



# Suprathreshold compound action potential amplitude as a measure of auditory function in cochlear implant users

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## Abstract

Electrically evoked compound action potential (eCAP) amplitudes elicited at suprathreshold levels were assessed as a measure of the effectiveness of cochlear implant (CI) stimulation. Twenty-one individuals participated; one was excluded due to facial stimulation during eCAP testing. For each participant, eCAPs were elicited with stimulation from seven electrodes near the upper limit of the individual's electrical dynamic range. A reduced-channel CI program was created using those same seven electrodes, and participants performed a vowel discrimination task. Consistent with previous reports, eCAP amplitudes varied across tested electrodes; the profiles were unique to each individual. In 6 subjects (30%), eCAP amplitude variability was partially explained by the impedance of the recording electrode. The remaining amplitude variability within subjects, and the variability observed across subjects could not be explained by recording electrode impedance. This implies that other underlying factors, such as variations in neural status across the array, are responsible. Across-site mean eCAP amplitude was significantly correlated with vowel discrimination scores ( $r^2 = 0.56$ ). A single eCAP amplitude measured from the middle of the array was also significantly correlated with vowel discrimination, but the correlation was weaker ( $r^2 = 0.37$ ), though not statistically different from the across-site mean. Normalizing each eCAP amplitude by its associated recording electrode impedance did not improve the correlation with vowel discrimination ( $r^2 = 0.52$ ). Further work is needed to assess whether combining eCAP amplitude with other measures of the electrode-neural interface and/or with more central measures of auditory function provides a more complete picture of auditory function in CI recipients. Copyright © 2017, PLA General Hospital Department of Otolaryngology Head and Neck Surgery. Production and hosting by Elsevier (Singapore) Pte Ltd. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

**Keywords:** Cochlear implant; Compound action potential; Suprathreshold amplitude

## 1. Introduction

Cochlear implant (CI) recipients likely have some degree of spiral ganglion degeneration associated with their hearing loss, the extent of which is determined by individual factors, such as age, etiology of hearing loss, and duration of deprivation (Nadol et al., 1989), among others. As the target of CI stimulation, the status of peripheral auditory neurons affects the fidelity and

efficiency of signal transmission to more central structures. Thus, it is hypothesized that peripheral neural function underlies some of the variability in perceptual outcomes observed across CI users. Electrophysiological measures can be used as a tool to assess auditory nerve function, which would otherwise not be directly measurable in living CI recipients.

Both the compound action potential (CAP) and early components (i.e. wave I) of the auditory brainstem response (ABR) arise from the synchronous firing of peripheral auditory neurons excited by either acoustic or electric signals. Animal research has demonstrated that various aspects of the electrically evoked (e) peripheral responses (e.g., thresholds, rate of growth, suprathreshold amplitude, latency, sensitivity to interphase gap, recovery) are correlated with the number or

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density of surviving neurons and/or degree of myelination (Smith and Simmons, 1983; Hall, 1990; Miller et al., 1994; Zhou et al., 1995; Prado-Gutierrez et al., 2006; Ramekers et al., 2014, 2015). These results have motivated investigations of these gross potentials as they relate to auditory function in living human CI recipients.

A few reports have investigated the predictive ability of the slope of eCAP amplitude growth functions on speech perception (Brown et al., 1990; Gantz et al., 1994; Kim et al., 2010), but the majority have favored more sophisticated eCAP paradigms to investigate channel interaction (Hughes and Stille, 2008; Tang et al., 2011; van der Beek et al., 2012; Scheperle and Abbas, 2015; DeVries et al., 2016) or temporal responsiveness (adaptation: Zhang et al., 2013; recovery: Brown et al., 1990; Gantz et al., 1994; sensitivity to interphase gap: Kim et al., 2010). At present, the results have been largely inconclusive, which may be due in part to inconsistencies in methodology and choice of outcome measures (see van Eijl et al., 2016 for a detailed review). Of the various eCAP measures, suprathreshold amplitude has been minimally evaluated in humans because early observations were not promising. It was not uncommon for poor performers to have more robust eCAPs than “star” performers (Carolyn J. Brown, personal communication), and a formal comparison revealed only weak correlations (Brown et al., 1990; statistical significance not reported). One limitation of eCAP amplitude measures is that the electrical dynamic range in humans has an upper limit determined by loudness discomfort. This is not a limitation in anesthetized animals. Thus, in humans, the maximum amplitude of the response at the upper boundary of loudness tolerance is likely smaller than the true maximum amplitude that could be obtained with a higher stimulation level, and might hinder observing the results expected from the animal literature. A second limitation is that electrode impedance and location has greater potential to affect a recorded waveform (because electrodes are used for both stimulation and recording) than speech perception (because electrodes are only used for stimulation).

Despite these potential limitations, a growing body of evidence suggests that suprathreshold amplitude of gross peripheral responses should be revisited as a measure of auditory function in both non-CI and CI recipients. One line of supportive research has been directed toward identifying “hidden” hearing loss in non-CI users with a history of noise exposure. Noise trauma has been shown to preferentially impact auditory neurons, and in animals, suprathreshold amplitudes of gross neural potentials are sensitive to synaptic deficits and neural degeneration even when threshold measures are not (Kujawa and Liberman, 2009). Explorations in humans have been promising to date. Stamper and Johnson (2015) observed that ABR wave I amplitudes elicited with high sound levels (90 dB nHL) were significantly correlated with noise exposure background. More recently, the amplitude of the CAP (normalized to the summing potential) was also observed to be significantly correlated with various speech perception measures in a group of individuals with varied risk of acoustic trauma (Liberman et al., 2016). Although this essentially normal-hearing (per audiometric thresholds) population is different from the population of CI recipients who have

unaided audiometric thresholds consistent with severe-profound hearing loss, a common goal across both groups is exploring peripheral neural degeneration as an underlying mechanism of speech perception difficulties.

A second line of work involves the acquisition of acoustically evoked electrocochleographic (ECoG) measures just prior to cochlear implantation as an indicator of residual cochlear/neural health. In this paradigm, multiple frequencies are presented at high levels in an effort to sample cochlear/neural responses from across the length of the cochlea. The response amplitudes measured from the round window are summed into a total response, which has been shown to significantly correlate with post-operative speech perception measures (Fitzpatrick et al., 2014). If an acoustically evoked measure of residual cochlear/neural health is indicative of perceptual abilities following implantation, it is reasonable to assume that an electrically evoked measure, which more directly assesses residual neural function and response to stimulation from the implant, deserves further attention.

A third line of work is aimed at exploring various measures of the electrode-neural interface in CI recipients. Both electrode position and neural status contribute to this interface, and both will affect the transduction of the electrical stimulus to a neural response. Suprathreshold eCAP amplitude measures appear less sensitive to the medial-lateral placement of the electrode within the scala than other measures, such as eCAP channel interaction and behavioral thresholds (DeVries et al., 2016), which implies that amplitude measures may be more sensitive to neural status. Moreover, average eCAP amplitudes were significantly correlated with speech perception scores and accounted for 68% of the variability (DeVries et al., 2016). This result is inconsistent with the result reported by Brown and colleagues (1990); however, several factors may have contributed to the different outcomes.

One methodologic difference between the two studies is the number of electrode sites tested. In DeVries et al. (2016), all of the intracochlear electrodes were used as stimulation sites; whereas, in Brown et al. (1990), eCAPs were elicited at a single stimulation site. Although a broad (monopolar) stimulation mode and the use of relatively high current levels results in a broad spread of current and potential recruitment of neurons from across the cochlea, the neurons closest to the recording electrodes likely influence the amplitude more than neurons farther away (discussed in Miller et al., 2008). Amplitude of the recorded eCAP varies as the stimulation and recording sites are varied across intracochlear electrodes in CI users, even when the stimulation mode is broad (DeVries et al., 2016; Schwartz-Leyzac and Pflugst, 2016). Moreover, the amplitude profile varies in a manner that is unique to the individual. Therefore, a single measure is not likely a good representation of overall neural health.

A second methodologic difference between the two studies is the choice of materials used to assess speech perception. In DeVries et al. (2016), consonant and vowel discrimination was assessed using materials that provided minimal contextual information; whereas, in Brown et al. (1990), word and sentence materials were used to assess speech. Because eCAPs

are a peripheral response, choosing speech-perception measures that are minimally influenced by top-down processing might be necessary to examine how the two are related.

Another difference between the two studies is that the present population of CI recipients is more heterogeneous than in the early 1990s, when candidacy was restricted to adults with minimal residual hearing and often long durations of deafness. Candidacy criteria have relaxed, allowing individuals with greater amounts of residual hearing, and presumably better neural survival, to receive implants.

The recent findings from [DeVries et al. \(2016\)](#) together with the results from studies in related areas using acoustic stimulation, suggest that further exploration into the use of suprathreshold eCAP amplitude as a measure of auditory function in CI recipients is warranted. The purpose of this study is to re-evaluate the relationship between eCAP amplitudes evoked with suprathreshold stimulus levels and speech perception to test whether the findings of [DeVries et al. \(2016\)](#) are replicable in a different and larger sample of CI users. It is hypothesized that a positive correlation between eCAP amplitude and speech perception will be observed. Additionally, this study formally evaluates whether averaging the amplitudes obtained across the electrode array (i.e. the across-site mean) for an individual is a better predictor than the use of an amplitude measured from a single electrode site.

To reduce potentially confounding effects of top-down processing on the speech perception scores, this study used vowel stimuli to minimize contextual information. The relationship between eCAP amplitude and recording electrode impedance was also evaluated to determine the degree to which characteristics of the recording electrode might limit observing the relationship of interest ([Schvartz-Leyzac and](#)

[Pfungst, 2016](#)). The results of this study add to a growing body of literature investigating various ways to characterize the effectiveness of peripheral neural excitation resulting from electrical stimulation.

## 2. Material and methods

The procedures and use of human subjects in this study was approved by the University of Iowa Institutional Review Board.

### 2.1. Participants

Twenty-one adults implanted with the Nucleus CI24RE (N = 13) or CI512 (N = 8) receiver/stimulators with contour-advance precoiled electrode arrays participated. Eleven individuals were tested in 2012–2013 as part of a different study ([Scheperle and Abbas, 2015](#)). Ten individuals were recruited and tested in 2015–2016. Some of the methodology reported below reflects decisions specific to [Scheperle and Abbas \(2015\)](#). Because the methods did not interfere with the present purpose, they were replicated so that the old data set could be merged with a new data set, doubling the sample size.

For bilateral CI recipients, the test ear with the desired receiver/stimulator and electrode array was chosen. If equivalent, the ear was selected at random. All participants had over 15 months of experience with their CI at the time of testing. Etiology was varied, but the majority of participants were postlingually deafened. For two individuals (E51 and F2L), hearing loss was perilingual, and progressive. Both of these individuals used hearing aids as children and were oral communicators. [Table 1](#) includes additional demographic information. Data from E89R were excluded due to facial

Table 1  
Participant information.

ID	Age (yrs)	Sex	Test ear	Reported etiology	Internal device	Age at IS (yrs)	Months post IS	Vowel (%)	Year tested
E40R	50	M	R	Otosclerosis	24RE	44	79	54	2013
E51	27	F	R	Pendred, progressive	24RE	26	15	29	2013
E55R	63	F	R	Genetic?	24RE	57	74	49	2013
E60	86	F	R	Unknown	24RE	80	65	50	2012
E68L	57	F	L	Unknown	24RE	52	62	38	2013
F18R	66	F	R	Meniere's?	CI512	63	28	35	2013
F19R	78	M	R	Unknown	CI512	76	27	29	2012
F25R	60	F	R	Genetic	CI512	57	36	27	2013
F26L	53	F	L	Unknown	CI512	51	22	65	2013
F2L	58	M	L	Congenital, progressive	CI512	55	35	38	2013
F8R	70	F	R	Unknown	CI512	68	26	24	2013
E18	78	M	R	Noise exposure	24RE	68	120	38	2015
E22	82	M	R	Noise exposure	24RE	72	119	35	2015
E58	58	M	L	Meniere's?	24RE	50	99	56	2015
E83R	75	M	R	Unknown	24RE	69	78	36	2015
E89R <sup>a</sup>	70	F	R	Otosclerosis	24RE	64	69	67	2015
E97L	71	M	L	Noise exposure	24RE	67	45	32	2015
E101R	79	M	R	Genetic?	24RE	77	25	37	2015
E105L	64	M	L	Noise exposure	24RE	57	83	42	2016
F10L	63	F	L	(Progressive)	CI512	58	60	58	2016
F13L	63	M	L	Labyrinthitis	CI512	57	66	32	2015

Identifier (ID); Initial Stimulation (IS).

F2L and E51 had childhood onset hearing loss that progressively worsened. Both were pediatric hearing aid users. All other participants had histories consistent with post-lingual onset hearing loss.

<sup>a</sup> Participant was excluded due to facial nerve stimulation to high-level eCAP stimuli. Recordings were obtained, but stimulation was below the desired level.

stimulation during electrophysiological testing which limited the current level below the desired level.

## 2.2. Electrode selection

The study design for [Scheperle and Abbas \(2015\)](#) involved assessing speech perception under reduced-channel processor settings. One of those settings was chosen to be included in and replicated for the present study. Specifically, seven electrodes were selected as the active electrodes, which were used both for eCAP stimulation and for the novel processor settings. Electrodes 6, 8, 10, 12, 14, 16 and 18 were selected for all but one participant. For F19R, previous data were available on electrodes 7, 9, 11, 13, 15, 17 and 19 ([Scheperle and Abbas, 2015](#)) and were used in this study for convenience since the electrode spacing was comparable. A laboratory owned Freedom processor was used for both physiological and speech perception testing to avoid any concern participants may have had with changing their personal processor settings and to maintain consistency across the merged data set. Some individuals in 2015/2016 were using a newer generation processor for personal use.

## 2.3. Electrically evoked compound action potentials

Custom Sound EP was used for evoking and recording eCAPs. The extracochlear return electrode for stimulation was MP1 (placed under a muscle), and the extracochlear return electrode for recording was MP2 (on the receiver/stimulator case). The suprathreshold current levels used to elicit eCAPs reflected the contour of the loudness-balanced maximum comfort (C) levels used to limit the processor output (explained in Section 2.5).

Forward-masking subtraction was used for artifact reduction ([Brown et al., 1990](#); [Dillier et al., 2002](#)). Both masker and probe signals were symmetrical, biphasic pulses (25  $\mu$ s/phase, 7- $\mu$ s interphase gap) routed to the same electrode, and separated in time by 400  $\mu$ s. Current levels for each masker–probe pair were equal. The active recording electrode was located two electrodes apical to the probe. Recording delay and amplifier gain were adjusted to optimize the recordings for the individual, but were most often within the ranges of 122–161  $\mu$ s and 50–60 dB, respectively. One hundred sweeps were averaged, and peak-to-peak ( $N_1$ - $P_2$ ) amplitudes were calculated in Custom Sound EP. Test order of each of the seven active electrodes was randomized.

## 2.4. Electrode impedance

Electrode impedance was measured in CustomSound EP using default parameters. The impedances calculated using MP2 as the reference electrode were used for further analysis to match the eCAP recording configuration. Due to the offset between stimulating and recording electrodes for eCAP measures, the impedance values for electrodes 8, 10, 12, 14, 16, 18, and 20 (or 9, 11, 13, 15, 17, 19, and 21 for F19R) were used for further analysis.

## 2.5. Novel processor settings

Threshold (T) and C levels were measured for each of the activated electrodes using MP1 as the return electrode to match the eCAP stimulation configuration. Stimuli were symmetrical, biphasic pulses (25  $\mu$ s/phase, 8- $\mu$ s interphase gap) delivered at a rate of 900 pps in 500-ms bursts. Participants were given a ten-point loudness rating chart, and stimuli were presented using an ascending procedure and step size of 5 current level (CL) units. After the electrical dynamic range was determined for each of the activated electrodes individually, a “sweep” was used to check for loudness balance across electrodes both at a low level (25% of the dynamic range) and at 5 CL below the loudness rating of 10 (C). Adjustments were made to T and C levels as needed. The loudness balanced C levels were the current levels used for eCAP measurements.

The lower and upper frequency boundaries of the frequency allocation table were adjusted to 350 Hz and 5600 Hz for this reduced electrode program. The decision to alter the frequency allocation table was specific to the design of [Scheperle and Abbas \(2015\)](#). A potential benefit for the present study is that it contributed to the novelty of the reduced-channel program used for speech-perception measurements. Additionally, the processing strategy was Advanced Combination Encoder (ACE) with seven maxima, which effectively is a Continuous Interleaved Sampling (CIS) strategy. The device was set to “live” mode to check for overall loudness comfort, and global adjustments to the C levels were made until the individual reported that the author's voice (reciting days of the week/months of the year) was a comfortable volume. All pre-processing options were turned off, and the auxiliary-to-microphone ratio was set to 10:1.

## 2.6. Speech discrimination

Medial vowel discrimination was assessed in an initial/h/, final/d/context using tokens spoken by ten female talkers ([Hillenbrand et al., 1995](#)). Each talker produced ten tokens (“had”, “hayed”, “head”, “heard”, “heed”, “hid”, “hood”, “hoed”, “hud”, “who'd”), resulting in a total of 100 stimuli. The stimuli were presented at a 55 or 60 dBA equivalent level through the auxiliary port. Prior to testing, each stimulus was displayed on a computer screen with simultaneous auditory input to familiarize the participant with the sound of the new processor settings. A sentence from the rainbow passage (“The rainbow is a division of white light into many beautiful colors.”) was also presented in auditory-visual mode. The sentence was spoken six times, each by a different female talker. For the test, each /h/vowel/d/ token was chosen using random selection without replacement, until all 100 stimuli had been presented. The ten possible tokens were displayed in print on a computer screen at all times. Participants responded by selecting the printed display corresponding to their perception, either with a touch pad or mouse click. Scores were calculated as percent correct (displayed in [Table 1](#)).

## 2.7. Analysis

Analyses were conducted in MATLAB (Mathworks, Inc.; version 2008). Correlation and regression analyses were used to evaluate several relationships: (1) recording electrode impedance with eCAP amplitude and (2) eCAP amplitude and vowel discrimination scores. For the latter comparison, the eCAP data were quantified three ways. First, each participant's eCAP data were reduced to a single value by averaging the eCAP amplitudes of the tested electrodes (i.e., the across-site mean). A second comparison used the eCAP amplitude for a single electrode in the middle of the array. The final comparison used the across-site mean of eCAP amplitudes that had been normalized by the respective recording electrode impedance. Correlations between eCAP amplitudes and vowel discrimination scores were compared using the Fisher  $r$  to  $Z$  score transformation.

## 3. Results

### 3.1. eCAP amplitude profiles

Consistent with previous reports, a high degree of variability was observed in the responses elicited by tested electrodes within an individual, and the  $N_1$ - $P_2$  amplitude profiles were specific to the individual. The amplitude profiles (normalized to the maximum amplitude for each individual for display purposes) are provided in Fig. 1. Each panel contains data from a different participant, arranged according to their across-site mean amplitude (smallest: top left; largest: bottom right). Responses were elicited from each of the test electrodes in all participants; however, the  $N_1$ - $P_2$  amplitudes ranged from just above the noise floor of the implant system ( $5.26 \mu\text{V}$ ) to  $621.24 \mu\text{V}$ .

### 3.2. Recording electrode impedance

Electrode impedances ranged from  $3.96$  to  $18.28 \text{ k}\Omega$  across all participants and all electrodes. Because a higher recording electrode impedance can result in a smaller amplitude waveform, it was important to assess how much of the eCAP amplitude variability was due to using intracochlear electrodes with different impedance values, as opposed to other factors presumed to be more relevant to speech perception, such as neural status. Fig. 2 displays scatter plots of eCAP amplitude (normalized for display) as a function of recording electrode impedance for each of the twenty participants in a separate panel. Regression lines are shown when the expected negative correlations were significant ( $p \leq 0.05$ ). The slopes and intercepts were calculated using both the normalized and absolute amplitudes. No pattern was apparent in either set of values.

Because the primary measure of interest was eCAP variability across participants as a measure of variability in auditory function, data were collapsed across participants to evaluate a possible (interfering) relationship between eCAP amplitude and electrode impedance (Fig. 3). No correlation

was observed, indicating that eCAP amplitude variability observed across participants is dominated by factors other than recording electrode impedance differences.

### 3.3. Relationship between eCAP amplitude and vowel discrimination

Positive correlations ( $p < 0.01$ ) between vowel discrimination scores and suprathreshold eCAP amplitudes were observed regardless of how the eCAP data were quantified. Scatterplots relating vowel discrimination scores to suprathreshold eCAP amplitudes are provided in Fig. 4. In the top panel, eCAP data were reduced to a single value for each participant by taking the across-site mean. This value accounts for 56% of the variability in vowel discrimination scores ( $b = 29.88$ ,  $m = 0.10$ ,  $r = 0.75$ ).

The positive correlation between eCAP amplitude associated with a single stimulation site in the middle of the array and vowel-discrimination scores remained significant (Fig. 4, middle panel). Although the single electrode eCAP amplitude accounted for less of the variability in vowel discrimination scores (37%) compared to the across-site mean (56%), the correlation coefficients were not significantly different ( $Z = 0.78$ ;  $b = 32.96$ ,  $m = 0.08$ ,  $r = 0.61$ ).

Because a relationship between recording electrode impedance and eCAP amplitude exists (though only in a subset of individuals), eCAP amplitudes were normalized by the impedance of the associated recording electrode prior to averaging across electrode site. These eCAP values are shown in the bottom panel of Fig. 4. Although the correlation remains significant ( $b = 29.82$ ,  $m = 0.67$ ,  $r = 0.72$ ), the normalization procedure did not account for a greater amount of variability than the non-normalized, actual eCAP amplitudes (top panel).

## 4. Discussion

The significant positive correlation between average eCAP amplitude and vowel perception observed in the present study is consistent with the data of DeVries et al. (2016), despite the fact that different devices were used in the two studies (Cochlear and Advanced Bionics, respectively). This replicable result is consistent with the hypothesis and more promising than the early reports (Brown et al., 1990). Together, these more recent findings indicate that suprathreshold eCAP amplitude should be reconsidered as a tool to characterize some aspects of auditory function in CI users. However, the tool needs to be used within the context of its limitations.

### 4.1. Electrode location

In the present study, eCAP amplitude was considered an indirect measure of neural status. In addition to the status of spiral ganglion neurons, the position of the electrode relative to stimutable neurons is another factor that contributes to the effectiveness of cochlear implant stimulation. Although insertion depth is not likely indicated by eCAP measures, it is

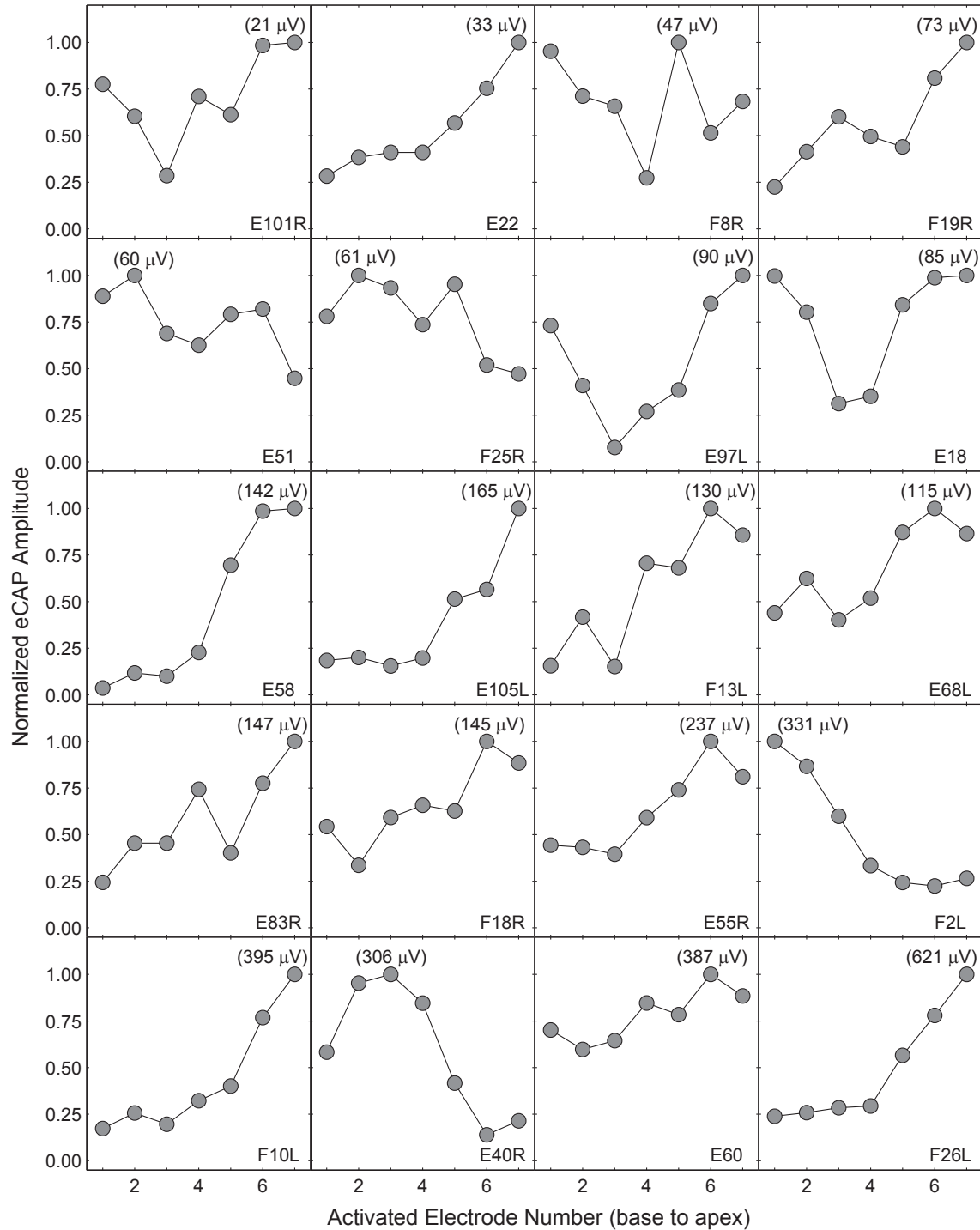


Fig. 1. Suprathreshold eCAP amplitude profiles for each participant (identifier is displayed in the lower right corner of each panel). Amplitudes were normalized to each participant's maximum (see number in parentheses) for plotting purposes. The panels are ordered by the across-site means of the eCAP amplitudes. Electrode position is displayed on the abscissa; the numbering reflects system used for this study and not the numbering system of the implant manufacturer. For all but one participant, the standard manufacturer electrode numbers used in the study were 6 (most basal; indicated as “1” for the study), 8, 10, 12, 14, 16 and 18. For F19R, electrodes 7 (most basal; indicated as “1” for the study), 9, 11, 13, 15, 17 and 19 were activated.

presumed that measured eCAP amplitude would reflect the distance between the electrode and stimulated neural elements. Contrary to the expectation, eCAP amplitude (elicited with suprathreshold, loudness balanced stimuli) appears less sensitive to medial-lateral electrode placement (estimated with post-operative imaging) than other metrics, such as behavioral

thresholds and eCAP channel-interaction measures (DeVries et al., 2016). This could be viewed as a benefit when there is a desire for a measurement with minimal information about electrode location. However, electrode position is also related to speech perception outcomes (e.g. Skinner et al., 2002; Holden et al., 2013), and thus was a limitation to the goals

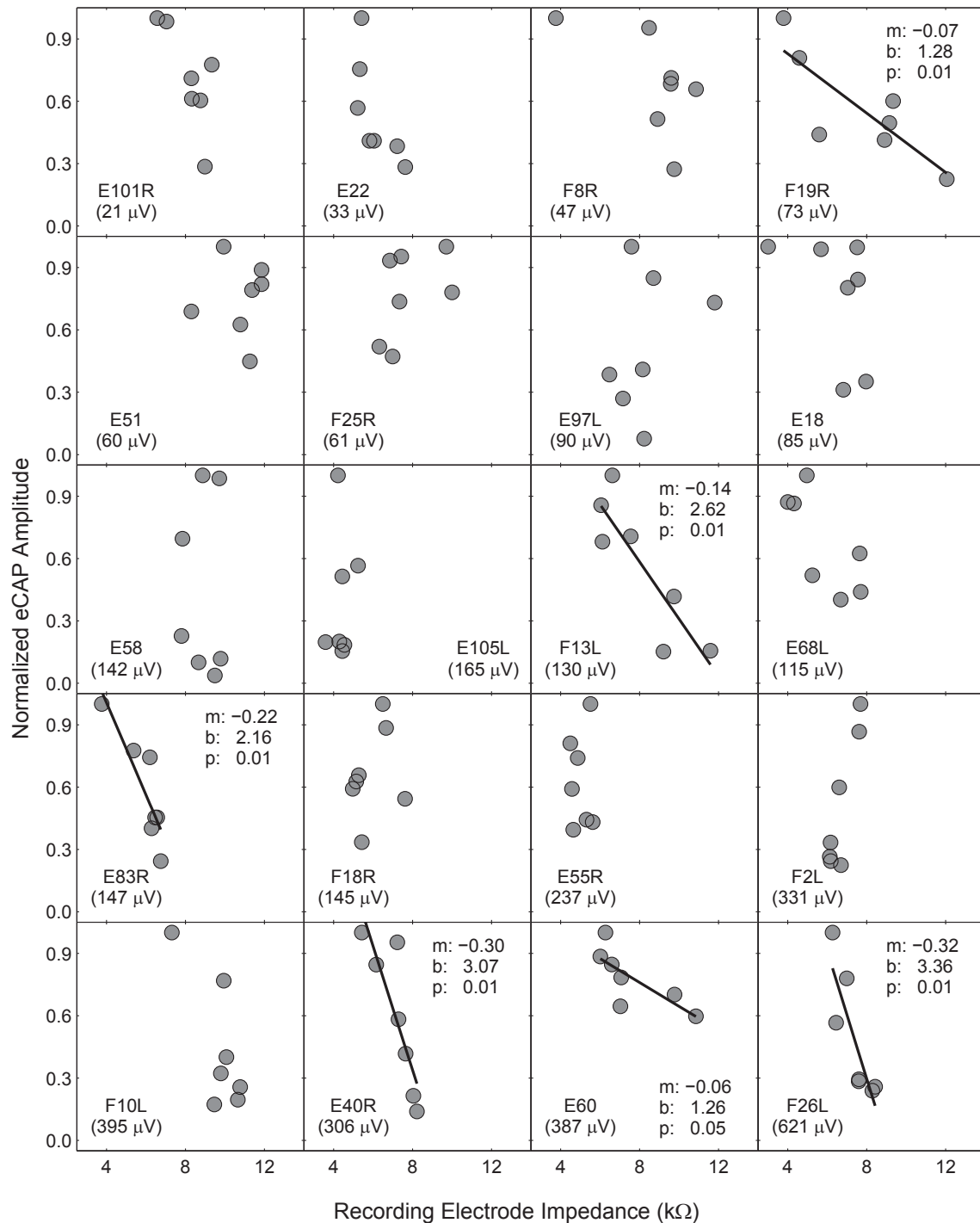


Fig. 2. Scatterplots relating eCAP amplitudes (normalized, as in Fig. 1) to recording electrode impedance (kΩ) within subjects. The participants are arranged in the same order as in Fig. 1. The normalization amplitude is provided in parentheses below the participant ID at the bottom of each panel. Regression lines and model parameters are displayed in the panels with significant negative correlations between eCAP amplitude and recording electrode impedance ( $p \leq 0.05$ ).

of the present study. Combining eCAP amplitude with an estimate of electrode position would have been more ideal.

#### 4.2. Recording electrode impedance

A benefit of eCAP measures over other electrophysiological measures is the nearness of the intracochlear recording electrode to the response generator site. However, this benefit

may be partially offset by the fact that electrode impedance is not under experimental control. Although no correlation was observed between electrode impedance and eCAP amplitude when considering all of the data available across participants in the present study, negative correlations have been observed between electrode impedance and eCAP amplitude for within-subject comparisons (Schvartz-Leyzac and Pflugst, 2016 and the present study). In the present study the MP2 extracochlear

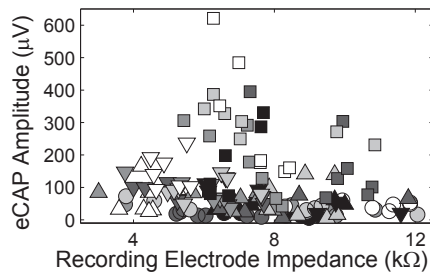


Fig. 3. Scatterplot relating eCAP amplitudes ( $\mu\text{A}$ ) to recording electrode impedance ( $\text{k}\Omega$ ) across all participants. A unique symbol/color combination is used for each participant.

electrode was chosen as the reference to reflect the recording electrode configuration used during eCAP measures as compared to using all non-active intracochlear electrodes as the return for the active electrode in a common ground mode (Schvartz-Leyzac and Pfingst, 2016). Even so, the results of the two studies are consistent. Correlations were significant in 30% of both samples (note: the present study used a more relaxed  $p$  value criterion).

Because the focus of the present study was across-subject variability, the within-subject variability in electrode impedance likely had a minimal effect. This is demonstrated by essentially no change in the correlation with vowel discrimination scores when eCAP amplitudes were first normalized to the respective recording electrode impedance prior to taking the across-site mean. For research aimed at understanding within-subject across-site patterns with goals to use the electrode profiles as a way to optimize stimulation for an individual, the relationship between eCAP measures and recording electrode impedance is likely more relevant. In these situations, measures that are less sensitive to recording electrode impedance may be more optimal. For example, Schvartz-Leyzac and Pfingst (2016) found that sensitivity to an interphase gap (i.e. the amplitude or slope difference for stimuli with short versus long interphase gaps) was less affected by recording electrode impedance than single measures of eCAP amplitude or slope.

#### 4.3. eCAP amplitude profile

eCAP amplitudes varied across electrode sites within an individual, and the pattern was unique to the participant, which is consistent with previous reports (DeVries et al., 2016; Schvartz-Leyzac and Pfingst, 2016). Although not statistically different in the present study, the correlation between vowel discrimination scores and single-electrode eCAP amplitudes was weaker than the correlation when the across-site mean eCAP amplitude was used. This result supports the assumption that including information from multiple stimulation/recording sites is more reflective of overall neural status than a measure from a single cochlear site, even when the stimulation mode is broad. Thus, as previously speculated, the null outcomes of Brown et al. (1990) may be partially attributed to the use of a single electrode. Although the across-site mean appears an improvement over a single-electrode measure, this

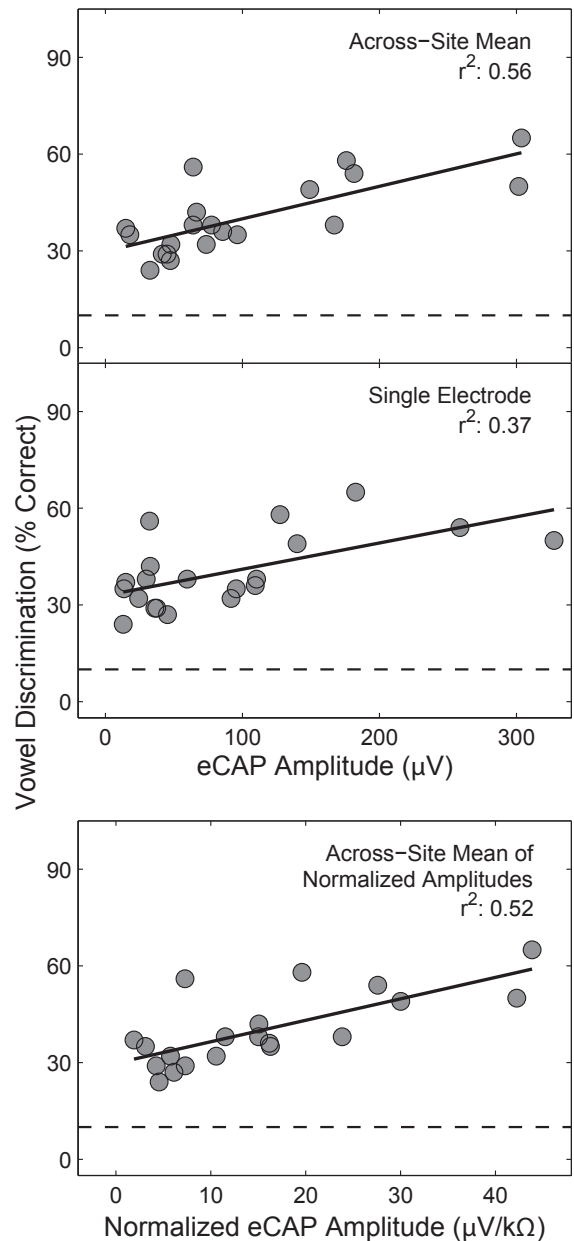


Fig. 4. Scatterplots relating vowel-discrimination scores (percent correct) to suprathreshold eCAP amplitudes. The three methods used to quantify eCAP amplitudes are shown in separate panels. Top panel: across-site mean of the eCAP amplitudes. Middle panel: amplitude for the electrode in the middle of the reduced-channel array. Bottom panel: eCAP amplitude normalized by the recording electrode impedance and averaged across the array. Simple linear regression fits are displayed as solid lines. Chance performance is 10% for this closed-set task (dashed horizontal line).

calculation is not ideal in that a mean eliminates some presumably relevant information about consistency of the excitation pattern as stimulation is swept across the array. Additional metrics that capture the variability should also be considered for cross-subject comparisons.

#### 4.4. Additional eCAP measures

The present study focused on using suprathreshold eCAP amplitude as a measure of peripheral neural status, but positive



correlations between slope of the eCAP amplitude growth function and speech perception have also been observed (e.g. Kim et al., 2010). Because half of the reported data set was collected as part of another study, only single-point amplitude measures were available. While a single-point amplitude measure has a practical advantage of requiring less data collection than required for slope measures, slope of the eCAP amplitude growth function is potentially less affected by loudness limitations or inconsistencies in loudness judgements than a single-point measure. This metric deserves further attention.

The eCAP also can be elicited using various stimulation paradigms to tap into more specific aspects of peripheral excitation. For instance, spatial selectivity can be assessed by eliciting eCAPs within channel-interaction paradigms. To date, significant correlations between eCAP channel interaction and speech perception have only been observed when channel interaction was manipulated within an individual, but not when attempting to explain the variable perceptual abilities observed across individuals (Hughes and Stille, 2008; Tang et al., 2011; van der Beek et al., 2012; Scheperle and Abbas, 2015; DeVries et al., 2016). Temporal response properties of the peripheral system can also be assessed via eCAP measures (e.g. Kim et al., 2010; Zhang et al., 2013; Schwartz-Leyzac and Pfungst, 2016), but correlations with speech perception are observed inconsistently (see van Eijl et al., 2016 for review). These results demonstrate the need for additional information to explain the inconsistencies, and for exploration into alternative applications of eCAP measures.

#### 4.5. Central auditory nervous system

Because perceptual measures are dependent upon the processing of the auditory pathway that extends beyond the auditory nerve, it is not expected that any eCAP measure will fully explain the variable perceptual abilities observed across CI users. In the present study, 56% of the variability in vowel discrimination scores was explained by the across-site mean eCAP amplitude, which is similar but lower than observed by DeVries et al. (2016; 68%). Although test materials were not formally evaluated, speech-perception metrics, such as vowel and consonant discrimination as used in both studies, are likely more appropriate to use when assessing the impact of peripheral processing on perception than measures that contain additional phonemic and linguistic context, and are likely to reflect differences in central and top-down processing across individuals. In the present study, a novel CI program was also used, which may have minimized any learning differences across participants in terms of the amount of time and familiarity with their personal programs (though all participants were experienced CI users). A within-subject test design for bilateral CI users is another option to minimize the differences in linguistic abilities and cognition across subjects (e.g. Zhou and Pfungst, 2014; Schwartz-Leyzac and Pfungst, 2016). These methodological issues are important to consider during the study design

phase, but even so, the perceptual differences among CI recipients is not expected to be fully explained by a peripheral measure.

#### 4.6. Individual optimization of cochlear implant stimulation

The present study focused on assessing whether eCAP amplitude could explain *cross*-subject perceptual variability. There is also a need to understand the functional variability observed when stimulating different electrodes along the array (*within*-subject variability), especially as it relates to individualized programming to ensure optimal outcomes for each CI recipient. A number of behavioral (e.g. thresholds, modulation detection, multipulse integration), electrophysiological (e.g., eCAP channel interaction, amplitude, slope, sensitivity to interphase gap, and sensitivity to stimulus polarity), and imaging (e.g. computerized tomography) measures have been used to characterize the functionality of each electrode site (e.g. Pfungst et al., 2004; Bierer and Faulkner, 2010; Garadat et al., 2012; Noble et al., 2013; Zhou and Pfungst, 2014; Long et al., 2014; Scheperle and Abbas, 2015; Hughes et al., 2015; DeVries et al., 2016; Schwartz-Leyzac and Pfungst, 2016). Because the across-site pattern is not the same for all measures (e.g. Pfungst et al., 2015), more work is needed to determine how these measures are related, and what they tell us about various mechanisms underlying auditory function. For instance, some measures, such as behavioral thresholds and eCAP channel interaction, appear more sensitive to electrode position than, for example, eCAP amplitude (Long et al., 2014; DeVries et al., 2016). These results imply that a combination of complementary measures might be necessary to gain a full picture of electrode functionality.

Even with our limited understanding of the various measures of auditory function, processing strategies that individually optimize stimulation patterns according to these measures have been shown to improve perceptual abilities in some, but not all CI users (e.g. Garadat et al., 2013; Bournique et al., 2013; Noble et al., 2014; Bierer and Litvak, 2016). More work in this area is needed. Suprathreshold eCAP amplitude has yet to be assessed as a measure upon which to base programming decisions.

## 5. Conclusions

In this group of CI recipients, suprathreshold eCAP amplitude explained a significant proportion of the variability in their vowel discrimination scores. These results provide empirical support to the hypothesis that peripheral neural status is an important factor when considering outcomes from CI stimulation, and that eCAP measures, as a reflection of peripheral neural status, provide relevant information about perception. This study focused on a single electrophysiological measure, but a combination of measures is likely needed for a more complete understanding of the factors underlying the effectiveness of CI stimulation to excite peripheral

auditory neurons. Further exploration into measures that characterize stimulation effectiveness *within* an individual across electrode sites deserves further attention, as does exploration into measures used to evaluate the variable outcomes observed *across* CI recipients. Various eCAP metrics, such as rate of growth, latency, spatial selectivity and temporal responsiveness, deserve further attention for both applications.

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