming process are similar for patients with ABIs and patients with cochlear implants (CIs). Nevertheless, clinicians who work with patients with ABIs face unique challenges. One challenge is to determine which electrode(s) should be deactivated because their activation results in non-auditory sensation. This challenge is a result of the electrode pad design and the anatomical location of electrode placement of the ABI. The Cochlear Corporation N24 ABI was used for all subjects in this study. With this device, electrodes align tightly in three rows of seven electrodes per row on an oval-shaped electrode pad that is 8.5 mm × 3.0 mm in dimension. Due to the small size of electrode pad, electrical stimulation can spread and activate adjacent neural tissue. The surgical goal of ABI implantation is to place the electrode pad on the ventral cochlea nucleus in the lateral recess of the fourth ventricle. The length of cochlear nucleus (primarily the ventral cochlear nucleus) located within this place is only about 7.6 mm (Quester & Schroder, 1999). The landmarks for identifying the lateral recess of the fourth ventricle may be difficult to locate in some patients due to anatomical distortions/variations. Therefore, the optimal electrode placement cannot be ascertained for individual patients at the time of surgery. The lateral recess of the fourth ventricle is surrounded by many neural structures, including the flocculus of the cerebellum, as well as the origins of facial, vestibulocochlear, glossopharyngeal and vagal nerves. These neural structures can be activated by electrical stimulation of the ABI due to current spread and/or less than optimal electrode placement. As a result, patients with ABIs often report non-auditory sensations when the device is activated (Colletti et al., 2005; Frohne et al., 2000; Goffi-Gomez et al., 2012; Herrmann et al., 2014; Marangos et al., 2000; Nevison et al., 2002; O'Driscoll et al., 2011b; Otto et al., 2002). To avoid unwanted side effects of stimulation, any electrodes that evoke non-auditory sensations should either be deactivated, or have limited maximum current level during the programming process. It is possible to identify these electrodes in post-lingual adult ABI recipients during programming, because they can discriminate auditory from non-auditory sensations, and can provide reliable feedback. However, determining which electrodes, when activated, evoke non-auditory sensations in children with pre-lingual onset of deafness with ABIs is difficult, if not impossible, because of their lack of language and experience with sound. Having an objective tool for identifying electrodes that produce non-auditory stimulation would be useful to optimize program settings for pediatric ABI recipients.

To program the speech processor of an ABI, estimates of the minimum amount of charge that patients can detect (T level) for multiple stimulating electrodes are needed. Even though the importance of accurate T levels has not been established in ABI recipients, it has been shown to be critical for understanding of low-level speech and speech presented in noise in CI users (Baudhuin et al., 2012; Dawson et al., 2007; Davidson et al., 2009; Firszt et al., 2004; Holden et al., 2007, 2011; James et al., 2003; Skinner et al., 1997, 1999, 2002; Spahr et al., 2007; van der Beek et al., 2015). Measuring T levels for multiple stimulating electrodes requires a significant amount of attention and effort to accomplish. Complicating programming efforts is the fact that many pediatric ABI recipients have multiple disabilities or medical conditions that limit their abilities to provide reliable behavioral responses regardless of age. Therefore, having objective tools for determining T level would be especially useful for pediatric ABI recipients.

The electrically-evoked auditory brainstem response (eABR) has been used to guide electrode placement and to assist in the programming process in patients with ABIs (Colletti et al., 2001, 2002, 2004a, 2004b, 2005; Herrmann et al., 2014; Goffi-Gomez et al., 2012; O'Driscoll et al., 2011a, 2011b). However, results of recent studies reveal a poor association between the presence/absence of the eABR and auditory stimulation in ABI recipients (Nevison et al., 2002; Goffi-Gomez et al., 2012; O'Driscoll et al., 2011a, 2011b). In addition, the morphology of the eABR can vary between and within test sessions (O'Driscoll et al., 2011b), and reveal conflicting evidence regarding the ability of the eABR to distinguish between auditory and non-auditory stimulation (Herrmann et al., 2014; O'Driscoll et al., 2011b). Finally, the association between behavioral T levels and eABR thresholds can vary across test sessions (O'Driscoll et al., 2011b). Overall, these results bring into question the value of the eABR as a tool for assisting the programming process in ABI recipients.

However, it should be noted that while the bipolar stimulation mode was used in eABR measures, the monopolar stimulation mode was typically used in programming maps in these studies. It is unclear whether the discrepancy between results of the eABR measures and the behavioral procedures can be accounted for by the difference in stimulation mode.

In addition to the eABR, Herrmann et al. (2014) measured the electrically evoked middle latency responses (eMLR) in four adult ABI recipients. Their results showed inter-subject variations in morphological characteristics of the eMLR. While the presence of an eMLR was indicative of an auditory sensation of the bipolar pair, the absence of an eMLR did not rule out an auditory perception.

The electrically-evoked cortical auditory event-related potential (eERP) is a response generated in the central auditory system that can be recorded from surface electrodes placed on the scalp. The presence of the onset eERP is indicative of auditory detection. One advantage the eERP has over the eABR and the eMLR is that it can be recorded in awake patients using the same stimuli as those used during the device programming process. Previous results have established an association between auditory perception and ERPs evoked by acoustic and electrical stimulation in human listeners (e.g. Chang et al., 2012; Cone & Whitaker, 2013; He et al., 2012; 2013, 2015a; Lightfoot & Kennedy, 2006; Visram et al., 2015). Additionally, morphological characteristics of onset eERPs that are associated with non-auditory sensations are different from those evoked by auditory stimulation in CI patients (He et al., 2012). Thus, the eERP holds promise as an objective tool to assist the programming process in ABI recipients.

The literature related to eERPs in ABI patients is scarce. Our previous report is the first study that described eERPs in human ABI recipients (He et al., 2015b). These preliminary results suggested that other neural systems, in addition to the auditory system, might contribute to the "eERP" recorded in some patients with ABIs. Therefore, even though the term "eERP" is still used in this study to refer to cortical responses evoked by electrical stimulation of the ABI, these neural responses may not be generated solely in the auditory system. While He et al. (2015b) demonstrated the feasibility of measuring eERPs in non-tumor pediatric ABI recipients, it remains unknown whether eERPs can be recorded in patients with Neurofibromatosis Type II (NF2), who may have additional damage to the auditory system caused by the tumor and/or surgical procedures used to remove the tumor. More importantly, the eERP morphology has not been characterized in ABI patients. Finally, the association between eERP morphology and auditory vs non-auditory stimulation has not been explored in ABI recipients with NF2. Therefore, the first aim of this study was designed to address the following three questions: 1) what is the feasibility of measuring eERPs in NF-2 ABI patients, 2) what are the morphological characteristics of eERPs measured in both NF2 and non-NF2 patients with ABIs; and 3) what is the association between onset eERP morphology and auditory vs non-auditory stimulation.

As previously mentioned, morphological characteristics of the eABR change over time in patients with ABIs (O'Driscoll et al., 2011b). Although underlying mechanisms for these changes are not known, it is unlikely that they are caused by developmental changes in the auditory system because the measurements were repeated with a short time interval (i.e., approximately eight weeks) between test sessions. This observation raises an additional question as to whether eERPs in ABI patients are repeatable across testing sessions. Like other auditory evoked potentials, it is important to demonstrate that these neural responses can be reliably measured if they are to be used clinically. Therefore, the second aim of this study was to assess the test-retest reliability of onset eERPs measured in ABI recipients.

Effects of stimulation levels on onset ERP responses have been investigated in normal-hearing (NH) listeners (Beagley & Knight, 1967; Buchsbaum, 1976; Bruneau et al., 1985; Cone & Whitaker, 2013; Davis & Zerlin, 1966; Hensch et al., 2008; Lightfoot & Kennedy, 2006; McCandless & Best, 1966; Pitcon et al., 1977; Purdy et al., 2013; Rapin et al., 1966). Overall, these studies showed that ERP amplitude increased as stimulation level increased up to 40-60 dB sensation level (SL). Further increases in stimulation levels caused amplitude saturation in some listeners. Changes in stimulation level show similar effects on eERP amplitudes measured in CI users (Firszt et al., 2002; Visram et al., 2015). The observation of similar level effects on response amplitude reported in NH listeners and CI users is not surprising. Previous studies have shown that central processing of intensity information can be described using the same temporal integration model for both listener groups (McKay & McDermontt, 1998; McKay et al., 2003). This model is based on the assumption that the amount of neural activity in the auditory nerve is the input information that the central auditory system relies on for encoding level cues in both subject groups. In comparison, studies assessing effects of stimulation level on response latency reported inconsistent results. While some studies reported decreases in response latencies as stimulation level increased (e.g. Cone & Whitaker, 2013; Hensch et al., 2008; Purdy et al., 2013), other studies have not observed these effects (Firszt et al., 2002). Differences in stimuli (speech vs. non-speech, acoustic vs. electrical stimulus), presentation levels (supra-threshold vs. near-threshold level) and subject groups (NH vs. CI listeners) may account for discrepancies in the results reported in these studies.

Under ideal conditions, electrical stimulation of the ABI is directly sent to the CN. In all mammals, the CN has multiple types of neurons with different neural response properties (McCreery, 2008; Møller, 2001; Pickles, 1988; Young, 2010). These neurons are sensitive to different stimulus features and have complex excitatory and inhibitory connections. In addition, results of previous studies suggested that unlike the auditory nerve, the “summed neural response” is not the only code that is used for neural encoding of intensity at the CN (Young, 2010). As a result, the intensity processing in the CN is much more complicated than that of the auditory nerve. In cases where neurons other than the CN are activated, changes in neural responses with intensity may be even more complicated and difficult to predict. To date, effects of stimulation levels on eERPs have not been investigated in ABI recipients. Therefore, the third aim of this study was to evaluate effects of stimulation levels on onset eERPs in patients with ABIs.

The association between the onset ERP and auditory detection threshold has been evaluated in NH listeners (Lightfoot & Kennedy, 2006), infants with sensorineural hearing loss (Chang et al., 2012), patients with auditory neuropathy spectrum disorder (He et al., 2012), and adult CI users (Visram et al., 2015). Results of these studies showed a strong correlation between thresholds measured using onset ERP measures and behavioral procedures. The extent to which an association exists in patients with ABIs has not been examined. The fourth aim of this study was to evaluate the feasibility of using the onset eERP to estimate the behavioral T levels in patients with ABIs.

In summary, this study aimed 1) to characterize eERP morphology and explore its potential association with auditory vs non-auditory stimulation; 2) to assess the test-retest reliability of onset eERPs; 3) to investigate effects of stimulation level on onset eERPs; and 4) to explore the feasibility of using the onset eERP to estimate T levels in patients with ABIs. We hypothesize that 1) morphological characteristics of onset eERPs evoked by non-auditory stimulation will be different from those elicited by auditory stimulation; 2) onset eERPs measured in individual ABI recipients will be repeatable across test sessions; 3) onset eERPs in ABI recipients will decrease in amplitude and increase in latency as stimulation level decreases; and 4) behavioral T levels will be correlated with the onset eERP thresholds in these patients.

## METHODS

### Subjects

Study participants included five pre-lingual deaf children (S1 – S5) and two post-lingual deaf adults (S6 and S7). All subjects were unilaterally implanted with a Cochlear Nucleus 24M ABI and had at least two months of listening experience with their ABIs prior to participating in this study. All pediatric ABI recipients were diagnosed with cochlear nerve deficiency. S6 and S7 were diagnosed with neurofibromatosis II (NF2) and implanted with an ABI after the surgical removal of the tumors. Pediatric ABI recipients ranged in age between 2.6 and 10.2 years (mean: 5.7 years; SD: 2.8 yrs) at the time of testing. S6 and S7 were 21.2 and 24.6 years of age at the time of testing. S3 had a Cochlear Nucleus System 5 (N5) CI and S5 had a Cochlear Nucleus Freedom (24RE) CI in the other ear. Electrically evoked intra-and post-operative eABRs were recorded for electrodes tested in this study in S2-S6. The presence/absence of the intra- or post-operative eABR in S1 and S7 is unknown because they were implanted at other medical centers.

ABI devices for all subjects were programmed using a SPEAK processing strategy. The stimuli used in their programming maps were presented with a pulse rate of 250 pulses per second (pps) per channel in monopolar-coupled stimulation mode (MP1+2). The pulse phase duration ranged from 100 to 300 µs per phase and the interphase gap was 45 µs. Active electrodes for the ABIs were initially selected based on the presence of intra- and post-operative eABRs in S2-S5 and S6. However, in later programming sessions, one electrode was deactivated in S2, one electrode was deactivated in S3, four electrodes were deactivated in S4, ten electrodes were deactivated in S5, and one electrode was deactivated in S6 due to non-auditory stimulation or lack of reliable behavioral responses when electrical stimulation was delivered to these electrodes. The number of active electrodes at the time of testing ranged from 7 to 17. All subjects demonstrated reliable responses to electrical stimulation with their ABI devices.

For S3 and S5, their CIs were also programmed with SPEAK progressing strategy. The programming rate used in their CI speech processor program was 250 pps per channel with an interphase gap of 45 μs. Both subjects had 20 active electrodes in their CI programming maps. S3 was using a pulse phase duration of 88 μs per phase. The pulse phase duration ranged from 75 to 88 μs per phase for S5. For these two subjects, onset eERPs were also measured with stimuli delivered to their CI sides.

Detailed demographic information of these subjects is listed in Table 1. Also shown are their averaged hearing thresholds with the ABI and/or the CI for 500, 1000 and 2000 Hz measured in the most recent test session. All subjects received payment for their participation. This study was approved by the local Biomedical Institutional Review Board. Written informed consent was obtained from all subjects and/or their legal guardians prior to participation.

## Procedures

Data were collected during multiple visits. During each visit, the subject's behavioral T and C levels were measured. Other audiologic tests, including hearing thresholds measured in sound field were also measured or attempted in each subject. In addition to the hearing tests, each subject participated in eERPs measurements. These two procedures were undertaken in two sessions scheduled on the same day. Stimuli used for determining T and C levels had the same pulse rate and duration as those used for eERP recordings. Due to variations in subject's availability and subject compliance, not all subjects were able to participate in projects designed for all aims. The specific electrodes used for each subject can be found in Table 2.

**Behavioral Measures—**Prior to eERP measurements, during speech processor programming, behavioral T and C levels were estimated for each subject by using an ascending and bracketing method. The stimulus was initially presented at a very low level of charge, manipulating both pulse phase duration and current level, and gradually increased by a step size of 5 Current Level (CL). Response modes typically included conditioned play audiometry tasks, or for older pediatric and adult subjects, a pictured loudness scale was used. Communication mode for S1-S5 included sign language or Cued Speech. They were monitored for signs of non-auditory stimulation (facial stimulation, swallowing, coughing or other indications of discomfort with stimulation) as they lacked the experience to report these sensations except by sign, gestures, and involuntary behaviors. S6 and S7 provided verbal descriptions about the stimulation, and they were asked to indicate whether they had auditory perception only, auditory perception plus non-auditory sensation (e.g. tactile, vertigo, bad taste, shoulder pain, facial twitching and etc.), or non-auditory sensation only when each electrode was stimulated. The map parameters used in the speech-processor programs, including the T and C levels and pulse phase duration, were used for electrophysiological measures.

### Electrophysiological Measures

**Stimuli:** During eERP measurements, the ABI speech processor was bypassed. The stimulus was a 100-ms train of biphasic charge-balanced electrical pulses with a pulse rate of 250 pps per channel presented in a monopolar-coupled stimulation mode (MP1+2). It was created using custom-designed software incorporating Nucleus Interface Communication programming routines (NIC v2) and was delivered directly to individual electrodes. Prior to electrophysiological recordings, the stimuli were presented at the previously measured C level to each stimulating electrode to confirm that the subject did not experience any discomfort and/or could tolerate non-auditory stimulation if there was any.

For the onset eERP measurements, the stimulus was presented at C levels measured for all except two stimulating electrodes that were not associated with any obvious sign of non-auditory stimulation. For two electrodes that clearly evoked non-auditory sensation (i.e. electrode 22 in S2 and electrode 19 in S6), the stimulus was presented at least 5 CL below the C level measured for these electrodes. The pulse train was presented at stimulation levels ranging from C to subthreshold levels for intensity series of eERPs. The same stimulating and recording parameters were used to evoke eERPs in two test sessions designed to evaluate test-retest reliability of the response. The inter-stimulus interval was 1000 ms.

**Electrophysiological recordings:** Each session lasted approximately two hours. Subjects were tested in a single-walled sound booth. They were seated in a comfortable chair or on a caregiver's lap and watched a silent movie with closed captioning or engaged in quiet play during testing. Breaks were provided as necessary.

Electroencephalographic (EEG) activity was recorded using a Neuroscan system (version 4.4) and a SynAmp$^2$ amplifier (Compumedics, Charlotte, NC). Disposable, sterile Ag-AgCl surface recording electrodes were used to record the EEG. The EEG was recorded differentially from high forehead ($F_z$, active) to contralateral mastoid ($A_{1/2}$, reference) relative to a ground electrode placed at the low forehead ($F_{pz}$) in the initial test sessions with S1-S5. For S6-S7 and later test sessions with S2-S5, the EEG was recorded differentially between five active recording electrodes (Fz, FCz, Cz, C3 and C4) and $A_{1/2}$, with the ground electrode placed on $F_{pz}$. These recording electrode sites were chosen since maturation of ERPs in children recorded at these sites is well described in previously published studies (e.g. Ponton et al., 2000; Wunderlich et al., 2006). Eye-blink activity was monitored by a pair of electrodes placed above and below the eye contralateral to the ABI or the CI. Electrode impedances were below 5000 Ω and the inter-electrode impedance difference was less than 2000 Ω. The recording window was 900 ms in length and included a 100-ms pre-stimulus baseline. The EEG was sampled at 1000 Hz, amplified with a gain of 10, baseline corrected, and online filtered between 0.1 and 100 Hz (12 dB/octave roll off). Responses exceeding 120 μV were rejected from averaging. After artifact rejection, the remaining artifact-free sweeps were averaged and at least two averaged responses of at least 100 sweeps were recorded for each stimulation condition in each subject. These recordings were digitally filtered between 1-30 Hz (12 dB/octave roll-off) offline before response identification. Replications measured in the same stimulation condition were averaged together and the averaged response was used for amplitude and latency measurements. The time interval between test sessions evaluating the test-retest reliability of the onset eERP was three months for S3, six months for S4 and two months for S5.

## Data Analysis

Both inter- and intra-subject variability in morphological characteristics of eERPs in ABI recipients was observed. Overall, eERPs measured in these subjects were categorized into two groups based on their morphologies. The first group of responses primarily consisted of a single vertex positive peak and a trough. For this type of response measured in pediatric ABI recipients, eERPs showed a vertex positive peak with a latency of 40-180 ms followed by a trough occurring approximately 100-220 ms later. In contrast, adult NF2 ABI recipients produced responses that were dominated by a trough with a latency around 50-100 ms followed by a vertex peak occurring around 150-220 ms after stimulus onset. To be consistent with results reported in our previous study (He et al., 2015b), this type of response was referred to as a Type I response. The other group of responses showed complex waveforms and consisted of up to three groups of positive and negative peaks within a time window of 25-500 ms after stimulus onset. This type of neural response was observed in both adult and pediatric ABI recipients and was referred to as a Type II response. Traditional peak labels (i.e. P1 and N2 for responses measured in children; P1, N1 and P2 for responses recorded in adults) are associated with specific neural generators. Neural sources of peaks observed in this study may be different from neural generators that are associated with those traditional peak labels. Therefore, all peaks in this study are described in terms of latency in order to avoid confusion. For example, P115 and N230 refer to a positive peak occurring 115 ms and a trough occurring 230 ms after stimulus onset, respectively.

Replicated responses measured for each stimulation condition within the same test sessions were overlapped to show their repeatability. Neural responses were considered present only if all replications recorded for the same stimulation condition at all recording sites were repeatable. Responses were independently evaluated by two judges. The second judge was blind to subject identification and stimulation condition. eERPs were recorded for 153 stimulation conditions in all subjects. Initial decisions regarding peak identification between the two judges were consistent for eERPs recorded for 142 stimulation conditions (i.e. approximately 92.8% inter-judge reliability). The disagreements were resolved through discussion for eERPs measured for nine stimulation conditions. One remaining disagreement was the lowest stimulation level that eERPs were recorded for electrode 2 in S4. In this case, the objective T level, defined as the lowest stimulation level that could evoke the onset eERP response, was taken as the lowest stimulation level for which both judges agreed that the eERP was recorded. The other disagreement was where the first positive peak located for eERPs recorded for electrode 21 in S2. The first judge chose the point with the largest amplitude immediately preceding the trough with a latency around 110 ms. The second judge chose the point with the largest amplitude around 30 ms post stimulus onset. In this case, the midpoint between peaks picked by two judges was used for peak amplitude and latency measures.

After peak identification was completed by these two judges, amplitude and latency of identified peaks were measured using custom-designed MATLAB (Mathworks) software. The peak-to-peak amplitude of Type I response was measured as the difference in volts between the vertex positive peak and the following trough in children and between the trough and the following vertex positive peak for adults. The peak-to-peak amplitude of

Type II response was measured as the difference in volts between each vertex positive peak and its following trough for both adult and pediatric ABI recipients. The intra-class correlation test was used to evaluate test-retest reliability of eERPs measured between test sessions. This statistical test has been successfully used for the same purpose in several previously published studies (Friesen & Tremblay, 2006; He et al., 2013; Tremblay et al., 2003). Effects of stimulation level on eERP amplitudes and latencies were not evaluated using any statistical analysis test due to limited range of stimulation levels for which responses could be measured in most subjects. Related Samples Wilcoxon Signed Rank test was used to compare objective and behavioral T levels. The association between these two T levels was evaluated using a One-way Spearman Rank correlation test.

# RESULTS

## Electrodes with Non-Auditory Stimulations

Non-auditory stimulation was observed in several subjects. Due to limited communication skills, S1 did not indicate non-auditory sensation before or during eERP measures when electrode 21 was stimulated at the C level. However, he reported a “tingling” sensation in the ipsilateral neck in addition to auditory perception when this electrode was stimulated after eERP measures were completed. S2 pointed to his throat when electrode 22 was stimulated at the C level. S6 reported a vibrotactile sensation in the ipsilateral chest when electrode 19 was stimulated at C levels. For these two subjects, the stimulation was decreased to a level that could be tolerated by the subject (at least 5 CL below the C level). Electrophysiological recordings were conducted at these low levels. Electrode 19 was deactivated for S6 in a following programming session scheduled four months later. S3 showed a balance sway when electrode 9 was stimulated. S5 showed sign of discomfort in the ipsilateral neck when electrodes 21 and 22 were stimulated and also had a clear balance sway when electrode 13 was stimulated. These electrodes were subsequently deactivated and were not tested for electrophysiological recordings. No other non-auditory stimulation was reported, indicated or observed.

## Morphological Characteristics of eERPs in ABI recipients

Figures 1 and 2 show onset eERPs recorded at Fz in five non-NF2 pediatric ABI recipients (S1-S5) and in two NF2 adult ABI recipients (S6 and S7), respectively. Each block of waveforms belongs to one subject, indicated by subject number in each panel. Due to variations in responses recorded among these subjects, different amplitude scales are used in these blocks. Responses measured in the same stimulation conditions are overlapped. Stimulating electrodes used to evoke these responses are noted on the right side of the waveforms. It should be pointed out that a subset of results recorded in S1-S4 was reported in our previous brief report (He et al., 2015b). However, the aim of that study was to establish the feasibility of measuring onset eERPs in non-NF2 pediatric patients with ABIs. Amplitude and latency of these onset eERPs have not been reported previously. Therefore, they were included in this study. Identifiable neural responses were not recorded for electrodes 8 and 11 in S5. Repeatable neural responses were recorded for all other electrodes. Black triangles are used to note the positive peaks identified in each set of responses. For the purpose of ease of visualization, troughs are not labeled in these figures.

Some of these responses (e.g., responses recorded in S4 and S7) contained a small positive peak at 0 ms, which represents stimulus artifact. Taken together, the eERPs shown in Figures 1 and 2 are characterized by inter- and intra-subject variability in morphological characteristics. While eERPs recorded in S4 are similar for different stimulating electrodes, responses recorded in other subjects (e.g., S2 and S3) are more variable. Overall, Type I responses were observed when stimuli were delivered to 42 of 55 stimulating electrodes (~76%) used in this study. The averaged peak-to-peak amplitude of Type I response ranged from 2.08 to 5.29 μV. For pediatric ABI recipients, the averaged latency of the positive peak ranged from 54 to 145.83 ms and the averaged latency of the trough ranged from 159.86 to 266.5 ms. The averaged latency of the troughs measured in S6 and S7 were 72.83 ms and 57 ms, respectively. The vertex positive peak occurred around 140 ms later in both subjects. Type II responses were observed when stimuli were delivered to 13 of the 55 stimulating electrodes (~24%). These responses show larger inter-subject variations in response amplitudes and latencies than those measured for Type I responses. Table 3 lists electrodes where Type I and Type II responses were recorded in this study. Means and standard deviations of amplitudes are listed in Table 3.

In addition to the ABI, S3 and S5 used a CI in the other ear, which provides an opportunity for comparing eERPs evoked by ABIs to those elicited by CIs. The left and right panels of Figure 3 show onset eERPs evoked by electrical stimulation of the CIs in S3 and S5. Onset eERP responses recorded at recording site Fz are shown in order to facilitate comparison with results shown in Figure 1. Electrode numbers that were stimulated to evoke these responses are labeled at the right side of each set of responses. Vertex positive peaks are indicated using black triangles. Several waveforms contain a positive peak occurring at the stimulus onset, which is the result of contamination due to electrical stimulus artifact. For S3, responses evoked by electrical stimulation of CI electrodes are more uniform compared to those elicited by stimulating ABI electrodes. These CI-elicited eERPs consist of two vertex positive peaks followed by a trough within a time window of 120-480 ms, which is similar to morphology of eERPs evoked by stimulating electrode 21 of her ABI device. However, eERPs after stimulation of electrode 21 of her ABI showed larger peak-to-peak amplitudes than those measured for eERPs evoked following CI stimulation. For S5, the overall morphological characteristics of eERPs evoked by the CI are similar to those elicited by the ABI. Variations in eERP morphology are also observed across CI stimulating electrodes in this subject. Whereas eERPs evoked by stimulating electrode 12 of the CI are dominated by a vertex positive peak occurring at around 160 ms, eERPs observed following stimulation of other electrodes show more complex waveforms. The mean and the standard deviation of amplitudes and latencies measured for eERPs evoked by CI stimulation are also listed in Table 3.

## Test-Retest Reliability of the eERP

Figure 4 shows onset eERPs recorded in two test sessions in S3, S4 and S5. Onset eERPs recorded in the first and the second test session are indicated using solid and dashed lines, respectively. The time interval between two test sessions ranged from two to six months. Each panel shows data recorded in one subject with subject numbers indicated in the bottom right corner. Onset eERP responses were only recorded at recording electrode site Fz in the first test session. Therefore, only onset eERPs recorded at Fz are shown in this figure even though onset eERPs were recorded at five surface electrode locations in the second test session. In general, these results show that onset eERPs recorded for the same stimulating and recording conditions are stable across test sessions. The intra-class correlation coefficients (ICCs) range from 0.5 to 0.96 with a mean of 0.81 (SD = 0.14).

## Effects of Stimulation Levels on eERPs

Figure 5 shows eERP intensity series in six subjects. Responses were recorded from a recording electrode located at Cz. Intensity series of onset eERP were recorded for two stimulating electrodes in S3 and S5, and for thee stimulating electrodes in S4. Only one intensity series is shown for these three subjects in this figure. Each graph shows results measured in one subject. Vertex positive peaks for these traces are indicated using black triangles. These data show that onset eERPs were recorded for a range of intensities in all six subjects. Overall, onset eERPs showed broader peaks with reduced amplitude as the stimulation level decreased. However, effects of stimulation level on response component latencies are less consistent across subjects. Results measured in S1-S3 and S6 show longer latencies as stimulation levels decreased. This systematic change in latency is not observed for eERPs measured in S4 and S5. In addition, some response components of eERPs measured for electrode 16 in S5 were only recorded at high stimulation levels.

Figure 6 shows amplitudes, peak and trough latencies of the eERP responses plotted as a function of stimulation level (i.e. input-out function) for each subject as indicated by different symbol types. For onset eERPs recorded for seven stimulating electrodes in five subjects, the response components that could be consistently identified with decreased stimulation levels were the vertex positive peak followed by a trough 35-300 ms after stimulus onset. Input-output (I/O) functions of peak and trough latencies and peak amplitude of these eERPs are shown in the left column of Figure. 6. In general, amplitudes increased with stimulation level, although this effect was non-monotonic. Effects of stimulation level on peak and trough latencies are less consistent across subjects. While responses recorded in S1, S2 and S6 generally showed longer latencies with decreased stimulation levels for both the peak and the trough, responses recorded in other subjects did not follow this trend.

For responses evoked by stimulation of electrode 18 in S3 and electrode 19 in S5, two positive peaks and troughs were recorded within 25-480 ms after stimulus onset (right column, Figure. 6). While the responses from both subjects consist of two peaks followed by troughs and increasing stimulation level increased peak amplitudes, these eERPs showed different characteristics. First, eERPs measured for electrode 19 in S5 have longer latencies and larger amplitudes than those observed in S3. Second, whereas peak and trough latencies in S3 decreased as stimulation level increased, response latencies in S5 are not affected by stimulation level.

Figure 7 shows intensity series of eERPs measured at Cz in two test sessions using the same stimulating and recording parameters in S4 and S5. The time intervals between test sessions were three and two months for S4 and S5, respectively. Negative troughs are labeled for these traces. Despite variations in amplitude and latency between the two test sessions, these eERPs demonstrate good test-retest reliability. The ICCs measured in S4 ranged from 0.38

to 0.83 with lower ICCs measured at lower stimulation levels (mean = 0.56; SD = 0.20). The ICCs for S5 ranged from 0.45 to 0.92 (mean = 0.74; SD = 0.20). Most importantly, intensity series from two recording sessions yielded the same objective T levels in both subjects.

### Association between Objective and Behavioral T Levels

Figure 8 plots behavioral T level as a function of objective T levels for all six subjects. It should be pointed out that more than one stimulating electrode was tested in S3-S5. Results shown in Figure 8 are data collected for all stimulating electrodes in these six subjects. The solid line represents a linear regression fit to the data, which accounted for 85% of variance. The slope of the regression line is 0.89, which is statistically significantly different from zero ($p<0.01$). Results of Related Samples Wilcoxon Signed Rank test show that objective T levels are significantly higher than behavioral T levels ($p<0.05$). Results of a one-way Spearman Correlation test show a correlation between objective and behavioral T levels for these subjects ($\rho= 0.91$; $p<0.001$).

## DISCUSSION

### eERP Morphological Characteristics

The feasibility of measuring eERPs in pediatric non-NF2 subjects with ABIs was demonstrated previously (He et al., 2015b). Results of this study show that onset eERPs can also be recorded in NF-2 patients despite the potential damage to the auditory system caused by the tumor and/or surgical procedures used to remove the tumor. Similar to our previous findings, onset eERPs in the present study were variable across subjects, as well as across stimulating electrodes within individual subjects. Based on the number of identifiable peaks, these responses were categorized into two types of responses, and inter- and intra-subject variations in amplitudes and latencies were observed for both response types. Type I responses consist of a single vertex peak followed by a trough. Averaged peak-to-peak amplitude of this type of responses ranged from 2.08 to 5.29 μV, which is similar to those measured in pediatric and adult CI users (e.g. Brown et al., 2008, 2015; Firszt et al., 2002; Gordon et al., 2005, 2011; Sharma et al., 2002, 2009). Type 1 responses accounted for 76% of total responses recorded in the present study. The remainders of onset eERPs were classified as Type II responses. The Type II response has a complex waveform consisting of multiple vertex peaks followed by troughs occurring within 25-480 ms following stimulus onset. Averaged maximum peak-to-peak amplitude of this response was 24.28 μV, which is larger than what has been reported for onset eERPs measured in CI users (e.g. Brown et al., 2008, 2015; First et al., 2002; Gordon et al., 2005, 2011; Sharma et al., 2002, 2009). Neural generators for onset eERPs recorded in ABI patients remain unknown. Results of this study do not suggest a clear association between onset eERP morphology and electrode location on the electrode pad. Although eERPs have been described in pediatric and adult CI users (e.g. Brown et al., 2008, 2015; First et al., 2002; Gordon et al., 2005, 2011; Sharma et al., 2002, 2009), a direct comparison between responses recorded in ABI and CI patients are difficult due to differences in etiology, electrode design and placement, and potential differences in neural pathways activated by these devices.

Inspection of Figures 1 and 2 suggests that onset eERPs evoked by ABI electrical stimulation, especially in S3 and S5, show morphological variations. Due to their young age and limited listening experiences, these two subjects were not able to report on their perceptions of electrical stimulation delivered by different ABI electrodes. Therefore, underlying mechanisms or associations with auditory perception of these variations are unknown. These morphological variations could be due to multiple factors including, but not limited to, anatomical variations in the auditory system and surgical placement of electrode pad. Response components originating from other systems could also contribute to these variations. For example, the positive peak occurring around 30 ms in eERPs recorded for electrode 18 in S3 could be post-auricular muscle response. Further studies are needed to investigate this possibility.

### eERP Morphology and Auditory vs Non-Auditory Stimulation

The association between onset eERP morphology and auditory vs. non-auditory stimulation was explored in this study. We hypothesized that eERP morphology as a result of non-auditory stimulation would be different from those elicited by auditory stimulation. Overall, results of our study did not provide conclusive evidence to support this hypothesis.

On one hand, onset ERPs recorded for electrode 21 in S1, electrode 22 in S2, and electrode 19 in S6 had complex waveforms with large amplitudes. These subjects provided evidence of non-auditory sensations when these electrodes were stimulated. In addition, intensity series when stimuli were delivered to electrode 16 in S5 (see Figure 5) showed that the large peaks occurring between 230 and 400 ms after stimulus onset vanished rapidly as stimulation level decreased, which suggested that these peaks might indicate myogenic activity. On the other hand, these complex waveforms were also observed for onset eERPs recorded for stimulating electrodes where subjects who did not report non-auditory sensations. For example, waveforms as a result of stimulation of electrodes 17 and 22 in S2 had similar morphologies. Non-auditory responses were indicated only when electrode 22 was stimulated. In addition, non-auditory stimulation was not observed in S3 despite the fact that onset eERPs recorded for electrodes 15, 18 and 21 showed complex waveforms with amplitudes that were at least one magnitude larger than those recorded in any other subjects. Factors accounting for this discrepancy are unclear. It should be pointed out that the lack of any sign of discomfort does not guarantee the absence of non-auditory stimulation. It is possible that subjects might have experienced *tolerable* non-auditory sensations and they did not show any sign of discomfort when these electrodes were stimulated.

Furthermore, reliable behavioral responses to electrical stimulation were not observed for stimuli delivered to electrodes 6, 7, 10 and 12 in S5 after six months of ABI use even though repeatable neural responses were observed following stimulation of these electrodes. Because of absent behavioral responses, these electrodes were deactivated in the programming map. The underlying mechanisms responsible for the lack of behavioral responses to electrical stimulation delivered through these electrodes in this subject are not well understood. Retrospective review of this patient's medical record suggested that several factors that might have contributed to her lack of response to stimulation of these electrodes. First, this patient did not use her ABI on a full time basis and had not received consistent speech therapy within the six months prior to testing. Second, this subject was only 2.8 years of age when these electrodes were deactivated. It is challenging to obtain reliable behavioral responses at this young age from individuals who have a paucity of auditory experience thus far in their lives. Finally, these neural responses were not necessarily evoked by auditory stimulation.

In summary, the results of this study do not provide conclusive evidence for the association between onset eERP morphology and auditory vs non-auditory stimulation. Further work with more adult, post-lingual ABI recipients is warranted in order to better understand the relation between response morphology and stimulation type.

## Test-Retest Reliability of the eERP

The second of aim of this study was to evaluate the test-retest reliability of onset eERPs in subjects with ABIs. Onset eERPs were recorded in two test sessions in three subjects using the same stimulating and recording parameters. In addition, test-retest reliability was evaluated by measuring an intensity series for one electrode in two subjects. Overall, our results demonstrated that onset eERPs recorded in these subjects were stable across test sessions. For response measured at the C level, the ICCs ranged from 0.50 to 0.96 with a mean of 0.81 (SD = 0.14), which is consistent with results in young listeners with normal hearing (Beauducel et al., 2000; Carrillo-de-la-Pena, 2001; Hegerl et al., 1988; Hensch et al., 2008; Sandor et al., 1999), elderly listeners (Tremblay et al., 2003), and CI users (He et al., 2013; Friesen and Tremblay, 2006).

Due to time constraint, the test-retest reliability was only evaluated for intensity series of eERPs measured for electrode 4 in S4 and electrode 19 in S5. These results showed that ICCs decreased as the stimulation level decreased, which is expected since the signal-to-noise ratio decreased as stimulation levels decreased. Similar effects of stimulation levels on reliability coefficients have been reported for ERPs measured in NH listeners in Hensch et al. (2008).

In pediatric CI users, morphological characteristics of eERPs change as listening experience with CI increases (e.g. Dorman et al., 2007; Ponton et al., 2001; Sharma et al., 2009). Specifically, eERPs measured in these listeners typically show decreased peak latencies within the first year of CI use. In comparison, eERPs recorded in our pediatric ABI patients did not show noticeable morphological changes across testing sessions. Differences in listener groups (CI vs ABI recipients) and relatively short time intervals between test sessions used in this study might account for this discrepancy.

## Effects of Stimulation Level on eERPs

The third aim of this study was to evaluate effects of stimulation level on onset eERP amplitude and latency in patients with ABI. Onset eERPs were expected to show increased amplitude and reduced latency as stimulation level increased. Results of this study showed that eERPs measured in all subjects had non-monotonic increases in amplitude as stimulation level increased, which is consistent with our hypothesis and results measured in CI users (Firszt et al., 2002; Visram et al., 2015). Amplitude saturation was observed for responses measured for electrodes 2 and 4 in S4 and electrode 18 in S3, which is consistent with results reported for CI users in Firszt et al. (2002). .

Despite the general association between stimulation level and eERP amplitude, variations in the I/O function of eERP amplitude were observed across subjects. While a linear I/O function was recorded in S1, functions recorded in other subjects showed two or even three stages of amplitude increase (e.g. S2 and S4). In addition, I/O functions measured for different components of eERPs recorded for the same electrode (i.e. electrode 18 in S3 and electrode 19 in S5) differed in slope and shape (see Figure 6). eERPs recorded in this study represents the synchronous firing of a large population of electrically stimulated neurons. Many types of neurons with different excitatory and/or inhibitory properties are likely activated. Therefore, the recorded eERP represents the results of a complicated interaction of neural excitations and inhibitions. Due to the nature of eERP responses, our results could not provide information about underlying mechanisms for observed variations of I/O functions. We can only speculate that responses recorded across subjects and electrodes might have different generators with different response properties.

eERPs latency increased with decreased stimulation levels in four subjects (S1-S3 and S6), which is consistent with results reported in CI users by Firszt et al (2002). However, effects of stimulation levels on eERP latencies were not obvious in S4 and S5. Latency has been interpreted as the speed of neural transduction. In CI users, as the stimulation level increases, more neurons are recruited and neural firing becomes more synchronized which contributes to larger responses. Given the same neural diameter and myelination status, larger neural response tends to transduce at a fast rate, which may result in shorter eERP latencies. Nevertheless, situations are more complex in the case of ABI recipients because eERP latency could be affected by other factors, including, for example, the spread of excitation changes with stimulation level. As a result, neurons responding to low stimulation levels might be different from those recruited at high stimulation levels. Therefore, neural resources of recorded eERPs could potentially be different at different stimulation levels.

## eERP Threshold and Auditory Detection

The fourth aim of this study was to explore the feasibility of using the onset eERP to estimate behavioral T levels for device programming in ABI recipients. We observed a correlation between onset eERP threshold and behavioral T levels, which is consistent with results of previous studies (Chang et al., 2012; Lightfoot & Kennedy, 2006; Visram et al., 2015). This result suggested that the onset eERP holds promise as an objective tool for estimating T levels in ABI recipients. It should be emphasized that the association between onset eERP threshold and behavioral T levels does not provide information that would allow one to determine whether ABI patients use auditory and/or non-auditory sensation to detect electrical stimulation. This ambiguity is due, at least in part, to the fact that neural responses generated by both auditory and/or non-auditory systems would have been recorded through surface electrodes in this study.

### Study Limitations

Despite these findings, this study has several limitations. One limitation is the relatively small number of subjects who could provide meaningful description of how electrical stimulation of the ABI was perceived. Due to this limitation, results of this study did not provide answers to the critical question of whether eERP can be used to identify electrodes with non-auditory stimulation. A second limitation of this study is that stimulation levels used to elicit eERPs were based on behavioral T and C levels in individual subjects. This procedure might have introduced a subjective bias into our results that would favor the observation of an association between objective and behavioral T levels. However, over-stimulation can be life threatening for ABI patients. This procedure was chosen to assure subject safety. A third limitation of this study is that stimulation levels that were used to measure eERP I/O functions were not well controlled across subjects. In many subjects, only a few stimulation levels were used due to time constraint and subject compliance. This limited the extent to which the effects of stimulation level on eERP amplitudes and latencies could be investigated. Finally, subjects tested in this study varied in age (young children vs adult) and etiology (i.e. CND vs NF2). Therefore, results of this study do not provide information about whether eERPs in ABI patients are subject to the same developmental impact as that reported in CI users (e.g. Dorman et al., 2007; Ponton et al. 2001; Sharma et al., 2009). Due to these limitations, the results from this study should be considered as descriptive or exploratory. Further study with a larger group of adult subjects and with well controlled stimulating parameters is warranted in order to better understand the predictive value of onset eERPs for determining stimulation type (i.e., auditory versus non-auditory) and behavioral thresholds that might be useful in programming ABIs. In addition, longitudinal studies with individual pediatric ABI recipients are needed to investigate developmental effects on eERPs in ABI recipients.

## CONCLUSIONS

The eERPs were recorded in both non-NF2 and NF2 ABI patients. eERPs in both ABI patient groups show inter- and intra-subject variability in morphological characteristics. However, onset eERPs measured in similar stimulating conditions within the same subject in this study tended to be stable across two test sessions. Onset eERPs potentially can be used to estimate behavioral T levels in patients ABI. Further studies with more adult ABI patients are warranted to investigate whether onset eERP can be used to identify electrodes with non-auditory stimulations.

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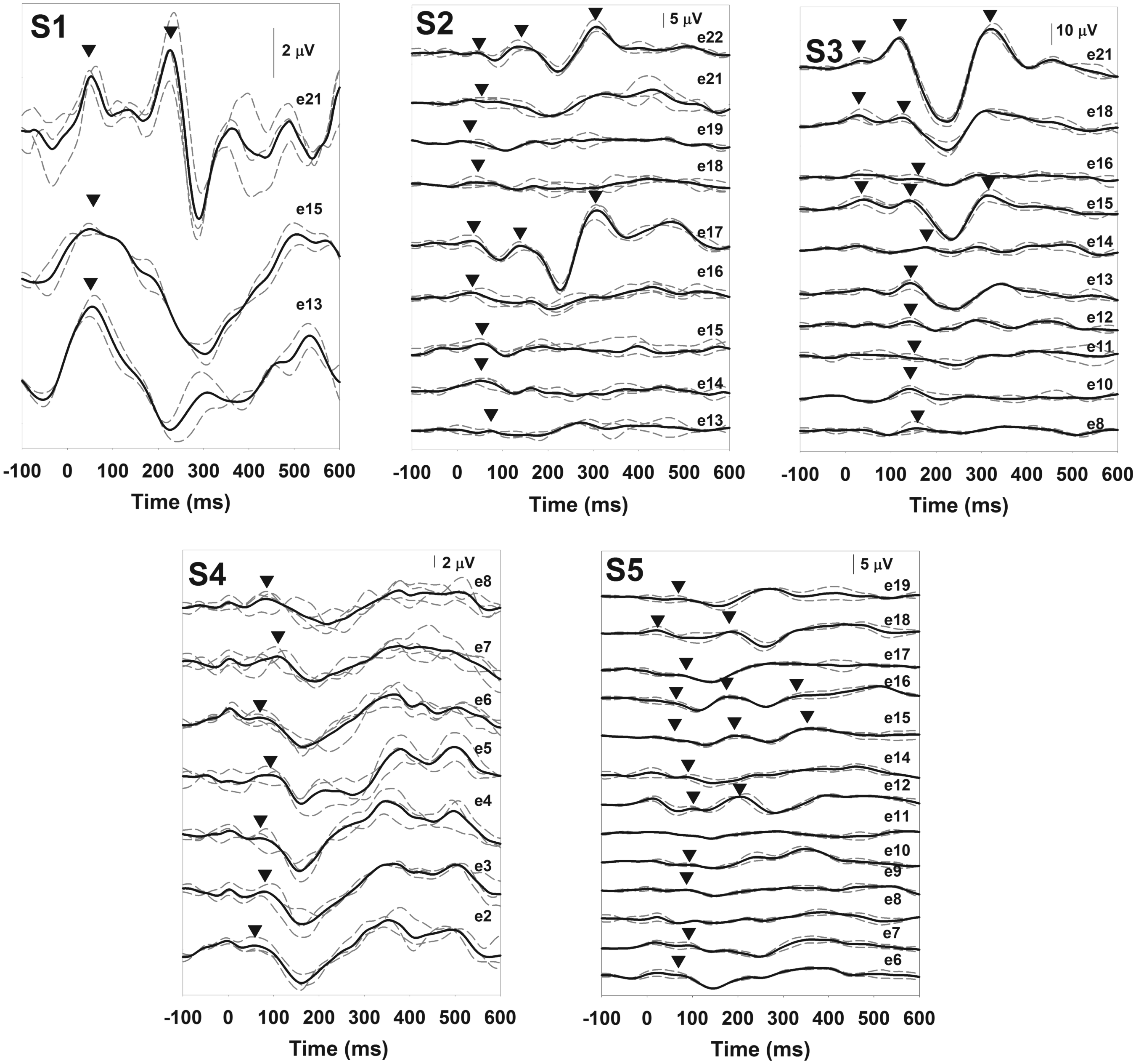

**Figure 1.**

eERPs recorded at Fz in five pediatric ABI recipients (S1-S5). Each graph shows results recorded in each subject. Grey dashed lines represent replications recorded at each stimulating electrode and black lines represent the averaged responses of these replications.

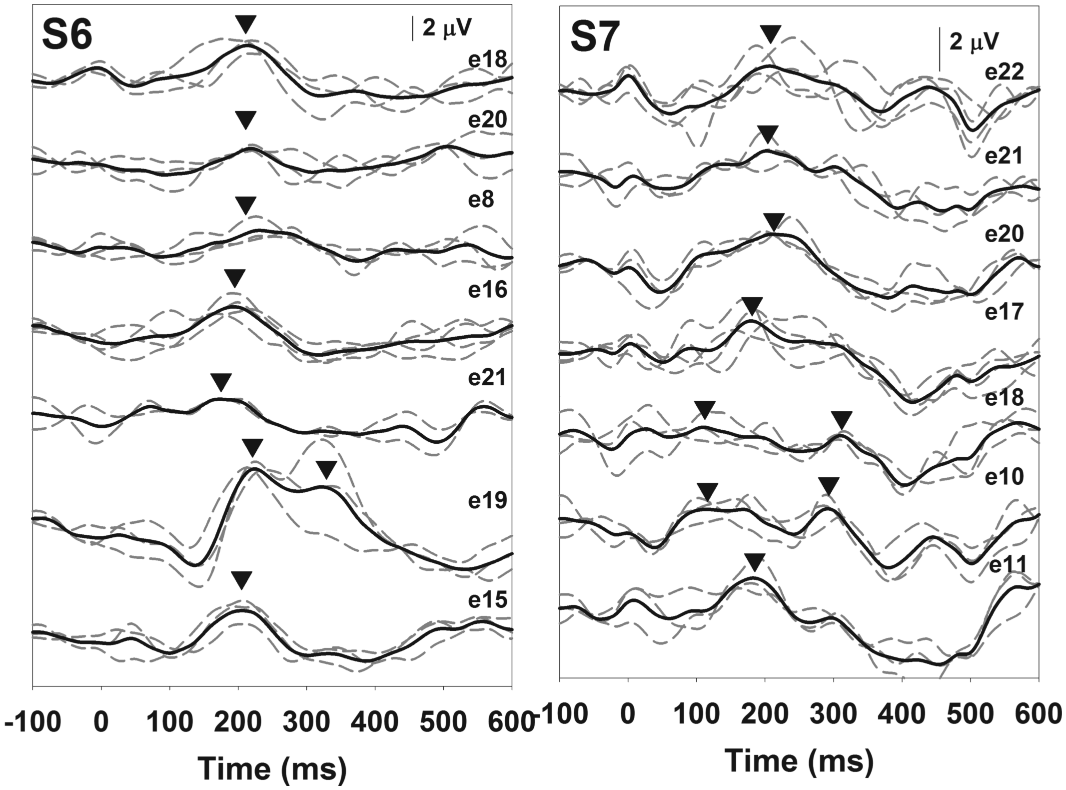

**Figure 2.**

eERPs recorded at Fz in two adult ABI recipients (S6 and S7). Results recorded in S6 and S7 are shown in the left and right panel, respectively. Grey dashed lines represent replications recorded at each stimulating electrode and black lines represent the averaged responses of these replications.

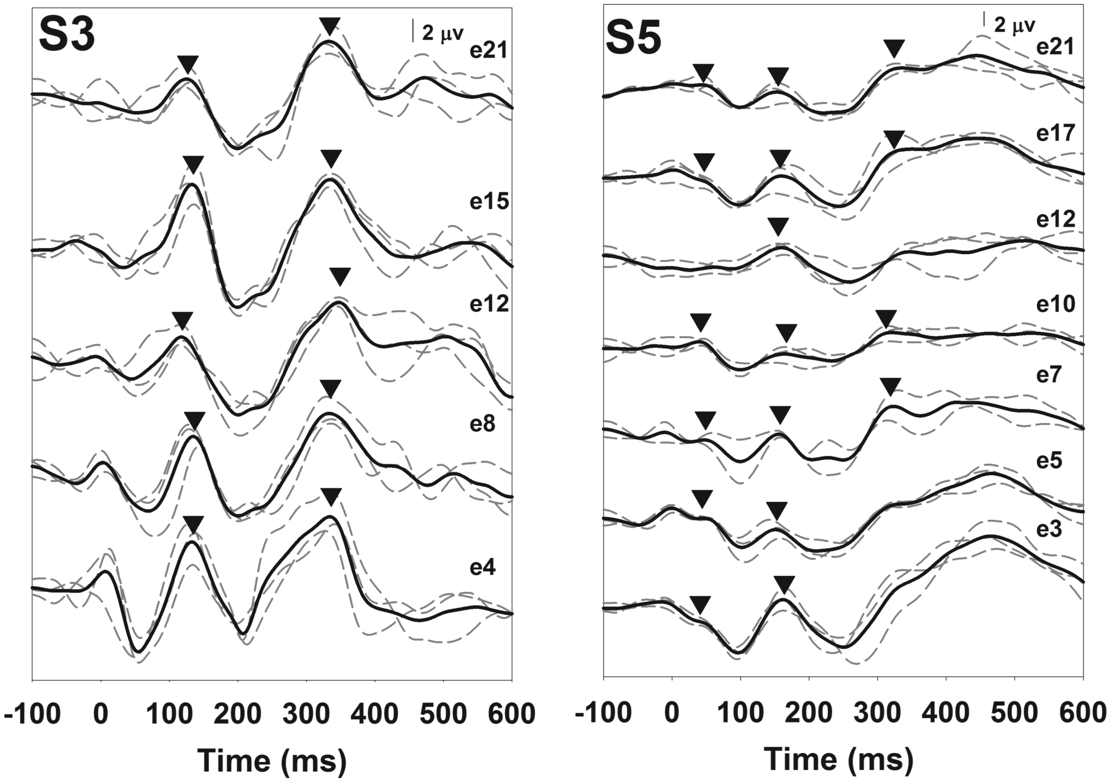

**Figure 3.**

eERPs evoked by electrical stimulation of cochlear implants in two subjects (S3 and S5). Grey dashed lines represent replications recorded at each stimulating electrode and black lines represent the averaged responses of these replications. Identifiable vertex positive peaks are indicated with black triangles.

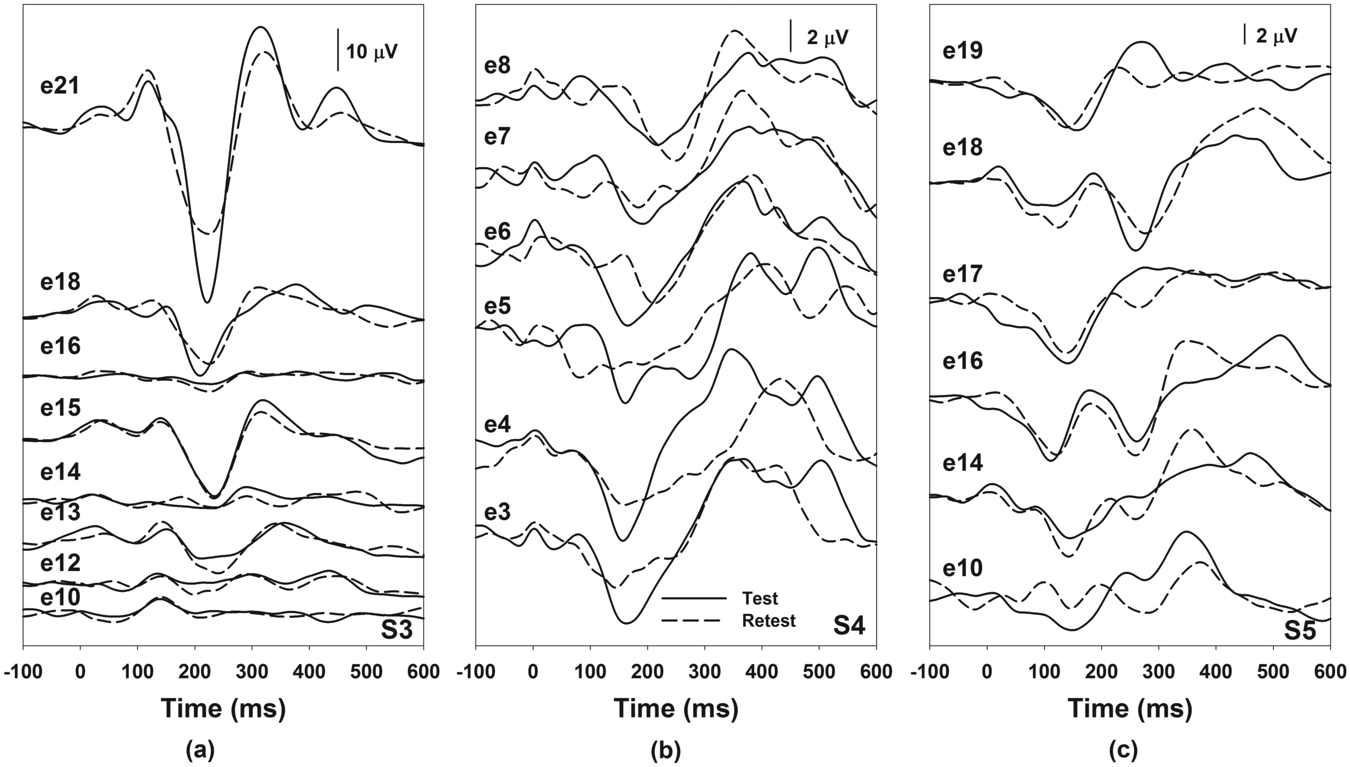

**Figure 4.**

eERPs recorded in two test session for S3, S4 and S5. Each line represents an average of 300-artifact free sweeps. Solid and dashed lines show results recorded in the first and second test session, respectively. The electrode number that was used to evoke these responses is labelled for these traces.

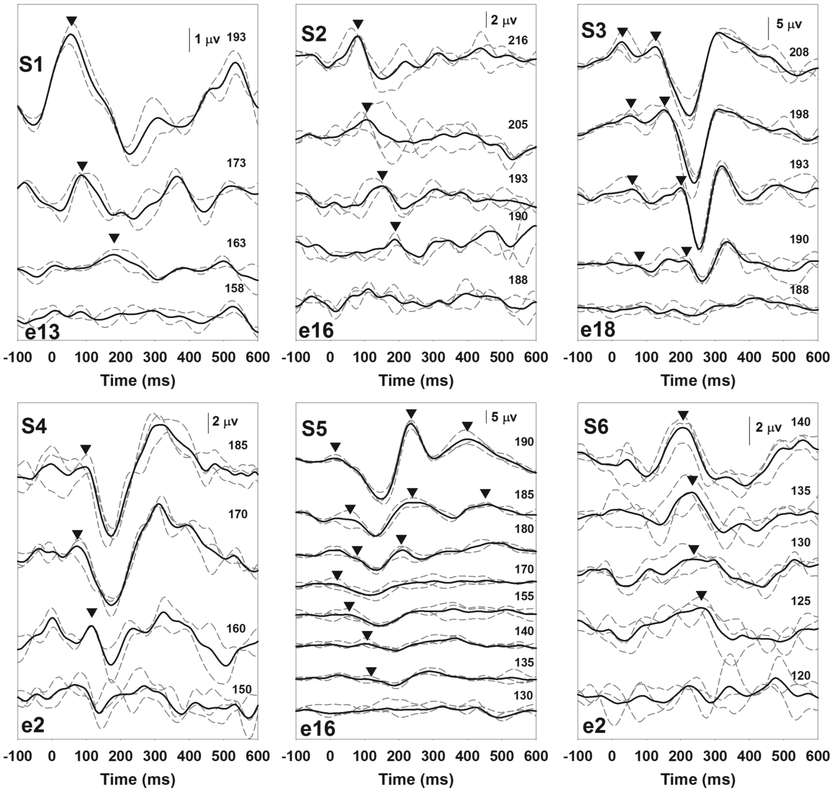

**Figure 5.**

Intensity series of the eERP recorded in six subjects. Grey dashed lines represent replications recorded at each stimulation level and black lines represent the averaged responses of these replications. Stimulation levels used to evoke these responses are labelled for these traces. Identifiable vertex peaks are indicated using black triangles. Subject number and electrode are shown in each graph.

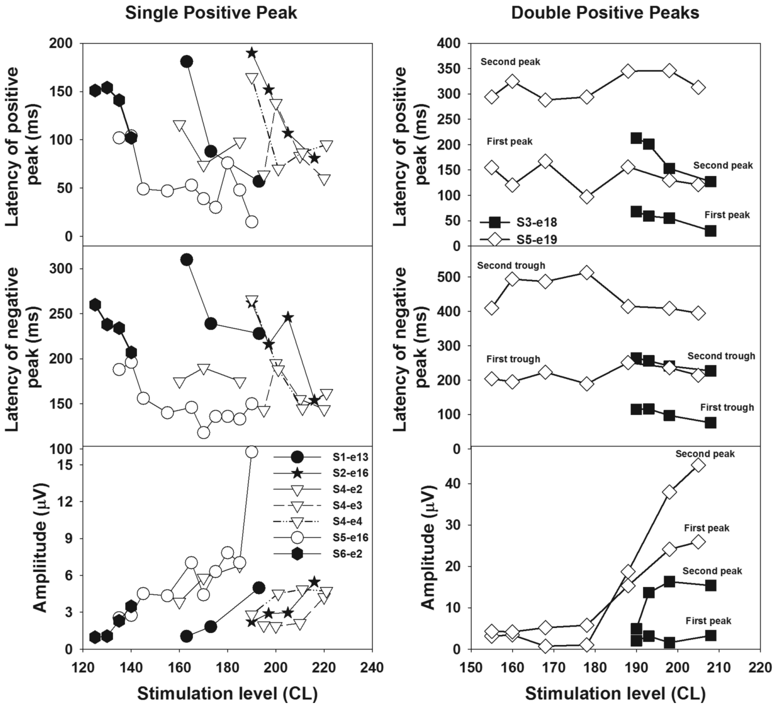

**Figure 6.**

Input-output functions of eERPs amplitudes and latencies recorded in six subjects. Left column shows results measured for the Type I responses recorded for seven electrodes in five subjects (S1, S2, and S4-S6). Right column shows results measured for the Type II response recorded in two subjects. Results recorded for different electrodes in these subjects are indicated using different symbols.

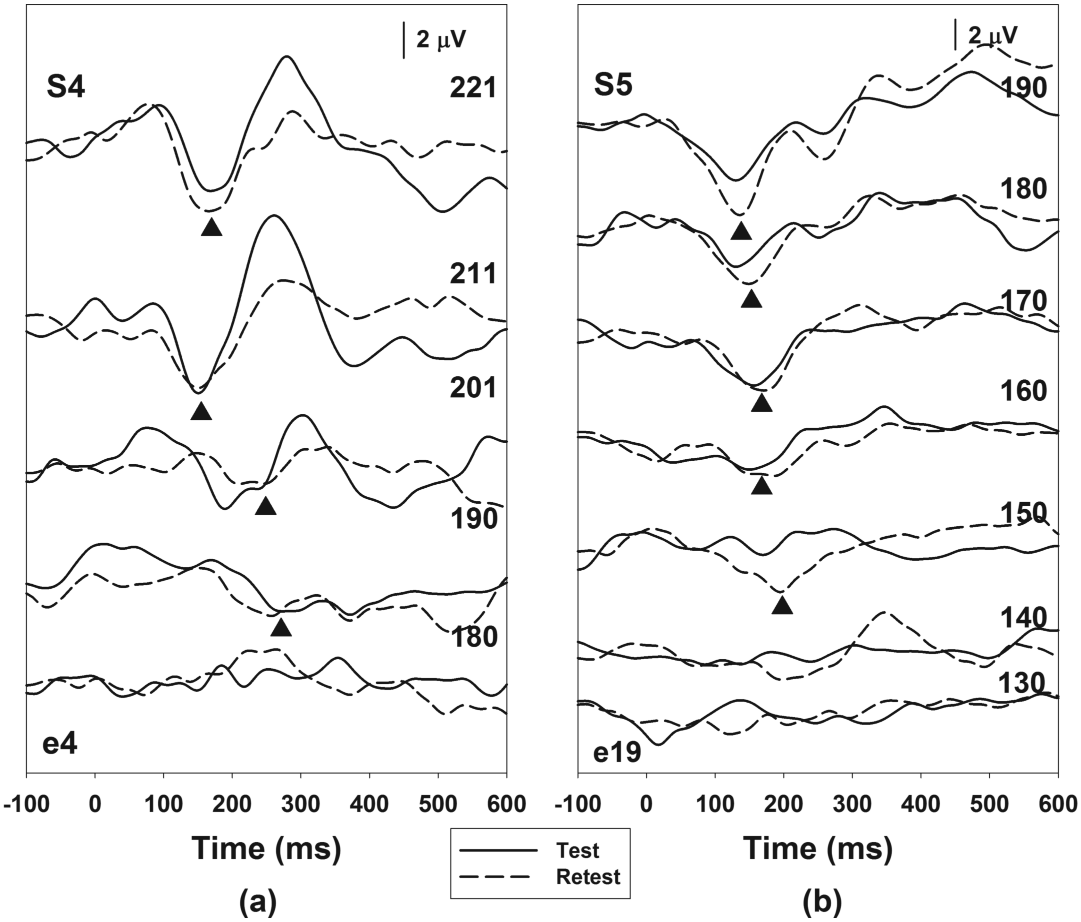

**Figure 7.**

Intensity series of eERPs recorded in two test sessions for electrode 4 in S4 [panel (a)] and electrode 19 in S5 [panel (b)]. Solid and dashed lines represent results recorded in the first and second test sessions, respectively. Stimulation levels used to evoke these responses are labelled for these traces.

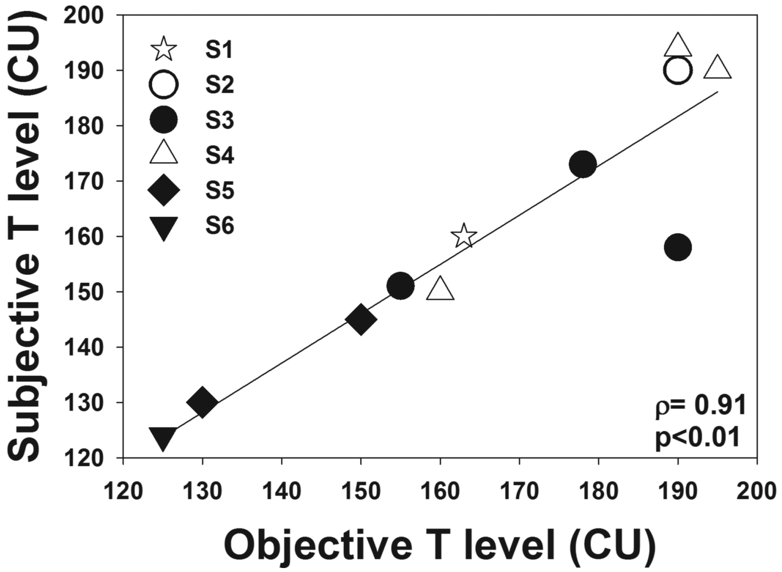

**Figure 8.**

Subject T levels plotted as a function of objective T levels. Results of one-way Spearman Rank correlation test are in the lower right corner.

## Table 1

Demographic information of subjects who participated in this study. CND: cochlear nerve deficiency; ABI: auditory brainstem implant; CI: cochlear implant; PTA: pure-tone average

| Subject number | Gender | Etiology | Device implanted | Age at implantation (yrs) | Age at testing (yrs) | Ear tested | Number of active electrodes | Pulse width (μs) | 3-Frequency hearing thresholds average (dB HL) | Non -auditory sensation |
|---|---|---|---|---|---|---|---|---|---|---|
| S1 | M | Goldenhar syndrome | 24 ABI | 3.3 | 10.2 | R | 17 | 100-200 | 28.3 | tactile |
| S2 | M | CHARGE syndrome | 24 ABI | 3.3 | 4.9 | L | 9 | 100-150 | 26.7 | Cough, facial twitch |
| S3 | F | unknown | 24 ABI | 5.5 | 6.2 | R | 13 | 100 | 35 | Vestibular stimulation |
|  |  |  | 24RE |  | 6.2 | L | 20 | 88 |  | None |
| S4 | M | CHARGE syndrome | 24 ABI | 3.5 | 4.5 | R | 6 | 150-300 | 45 | None |
| S5 | F | unknown | 24 ABI | 2.2 | 2.6 | R | 6 | 150 | 35 | Vestibular stimulation, discomfort in ipsilateral neck |
|  |  |  | N5 |  | 2.6 | L | 20 | 75-88 | 43 | None |
| S6 | F | NF2 | 24 ABI | 21.2 | 22.0 | L | 7 | 100 | 40 | tactile |
| S7 | F | NF2 | 24 ABI | 24.4 | 24.6 | R | 13 | 150 | 48 | None |

### Table 2

Electrodes stimulated in each subject for different studies. eERP: electrically evoked auditory-event related potential; ABI: auditory brainstem implant; CI: cochlear implant; T level: auditory detection level.

| Subject number | Device | Onset eERP | Test-retest reliability of the onset eERP | Effects of stimulation level on eERPs | Association between object and subject T levels |
|---|---|---|---|---|---|
| S1 | ABI | 13, 15, 21 | | 13 | 13 |
| S2 | ABI | 13, 14, 15, 16, 17 18, 21, 22 | | 16 | 16 |
| S3 | ABI | 8,10, 12, 13, 14, 15, 16, 18, 21 | 10, 12, 13, 14, 15, 16, 18, 21 | 18, 21 | 18, 21 |
| | CI | 4, 8, 12, 15, 21 | | | |
| S4 | ABI | 2, 3, 4, 5, 6, 7, 8, | 3, 4, 5, 6, 7, 8 | 2, 3, 4 | 2, 3, 4 |
| S5 | ABI | 6, 7, 10, 14, 16, 17, 18, 19 | 10, 14, 16, 17, 18, 19 | 16, 19 | 16, 19 |
| | CI | 3, 5, 10, 12, 17, 21 | | 12 | 12 |
| S6 | ABI | 2, 4, 5, 8, 10, 11, 14 | | 2 | 2 |
| S7 | ABI | 2, 10, 12, 13, 15, 18, 19 | | | |

## Table 3

Response type, latency and amplitude of eERPs recorded at different electrodes of auditory brainstem implants.

| Subject number | Device | Type I response | | | | Type II Response | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | Electrode number | Latency (ms SD) | | Amplitude (µV SD) | Electrode number | Latency (ms SD) | | | | | | Amplitude (µV SD) | | |
| | | | Positive | Trough | | | 1st Peak | 1st Trough | 2nd Peak | 2nd Trough | 3rd Peak | 3rd Trough | 1st Peak | 2nd Peak | 3rd Peak |
| S1 | ABI | 13, 15 | 54 | 266.5 | 5.01 | 21 | 50 | 90 | 227 | 290 | | | 1.56 | 6.82 | |
| S2 | ABI | 13, 14, 15, 16, 18, 21 | 49.67 (19.96) | 178.17 (51.91) | 4.12 (1.67) | 17, 22 | 38 | 84 | 134.5 | 222 | 310.5 | 369.5 | 4.58 | 12.09 | 8.56 |
| S3 | ABI | 8, 10, 11, 12, 13, 14, 16 | 145.83 (27.44) | 230.71 (18.84) | 4.98 (3.44) | 15, 18, 21 | 32.67 (6.50) | 72 (19.69) | 124 (10.14) | 226.33 (5.51) | 315.67 (5.68) | 403.67 (20.81) | 2.32 (1.76) | 24.28 (13.07) | 9.47 (7.41) |
| | CI | | | | | 4, 8, 12, 15, 21 | 130.6 (7.53) | 203.40 (3.78) | 338 (6.21) | 443.8 (29.06) | | | 7.75 (1.83) | 6.20 (1.97) | |
| S4 | ABI | 2, 3, 4, 5, 6, 7, 8 | 81.28 (16.86) | 175.71 (22.14) | 5.29 (0.79) | | | | | | | | | | |
| S5 | ABI | 9, 6, 7, 10, 14, 17, 19 | 74.71 (13.20) | 159.86 (27.41) | 3.87 (1.65) | 12, 15, 16, 18 | 79.67 (19.03) | 130.36 (19.75) | 217.35 (36.10) | 315.60 (40.09) | | | 3.35 (21.92) | 4.65 (2.47) | |
| | CI | 12 | 160 | 259 | 4.77 | 3, 5, 7, 10, 17, 21 | 45.67 (2.42) | 100.83 (2.14) | 159.83 (5.42) | 236.83 (16.66) | 326.83 (4.89) | 367.59 (6.67) | 3.97 (0.78) | 3.56 (1.87) | 0.88 (0.52) |
| S6 | ABI | 8, 15, 16, 18, 19, 21 | 201.67 (14.59) | 72.83 (24.32) | 2.42 (0.91) | 19 | 222 | 139 | 322 | 281 | | 524 | 1.80 | 6.74 | |
| S7 | ABI | 10, 11, 17, 18, 20, 21, 22 | 198.2 (14.31) | 57 (6.56) | 2.08 (0.37) | 10, 18 | 114 | 51 | 302.5 | 248 | | 399 | 1.11 | 2.22 | |