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Peripheral and Central Contributions to Cortical Responses in Cochlear Implant Users

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Abstract

Objectives—The primary goal of this study was to describe relationships between peripheral and central electrophysiological measures of auditory processing within individual cochlear implant (CI) users. Specifically, we evaluated the distinctiveness of neural excitation patterns resulting from the stimulation of different electrodes, which we refer to as “spatial selectivity.” The hypothesis was that if central representations of spatial interactions differed across participants semi-independently of peripheral input, then the within-subject relationships between peripheral and central electrophysiological measures of spatial selectivity would reflect those differences. Cross-subject differences attributable to processing central to the auditory nerve may help explain why peripheral electrophysiological measures of spatial selectivity have not been found to correlate with speech perception.

Design—Eleven adults participated in this and a companion study. All were peri- or post-lingually deafened with more than 1 year of CI experience. Peripheral spatial selectivity was evaluated at 13 cochlear locations using 13 electrodes as probes to elicit electrically evoked compound action potentials (ECAPs). Masker electrodes were varied across the array for each probe electrode to derive channel-interaction functions. The same 13 electrodes were used to evaluate spatial selectivity represented at a cortical level. Electrode pairs were stimulated sequentially to elicit the auditory change complex (ACC), an obligatory cortical potential suggestive of discrimination. For each participant, the relationship between ECAP channel-interaction functions (quantified as channel-separation indices) and ACC N₁-P₂ amplitudes was modeled using the saturating exponential function $y = a * (1 - e^{-bx})$. Both a and b coefficients were varied using a least-squares approach to optimize the fits.

Results—Electrophysiological measures of spatial selectivity assessed at peripheral (ECAP) and central (ACC) levels varied across participants. The results indicate that differences in ACC amplitudes observed across participants for the same stimulus conditions were not solely the result

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of differences in peripheral excitation patterns. This finding supports the view that processing at multiple points along the auditory neural pathway from the periphery to the cortex may vary across individuals with different etiologies and auditory experiences.

Conclusions—The distinctiveness of neural excitation resulting from electrical stimulation varies across CI recipients, and this variability was observed both in peripheral and cortical electrophysiological measures. The ACC amplitude differences observed across participants were partially independent from differences in peripheral neural spatial selectivity. These findings are clinically relevant because they imply that there may be limits (1) to the predictive ability of peripheral measures and (2) in the extent to which improving the selectivity of electrical stimulation via programming options (e.g., current focusing/steering) will result in more specific central neural excitation patterns or will improve speech perception.

INTRODUCTION

The first stage of auditory processing for a cochlear implant (CI) user is the peripheral neural excitation pattern resulting from electrical stimulation. The number, functionality, and location of surviving auditory neurons, the location of the electrodes relative to stimutable neurons, and the impedance pathway for current spread varies across individuals and across the electrode array (e.g., Nadol, 1997; Kawano et al. 1998; Fayad & Linthicum 2006; Long et al. 2014). These factors affect the extent to which stimulation from different electrodes results in unique neural excitation patterns. Considering the tonotopic organization of the auditory system, the distinctiveness of neural excitation in the spatial domain (i.e. spatial selectivity) presumably is responsible for some of the variable perceptual abilities observed across CI users (e.g., Tyler et al. 2000; Firszt et al. 2004; Won et al. 2011; Jones et al. 2013).

The most direct measure of peripheral neural excitation in CI users is the electrically evoked compound action potential (ECAP). The spatial selectivity of electrical stimulation can be assessed by evoking the ECAP within a forward-masking/channel-interaction paradigm. Although influenced by many factors, an ECAP channel-interaction function reflects the neural excitation pattern resulting from the probe stimulus. The shape of the function resembles that of an auditory filter (though derived using responses obtained at suprathreshold stimulation levels). The magnitude, breadth, and overall shapes of ECAP channel-interaction functions differ across CI users and probe electrodes (e.g., Cohen et al. 2003; Abbas et al. 2004; Eisen & Franck 2005); however, significant correlations with speech perception have not been observed (Cohen et al. 2003; Hughes & Abbas 2006; Hughes & Stille 2008; Tang et al. 2011; van der Beek et al. 2012).

One potential explanation for the lack of correlation between ECAP channel-interaction functions and speech perception is that although the periphery is the foundation for further processing, variability of central processing must be considered, particularly in long-term, hearing-impaired ears. Auditory deprivation and experience affect the organization and development of the central auditory system (e.g., Kral et al. 2005; also reviewed in Dahmen & King 2007; Moore & Shannon 2009), and contribute to speech perception (e.g., Blamey et al. 2013). Although often considered within the context of a sensitive period for the

immature auditory system, plasticity, which includes the capacity for tonotopic reorganization of the cortex, is retained throughout adulthood (Dahmen & King 2007).

Cortical electrophysiological responses have been used to explore central neural maturation and plasticity in CI recipients. Waveform morphology is sensitive to duration of deafness and auditory experience (e.g., Ponton et al. 1996; Sharma et al. 2005). Although longitudinal measures of cortical activity for an individual may provide information about changes in auditory processing abilities (e.g., Sharma et al. 2005), interpreting a single measure for an individual and/or comparing measures across individuals, particularly CI users, is complicated by the fact that central responses reflect cumulative processing along the auditory pathway. In normal-hearing individuals, peripheral input is relatively uniform, and differences observed at cortical levels would suggest differences in processing central to the auditory nerve. For individuals with CIs, uniformity of peripheral input cannot be assumed. Moreover, the development, maturation, and organization of more central structures are likely more variable across this population than across a group of normal-hearing individuals. It would be useful to understand the relative contributions of different stages of auditory processing, as the information may improve our ability to predict perception resulting from CI stimulation for individuals and/or could be used to inform clinical decisions about (re)habilitation and management strategies.

A few investigators have measured electrophysiological responses at multiple levels of the auditory system (e.g., brainstem, midbrain, cortex) within individual CI recipients to evaluate the influence of peripheral processing on central measures (Makhdoum et al. 1998; Firszt et al. 2002a). When pooling data across participants, significant correlations between brainstem, midbrain, and cortical component amplitudes or component latencies have not been consistently observed. These null findings suggest that the cross-subject differences observed at cortical levels are not simply a reflection of cross-subject differences at peripheral levels. Although central processing is dependent upon peripheral processing, these studies demonstrate that peripheral differences were not sufficient to explain the variability observed at more central levels. Neither Makhdoum nor Firszt and colleagues performed within-subject analyses to describe how the relationships between peripheral and central processing varied across their participants, and neither included the most peripheral measure available in CI users: the ECAP.

The purpose of this study was to characterize the relationship between peripheral and central processing for individuals by performing multiple peripheral and cortical electrophysiological measures for each participant. Spatial selectivity was evaluated because the goal was to extend this work to predictions of speech perception (Scheperle & Abbas, submitted). ECAP channel-interaction functions were obtained on more than half of the electrode array, which allowed a more thorough characterization of peripheral spatial selectivity for each participant than the relatively sparse sampling of previous studies (Cohen et al. 2003; Hughes & Stille 2008; Tang et al. 2011; van der Beek et al. 2012). The cortical electrophysiological measure of spatial selectivity was the acoustic/auditory change complex (ACC; Ostroff et al. 1998; Brown et al. 2008).

The ACC is an obligatory cortical auditory evoked potential (CAEP) elicited when some feature in an ongoing stimulus is changed (e.g., Jerger & Jerger 1970; Won et al. 2011). One stimulus paradigm used to elicit the response in CI users is the presentation of pulse trains on two sequentially stimulated electrodes (Brown et al. 2008; Hoppe et al. 2010; He et al. 2013). The ACC elicited with this stimulus paradigm can be considered an objective measure of electrode discrimination, and permits a central measure of spatial selectivity using only a slightly more complex stimulus (high-rate pulse trains) than the stimulus used in the ECAP channel-interaction paradigm (low-rate pulse trains). Like the ECAP, the size of the ACC is partially dependent upon the degree with which the two electrodes stimulate non-overlapping neural populations. ACC amplitude generally increases as the electrode pairs are spaced farther apart, although nonmonotonicities also are observed (Brown et al. 2008; He et al. 2013). Significant correlations have been observed between the ACC and behavioral measures of electrode discrimination (Hoppe et al. 2010; He et al. 2013) and speech perception in children identified with auditory neuropathy spectrum disorder (He et al. 2013).

This study compared amplitudes of the ACC evoked using pairs of sequentially stimulated electrodes with channel-separation indices calculated from ECAP channel-interaction functions obtained for the same pairs of electrodes. A channel-separation index captures the response-amplitude *differences* across two ECAP channel-interaction functions, thus reflecting the extent to which the neural excitation patterns differ across two probe electrodes. The index has been found to correlate with behavioral measures of pitch ranking (Hughes 2008). This study extends the findings of Hughes (2008) by comparing the index with an objective measure of electrode discrimination. A positive correlation between the two measures of spatial selectivity (ECAP channel-separation indices and ACC amplitudes) was expected for all subjects. We hypothesized that the *relationships* (e.g., growth rates and saturation) would reveal variability across participants attributable to processing central to the auditory nerve.

MATERIALS AND METHODS

Participants

Eleven adult recipients of either a Nucleus CI24RE or CI512 device (Cochlear Ltd., Macquarie, NSW, Australia) participated in this and the companion study. Both internal devices contain the same amplifier, resulting in similar noise floors for ECAP measures. All participants were implanted with the Contour Advance intracochlear electrode array, which is pre-curved with 22 half-banded electrodes numbered from base (1) to apex (22). Two extracochlear electrodes (MP1, positioned under the temporalis muscle; MP2, located on the case of the receiver-stimulator) are available for monopolar stimulation modes (Patrick et al. 2006). The measurements for this and the companion study (Scheperle & Abbas, submitted) were obtained using a laboratory Freedom processor and headpiece.

All participants were native English speakers with more than one year of CI experience. For individuals with bilateral CIs, only one ear was tested. The test ear was chosen to avoid deactivated electrodes or older internal devices. Two participants (E51 and F2L) had progressive hearing loss identified during childhood and initially managed with hearing-aid

use. All other participants had histories consistent with adult-onset deafness. Additional demographic information is included in Table 1.

The data collected for this and the companion study (Scheperle & Abbas, submitted) required a total of 12–20 hours of participation for most individuals. Each session ranged from 4–8 hours, and the time between the first and last sessions ranged from approximately 1 week to 7 months. Participants were compensated for their time. This study was conducted in accordance with guidelines set forth by the Institutional Review Board of the University of Iowa.

Stimulation Levels

Ideally, the peripheral and cortical electrophysiological measures would be elicited using identical stimulation levels because spatial spread of current and the resulting excitation pattern can be affected by stimulation level (e.g., Cohen et al. 2003; Abbas et al. 2004). The different stimulation rates used for the peripheral and cortical measures complicate the experimental design because temporal integration results in greater loudness for high-rate compared to low-rate stimuli. Although we did not equate absolute stimulation levels across the two outcome measures, we attempted to retain the stimulus contour (relative electrode-specific stimulation levels) across measures for each individual.

Custom Sound (version 3.2) software was used to present 500-ms bursts of charge-balanced biphasic pulses (900 pulses per second, 25- μ sec/phase, 8- μ sec interphase gap) to each intracochlear electrode using MP1 as the return. An ascending method was used to find current levels associated with behavioral threshold (T) and uncomfortable (U) loudness for all 22 electrodes. Stimulus level was raised in 5 current-level (CL) steps (1 CL $\approx$ 0.175 dB). Participants rated perceived loudness on a scale from “0” (no sound) to “10” (too loud). Threshold was considered the highest CL resulting in a rating of “2” due to limited loudness growth at low levels for a number of subjects (this is sometimes referred to as a “ T -tail”; Waltzman & Roland, 2006). U level was considered the CL rated as a “10” or the highest CL before reaching voltage compliance limits of the device.

Loudness balancing was performed across the electrode array at two stimulation levels: 5 or 10 CL below U level and at 25% of the behavioral dynamic range (difference between T and U). Groups of four electrodes were stimulated sequentially in an apical-to-basal direction. The last electrode in each group became the first electrode stimulated in the subsequent group. Individual electrode levels were adjusted as needed to achieve equal loudness across adjacent electrodes.

The loudness-balanced current levels based on the 900-pps rate stimuli were used for ECAP measures so that relative stimulation levels across electrodes would reflect the contour of the stimuli used to elicit the ACC (this study) and of the participants’ comfort (C) levels of experimental processor programs used for the companion paper (Scheperle & Abbas, submitted). Because channel-interaction functions require *suprathreshold* ECAP amplitudes, a screening was initially performed at the 900-pps U level as an initial attempt to determine a level high enough to evoke an ECAP but one that would not be uncomfortable. For six participants, screening levels were sufficient to evoke suprathreshold ($> 30 \mu$ V) responses.

For one participant (F2L) stimulus artifact was large, and levels were lowered by 25 CL across the array to maintain the contour across electrodes. For the remaining five participants, masker and probe levels for the majority of electrodes were increased by different amounts (range: 2–25 CL) as necessary to observe response amplitudes $>30 \mu\text{V}$. For E40R, the device's voltage compliance limited stimulus levels for a number of high-impedance electrodes. In all cases, stimulation levels for CAEPs were set at 80% of the dynamic range between loudness-balanced *T* and *U* levels.

General Procedures

Participants were seated in a reclining chair and asked to engage in a quiet activity (e.g., watch closed-caption TV or video, read, use computer/iPad). For the ECAP measures, participants were allowed to sleep. During the CAEP measures, participants were asked to minimize movements and to remain awake and alert. Breaks were offered regularly and given as requested by the participant.

Spatial selectivity was evaluated for the 13 cochlear locations associated with electrodes 3, 6, 8, 9, 10, 11, 12, 13, 14, 15, 16, 18 and 21. Electrode pairs always included electrode 12. For participant F19R, ECAPs were small/absent when stimulating probe electrodes 3–6 within loudness tolerance. For this individual, the set was modified to include electrodes 2, 7, 9, 10, 11, 12, 13, 14, 15, 16, 17, 19 and 22, and electrode 13 was always included in the pair. Thus, the relative spacing between electrodes was identical to that of all other subjects, except for the most basal electrode.

Peripheral Measures of Spatial Selectivity

The Custom Sound EP (version 3.2) Neural Response Telemetry (NRT) system was used to elicit and record ECAPs. The following default parameters were used: MP1 reference for probe stimulation, MP2 reference for masker stimulation, 80-pps stimulation rate, 400- μsec masker-probe interval. Other measurement parameters (e.g., delay, recording electrode, and gain) were adjusted as needed for each participant (Abbas et al. 1999; Dillier et al. 2002). Typically the recording electrode was two electrodes apical to the probe for basal maskers and two electrodes basal to the probe for apical maskers. Across participants and probe electrodes, the optimal recording delay ranged from 78–160 μsec and amplifier gain from 40–60 dB. One hundred recordings were averaged for each masker-probe pair.

ECAP channel-interaction functions were obtained using the individually optimized stimulation and recording parameters and a forward-masking subtraction paradigm to derive the probe response (e.g., Cohen et al. 2003; Abbas et al. 2004). The current levels described previously were used for both masker and probe stimulation. Thus, maskers and probes were stimulated at equal (or close to equal) loudness levels rather than equal current levels. The order in which the channel-interaction functions were collected was randomized. For each series of measurements, the location of the probe was fixed and the location of the masker varied randomly across all 22 electrodes. ECAP channel-interaction functions were obtained on all 13 probe electrodes in < 1 hour.

An example of one series of ECAP waveforms obtained for participant E55R is provided in Figure 1. The waveforms are offset vertically by masker electrode and arranged in order from 1 (top) to 22 (bottom); electrode 12 was the probe for all conditions. For each waveform, ECAP amplitude was calculated as the difference between negative (N_1) and positive (P_2) peaks, which were manually set by the examiner using a custom MATLAB (MathWorks, Inc. 2012a, Natick, MA) program. These peaks are marked with crosses in Figure 1. Because of the subtraction paradigm used to reduce stimulus artifact, no response is observed when the masker is distant from the probe, and each electrode presumably excites different populations of neurons. Response amplitudes tend to increase when the masker nears the probe.

ECAP amplitudes at the peaks of the channel-interaction functions ranged from approximately 30 μ V to > 600 μ V across participants of this study. For cross-subject comparisons, ECAP amplitudes often are normalized to the largest amplitude within each function. The goal of this study was within-subject analyses, and normalization was not necessary. However, because cross-subject analyses were of interest for the companion paper, ECAP amplitude was normalized to the single largest amplitude observed across all 13 channel-interaction functions for a given person (Hughes 2008; Hughes et al. 2013). This normalization allowed for comparisons across individuals while preserving the relative magnitude differences of excitation patterns across the electrode array within each person.

To compare ECAP channel-interaction functions with ACC response amplitudes, we calculated channel-separation indices for pairs of probe electrodes using a formula similar to Hughes (2008):

$$\frac{\sum |a_{xi} - a_{yi}|}{n}. \quad (1)$$

For a pair of ECAP channel-interaction functions associated with probes x and y , the absolute differences in normalized ECAP amplitudes (a) for each masker electrode ($i = 1-22$) were summed and divided by the total number of masker electrodes ($n = 22$). This index reflects the non-overlapping areas of two functions, capturing both location and shape differences. Although any two channel-interaction functions can be paired to calculate a channel-separation index, for this study, indices were calculated for all ECAP channel-interaction functions paired with that of the center electrode (13 for F19R and 12 for all others).

The left panels of Figure 2 display a subset of normalized channel-interaction functions for participant E55R to illustrate how the channel-separation index was calculated. Probe electrodes are indicated by dotted vertical lines in each panel. The top panel displays the single function for probe 12 (by definition, the channel-separation index = 0). In the lower three panels, amplitude differences between the function for probe 12 (filled circles) and a comparison probe (open circles) are indicated by solid vertical lines. The average of those differences (the channel-separation index: CSI) is displayed in the upper right corner of each panel. For the examples shown in this figure, the channel-separation index increased as the spatial separation between probe electrodes increased.

Central Measures of Spatial Selectivity

Custom software developed to call Nucleus Implant Communicator (NIC, version 2) routines was used to directly control electrode stimulation for evoking CAEPs. Electrode 12 (13 for subject F19R) was always included as one electrode in the pair. The second electrode was randomly selected without replacement from the remaining electrodes within the set listed previously. Stimulation consisted of an 800-ms train of charge-balanced biphasic pulses (900 pps, 25 μ sec/phase). For the control condition, stimulation was presented via electrode 12 (13) for the entire 800 ms. For all other conditions, the pulse train was output by one electrode in the pair for 400 ms and by the second electrode for the remaining 400 ms. The stimulus change in both basal and apical directions ranged from 0 (control condition where the same electrode is stimulated) to 9 electrodes (12-3; 12-21) for most participants. The largest stimulus change was 11 electrodes for F19R (13-2). The return electrode was MP1 to match the stimulation mode used for ECAPs. Electrode pairs were stimulated approximately once every 3 seconds. A single pulse synchronized with the stimulus onset was routed to a second computer to trigger recordings.

Two differential recordings were obtained simultaneously using disposable surface Ag/AgCl electrodes: vertex (+) to contralateral mastoid (–), and vertex (+) to inion (–). An electrode placed off-center on the forehead served as the ground, and a pair of vertically placed electrodes above and below the eye were used to monitor eye blinks. At the beginning of each recording session, electrode impedance was $< 5 \text{ k}\Omega$ for each electrode, and differences were $< 2 \text{ k}\Omega$ across electrodes. Electroencephalographic (EEG) signals were routed to an OptiAmp 1.10 amplifier (Intelligent Hearing Systems). The amplifier filtered the EEG signals between 1–30 Hz and applied a gain of 10,000. The analog EEG signals were digitized with a National Instruments DAQ soundcard (6062E) using a sampling rate of 25,000 per second. LabVIEW (version 9.0.1, National Instruments, 2009) was used for online display of the EEG activity and artifact rejection during recording, and for averaging and storing sets of 100 non-rejected sweeps. The amplitude criterion used for artifact rejection was adjusted for each individual.

Recording late potentials evoked with long-duration stimuli in CI users can be problematic due to electrical artifact from the device that overlaps the neural response in the time domain. By balancing impedances across the recording electrodes, we reduced direct-current (DC; or, “pedestal”) artifact. The amplifier low-pass filter cut-off frequency reduced the high-frequency artifact (McLaughlin et al. 2013). For each pair of electrodes, 100 sweeps were collected when using electrode 12 to elicit the onset response and 100 sweeps when using electrode 12 to elicit the ACC. The two waveforms for the same electrode pairs presented in reverse order were averaged together offline. Additionally, the differential waveforms obtained with the two inverting recording sites were averaged together. Before analysis, the averaged waveforms were smoothed using a two-stage filter (down-sampling by averaging across 25 samples and application of a 20-sample rectangular window), and any remaining DC offset was removed via subtraction. Together, these procedures minimized the effects CI artifact and biological noise on the measurement of the neural potential.

A custom MATLAB peak-picking algorithm was used to identify minima (N_1) and maxima (P_2) in the time window following the stimulus change (i.e. 75–300 ms post stimulus change). Accuracy was visually confirmed and peak locations were modified if necessary by the examiner. For participant F2L, the positivity before the N_1 component (P_1) appeared more sensitive to the specific stimulus condition than P_2 . Thus for this person, the reported ACC amplitudes are P_1 - N_1 instead of N_1 - P_2 . Although peak-to-peak amplitudes were used to quantify central spatial selectivity, rms amplitudes across the ACC time window were used to identify points to exclude. If the rms amplitude for an electrode pair was less than that of the control condition (one electrode stimulated for the entire 800 ms), it was assumed that the response was noisy. This exclusion criterion is similar to that reported by Martin and Boothroyd (2000).

Examples of the averaged waveforms associated with four test conditions are shown in the right panels of Figure 2 for participant E55R. The electrodes used for stimulation are displayed in the upper left corners and match the probe electrodes used for the ECAP channel-interaction functions displayed in the left panels. The gray area spans the time window used for the rms calculation. Negative (N_1) and positive (P_2) peaks of visually identifiable onset and change responses are indicated by crosses, and N_1 - P_2 amplitudes of the ACC are noted in the upper right corners. For the examples shown in this figure, ACC amplitude increased as the stimulus change increased.

Modeling the Relationship Between Peripheral and Central Spatial Selectivity

Martin and Boothroyd (2000) modeled group-mean ACC amplitude as a function of the stimulus change (level in dB) with a saturating exponential. Although we were primarily interested in modeling *individual* data, we used group means to evaluate the validity of the exponential function to characterize the relationship between ACC amplitude and stimulus change in the *spatial* domain. We then applied the model to individual data. We assumed that a given stimulus change would likely result in different peripheral excitation patterns across individuals. Thus, for individual applications, we modeled ACC amplitude as a function of the ECAP channel-separation index, an individualized *measure* of peripheral excitation resulting from the stimulus change. We viewed a single ECAP channel-interaction function as a way to characterize the neural excitation pattern for one stimulation site (the site of the probe electrode). The channel-separation index, calculated using two channel-interaction functions, quantifies how different neural excitation patterns are for two stimulation sites. The CAEPs were evoked with sequential stimulation of two electrodes (i.e. two stimulation sites). The ACC is the response to the second electrode, and the size of the response indicates how different the excitation pattern from the second site of stimulation is relative to the first site. Thus, our primary interest was modeling the relationship between the ECAP channel-separation index and ACC amplitude for individuals.

RESULTS

The results for both peripheral and cortical measures of spatial selectivity are discussed as a function of the change in stimulation site (displayed using number of electrodes). Spacing between electrodes of the Contour Advance array is not constant, but graded from base to

apex, presumably to account for distance from the neural elements within the spiraled cochlea. Therefore, there may be differences in the overlap of electrical stimulation among "equally spaced" electrode pairs as defined by number of electrodes. Because all participants were implanted with the same electrode array, specifying the stimulus change in terms of electrodes was deemed appropriate for displaying and discussing the initial results (Figs. 3, 4, 5). The channel-separation index, not electrode spacing, was used for the ultimate within-subject analyses used to characterize the relationship between peripheral and cortical measures of spatial selectivity.

Peripheral Measures of Spatial Selectivity

Figure 3 displays the ECAP channel-separation index as a function of the separation between stimulation sites (i.e. probe electrodes) relative to the center electrode. The label "stimulus change" is used to parallel the displays of the ACC data (Figs. 4 and 5). Negative and positive numbers are used to denote basal and apical directions, respectively. Each panel contains the data from a different participant. ECAP channel-separation indices generally increase with electrode separation in either the basal or apical directions, although some nonmonotonic changes are evident (e.g., basal and apical electrodes for E51), and the index appears to saturate for some individuals (e.g., the most apical electrodes for E40R). The nonmonotonicities and saturation may be reflecting how spatial selectivity varies across the electrode array, but also may be influenced by noise in the recording or "edge effects" for channel-interaction functions near the ends of the electrode array (see Discussion). The variability observed across subjects for the same stimulus conditions suggests differences in peripheral spatial selectivity.

Central Measures of Spatial Selectivity

Figure 4 is identical to Figure 3, except that it displays ACC amplitude on the y axis. Similar to what was observed with the peripheral ECAP data, and consistent with previous studies (Brown et al. 2008; He et al. 2013), ACC amplitude tends to increase with increased distance between stimulated electrodes, and both saturation and nonmonotonicities can be observed with electrode separations in both apical and basal directions. In general ACC data appear noisier than the peripheral measures. We expect that saturation and nonmonotonicities are partially the result of peripheral excitation, but may also be reflecting additional noise in the far-field recordings compared to the peripheral measures as well as processing central to the auditory nerve.

Model Validation

Group-mean ACC amplitudes (± 1 standard deviation; SD) are shown in Figure 5. In contrast with the two previous figures, the stimulus change is displayed using only positive numbers; however, data for basal (black) and apical (gray) electrode pairs are shown separately. Data for the apical electrodes are shifted on the x-axis for visualization purposes only. The group means for apical and basal electrode pairs were averaged together and fit with the function $y = a*(1-e^{-bx})$ using the MATLAB *fit* command and a least-squares approach to determine the a and b coefficients. The a coefficient is related to the magnitude and asymptote, and the b coefficient is related to the slope of the function. The group-mean

data provide empirical support for the use of this function for modeling the ACC evoked by stimulus changes in the spatial domain. We assumed that the same function would underlie individual data, and that individual differences would primarily be characterized by changing the coefficients.

Within-Subject Relationship Between Peripheral and Central Spatial Selectivity

The primary question of this study is not how ECAP channel-separation indices or spatial ACC amplitudes vary as a function of the stimulus condition, but how these two electrophysiological measures are related within an individual. Characterizing peripheral spatial selectivity as ECAP channel-separation indices, and relating this metric with the ACC in effect normalizes for peripheral processing differences across individuals and highlights differences in central processing. The ECAP channel-separation index for two probe electrodes was compared with the amplitude of the ACC when the same two electrodes were stimulated sequentially (13 pairs). These comparisons are shown in Figure 6. Similar to Figures 3 and 4, each participant's data are displayed in a different panel. The gray dots are the data points that were excluded from analysis because the rms amplitude across the ACC time window was smaller than the no-response, control condition. The rms exclusion criterion resulted in 1–5 points being excluded from the regression analysis for F18R, F19R, F25R, F2L.

Within an individual's data set, larger ACC amplitudes generally are associated with larger ECAP channel-separation indices, although ACC amplitudes tend to saturate and display nonmonotonic growth patterns that are not explained by the peripheral measures. The range of ECAP channel-separation indices differs across participants for the same stimulus conditions; however, the differences in overall ACC amplitude and growth rates exceed the differences observed in the peripheral measures. To quantify these qualitative observations, each person's data were fit with the exponential function used to model the group mean data. For the least-squares fitting procedure, the starting point for both coefficients was set to 1.0. No lower constraint was used. The a coefficient was constrained at or below 10, and the b coefficient was constrained at or below 50. These constraints were specifically in place for participants F19R and F18R, respectively, and did not affect the r^2 values for these two participants or the solutions for the other participants. The correlations were significantly greater than zero ($p < 0.01$) for all individuals. The coefficients are shown in the top left corner of each panel. The differences in a and b coefficients across individuals is evidence of processing differences attributable to structures central to the auditory nerve.

For some individuals, the model fit was better than others. Asterisks next to the participant ID indicate those individuals for whom the stimulus-level contour for the ECAP measures was adjusted. Although level adjustments were necessary for the participant with the poorest fit (E40R: $r^2 = 0.44$), subject E55R did not require level adjustments for ECAPs, and the data reveal a number of high-amplitude ACC responses that are not characterized well by the model. The poorest model fits are not coincident with the necessity for stimulus level adjustments.

The data for E40R are re-plotted in Figure 7, with basal and apical electrode pairs shown separately (black and gray colors, respectively). For most individuals, there were no

apparent differences in the relationship between peripheral and central spatial selectivity for basal and apical electrode pairs, but for this person, there were. For basal electrode pairs, as the ECAP channel-separation index increases, ACC amplitude appears to saturate. For apical electrode pairs, the relationship appears more linear and saturation is not observed. Disregarding these differences resulted in a relatively poor “average” fit.

An alternative method to quantify the ACC is to normalize the amplitude to the onset. This has a theoretical advantage of reducing noise due to subject state/fatigue/restlessness, which may change over the course of lengthy test sessions. We performed the analyses illustrated in Figures 5 and 6 using normalized amplitudes, and results did not change appreciably. When modeling the group-mean data (Figure 5), the r^2 values were 0.97 and 0.95 for the respective normalized and absolute ACC amplitudes. When modeling individual data (Figure 6), the goodness of fit (visually determined and assessed with r^2 values) did not change consistently across participants. For some individuals, the normalized amplitude improved the model fit to the data, but for others, the absolute amplitude improved the model fit. Because we did not observe consistent benefit of normalizing the ACC to the onset, we opted to report absolute amplitudes.

DISCUSSION

There are a number of potential reasons why studies to date have not been able to demonstrate a direct relationship between ECAP measures of spatial selectivity and speech perception (Cohen et al. 2003; Hughes & Abbas 2006; Hughes & Stille 2008; Tang et al. 2011; van der Beek et al. 2012). One limitation is that ECAPs do not reflect processing beyond the auditory nerve. The purpose of this study was to evaluate and describe the differences in central processing across a group of CI users. By making multiple recordings at both peripheral and cortical levels, we were able to provide evidence that although cortical responses reflect peripheral processing, which varies considerably across CI users, the cortical representations were more variable than what could be explained by the periphery. It is worth emphasizing that variability attributable to processing beyond the auditory nerve was identified even with the use of relatively simple stimuli and the use of the obligatory cortical evoked response. These results suggest that adding information about central processing to measures of peripheral processing for the purpose of predicting speech perception is worth further exploration. This was the investigated in the companion paper (Scheperle & Abbas, submitted).

Peripheral Measures of Spatial Selectivity

Consistent with Hughes (2008), we observed larger ECAP channel-separation indices with greater distance between probe electrodes. Our work extends that of Hughes (2008) by showing data for individual subjects and for a greater number of electrode pairs. Additionally, we extend her findings by demonstrating a relationship between the index and an objective measure of electrode discrimination: the ACC. In both this study and in Hughes (2008), the channel-separation index was used for within-subject analyses. In the companion paper, we will explore its usefulness for cross-subject analyses (Scheperle & Abbas, submitted).

A notable quality of the channel-separation index is that two functions that are entirely separate (no overlap) will rarely have an index of 1.0. Although an index of 1.0 is theoretically possible, it is not likely to be observed empirically. This is in contrast to the channel-interaction index calculated from behavioral thresholds (discussed in Jones et al. 2013). Psychophysical channel-interaction indices can be observed across the entire normalized range from 0 (no interaction) to 1.0 (complete overlap). Complete overlap quantified with the ECAP channel-separation index will have a value of 0. However, “no interaction” between two functions can result in many different indices. This is because the channel-separation index is sensitive to overall extent of neural excitation as indicated by the ECAP amplitudes and breadth of the channel-interaction functions. It can be considered an “index of differential excitation”.

Because the index is sensitive to overall extent of neural excitation, there were instances within this data set when the channel-separation index associated with two non-overlapping functions was smaller than the index associated with two overlapping functions. This scenario is exemplified in Figure 8 using data from participants F19R (top panel) and E60 (bottom panel). Channel-interaction functions for probes 9 and 16 are displayed for both subjects; the channel-separation indices (CSI) are in the top, right corners. Although the functions for F19R are entirely separate, the index is smaller than that calculated for E60, whose functions are overlapping. We did not view this as a limitation of the channel-separation index. Instead, we viewed this index as a way to retain information about the overall area of excitation resulting from electrode stimulation. Broader excitation areas might not always be detrimental to performance as long as excitation patterns across electrodes are different.

As mentioned previously, the channel-separation index was observed to saturate for many subjects at large electrode separations. The saturation may be reflecting that differences in neural-excitation areas remain the same once the distance between probe electrodes increases beyond a certain point. Alternatively, the saturation may be reflecting a limitation of the ECAP channel-interaction functions used to characterize the neural-excitation area. If a channel-interaction function is not fully characterized (i.e., ECAP amplitudes have not decreased to 0 when the masker is at the physical limits of the device: electrodes 1 and 22 for this study), then the channel-separation index will be smaller than the actual differences in neural excitation areas associated with the electrode pair. This scenario is exemplified in Figure 9 using data obtained for subject F26L. The top panel displays channel-interaction functions for probes 9 and 16; the bottom panel displays channel-interaction functions for probes 9 and 21. The channel-separation index (CSI) is noted in the top, right corners. Although the electrode spacing is greater for electrodes 9 and 21 than for electrodes 9 and 16, the channel-separation index is smaller. Notice that the channel-interaction function for probe 21 does not decrease to 0 on the apical side (i.e., ECAP amplitude is approximately 0.6 for masker electrode 22). This “edge effect” likely contributes to the lower channel-separation index.

Central Measures of Spatial Selectivity

Previous studies have reported on the use of an electrode-discrimination paradigm to elicit the ACC in CI users (Brown et al. 2008; Hoppe et al. 2010; He et al. 2013). Consistent with previous observations, ACC amplitude generally increased and saturated as a function of electrode separation, although nonmonotonic amplitude variations were also present for individuals. Martin and Boothroyd (2000) used a saturating exponential to describe group mean ACC amplitudes as a function of stimulus intensity changes for normal-hearing individuals. We applied the same model to the CI users' group-mean data as a function of changes in the location of the stimulating electrode. Our data, in combination with the data reported by Martin and Boothroyd (2000), suggest that cortical responses evoked with acoustic or electrical stimulation for individuals with and without hearing loss, and for stimulus changes in different domains, can be characterized by the same underlying function. Although this study was primarily focused on characterizing individual differences for the purpose of exploring mechanisms of variability, the group-mean data suggest a general consistency with regards to encoding and responsiveness of the auditory pathway. The saturation of ACC amplitude as the stimulus change, reflected in the peripheral response, continues to increase may be an important characteristic of the cortical responses. That is, signal processing in the auditory system changes from peripheral excitation patterns that primarily reflect the stimulus to more complex patterns that are ultimately translated to perception.

Previously reported ACC data reveal variability across individuals with respect to overall amplitudes and growth rates as a function of electrode separation. Interpreting the mechanisms underlying this variability is limited because investigators did not include measures of peripheral spatial selectivity. Thus, the extent to which differences across participants reflect differences in peripheral excitation patterns or differences in processing central to the auditory nerve cannot be determined. In this study, peripheral spatial selectivity was measured for each individual and stimulus condition, and quantified as the ECAP channel-separation index. We modeled ACC amplitude as a function of the peripheral measure. This allowed us to interpret the differences in a and b coefficients across participants as evidence of differences in central processing independent from differences in peripheral processing. Although our number of participants was small, they comprised a heterogeneous group with respect to age (range: 27–86 yrs), etiology, and auditory experience pre- and post-implantation (Table 1). Given these factors and the link between sensory experience and cortical plasticity (e.g. Dahmen & King, 2007) it is not surprising that our results attribute some of the differences in ACC amplitudes to processing central to the auditory nerve.

Although the fit of the saturating exponential model to the group-mean data is convincing, the model did not fit individual data sets with the same accuracy. For E40R, the poor fit appeared the result of differences observed across apical and basal electrode pairs. Since hearing loss is often frequency dependent (e.g., steeply sloping, high-frequency hearing loss), and cortical tonotopic organization may be disrupted for some frequencies but not others (e.g. Dahmen & King, 2007), it may be that cortical processing in some individuals is place (frequency) specific. Though speculative, this factor may account for differences

observed in basal versus apical processing. An alternative explanation for the poor individual fits is that stimulus level may have been a confounding factor. To simplify data collection, we attempted to equate loudness across electrodes in order to isolate spatial cues from intensity cues. Martin and Boothroyd (2000) used a more complex function to model the ACC evoked by stimuli that combined amplitude and spectral changes. It is possible that variations in stimulus level may have affected the accuracy of exponential fits in Figure 6. Because a broader goal of our work was to relate the ECAPs and ACC to speech perception (Scheperle & Abbas submitted), the loudness equalization was deemed necessary.

Implications for Predictions of Speech Perception

A few studies have investigated the relationship between cortical potentials and speech perception in CI users. Makhdoum and colleagues (1998) elicited the onset cortical response using a tone burst, and observed a significant correlation between response amplitude and speech perception (spondee discrimination). Firszt and colleagues (2002b) did not observe a statistically significant relationship between component amplitudes or latencies of the onset cortical response and speech perception (sentences in quiet and noise). One potential limitation of the onset response is that it reflects detection, and discrimination abilities are relevant for speech perception.

The mismatch negativity (MMN) and ACC both may be better suited for comparing with speech perception. Like the ACC, the MMN reflects discrimination abilities and does not require active listening by the participant; however, it is a small, derived response, susceptible to noise, and is most often used to make group comparisons (e.g., Martin et al. 2008). Wable and colleagues (2000) elicited the MMN within a group of CI users using an electrode-discrimination paradigm; however, the response was *not* significantly related to any of the speech perception measures (consonants, phonemes, words, key words). To date, only one study has evaluated the relationship between the ACC as a measure of electrode-discrimination and speech perception (He et al. 2013). A significant correlation was observed between discrimination thresholds determined from ACC amplitude and word identification scores in children identified with auditory neuropathy spectrum disorder. It is noteworthy that speech scores were categorized as “good” and “poor” performance rather than assessed as a continuous variable. Although these results provide some evidence that central processing may be important for predicting speech perception, the role of peripheral processing on the reported findings is uncertain. The contributions of peripheral and central processing to speech perception for a more heterogeneous population of CI users were evaluated in the companion paper (Scheperle & Abbas, submitted).

CONCLUSIONS

The two electrophysiological measures of spatial selectivity included in this study provide evidence that both peripheral and central processing differ across CI users. Although cortical responses reflect peripheral input, this study was able to highlight differences in central processing independent of the periphery, providing evidence that auditory structures central to the auditory nerve function differently across CI users. The companion study evaluates

whether information about central processing may improve predicting speech perception from electrophysiologic responses.

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REFERENCES

- Abbas PJ, Brown CJ, Shalloo JK, et al. Summary of results using the nucleus CI24M implant to record the electrically evoked compound action potential. *Ear Hear.* 1999; 1:45–59. [PubMed: 10037065]
- Abbas PJ, Hughes ML, Brown CJ, et al. Channel interaction in cochlear implant users evaluated using the electrically evoked compound action potential. *Audiol Neurotol.* 2004; 4:203–213. [PubMed: 15205548]
- Blamey P, Artieres F, Baskent D, et al. Factors affecting auditory performance of postlingually deaf adults using cochlear implants: An update with 2251 patients. *Audiol Neurotol.* 2013; 18:36–47.
- Brown CJ, Etler C, He S, et al. The electrically evoked auditory change complex: preliminary results from nucleus cochlear implant users. *Ear Hear.* 2008; 5:704–717. [PubMed: 18596644]
- Cohen LT, Richardson LM, Saunders E, et al. Spatial spread of neural excitation in cochlear implant recipients: comparison of improved ECAP method and psychophysical forward masking. *Hear Res.* 2003; 1–2:72–87.
- Dahmen JC, King AJ. Learning to hear: plasticity of auditory cortical processing. *Current Opinion in Neurobiology.* 2007; 17:456–464. [PubMed: 17714932]
- Dillier N, Lai WK, Almqvist B, et al. Measurement of the electrically evoked compound action potential via a neural response telemetry system. *Annals of Otology Rhinology and Laryngology.* 2002; 5:407–414.
- Eisen MD, Franck KH. Electrode interaction in pediatric cochlear implant subjects. *J Assoc Res Otolaryngol.* 2005; 2:160–170. [PubMed: 15952052]
- Fayad JN, Linthicum FH. Multichannel cochlear implants: relation of histopathology to performance. *The Laryngoscope.* 2006; 116:1310–1320. [PubMed: 16885730]
- Firszt JB, Holden LK, Skinner MW, et al. Recognition of speech presented at soft to loud levels by adult cochlear implant recipients of three cochlear implant systems. *Ear Hear.* 2004; 4:375–387. [PubMed: 15292777]
- Firszt JB, Chambers RD, Kraus N, et al. Neurophysiology of cochlear implant users I: effects of stimulus current level and electrode site on the electrical ABR, MLR, and N1-P2 response. *Ear Hear.* 2002a; 6:502–515. [PubMed: 12476088]
- Firszt JB, Chambers RD, Kraus N. Neurophysiology of cochlear implant users II: comparison among speech perception, dynamic range, and physiological measures. *Ear Hear.* 2002b; 6:516–531. [PubMed: 12476089]
- He S, Grose JH, Teagle HFB, et al. Objective measures of electrode discrimination with electrically evoked auditory change complex and speech-perception abilities in children with auditory neuropathy spectrum disorder. *Ear Hear.* 2013; 34:733–744. [PubMed: 23722354]
- Hoppe U, Wohlbered T, Danilkina G, et al. Acoustic change complex in cochlear implant subjects in comparison with psychoacoustic measures. *Cochlear Implants International.* 2010; 11:426–430. [PubMed: 21756665]

- Hughes ML. A re-evaluation of the relation between physiological channel interaction and electrode pitch ranking in cochlear implants. *J Acoust Soc Am*. 2008; 5:2711–2714. [PubMed: 19045758]
- Hughes ML, Abbas PJ. The relation between electrophysiologic channel interaction and electrode pitch ranking in cochlear implant recipients. *J Acoust Soc Am*. 2006; 3:1527–1537. [PubMed: 16583898]
- Hughes ML, Stille LJ. Psychophysical versus physiological spatial forward masking and the relation to speech perception in cochlear implants. *Ear Hear*. 2008; 3:435–452. [PubMed: 18344869]
- Hughes ML, Stille LJ, Baudhuin JL, et al. ECAP spread of excitation with virtual channels and physical electrodes. *Hear Res*. 2013; 306:93–103. [PubMed: 24095669]
- Jerger J, Jerger S. Evoked response to intensity and frequency change. *Archives of Otolaryngology*. 1970; 5:433–436. [PubMed: 5442735]
- Jones GL, Won JH, Drennan WR, et al. Relationship between channel interaction and spectral-ripple discrimination in cochlear implant users. *J Acoust Soc Am*. 2013; 133:425–433. [PubMed: 23297914]
- Kawano A, Seldon HL, Clark GM, et al. Intracochlear factors contributing to psychophysical percepts following cochlear implantation. *Acta Oto-Laryngologica*. 1998; 118:313–326. [PubMed: 9655204]
- Kral A, Tillein J, Heid S, et al. Postnatal cortical development in congenital auditory deprivation. *Cerebral Cortex*. 2005; 15:552–562. [PubMed: 15319310]
- Long CJ, Holden TA, McClelland GH, et al. Examining the electro-neural interface of cochlear implant users using psychophysics, CT scans, and speech understanding. *J Assoc Res Otolaryngol*. 2014; 15:293–304. [PubMed: 24477546]
- Makhdoum MJ, Groenen PAP, Snik AFM, et al. Intra- and interindividual correlations between auditory evoked potentials and speech perception in cochlear implant users. *Scand Audiol*. 1998; 1:13–20. [PubMed: 9505287]
- Martin BA, Boothroyd A. Cortical, auditory, evoked potentials in response to changes of spectrum and amplitude. *J Acoust Soc Am*. 2000; 107:2155–2161. [PubMed: 10790041]
- Martin BA, Tremblay KL, Korczak P. Speech evoked potentials: from the laboratory to the clinic. *Ear Hear*. 2008; 3:285–313. [PubMed: 18453883]
- McLaughlin M, Lopez Valdes A, Reilly RB, et al. Cochlear implant artifact attenuation in late auditory evoked potentials: A single channel approach. *Hear Res*. 2013; 302:84–95. [PubMed: 23727626]
- Moore DR, Shannon RV. Beyond cochlear implants: awakening the deafened brain. *Nat Neurosci*. 2009; 6:686–691. [PubMed: 19471266]
- Nadol JB. Patterns of neural degeneration in the human cochlea and auditory nerve: implications for cochlear implantation. *Otolaryngology--Head and Neck Surgery*. 1997; 117:220–228. [PubMed: 9334769]
- Ostroff JM, Martin BA, Boothroyd A. Cortical evoked response to acoustic change within a syllable. *Ear Hear*. 1998; 4:290–297. [PubMed: 9728724]
- Patrick JF, Busby PA, Gibson PJ. The development of the Nucleus® Freedom™ cochlear implant system. *Trends Amplif*. 2006; 10:175–200. [PubMed: 17172547]
- Ponton CW, Don M, Eggermont JJ, et al. Maturation of human cortical auditory function: differences between normal-hearing children and children with cochlear implants. *Ear Hear*. 1996; 17:430–437. [PubMed: 8909891]
- Scheperle RA, Abbas PJ. Relationships among peripheral and central electrophysiological measures of spatial and spectral selectivity and speech perception in cochlear implant users. *Ear Hear*. submitted.
- Sharma A, Dorman MF, Kral A. The influence of a sensitive period on central auditory development in children with unilateral and bilateral cochlear implants. *Hear Res*. 2005; 203:134–143. [PubMed: 15855038]
- Tang Q, Benítez R, Zeng FG. Spatial channel interactions in cochlear implants. *J Neural Eng*. 2011; 8
- Tyler RS, Rubinstein JT, Teagle H, et al. Pre-lingually deaf children can perform as well as post-lingually deaf adults using cochlear implants. *Cochlear Implants International*. 2000; 1:39–44. [PubMed: 18791992]

- van der Beek FB, Briare JJ, Frijns JHM. Effects of parameter manipulations on spread of excitation measured with electrically evoked compound action potentials. *Int J Audiol*. 2012; 51:465–474. [PubMed: 22315988]
- Wable J, van den Abbeele T, Gallego S, et al. Mismatch negativity: a tool for the assessment of stimuli discrimination in cochlear implant subjects. *Clinical Neurophysiology*. 2000; 111:743–751. [PubMed: 10727926]
- Waltzman, SB.; Roland, JT., editors. *Cochlear Implants*. Inc., NY: Thieme Medical Publishers; 2006.
- Won JH, Clinard CG, Kwon S, et al. Relationship between behavioral and physiological spectral-ripple discrimination. *J Assoc Res Otolaryngol*. 2011; 3:375–393. [PubMed: 21271274]

Figure 1. ECAP waveform series used to generate a channel-interaction function for participant E55R. Each waveform is the derived ECAP resulting from 100 averaged recordings using electrode 12 as the probe. The vertical offset separates waveforms obtained with different masker electrodes in order from 1 (top) to 22 (bottom). Negative (N_1) and positive (P_2) peaks of neural responses are marked with crosses. The N_1 - P_2 amplitudes from this waveform series comprise the ECAP channel-interaction function for probe 12 displayed in the left panels of Figure 2 (filled circles).

Figure 2.

Examples of peripheral and central measures of spatial selectivity for E55R. Left: ECAP channel-interaction functions for a subset of probe electrodes (indicated by dotted vertical lines). Amplitude differences between two channel-interaction functions are marked by solid black vertical lines (rows 2–4). The average of the differences (i.e., the channel-separation index: CSI) is displayed in the top right corners. Right: Cortical waveforms elicited with the electrode-discrimination paradigm for the corresponding conditions. The electrode pairs are indicated in the top left corners. Vertical lines at 0.0 sec mark the onset of stimulation from one electrode, and vertical lines at 0.4 sec mark the change in stimulation to another electrode. The gray area spans the time window used to calculate the rms amplitude. Onset and change N₁ and P₂ peaks are marked with crosses, and change (ACC) N₁-P₂ amplitude is displayed in the top right corner of each panel.

Figure 3.

Peripheral measures of spatial selectivity. Thirteen ECAP channel-separation indices were calculated for each participant by pairing each channel-interaction function with that of the center electrode (probe 13 for F19R and probe 12 for all others). The stimulus change (distance between probe electrodes) is negative when the comparison probe is basal to the center electrode and positive when apical to the center electrode. Data for each participant are separated into different panels.

Figure 4.

Central measures of spatial selectivity. ACC amplitude as a function of the stimulus change (distance between the pairs of sequentially stimulated electrodes). Electrode 12 (13 for F19R) was always one of the two electrodes stimulated. The zero point on the abscissa is the no-response control condition (e.g., stimulation on the center electrode for 800 ms). Negative and positive numbers denote basal and apical electrode pairs, respectively. Data for each participant are separated into different panels.

Figure 5.

Group-mean ACC amplitude (± 1 SD) as a function of the stimulus change. Black symbols denote basal electrode pairs. Gray symbols, shifted on the x axis for visualization, denote apical electrode pairs. Basal and apical data were averaged at each stimulus change and the averages were fit with an exponential function (line). Coefficients are displayed in the top left corner.

Figure 6. Within-subject relationships between peripheral and central electrophysiological measures of spatial selectivity. Data for each participant are separated into different panels. Asterisks identify the participants who required stimulation-level adjustments for the ECAP data. ACC amplitude is plotted as a function of ECAP channel-separation index for thirteen electrodes pairs. The gray dots indicate data points that were not included in the exponential fit (lines). Coefficients are displayed in the top left corner of each panel.

Figure 7.

Exploring the poor fit of E40R's data set. A difference is observed between basal (black symbols) and apical (gray symbols) electrode pairs. This difference was not considered when modeling the relationship between peripheral and central measures of spatial selectivity, and informs the poor fit shown in Figure 6.

Figure 8. Example of a larger channel-separation index with overlapping ECAP channel-interaction functions. Channel-interaction functions for probes 9 and 16 are displayed in both panels for two participants (top: F19R, bottom: E60). Probe electrodes are indicated by the dotted vertical lines. Amplitude differences between the two functions are indicated with solid vertical lines. The channel-separation indices (CSI) are displayed in the top, right corners. Even though the channel-interaction functions show greater overlap for E60 than for F19R, the channel-separation index is larger for participant E60 than for F19R.

Figure 9.

Example of “edge effects” on the calculation of the channel-separation index using data from participant F26L. ECAP channel-interaction functions for probes 9 and 16 and for probes 9 and 21 are displayed in the top and bottom panels, respectively. Probe electrodes are indicated by the dotted vertical lines. Amplitude differences between the two functions are indicated with solid vertical lines. The channel-separation indices (CSI) are displayed in the top, right corners. The “edge effect” is illustrated most clearly by probe 21 (bottom panel, open circles): ECAP amplitude is 0.6 when the masker electrode 22. The channel-

separation index is smaller for the example in the bottom panel, even though the probe electrodes are spaced farther apart than the pair shown in top panel.

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Table 1

Participant demographic data.

ID	Age (yrs)	Sex	Test Ear	Reported Etiology	Internal Device	Age at IS (yrs)	Months Post IS
E40R	50	M	R	Otosclerosis	24RE	44	79
E51	27	F	R	Pendred (Progressive)	24RE	26	15
E55R	63	F	R	Suspected Genetic	24RE	57	74
E60	86	F	R	Unknown	24RE	80	65
E68L	57	F	L	Unknown	24RE	52	62
F18R	66	F	R	Suspected Ménière's	CI512	63	28
F19R	78	M	R	Unknown	CI512	76	27
F25R	60	F	R	Genetic	CI512	57	36
F26L	53	F	L	Unknown	CI512	51	22
F2L	58	M	L	Congenital (Progressive)	CI512	55	35
F8R	70	F	R	Unknown	CI512	68	26

Identifier (ID); Initial Stimulation (IS)