Neuronal Responses in Cat Primary Auditory Cortex to Electrical Cochlear Stimulation: IV. Activation Pattern for Sinusoidal Stimulation

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Submitted 16 May 2002; accepted in final form 17 February 2003

Raggio, Marcia W. and Christoph E. Schreiner. Neuronal responses in cat primary auditory cortex to electrical cochlear stimulation: IV. Activation pattern for sinusoidal stimulation. J. Neurophysiol. 89: 3190–3204, 2003; 10.1152/jn.00341.2002. Patterns of threshold distributions for single-cycle sinusoidal electrical stimulation and single pulse electrical stimulation were compared in primary auditory cortex of the adult cat. Furthermore, the effects of auditory deprivation on these distributions were evaluated and compared across three groups of adult cats. Threshold distributions for single and multiple unit responses from the middle cortical layers were obtained on the ectosylvian gyrus in an acutely implanted animal; 2 wk after deafening and implantation (short-term group); and neonatally deafened animals implanted following 2–5 yr of deafness (long-term group). For all three cases, we observed similar patterns of circumscribed regions of low response thresholds in the region of primary auditory cortex (AI). A dorsal and a ventral region of low response thresholds were found separated by a narrow, anterior-posterior strip of elevated thresholds. The ventral low-threshold regions in the short-term group were cochleotopically arranged. By contrast, the dorsal region in the short-term animals and both low-threshold regions in long-term deafened animals maintained only weak cochleotopy. Analysis of the spatial extent of the low-threshold regions revealed that the activated area for sinusoidal stimulation was smaller and more circumscribed than for pulsatile stimulation for both dorsal and ventral AI. The width of the high-threshold ridge that separated the dorsal and ventral low-threshold regions was greater for sinusoidal stimulation. Sinusoidal and pulsatile threshold behavior differed significantly for electrode configurations with low and high minimum thresholds. Differences in threshold behavior and cortical response distributions between the sinusoidal and pulsatile stimulation suggest that stimulus shape plays a significant role in the activation of cortical activity. Differences in the activation pattern for short-term and long-term deafness reflect deafness-induced reorganization changes based on factors such as differences in excitatory and inhibitory balance that are affected by the stimulation parameters.

INTRODUCTION

The use of cochlear implants for the treatment of deafness has revealed significant improvements in the auditory capabilities for both pediatric and adult recipients (e.g., Hollow et al. 1995; Skinner et al. 1997; Tyler et al. 1997). Duration of deafness, age at implantation, and duration of implant use play a major role in patient performance (Blamey et al. 1996; Cowan et al. 1995; Dawson et al. 1992; Miyamoto et al. 1994; Osberger et al. 1998; Snik et al. 1997; Tyler et al. 1997; Waltzman 1997). In addition, variations in speech understanding by cochlear implant patients can be attributed to issues surrounding electrode design, speech coding strategies, and stimulus characteristics. It appears that anatomical limitations, and subsequent physiological alterations in central auditory nervous system processing capacities, also can be responsible for patient performance (Ponton et al. 1996; Shepherd et al. 1997). Two main principles of stimulus delivery to electrodes of cochlear prostheses are in use: simultaneous delivery of analog waveforms and nonsimultaneous interleaved delivery of pulsatile stimuli. Both strategies have been shown to be useful; however, their respective effectiveness may differ among patients (Loeb and Kessler 1995; Stollwerck et al. 2001; Tyler et al. 1996; Wilson et al. 1991, 1995). While there are a number of significant spatial and temporal differences in the stimulus delivery between these two strategies, the stimulus shape itself—short pulses versus long sinusoids—may give rise to a number of central auditory consequences in the signal representation.

To explore the effects of auditory deprivation on performance and the efficacy of electrical stimulation on the representation of sounds in the auditory system, it is essential to evaluate the physiology of the central auditory system in animals deafened for different lengths of time, using various electrical stimulation strategies (Bierer and Middlebrooks 2002; Dinse et al. 1997; Klinke et al. 1999; Middlebrooks and Bierer 2002). Previously, we explored the response distribution of primary auditory cortical neurons to single pulses of electrical current with regard to the effects of age at deafness onset and duration on the functional organization of primary auditory cortex (AI) (Raggio and Schreiner 1994, 1999; Schreiner and Raggio 1996). The spatially nonuniform distribution of evoked cortical responses to acoustic stimulation (Heil et al. 1992; Schreiner and Mendelson 1990; Schreiner et al. 1992, 2000) offers a systematic functional framework against which the central representation of peripheral electrical stimulation can be compared.

This study was undertaken to evaluate the following questions. 1) How do spatial distributions of responses from cochlear implant stimulation differ for pulsatile and sinusoidal...
inputs in cat AI? 2) How are these differences affected by short-term deafening with nearly complete spiral ganglion cell survival and by long-term neonatal deafening with a high degree of degeneration of spiral ganglion cells?

The data set contains only conditions in which both, sinusoidal and pulsatile responses, were obtained. Some of the most relevant parameters for implants serve as independent variables: location of stimulation, spatial pattern of stimulation (monopolar, bipolar, radial, longitudinal), and duration and onset of deafness. Dependent variables include sensitivity to electrical stimulation (response threshold) and spatial distribution of response sensitivity across AI.

**Methods**

Most technical details of this study have been described in some detail in previous reports from this series of studies (e.g., Raggio and Schreiner 1994, 1999) and therefore will be summarized only briefly.

Neuronal responses in the auditory cortex evoked by electrical stimulation of the cochlea were recorded from the right hemisphere of healthy, adult cats (*Felis catus*) after each animal received a left scala tympani cochlear implant. Animals were segregated into three groups according to the duration of deafness. The first group consisted of four adult, neonatally deafened cats that were implanted between 2 wk and 4 mo before the electrophysiological evaluation and studied 33–69 mo after birth (long-term group). Two of the four long-term deafened animals (K55 and K56) received some chronic electrical stimulation of the cochlear implant for several months immediately prior to the electrophysiological evaluation of cortex. Both animals were stimulated for 2–6 h/day either passively or as part of behavioral detection or discrimination tasks. The two other groups were normal hearing adult cats that were either implanted 2 wk before study (short-term group, *n* = 3) or implanted acutely (acute group, *n* = 1). Since only one acutely deafened control animal was studied for both pulsatile and sinusoidal stimulation, the statistical analysis and discussion concentrates on the comparison of short-term and long-term animals.

**Deafening procedures**

Prior to implantation of the intracochlear electrode and recording from cortical cells, the animals were deafened using one of three procedures.

**Long-term group.** Beginning 24 h after birth, intramuscular injections of neomycin sulfate were administered for 14–21 days at 50 mg/kg/d (Snyder et al. 1990).

**Acute group.** Monaural hearing loss was induced by intrascalar injection of neomycin sulfate (50 mg/ml) followed by electrode insertion several hours before recording from auditory cortex.

**Short-term group.** Bilateral deafening was induced by a single subcutaneous injection of kanamycin (400 mg/kg) followed by slow intravenous infusion of ethacrynic acid (10–25 mg/kg) (Leake et al. 2000). All procedures involving animals were approved by the Institutional Review Board and followed national guidelines of animal care.

**Implantation and surgery**

Animals from the short-term and long-term groups were implanted under sterile conditions at least 2 wk before the electrophysiological mapping experiment. Animals were sedated with an intramuscular injection of a 4:1 mixture of ketamine hydrochloride (10 mg/kg) and acepromazine maleate (0.10 mg/kg). After venous cannulation, an initial dose of sodium pentobarbital (15–30 mg/kg iv) was administered. Anesthesia was maintained at alveolar levels with supplementary intravenous injections of sodium pentobarbital and during experimental procedures with a continuous infusion of sodium pentobarbital (2 mg/kg/h) in lactated Ringer solution (infusion volume approximately 3.5–5 ml/h). The animals were also administered dexa-methasone sodium phosphate (0.14 mg/kg), atropine sulfate (0.04 mg/kg im), and prophylactic antibiotic treatment (Penicillin G 100K units). A tracheotomy was performed, and a tracheal tube placed to ease breathing. The body temperature of the animals was maintained at 37.5°C by means of a heated water blanket with feedback control. An elliptical incision was made through the scalp, and a posterior temporalis muscle flap created. The bulla was then exposed and opened, thereby exposing the round window. The round window membrane was opened and the intracochlear electrode inserted into the scala tympani. Once in place, the silastic electrode carrier was secured to the promontory and under the temporalis flap using a butyl cyanoacrylate adhesive (Histocryl).

For the recording session, the animal’s head was mounted in a standard mouth-bar head holder. The temporalis muscle was then retracted and the right lateral cortex was exposed. The exposed cortical region was covered with silicone oil and a video image of the surface vasculature obtained. Electrode penetration sites were marked on a video picture of the cortical surface.

For the neonatally deafened animals, spiral ganglion cell density was evaluated in radial sections of the cochlea and expressed as a percentage of normal cell density (Leake et al. 1991; Rebscher et al. 2001). The mean spiral ganglion cell survival for animals in this long-term deafened group was approximately 9%, in close agreement with a larger, partially overlapping group of similarly treated cases (Rebscher et al. 2001).

**Stimulus generation and presentation**

Electrical stimuli were generated and controlled by a signal processing computer (TMS32010) and converted to an analog signal by a 16 bit D/A converter running at a 60-kHz sampling rate. A low impedance attenuator was used to control electrical current in a range from 1 to 30 mAmmps (Vureck et al. 1981). Stimuli were then delivered to an electrode pair switch box connected by cable to the electrode connector at the animal’s head. Electrical stimuli consisted of capacitively coupled, charge-balanced, single biphasic square wave pulses of 200 μs per phase or a single cycle of a 100-Hz sinusoid, delivered at 1–2 Hz. Electrical peak current levels are expressed in dB (100μA/A→). This convention is used for both stimulus types. Due to the longer duration and difference in waveform, the total charge delivered by the sinusoid is 24 dB higher than for the pulse stimulus when both have the same peak current.

Single pulses and sinusoids were used to avoid contamination of the cortical response by electrical stimulus artifacts. Most cortical neurons only respond poorly to repetitive stimuli presented at rates >20 Hz (Schreiner and Raggio 1996), and unmodulated continuous pulsatile or sinusoidal stimulation at rates of 100 Hz would be characterized by the virtual absence of spiking activity following the brief onset activity.

**Recording procedure**

Experiments were conducted in a double-walled, sound shielded room (IAC). Parylene-coated tungsten microelectrodes (Microprobe) with impedances of approximately 0.8–1.2 MΩ/sm at 1 kHz were introduced into the auditory cortex with a hydraulic microdrive (KOPF) remotely controlled by a stepping motor. All penetrations were essentially orthogonal to the brain surface. Recordings were obtained at intracortical depths ranging from 850 to 1,050 µm, as determined by the microdrive setting, corresponding to layers IIb and IV. Dimpling of the cortical surface was largely eliminated by advancing the electrode beyond the targeted recording depth and then retracting until the surface was flat as observed under the microscope. Activity of small clusters of neurons or single neurons was amplified,
band-pass filtered, and monitored on an oscilloscope and an audio monitor. Spike activity was isolated from background noise with a window discriminator (DIS-1, Microprobe). Threshold mapping was the singular goal of electrical stimulation in this portion of the study. Audiovisual criteria of minimum driven spike activity from single units or small cluster of units were used to determine the minimum threshold values for a peak current range of 30–300 μAmps. A single measure of threshold determination was made at each penetration site using an ascending/bracketing method for each electrode configuration. Several designs of scala-tympani electrodes were used, resulting in various spacings of the bipolar pairs and locations of the individual electrode contacts. Since only a few actual stimulation electrode positions could be obtained at the conclusion of the experiment, estimates of the positioning of the electrodes were obtained relative to the electrode cuff at the round window and the distance of the electrode contacts from the cuff (for details, see Raggio and Schreiner 1999).

Data representation

One method of data reconstruction and representation throughout these studies is the use of two- and three-dimensional spatial plots that represent the distributions of parametric responses across the primary auditory cortical surface (see Fig. 1). These reconstructions were performed with a software package (Surfer Golden Software) using standard methods for pseudo-three-dimensional representation applied in geological studies to represent terrain. The methods are based on an interpolation algorithm that weighs the values of the two nearest neighboring points in each quadrant according to an inverse square distribution. Penetration sites were chosen to evenly cover the high-frequency region of the primary AI. Spacing of the penetrations was between 300 and 600 μm and approximately equal across each map to minimize spatial biases. Since in most of these cases no physiological measures of the actual location of AI were available, such as the tonotopic gradient (Merzenich et al. 1975) or the location of the sharply tuned region in AI (Schreiner and Mendelson 1990), distinct anatomical features had to serve as main landmarks. In general, the mapping was limited to the region between the anterior and posterior ectosylvian sulci, in the rostro-caudal direction, and between the supra-sylvian sulcus and a line approximately 2–3 mm ventral to the connection line between the dorsal tips of the anterior and posterior ectosylvian sulci. This region usually spans the full iso-frequency extent of AI. Details about the cases, including extent and mapping density, are shown in Table I (see also Raggio and Schreiner 1999).

Pattern of threshold distribution in primary auditory cortex

For each configuration of the scala-tympani electrode, a distinct spatial pattern of response thresholds across the mapped region was observed. Local regions of low-threshold responses were separated from regions with high-threshold responses or unresponsive areas. Usually two low-threshold regions were encountered in AI for both pulsatile stimulation (Raggio and Schreiner 1999) and sinusoidal input, one in

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**Fig. 1.** Reconstruction of spatial response threshold distribution. A: relative position of recording locations in auditory cortex (AI). Cortical distances are plotted along the ventral-dorsal and caudal-rostral axes of AI and are given in millimeters. The origin of the coordinate system arbitrarily is chosen to be near the most ventral and most caudal excursions of all recording locations (in this case: radial pair 1.2; C163). For each recording site, the minimum response threshold for a given electrode configuration is noted at the corresponding site in the map. Iso-threshold contours are determined on the basis of the spatial distribution pattern. For this example, the approximate location of iso-threshold contours for 15, 25, and 35 dB (100 μAmp) are indicated: B: from the resulting interpolated spatial pattern, 3 quantitative measures were obtained. 1) Caudal-rostral spatial extent or spatial tuning width (STW) 6 dB above minimum threshold for dorsal and ventral AI. 2) Cortical area occupied by locations with thresholds not more than 6 dB above minimum threshold (thick solid line). 3) Width of the high-threshold ridge (RW) separating dorsal and ventral low-threshold regions.

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Statistical analyses of the data, including pairwise t-test, principal component analysis, and Pearson regression, were performed using Statview 4.5 (Abacus Concepts). Generally, only statistically secure results with P values less than 0.05 are reported.
dorsal AI and a second region in ventral AI, separated by a ridge of higher response thresholds.

Examples of the reconstructed cortical response-threshold distributions for different locations of the cochlear stimulation electrodes are shown in Figs. 2 and 3. The response-threshold maps illustrated in Fig. 2 are from an animal that was deafened neonatally and mapped after 68 mo of deafness. However, the animal did receive several months of chronic electrical stimulation of one radial pair immediately prior to mapping. The approximate location of the mapped region on the right ectosylvian gyrus is indicated in a small schematic plot. The threshold distributions for pulsatile (Fig. 2, left) and sinusoidal (Fig. 2, right) stimuli are shown for two electrode configurations, one monopolar condition (top row) and one longitudinal pair (bottom row). Each panel shows the interpolated threshold distribution based on 99 recording sites (black dots). Actual threshold values were transformed into a color code shown at the bottom right.

Inspection of the different threshold distributions reveals clusters of penetrations with equally high (red to orange) or low (purple to blue) thresholds. Characteristically, along the ventral-dorsal axis of the map one can distinguish two regions of lower thresholds that are separated by a narrow ridge of higher response thresholds. The rostro-caudal location of the ventral and dorsal low-thresholds regions is quite similar. For both electrode configurations, the sinusoidal stimuli have lower response thresholds (measured at peak amplitude; see corresponding color scale in Fig. 2) and show a more restricted extent of the low-threshold region along the rostro-caudal and the dorso-ventral axis than the pulsatile stimuli. This effect is more pronounced for the monopolar electrode configuration. A high-threshold ridge between the dorsal and ventral low-threshold regions is clearly expressed for both stimuli and for both electrode configurations.

Another example of threshold maps from a long-term deafened animal is shown in Fig. 3. It depicts one of the most diffuse and patchy patterns of low- and high-threshold regions that were encountered. This type of pattern is only seen in some long-term cases. Several circumscribed regions of low-threshold are present for both stimuli but no clear central ridge separates dorsal and ventral threshold minima. The sinusoidal
thresholds (peak amplitude) generally are 8–10 dB below the pulsatile threshold. However, the overall distribution pattern of response thresholds is quite similar for the two stimuli.

In summary, the examples demonstrate some general principles of the spatial organization of Al for the response sensitivity to cochlear electrical stimulation. Two regions of low-response thresholds, separated in the dorso-ventral domain by a high-threshold ridge, generally appear with electrical cochlear stimulation of either type. However, details of the spatial pattern, such as extent and relative location of regions with low response thresholds, can vary with the specific electrode configuration, with the deafening history of the animals, and with the stimulus configuration. In the next sections, several specific aspects of the spatial distribution pattern are analyzed and compared for the different stimuli and deafness histories.

Electrode configuration effects on cortical response parameters

Potentially confounding the results is the use of several different designs and stimulation configurations of the feline scala-tympani electrode, the UCSF electrode and the UCSF wing electrode (Rebscher et al. 2001). This variability in the experimental design was due to advances in electrode technology over the extended time frame of the study (>8 yr) and limited availability of some electrode types. As a consequence, some details of the size and position of the electrode contacts as well as the longitudinal and radial spacing of the bipolar electrode configuration varied between and within experimental groups (see Raggio and Schreiner 1999). For pulsatile stimulation, a number of significant differences between the narrowly spaced radial electrode configurations and the more widely spaced longitudinal configurations, as well as the monopolar configurations, were observed for cortical response properties (Raggio and Schreiner 1999). Accordingly, the following analysis of sinusoidal stimulation will also distinguish between bipolar radial configuration (≤1 mm longitudinal spacing); bipolar longitudinal configuration (2–6 mm longitudinal spacing); and monopolar configuration (single intracochlear contact with extracochlear return electrode of >20 mm separation). A direct comparison of group data and individual conditions for pulse and sinusoidal stimulation is feasible because the data are based only on those electrode configurations that were tested for both stimulus types.

Cochlear electrode position effects on location of threshold minima in cortex

Among the main aspects of cortical activation patterns that can be deduced from the individual maps (e.g., Figs. 2 and 3) is that the cortical position of the region(s) with lowest response threshold can co-vary with the position of the stimulation electrode in the cochlea. We tested the hypothesis that cortical activation by sinusoidal electrical cochlear stimulation reflects the same cochleotopic organization of Al as seen in normal, hearing animals. After establishing the relative relationship between cochlear position (expressed as distance of basilar membrane in percent from the cochlear base) and rostro-caudal cortical distance (expressed in millimeter), the cortical position of lowest threshold for focal cochlear stimulation could be obtained (for procedural details, see Raggio and Schreiner 1999). The relative cortical positions for both the dorsal and ventral threshold minima were plotted as a function of the electrode position in the cochlea (Fig. 4). The location data for the radial bipolar and the monopolar electrode configurations were combined since both showed distinct, spatially confined threshold minima. The cortical positions for different stimulation electrode locations were first plotted separately for each individual case, and a regression analysis was performed. The individual regressions were adjusted to align arbitrarily the cochlear position of 47% with the cortical position of 0 mm. After pooling the cases relative to this reference, a global regression analysis was performed. The solid lines and the

<table>
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<tr>
<th>Animal</th>
<th>Deafening Procedure</th>
<th>Deafness Duration, mo</th>
<th>No. of Cortical Sites</th>
<th>Cortical Area, mm²</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute C603</td>
<td>Aminoglycoside intrascalar</td>
<td>0</td>
<td>60</td>
<td>6.6 × 2.4</td>
</tr>
<tr>
<td>Short-term C637</td>
<td>Aminoglycoside adult SQ</td>
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<td>93</td>
<td>8.2 × 4.6</td>
</tr>
<tr>
<td>C617</td>
<td>Aminoglycoside adult SQ</td>
<td>0.5</td>
<td>65</td>
<td>7.4 × 5.6</td>
</tr>
<tr>
<td>C518</td>
<td>Aminoglycoside adult SQ</td>
<td>0.5</td>
<td>62</td>
<td>6.4 × 6.6</td>
</tr>
<tr>
<td>Long-term K73</td>
<td>Aminoglycoside neonatal IM</td>
<td>33</td>
<td>147</td>
<td>7.5 × 9.6</td>
</tr>
<tr>
<td>K55</td>
<td>Aminoglycoside neonatal IM</td>
<td>68</td>
<td>109</td>
<td>4.4 × 5.0</td>
</tr>
<tr>
<td>K56</td>
<td>Aminoglycoside neonatal IM</td>
<td>68</td>
<td>99</td>
<td>5.4 × 6.8</td>
</tr>
<tr>
<td>K51</td>
<td>Aminoglycoside neonatal IM</td>
<td>69</td>
<td>110</td>
<td>4.2 × 5.6</td>
</tr>
</tbody>
</table>

FIG. 3. Reconstruction of cortical response threshold distributions for another long-term deafened animal (K73, n = 147). Response thresholds for pulsatile and sinusoidal stimulation of electrode pair 2, 3 are shown. Same conventions as described for Fig. 2. The interval between iso-threshold contours is 5 dB.
equations in each panel of Fig. 4A show the result of that analysis for the short- and long-term deafness and for dorsal (solid line) and ventral (dotted line) locations of cortical threshold minima. The dashed line in each panel represents the normal relationship between cortical position and cochlear position via the CF relationships in hearing animals (Raggio and Schreiner 1999).

The cortical position of the minimum threshold for three of the electrodes of the acutely deafened animal (Fig. 4A, red symbols) corresponded well to the normal cochleotopic organization. Only the most caudal electrode, which had the highest thresholds for both dorsal and ventral sites, deviated from the predictions. For the short- and long-term deafened animals, the regression lines were significantly different from zero and had the same sign as for the normal hearing animals, with the exception of the ventral part of the long-term deafened animals. Consequently, the shift in cortical position with variations of cochlear stimulation locus was consistent with a maintained global cochleotopic gradient. However, the slope of the regression line was significantly shallower than in the normal, hearing animals. This was especially true for the long-term cases which showed no clear spatial variation with changes in cochlear position. Accordingly, the cochleotopic organization in AI appears to have deteriorated during long-term deprivation from sound input. The reduced cochleotopic order for the short-term group in ventral, and especially in dorsal AI is in contrast to the pulsatile stimulation, in which both regions showed a nearly normal cochleotopic profile.

The locations of threshold minima for pulsatile and sinusoidal stimulation were significantly correlated (Fig. 4B) for short-term and long-term cases. However, the regression slope for all four configurations was significantly below unity, i.e., variations in the position of the threshold minima with electrode position were smaller for sinusoidal stimuli than for pulsatile. These findings suggest that the cochleotopic axis in AI for short-term, and especially, long-term deafened animals is significantly compressed or even absent for sinusoidal stimuli and that stimulus configuration has a significant influence on the expression of the cortical activation pattern and issues of cortical channel separation. For the acutely deafened case, the regression was not significantly different from unity.

**Effects of electrode configuration and deafness duration on minimum threshold**

One of the main questions of this study was whether long-term deafening introduces a decrease in response sensitivity of cortical neurons reflected in an increase of the minimum response threshold in cortex. The lowest response threshold to sinusoidal stimulation encountered for each electrode configuration and for each case was determined (Fig. 5). Since no significant difference between the minimum thresholds in dorsal and ventral AI was detected, only the absolute minimum was considered for further analysis of threshold properties.

Figure 5A shows the minimum sinusoid thresholds for the three electrode configurations and the different deafness histo-
Across all electrode configurations, the thresholds of the short-term cases (-18.0 ± 9.5 dB) were significantly below those of the long-term animals (-2.4 ± 9.0 dBpeak; Scheffe, P < 0.0001). The monopolar and the radial conditions both showed a significant difference between short-term and long-term deafening. For the short-term condition, the thresholds between radial and monopolar conditions were significantly different. Finally, the thresholds of the acute animal were significantly higher than short-term conditions for the radial electrode configuration. Pulsatile thresholds had not revealed significant threshold differences between short- and long-term deafened animals (Raggio and Schreiner 1999). There was no statistically significant interaction effects between the electrode conditions and the deafness conditions.

A pairwise comparison between minimum sinusoidal and pulsatile response threshold is given in Fig. 5B for all electrode conditions. The minimum thresholds for both stimuli are highly correlated (r = 0.81; P < 0.0001). The slope of the regression line is significantly steeper than unity. Cortical locations with the lowest minimum thresholds showed a closer correspondence to an equal charge per phase for the two stimuli than stimulation sites with higher thresholds. (The equal charge condition for the two stimuli is indicated by the dashed line in Fig. 5B.) For locations with minimum pulsatile thresholds above 10 dB, the corresponding sinusoidal threshold tended to be approximately 10 dB higher than an equal-charge condition would entail. Monopolar conditions (red symbols) and short-term cases (squares) showed the lowest thresholds for both pulsatile and sinusoidal stimulation. A possible source of the threshold behavior could be the location of the electrode contacts within the scala tympani and concomitant systematic changes in the proximity of the electrode contacts to the spiral ganglion. However, analysis of the relationship between the magnitude of minimum threshold differences for the two waveforms and the distance of the stimulation electrodes from the base of the cochlea showed no orderly, statistically significant relationship (Pearson regression, P > 0.3).

In summary, the lowest encountered minimum threshold responses can be evoked by 100-Hz sinusoidal and 0.2-ms pulsatile stimuli of approximately equal total charge. However, at locations with higher minimum response thresholds, the total delivered charge for the longer sinusoidal stimuli exceeded that for short, pulsatile stimuli by a factor of 3. This suggests that stimulus waveform and/or duration may influence the peripheral or central integration mechanisms that lead to a cortical response. In contrast to pulsatile stimuli, long-term deafness significantly elevates minimum response thresholds for sinusoidal stimuli compared with short-term deafness.

Differences in the relationship between sinusoidal and pulsatile stimulus parameters are not limited to the conditions of minimum threshold. Figure 6 shows the response thresholds evoked for three electrode configurations for all cortical sites sampled in these cases. Due to the spatial tuning of responses across cortex (e.g., Figs. 2 and 3), response thresholds vary over a wide range of stimulus amplitudes. As for minimum thresholds, sinusoidal and pulsatile response thresholds for all recording sites are highly correlated and only show substantial scatter at the highest thresholds. However, the slope of the threshold regression varies substantially between electrode configurations with very low minimum thresholds compared with less sensitive configurations. The regression coefficients (slopes) for all electrodes and deafness durations show a significant dependence on minimum threshold (Fig. 7B). For electrode configurations or deafness histories that result in high minimum thresholds, the slopes are near unity and reflect a dependence of stimulus strength and cortical location that is very similar for the two stimulus modes. Note, again, that the sinusoidal threshold values are not compatible with the assumption of equal charge for pulses and sinuosoids at threshold.

By contrast, implant conditions that result in low minimum thresholds show very steep slopes (Fig. 7, A and B) that start at stimulus amplitudes that are compatible with equal charge for both stimulus configurations. This suggests two modes of
spatial-temporal integration for sinusoidal stimulation: a low-threshold, highly energy efficient mode that is limited to a narrow range of current levels, and a high-threshold, less energy efficient mode that spans a wide range of stimulus amplitudes.

Effects of electrode configuration and deafness duration on size of low-threshold area

Next to stimulus sensitivity, the spatial extent of activation plays a major role in the representation, and potentially, discrimination of sounds and electrical cochlear stimuli. We used several measures of the activated cortical area to evaluate the spatial extent of activation (see METHODS and Fig. 1). For this purpose, the low-threshold area was defined as that region of activated cortex that was within 6 dB of the minimum threshold for a given electrode configuration. We expressed this areal measure relative to the extent of the total mapped region (see Raggio and Schreiner 1999). The mean extent of the low-threshold area is shown in Fig. 8A for different electrode configurations. No significant differences between the short- and long-term deafness conditions were observed for sinusoidal stimuli. This is in contrast to the pulsatile condition in which the average short-term area was approximately 40% larger than the average area in the long-term cases. Similarly, no significant differences were observed between the different electrode configurations. For pulsatile stimuli, radial electrode pairs occupied the smallest low-threshold area.

A direct comparison between pulsatile and sinusoidal stimuli (Fig. 8B) shows no clear correlation for this areal measure. However, it is obvious that the low-threshold area for the sinusoidal condition is generally smaller than that for pulsatile activation. The mean pairwise difference was 23.1% ($P < 0.0001$; df 35) of the total mapped area. In relative terms, the sinusoidal low-threshold area was about one-half the size of the pulsatile area.

Effects of electrode configuration and deafness duration on spatial tuning width

While the area of low-threshold responses is a useful measure of the extent of cortical activation, the spread of excitation along the cochleotopic axis is of particular interest. Such a measure is more suitable for considerations of channel interaction and activation overlap along the cochleotopic axis than the areal measure alone. The measure of spatial tuning width has been used previously (e.g., Bierer and Middlebrooks 2002; Kral et al. 1998; Raggio and Schreiner 1999; Snyder et al. 1990) for expressing spread of excitation along the cochleotopic axis. In the case of the auditory cortex, two spatial...
tuning measures have to be considered: one for the dorsal activation region and one for the ventral region.

The mean spatial tuning width (in mm of cortical distance) for the different conditions is shown in Figs. 9 and 10 for dorsal and ventral AI, respectively. No consistent and statistically significant difference in the spatial tuning width was found for the two deafness condition in either dorsal or ventral AI. This is consistent with the findings for pulsatile stimuli (Raggio and Schreiner 1999). For electrode configurations, the radial acute tuning width was significantly more narrowly tuned than the short-term cases in ventral AI (mean pairwise difference: 2.52 mm, \( P < 0.02 \)). Although there was a tendency for broader tuning in longitudinal electrode pairs, this difference was not statistically significant.

Direct comparison of sinusoidal versus pulsatile spatial tuning width (Figs. 9B and 10B) reveals a significant correlation for both dorsal and ventral AI. For both regions, the slope of the regression line is significantly below unity (dorsal slope: 0.68, \( r^2 = 0.33; P < 0.0006 \); ventral slope: 0.72; \( r^2 = 0.40; P < 0.0001 \)). This means that the spatial tuning width for sinusoidal stimulation is narrower than for pulsatile stimulation by a factor of approximately 0.7. The mean difference was 1.08 mm (\( P < 0.00001; df 36 \)) and 1.10 mm (\( P < 0.0001; df 36 \)), respectively, for dorsal and ventral AI.

Effects of electrode configuration and deafness duration on high-threshold ridge

A characteristic of the activity distribution across AI was a narrow ridge of high-threshold or unresponsive locations spanning usually the whole rostro-caudal length of the mapped areas, thus separating dorsal from ventral low-threshold regions (see Fig. 2). The width of the ridge between the dorsal and ventral low-threshold regions (12 dB above minimum threshold) varied quite dramatically between some of the configurations for pulsatile stimulation and was essentially absent in short-term animals (Raggio and Schreiner 1999). The lower total number of configurations contributing to the analysis of this parameter is due to the fact that not all cases could be mapped sufficiently to assess the full width of the central ridge. The mean width of the central ridge for sinusoidal stimulation is shown in Fig. 11A for different deafness durations and

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**FIG. 8.** A: bar graphs of mean low threshold area. For each case (\( n = 8 \)), the cortical area with threshold values <6 dB above minimum threshold was determined for each electrode configuration and for 3 durations of deafness. Number in each bar gives the size of the sampled electrode configurations. B: comparison of cortical activation area for sinusoidal and pulsatile stimulation. Solid line indicates equal size of low threshold areas.

**FIG. 9.** A: bar graphs of mean spatial tuning width (STW) in dorsal AI. For each case (\( n = 17 \)), the STW was determined 6 dB above minimum threshold for each electrode configuration. Mean STW for different deafness durations separated into subgroups for electrode configurations. Number in each bar gives the size of the sampled conditions. B: comparison of dorsal spatial tuning width for sinusoidal and pulsatile stimulation. Solid line indicates tuning of the same width for both stimulus conditions. For reference, the dashed line corresponds to a spatial tuning of the sinusoidal one-half the width for pulsatile stimulation.
different electrode configurations. Substantial differences in the ridge width were seen between the long-term cases and the short-term cases for pulsatile stimuli with largely absent or very narrow ridges in the short-term cases. For sinusoidal stimulation, the situation was quite different. Across all electrode configurations, the short-term cases did exhibit distinct high-threshold ridges and they were substantially wider (on average by 0.37 mm, Scheffe $P = 0.038$) than the ridges in the long-term cases. Analyzed by electrode configuration, this difference was significant for the monopolar condition only. No significant differences in ridge width were found between electrode configurations within each deafness group. Comparison between sinusoidal and pulsatile stimuli showed a significant difference for the short-term cases but not for the long-term cases.

**Correlation analysis of parameters**

Correlation analysis between the main measures across all electrode and deafness conditions estimates the shared information provided by the different descriptors for sinusoidally evoked responses. The correlation coefficients and the significance values are shown in Table 2. Measures taken independently for dorsal and ventral AI, such as spatial tuning width and rostro-caudal position of minimum threshold, were highly correlated (see Table 2). Measures of response sensitivity, i.e., minimum threshold and slope of the relationship between pulsatile and sinusoidal threshold, were inversely correlated. Minimum threshold was weakly and inversely related to the ventral spatial tuning width and the ridge width: the lower the threshold, the broader was spatial tuning and ridge width. The spatial tuning width (ventral AI) was related to the threshold relationship between sinusoids and pulses: broader tuning was found in conditions that had steeper slopes. The measures of the cortical extent of activation, spatial tuning width, and low-threshold area, did not covary significantly, in contrast to the pulsatile case (Raggio and Schreiner 1999).

A principal component analysis was performed for the response parameters derived from the radial and monopolar electrode configurations and spiral ganglion density combined for sinusoidal and pulsatile stimulation and for short-term and long-term deafness. This analysis helps to determine which of

![FIG. 10. A: bar graphs of mean spatial tuning width (STW) in ventral AI. For each case ($n = 17$), the STW was determined 6 dB above minimum threshold for each electrode configuration. Mean STW for different deafness durations separated into subgroups for electrode configurations. Number in each bar gives the size of the sampled conditions. B: comparison of ventral spatial tuning width for sinusoidal and pulsatile stimulation. Solid line indicates tuning of the same width for both stimulus conditions.](image)

![FIG. 11. A: bar graphs of mean width for central high-threshold ridge. For each case ($n = 17$), the width of the horizontal ridge in central AI was determined that separates dorsal and ventral low-threshold regions. The dorso-ventral ridge width was determined near the line connecting the locations of minimum threshold in dorsal and ventral AI 12 dB above lowest threshold. Mean ridge width for different deafness durations are shown separated into subgroups for electrode configurations. Statistically significant differences between conditions are indicated by brackets ($*P < 0.05$). B: comparison of central ridge width for sinusoidal and pulsatile stimulation. Solid line indicates tuning of the same width for both stimulus conditions.](image)
TABLE 2. Correlation coefficients and P values of regression analysis of the eight descriptive parameters for sinusoidal stimulation of radial and monopolar electrode conditions

<table>
<thead>
<tr>
<th></th>
<th>Thr min</th>
<th>Pos d</th>
<th>Pos v</th>
<th>STWd</th>
<th>STWv</th>
<th>RW</th>
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<td>Thr min</td>
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<tr>
<td>Pos v</td>
<td>—</td>
<td>&lt;0.0001</td>
<td>1.00</td>
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<tr>
<td>STW d</td>
<td>&lt;0.05</td>
<td>—</td>
<td>—</td>
<td>1.00</td>
<td>0.57</td>
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<tr>
<td>STW v</td>
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<td>&lt;0.001</td>
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<td>RW</td>
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<td>Area</td>
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<td>Slope</td>
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Statistically significant correlation coefficients (r) are shown above the diagonal, P values below the diagonal. Non-significant correlations are indicated by dashes. Thr, minimum threshold; Pos, rostro-caudal position of minimum threshold; STW, spatial tuning width; RW, ridge width; Area, low-threshold area; Slope, regression of sinus vs. pulse thresholds; d, dorsal; v, ventral.

The obtained measures of the spatial excitation patterns provide necessary and independent information about the effects of deafness duration and stimulus waveform. From the 11 measures, 5 orthogonal or independent factors (Eigen values > 1.0) emerged that accounted for 85% of the total variance of the data. The strongest factor (F1) accounted for 32% of the total variance and was comprised of five measures: minimum response threshold for pulses and sinusoids (Pearson correlation coefficient between variable and factor: +0.86 and +0.80, respectively), sinusoidal area (+0.74), the width of the pulsatile high-threshold ridge (+0.55), and the spiral ganglion density (−0.63). This means that a low spiral ganglion density is predictive of higher minimum thresholds, larger sinusoidal activation areas, and wider pulsatile central ridges. The second strongest factor (F2) accounted for 19% of the variance and corresponded to two parameters: the spatial tuning width for both sinusoidal and pulsatile waveforms (+0.92 and +0.83, respectively). F2 was dominated by a spatial measure that appears to be largely independent from spiral ganglion density. The third factor (F3, 13% of variance) was comprised of the ridge width in the sinusoidal condition (+0.94). The pulsatile ridge width had the second strongest load on this factor (+0.46) but contributed more strongly to F1. Factor four (F4) was comprised of the low-threshold area for pulsatile stimulation (+0.93) and the spiral ganglion density (+0.63). This reflects the finding that the extension of the excitation area was larger for the short-term cases than for the long-term cases, which also had very low spiral ganglion survival. However, influences of alteration in inhibitory properties (Rajan, 1998; Raggio and Schreiner 1999) that are not directly captured by the obtained parameters may play a larger role in the expansion of the activated area than spiral ganglion survival per se. Finally, factor five (F5) captures the caudal-rostral or cochleotopic position of the cortical excitation for both pulsatile (+0.93) and sinusoidal (+0.56) stimulation. Note that this analysis explores the redundancy in the used physiological measures and does not differentiate between the experimental variables of deafness history and electrode configurations with the exception of spiral ganglion density.

In summary, the correlation analysis and the more global principal component analysis show that the investigated parameters capture different aspects of the relationship between deafness duration, stimulus form, and cortical excitation. The main variables for both stimulus types appear to be response sensitivity, spatial tuning width, and cochleotopic position. Additional factors are size of cortical excitation area and ridge width that both appear to be sensitive to the type of stimulus used. Low spiral ganglion density is predictive of higher thresholds, larger sinusoidal area, and small activated area with pulsatile stimulation.

Discussion

In this study, the effect of sinusoidal cochlear stimulation on properties of cortical activation was parametrically evaluated for different deafness durations in the adult cat. We compared animals that were deafened shortly after birth with adult animals deafened 2 wk prior to being studied. The study confirmed a number of observations previously made with pulsatile electrical stimulation in a partially overlapping set of animals (Raggio and Schreiner 1999); however, some significant differences in cortical response sensitivity and distributions were noted that demonstrate the role of stimulus-specific effects in the expression of cortical responses. The data reported here are derived from cases in which both stimulus types were explored and a pair-wise analysis designs could be implemented. A detailed discussion of experimental limitations and caveats in this study is given in the description of the pulsatile responses (Raggio and Schreiner 1999).

The use of sinusoidal electrical stimulation confirms the presence of two circumscribed regions of low response thresholds on the ectosylvian gyrus as obtained with pulsatile cochlear stimulation (Raggio and Schreiner 1999) and also observed in evoked potential studies (Volkov and Dembrovetskii 1979). These two regions are separated dorsal-ventrally by a ridge of high response thresholds. While some details of the spatial patterns of threshold representation varied across deafness histories, electrode configurations, and stimulus waveform, the observed functional partitioning is consistent with the general spatial organization of AI in hearing animals. It reflects a segregation of the dorsal-ventral or iso-frequency domain of AI into functionally distinct subregions that had been noted for acoustical stimulation (Read et al. 2001; Schreiner and Mendelson 1990; Schreiner et al. 1992; Sutter and Schreiner 1995). For acoustic stimulation, dorsal and ventral AI are separated by a band of neurons, running rostro-caudally, with low thresholds and narrow frequency tuning. Neurons dorsal and ventral to this band demonstrate generally higher thresholds and often broader tuning. The cortical distribution pattern seen with electrical cochlear stimulation reveals a threshold pattern that appears to be inverted: a narrow band of high-threshold locations is located between two larger areas of low thresholds.
(Raggio 1992). Interestingly, acoustical studies have revealed not just one central band of sharp tuning across AI but a second, narrower band of more sharply tuned neurons approximately 1.7 mm dorsal to the main central region of sharp tuning (Read et al. 2001). However, the electrical studies with pulsatile and sinusoidal stimuli did not reveal a second band of high response threshold at a corresponding dorsal distance from the central ridge. This suggests that the two narrowly tuned functional modules are likely to differ in response properties other than sharpness of tuning since they are not equivalently engaged by electrical stimulation.

Cochleotopy

The cochleotopic organization of AI for electrical cochlear stimulation with sinusoidal waveforms appears to be clearly diminished in long-term deafened adult animals as well as in animals that had only 2 wk of deprivation from auditory input. Both dorsal and ventral low-threshold regions of AI show slopes of cochlear position versus cortical position that are significantly below that of normal, hearing animals. Only the ventral region in the short-term animals maintained a global cochleotopic gradient, although with a shallower gradient than in normal animals. Previous studies (Dinse et al. 1997; Hartman et al. 1997; Klinke et al. 1999; Taniguchi et al. 1997) and our results from pulsatile stimulation (Raggio and Schreiner 1999) suggested that long-term deafening, or the sustained absence of auditory input, and the profound reduction in peripheral innervation density cause a reduction of cortical cochleotopy. The more extensive reduction of cochleotopy with sinusoidal compared with pulsatile stimulation indicates that other factors than auditory deprivation and loss of spiral ganglion density contribute to the transformation of cochlear stimulation location to cortical response location. How differences in stimulus waveform may contribute to differences in the location of highest stimulus sensitivity in cortex remains unclear. At least two potential factors may play a role. In the periphery, longer stimulus rise-time and overall stimulus duration may affect the current spread and the excitation process by favoring current paths of lower resistance, e.g., resulting in hot spots of excitation determined by electrical idiosyncrasies of the modiolar wall of the scala tympani. Centrally, details of receptive field properties and response location relative to the cochleotopic arrangement may be influenced by specific properties of the electrical stimuli, including rise-time (Heil 1997) and duration (He 1997).

Stimulus effects on cortical response sensitivity

Response thresholds for sinusoidal stimulation were below those of pulsatile stimulation when expressed relative to peak current. The threshold difference was on the order of 10 to 20 dB. These values are in good agreement with previous findings of thresholds for various phase durations of stimuli in the auditory nerve (Hartmann et al. 1984; Sheperd and Javel 1997; Sheperd et al. 1993), the inferior colliculus (Leake et al. 2000; Snyder et al. 1990), and for psychophysical assessments of response sensitivity (Beitel et al. 2000a,b; Moon et al. 1993; Pfingst and Morris 1993; Smith and Finley 1997; Smith et al. 1994). Several animal studies indicate that 100-Hz sinusoidal stimulation results in the lowest neural thresholds (e.g., Glass 1983; Hartmann and Klinke 1990; Hartmann et al. 1984; Miller et al. 1999).

Based on a simple integrate-and-fire model of nerve excitation, the difference in thresholds for pulsatile and sinusoidal stimuli in this study, at least partially, can be attributed to the difference in stimulus duration. Indeed, when comparing the total current/phase delivered by pulses and sinusoids rather than the peak amplitude, the threshold difference is greatly diminished (see Fig. 5B) for the cortical locations with the lowest thresholds. However, this equivalency is not maintained at cortical locations with higher minimum response thresholds. For those sites, the current/phase necessary to reach response threshold is larger for sinusoids than for pulses (however, the peak current for the sinusoids remains below that for the pulses). The cause for the discrepancy in threshold values for insensitive locations is unclear but may be related to nonoptimal positioning of the cochlear electrodes relative to the excitable elements. As a consequence, slower changes in current, as in the case of sinusoidal stimuli, which result in small temporal synchrony (Heil 1997), may be less effective than rapidly rising waveforms that maintain higher synchrony even near threshold.

The wide range of minimum thresholds observed for both stimuli is less influenced by stimulus conditions, but may result from peripheral manifestations of deafness history and electrode placement. However, the large variations of response thresholds for any given electrode condition across AI indicate that cortical thresholds are not a simple reflection of peripheral stimulation efficacy but reflect central influences from networks of neurons.

The effects of deafness duration, and consequently, spiral ganglion survival on thresholds was more profound for sinusoidal than pulsatile stimulation. The spiral ganglion density in the long-term animals was approximately 9% of normal and short-term animals (Rebscher et al. 2001 and personal communication). Short-term thresholds for sinusoids were 10–20 dB below thresholds in long-term animals, whereas there was no significant difference for the pulsatile stimuli (Raggio and Schreiner 1999). The findings for sinusoids support previous studies suggesting that loss of spiral ganglion density can cause an increase in response threshold (e.g., Beitel 2000a; Nadol et al. 1989; Pfingst et al. 1981; Shepherd and Javel 1997). However, it is not clear why pulsatile stimuli did not reveal a similar difference for deafness duration despite the fact that all conditions in studying the two stimulus waveforms were identical. Perhaps the consequences of reduced synchrony for near threshold sinusoids is exacerbated in cases of low spiral ganglion survival.

Comparison of sinusoidal and pulsatile thresholds—either for minimum thresholds per electrode configuration or for all cortical sites per electrode configuration—reveals two functionally distinct regions of operation: for locations with relatively high pulsatile thresholds, the relationship to sinusoidal thresholds is nearly 1:1, i.e., cortical locations with pulsatile thresholds 10 dB higher than other sites have sinusoidal thresholds that are shifted by nearly the same amount. In addition, the sinusoidal stimuli at threshold are approximately 10 dB higher in total charge/phase than for pulses. By contrast, for sites with lower pulsatile thresholds, site-by-site threshold comparison shows a much more rapid growth of sinusoidal threshold relative to changes in pulsatile thresholds. In addition, the
lowest sinusoidal thresholds are matched to the pulsatile thresholds in total charge/phase. The properties that lead to two regions of operation are unclear. The compression of the pulsatile or expansion of the sinusoidal efficacy was observed mostly in short-term cases of highest sensitivity. However, it was not limited to those cases (see Fig. 7B). Accordingly, this behavior is unlikely to be exclusively a consequence of deafness duration or spiral ganglion density, but may reflect other, potentially nonlinear processes that affect the efficacy of stimulation for the most sensitive conditions. Psychophysical studies of waveform differences of threshold behavior have lead to a model of peripheral integration of excitation with two modes (Shannon et al. 1989): envelope coding for continuous presentation of short-duration elements and a compressive process for longer duration elements. The latter process is perhaps related to activation of peripheral processes of spiral ganglion cells (van den Honert and Stypulkowski 1984) and affected by spread of activation and the survival of ganglion cells (Pfingst et al. 1981). This might explain the observation that there was a large threshold difference between short-term and long-term cases for sinusoidal stimuli but not for pulsatile stimuli. However, threshold mechanisms may reflect additional properties such as degree of synchronization, central integration properties (Shannon et al. 1989), and refractory and accommodation processes (Miller et al. 1997). Electrode configuration had an effect on the response thresholds. In particular, the radial conditions were approximately 12 dB less sensitive than the monopolar condition, however, only for the short-term animals. A similar trend was present for the pulsatile stimulation, although limited to the long-term condition. This overall behavior is compatible with an increase in threshold for increasingly more focal stimulation modes in animals (Bierer and Middlebrooks 2002) and in psychophysical studies (Chatterje et al. 2000; Morris and Pfingst 2000).

**Stimulus effects on cortical response distribution**

Sinusoidal stimulation results in a tri-sectored pattern of dorsal and ventral low-threshold neurons separated by a central area of high thresholds. This pattern is visible for short-term and long-term deafness, although the pattern is more “patchy” in some long-term cases. A similar distribution has been seen for pulsatile stimulation (Raggio and Schreiner 1999). The areal extent of low-threshold regions was approximately 23% smaller for sinusoidal than for the pulsatile stimulation; short-term and long-term animals exhibited about the same activated regions. This is in contrast to pulsatile stimulation that showed a significantly larger area in the short-term cases than in the long-term cases. The reason for this discrepancy may again be related to the differences in threshold behavior for sinusoids and pulses as observed in low-threshold region for pulsatile stimulation, and may result in an overestimation of the extent of the most sensitive cortical areas for pulsatile stimulation.

The spatial tuning width along the cocheleotopic axis was slightly narrower for sinusoidal stimulation both in dorsal and ventral response regions of AI. The differences correspond to approximately 0.6 octaves in frequency spread when related to the normal frequency versus cortical distance relationship in AI (see Raggio and Schreiner 1999). A similar difference between pulsatile and sinusoidal spatial tuning has been observed in the IC (Leake et al. 2000). This would suggest that central, neural channel interactions, compared with peripheral, electrical interactions, are reduced with sinusoidal stimulation. The finer spatial resolution observed with sinusoidal stimuli may make this stimulus paradigm more suitable for assessing plastic changes than a pulsatile regimen. The tuning for radial pairs in the short- and long-term groups averaged to a frequency extent of approximately 1.5 octave, closely matching the width of approximately 1.3 octaves observed in the IC of cats (Leake et al. 2000). For acute cases, the sinusoidal STC in the IC was approximately 0.8 octaves wide (Leake et al. 2000) compared with 0.6–1 octave in cortex. In an acute guinea pig auditory cortex study (Bierer and Middlebrooks 2002), the narrowest observed width of excitation for a bipolar pair corresponded to a subtended frequency range of approximately 1.9 octaves for their pulsatile stimulation. We observed a tuning width of approximately 0.9–1 octave in the cat. This almost twofold difference is likely related to the more radial arrangement of the electrode pairs in the cat study and a longitudinal arrangement in the guinea pig study. Differences in the monopolar conditions between cat and guinea pig are less easily explained. In the guinea pig, the monopolar conditions resulted in spatial tuning curves clearly wider than for the bi- or tri-polar conditions (Bierer and Middlebrooks 2002). By contrast, the monopolar conditions in our study showed a tuning width that was nearly equal to the radial bipolar conditions for pulsatile and sinusoidal conditions and for both deafness groups. Peripherally, narrow tuning for monopolar stimulation has been observed in some instances (van den Honert and Stypulkowski 1987); however, generally it seems to evoke broad excitation patterns (Hartmann et al. 1984; Kral et al. 1998). Whether specific peripheral conditions, such as electrode size and position, or central effects, such as engagement of sharpening mechanisms, account for the observed monopolar tuning, remains to be answered.

The largest difference in the spatial patterns of sinusoidal and pulsatile stimulation was evident in the high-threshold ridge that separates dorsal from ventral low-threshold regions. In particular, the ridge was clearly expressed in short-term animals for sinusoidal stimulation but was largely absent for pulsatile stimulation. As a potential explanation for the lack of a pulsatile high-threshold region in short-term cases, we had suggested a potential, perhaps temporary, reduction of inhibition (Raggio and Schreiner 1999). It was argued that the presence of the ridge in acute and long-term cases reflects strong local inhibitory influences that result in elevated thresholds or reduced responsiveness for broadband stimuli. The presence of a ridge with sinusoidal stimulation even in short-term cases now indicates that inhibitory influences are present but that they may be less strongly evoked by highly synchronized activity from pulsatile inputs. The high response thresholds in the central ridge region are potentially the consequence of strong inhibitory effects. It appears (Raggio 1992) that this region coincides with the most sharply tuned region in AI of normal hearing animals. One of the mechanisms that contribute to the generation of sharp frequency tuning in that region is the presence of strong inhibitory side-bands (Sutter et al. 1999).

The side-bands are already reflected in the thalamo-cortical projection to this region, but may be strengthened by intrinsic cortical mechanisms (Miller et al. 2002), as suggested by a relatively high local density of GABAAergic neurons in or near this region (Prieto et al. 1994; Wang et al. 2000). These strong
inhibitory influences result in weaker responses to broad-band stimuli in sharply tuned regions compared with broadly tuned regions (Schreiner and Mendelson 1990). The high thresholds along the central ridge for electrical stimulation thus may reflect consequences of a relatively broad peripheral excitation pattern in combination with strong central inhibitory effects.

These observations may be related to the finding that patients preferring simultaneous analog stimulation (SAS) stimulation appear to have lower response threshold (Battmer et al. 1999) and do better in the initial 3 mo of stimulation than continuous interleaved sampler (CIS) patients (Osberger and Fisher 1999). Perhaps low-threshold sinusoidal stimulation is more effective in providing better central channel segregation, at least initially, by engaging the natural central inhibitory sharpening mechanisms.

Overall, this assessment of the responsiveness and organization of the cortical responsivity distribution in deafened animals provides further evidence that a modular functional organization of AI is maintained even after prolonged duration of deafness. The response patterns evoked by long-phase duration sinusoidal stimulation share many aspects with those evoked by short-duration pulsatile responses while also revealing a number of stimulus specific aspects. These data contribute to the background for the exploration of the effects of different strategies of chronic electrical stimulation for the full restoration of cortical auditory functions with electrical cochlear stimulation.

We thank Dr. Patricia Leake for continued support and help with the deafening procedures, implantations of some of the electrodes, and information about the spiral ganglion cell densities. We thank S. Rebscher for skilful manufacturing of the cochlear implant electrodes. We also thank Drs. Ralph Beitel and Maike Vollmer for help in the data collection in some of the manufacturing of the cochlear implant electrodes. We also thank Drs. Ralph Beitel and Maike Vollmer for help in the data collection in some of the long-term cases.

This study was supported by National Institute of Deafness and Other Communication Disorders Grants No1-DC-0-2108 to P. A. Leake and DC-02260 to C. E. Schreiner, the Coleman Fund, and by Hearing Research.

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