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#### Research paper

## Assessment of responses to cochlear implant stimulation at different levels of the auditory pathway



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#### ABSTRACT

This paper reviews characteristics of both the electrically evoked compound action potential (ECAP) and analogous measures of cortically evoked responses (CAEP) to electrical stimulation in cochlear implant users. Specific comparisons are made between the two levels of processing for measures of threshold, growth of responses with increasing stimulus level, changes in stimulation electrode and, finally, in temporal response properties. The results are interpreted in a context that ECAPs primarily reflect the characteristics of the electrode-neural interface for an individual ear. CAEPs clearly are dependent on those peripheral responses but also reflect differences in central processing among individual implant users. The potential applicability of combined measures in clinical situations is discussed.

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#### 1. Introduction

A number of factors can affect the ability of a cochlear implant (CI) user to identify and discriminate acoustic signals in the environment: the way the speech processor is programmed, the number of electrodes that are available, the extent to which temporal fine structure in the acoustic stimulus is transmitted. All of these factors can impact the way an acoustic signal is perceived. However, even when these device-related factors are held constant, crosssubject variability on almost all measures of post-operative performance with a CI is large (Tyler et al., 2000). Another factor that may contribute to variance in performance with a CI is the interface between the intracochlear electrodes and the neurons of the auditory nerve. Electrode insertion depth, the extent of fibrous tissue growth and the effective distance between the electrode contact and the stimulable neural elements will all have an impact on the way the auditory nerve responds to electrical stimuli both at threshold and suprathreshold levels and could potentially limit the amount of information transferred to the auditory nervous system (Shepherd et al., 1993; Frijns et al., 2001; Miller et al., 1993). For example, the extent to which electrical current spreads across the cochlea will influence the size of the neural population that is activated and how much overlap there is in neural populations stimulated by adjacent intracochlear electrodes (Miller et al., 1993; Shepherd et al., 1993; Liang et al., 1999; Kral et al., 1998). Results of animal studies show that the status of the auditory nerve can influence basic response properties like neural refractoriness and adaptation and as a result, have an impact on how sequences of electrical pulses presented by the CI are coded by the auditory nerve (Miller et al., 2001; Matsuoka et al., 2000). Many of these factors are also likely to be affected by neural degeneration typical in ears with sensorineural hearing loss. Cross-subject variance in the electrode neural interface and the status of the peripheral auditory nerve itself could affect sensitivity to electrical stimulation, spatial selectivity and how well the temporal fine structure in a signal is coded at the level of the auditory nerve.

Several studies have suggested that variations in performance among CI users may also be due, in part, to differences in central nervous system function (Firszt et al., 2002b; Kelly et al., 2005; Kraus et al., 1993; Micco et al., 1995). Cochlear damage can lead to degeneration of spiral ganglion cells (Leake and Hradek, 1988) and subsequently to significant changes in the central auditory pathways (Webster and Webster, 1977; Kitzes and Semple, 1985; Kral et al., 2005). Consequently, even if the response of the auditory nerve to electrical stimulation was "normal", central processing in a long-term deafened ear may be different than in someone with a short duration of deafness or normal hearing. Several studies have shown that congenital hearing loss alters the way the central auditory system develops and that late implantation can have a significant impact on outcome with a CI (Ponton et al., 1996; Ponton and Eggermont, 2001; Sharma et al., 2002, 2005; Kral and Sharma, 2011). As a result, the processing of a signal transmitted to the

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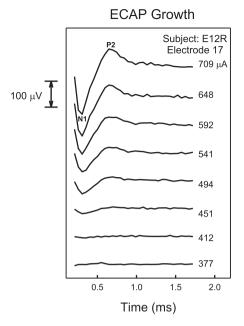
central auditory nervous system by the cochlear implant may vary significantly across individuals and the ability of those individual CI users to adapt to the novel neural patterns may also vary. Finally, psychophysical studies attempt to characterize the relationship between an acoustic signal and perception and typically relay on either detection, discrimination and/or identification paradigms.

Our early work focused on development of methods to understand how auditory signals are processed in the auditory periphery. Most of that work relied on the use of neural telemetry systems that allow us to record the electrically evoked compound action potential (ECAP) from an intracochlear electrode. ECAPs proved to be an important way we could characterize how acoustic signals were processed at the level of the auditory nerve (Abbas et al., 2006). Our recent work has focused on recording CAEPs. These evoked responses can be measured using surface electrodes placed on the scalp. The paradigm we typically use involves presentation of a sequence of two long duration sounds. A response is generated at the onset of the stimulus and is generally interpreted as evidence that a stimulus has been detected. A similar evoked potential is recorded if the listener perceives a change in the ongoing stimulus. The cortical change responses can provide a non-behavioral measure of how well two stimuli are able to be discriminated. Comparison of ECAPs and CAEPs can provide some insight into the relative contributions of neural processing both at the periphery and within the central auditory pathways.

Understanding the nature and the locus of the limitations on signal processing in an individual implant user could be potentially important in developing appropriate treatment strategies. For instance, adjusting stimulation parameters at the periphery could be effective in reducing current spread and potentially reduce effects of channel interaction. Alternatively, if the limitation in electrode discrimination appears to be more central in origin, some type of training program might be a more effective intervention strategy. These issues might be particularly relevant in children where differences in the neural degeneration may be large and where, depending upon age of implantation, the processing within the central auditory pathway may be quite variable. Further, in children who are too young to perform complex listening tasks, the use of physiological measures may be particularly informative. Our goal in this paper is to summarize the results of several studies conducted in our laboratory that have addressed the similarities and differences between peripheral and central responses to cochlear implant stimulation.

#### 2. Summary of experimental methods

The ECAP is a measure of the response of the auditory nerve to electrical stimulation. It is typically recorded from an intra-cochlear electrode. The proximity of stimulating and recording electrodes coupled with the short latency of the ECAP makes contamination of the neural response by stimulus artifact a problem. We originally made ECAP measures in Ineraid implant users by accessing the intracochlear electrodes directly via the percutaneous plug (Brown et al., 1990). A subtraction technique was developed that takes advantage of the refractory properties of neurons to isolate and minimize the stimulus artifact. Contemporary cochlear implants do not use percutaneous connection between the speech processor and the implanted electronics. ECAPs are measured using a reverse telemetry system and an artifact subtraction technique similar to the one we originally described (Abbas et al., 1999; Frijns et al., 2002; Jeon et al., 2010; Bahmer et al., 2010). Fig. 1 shows a series of such ECAPs recorded at different stimulus levels. The responses are relatively short latency, typically less than 0.5 ms. They are typically measured using a single biphasic current pulse delivered through a single electrode bypassing the speech processor of the CI.



**Fig. 1.** Plots of electrically evoked compound action potentials (ECAP) recorded from a Nucleus cochlear implant user. Stimulation is on electrode 18, recording from electrode 19. Level of the probe stimulus is indicated by each waveform.

The ECAP is characterized by a negative peak (N1) followed by a positive peak (P2). The amplitude of that peak (N1–P2) grows as current level is increased. This response is thought to be a weighted sum of neural activity from the auditory nerve recorded in response to a single stimulus pulse.

ECAPs can be used to evaluate the characteristics of the peripheral electrode-neural interface. For example, they are affected by both the choice of stimulating and recording electrode and vary considerably both across individuals and across stimulating electrodes within individuals (Brown et al., 2000; Dillier et al., 2002). Shepherd et al. (1993) showed that ECAPs are sensitive to electrode placement and nerve survival in a particular location in the cochlea. The primary advantage that ECAP have over other evoked potential measures is that they can be recorded quickly from CI users of all ages and doing so does not require application of surface recording electrodes. The measurements themselves are not dependent on attention, are not affected by muscle artifact nor are they adversely affected by sleep or sedation. All of these factors led to the use of ECAP measures in clinical practice. The primary clinical application for these measures is as a guide to programming the speech processor (Brown et al., 1995; Hughes et al., 2000). They have not proven to be useful predictors of word recognition or overall performance levels. The lack of predictive value is most likely a reflection of the fact that the ECAP represents neural responses from the auditory periphery and does not reflect contributions to neural processing at more central levels within the auditory system.

Cortical auditory evoked potentials (CAEP), recorded from surface electrodes on the scalp, can include a wide variety of different responses but here we focus on what is commonly referred to as the P1–N1–P2 response with latencies in the 50–200 ms range (Näätänen and Picton, 1987; Hyde, 1997). These potentials are thought to reflect neural processing at cortical or pre-cortical levels and have been successfully recorded in CI users (e.g. Beynon et al., 2002; Firszt et al., 2002a,b; Kelly et al., 2005). When evoked using an electrical stimulus, the P1–N1–P2 response has a similar morphology to those recorded using acoustic stimulation. They can be recorded in passive listening paradigm but are adversely affected by sleep. Recordings reported here are made using electrodes

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