Immediate Changes in Tuning of Inferior Colliculus Neurons Following Acute Lesions of Cat Spiral Ganglion

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Snyder, Russell L. and Donal G. Sinex. Immediate changes in tuning of inferior colliculus neurons following acute lesions of cat spiral ganglion. J Neurophysiol 87: 434–452, 2002; 10.1152/jn.00937.2000. In previous studies, we demonstrated that acute lesions of the spiral ganglion (SG), the cells of origin of the auditory nerve (AN), change the frequency organization of the inferior colliculus central nucleus (ICC) and primary auditory cortex (AI). In those studies, we used a map/re-map approach and recorded the tonotopic organization of neurons before and after restricted SG lesions. In the present study, response areas (RAs) of ICC multi-neuronal clusters were recorded to contralateral and ipsilateral tones after inserting and fixing-in-place tungsten microelectrodes. RAs were recorded from most electrodes before, immediately (within 33–78 min) after, and long (several hours) after restricted mechanical lesions of the ganglion. Each SG lesion produced a “notch” in the tone-evoked compound action potential (CAP) audiogram corresponding to a narrow range of lesion frequencies with elevated thresholds. Responses of contralateral IC neurons, which responded to these lesion frequencies, underwent an elevation in threshold to the lesion frequencies with either no change in sensitivity to other frequencies or with dramatic decreases in threshold to lesion-edge frequencies. These changes in sensitivity produced shifts in characteristic frequency (CF) that could be more than an octave. Thresholds at these new CFs matched the prelesion thresholds of neurons tuned to the lesion-edge frequencies. Responses evoked by ipsilateral tones delivered to the intact ear often underwent complementary changes, i.e., decreased thresholds to lesion frequency tones with little or no change in sensitivity to other frequencies. These results indicate that responses of IC neurons are produced by convergence of auditory information across a wide range of AN fibers and that the acute “plastic” changes reported in our previous studies occur within 1 h of an SG lesion.

INTRODUCTION

In the auditory system, the systematic topographic representation of tone frequency, tonotopy, is a fundamental and thoroughly documented principle of auditory system organization. In the peripheral auditory system, basilar membrane tuning and point-to-point (labeled-line) connections are responsible for this organization (see Dallos et al. 1996). In the central auditory system, however, tonotopy coexists with convergent projections across frequency channels at all levels of the system (see Ehret 1997 for review). This convergence along with the extensive spread of central auditory dendrites (e.g., see Rhode 1991) make relayed or labeled-line mechanisms for tonotopy unlikely.

Moreover, central tonotopic organization has been shown to be plastic. It has long been known that in young or neonatal mammals, chronic alterations in auditory input produce functional and structural changes in central auditory organization (see Kitzes 1996; Tierney et al. 1997, for review). More recently, chronic alterations in auditory input, usually in the form of focal ablations of the basilar membrane and/or organ of Corti, have been shown to produce tonotopic reorganization in adults (see Palmer et al. 1998, Weinberger 1995 for review). These changes have been most thoroughly documented in the primary auditory cortex comparing chronic lesioned animals with normal animals (Irvine et al. 2000; Rajan et al. 1993; Robertson and Irvine 1989; Wang et al. 1996; Willott 1984, 1996; among others). These chronic lesion studies have reported expanded representations of lesion-edge frequencies in the auditory cortex, inferior colliculus, and cochlear nucleus. However, some of these expansions, especially those in subcortical areas, have been shown to occur with concomitant decreases in overall sensitivity. Because these alterations can be attributed to changes in peripheral sensitivity, they have been termed “pseudoplasticity” (Kaltenbach et al. 1992, 1996) or to recordings of “residual” responses (Rajan and Irvine 1998b; Rajan et al. 1993; Robertson and Irvine 1989). Nevertheless, some chronic studies have revealed expansions of cortical representations of lesion-edge frequencies in adults without consistent elevations in overall thresholds (e.g., Egg-ermont and Komiyao 2000; Rajan and Irvine 1998a; Rajan et al. 1993; Robertson and Irvine 1989; Willott 1984).

Because these studies were done in the cortex of animals with chronic peripheral lesions, they give us little insight into the time course of the tonotopic changes and leave open the existence of subcortical changes. Several studies examining the subcortical effects of chronic peripheral lesions have either failed to detect tonotopic reorganization (Kaltenbach et al. 1992, 1996; Rajan and Irvine 1998b) or failed to detect it consistently (Irvine and Rajan 1994; Rajan and Irvine 1996; Salvi et al. 1996).

Recently, we (Snyder and Sinex 1998; Snyder et al. 2000) described tonotopic reorganization in auditory cortex and central nucleus of the inferior colliculus (ICC) after acute mechan-
ical destruction of restricted (~1 mm) sectors of the spiral ganglion (SG). This procedure leaves the tuning and sensitivity of the basilar membrane/organ of Corti intact and allows lesion-induced changes in the central auditory system to be examined immediately after the lesions. The results of these map/re-map studies revealed consistent lesion-induced changes without any overall changes in threshold. By comparing the response areas (RAs) recorded from comparable ICC locations before and after the lesions in the same animal, it could be inferred that the frequency response properties of ICC neurons were altered. Among these alterations were shifts in characteristic frequency (CF), broadened tuning, and losses of excitability (“holes”) in the neuron’s frequency responses across the narrow range of lesion frequencies.

In the present experiments, we confirmed and extended our previous IC results by recording RAs in the ICC with fixed in-dwelling electrodes before and after restricted SG lesions. This approach gives us more confidence that we are recording lesion-induced changes in the same neurons and allows us to specify more precisely the time course of those changes. Results indicate that restricted SG lesions produced ICC neurons with decreased sensitivity (elevated thresholds) to contralateral tones at frequencies affected by the lesion. This decreased sensitivity produced gaps in the excitatory regions in the RAs of many ICC neurons. These gaps were often less than 1/3 octave wide, were 60 dB deep, and corresponded precisely to frequencies affected by the lesion. In addition, SG lesions produced narrow regions of increased sensitivity (lowered threshold and increased suprathreshold responses) to contralateral tones at lesion-edge frequencies. These increases in sensitivity often produced shifts of more than an octave in the CFs of some ICC neurons. In addition, some ICC neurons displayed increased sensitivity to ipsilateral tones at the lesion frequencies.

METHODS

Experiments were conducted in five normal cats. All animals were maintained in a facility approved by American Association for Accreditation of Laboratory Animal Care. All procedures were approved by the University of California at San Francisco Committee on Animal Research and were conducted in accordance with the guidelines provided by the PHS/National Institutes of Health Guide for the Care and Use of Laboratory Animals.

Surgical preparation

Each animal was tranquilized with an intramuscular injection of ketamine HCl (25 mg/kg) and acepromazine (0.2 mg/kg). An intravenous catheter was inserted into the cephalic vein, and a surgical level of anesthesia was induced and maintained by infusion of pentobarbital sodium. A tracheal canula was inserted via a tracheostomy. Body temperature was continuously monitored and maintained using a rectal thermal probe and a thermostatically controlled warm-water recirculating blanket. Blood oxygenation, respiratory rate, and heart rate were continuously monitored using a blood oximeter (Ohmeda). In addition, somatic reflexes (e.g., corneal reflex and forelimb withdrawal reflexes) were monitored to ensure that a surgical (areflexic) level of anesthesia was maintained. A urinary catheter was inserted into the urethra, and the urine output was collected and monitored. Lactated Ringer solution was continuously infused throughout the experiments to maintain normal levels of hydration. Prophylactic injections of antibiotics (e.g., Cefazolin 22 mg/kg) were administered twice daily. In addition, prophylactic doses of dexamethazone (1 mg · kg⁻¹ · h⁻¹ · iv) and mannitol (1–2 mg · kg⁻¹ · h⁻¹ · iv) were given to prevent cerebral edema. The head was immobilized and held in position using a mouth-bar head-holder, which was mounted in a magnetic base. The external ear canals on both sides were opened near the bony annulus, and rigid plastic tubes connected to sealed earphones were inserted into the canals and sealed in place. The auditory bulla on the left side was surgically exposed and then opened to permit clear visualization of the round window.

Sound generation and delivery

A PC/AT compatible computer controlled presentation of acoustic stimuli with hardware for generating digital waveforms (Tucker-Davis Technologies, System II). The effective upper limit of this signal generation system is 32 kHz. Two waveform channels were used to deliver stimuli to the two ears. Acoustic stimuli were presented through closed acoustic systems consisting of Radio Shack super tweeters coupled via metal casings to a plastic tube that could be inserted into the external auditory meatus, as noted above. The assembly incorporated a B&K probe tube microphone (type 4182) with a known transfer function, and the acoustic system was calibrated for each ear in each experiment.

CAP audiograms

A silver ball “active” electrode was placed in the round window niche of the left cochlea and fixed in place with cyanoacrylate glue. A silver wire “reference” electrode was placed in the skin of the neck, and a silver wire ground electrode was inserted into the skin below the right ear. The output of these electrodes was amplified (WPI, DAM50 and Tektronix 5A22N) with band-pass settings of 100 Hz to 10 kHz and amplified 100,000 times. The amplified output was displayed on an oscilloscope and digitized by an A/D converter sampling at a rate of 20 kHz. The left cochlea was stimulated with 15-ms tone bursts with 1-ms rise/fall times. Every other tone burst was inverted to cancel the cochlear microphonic. Responses to 50–100 tone bursts were averaged at each stimulus frequency and level. Frequency was usually varied in steps of one-fourth octaves. Averaged responses from below threshold to 30 dB above threshold were obtained for each tone frequency. CAP audiograms were recorded both immediately before and immediately after cochlear lesions. In some experiments, a third CAP audiogram was recorded at the end of the experiment.

Electrophysiological recording

Multi-unit cluster recordings were made at 16 locations within the central nucleus of the inferior colliculus (ICC) in the six animals using procedures described in previous publications (see Snyder et al. 1990, 2000). Through a mid-line skin incision, the dorsolateral aspect of the right calvarium was exposed, and a craniotomy was made in the parietal bone over the occipital cortex. The dura was incised and reflected. The occipital cortex was removed by aspiration, and a wedge of the bony tentorium cerebelli was removed exposing the entire dorsal and dorsolateral surface of the right inferior colliculus.

Multiple unit activity evoked by 50-ms pure tones was recorded using parylene-C insulated tungsten microelectrodes (1–2 MΩ at 1 kHz, Microprobe) mounted in glass tubes with an internal diameter of 1 mm. The ends of these tubes were sealed with epoxy resin. Electrodes were held in a micromanipulator (Narishige) and advanced manually into the ICC along a standardized trajectory, tilted 45° off the sagittal plane in the coronal plane. This trajectory compensates for the tilt of the “frequency band lamina” in the ICC. On this axis, penetrations pass through the full range of frequencies represented in the ICC (Snyder et al. 1990, 2000). Multunit neural activity was amplified (100,000–200,000 times) with a band-pass of 300 Hz to 3 kHz using a battery-powered preamplifier (DAM50) and Tektronix 5A22N post-
amplifier. Neural activity was isolated from background activity using a spike window discriminator (BAK DIS-1). The responses, acoustic stimuli, and discrimination acceptance pulses were monitored on an oscilloscope. The time of occurrence of each acceptance pulse from the window discriminator was recorded and stored with an accuracy of 10 µs. Electrodes were inserted simultaneously into the right ICC until recorded neural activity on a selected electrode was tuned to an appropriate frequency, usually between 10 and 20 kHz. Up to six electrodes (2 sets of 3) were inserted into the IC of any given animal. However, in no case were we able to record neural activity on all electrodes. The reasons for these failures were not always known. In one case, however, the seal at the distal end of one glass tube was defective. This allowed cerebrospinal uid to slowly wick from the subcranial space into the glass tube holding the electrodes. We assume that this fluid shorted the electrodes in that tube because all three electrodes (50% of our electrode failures) became simultaneously silent during the course of the prelesion recordings.

When the electrodes had been inserted to an appropriate location, a series of response areas (1 RA from each electrode, see following text) was recorded using contralateral tones 50 ms in duration. Then the cortical deicit was filled with 2% agar in Ringer solution. Once solidiﬁed, the agar and surrounding calvarium were covered with dental acrylic, which sealed the bony deicit and ﬁxed the electrodes in place. The ﬁxed electrodes were released from the micromanipulator, and a second series of response areas was recorded to ensure that the recorded neural responses were not substantially changed. The animal was then rotated head-to-tail and right ear up to right ear down so that the left cochlear bulla could be exposed. The bulla was exposed and opened to expose the round window. A round window electrode was placed in the round window niche, and a third series of RAs was recorded. Then in most cases, responses to contra (left) and ipsi (right) tones were recorded from each electrode. A pre lesion CAP audiogram (see preceding text) was also recorded using tones presented to the left (pre lesion) ear. After this audiogram and pre lesion RAs were recorded, a small slit was made in the round window membrane, and a lesion was made in the spiral ganglion (described in the following text). Following the lesion, a series of RAs was recorded to contralateral and ipsilateral tones at post lesion intervals ranging from 10 min to 22 h after the lesion. During this post lesion interval, a second post lesion CAP audiogram also was recorded.

Data collection and analysis

Window discriminator pulses were stored in an Intel based microcomputer for display as RAs and were saved in a disk ﬁle along with stimulus information for later analyses. Tones were presented in randomized order over a range of frequency and SPL. Tone frequencies usually varied across three to ﬁve octaves. The exact frequency limits varied among animals, depending on the CF at the recording site(s), but these limits were usually held constant within an animal for an entire experiment. In no animal did we present tones below 2 kHz or above 32 kHz (the upper limit of our system). SPL usually varied over a range of 60–80 dB in steps of 5–10 dB. RAs were displayed in a frequency versus SPL space with responses represented by lines whose length represented the driven response magnitude (spontaneous activity was subtracted) elicited by each 50-ms tone at its frequency-SPL (F/L) combination and plotted at the appropriate F/L coordinate and scaled to ﬁt into the space allotted to them. CF and threshold at CF were estimated from these line plots. Threshold was estimated at the lowest stimulus level to evoke a response consistently greater than spontaneous activity. CF was estimate as the frequency that evoked the largest response at threshold. If two or more frequencies elicited the same response amplitude at threshold, CF was estimated as the mean of those frequencies. Since RAs were constructed using 6–8 frequency steps per octave and level steps of 5 dB (or in a few cases 10 dB), CF was estimated with a maximum accuracy of ±1/12 octave, and threshold was estimated with a maximum accuracy of ±5 dB. Normalized difference RAs were computed by subtracting spontaneous activity from the responses to estimate driven rates in the last pre lesion RA before the lesion and a representative, stabilized post lesion RA. The pre- and post lesion rates were 3 point smoothed and normalized relative to the maximum rate for that RA. Thus normalized pre- and post lesion rates varied from 0 to 1. Rate differences were computed by subtracting the smoothed and normalized pre lesion rate from that of the post lesion rate at each F/L combination. If there was a net offset from zero, it was eliminated by adding a constant to one set so that the mean difference in rates was zero. Elimination of this

FIG. 1. A post-mortem view of the hook region of the osseous spiral lamina (osl) in a cat cochlea as seen through the round window. For the purposes of this ﬁgure, the round window membrane and all the perilymph has been removed. The basilar membrane is visible as the medium gray crescent (black arrows) below the margin of the round window. The extreme basal end of the cochlear spiral is toward the right. The scala tympani spirals counterclockwise and away into the basal turn at the bottom left of the round window. The modiolus (large asterisk) is toward the bottom. The white arrow indicates a 1-mm spiral ganglion lesion. The lesion is visible due to extravasated blood in Rosenthal’s canal, which can be seen as a light gray crescent (small asterisk) in the osseous spiral lamina.
offset was necessary in order for all difference RAs to centered on the same medium gray of the gray scale. Once these rate differences were computed, they were plotted as a gray-scale patch plots with gray-scale value of each patch representing the rate difference (post minus pre) along a standardized gray scale, which had a mean of zero and a range of $-0.5$ (black) to $+0.5$ (white). Finally, the gray-scale value of each patch was smoothed by bilinear interpolation of the gray level at its four vertices relative to those of adjacent vertices. These difference RAs indicate by their gray-scale values the smoothed relative withdrawal of excitation (darker shades) or relative addition of excitation (lighter shades) induced by the lesion.

**SG lesions**

Acute SG lesions were created after recording an initial CAP audiogram and after initial series of RAs had been recorded. The SG was visualized directly by incising the round window membrane and partial aspiration of the perilymph. Rosenthal’s canal could be seen as a dark arc within the bony spiral lamina. Using an operating microscope (Zeiss, OPMI), the bone overlying an approximate 1 mm segment of Rosenthal’s canal was removed by manual curettage with a 34-gauge hypodermic needle and the subjacent SG destroyed. After the lesion was complete and all bleeding had been stopped, the intracochlear location of the lesion was recorded using a high-resolution color video camera (Panasonic, KS102) attached to the operating microscope. The video image was digitized and stored on a Macintosh Quadra 800. After the perilymph had been replenished, the round window was re-sealed using a disk of Suranwrap to prevent further leakage of the perilymph.

**RESULTS**

**SG lesions and CAP audiograms**

We examined the response properties of IC neurons at 16 locations before and immediately after acute focal SG lesions. These lesions were centered $\sim 5$ mm from the basal end of the spiral ganglion at the junction of the hook and basal turn of the cochlea in adult cats. Figure 1 shows a typical SG lesion in view through the round window showing the osseous spiral lamina (osl) of a postperfusion cochlea.

We have documented the physiological effects of SG lesions on cochlear function by constructing tone-evoked CAP audiograms before and after the lesion. Figure 2A illustrates a pre- and postlesion (×) CAP audiogram from one animal. The difference audiogram (●) is computed by subtracting prelesion from postlesion thresholds. Approximately 45 min separated the pre- from the postlesion threshold estimates. Figure 2, B–D, illustrates three additional difference audiograms. These difference audiograms indicate that the SG lesions produced elevated CAP thresholds across a range of frequencies that span slightly more than an octave, $\sim 12$ to $30$ kHz. In all cases, maximum loss in sensitivity occurred at frequencies between 15 and 20 kHz (●). These audiograms are typical of those observed in these experiments.

**RAs to contralateral tones**

The effects of SG lesions on a given neuron’s responses will be seen to depend on the relationship between the neuron’s CF and the CF of the damaged AN fibers. It might be expected that sites, which are tuned to the lesion center frequencies, might be most affected by the lesions. We will consider these sites first. Next, we consider sites that one might expect to be least affected, namely those sites tuned to progressively higher (or lower) contralateral frequencies. Finally, we consider those sites that might be expected to be least affected by the lesions, i.e., responses evoked by tones delivered to the intact ipsilateral ear.

RAs recorded from intact animals with fixed, in-dwelling electrodes have excitatory regions evoked by contralateral stimulation...
that are stable for many hours if the physiological status of the animal remains unchanged. CF and minimum threshold change little in the absence of changes in cochlear sensitivity. However, immediately after SG lesions, postlesion changes occurred, including shifts in CF and the introduction of notches in the excitatory response regions of neurons tuned to these lesion frequencies. These changes are similar to those described previously (Snyder et al. 2000), and they were seen at 13 of 16 IC locations. Figure 3 illustrates an example of a series of four prelesion RAs recorded from a single, fixed electrode at four time intervals prior to a SG lesion. The time of each recording relative to the lesion is indicated at the top of each RA. Responses in Fig. 3A were recorded 7 h prior to the lesion immediately after the electrode had been cemented in place with its tip in the left IC. The estimated CF (23 kHz) and minimum threshold (20 dB SPL) are indicated by the arrow. Responses in Fig. 3B were recorded ∼3.5 h later, 3.5 h prior to the lesion. During this interval, all acoustic and electrical connections had been removed from the animal, it had been turned head-to-tail and left-ear-up to right-ear-up to provide access to the right cochlea, all electrical connections were replaced, the right cochlea was exposed and the prelesion CAP audiogram had been recorded. Response magnitudes are virtually identical to those seen 3.5 h earlier. The responses in Fig. 3, C and D, were recorded 2.5 and 1.5 h prior to the lesion respectively without any further manipulations. The CF and threshold were essentially unchanged over this entire 7-h interval.

After these prelesion RAs had been recorded, a lesion was made in the spiral ganglion. The postlesion CAP difference audiogram indicates a maximum elevation in threshold of ∼30 dB at 16 kHz (Fig. 2C). Figure 4 illustrates RAs recorded at four intervals after the lesion. In this example, the postlesion IC recordings were made after a CAP audiogram was recorded. The first RA (Fig. 4A) was recorded 1 h 51 min after the lesion. Comparison of the estimated prelesion CF (small arrow) and the postlesion CF (large arrow) indicates that the lesion had caused an immediate shift in the CF at this location from 20 to 12 kHz. This shift was seen consistently in the three additional postlesion recordings (Fig. 4, B–D). The minimum threshold

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**Figure 3.** A–D: prelesion response areas recorded using contralateral tones from a fixed in-dwelling electrode (6 in cat 7/31/00). RAs were recorded at successive intervals. A: 7 h prior to the lesion immediately after electrodes had been cemented in place. B: 3 h 20 min prior to the lesion. C: 2 h 20 min prior to the lesion. D: 1 h 37 min prior to the lesion. The gray arrows indicate the estimated characteristic frequency (CF) and threshold in each response area (RA).
Post-lesion Contralateral Stimulation

(at the new CF) increased slightly, ∼5 dB, but there was a loss of sensitivity at the prelesion CF of 15 to 20 dB and an even greater loss at the 16 kHz lesion-center-frequency of 30–35 dB (asterisks).

The changes produced at this location by the SG lesion are most easily appreciated by an examination of the normalized difference RA (Fig. 5). This difference RA demonstrates that the cochlear lesion had two major effects. First, it produced a loss of excitation (black regions) primarily across the lesion-frequencies (arrowhead) and below the prelesion CF (small arrow), which occurred across a broad range of stimulus levels from 20 to 70 dB SPL. Second, the lesion produced an increase in excitation (white regions) primarily at high stimulus levels at frequencies above the prelesion CF. This difference RA emphasizes that the lesion induced a loss of excitation across the lesion frequencies. This loss of excitation is responsible for the apparent shift in CF observed in Fig. 5 rather than an increase of excitation at and sensitivity to juxta-lesion frequencies.

Approximately 2 h separated the pre- and postlesion recordings illustrated in Figs. 3 and 4 because the postlesion CAP audiogram was recorded immediately after the lesion. However, most postlesion RAs were recorded after recording the postlesion CAP thresholds. Thus postlesion responses could be recorded only 33–78 min after making the lesion. Figure 6 illustrates an example of one such experiment. Two prelesion RAs are illustrated, one 3 h prior to the lesion and after the fixation of the electrodes in the IC (Fig. 6A) and another after the electrode has been fixed in place and the animal had been repositioned for making the lesion (Fig. 6B). The excitatory regions in these RAs have the standard V shape that is almost invariably seen in normal cats under barbiturate anesthesia. The estimated CFs (16 kHz) and minimum thresholds (10–20 dB)
were similar for these two RAs. The prelesion CAP responses were then recorded, and a spiral ganglion lesion was made. This lesion produced a 35 dB peak (loss) in the difference audiogram centered at ~17 kHz (Fig. 2A). The first postlesion RA (Fig. 6C) demonstrates that 10 min after the lesion there was an immediate reduction in overall sensitivity of 20–30 dB in the neurons at this location. This loss of sensitivity occurred across a range of frequencies of ~1 octave (12–22 kHz) that included the prelesion CF (arrow) and that approximated the lesion frequencies (horizontal gray bar). It is difficult to estimate a CF at this location at this time because of the elevated thresholds. However, after an additional 37 min (Fig. 6D), the sensitivity of these neurons had recovered somewhat, and the postlesion CF was estimated to be 11 kHz and the minimum threshold estimated to be 30 dB SPL. After these postlesion RAs were recorded, the postlesion CAP thresholds were estimated. Then a third postlesion RA was recorded (Fig. 6E) ~3 h after the previous RA. At this time, the sensitivity of the neurons had completely recovered; the postlesion minimum threshold matched that seen before the lesion. However, the estimated CF had shifted to a lower frequency (10 kHz), approximately half octave below its prelesion CF of 17 kHz. Moreover, there was a clear notch or gap (asterisk) in the postlesion excitatory region corresponding to the lesion frequencies. This notch and the change in CF persisted in subsequent recordings made 5.5 h after the lesion and they remained unchanged over the next 5 h. The normalized difference RA (Fig. 6F) illustrates that the asymptotic CF changes were due not only to a withdrawal of excitation (black region) across the lesion frequencies but also to an addition of excitation (white region) centered at the new postlesion CF.

Figure 7 illustrates an example of a lesion-induced shift in CF comparable to that seen in the previous three figures. The prelesion RA has a CF of ~23 kHz and a minimum threshold of 10 dB SPL (Fig. 7A). In contrast to the previous examples, the postlesion sensitivity of responses to frequencies above the lesion frequency were relatively unaffected. The postlesion thresholds to frequencies above 20 kHz are not substantially different from their prelesion counterparts (Fig. 7B). However, there is a suggestion of a postlesion “hole” in the excitatory region (asterisk, 7C) with clear augmentation of excitation on low frequency side of this hole. The increase in excitation below the lesion frequencies extends the sensitivity of these neurons by ~20 dB to frequencies across a narrow range of frequencies centered at 11 kHz. The increased sensitivity results in a downward shift in estimated CF of an octave from 27 to 11 kHz.

This pattern of withdrawal of excitation across lesion frequencies and addition of excitation at frequencies below and/or above the lesion frequencies was observed at half the locations in these experiments. Figure 8 illustrates an example where no shift in CF occurred because the prelesion CF is below the lesion center frequency. The prelesion RA (Fig. 8A) indicates that the prelesion CF and minimum threshold at this location for responses to contralateral tones are 14 kHz and 10 dB SPL, respectively (small arrow). Twenty-eight minutes after the lesion, the postlesion CF and minimum threshold (Fig. 8B) were virtually unchanged (13.5 kHz and 20 dB SPL, large arrow). In this case, the cochlear lesion produced a minimal elevation in threshold (~10 dB) without a clear CF shift. The difference RA (Fig. 8C) demonstrates that there was an obvious withdrawal of excitatory drive (at the lesion frequencies, black region) similar to that illustrated in Fig. 7, which reduced the sensitivity of these neurons by 10 dB.

In these examples, prelesion CFs were at or near the center of the lesion frequencies. Figure 9 illustrates an example of the effects of a SG lesion on responses at an IC location with a prelesion CF (10 kHz, Fig. 9A) that is at the lower edge of the lesion frequencies (Fig. 2D). In this case, the cochlear lesion produced a dramatic loss of excitatory responses across a narrow range of frequencies (arrowhead) above CF corresponding to the lesion frequencies without substantially changing the CF of the postlesion responses (Fig. 9B). This loss in excitation occurred across a broad range of intensities and produced a “hole” in the excitatory region (asterisk), which had a sharp low-frequency border. This border extended vertically from ~15 to 65 dB SPL, the highest intensity presented. The difference RA (Fig. 9C) indicates that there were also minor losses of excitation across a broad range of frequencies below CF. Between these two regions, there is a region of increased excitation, which extends across a narrow range of frequencies roughly centered on the location’s CF.

RAs illustrated in the preceding text describe responses at locations that have prelesion CF’s at or near the lesion frequencies. This study has focused on these locations to document the effects of SG lesions on such responses. However, three electrodes were fixed at locations where the recorded CFs were far from the lesion frequencies. The RAs in Figs. 10 and 11 illustrate two of the three RAs that were not (or only slightly) altered by the lesion. Neurons at these locations had CFs that were far below (Fig. 10) and above (Fig. 10) the lesion frequencies. In Fig. 10A, the prelesion CF is estimated at 3 kHz and the minimum threshold is estimated at 15 dB SPL. After a
A lesion, which produced a 45 dB peak in the difference audioogram centered at 19 kHz (not shown), the postlesion RA at this location is essentially unchanged (Fig. 10B). The CF is still 3 kHz and the minimum threshold is 15 dB SPL. In Fig. 11A, the prelesion CF is estimated at 22 kHz and the minimum threshold is 15 dB SPL. Following the lesion, which is centered at \(\sim 16\) kHz (see Fig. 2D), the RA is only slightly changed. The CF has increased to 28 kHz, but the minimum threshold (15 dB SPL) has remained unchanged. There is a loss of excitatory responses at the prelesion CF and the suggestion of a hole in the excitatory response area in the postlesion RA (asterisk).

There is an addition of excitation centered at the postlesion CF but no addition of excitation in the previously silent regions.

The lesion-induced changes in ICC neuronal responses to contralateral stimulation at all recording sites are summarized in Table 1. Substantial changes in CF without overall elevations in threshold were observed at 9 of 16 recording locations. As noted above, some of these shifts were small, but others were more than one half octave. Of the seven cases at which no clear or substantial shift in CF occurred, responses at four of these location were tuned to frequencies that were sufficiently above or below the lesion frequencies that their CFs and minimum thresholds were
unaffected by the lesion. In all but one of these cases (see Fig. 11), notches corresponding to the lesion frequencies could be discerned in the excitatory response areas above or below the postlesion CF (e.g., Figs. 7–9). At two locations, two frequencies gave low threshold responses suggesting that there were two CFs (see Table 1, animal 12/27/99, E5 and E6).

As illustrated in Fig. 12, RAs at the remaining four locations were changed in a manner consistent with recordings of the “residue of prelesion responses” (see Rajan et al. 1993). Three of these locations were recorded in one animal, 7/31/00. Responses at these locations simply became less sensitive to the lesion frequencies with no lesion-induced increases in sensitivity to nonlesion frequencies (Fig. 12B). Thus these neurons displayed no postlesion CF shift. Losses of sensitivity to lesion

FIG. 7. A: prelesion RA recorded from electrode 6 in cat 12/27/99. The minimum threshold and estimated CF (gray arrow) are −10 dB and 27 kHz. B: postlesion RA from the same fixed, in-dwelling electrode. The lesion (see Fig. 1B, arrow) produced a peak in the difference CAP audiogram, which was centered at 19 kHz. The estimated CF and threshold of this postlesion RA has shifted to −11 kHz and 0 dB SPL (black arrow). The asterisk indicates a gap at the lesion frequency. This recording was made −65 min after the lesion. C: gray-scale difference RA illustrating the difference between the normalized pre- (A) and postlesion (B) responses (post minus pre).

FIG. 8. A: prelesion contralateral RA recorded with an in-dwelling, fixed electrode (electrode 1 in cat 7/27/99). The estimated prelesion CF and threshold (gray arrow) for this response are 14 kHz and 10 dB SPL, respectively. B: postlesion RA recorded from the same in-dwelling electrode as A after an SG lesion. This lesion (arrowhead) produced a notch in the difference CAP audiogram centered at 17 kHz. The postlesion CF and threshold are 13.5 kHz and 20 dB SPL, respectively (black arrow). This recording was made −28 min after the lesion. C: gray-scale difference RA illustrating the difference between the normalized pre- (A) and postlesion (B) responses (post minus pre).
frequencies produced broad, higher threshold (20–40 dB higher) excitatory regions, which were centered more or less at the prelesion CF, whereas thresholds to nonlesion frequencies were largely unaffected. At all other locations, SG lesions produced dramatic decreases (>40 dB) in sensitivity to lesion frequencies and no change or an increased sensitivity to lesion-edge frequencies. The single exception (Fig. 10) was tuned to 3 kHz and had no responses to the lesion frequencies either before or after the lesion.

Responses to ipsilateral stimulation

The RAs illustrated in all the previous figures were recorded using contralateral stimulation. This emphasis on contralateral

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**FIG. 9.** A: prelesion RA recorded with a in-dwelling, fixed electrode (electrode 2 in cat 11/12/99). The estimated CF and threshold (gray arrows) for this response are 10 kHz and 5 dB SPL, respectively. B: postlesion RA from the same fixed, in-dwelling electrode as A. The SG lesion (arrowhead) produced a notch in the difference CAP audiogram centered at 17 kHz. The estimated CF and threshold of this postlesion RA was virtually unchanged 9.5 kHz and 10 dB SPL, respectively (black arrow). There is a clear notch (asterisk) on the high-frequency side of the excitatory region of this RA recorded ~76 min after the lesion. C: gray-scale difference RA between the normalized pre- (A) and postlesion (B) responses (post minus pre).

---

**FIG. 10.** A: prelesion RA recorded on a fixed, in-dwelling electrode (4 in cat 9/17/99). The CF and minimum threshold are estimated to be 3 kHz and 15 dB SPL (gray arrow). B: postlesion RA from the same fixed, in-dwelling electrode. The estimated CF and threshold are estimate to be 3 kHz and 10 dB SPL (black arrow). This recording was made ~65 min after the lesion. The lesion produced a notch in the difference CAP audiogram, which was centered at 19 kHz (arrowhead). C: gray-scale difference RA illustrating the difference between the normalized pre- (A) and postlesion (B) responses (post minus pre).
stimulation arises from the fact that virtually every IC neuron responds to contralateral stimulation, whereas only 42% of all IC neurons respond to ipsilateral stimulation (Kitzes and Semple 1985). Thus most IC neurons are so-called EO neurons with a minority classified as EE neurons. Thresholds in response to ipsilateral CF tones of these EE neurons are higher (15 dB on average) than their contralateral thresholds and the maximum discharge rates are lower (Semple and Kitzes 1985). Thus IC neurons in normal animals are much less sensitive to ipsilateral stimulation than to contralateral stimulation. This differential sensitivity to contralateral stimulation is especially true for IC neurons with CFs higher than 8 kHz. Among these high CF neurons <10% respond to ipsilateral stimulation (Aitkin 1991; Schreiner and Langner 1988). Since the SG lesions made in this study were centered at such high frequencies between 16 and 20 kHz, it focused on locations with CFs >8 kHz. Thus a minority of locations recorded in this study responded to ipsilateral stimulation. However, at some locations, responses to ipsilateral stimulation were observed, and the responses at these locations were often changed by SG lesions. The RAs presented in Fig. 13 were recorded in response to ipsilateral stimulation with the same electrode at the same IC location as the RAs to contralateral stimulation illustrated in Figs. 3–5. The RA in Fig. 13A was recorded 30 min

**TABLE 1. Contralateral stimulation**

<table>
<thead>
<tr>
<th>Experiment</th>
<th>Electrode</th>
<th>No. of RAs</th>
<th>CF (kHz) ± SD</th>
<th>Threshold (dB) ± SD</th>
<th>No. of RAs</th>
<th>CF (kHz) ± SD</th>
<th>Threshold (dB) ± SD</th>
<th>Diff, kHz</th>
<th>Diff, dB</th>
</tr>
</thead>
<tbody>
<tr>
<td>2/27/99</td>
<td>E1</td>
<td>3</td>
<td>17.1 ± 0.7</td>
<td>12 ± 3</td>
<td>3</td>
<td>11.5 ± 1.7</td>
<td>20.0 ± 0.0</td>
<td>5.6</td>
<td>8.3</td>
</tr>
<tr>
<td></td>
<td>E2</td>
<td>3</td>
<td>15.8 ± 0.0</td>
<td>15 ± 0</td>
<td>2</td>
<td>10.1 ± 1.4</td>
<td>12.5 ± 3.5</td>
<td>5.7</td>
<td>2.5</td>
</tr>
<tr>
<td>9/17/99</td>
<td>E1</td>
<td>6</td>
<td>20.6 ± 1.9</td>
<td>11 ± 4</td>
<td>3</td>
<td>35.3 ± 1.5</td>
<td>30.0 ± 0.0</td>
<td>-14.8</td>
<td>19.2</td>
</tr>
<tr>
<td></td>
<td>E2</td>
<td>5</td>
<td>14.0 ± 0.4</td>
<td>7 ± 4</td>
<td>4</td>
<td>10.8 ± 0.6</td>
<td>11.3 ± 2.5</td>
<td>3.4</td>
<td>4.3</td>
</tr>
<tr>
<td></td>
<td>E3</td>
<td>4</td>
<td>2.9 ± 0.4</td>
<td>11 ± 3</td>
<td>3</td>
<td>2.7 ± 0.1</td>
<td>8.3 ± 2.9</td>
<td>5.6</td>
<td>2.9</td>
</tr>
<tr>
<td>11/12/99</td>
<td>E1</td>
<td>2</td>
<td>10.0 ± 0.5</td>
<td>-5 ± 7</td>
<td>2</td>
<td>9.4 ± 0.1</td>
<td>7.5 ± 3.5</td>
<td>0.5</td>
<td>12.5</td>
</tr>
<tr>
<td></td>
<td>E2</td>
<td>2</td>
<td>9.9 ± 0.0</td>
<td>0 ± 0</td>
<td>2</td>
<td>9.6 ± 0.1</td>
<td>7.5 ± 10.6</td>
<td>0.3</td>
<td>7.5</td>
</tr>
<tr>
<td></td>
<td>E3</td>
<td>3</td>
<td>22.7 ± 1.6</td>
<td>27 ± 10</td>
<td>4</td>
<td>28.0 ± 1.4</td>
<td>13.8 ± 4.8</td>
<td>-6.0</td>
<td>-12.9</td>
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<tr>
<td>12/27/99</td>
<td>E1</td>
<td>3</td>
<td>14.4 ± 2.1</td>
<td>15 ± 10</td>
<td>3</td>
<td>27.2 ± 1.8</td>
<td>21.7 ± 12.6</td>
<td>-12.8</td>
<td>6.7</td>
</tr>
<tr>
<td></td>
<td>E2</td>
<td>4</td>
<td>11.5 ± 2.4</td>
<td>18 ± 17</td>
<td>6</td>
<td>12.7 ± 1.0</td>
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<td>E3</td>
<td>4</td>
<td>14.4 ± 1.8</td>
<td>10 ± 9</td>
<td>4</td>
<td>15.8/30.4 ± 0.6</td>
<td>13.8 ± 2.5</td>
<td>-13.9</td>
<td>3.8</td>
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<tr>
<td></td>
<td>E4</td>
<td>3</td>
<td>26.9 ± 1.6</td>
<td>18 ± 14</td>
<td>4</td>
<td>11.6/28.3 ± 0.6</td>
<td>13.8 ± 7.5</td>
<td>15.4</td>
<td>-4.6</td>
</tr>
<tr>
<td>7/31/00</td>
<td>E1</td>
<td>5</td>
<td>20.8 ± 1.95</td>
<td>21 ± 2</td>
<td>NR</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>E2</td>
<td>4</td>
<td>22.4 ± 0.7</td>
<td>20 ± 0</td>
<td>5</td>
<td>22.7 ± 0.1</td>
<td>38.0 ± 6.7</td>
<td>-0.3</td>
<td>18.0</td>
</tr>
<tr>
<td></td>
<td>E3</td>
<td>4</td>
<td>18.3 ± 0.7</td>
<td>23 ± 3</td>
<td>6</td>
<td>16.8 ± 1.6</td>
<td>51.7 ± 2.6</td>
<td>1.4</td>
<td>29.2</td>
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<tr>
<td></td>
<td>E4</td>
<td>4</td>
<td>18.9 ± 0.2</td>
<td>21 ± 3</td>
<td>4</td>
<td>19.5 ± 1.9</td>
<td>51.0 ± 4.2</td>
<td>-0.6</td>
<td>29.8</td>
</tr>
<tr>
<td></td>
<td>E5</td>
<td>4</td>
<td>22.0 ± 0.8</td>
<td>21 ± 2</td>
<td>6</td>
<td>12.5 ± 1.1</td>
<td>36.0 ± 9.6</td>
<td>9.5</td>
<td>15.2</td>
</tr>
</tbody>
</table>

Values are means ± SD. RA, response area; CF, characteristic frequency; underline, double CFs.
prior to a SG lesion. Its CF (16 kHz, arrow) is somewhat lower than the prelesion CF evoked by contralateral stimulation (20 kHz). The minimum threshold (50 dB SPL) is substantially higher than that to contralateral stimulation (25 dB SPL). After the lesion (Fig. 13B), the ipsilaterally evoked CF increased to 21 kHz, which closely approximates the prelesion contralateral CF, and postlesion minimum threshold decreased to 15 dB SPL (black arrow). This is a decrease of ~30 dB from the prelesion threshold at this shifted postlesion CF and overall a decrease of 25 dB from the minimum threshold seen before the lesion (gray arrow). These changes indicate that the lesion produced a clear increase in sensitivity to ipsilateral, lesion-frequency tones at this location. This lesion-induced shift in sensitivity persisted essentially unchanged as long as the responses were recorded 14 h after the lesion (Fig. 13C).

Given that most IC neurons with CFs 8 kHz are insensitive to ipsilateral stimulation (Aitkin 1991; Schreiner and Langner 1988), it is perhaps not surprising that the most prominent effect of a restricted SG lesion on ipsilateral responses is the addition of excitation at previously subthreshold F/I combinations. However, it is surprising that so few locations showed such additions of excitation. In those cases where it was seen, the ipsilaterally evoked difference RAs (e.g., Fig. 13D) demonstrate that the primary lesion-induced effect on ipsilaterally evoked responses is an increase in excitation (white region). This increase in excitation is restricted to a narrow range of frequencies, which is centered at the prelesion contralateral CF at the upper edge of the lesion frequencies. It occurs at all ipsilateral stimulus levels from 15 to 70 dB SPL. The postlesion changes in contralaterally evoked responses are observed at every location tuned to the lesion frequencies; however, comparable ipsilaterally evoked changes are observed in only half the locations that respond to ipsilateral tones.

The effects of SG lesions on ipsilateral responses are tabulated in Table 2. Pre- and postlesion CFs could be estimated at five locations. In three cases, ipsilateral CFs shifted (Table 1, underline) as in Fig. 14. In two cases, they shifted to match the postlesion contralateral CF (E1 and E2, cat 7/27/99) and in the third case, to match the contralateral prelesion CF (E6, cat 7/31/00). In four of five cases, the thresholds decreased from higher than contralateral threshold to lower than contralateral threshold (Table 2, underline). In the remaining case, the prelesion ipsilateral threshold was comparable to the contralateral threshold and it increased slightly while CF decreased by more than half octave.

**DISCUSSION**

This study corroborates our previous observations (Snyder et al. 1996, 2000) on the effects of acute SG lesions on the response properties of ICC neurons. They extend these observations to recordings made with the same electrodes at the same ICC locations before and after an SG lesion. The previous observations were made by comparing recorded responses to an acute lesion and then complete a postlesion IC penetration. In this study, postlesion observations could be made as early as 10 min after the lesion but usually at longer postlesion intervals (33–78 min). The results corroborate those previously reported. SG lesions across restricted cochlear sectors produce losses of sensitivity across a restricted range of frequencies. This loss in sensitivity was found to produce three major effects on ICC neuronal responses: a decrease in the excitation evoked by contralateral tones at frequencies corresponding to the lesion frequencies, an increase in excitation evoked by contralateral tones at lesion-edge frequencies, and an increase in excitation...
produced by ipsilateral tones at lesion frequencies. This last effect was restricted to the minority of sites that displayed a response to ipsilateral stimulation.

After contralateral SG lesions, decreased excitatory activity was most prominent in IC responses to contralateral tones whose frequencies corresponded to the frequencies most affected by the SG lesions (as indicated by the pre- and postlesion CAP audiograms). This decrease in excitation is striking because it was observed across such a narrow range of frequencies (often less than an octave), because it occurred across a broad range of intensities (often 40 dB), and finally because it occurred across the same range of frequencies in neurons tuned to a wide range of CFs. It was not restricted to neurons tuned to the lesion-center frequency, and it did not silence any IC locations, results one might expect if AN fiber responses were simply relayed to the IC (see following text). Rather, SG lesions produced a notch in the excitatory region of RAs in 13 of 15 IC neurons that were excited by lesion frequency stimulation at any level prior to the lesion. These notches were always confined to the relatively restricted range of lesion frequencies. Thus they are not equivalent to the broad decreases in sensitivity observed following acute high-intensity noise or tone-induced hearing losses in AN fibers and IC neurons. These sound induced losses occur primarily at the neuron’s CF (Liberman and Mulroy 1982; Salvi et al. 1996; Wang et al. 1996). In addition, acoustic lesions often produce increases in sensitivity to low-frequency tones below CF across several octaves. These increases in low-frequency sensitivity results in low-frequency, high-intensity “tails” on the excitatory tuning curves of the affected neurons. Thus these acoustic

![FIG. 13. Response areas recorded using ipsilateral tones from the same fixed, in-dwelling electrode (6 in cat 7/31/00) as used in Figs. 3 and 4. A: prelesion RA recorded 30 min prior to the lesion. The gray arrow indicates the estimated CF and threshold. B: postlesion RA recorded 11 h after the lesion centered at ~18 kHz (see arrow Fig. 2C). The black arrow indicates the estimated CF and threshold. C: postlesion RA recorded 14 h after the lesion. The postlesion and prelesion estimates of CFs and thresholds are indicated by the black and gray arrows, respectively. D: gray-scale difference RA illustrating the difference between the normalized pre- (A) and postlesion (B) responses (post minus pre).](http://jn.physiology.org/doi/abs/10.1152/jn.00184.2001)
lesions only rarely result in sufficient increases in sensitivity to produce a CF change. They simply lower the high-intensity, low-frequency thresholds of auditory neurons and produce changes in tuning that are only weakly related to the lesion frequencies (Calford et al. 1993; Liberman and Mulroy 1982; Salvi et al. 1996; Wang et al. 1996).

In contrast to the sensitivity changes evoked by high-intensity tones or noise, the increases in sensitivity to contralateral lesion-edge frequency tones produced by SG lesions could occur across narrow frequency ranges that were both above and below the lesion frequencies. In addition, SG lesions induced increases in sensitivity to tones at very low stimulus levels; often below the threshold at the prelesion CF. Increased sensitivity was most prominent at lower-edge frequencies. At these frequencies, SG lesions induced the greatest differences in pre- and postlesion firing rates. It was also at these lower-edge frequencies that changes occurred at the lowest stimulus levels. This difference in prominence between lower- and upper-edge frequencies is due in part to the fact that our SG lesions were located in basal (high frequency) cochlea producing losses on the rising high-frequency section of the cat’s audiogram. Thus tones below the lesion frequencies have lower thresholds. In addition, any nonspecific changes in threshold that result from opening the round window and partially draining the perilymph from the scala tympani would be expected to depress preferentially high-frequency (basal) responses. For both these reasons, any nonspecific changes in response threshold would be expected to be much more prominent at the lower edge frequencies than at higher edge frequencies.

In some instances, increased excitation occurred at F/L combinations that were clearly excitatory prior to the lesion, i.e., it produced enhancement of previously excitatory responses. In other instances, the lesions resulted in excitatory responses at previously silent F/L combinations. At most IC locations, responses increased for some F/L combinations in both categories. When the first two effects (decreased sensitivity at lesion frequencies and increased sensitivity at lesion-edge frequencies) were seen at one location, the result was a postlesion CF shift without a change in overall threshold. Such CF shifts could be large (half an octave or more) for neurons tuned to lesion-center frequencies or could be small for neu-

<table>
<thead>
<tr>
<th>Experiment</th>
<th>Electrode</th>
<th>No. of RAs</th>
<th>CF</th>
<th>Threshold</th>
<th>No. of RAs</th>
<th>CF</th>
<th>Threshold</th>
<th>Diff, kHz</th>
<th>Diff, dB</th>
</tr>
</thead>
<tbody>
<tr>
<td>7/27/99</td>
<td>E1</td>
<td>3</td>
<td>15.7 ± 1.46</td>
<td>20.0 ± 0.00</td>
<td>2</td>
<td>12.5 ± 0.72</td>
<td>23.3 ± 5.77</td>
<td>-3.2</td>
<td>3.3</td>
</tr>
<tr>
<td></td>
<td>E2</td>
<td>3</td>
<td>16.7 ± 0.57</td>
<td>12.5 ± 3.5</td>
<td>2</td>
<td>12.6 ± 0.57</td>
<td>10.0  ± 0.00</td>
<td>-4.1</td>
<td>-2.5</td>
</tr>
<tr>
<td>7/31/00</td>
<td>E1</td>
<td>1</td>
<td>19.2</td>
<td>55.0</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td></td>
<td>E2</td>
<td>1</td>
<td>18.5</td>
<td>50.0</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td></td>
<td>E4</td>
<td>1</td>
<td>18.5</td>
<td>50.0</td>
<td>2</td>
<td>18.6 ± 0.07</td>
<td>32.5 ± 3.54</td>
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<td></td>
<td>E5</td>
<td>1</td>
<td>18.8</td>
<td>55.0</td>
<td>2</td>
<td>17.8 ± 0.07</td>
<td>22.5 ± 3.54</td>
<td>-1.1</td>
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</tr>
<tr>
<td></td>
<td>E6</td>
<td>1</td>
<td>16.1</td>
<td>50.0</td>
<td>2</td>
<td>21 ± 0.00</td>
<td>15 ± 0.00</td>
<td>4.9</td>
<td>-35.0</td>
</tr>
</tbody>
</table>

Values are means ± SD.
rons tuned to the lesion-edge frequencies. In either case, the CF shifts often occurred with little or no change in the overall sensitivity of the neurons or any change in the bandwidth of the excitatory region (BW<sub>20</sub>). The change in minimum threshold (threshold at CF) was often less than ±10 dB despite shifts in CF of half octave. The responses of neurons that were unresponsive to the lesion frequencies were unaffected by the lesions. Thus the observed lesion-induced CF shifts are not simple reflections of changes in cochlear sensitivity and are not reflections of pseudoplasticity (see Kaltenbach et al. 1992) or recording of the “residue” (see Rajan et al. 1993). These lesions often produced CF shifts across specific regions with clear increases in lesion-edge frequency sensitivity without increasing overall response thresholds.

The final major effect of SG lesions was to an immediate increase in sensitivity to previously subthreshold ipsilateral tones at several ICC locations. Increased ipsilateral sensitivity occurred to tones only over a very restricted range of frequencies. It was not a generalized, broadband increase. Postlesion BW<sub>20</sub>’s were all >1 and equal to or greater than prelesion BW<sub>20</sub>’s at four of five locations. At three locations, SG lesions produced an overall decrease in threshold to ipsilateral tones of 30 dB.

Increased sensitivity to ipsilateral acoustic stimuli in adults has been reported after neonatal destruction of the contralateral cochlea (Kitzes 1984; Kitzes and Semple 1985; McAlpine et al. 1997; Reale et al. 1987) and after chronic destruction in adults (McAlpine et al. 1997; Popelar et al. 1994). For example, Kitzes and Semple (1985) reported lower mean thresholds (~8 dB lower) to ipsilateral tones in adult gerbil IC neurons after unilateral destruction of the cochlea in neonates. They also reported shorter median latencies (~3 ms shorter), higher median maximum driven rates (an increase from 1 to 6 spikes/100-ms CF tone) to ipsilateral tones. By all these measures, ipsilateral responses to CF tones in adults with neonatal contralateral cochlear destruction were more sensitive than normal ipsilateral responses; they matched the responses of normal contralateral responses. Reale et al. (1987) reported increased responsiveness of neurons in AI of adult cats to ipsilateral tones following neonatal destruction of the contralateral cochlea. They also reported a dramatic increase in the responsiveness of AI neurons to ipsilateral tones in one of two adult cats, which were studied in a map/re-map paradigm after acute cochlear destruction. In a subsequent study, McAlpine et al. (1997) reported that neonatal destruction of one cochlea in ferrets produced nearly a threefold increase in the number of IC neurons that responded to ipsilateral tones at adulthood as compared with normal adult ferrets. They also reported increases in the number of IC neurons that responded to ipsilateral tones after both acute (2 times) and chronic (3 times) cochlear destruction in adult ferrets. Mossop et al. (2000) recorded multineuronal responses to ipsilateral tones in penetrations through the IC of adult gerbils before and after destruction of the contralateral cochlea. They reported responses to ipsilateral tones at 30 of 75 sites that had been unresponsive to ipsilateral tones prior to cochlear destruction. Thus several previous studies have reported increases in ipsilateral driving after contralateral cochlear damage. However, the present results are the first to define the frequency and intensity specificity of these increases.

**Time course of acute response changes produced by restricted cochlear lesions**

As with all plasticity, interpretation of the “plastic” changes induced by partial hearing losses depends on their time course. Spinal shock, the immediate and total, but transient, suppression of all segmental reflexes after spinal cord transection, is not normally considered a form of sensory/motor plasticity. Rather it is considered a passive response to withdrawal of descending tonic excitation (Little et al. 1999; Naciemento and Noth 1999). However, the recovery of segmental reflexes and their eventual hyperactivity over the succeeding days after transection would be considered plasticity (Ko et al. 1999). Likewise, decrebribud rigidity, the instantaneous hyperactivity of all stretch reflexes following transection of the rostral midbrain, is not normally considered plasticity. It is normally considered the result of “release” of excitatory activity in spinal neurons from tonic descending inhibition (Burke 1999).

However, the subsequent recovery of near-normal stretch reflexes, which requires weeks, is considered a form of plasticity. The time course of “plastic” changes also limits the types of mechanisms that can be considered to underlie them. Changes that require days or even months may arise by several mechanisms including anatomical sprouting, cell atrophy and cell death. Changes that occur over a shorter time course (several hours to days) require different mechanisms e.g., long-term potentiation (LTP) or depression (LTD). However, changes that occur instantly or in a matter of minutes must be accounted for by still other mechanisms.

The changes in IC tuning and sensitivity described in this study occur within a few minutes to a few tens of minutes. It is difficult to be more precise about their time course because the process of making a SG lesion itself (opening the round window, draining the perilymph, curling a hole in Rosenthal’s canal) undoubtedly produces some transient changes in cochlear sensitivity. These incidental sensitivity changes are likely to be more generalized and of a different nature than those produced by the destruction of the spiral ganglion per se. Recovery from these incidental changes occurs over a time course that progresses concurrently with those produced by destruction of a SG segment. For example, it takes time for the perilymph in the basal cochlea to be replenished, and normal inner hair cell sensitivity in the basal cochlea will not fully recover until that occurs. Thus the precise timing of all the described effects is difficult to determine. However, one can say that virtually all of them are stable for several hours within 60–90 min after the lesion. This relatively rapid time course presumably precludes some mechanisms, such as anatomical sprouting, which require days to months.

It is possible that at least some of the changes observed in these experiments could result from changes in descending pathways. Suga and co-workers (Gao and Suga 1998; Yan and Suga 1998; Zhang and Suga 2000; Zhang et al. 1997) have reported that in bats a number of procedures, which influence cortical activity, can rapidly alter tuning in IC and thalamic neurons. For example, they reported that focal cortical electrical stimulation at a specific frequency location for 7 min could augment or depress the response amplitudes of IC and thalamic neurons tuned to that frequency. They also reported that such stimulation could change the tuning of subcortical neurons tuned to adjacent frequencies (Yan and Suga 1998; Zhang and
Suga 2000; Zhang et al. 1997). Conversely, cortical inactivation by application of lidocaine or muscimol could block these effects. These results bear some resemblance to the changes reported here in postlesion responses to contralateral tones.

However, there are a number of differences. First, the CF shifts reported by Suga and collaborators are small (~1 kHz for CFs at 60 kHz) and transient (lasting ~30–180 min). Those reported here and previously (Snyder and Sinex 1998; Snyder et al. 1996, 2000) were relatively large (nearly an octave at 16 kHz) and lasted at least as long as the longest experiment (4 days). Second, response areas in the bat’s IC were indeed “shifted,” i.e., they changed CF with little or no change in shape. Although some had minor changes in their bandwidths, these changes were small (<0.5 at 60 kHz) and none were reported to have notches or holes in their excitatory regions. Therefore although the role of the cortex in modulating the effects reported here is an open empirical question, we believe that the basic phenomena arise largely from interactions among ascending auditory pathways.

Numerous studies of the chronic effects of partial hearing losses have reported plasticity in the topographic organization in the auditory CNS (Harrison et al. 1991, 1993, 1996; Rajan et al. 1993; Reale et al. 1987; Robertson and Irvine 1989; Salvi et al. 1996; Schwaber et al. 1993; Willott 1984, 1996; Willott et al. 1994; among others). However, none of these studies, with the exception of Robertson and Irvine (1989) and Reale et al. (1987), examined their preparations for acute effects of their lesions. Robertson and Irvine (1989) found no evidence for plasticity but rather only “residual” responses in their acute controls, although Reale et al. (1987) found dramatic changes in at least one of their acutely lesioned adult controls. Since “plastic” topographic changes can be mimicked by the acute effects of altered AN input (Snyder et al. 1996, 1998, 2000, this publication), much of this plasticity may simply reflect acute withdrawal of excitation and/or release from inhibition.

Differences between SG lesions and other procedures producing partial hearing losses

The results presented here are clearly different from those reported by other studies of the effects of frequency specific (i.e., partial) hearing losses. These differences are undoubtedly due to the differences between lesions that remove a sector of the spiral ganglion and those that damage sector(s) of the basilar membrane and/or organ of Corti. SG lesions leave the organ of Corti and basilar membrane intact. Most other procedures damage broad areas of cochlea. Acoustic lesions and lesions produced by ototoxic drugs can produce partial hearing losses, but these losses are often accompanied by widely distributed and idiosyncratic destruction of the inner and outer hair cells (e.g., Harrison et al. 1996; Liberman and Mulroy 1982; Salvi et al. 1982). The resulting hearing losses may take days, weeks, or even months to stabilize. In so doing, they disrupt the signal processing capacity and sensitivity of the cochlea. SG lesions leave that capacity and sensitivity intact except across a highly restricted and predictable range of frequencies.

It is important to distinguish between the postlesion responses of IC neurons and those that would be expected in AN neurons. First, if there are no differences, then the postlesion changes in the IC can be attributed to pseudoplasticity or recording of the “residue,” i.e., changes in CF due to losses in sensitivity at the tuning curve tip. Second, they clearly differentiate IC excitatory response regions from those of AN neurons, which they superficially resemble.

The most striking difference between postlesion responses of these two types of neurons is in the postlesion loss of excitation. SG lesions can be expected to completely silence the relatively small number of AN neurons directly damaged by the lesion while leaving intact the responses of the remaining nerve fibers. Thus across the AN population one would expect a lesioned SG sector with silent AN fibers which is flanked by two normal SG sectors with AN fibers with normal thresholds. This is very different from the AN seen after noise damage of the cochlea. Liberman and Mulroy (1982) found that only AN fibers with CFs at noise center frequency and an octave above it were affected by the exposure. Neurons with CFs centered half an octave above the noise center frequency were most affected, and they displayed a 60 dB decrease in sensitivity at prelesion CF. However, sensitivity across the low-frequency “tails” and high-frequency edges of their tuning curves were often unaffected by the noise exposure. Many AN fibers lost the low-threshold “tips” of their tuning curves, but their sensitivity at other frequencies was unaffected. If the RAs of ICC neurons were relayed replicas of those in AN fibers, then SG lesions would produce a silent region (or at least a region of highly elevated thresholds) in the IC corresponding to the neurons that receive their relayed input from the lesioned SG sector. A model of such a system is presented in Fig. 14. In this model, the output of the intact organ of Corti is illustrated as series of colored triangles (top of the figure) representing the tuning curves of intact inner hair cell (IHCs). These tuning curves are arrayed with the red triangles on the left representing the tuning curves of IHCs with low frequency CFs and the purple triangles on the right representing IHCs with high-frequency CFs. Thus the apical cochlea is represented on the left and the basal cochlea is represented on the right. Each inner hair cell is innervated by a unique cluster of spiral ganglion cells (vertical lines with circles in the middle). These are bipolar cells are arrayed along the cochlear spiral with their peripheral processes innervating a single inner hair cell and their central process innervating entering the CNS, i.e., a restricted region of the cochlear nucleus (not illustrated, but see Leake and Snyder 1989; Snyder et al. 1997). Ultimately, activation reaches the inferior colliculus (bottom row of triangles, Fig. 14). In this model, a lesion across a restricted region of the ganglion (dotted vertical lines and circles), removes the cochlear output across a restricted frequency region in the IC (dotted triangles). If the auditory system consisted of a parallel series of tuned channels without convergence, then such a lesion should result in an IC region within which the neurons would be either silent (dashed triangles at the bottom) or would have dramatically elevated thresholds. In these experiments, elevated thresholds were observed at some IC locations (Fig. 12) but far less frequently than locations at which the minimum

Differences between responses of AN fibers and IC neurons to restricted cochlear lesions

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threshold was unchanged and the excitatory regions had a clear notch or gap corresponding to the lesion frequencies (e.g., see Figs. 4, 6, 7, and 9).

In contrast to the model in Fig. 14, restricted SG lesions produce a loss of excitation across the narrow range of lesion-frequencies in neurons tuned to a wide range of CFs distributed across a range of depths within the IC. In addition, they produce regions of additional sensitivity across lesion-edge frequencies. We have tried to represent these results in Fig. 15 by illustrating the tuning curves in five IC neurons distributed across the depth of the IC. As in Fig. 14, the prelesion tuning curves are indicated by the dotted triangles. Prior to the lesion, neurons located at IC depths far above or far below those tuned to the lesion frequencies (i.e., neurons tuned to much lower or higher frequencies) do not respond to or respond only very weakly to the lesion frequencies. Therefore their postlesion responses are unaffected by the lesion (e.g., see Fig. 10). The tuning curves of such neurons are represented by the triangles at the far-left and far-right bottom of Fig. 15. Neurons at IC locations between these unaffected populations are represented by the three triangles at the bottom, center of Fig. 15. Before the lesion, their tuning curves have the normal V shape. After the lesion, they have notches or gaps in their excitatory regions corresponding to the lesion frequencies. These notches can be above, at, or below the neurons’ prelesion CF, depending on the relationship of their prelesion CF relative to the lesion frequencies. Neurons with prelesion CFs tuned to the lower lesion-edge frequencies (middle left triangle Fig. 15) have the high-frequency side of their excitatory regions pared-off (e.g., see Figs. 3, 4, and 12). In addition, they may have excitation added at previously silent F/lg tone combinations. This additional excitation may shift their postlesion CFs to either lower (Fig. 7) or higher frequencies (Fig. 11) depending on their prelesion CFs relative to the frequencies affected by the lesion and their sensitivity to the added excitatory input (bottom center, Fig. 15). Neurons with prelesion CFs tuned to upper lesion-edge frequencies have notches in their low frequency tails or shifts in their CF, if they are exceptionally sensitive to the added excitation (bottom right, Fig. 15).

The results presented here (in barbiturate-anesthetized cats) reinforce a conclusion that can be drawn from studies of ICC responses in the un-anesthetized cat (Davis et al. 1999; Ramachandran et al. 1999), namely, that response areas of IC neuron are not relayed replicas of AN fiber responses. In addition, however, this study suggests that frequency responses of ICC neurons are composites or mosaics of discrete frequency channels arrayed across the response areas. Each channel evokes activity across a narrow range of frequencies, and this activity is ultimately traceable to a specific restricted sector of the spiral ganglion. Excitation evoked by 18–20 kHz tones in a given IC neuron’s RA is dependent on and ultimately derived from AN fibers with CFs at 18–20 kHz. Destruction of these AN fibers removes the excitation evoked across that frequency range but leaves intact excitation evoked by tones in adjacent frequency ranges (e.g., 16–18 and 20–22 kHz) and may release excitation at these frequencies. Conversely, the AN fibers tuned to 18–20 kHz supply the 18–20 kHz excitation to all (or most) IC neurons. Their removal results in loss of excitation across this frequency range in many (most) IC neurons, which respond to these frequencies, i.e., those with CFs 10 kHz. Thus the loss of excitation in these high-frequency neurons occurs at the lesion frequencies regardless of their CF (location in the nucleus).

In addition to the withdrawal of excitation, there is rapid withdrawal of inhibition and/or addition of excitation. Postlesion stimulation at intact, nonlesion frequencies produces IC responses at stimulus levels below those that were effective in prelesion stimulation (e.g., Figs. 4, 7, and 11). Loss of excitatory input within an excitatory region may be accompanied by rapid, frequency-specific loss of inhibition and/or the addition of excitation to all (or most) IC neurons. Their removal results in loss of excitation across this frequency range in many (most) IC neurons, which respond to these frequencies, i.e., those with CFs 10 kHz. Thus the loss of excitation in these high-frequency neurons occurs at the lesion frequencies regardless of their CF (location in the nucleus).

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of excitation within previously “silent” regions. The addition of excitation suggests that these silent regions are silent not because there is no excitatory drive at these F/L combinations. Rather, they are silent because the existing excitatory drive is subthreshold or suppressed by inhibition. If it is suppressed, the suppression is supplied by activity in normally excitatory pathway(s). These results lead us to hypothesize that SG lesions produce a release from inhibition that acts across specific nonlesion frequency representations. Tones, which excite intact cochlear regions in the lesioned ear, evoke supra-threshold excitation in contralateral IC neurons at levels that were subthreshold before the lesion. Thus for example, removal of SG sectors in the left ear that are tuned to 15–20 kHz releases excitatory activity in the right IC to tones at 10–15 kHz in that ear and tones at 15–20 kHz in the right ear.

This view of IC response areas is similar to that suggested for cortical neurons by Phillips and Hall (1992), who suggested that cortical response areas represent a series of overlapping V-shaped inputs. Our hypothesis is similar with the difference that our data suggest that IC response areas consist of a series of I-shaped or level-insensitive excitatory and inhibitory inputs (Ramachandran et al. 1999; Suga and Tsuzuki 1985), each acting across a specific (perhaps nonoverlapping) frequency range whose frequency limits change little with stimulus intensity. Removal of one of these I-shaped input regions (by complete destruction of a SG sector) results in a gap in the excitatory region of an IC neuron’s RA that has nearly vertical sides (see black regions in difference RAs in Figs. 5, 6, and 8). The balance between excitation and inhibition within each input region (frequency) produces the threshold and rate/intensity function at that frequency.

This view might help to explain a number of otherwise inexplicable phenomena. For example, it helps to explain the dramatic differences seen in the response areas of IC neurons recorded in barbiturate-anesthetized cats with those recorded from unanesthetized cats. Ramachandran et al. (1999) reported that only 12% of the neurons recorded in decerebrate, unanesthetized cats had V-shaped excitatory regions (the type seen almost exclusively in normal, barbiturate-anesthetized cats, see prelesion excitatory regions in this study). The remaining 88% had excitatory response regions that were either I-shaped (similar to level insensitive neurons described by Suga and Tsuzuki 1985) or O-shaped (similar to Type IV units described in the DCN by Young and Voigt 1982). Barbiturate anesthesia simply biases the balance toward excitation at all frequencies except those at or near CF. It also helps to explain the dramatic topographic (tonotopic) reorganizations seen after partial hearing losses (Rajan et al. 1993; Robertson and Irvine 1989). Any cochlear lesion that affects a restricted range of frequencies will produce changes in the balance between excitation and inhibition and may produce immediate and, in some cases, dramatic changes in the tuning of IC neurons. Thus these plasticity effects in the auditory system may be more related to phenomena like spinal shock (withdrawal of excitation) and decerebrate rigidity (release from inhibition) than to adaptive cortical reorganization/re-calibration and use-dependent plasticity (Gilbert et al. 1996).

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