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Clinical role of electrocochleography in children with auditory neuropathy spectrum disorder

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ABSTRACT

Objectives: To assess electrocochleography (ECochG) to tones as an instrument to account for CI speech perception outcomes in children with auditory neuropathy spectrum disorder (ANSD).
Materials & methods: Children (<18 years) receiving CIs for ANSD (n = 30) and non-ANSD (n = 74) etiologies of hearing loss were evaluated with ECochG using tone bursts (0.25–4 kHz). The total response (TR) is the sum of spectral peaks of responses across frequencies. The compound action potential (CAP) and the auditory nerve neurophonic (ANN) in ECochG waveforms were used to estimate nerve activity and calculate nerve score. Performance on open-set monosyllabic word tests was the outcome measure. Standard statistical methods were applied.
Results: On average, TR was larger in ANSD than in non-ANSD subjects. Most ANSD (73.3%) and non-ANSD (87.8%) subjects achieved open-set speech perception; TR accounted for 33% and 20% of variability in the outcomes, respectively. In the ANSD group, the PTA accounted for 69.3% of the variability, but there was no relationship with outcomes in the non-ANSD group.
In both populations, nerve score was sensitive in identifying subjects at risk for not acquiring open-set speech perception, while the CAP and the ANN were more specific.
Conclusion: In both subject groups, the TRs correlated with outcomes but these measures were notably larger in the ANSD group. There was also strong correlation between PTA and speech perception outcome in ANSD group. In both subject populations, weaker evidence of neural activity was related to failure to achieve open-set speech perception.

1. Introduction

Auditory neuropathy spectrum disorder (ANSD) is hearing dysfunction characterized by compromised integrity of transmission to or within the auditory nerve with relative sparing of cochlear function [1,2]. The deficit is thought to stem from a dyssynchronous neural response to the acoustic signal, resulting in increased gap detection thresholds, poor sound localization and speech discrimination. In particular, postlingually deafened patients with ANSD demonstrate impaired speech perception out of proportion with the increase in their detection thresholds [3–5]. Commonly, ANSD is identified in infants who fail newborn hearing screening (NBHS) and are evaluated with auditory brainstem response (ABR) testing that reveals a cochlear microphonic (CM) but abnormal wave V [5,6]. Otoacoustic emissions may also be present indicating healthy outer hair cells [5,7,8]. ANSD is reported to affect 6.5%–15% of newborns with hearing loss [9,10]. It is associated with a wide range of etiologies and risk factors including premature birth, hyperbilirubinemia, genetic mutations and cochlear nerve deficiency (CND) [11–14].

Patients with ANSD are often treated with cochlear implants (CI), however, their outcomes are highly variable; some subjects perform as well as the best CI users with hearing loss due to non-

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ANSD etiologies, while others never achieve open-set speech perception [8,10–12,15,16]. When comorbidities are absent or controlled for, the outcomes in ANSD and non-ANSD CI recipients are not significantly different [17–19]. Still, no specific factors highly predictive of speech perception outcomes in ANSD patients have been identified [12,16,20]. The site-of-lesion appears to have prognostic significance: abnormalities restricted to the inner hair cells, the synapse, and the terminal dendrites of the auditory nerve allow for better CI outcomes than pathologies of spiral ganglion cells, myelination, or the central nervous system (CNS) [2,7,11,19,21–24]. However, most ANSD subjects do not have clinical indicators of the site-of-lesion which limits the utility of this distinction in current clinical practice.

Electrocochleography (ECochG) provides a possible objective measure to evaluate the peripheral auditory system of CI candidates including those diagnosed with ANSD [1,16,22,25,26]. By examining the origins and magnitude of the potentials recorded with ECochG we may improve our understanding of the variation in speech perception outcomes. The stimuli previously used for evaluation have typically been clicks or high frequency tone pips; the ECochG components produced by these are the CM, summating potential (SP) and compound action potential (CAP) [16,27–30]. Our approach is to utilize a wide range of tone frequencies, because most responses in CI subjects are to low frequencies [25,26,31,32]. In addition to the CM, SP and CAP, the response to low frequency tones also includes the auditory nerve neurophonic (ANN). From the responses to this series of tones, we've developed a 'total response' (TR) measure calculated by summing the significant spectral peaks of responses across a wide frequency range (250 Hz–4000 Hz) as a measure of overall cochlear health [25,26,32]. The objective of this study is to evaluate features of the inner ear electrophysiology including TR, CAP, and ANN as well as their influence on speech perception outcomes of pediatric CI recipients with ANSD.

2. Materials and methods

All aspects of this prospective observational cohort study were approved by the Institutional Review Board. Parental consent was obtained for all subjects and patient assent was obtained from children at least seven years old. All pediatric patients (eight months to eighteen years) who satisfied the criteria for CI at our institution were eligible for the study. Children with non-English speaking guardians, severe inner ear malformations or undergoing revision surgery were excluded from the study. Each subject underwent comprehensive evaluation at the Children's CI Center at University of North Carolina (CCIC at UNC) which included review of birth, medical, family and social history, molecular and genetic testing, ABR, MRI and/or CT imaging where indicated. ANSD was diagnosed based on ABR testing demonstrating a reduced/absent wave V in the presence of CM [7]. In ANSD subjects, the presence of risk factors such as hyperbilirubinemia, prematurity, neonatal intensive care unit stay with requirement of mechanical ventilation (NICU), and temporal bone abnormalities was noted. Additional comorbidities such as CNS abnormalities, systemic illnesses, prelingual deafness and developmental delay were also considered. Bilateral implantations were considered as individual cases. Audiometric thresholds were obtained using developmentally appropriate techniques for each subject. When the highest level of stimulation elicited no response, 120 dB HL was recorded as the threshold for that particular frequency. Pure tone average (PTA) was calculated as the average of threshold at 500 Hz, 1000 Hz and 2000 Hz.

2.1. Operative set up and ECochG recording

All ECochG recording procedures were performed during each subjects' CI procedure under general anesthesia. Acoustic stimulation and recording were performed using a *Biologic Navigator PRO* (Natus Medical Inc., San Carlos, CA). The stimuli were delivered through a foam insert attached to a speaker (Etymotic 3b). A ground electrode was placed on the glabella and the reference electrode on the mastoid contralateral to surgical site. The round window was exposed to insert the CI by using the standard transmastoid facial recess approach. Just prior to insertion of the CI electrode array, a recording probe (Neurosign; Magstim Co., Wales, UK) was placed at the round window. Electrode impedances were less than 16 kOhm.

Acoustic stimuli included tone bursts (250–4000 Hz) presented with alternating phases at 90 dB nHL (95–107 dB SPL). In most cases, 2 to 3 frequencies at 90 dB SPL were tested with the sound tube crimped to test for the absence of electrical artifact.

2.2. Signal analysis

Recorded responses to the acoustic stimuli were processed using custom MATLAB programs (Mathworks, Natick, MA, USA). An example of recorded waveform and its spectrum is shown in Fig. 1A. The energy spectrum is derived from the ongoing, or steady-state portion of the response (shaded box), that occurs after the CAP and lasts until the stimulus is turned off. The TR was derived by adding the amplitudes of significant responses at the first three harmonics, summed across all stimulus frequencies (only the response to 500 Hz, with two significant peaks, is shown). To be considered 'significant', the spectral peaks had to exceed the mean noise level by at least 3 standard deviations. The noise and its variance were determined from six bins, three on each side of the target frequency, starting two bins away from the peak. The lowest detectable signal levels were typically on the order of 0.02 μV.

Neural activity was assessed based on the presence of CAP and ANN in the ECochG waveforms. Only subjects with a TR greater than −6 dB μV (0.5 μV) were included in this analysis because in smaller responses the signal to noise ratio was too low for these neural features to be detected. In CI subjects a CAP is often visible as a pronounced negative deflection of the potential at the onset of the response (Fig. 1A, portion in red), but across subjects the morphology is highly variable and difficult to quantify [33]. Similarly, the presence of an ANN is detectable by distortions in the ongoing portion of the response but its magnitude is difficult to quantify because it is mixed with the CM (Fig. 1 A, in the blue box). Consequently, a subjective scale ranging from 0 to 2 was used to independently grade the evidence of CAP and ANN in each waveform. On this scale, 0 indicates complete absence, 1 indicates presence of even the smallest evidence of the potential, and 2 indicates that the potential were clearly discernable. The scores for CAP and ANN were added to produce a composite 'nerve' score. Examples of the different morphologies and scores are provided in Fig. 1B.

2.3. Speech perception testing

A battery of age and developmentally appropriate speech perception tests was employed at follow-up audiology appointments [34]. Results from open-set monosyllabic word tests, usually the phonetically balanced kindergarten word test (PB-k), were selected as the outcome measure. The PB-k lists are composed of 25 words found in average vocabulary of a kindergarten-aged child and is scored as 'percent correct' [35–37]. Pediatric CI recipients may continue improving in their speech perception performance