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COCHLEAR IMPLANT ELECTRODE CONFIGURATION EFFECTS ON ACTIVATION THRESHOLD AND TONOTOPIC SELECTIVITY

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Abstract

The multichannel design of contemporary cochlear implants (CIs) is predicated on the assumption that each channel activates a relatively restricted and independent sector of the deaf auditory nerve array, just as a sound within a restricted frequency band activates a restricted region of the normal cochlea. The independence of CI channels, however, is limited; and the factors that determine their independence, the relative overlap of the activity patterns that they evoke, are poorly understood. In this study, we evaluate the spread of activity evoked by cochlear implant channels by monitoring activity at 16 sites along the tonotopic axis of the guinea pig inferior colliculus (IC). “Spatial tuning curves” (STCs) measured in this way serve as an estimate of activation spread within the cochlea and the ascending auditory pathways. We contrast natural stimulation using acoustic tones with two kinds of electrical stimulation either (1) a loose fitting banded array consisting of a cylindrical silicone elastomer carrier with a linear series of ring contacts; or (2) a space-filling array consisting of a tapered silicone elastomer carrier that is designed to fit snugly into the guinea pig scala tympani with a linear series of ball contacts positioned along it. Spatial tuning curves evoked by individual acoustic tones, and by activation of each contact of each array as a monopole, bipole or tripole were recorded. Several channel configurations and a wide range of electrode separations were tested for each array, and their thresholds and selectivity were estimated.

The results indicate that the tapered space-filling arrays evoked more restricted activity patterns at lower thresholds than did the banded arrays. Monopolar stimulation (one intracochlear contact activated with an extracochlear return) using either array evoked broad activation patterns that involved the entire recording array at current levels < 6dB SL, but at relatively low thresholds. Bi- and tripolar configurations of both array types evoked more restricted activity patterns, but their thresholds were higher than those of monopolar configurations. Bipolar and tripolar configurations with closely spaced contacts evoked activity patterns that were comparable to those evoked by pure tones. As the spacing of bipolar electrodes was increased (separations > 1 mm), the activity patterns became broader and evoked patterns with two distinct threshold minima, one associated with each contact.

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Keywords

Cochlear implant; cochlear prosthesis; deafness; auditory nervous system; multichannel recording; auditory prosthesis; inferior colliculus

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INTRODUCTION

Approximately 100,000 cochlear implants (CIs) have been implanted in deaf and hearing impaired people world wide. Typically, these highly successful prosthetic devices consist of an external microphone, a speech processor-transmitter, an implanted receiver-stimulator, and an intrascalar electrode array. These electrode arrays consist of a flexible silicone elastomer carrier, platinum connecting wires and a linear array of contacts distributed longitudinally along the cochlear spiral. Although generally similar, commercial CI arrays differ in detail. They differ in the number of contacts (from 12 to 22), the spacing between contact centers (from 0.75 to 2.4 mm), contact size, contact shape, and carrier size and shape. In some arrays, the contacts are large bands that encircle the carrier; in others the contacts are smaller hemi-bands or spheres placed on the inner curvature of the cylindrical carrier. In addition, the flexible electrode arrays differ in shape and diameter. Some are straight rods with constant relatively small diameters; others are tapered and curved in an attempt to make them more closely approximate the taper and curvature of the human scala tympani.

Upon insertion, straight carriers ride along the outer wall of the spiraled scala tympani at the maximum distance from the modiolus, whereas curved tapered carriers are intended to place the stimulating contacts closer to the modiolus. When the effects of these two placements (nearer the modiolus vs. nearer the lateral wall) have been compared in CI users, closer approximation of electrode contacts by curved carriers appear to evoke responses at lower thresholds, however, effects on other measures of performance, e.g., speech reception, are inconsistent (Cohen et al., 2003, Cohen et al., 2005).

Although all these array designs allow the reception of speech in many but not all subjects, the functional significance of their design differences are poorly understood. In order to understand the functional consequences of these differences in electrode design, we have begun to examine which characteristics most strongly influence the selectivity and sensitivity of intracochlear electrodes (Bierer and Middlebrooks, 2002; Snyder et al., 2004).

In the current studies we have compared activation of the ascending auditory pathways in an animal model, the acutely deafened guinea pig, using two types of intracochlear arrays: a modified conventional human array (which is a loosely fitting array), and an experimental array, specifically designed to be space filling within the scala tympani of our animal model. We inserted these arrays successively into the same animal and recorded the responses evoked by each using a recording probe that had been previously fixed in place in the inferior colliculus. Thus, we were able to compare directly the differences in the activity patterns evoked by these two arrays. We observed striking differences in sensitivity and selectivity between the two intracochlear array types across several electrode configurations. These differences highlight some of the factors that limit selectivity and affect threshold. These important factors include 1) electrode position (distance of the electrode from the osseous spiral lamina), 2) location of the return electrode(s) and 3) electrode separation.

METHODS

Anesthesia, Surgery and Recording

The procedures used for anesthesia, surgery and inferior colliculus (IC) recording were similar to those used in a previous study (Snyder et al., 2004). In brief, 6 pigmented guinea pigs were anesthetized with mixture of ketamine and xylazine. The right IC was exposed and a 16 channel silicon probe (NeuroNexus Technologies, Ann Arbor, MI) was inserted along a standardized trajectory parallel to the IC tonotopic axis. When the probe reached a suitable depth, it was fixed in place. Then the animal was re-positioned to allow access to the left cochlea, control acoustic recordings were made using a sealed and calibrated acoustic delivery system. Using tones, the acoustic response areas (response amplitude as a function of tone intensity and frequency) were recorded at each site. Once the acoustic recordings were made, the cochlea was acutely deafened with an intrascalar injection of neomycin. Previous studies have shown that such injections produce profound deafness and the elimination of all spontaneous activity in the auditory nerve within minutes of the injection (Leake et al., 1982, 1992; Snyder et al., 1990, 2004; Miller et al., 2001; Bierer and Middlebrooks, 2002). After deafening, one of the intracochlear arrays was inserted and tested. After the responses using this array were recorded, the first array was removed and the second array was inserted and tested. After insertion of each array, we routinely inspected the scala tympani through the round window for any signs of damage. In some cases we conducted post-mortem dissections of the cochleas with the electrodes left *in situ*. These inspections and dissections were conducted to verify the position of the array contacts, document the depth of array insertion and to check for any gross insertion trauma. No signs of gross or dramatic insertion trauma (ruptures of the basilar partition, fractures of the osseous spiral lamina, etc.) were observed. However, incidences of minor insertion trauma could have been overlooked.

Intracochlear Arrays

In these experiments we recorded and compared the responses evoked by two types of intracochlear stimulating arrays: 1) an animal version of the clinical Nucleus-22 banded electrode array (Cochlear Americas, Englewood, Colorado, USA) and 2) a space-filling array fabricated in our laboratory. The space-filling array and the methods used to fabricate it have been described in detail elsewhere (Rebscher et al., 2007).

Banded array—This array consisted of the distal 6 platinum bands of a Nucleus-22 array. The bands were 450 μm in diameter and 300 μm wide. They were arrayed on a silicone-elastomer carrier with a center-to-center spacing of 750 μm (see, Figure 1, lower inset). The cylindrical carrier was approximately 450 μm in diameter (slightly larger at the tip) and was $\frac{1}{3}$ to $\frac{2}{3}$ the diameter of the tapered scala tympani in the guinea pig basal turn. Banded arrays were inserted manually until the tip met with resistance or until the most proximal band fit just inside the ventro-rostral edge of the round window.

Space-filling array—Space-filling arrays were custom designed and fabricated to fit into and fill the guinea-pig scala tympani (Figure 1). It had 8 – 16 spherical platinum-iridium contacts arranged in a longitudinal series; approximately half of each contact was exposed forming a hemispheric surface for charge transfer. The wires and contacts were embedded in a soft silicone elastomer carrier. In addition, the wires were insulated with parylene-C. The contacts had diameters $\sim 125 \mu\text{m}$ and center-to-center spacing of $\sim 500 \mu\text{m}$. The tapered carrier was designed to nearly fill the scala tympani from the beginning of the basal first turn to the middle of the 2nd turn. The carrier was considerably less space filling in the hook region where the scala tympani is largest, in part because it must be inserted through the relatively small round window annulus. The carrier was designed to place the stimulating contacts close to the osseous spiral lamina and to minimize shunting of current directly between contacts though

the perilymph. It was inserted manually until the enlarged basal segment went beyond the round window and the region indicated by the red dashed line in Figure 1 lay just inside the round window. Figure 1 (inset) illustrates the approximate position of the contacts along a cast of the guinea pig scala tympani. The eight contacts in this figure are shown arrayed longitudinally along the habenula at a radial position that is close to the osseous spiral lamina. Although the space-filling dimensions of the carrier ensure that the contacts were close to the osseous spiral lamina, the carrier could twist during insertion and the exact radial position of the contacts could vary from animal to animal and from insertion to insertion in the same animal.

Stimulus Generation

Sound stimuli were digitally generated (System 3 equipment from Tucker-Davis Technologies; Alachua, FL, USA), amplified using an audio amplifier (model 260, Samson Technologies Corp., Hauppauge, NY, USA) and presented using a speaker (super-tweeter, Radio Shack, Fort Worth, TX, USA) attached to a custom ear bar that was inserted and sealed into the left ear canal. Sound levels were calibrated using a probe tube microphone (model 4182, Brüel & Kjær Norcross, Georgia, USA) with the probe tube inserted through the ear bar so that the tip rested near the tympanic membrane. The calibrated acoustic signal was adjusted so that the tone transfer function at the ear canal was flat within ± 2 dB over the range between 2 kHz and 41.5 kHz up to 80 dB SPL.

After recording responses to tones under normal-hearing conditions in each animal, the round window of the left cochlea was exposed and left cochlea was deafened with a 50 – 100 μ L injection of 10% Neomycin sulfate through the opened round window. Spot checks of click-evoked CAPs indicated that thresholds were above the maximum output of our system (120 dB SPL) in 30 – 60 minutes after injection. After deafening, one of the intracochlear stimulating electrode arrays was inserted into the scala tympani and IC responses to electrical stimulation using that array were recorded. After testing of that array, it was removed and the cochlea was examined for any signs of trauma. If there was no sign of trauma (the usual result), the second array was inserted and tested. The order of array insertion (banded first or space-filing first) had no discernible effect on the results of stimulation. In addition in several instances, we had occasion to insert, remove and then re-insert each array. In every instance re-insertion of either array had only minor influences on the subsequent thresholds and selectivity. Finally, the results reported here are completely consistent with those from previous and subsequent experiments in which only one array was inserted and tested.

Electrical stimuli were generated by a custom multichannel constant current source controlled by a multichannel D/A converter (RX8, Tucker-Davis Technologies; Alachua, FL, USA). Stimuli were 2 symmetric biphasic current pulses, 200 μ s per phase, delivered with a 50 ms interpulse interval. In the monopolar (MP) configuration, the activating current was applied to an intracochlear electrode, and an extracochlear silver wire that had been inserted through the ipsilateral external ear canal served as the return electrode. Different MP configurations were identified by the number of the active electrode, increasing from apex to base. Different bipolar (BP) configurations were identified by listing the electrodes, the activating cathodic current was applied to the first intracochlear electrode and second intracochlear electrode provided the return current path; e.g., “3,4” indicates active electrode #3 and return electrode #4. Bipolar pairs were tested with varying separations of active and return electrodes, and are indicated as BP+n, where n indicates the number of inactive electrodes lying between the active and return electrodes. In the tripolar (TP) configuration, activating current was applied to one intracochlear electrode, and the return current was divided equally between the two adjacent electrodes. Tripolar configurations were identified by listing the electrodes in order; e.g., “3,4,5”, where the active electrode was #4 and the return electrodes were #3 and #5.

Data Analysis

In each electrical stimulation series, biphasic current pulses were presented in 1 or 2 dB increments over a range of intensities beginning at levels below minimum threshold among all recording sites up to levels that evoked saturated activity on at least one recording site. The maximum level permitted by the stimulator was 1.6 mA. Response amplitudes to single pulses were recorded over the post-stimulus interval from 5 – 30 ms and were plotted as a function of depth in the IC (recording array site number) and pulse intensity to create a spatial tuning curve (STC, see Figure 2) for each stimulus configuration. The strength of the neural response at each site/intensity combination was encoded using a color scale to represent the strength of the neural response from spontaneous activity (blue) to the maximum response recorded (red). For each STC, rate/level curves for each recording site were computed across all tested stimulus conditions. The maximum firing rate across all stimulus conditions was computed for each IC recording site. Spontaneous response rates at each site were estimated by averaging the activity during the stimulus-free periods preceding each current pulse. All driven responses were normalized between 0 and 1 using the formula:

$$RN_i = (R_i - S_i) / (M_i - S_i)$$

Where RN_i equal the normalized rate, R_i equals the recorded firing rate, S_i is the spontaneous rate and M_i is the maximum rate on the i th electrode for any stimulus. Responses were smoothed using a weighted average by convolving the STC with a kernel of the values: [0.0566, 0.0801, 0.0566; 0.0801, 0.4531, 0.0801; 0.0566, 0.0801, 0.0566].

The minimum threshold at each site was identified as the stimulus level inducing a normalized response exceeding 0.2, corresponding to the spike rate that exceeded the spontaneous rate by 20% of the difference between maximum and spontaneous rates. The overall threshold was taken to be the minimum threshold among the sixteen recording sites.

STC width was determined at 6 dB above the overall minimum threshold, and was computed as the distance between the deepest and the most superficial recording sites whose normalized response rates exceeded 0.2 (see Figure 2). A large number of spatial tuning curves, especially MP curves, were too broad to measure a 6 dB width. In these cases, where the range of thresholds was less than 6dB, STC widths were recorded as 1600 microns, i.e., the entire length of the recording probe.

RESULTS

Acoustic Stimulation

Each experiment began in normal-hearing conditions with measurements of responses to acoustic tones that varied in frequency and intensity. Tone evoked responses were assembled into frequency response areas (one for each recording site) like those shown in Figure 3, which are typical of those recorded in the central nucleus of the IC (ICC) of anesthetized guinea pigs. Most excitatory response areas had a “V” shape with a single minimum threshold at one frequency, the site’s characteristic frequency (CF). At most stimulus frequencies, response rates increased monotonically as stimulus intensity increased, and the maximum response at any intensity usually occurred at or near CF. At superficial sites, CFs were tuned to relatively low frequencies; at successively deeper sites CFs shifted systematically to higher frequencies consistent with the known tonotopic organization of the ICC. Estimates of CF established the relative location of each recording site within the ICC tonotopic organization, and the range of these CFs documented the position and trajectory of the recording probe. This positioning of the recording probe relative to empirical CFs, or “acoustic calibration”, allowed inferences to be made regarding the cochlear origins of electrically evoked activity in deafened animals (Snyder et al., 2004). In the experiment illustrated in Figure 3, CFs measured along a 1.5-mm

span of the tonotopic axis ranged from 3.5 kHz to 25 kHz, a range of approximately 3 octaves. That range corresponded approximately to the range of CFs expected at the cochlear locations activated by our basally located intracochlear arrays. The mean Q10 (CF divided by response bandwidth @ 10dB above threshold) for the curves illustrated in Figure 3 was 2.36. The mean for 92 curves in 7 animals was 2.8.

Figure 4 represents the same data re-plotted as spatial tuning curves (STCs) for each of 8 tone frequencies. Tone intensity is plotted on the abscissa; relative ICC depth is plotted on the ordinate, and normalized firing rate is represented by colors. These acoustic STCs were narrowly restricted in ICC depth and display a progressive shift to deeper ICC locations as tone frequency increases.

Electric Stimulation Using the Banded Array

Figure 5 illustrates the activity patterns evoked by stimulation of the banded array when it was activated in three different configurations (MP, BP+0, and TP) in the animal whose acoustic responses are illustrated in Figure 3. The schematic at the top of the figure illustrates the current flow in these configurations. In the MP configuration (top row, A), activation of each of the 6 electrode bands evoked broadly distributed activity across the ICC tonotopic organization. This broad activation occurred even at stimulus levels near minimum threshold and showed little tonotopic specificity. This is typical of responses to MP stimulation using the banded array. The spread of activity was so broad that it was not possible to estimate the 6 dB widths of these STCs, since the difference in threshold across the entire length of the recording probe did not exceed 6 dB. These results are consistent with previously published results using this banded array (Bierer and Middlebrooks, 2002; Snyder et al., 2004). Although the distribution of activity was broad for these monopoles, minimum thresholds were relatively low, about 30-100 μ A, and there was a trend for the minimum thresholds to increase as the activation site moved basally (i.e., from MP1 to MP6). This is also typical of stimulation with the banded array and is consistent with the widening of the scala tympani in the base relative to the array cross-section, which allows the array to be located further away from the modiolus.

In the BP+0 and TP configurations (Fig 5B & C), most of the activation patterns evoked by the banded arrays were more selective and had threshold minima that were tonotopically appropriate. The most apical bipolar pair (1,2) and the most apical tripolar combination (1,2,3), for example, evoked activity with minimum threshold centered on ICC site 7, which was tuned acoustically to 9.5 kHz, whereas the more basal bipolar pair 4,5 and the more basal tripolar combination 3,4,5 evoked activity with a minimum centered on ICC sites 14 & 15, which had CFs around 23 kHz. As was seen with the monopolar stimulation, thresholds for these bipoles and tripoles shifted systematically with their location; more apical pairs located in the narrower apical scala tympani evoked activity at lower current levels than the more basal pairs. The bipolar thresholds were 6 -12 dB higher and tripolar thresholds were 10 -16 dB higher than those for monopoles at corresponding active electrode locations. The higher thresholds for BP and TP result were consistent with current shunting directly between electrodes through the perilymph without engaging excitable neural elements in the modiolus.

Figure 6 illustrates the effect of bipolar electrode separation on STCs. As in the previous figure, adjacent bipolar bands often evoked selective, tonotopically appropriate ICC activation when the bands were located in the apical cochlea. In this case, however, selectivity was markedly degraded when the stimulating bands were located in the basal cochlea where the scala is much larger. Selectivity was also degraded when non-adjacent bands were employed. For example, the most apical BP+0 pair (1,2; top left panel) evoked relatively selective ICC activation, but this selectivity broadened when current was applied in BP+1 mode (1,3; second row) and it was virtually abolished when BP+2 stimulation was employed (pair 1,4; third row). It was seldom possible to estimate the 6 dB widths of the activity patterns evoked by non-adjacent

bands because their thresholds did not increase above 6 dB SL within the span of the recording probe. The separation between bands had little effect on threshold, except when the most basal and least efficient electrodes (5 & 6) were employed. There was a clear tendency for more basal electrodes to have higher thresholds regardless of their separation. This again is consistent with the wider cross-sectional diameter of the scala at more basal locations.

Electric Stimulation Using a Space Filling Array

STCs evoked using the space-filling array in MP (upper row), BP+0, and TP configurations are illustrated in Figure 7. Like the monopoles using the banded array, monopolar stimulation using the space-filling array evoked activity at relatively low thresholds but with relatively weak tonotopic selectivity. Bipolar and tripolar stimulation required higher stimulation currents but demonstrated clear tonotopic selectivity. Nevertheless, all of these configurations evoked activity patterns that were tonotopically appropriate. Activation of more apical (lower frequency) intracochlear contacts (on the left) evoked threshold activity at more superficial (lower frequency) ICC locations, and activation of successively more basal (higher frequency) contacts (right) evoked threshold activity at deeper (higher frequency) ICC locations. For example, the left-most bipolar electrode pair (1,2) evoked activity centered at site #6 (tuned to 13.5 kHz), whereas activation of a more basal bipolar pair (6,7) evoked activity centered around site #12, which was tuned to 20.7 kHz. Activation of the intermediate electrode pairs evoked activity at intermediate ICC locations tuned to intermediate frequencies. Tripolar stimulation (bottom row of STCs) evoked tonotopically appropriate activation of the ICC that was more selective than bipolar stimulation. Compare, for example, the difference between STCs evoked by activation of bipole 2,3 and tripole 2,3,4.

Figure 8 illustrates the effects of systematically altering the separation between bipolar contacts on the space-filling electrode array. STCs evoked by activation of adjacent bipolar pairs, BP +0 are shown on the top row and those evoked by progressively more widely separated pairs in successively lower rows. All BP+0 pairs produced relatively selective, tonotopically appropriate excitation patterns in the ICC and STCs exhibited a single clear minimum threshold. However, as the separation between the contacts increased (shown successively lower rows) the selectivity of stimulation decreased. Initially the wider separation evoked STCs that were only slightly broader than those evoked by adjacent (BP+0) pairs. And, as the separation between bipolar contacts was increased, the STCs exhibited two minima -- one associated with each constituent contact of the bipolar pair. The overlap and interaction of these two populations lead to a reduced tonotopically appropriate selectivity. For example, in the STCs evoked by BP+2 activation (third row from the top), stimulation using each electrode pair (1,4 through 4,7) evoked two partially overlapping, independent ICC responses (white arrows), one appropriate for each constituent contact. The peaks in these BP+2 STCs were approximately equally spaced, consistent with the equal spacing of the contact pairs, and they shifted down to higher frequency ICC locations as the stimulating contacts shifted to more basal (higher frequency) cochlear locations. Likewise, in the STCs evoked by bipolar channels that involved contact #1 (the 1st STC in each row), more widely spaced partially independent responses can be discerned in each successive row, consistent with the more widely spaced constituent contacts. Activation of the more closely spaced BP+2 contacts (pair 1,4) produced more closely spaced peaks than did the more widely spaced BP+3 contacts (1,5) and (1,6).

Figure 9 summarizes the effects of electrode configuration on threshold and STC 6 dB width. Mean thresholds were higher (Fig 9A) and median STC 6dB widths were wider (Fig. 9B) in all configurations (except MP) for the banded array than those for the space-filling array. In some cases thresholds for the banded array were as much as 18 dB higher than those for space-filling array. In most configurations, it is difficult to evaluate just how much broader the banded

array STCs were, since the 6dB widths for the banded array were broader than the extent of the recording probes.

Despite the differences in threshold and STC width between the two arrays, some trends were similar across configurations. Mean thresholds were lowest in the monopolar configurations for both arrays, whereas mean tripolar thresholds were the highest for both arrays. Likewise, mean STC widths were broadest for the monopolar configurations and were narrowest for tripolar configurations. Across bipolar configurations, thresholds for both arrays decreased systematically as electrode separation increased. The more widely spaced bipolar pairs tended to have broader STC widths than those evoked by more narrowly spaced pairs. At the extremes, adjacent bipoles (BP+0) with edge-to-edge separations of 400 μm (space-filling array) or 320 μm (banded array) had mean thresholds that were 3-7dB higher than those observed for widely spaced bipoles, i.e., those separated by 2000 μm or more (BP $\geq$ 3). The mean thresholds for these most widely spaced bipolar contacts were comparable to (or lower than) those for monopolar configurations. Mean thresholds for tripolar configurations were the highest, approximately equal to adjacent bipoles and 3 – 12 dB higher than those for monopoles. STC widths varied systematically with configuration and contact separation. Stimulation with closely spaced bipolar and tripolar configurations produced relatively narrow STCs. Stimulation with monopolar and widely spaced bipolar configurations produced relatively broad STCs.

DISCUSSION

In these experiments we compared the threshold and selectivity of ICC activity patterns evoked by intracochlear electrical stimulation using two different types of intracochlear electrode array using the same recording system in the same animals. With each electrode array we tested several different electrode configurations. Our goal was to determine which configurations and which array evoked the most selective activity at the lowest thresholds. The results are consistent with the design goals of contemporary cochlear implants which seek to place stimulating contacts near the modiolus and to displace conductive perilymph from the surrounding scala in order to minimize current shunting between electrodes and to evoke activation patterns which are similar in their selectivity to those elicited by tones under normal-hearing conditions.

Before discussing our results, some aspects of our experimental design (the multi-site & multi-unit recording in the ICC, and the use of acutely deafened animals) should be considered. Ideally studies of threshold and spread of excitation should measure the spread of activity evoked across a population of isolated auditory nerve fibers in deaf animals. The CFs of these fibers should be known and distributed across a broad range of frequencies. Some studies (Hartmann and Klinke, 1990, Kral et al., 1998 and Liang et al., 1999) have attempted this by determining the thresholds of single auditory nerve fibers to stimulation using intrascalar electrodes distributed longitudinally along the basal scala tympani. These single fiber curves (called “spatial tuning curves” by Hartmann and colleagues) are functionally most equivalent to low resolution acoustic frequency tuning curves that describe threshold as a function of the cochlear location of the stimuli. Although suggestive, the interpretations of these curves have certain limitations (see Liang et al., 1999) and should not be confused with the ICC spatial tuning curves reported here. The IC STCs reported here represent the activity evoked across the tonotopic organization of the ICC after stimulation of a single intracochlear location. Therefore, they are more like the “population responses” evoked by single acoustic tones reported by Kim and colleagues (Kim and Molnar, 1974; Kim and Parham, 1991) and the electrically evoked “spatial excitation patterns” reported by van den Honert and Stypulkowski (1987).

Multi site recording in the ICC

ICC spatial tuning curves reported here also have limitations as pointed-out by Finley et al. (1990). They are the product of many poorly understood patterns of spatiotemporal interaction/integration both within the colliculus and across its afferent sources. Nevertheless, they allow direct comparisons between the patterns evoked by different acoustic and electric stimuli in the same neurons in the same animals.

ICC multiunit vs. single unit recording

One shortcoming of the current experiments is that they are based on multiunit recordings. However, they qualitatively resemble single unit responses. The acoustic frequency to which each IC recording site is tuned varies systematically with recording site location (ICC depth). Virtually all multiunit frequency response areas (Figure 3) have excitatory response regions that are “V” shaped and are narrowly tuned. In addition these cluster responses are quantitatively similar to single IC unit responses measured with high impedance electrodes. For example, the cluster response areas with CFs between 4 – 25 kHz in the 7 ketamine anesthetized guinea pigs in this study ($N = 92$), had a mean Q_{10} of 2.8. This value is virtually identical to that measured for single unit responses (mean $Q_{10} = 2.5$) recorded using glass pipettes across this same CF range in similarly anesthetized guinea pigs (Syka et al., 2000). Thus the frequency tuning of multi-unit clusters is comparable to that observed in well isolated single ICC units and, therefore, the resulting multiunit STCs should be comparable to those that would result from populations of well isolated single ICC neurons.

IC and 8th nerve spatial tuning

The spatial distribution of cluster STCs recorded in the ICC are comparable to those recorded in auditory nerve fiber populations. The pure-tone cluster STCs illustrated in Figure 4, for example, represent activity evoked across sites with CFs distributed across a mean range of 1.2 octaves at 40 dB SL. This spread is similar to the 1-2 octave CF range of the population of well isolated single auditory nerve fibers activated by 5 kHz pure tones between 30 - 70 dB SPL (Kim and Parham, 1991). Thus we believe that the distribution of activity evoked by tones across the tonotopic axis of the ICC was comparable to that evoked across the auditory nerve array.

Hair cell survival and acute vs. chronic deafening

Acutely deafened animals offer a standardized if somewhat limited model of deafness in human CI users. Specifically, in the present study, each animal began with normal hearing and then was deafened by acute intracochlear administration of neomycin sulfate. Therefore, all or almost all spiral ganglion cells were intact along with their central axons and peripheral processes. This is very different from the situation in human CI users, who typically receive their first electrical stimulation months or years after the onset of deafness and who commonly have considerable and highly variable losses of spiral ganglion cells as well as partial or complete losses of their peripheral processes (Khan et al., 2005; Nadol and Eddington, 2006). Therefore, the current results may be applicable only to CI users with uniformly high dendrite and/or ganglion cell survival.

Electrical Stimulation

Effects of electrode configuration—The most influential parameter on activation spread was stimulus intensity. Regardless of all other parameters, spread of activation broadened with increasing stimulus intensity. Another influential parameter, however, is electrode configuration. The current results are in agreement with several previous animal studies (van den Honert and Stypulkowski, 1987; Hartmann and Klinke, 1990; Snyder et al., 1990, 2004; Shepherd et al., 1993; Brown et al., 1996; Kral et al., 1998; Bierer and Middlebrooks, 2002),

which have noted that monopolar stimulation evokes activity at lower thresholds with dramatically poorer selectivity as compared to bipolar (and in some experiments tripolar) stimulation. In addition some of these studies using banded arrays demonstrated that band separation had a strong influence on evoked activity threshold (Shepherd et al., 1993; Bierer and Middlebrooks, 2002) and selectivity (Bierer and Middlebrooks, 2002).

This trend across electrode configurations and electrode separations is not completely consistent with previously reported results in CI users (Lim et al., 1989; Pfingst et al. (1995); Cohen et al., 1996; Chatterjee et al., 2005; Kwon and van den Honert, 2006). Lim et al (1989) reported on the effects of electrode separation in a single Nucleus-22 user. This subject's bipolar thresholds decreased as electrode separation increased and his/her forward masking patterns broadened. Interestingly the masking patterns also broadened as masker level increased, an effect one might predict from the physiological data present here. Likewise Pfingst et al. (1995) and Chatterjee (2000) also reported that bipolar thresholds of Nucleus-22 CI users decreased and approached monopolar thresholds as electrode separation increased. Unfortunately, they didn't examine the masking patterns of their subjects. Cohen et al (1996) compared bipolar (BP+1) masking patterns in 6 Nucleus-22 users with those evoked by monopolar and pseudo-monopolar (common ground) stimulation. The results were "complex" but there were no clear differences between the selectivity of the three stimulation modes. Chatterjee et al. (2005) examined the effects of electrode separation on both thresholds and masking patterns in 3 Nucleus-22 users. Like Lim et al. (1989), they found that thresholds decreased and the masking patterns broadened slightly or developed two peaks as bipolar electrode separation increased. It should be noted, however, that very wide electrode separations (BP+9 or BP+18) were required for dual peak patterns to appear in these subjects, and unlike the patterns reported by Lim et al. (1989), the masking pattern shapes varied little with masker level, an effect that Chatterjee and Shannon (1998) had also observed. Kwon and van den Honert (2006) compared monopolar and bipolar (BP+1 or BP+2 depending upon the subject) thresholds and masking patterns in 4 Nucleus-24 (straight array) users. They found that, while monopolar thresholds were lower for all subjects, the masking patterns were "quite similar" at all levels within each stimulation mode, and that there appeared to be no consistent difference in selectivity between monopolar and bipolar masking patterns across subjects. Thus while the thresholds effects of electrode separation and configuration in CI user qualitatively agree with the results of physiological studies, the effects on stimulation selectivity are inconsistent. [Heh – "whilst" makes this sound like Alan Palmer.]

Effects of electrode type—Another influential parameter on threshold and selectivity in this study was array type. The space-filling array was much more selective and more efficient (i.e., evoked responses at lower thresholds) than the banded array. We attribute these differences to two factors: First, the space-filling array with its smaller contacts embedded its larger space-filling carrier limits shunting of currents between electrodes. Conversely, the relatively poor selectivity and high thresholds of the banded array can be attributed in part to the relatively large size and geometry of its contacts, which extend around the entire circumference of the carrier. This arrangement minimizes electrode impedance but maximizes shunting of current between contacts especially when an intracochlear return is used.

Second, the space-filling array places its contacts closer to the neural elements along its entire length (Rebscher et al., 2001; 2006). Therefore, it should lower thresholds and increase current density across the neural membranes for all its contacts. The banded array may do this only at its most apical contacts in the rapidly tapering, relatively small guinea pig scala. In the larger human scala, the banded array adopts only remote lateral positions along its entire length (Wardrop et al., 2005a,b). In this respect the apical contacts of banded arrays inserted into the guinea pig scala tympani may be more similar to the more recently developed "perimodiolar" arrays, which use large contacts embedded in a carrier designed to be "modiolar hugging" -

although not space-filling (Tykocinski et al., 2000, 2001; Balkany et al., 2002). Therefore, our results comparing space-filling and banded arrays in guinea pigs may minimize the selectivity differences that might be expected in CI users with similar arrays. Predicted differences in speech reception scores made from these results might also be minimized, since Throckmorton and Collins (1999) have demonstrated a strong correlation between activation selectivity and speech recognition scores in CI users.

In this context, it is important to note that, although different electrode designs and stimulation configurations are intended to evoke more selective activation, they are not always successful. For example, despite lowering thresholds somewhat in human CI users, the recently developed perimodiolar arrays appear to have little effect on activation selectivity and little influence on speech recognition scores (Boex et al., 2003; Cohen et al., 2004, 2005, Hughes and Abbas, 2006). Similarly, CI users of banded arrays show no difference in their forward masking patterns (Kwon and van den Honert, 2006) or speech reception performance (Pfungst et al., 2001) when activated in BP+0 and monopolar configurations. These results suggest that changing electrode configuration may not be sufficient to produce higher activation selectivity, since the bipolar stimulation using the banded array may have selectivity equivalent to monopolar stimulation,

Comparisons of Physiological and Psychophysical Studies of ICES Selectivity

Narrow dynamic ranges and broad excitation patterns are characteristic of monopolar stimulation in animal studies (van den Honert and Stypulkowski, 1987; Hartmann and Klinke, 1990; Snyder et al., 1990, 2004; Kral et al., 1998; Rebscher et al., 2001, Bierer and Middlebrooks, 2002). Nevertheless, psychophysical studies of CI users stimulated in the monopolar mode often report percepts that are consistent with relatively restricted, tonotopically appropriate excitation (Townshend et al., 1987; McDermott and McKay, 1994; Cohen et al., 1996, 2001, 2006; McKay et al., 1999; Pfingst et al., 1999). One possible way to reconcile the animal and user results is to assume that pitch percepts of CI user were evoked at near threshold levels (2-3 dB SL), where monopolar stimulation may evoke some tonotopically appropriate selectivity. However, electrode discrimination in CI users appears to *improve* slightly at *higher* stimulation levels, a result that suggests that the activity patterns become *more* selective as levels increase (McKay et al., 1999; Pfingst et al., 1999; Cohen et al., 2006). Likewise, Hanekom and Shannon (1998) found that gap detection tuning was relatively weak when the stimulus level was low (30% of comfortable loudness), but shifted in tonotopically appropriate directions as electrode location was shifted. At higher levels (83% of comfortable loudness) gap detection tuning was more robust, more sharply tuned and just as tonotopic (indicating *more* selective excitation). In contrast, increasing electrode separation or switching from monopolar to bipolar stimulation, which should have produced broader excitation, had little influence on estimates of gap detection tuning.

These results in CI users are difficult to explain using simple, direct models of excitation spread. They have led some investigators to consider more complex models of electrical excitation that incorporate central and as well as peripheral tuning mechanisms (see Hanekom and Shannon, 1998). They have led others to emphasize that CI pitch percepts are weak, complex, and multidimensional (Shannon, 1983; Collins et al., 1997; McKay et al., 1996). One study emphasizes that the pitch percepts evoked by electrical stimulation of the implanted ear of in CI users with residual hearing in their un-implanted ears bear little relation to tone evoked percepts in hearing ear (McDermott and Sucher, 2006). This disconnect between electrically evoked percepts and tone evoked pitch may be related to the weak correlation between electrode discrimination scores and speech recognition scores (e.g., Zwolan et al., 1997).

Physical and Computational Models of ICES Selectivity

Several studies have tried to model the spread of current within the cochlea to determine the factors that most influence the selectivity CI stimulation. These models fall roughly into two categories: physical models, which attempt to measure current spread in model systems such as saline tanks, or cadaver or live animal cochleas (Spelman et al., 1982, 1995; Black et al., 1983; Ifukube and White, 1987; Jolly et al., 1996; Kral et al., 1998), and computational models, which attempt to compute the spread of current from first principles (e.g., Finley et al., 1987, 1990; Frijns et al., 1995, 1996; Spelman et al., 1995; Briare and Frijns, 1996; Jolly et al., 1996; Hanekom, 2001; Rattay et al., 2001). Both model types predict the general results described here. For example, monopolar stimulation produces lower threshold currents but broader current spread than either bipolar or tripolar (sometimes called quadrupolar) stimulation. For example, rotationally symmetric and a spiral models of the electrically stimulated guinea pig cochlea (Frijns et al., 1995, 1996) and human cochlea (Briare and Frijns, 2000; Hanekom, 2001; Rattay et al., 2001) predict highly selective excitation of auditory nerve fibers within cochlear sectors immediately adjacent to bipolar point electrodes. These primary peaks could be highly selective with $Q_{10\text{ dB}}$ values between 1.42 and 2.4 with a average of 1.98 for symmetric biphasic pulses delivered various distances from the modiolus with various radial separations (Frijns et al., 1996). These values are in good agreement with our measurements of bipolar STC widths using space-filling arrays, which have $Q_{10\text{ dB}}$ values of 1.3 - 5.29 with an average of 2.35. They are also in good agreement with or slightly higher than the comparable $Q_{10\text{ dB}}$ values (mean of 1.25 and range of 0.53 – 2.62) reported for bipolar stimulation of the auditory nerve (van den Honert and Stypulkowski, 1987). Thus activation selectivity evoked by activation of the space-filling arrays is at least as selective as those predicted by these point-source models as well as selectivity previously reported for the nerve in hearing animals.

There are, however, discrepancies between the point-source model calculations and the experimental data. Both the rotationally symmetric model and spiral models (Frijns et al., 1995, 1996; Briare and Frijns, 2000; Hanekom, 2001; Rattay et al., 2001) predict ectopic excitation of fibers from the apical (3rd and 4th) turn fibers) when 2nd turn electrodes are activated. This ectopic excitation takes the form of secondary peaks in the excitation profiles, which could have thresholds in some cases less than 10dB lower than the primary peaks. The existence of such secondary peaks were sometimes suggested in the STCs evoked by the banded arrays, but were never observed in the STC evoked by space-filling arrays using monopolar, bipolar or tripolar configurations. The absence of secondary peaks in low frequency regions of STCs of the inferior colliculus is in good agreement with the activation profiles measured in the auditory nerve evoked by longitudinal bipolar electrodes (van den Honert and Stypulkowski, 1987a); in this study, secondary peaks were observed in only some of their monopolar spatial excitation patterns.

In some aspects, our results are not qualitatively consistent with one report of simulations of electrical stimulation in the human cochlea using a computational model. In a study that examined the effects of electrode separation for both banded and point-contacts arrays (Hanekom, 2001), the investigator concluded that there was little difference between the electrical tuning curves evoked by these electrodes. The activation patterns of both arrays were sharply tuned regardless of the radial location (closer to the lateral wall or closer to the modiolus) of the array, and the selectivity of both varied virtually identically with electrode separation from BP+0 to BP+3. In this simulation, dual peaked activation that was observed even with BP+0 became more pronounced as electrode separation increased to BP+3 and pseudo-monopolar (apical return) configurations. It is difficult to reconcile these results both with our comparisons using the banded and space-filling array (a point-contact array) and studies using banded arrays reported elsewhere. For example, Chatterjee et al (2005) were

unable to see double peaked forward masking patterns in their subjects until very wide separation (BP+9 or greater). Neither Kwon and van den Honert (2006) nor Chatterjee and Shannon (1998) saw double peaked excitation patterns in CI users stimulated in BP+2 configurations of Nucleus-22 devices..

Summary and Conclusions—Based on the results presented here we conclude that the electrodes in the banded arrays evoke excitation across broader frequency regions at higher thresholds levels than those in space filling arrays. The selectivity and thresholds of both arrays are strongly dependent upon the configurations of the contacts (MP vs. BP vs. TP), the degree of approximation of the contacts to the neural elements and the distance separating the contacts in the bipolar configuration. Monopolar configurations are less selective than bipolar which in turn are somewhat less selective than tripolar configurations. Contacts with less separation between them evoke more selective excitation but with higher thresholds than contacts with greater separation. In particular, widely separated bipolar contacts evoke broad excitation patterns that exhibit two excitation regions, one associated with each of the constituent electrodes.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Figure 1.

An image of the guinea pig electrode array used in these experiments. This array has 8 stimulating electrode contacts and connecting wires embedded in a elastomer carrier. The contacts are numbered with #1 being the most apical and #8 the most basal contact. The carrier is designed to be space-filling and to place the contacts in a longitudinal series along the osseous spiral lamina at a radial location that is somewhere between the habenula and Rosenthal's canal. The contacts have a diameter of about 125 microns and a center-to-center spacing of ~500 microns. Upon insertion, the round window will be located at approximately the red dashed line. Upper inset shows a cast of the guinea pig scala tympani with the approximate locations of the contacts when the electrode is inserted. The arrows indicate the the lateral edge of the basilar membrane and the red dashed line the round window. Lower inset shows an image of the modified conventional banded array, which has 6 bands.

Figure 2.

A diagram illustrating how the 6 dB width of a spatial tuning curve is estimated. The left ordinate is relative depth in the IC or recording site number. The right ordinate is site CF estimated from the acoustic stimulation. On the far right the color scale coding of normalized spike rate. On the far left is a diagram of a recording probe showing its 16 contacts. This diagram shows threshold (+20% re spontaneous activity) and the 6 dB width of an electrically evoked STC.

Figure 3.

Acoustic frequency response maps from GP91. Each panel represents a multi-unit frequency response map recorded in the right ICC at one of 16 probe recording sites. Each facet in a panel represents the response at that site to 4 repetitions of pure tone, whose frequency and intensity are indicated on the ordinate and abscissa respectively. Response amplitude is color coded (scale on right side) with dark red indicating the maximum evoked activity and dark blue indicating spontaneous activity. The numbers in the upper right of each panel indicate the relative depth in microns of each recording site.

Acoustic Spatial Tuning Curves 8 tones; 3.4 – 22.6 kHz in 1/4th Octave Steps

Figure 4.

Acoustic spatial tuning curves to 8 tones; 3.4 – 22.6 kHz in 1/4th octave steps. These 8 curves were constructed using the same data illustrated in Figure 3. Each panel represents the activity evoked by a single tone (indicated in the lower left corner), which is one of the 35 possible tones used in Fig. 3. Tone intensity in dB SPL is plotted on the abscissa and relative ICC depth or probe site number is plotted on the ordinate. The activity evoked by the lowest frequency tone is illustrated in the upper left and that evoked by the highest frequency tone is illustrated on the lower right.

Figure 5.

Spatial tuning curves (STCs) evoked by stimulation with the banded human electrode activated in three different configurations: monopolar (MP) in the upper row, adjacent bipolar (BP+0) in the middle row, and adjacent tripolar (TP+0) in the bottom row. The specific electrode combinations used to evoke activity in each STC are indicated in the upper right corner of the curve. In this and all subsequent figures, STCs within each row are arranged with the most apical electrode combination on the far left and the more basal combinations sequentially distributed to the right. The upper row of curves illustrates the effects of activation of the 6 MP configurations. The middle row of curves illustrate the effects of activation of all possible BP+0 combinations. The bottom row illustrates the activity patterns evoked by activation of all possible adjacent tripolar (TP+0) configurations. The characteristic frequencies (CFs) of each recording probe site, estimated from acoustic stimulation prior to deafening and implantation, are indicated to the right of the most basal bipolar STC. The cartoon at the top right defines the numbering system for the banded electrode contacts and its stimulus configurations, the blue arrow illustrates monopolar stimulation between band 1 and an extracochlear return electrode (E), yellow arrows illustrate bipolar stimulation between adjacent bands, the red arrows illustrate adjacent tripolar stimulation. The color scale on the right indicates response amplitude with red equal to the maximum response and blue equal to spontaneous activity. This scale applies to all subsequent curves.

Figure 6.

Spatial tuning curves evoked by activation of the banded electrode array in successively more widely spaced, bipolar configurations: adjacent bipolar electrodes (BP+0) in the top row to bipolar electrodes separated by 4 electrode contacts (BP+4) in the bottom row. The specific bipolar combinations are indicated in the upper right corner of each STC. The curves are arranged so that the activity patterns evoked by stimulation of the most apical electrode pair is on the far left and those from more basal pairs are placed successively to the right. The characteristic frequencies (CFs) of the recording sites, estimated from acoustic stimulation prior to deafening and implantation, of each recording probe site in this animal is indicated to the right of the bottom row.

Figure 7.

Spatial tuning curves (STCs) evoked by stimulation of the guinea pig electrode activated in three different configurations: monopolar (MP) in the upper row, adjacent bipolar (BP+0) in the middle row, and adjacent tripolar (TP+0) in the bottom row. The specific electrode combinations used to evoke activity in each STC are indicated in the upper left corner of the curve. Within each row, curves are arranged such that the activity resulting from stimulation of the most apical electrode combination is on the far left and those from the more basal combinations are sequentially distributed to the right. The upper row of curves illustrates the effects of activation of all 8 MP electrodes. The middle row of curves illustrate the effects of activation of all possible BP+0 combinations. The bottom row illustrates the activity patterns evoked by activation of all possible TP+0 combinations. Characteristic frequencies (CFs), estimated from acoustic stimulation prior to deafening and implantation, of each recording probe site is indicated to the right of the most basal bipolar STC. The scale on the right indicates the color coding with red equal to the maximum response and blue equal to spontaneous activity. This scale applies to all subsequent curves.

Figure 8.

Spatial tuning curves evoked by activation of our guinea pig electrode in successively more widely spaced, bipolar configurations: adjacent bipolar electrodes (BP+0) in the top row to bipolar electrodes separated by 5 electrode contacts (BP+5) in the bottom row. The specific bipolar combinations are indicated in the upper right corner of each STC. The curves are arranged so that the activity patterns evoked by stimulation of the most apical electrode pair is on the far left and those from more basal pairs are placed successively to the right. The characteristic frequencies (CFs) of the recording sites, estimated from acoustic stimulation prior to deafening and implantation, of each recording probe site in this animal is indicated to the right of the bottom row. The white and red arrows indicate interaction peaks that are resolvable in widely spaced bipolar pairs (see text). Although these data were recorded from a different animal than those presented in the previous figure, the top row of BP+0 responses in the two figures can be directly compared.

Figure 9.

Histograms of mean threshold (A) and median STC widths (B) for bipolar+n, monopolar and tripolar electrode configurations for the space-filling electrode and the human banded electrode. The numbers at the top of each bar in B indicate the number of STCs out of all STCs (n/total) that were too wide to measure at 6dB above threshold.