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Unilateral Auditory Cortex Ablation in Macaques Results in a Contralateral Hearing Loss

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SUMMARY AND CONCLUSIONS

1. The behavioral audiograms of four Japanese macaques (*Macaca fuscata*) were assessed before and after unilateral ablation of auditory cortex. The tones were presented via insertion earphones so that each ear could be tested separately.

2. Each animal had a hearing loss in the ear contralateral to the lesion, whereas the ipsilateral ear showed no change in sensitivity. The hearing loss initially appeared as a large shift in thresholds followed by rapid but incomplete recovery during the first 3–5 wk after surgery. The initial hearing loss ranged as high as 68 dB at some frequencies, although thresholds at other frequencies were occasionally unchanged. A threshold shift could be demonstrated with broadband noise as well as with tones. Although thresholds for some tones returned to normal within a few weeks, most were still elevated 16 wk after surgery when testing was discontinued. The largest long-term hearing losses occurred at frequencies from 4 to 25 kHz.

3. Analysis of the animals' psychophysical functions suggested that the hearing loss resembled a sensory deficit, as opposed to a nonsensory deficit in attention or vigilance.

4. Testing with binaural stimuli indicated that the hearing loss could best be described as a contralateral "ear" deficit, as opposed to a contralateral "auditory field" deficit.

5. It is suggested that a similar hearing loss occurs in humans after unilateral damage to auditory cortex.

INTRODUCTION

It has recently been shown that bilateral ablation of auditory cortex in Japanese macaques results in a significant hearing loss (Heffner and Heffner 1986, 1989b). This hearing loss is characterized by a sudden decrease in sensitivity to sound, which, in the case of lesions encompassing the entire superior temporal gyrus, may be a total failure to respond to sound followed by gradual but incomplete recovery. The existence of this hearing loss in macaques is of interest not only for its theoretical implications concerning the function of auditory cortex, but also because it appears to be identical to the phenomenon of cortical deafness in humans (Heffner and Heffner 1986).

If bilateral auditory cortex ablation results in a hearing loss in both ears, then the question arises as to whether unilateral ablation results in a hearing loss in one ear. Because the predominant excitatory projection from each ear is to the contralateral hemisphere (e.g., Phillips and Gates 1982), it is reasonable to expect that unilateral ablation of auditory cortex would result in a hearing loss in the contralateral ear. Indeed, an early indication of this possibility is found in the work of Ferrier, which demonstrated that monkeys were unresponsive to sound after unilateral auditory cortex lesions when the ear ipsilateral to the lesion was plugged with cotton-wool (Ferrier 1876). However, because it was long believed that even bilateral auditory cortex ablation did not result in a hearing loss (Masterton and Berkley 1974), previous studies of the effect of unilateral cortical ablation did not investigate the possibility of a contralateral hearing loss.

Nor does the clinical literature provide a clear answer regarding this question. Although one study demonstrated that hemiplegic patients have a small but statistically significant hearing loss in the ear contralateral to their damaged hemisphere (Karp et al. 1969), most studies of patients with unilateral temporal lobe damage have failed to note substantial hearing loss in the contralateral ear. Thus the prevailing opinion seems to be that unilateral damage to auditory cortex does not result in a large or permanent hearing loss in either ear, although the possibility of a small or transient deficit has not been ruled out (e.g., Chandler and Sedge 1987; Jerger et al. 1969).

The purpose of this paper is to present the results of a study of the effect of unilateral ablation of auditory cortex on absolute thresholds in Japanese macaques. As will be seen, these lesions consistently resulted in a significant hearing loss in the contralateral ear.

METHODS

The general design of the study was first to determine the preoperative audiograms of four monkeys for each ear separately with an avoidance procedure. The animals were then retested at various times after unilateral ablation of the superior temporal gyrus and the results compared with their preoperative thresholds. Thus any change in hearing could be precisely specified in terms of individual threshold shifts. Additional tests using binaural stimuli and noise were given to examine the animals' hearing further.

Subjects

Four 7-yr-old (adolescent) male Japanese macaques (*Macaca fuscata*) that had been born and reared in a free-ranging colony (Arashiyama West Institute) were used in this study. The animals, referred to as *M-207, M-214, M-267,* and *M-337,* were also used in a study of the effect of cortical ablation on the perception of primate vocalizations (Heffner and Heffner 1989a). They were individually housed in primate cages with free access to food and were trained with water reward. Each monkey was weighed daily to monitor its health and deprivational level. The ears of each animal were examined during testing and after death to ensure that they were free of damage or disease.

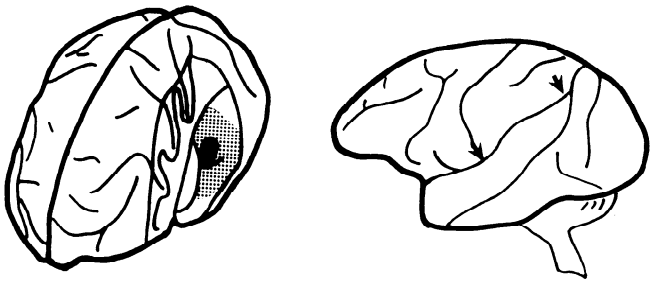

FIG. 1. Location of auditory cortex in the macaque. *Left*: Japanese macaque brain with the frontoparietal operculum removed to show the location of primary (blackened) and the surrounding belt of secondary (stippled) auditory cortex. More secondary auditory cortex is buried in the circular sulcus bounding the insula. *Right*: lateral surface of a Japanese macaque brain. Arrows mark the approximate limits of the primary and secondary auditory fields of the superior temporal plane [drawings based on the electrophysiological study of Merzenich & Brugge (1973)].

Surgical and histological procedures

SURGERY. Following preoperative training and testing, the four monkeys received unilateral lesions of the temporal lobe. For surgery, a monkey was initially sedated with ketamine (5 mg/kg) and given 0.5 mg of atropine sulfate and 100 mg of Lincocin (Upjohn). This was followed by halothane administered via endotracheal cannula, as needed, to maintain deep anesthesia. The animal's head was shaved and washed, the scalp opened, and the temporal muscle on one side dissected with a cautery. With the edges of the temporal muscle retracted, the portion of the cranium overlying the sylvian fissure was removed, the dura retracted, and the superior temporal gyrus removed by subpial aspiration with the aid of a surgical microscope. Aseptic procedures were followed throughout surgery.

After removal of cortical tissue, the lesion was packed with Gelfoam (Upjohn) to minimize subsequent distortion of the gyri, and Gelfilm (Upjohn) was placed over the opening and under the edges of the cranium to minimize adhesions of the overlying tissue with the pia. The temporal muscle was then apposed and sutured, a topical antibiotic powder (Neo-Predef, Upjohn) was applied, and the scalp incision was closed with silk suture. The animal was placed in a cage located in a dark, quiet room and given acepromazine as needed to minimize discomfort.

HISTOLOGY. After completion of behavioral testing, the monkeys were deeply anesthetized with pentobarbital sodium and perfused with isotonic saline followed by 10% Formalin. The brains were removed, photographed to aid cortical reconstruction, and prepared for frozen sectioning. Each brain was sectioned in the coronal plane at 40 μm, and two sets of sections at 200-μm intervals were stained: one with thionin and one with Protargol (Sterling). These sections were then used to reconstruct the lesions and resulting thalamic degeneration.

Procedure

BEHAVIORAL APPARATUS. A standard primate chair was modified to accommodate a "double" water spout. This spout consisted of two standard sipper tubes mounted parallel and close enough (1 cm apart) so that a monkey could comfortably place its mouth on both spouts. The two spouts, which were electrically isolated from each other, were connected to a contact switch that detected when the animal placed its mouth on them. One of the spouts was attached via plastic tubing to an electrically operated water valve and constant-pressure water reservoir. Using the double water spout eliminated the need to tie the animal's foot to complete the circuit for the contact switch, thus providing the animal with greater freedom of movement. Mild electric shock was provided by a shock generator connected to the two spouts.

Although the animal was able to turn about in the monkey chair, perfunctory head movements were restricted to prevent accidental dislodging of the insertion earphones through which the stimuli were presented. This was accomplished by mounting two vertical rods on the primate chair so that the animal placed its muzzle between them while drinking from the spout. A horizontal rod mounted on the two vertical rods above the animal's muzzle, and a back plate mounted behind the animal's head, completed the arrangement. This configuration enabled the animal to break contact easily with the water spout, while reducing the possibility of accidentally dislodging the earphones. However,

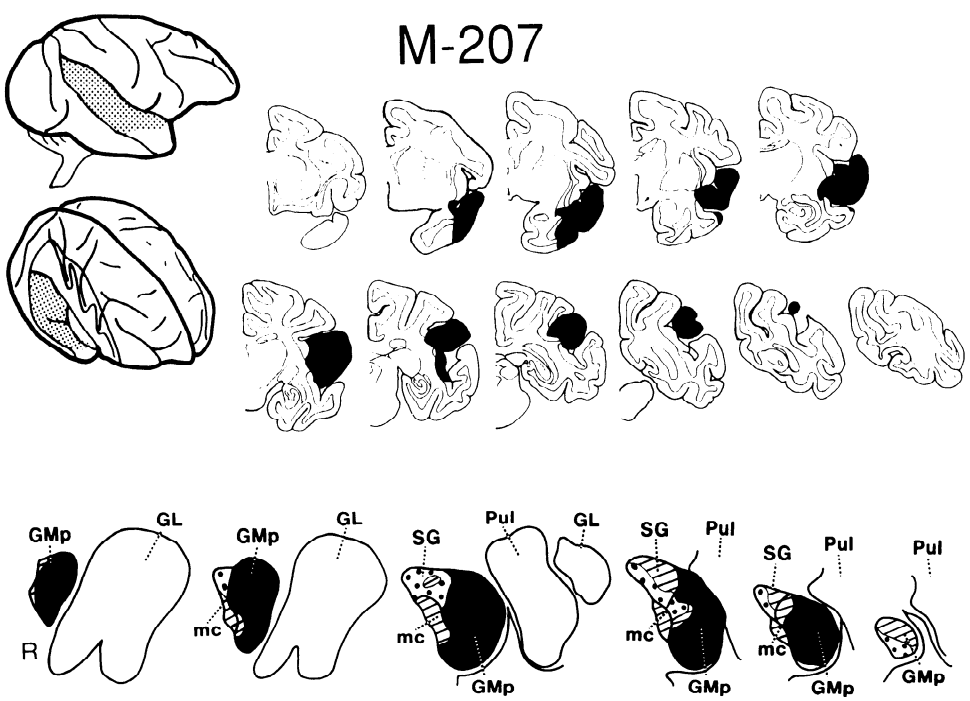

FIG. 2. Cortical reconstruction and medial geniculate degeneration for *M-207*. *Top left*: reconstruction of cortical lesion (stippling) showing surface views and views of the superior temporal plane with the parietal operculum removed. *Top right*: coronal sections, 3.6 mm apart, with ablated areas shown in black. *Bottom*: retrograde degeneration in the vicinity of the medial geniculate. Right thalamic sections (*top*) are shown posterior to anterior. Thalamic sections are 600 μm apart. GL, dorsal lateral geniculate; GMp, principal division of the medial geniculate; mc, magnocellular division of the medial geniculate; Pul, pulvinar; SG, suprageniculate nucleus. Blackened area indicates total degeneration, 95–100% cell loss; hatched area indicates severe degeneration, 70–95% cell loss; stippled area indicates moderate degeneration, 30–70% cell loss.

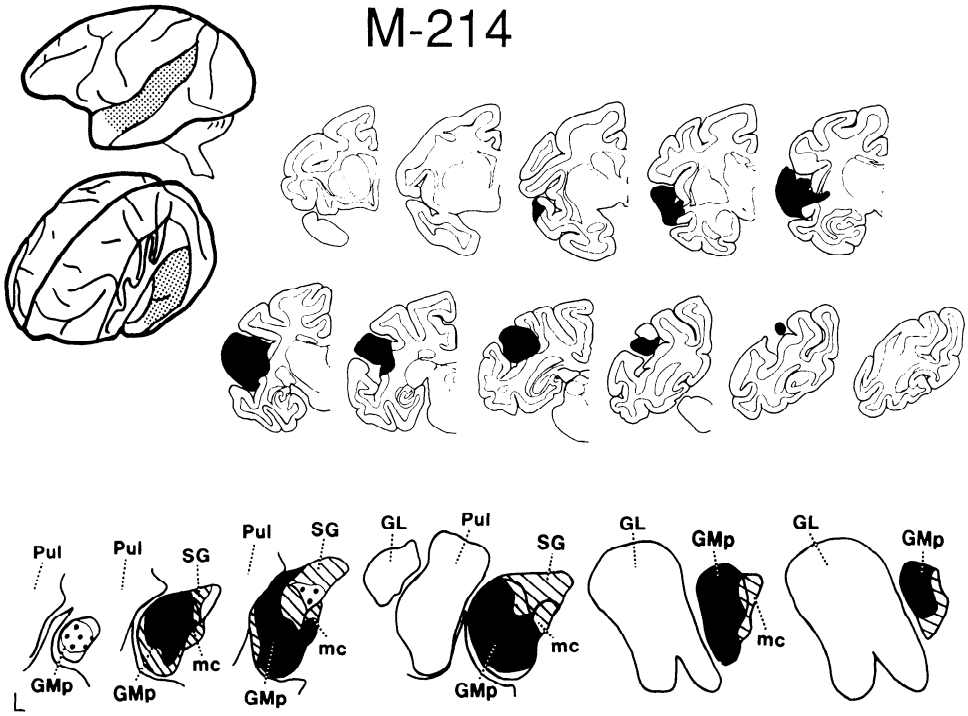

FIG. 3. Cortical reconstruction and medial geniculate degeneration for *M-214*. (See Fig. 2 for key.)

the animal was still able to turn around in the chair and face the door of the test chamber, an act which dislodged the earphones. As this usually occurred late in a session, it was taken as an indication that the animal wished to terminate the session, and the animal was then returned to its cage and given supplemental water as needed to maintain good health.

A 60-W light was mounted above the chair, and the entire apparatus was located in a double-wall sound chamber (2.7 × 2.5 × 2.0 m), the walls and ceiling of which were lined with egg-crate foam to reduce sound reflection. A microcomputer was used for behavioral programming.

ACOUSTICAL APPARATUS. Sine waves were produced by a generator (Hewlett-Packard 209A), and noise stimuli were produced by a Grason-Stadler white-noise generator (model 901A). The signal was switched by a rise-fall gate (Coulbourn S84-04) and pulsed two times per second (250 ms on, 250 ms off, 50 ms rise-decay for 63 Hz to 250 Hz, and 20 ms rise-decay for higher frequencies). The signal was then led to an attenuator (Hewlett-Packard 350B), bandpass filter (Krohn-Hite 3202), amplifier (Crown D75), and finally to headphones (Koss Pro 4X). The headphones, which were suspended over the animal's head, were fitted with a Plexiglas adapter and connected to molded ear pieces

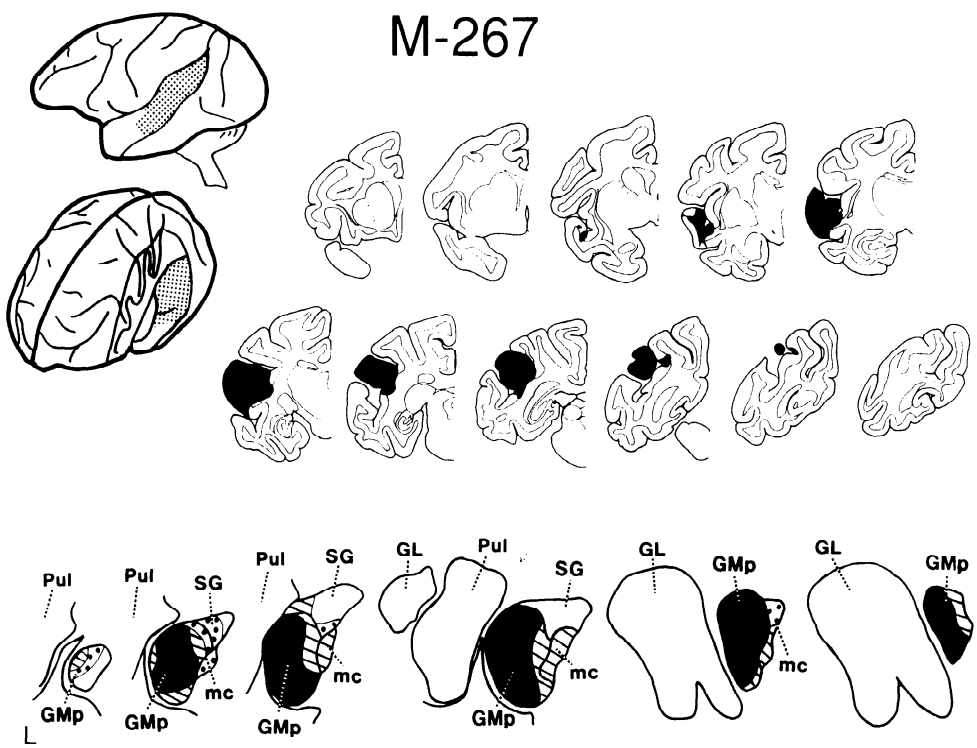

FIG. 4. Cortical reconstruction and medial geniculate degeneration for *M-267*. (See Fig. 2 for key.)

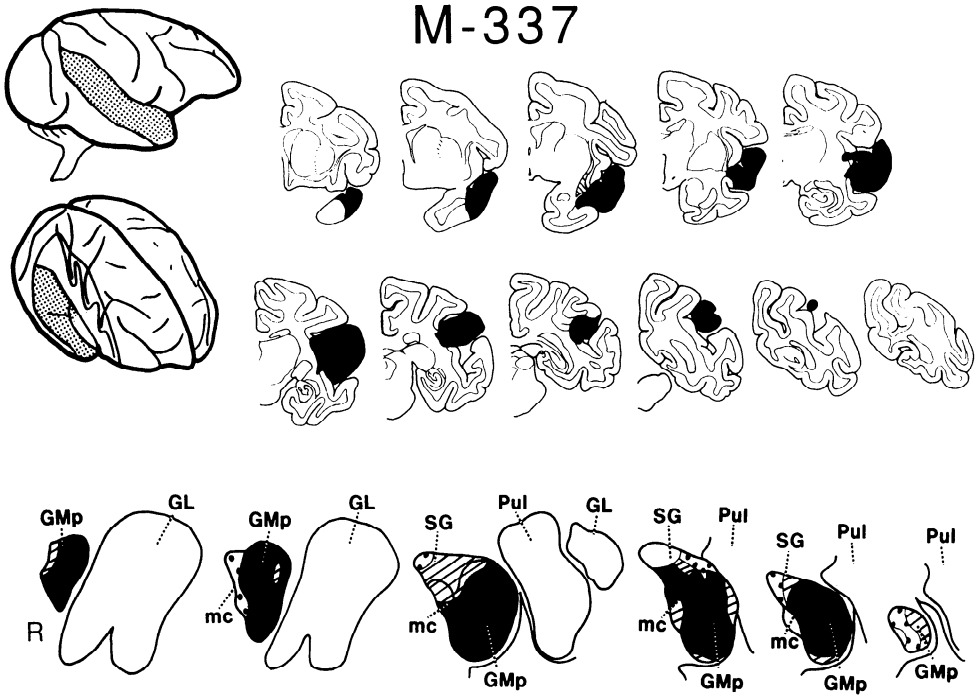

FIG. 5. Cortical reconstruction and medial geniculate degeneration for *M-337*. (See Fig. 2 for key.)

via a 25-cm length of plastic tubing (2 mm ID). This system permitted each ear to be stimulated independently while allowing the animal to move its head to break contact with the water spout. Thresholds were conducted in octave steps from 63 Hz to 32 kHz, with an additional threshold taken at 25 kHz.

The output of the headphones was periodically checked with a Brüel and Kjaer (B & K) sound-level meter (model 2203), 1-in. (2.54-cm) microphone (B & K 4144), octave filter (B & K 1613), and artificial ear (B & K 4152 with 2-ml coupler). Frequencies > 16 kHz were measured with a 0.5-in. (1.27-cm) microphone (ACO 7012), microphone amplifier (B & K 2608), external filter (B & K 1613 or Krohn-Hite 3550), and artificial ear (B & K 4152 with 2-ml coupler). In addition, the output of the microphone amplifier was led to an oscilloscope to verify the presence of the signal. All microphones were calibrated with a pistonphone (B & K 4220).

PSYCHOPHYSICAL PROCEDURE. A thirsty monkey was rewarded for climbing into the primate chair and placing its mouth on the water spout by providing a steady trickle of water (3–4 ml/min) as long as the animal maintained contact with the spout. Tones were then presented through the earphones at random intervals and followed at their offset by mild electric shock delivered across the double water spout. Once the animal had learned

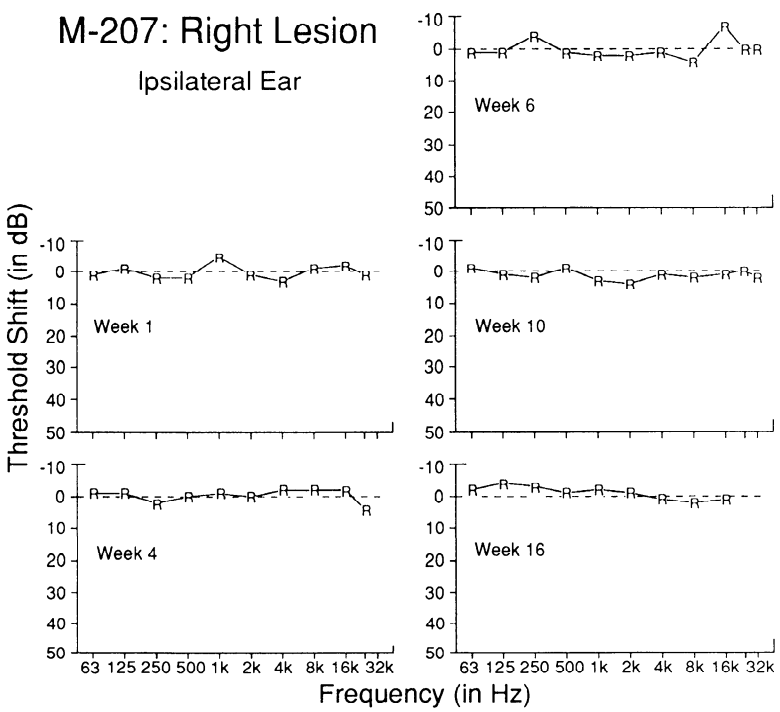

FIG. 6. Postoperative audiograms for the right ear of *M-207*. Note that thresholds in the ear ipsilateral to the lesion were unchanged. Thresholds (indicated by the letter R) are plotted relative to the preoperative audiogram.

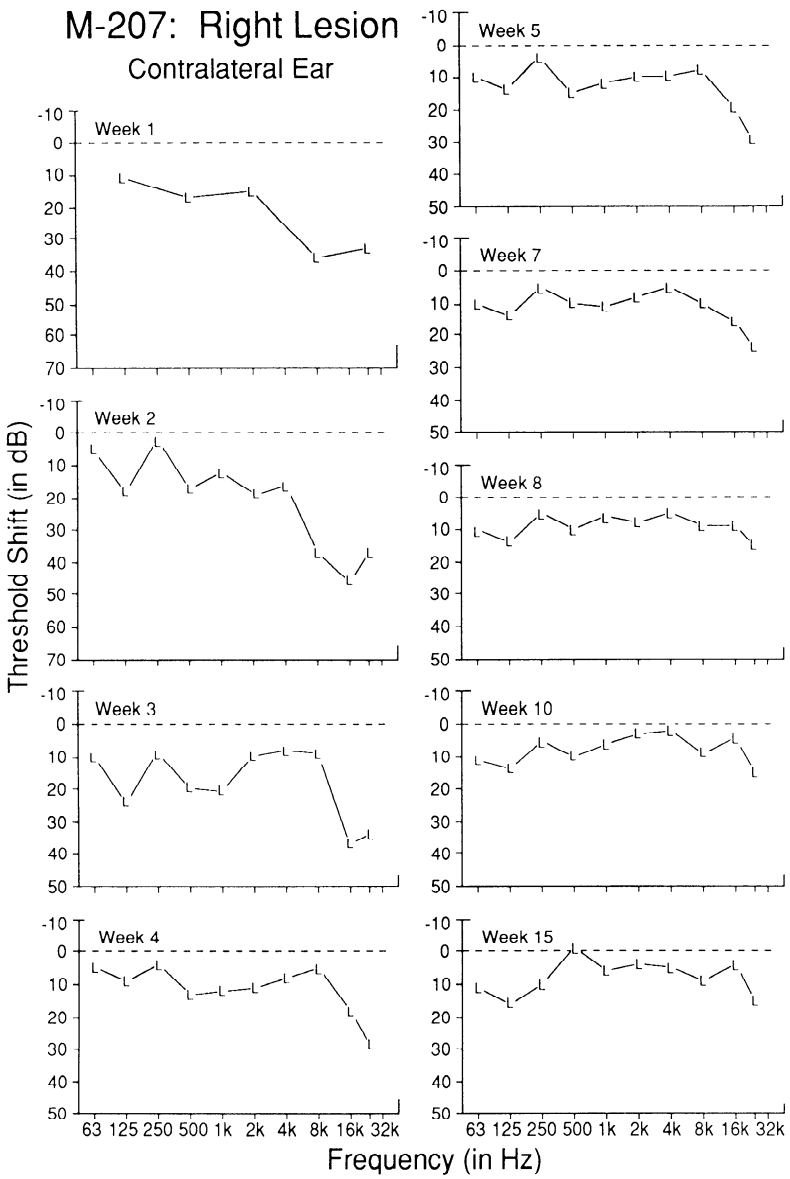

FIG. 7. Postoperative audiograms for the left (L) ear of *M-207*. Note that the lesion resulted in a hearing loss in the ear contralateral to the lesion.

to associate the tone with shock, it avoided the shock by breaking contact with the spout whenever a tone signaled impending shock. This cessation of contact was used to indicate that the animal detected the tone. The light above the primate chair was momentarily turned on after each warning trial to indicate that the shock had been delivered and that the animal could return to the spout.

The level of the shock was individually adjusted for each animal to the lowest level that would reliably produce an avoidance response. Because the animals never developed any fear of the water spout and returned to it without hesitation after receiving a shock, the shock level was designated as "mild."

The test procedure consisted of presenting 3.5-s trials with a 3.5-s intertrial interval (i.e., 1 trial every 7 s). Each trial was either a "safe" trial, during which no tone was presented, or a "warning" trial, which consisted of a 3.5-s train of tone pulses. Warning trials occurred randomly from one to seven trials after the previous warning trial with occasional "catch" trials inserted, in which no warning trial was presented on the seventh trial. The number of warning trials given in each of the trial periods (i.e., *periods 1* through *7*) was adjusted so that each trial period had the same probability (0.25) of containing a warning signal.

The response of the animal on each trial, i.e., whether it had made an avoidance response, was determined by noting whether the animal was in contact with the spout during the last 200 ms of the trial. Basing the response criterion on the last 200 ms allowed the animal sufficient time to break contact with the spout after presentation of a warning stimulus. To reduce the effects of occasional pauses in drinking, the results of a trial were automatically discarded if the animal was not in contact with the spout at any time during the 1 s immediately preceding the trial (although the trial was presented as usual).

The scores for a session were averaged separately for the silent or safe (S) trials and the tone or warning (W) trials for each frequency at each intensity. A measure of discrimination was then expressed in the form of a performance ratio, $(S - W)/S$, for each stimulus intensity, where S is the average score of the safe trials and W is the average score of the warning trials. In trained animals, this measure varies from ~ 0 (failure to detect the tone) to 1 (perfect detection).

Two procedures were used to determine auditory thresholds. Preoperative thresholds were first determined for each frequency by reducing the intensity of the tone in 5-dB steps until the animal could no longer distinguish tone trials from silent trials. Once a

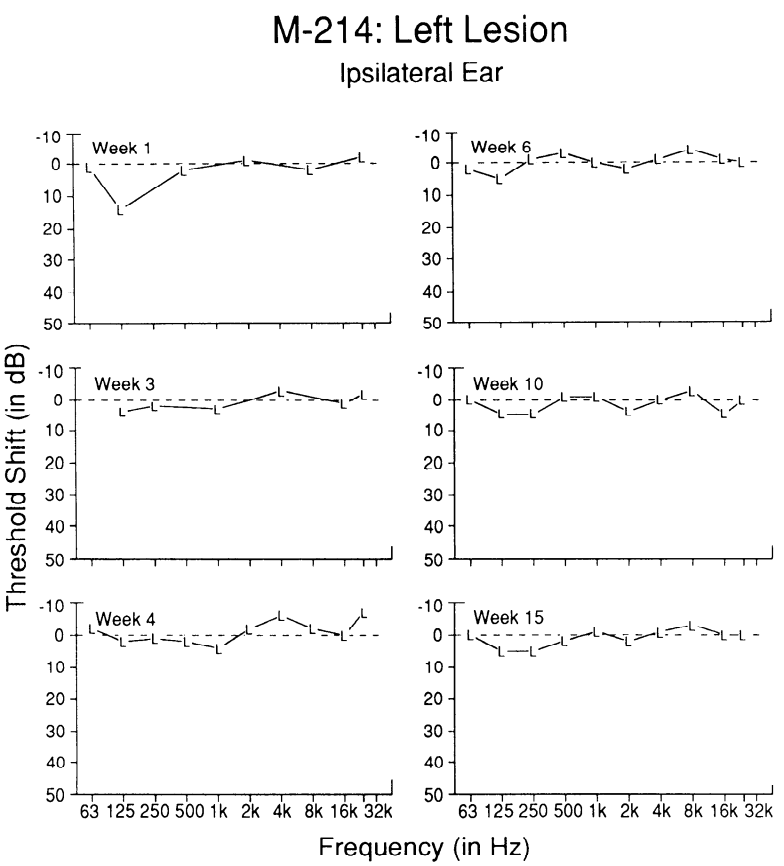

FIG. 8. Postoperative audiograms for the left (L) ear of *M-214*. Note the absence of a hearing loss in the ipsilateral ear.

preliminary threshold had been obtained, final threshold determination was conducted using the method of constant stimuli by presenting tones varying in intensity by 5-dB increments extending from 10 dB below to 10 dB above the estimated threshold. The trials at each intensity were presented in blocks of three to five warning trials, and the level of shock was varied to insure optimal performance. Threshold was defined as the lowest intensity that could be detected above the 0.01 level of chance, which was usually a score of 0.20. Chance level was calculated by comparing the occurrence of responses during the safe and warning trials with the use of the binomial distribution (Hays 1963).

Once initial preoperative thresholds had been determined, they were rechecked using the descending method of limits. This procedure consisted of decreasing intensity first in 10- and then 5-dB steps, with three to five warning trials given at each intensity, until the animal no longer responded to the stimulus. The thresholds obtained with this procedure were in close agreement with those obtained in the initial audiogram. This method was then used to rapidly assess postoperative thresholds. However, every stimulus for which a threshold shift was noted was tested at least once with the method of constant stimuli. No significant differences were noted between the results of the two procedures.

RESULTS

Anatomical results

The locus and extent of auditory cortex have been studied in the rhesus macaque by evoked response (Woolsey et al. 1972, 1982), microelectrode recordings (Merzenich and Brugge 1973), cytoarchitectural analysis (Galaburda and Pandya 1983; Pandya and Sanides 1973), and by tracing thalamocortical connections (Mesulam and Pandya 1973). Because Japanese and rhesus macaques are closely related and their brains are similar in appearance, information from these studies is useful in locating auditory cortex in the Japanese macaque.

Although the exact boundaries of auditory cortex can be difficult to define, both cytoarchitectural and electrophysiological studies have indicated that there is a central core area (primary auditory cortex) and a surrounding belt region of secondary auditory fields. Primary auditory cortex lies in the depths of the sylvian fissure on the middle one-third of the superior temporal plane and is surrounded by four secondary auditory fields (Fig. 1; for a review, see Heffner and Heffner 1986).

Other parts of the superior temporal gyrus may also be auditory. Auditory responses have been recorded on the superior temporal plane rostral to the secondary fields as well as on the lateral surface of the superior temporal gyrus, indicating that there are at least two other auditory fields (Merzenich and Brugge 1973). In addition, the cytoarchitectonics and cortical connections of the auditory fields suggest that all of the superior temporal gyrus may have auditory functions (Mesulam and Pandya 1973; Pandya and Sanides 1973). This conclusion is supported by behavioral evidence demonstrating that lesions restricted to the portion of the superior temporal gyrus rostral to the primary and surrounding auditory fields produce a hearing loss (Heffner and Heffner 1989b).

Although precise placement of auditory lesions requires prior electrophysiological mapping, the pattern of thalamic degeneration that follows cortical ablation gives a useful picture of the extent of a lesion (for details, see Heffner and

Heffner 1986). Ablation of primary auditory cortex results in severe degeneration of the anterior two-thirds of the principal division of the medial geniculate (GMp), with no noticeable degeneration in the magnocellular division (GMmc) or in the suprageniculate nucleus (SG). Ablation of the primary and surrounding secondary auditory fields results in severe degeneration throughout GMp, with the exception of the caudal tip, and partial degeneration of GMmc and SG. Finally, ablation of the entire superior temporal gyrus results in total degeneration of all of GMp, including the caudal tip, with severe degeneration in GMmc and SG.

EXTENT OF THE LESIONS. Cortical reconstruction and thalamic degeneration are illustrated for each of the four cases (Figs. 2–5). The lesions were confined to the superior temporal gyrus and differed primarily in the involvement of the rostral portion of the gyrus. All of the animals appeared to have complete lesions of the primary and surrounding auditory fields, with the exception of *M-267*, in which part of the rostral auditory field on the superior temporal plane may have been spared (Fig. 4).

Behavioral results

The lesions resulted in a deficit that appeared as a hearing loss in the ear contralateral to the lesion. There was no noticeable elevation of thresholds in the ipsilateral ear. The initial hearing loss was large and was followed by rapid but incomplete recovery, which left the animals with a small, permanent hearing loss.

The following is a description of each animal's hearing loss and the results of two tests concerning the nature of the deficit. The purpose of these additional tests was to determine if the hearing loss differed from the type of sensory deficit that would be expected to occur from direct damage to the ear alone.

MONKEY 207. Thresholds in the ear ipsilateral to the lesion were measured over a period of 16 wk and proved to be quite stable (Fig. 6). The thresholds varied from preoperative levels by −7 to +4 dB, with an average absolute deviation of +1.8 dB from preoperative baseline. Taking these thresholds as a sample of the normal variation in thresholds, a rank-ordering of the absolute deviations indicated

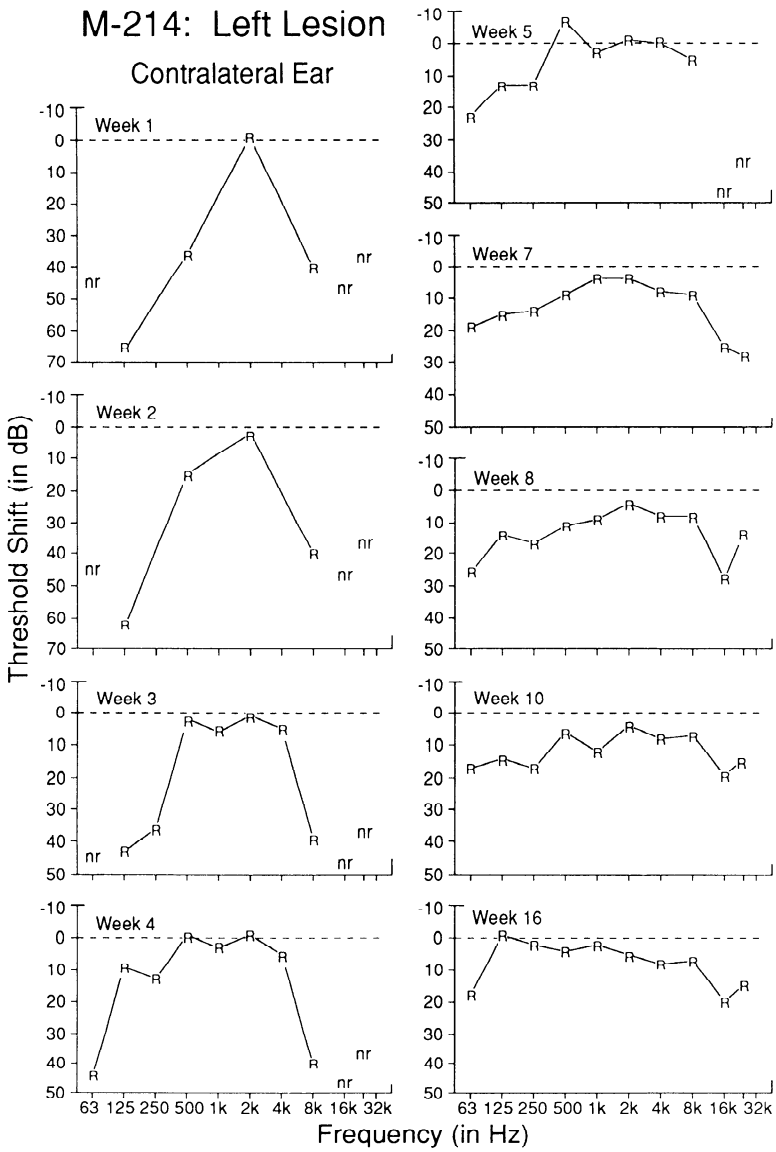

FIG. 9. Postoperative audiograms for the right (R) ear of *M-214*. Note the hearing loss in the contralateral ear. nr indicates that the animal was unable to respond to a tone at maximum intensity.

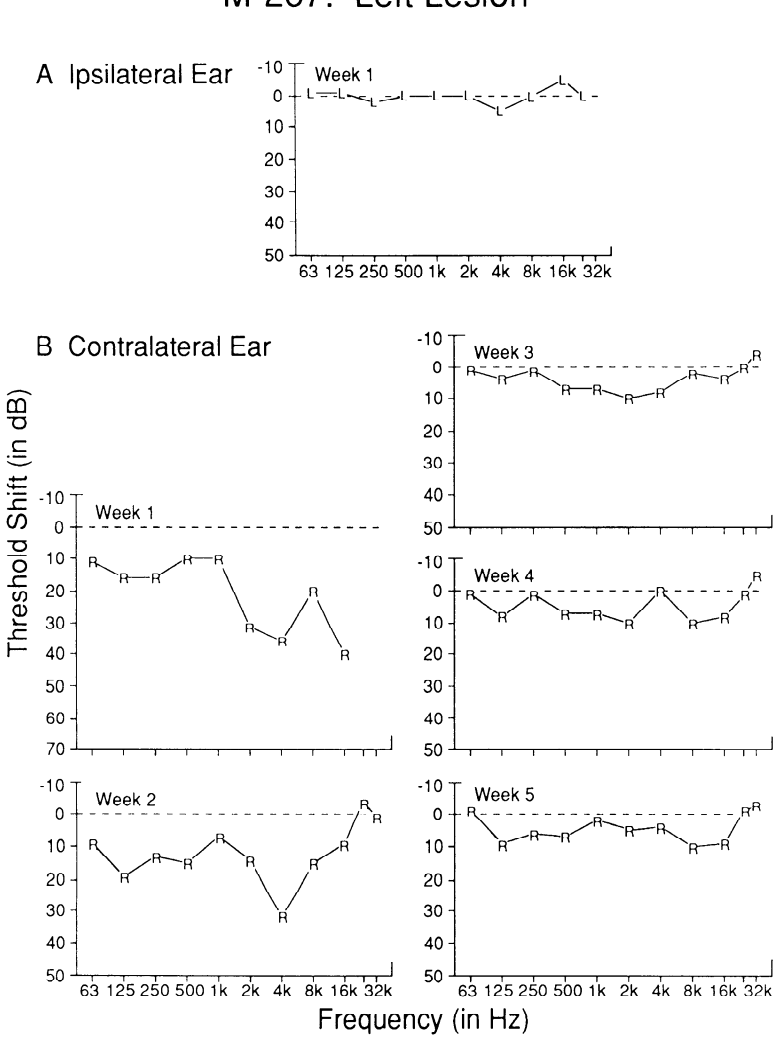

FIG. 10. Postoperative audiograms for the left (L) and right (R) ears of *M-267*. Note the hearing loss in the contralateral, but not the ipsilateral, ear.

that only those thresholds that deviated by >4 dB from preoperative baseline could be considered to be reliably deviant ($P < 0.05$).

Elevated thresholds were observed at all 10 frequencies in the contralateral ear, with the largest loss (45 dB) occurring at 16 kHz (Fig. 7, wk 2). Although there was some variability in thresholds, most gradually improved over time, with three (500 Hz, 2 kHz, and 16 kHz) returning to normal levels at the end of 15 wk.

MONKEY 214. Thresholds in the ear ipsilateral to the lesion varied from preoperative levels by −7 to +14 dB, with an average absolute deviation of +2.5 dB (Fig. 8). This sample of normal variation indicated that, for this monkey, only those thresholds which deviated by >5 dB could be considered to be reliably different ($P < 0.05$).

Elevated thresholds of ≤66 dB (at 125 Hz) were observed in the contralateral ear (Fig. 9). In contrast, no threshold shift was observed at 2 kHz. Again, thresholds improved over time, with those from 125 Hz to 2 kHz recovering to normal levels 16 wk after surgery.

MONKEY 267. Threshold shifts of ≤40 dB (at 16 kHz) were observed in the contralateral ear, whereas thresholds in the ipsilateral ear remained within 5 dB of preoperative levels (Fig. 10). This animal demonstrated the smallest hearing loss of any of the four monkeys, with 5 of the 11 thresholds returning to within 5 dB of preoperative thresholds by wk 5.

MONKEY 337. Threshold shifts of ≤68 dB (at 2 kHz) were observed in the contralateral ear, whereas thresholds in the ipsilateral ear remained within 5 dB of preoperative levels (Fig. 11). Substantial recovery occurred in this animal, with 6 of the 11 frequencies returning to within 5 dB of preoperative thresholds by wk 6.

NOISE THRESHOLDS. The contralateral hearing loss could be demonstrated with noise as well as with tones. As shown in Fig. 12, the two monkeys tested had raised thresholds in the contralateral ear for broadband noise, whereas there was little change in the ipsilateral ear. Because most of the energy in the noise spectrum was <10 kHz, these thresholds probably reflect the low- and middle-frequency portions of the animals' audiograms.

SENSORY VERSUS NONSENSORY DEFICIT. Although the hearing losses exhibited by the monkeys can be interpreted as a sensory deficit, it is not impossible that the results were because of some nonsensory factor. For example, the cortical lesions may have affected the "listening" ability of the

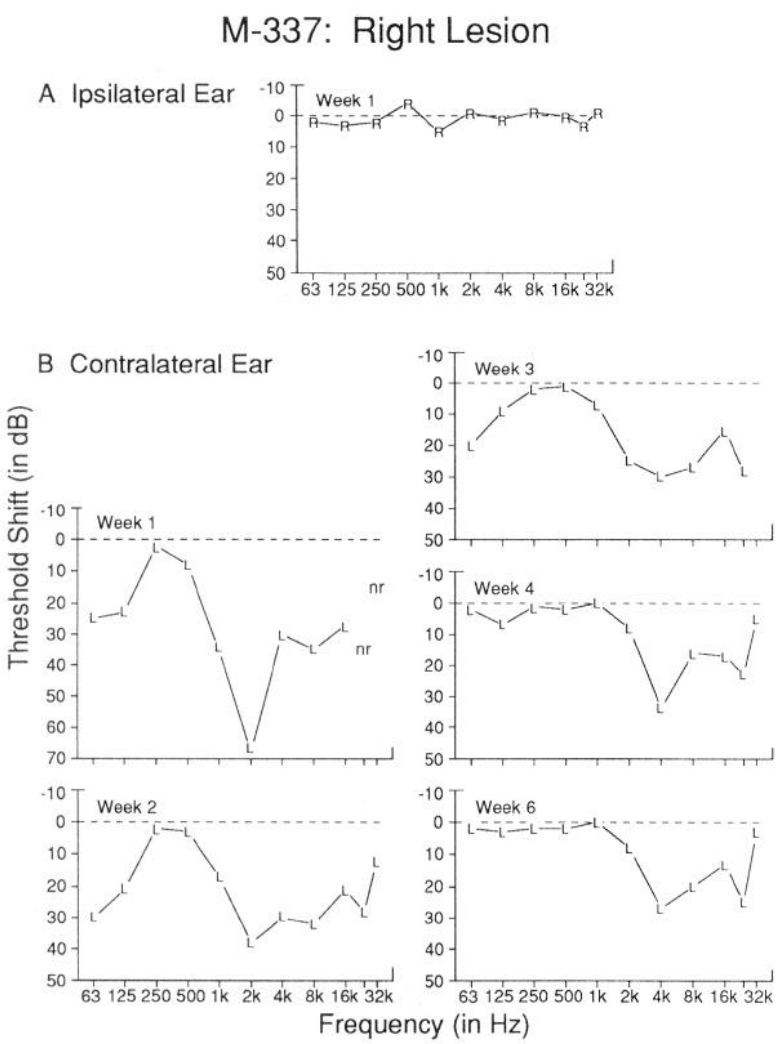

FIG. 11. Postoperative audiograms for the left (L) and right (R) ears of *M-337*. Note the hearing loss in the contralateral, but not the ipsilateral, ear. nr indicates that the animal was unable to respond to a tone at maximum intensity.

animals. Thus the question arises as to whether the deficit might be better described in terms of "vigilance," "auditory attention," or "sensory neglect."

Recently it has been noted that nonsensory deficits can occur as the result of auditory system lesions and that such deficits can sometimes be identified by examining the slope of the psychophysical function (Masterton and Granger 1988). That is, the performance of a well-trained animal usually remains high until the intensity of a stimulus approaches threshold, at which point performance falls rapidly to chance. Typically, the slope of the psychophysical function is fairly steep, with performance falling from asymptote to chance within 10 dB. However, a nonsensory deficit may result in a more gradual psychophysical function in that an animal's performance declines at higher intensities, whereas the intensity at which chance performance is reached remains unchanged.

The monkeys' pre- and postoperative psychophysical functions were analyzed by determining the range of intensities over which performance declined from 1.0 (perfect performance) to 0.10 (chance performance). As shown in Fig. 13, the psychophysical functions were fairly steep, averaging from 5.3 to 7.4 dB. More importantly, the lesions had no significant effect on the slopes of the psychophysical functions. Thus an analysis of the psychophysical functions

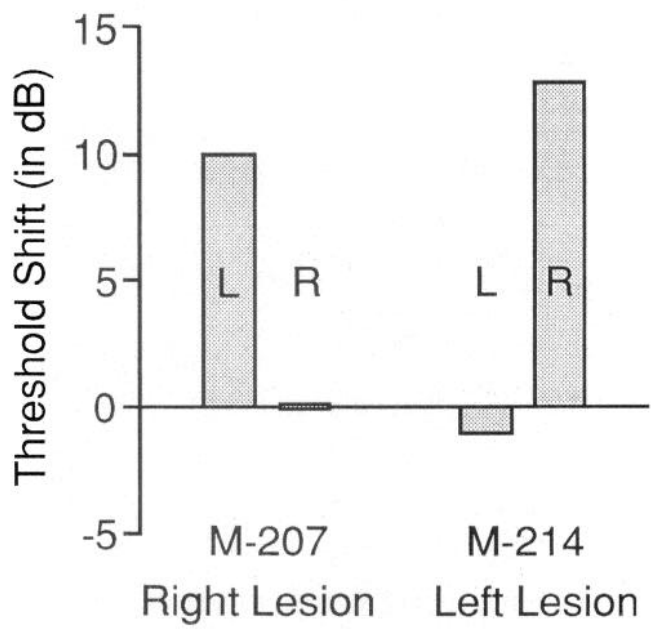

FIG. 12. Shift in noise thresholds for 2 monkeys (*M-207* and *M-214*). The animals' thresholds for noise increased in the ear contralateral to the lesion, whereas ipsilateral thresholds showed little change. Thresholds taken in the 2nd wk after surgery. L, left ear; R, right ear.

did not reveal any effect that would distinguish the hearing loss from a sensory deficit such as that arising from direct damage to the ear alone.

CONTRALATERAL EAR VERSUS CONTRALATERAL HEMIFIELD DEFICIT. So far we have described the deficit as a hearing loss in the ear contralateral to the lesion. Indeed, such a description is consistent with the view that although both ears are represented in each hemisphere, the contralateral ear is more "strongly" represented. However, an alternative view is that it is the contralateral *sound field*, rather than the contralateral *ear*, that is represented in each hemisphere (Glendenning and Masterton 1983; Phillips and Gates 1982). This view is derived from the observations that the majority of cells in auditory cortex are driven by sounds in the contralateral field and that unilateral ablation results in sound-localization deficits confined to the hemifield contralateral to the lesion (e.g., Middlebrooks and Pettigrew 1981; Jenkins et al. 1982, 1984).

Given this view, it is conceivable that the hearing loss observed in the monkeys might be a contralateral field, as opposed to a contralateral ear deficit. If so, then one would expect to find a hearing loss for sounds that reach both ears but are localized to the hemifield contralateral to the lesion. Such a condition would exist for sounds presented via a loudspeaker located in the contralateral hemifield or for dichotic stimuli that are lateralized to the contralateral ear with the use of binaural time- or intensity-difference cues.

To investigate this possibility two of the monkeys (*M-207* and *M-214*) were tested during the second postoperative week for their ability to detect 8-kHz tone pips presented either individually to each ear (monaural condition) or to both ears simultaneously (binaural condition). The intensities of the tones were set relative to preoperative thresholds (i.e., sensation level or SL) at 15-dB SL in the ear ipsilateral to the lesion and 35-dB SL in the ear contralateral to the lesion. In the monaural condition, the animals could hear the 15-dB tone in the ipsilateral ear but could not hear the 35-dB tone in the contralateral ear (Table 1).

The next step was to present both tones simultaneously, i.e., the binaural condition. Because of slight differences between the preoperative thresholds of each animal's ears, the 15-dB/35-dB SL settings resulted in an absolute intensity difference between the two ears of 21 dB (*M-207*) and 22 dB (*M-214*). These are large binaural intensity differences, which in normal monkeys produce a perception equivalent to the presentation of a tone to one ear only (Houben and Gourevitch 1979).

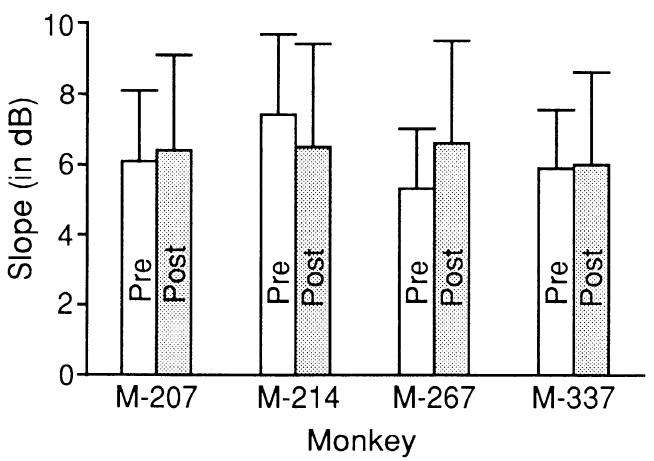

FIG. 13. Average and standard deviation of the pre- and postoperative slopes of the psychophysical functions for the 4 monkeys (*M-207, M-214, M-267,* and *M-337*). There was no significant change in the slopes of the functions after surgery.

TABLE 1. *Effect of unilateral cortical lesions on the ability to detect 8-kHz tones presented monaurally and binaurally*

Animal	Monaural Stimulation: Ipsilateral ear, 15 dB SL	Monaural Stimulation: Contralateral ear, 35 dB SL	Binaural Stimulation, Contralateral Image, 15 dB/35 dB SL
M-207	1.00*	0.09	1.00*
M-214	0.80*	0.00	0.80*

Tone intensity relative to preoperative thresholds (SL, sensation level). Binaural stimulation consisted of simultaneous presentation of the tones with a 20 dB SL intensity difference. Note that the animals had a hearing loss for tones presented to the ear contralateral to the lesion but not for a binaural stimulus that would normally be lateralized to that ear. *Statistically reliable detection ($P < 0.01$).

In contrast to the monaural condition, the monkeys were able to detect the binaural signal easily, even though normally it would have been lateralized to the contralateral ear. Indeed, the fact that their scores were identical to those when the 15-dB tone was presented monaurally to the ipsilateral ear suggests that their binaural performance was based on the ipsilateral ear alone. This result indicates that the animals had a hearing loss for sounds presented to the contralateral ear, but not for binaural stimuli that normally would be lateralized to that ear. The significance of this result is addressed in the DISCUSSION.

DISCUSSION

The results show that unilateral ablation of auditory cortex leads to a hearing loss in the contralateral ear with no noticeable effect on the ipsilateral ear. This hearing loss is not limited to the detection of tones but can be demonstrated with broadband noise as well. The following is a discussion of some of the noteworthy features of the hearing loss, including the rapid partial recovery of sensitivity, the observation that the loss resembles a sensory deficit, and the variation in the magnitude of the loss with frequency.

Recovery

RECOVERY RATE. With a few exceptions the animals' thresholds showed steady improvement over time. Most of the recovery took place in the first 3–5 wk, during which thresholds showed rapid improvement (Fig. 14). This initial period of recovery was followed by an abrupt leveling off in the recovery rate, with subsequent thresholds improving on average by <5 dB. Although it is possible that further recovery would have occurred after 16 wk, the slope of the recovery functions shown in Fig. 14 suggests that such recovery would probably be incomplete.

BASIS OF RECOVERY. There are a number of explanations that have been advanced to account for recovery of function that could be applied to the present situation (e.g.,

Finger et al. 1988). Such explanations include the temporary disruption of neural activity due to surgery (shock), the disruption of neural activity in other auditory centers brought on by the sudden removal of cortical input (diaschisis), incomplete lesions (sparing), recovery mediated by auditory cortex in the intact hemisphere, and recovery mediated by other cortical areas.

Much of the recovery seen here appears to be mediated by auditory cortex in the intact hemisphere. This is demonstrated by the fact that bilateral auditory lesions result in a greater initial hearing loss with substantially less recovery than is seen after unilateral lesions (Heffner and Heffner 1986). Thus the presence of intact auditory cortex in the other hemisphere lessens the initial severity of the hearing loss and provides for greater recovery. Subsequent removal of this cortex can be viewed as "reinstating" the hearing loss in the previously affected ear (as well as resulting in a hearing loss in the previously normal ear).

The present results indicate that each hemisphere is primarily involved with the contralateral ear. However, after unilateral ablation, the intact hemisphere can rapidly become involved with the detection of sound in the ipsilateral ear. The question arises, then, as to whether a hemisphere normally has a secondary role in detecting sounds in the ipsilateral ear or whether it acquires this role as a new function. That is, is the recovery mediated by neurons that already receive input from the ipsilateral ear, or are neurons previously unresponsive to ipsilateral stimulation acquiring a new function? In either case, the question also arises as to whether the increased responsibilities of the intact hemisphere would result in a noticeable decrease in its ability to process input from the contralateral ear.

Another possible mechanism in the recovery of absolute thresholds is sparing. It has previously been demonstrated that partial bilateral auditory cortex lesions result in smaller deficits than larger lesions (Heffner and Heffner 1989b). This fact is also evident in the present report, as the animal with the smallest lesion (*M-267*) showed the smallest deficit (cf. Fig. 14). Although the simplest interpretation is that animals with partial lesions show better recovery simply because the lesions resulted in a smaller initial deficit, it opens the possibility that the spared cortex may assume some of the functions of the cortex that was removed.

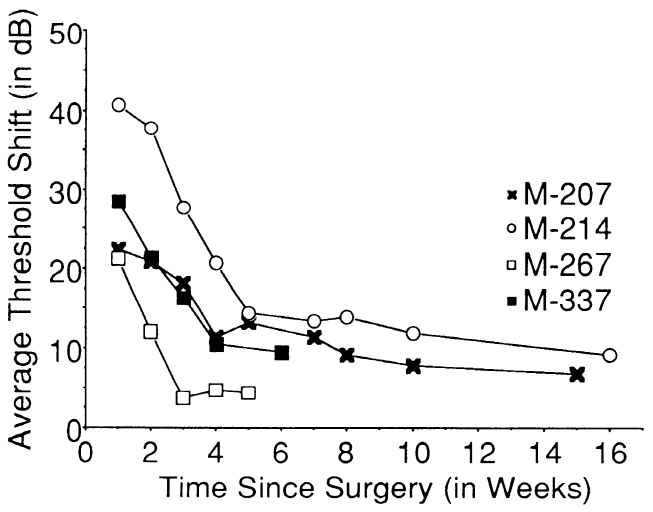

FIG. 14. Average threshold shifts of the 4 monkeys (*M-207, M-214, M-267,* and *M-337*) plotted over time. Maximal recovery took place within 3–5 wk.

Nature of the cortical deficit

In analyzing the nature of the hearing loss, we considered the possibility that the deficit might be better described in nonsensory terms such as attention, vigilance, or sensory neglect. Recently, Masterton and Granger (1988) have noted that a nonsensory deficit can significantly change the slope of the psychophysical function. They point out that although the animal may be equally *sensitive* after a lesion, it may *not* be equally *reliable*. The effect of such a deficit would be to make the slope of the psychophysical function less steep. This is because the animal's postoperative performance would decline at higher stimulus intensities, whereas the point at which performance falls to chance would shift little.

Close examination of the monkeys' performances gave no evidence of a nonsensory deficit. First, the thresholds were defined in terms of the level at which performance fell to chance, a definition which Masterton and Granger point out is relatively immune to nonsensory changes. Second, the slopes of the psychophysical functions did not show any significant change after surgery. Thus the hearing loss does not seem to be the result of a nonsensory deficit, nor, for that matter, can it be described as a combined sensory/nonsensory deficit. In addition, the hearing loss could be demonstrated with broadband noise, indicating that it was not limited to certain types of sounds, such as pure tones, that might be less likely to attract the animal's attention. Thus we currently have no reason to reject the conclusion that auditory cortex lesions in macaques result in a deficit that closely resembles a sensory hearing loss.

A second question was whether the hearing loss was for the contralateral ear or for sounds arising from the contralateral hemifield. This question was addressed by testing the animals with binaural tone pips that normally would be lateralized to the contralateral ear, but that monaural testing had indicated were inaudible to that ear. Failure to detect this binaural stimulus would indicate that the animals had a contralateral field deficit, whereas successful detection of the stimulus would suggest that the hearing loss was specific to the contralateral ear.

The fact that the animals easily detected the binaural tones indicated that they were responding to the tone in the ipsilateral ear. This result suggests that the animals had not lost the ability to detect sounds emanating from the hemifield contralateral to the lesion but that they simply had a hearing loss in the contralateral ear.

However, this result does not necessarily mean that each cortex is primarily concerned with the contralateral ear as opposed to the contralateral hemifield. This is because the lateralization test rests on at least two assumptions that may not be valid. The first is that a lateralized sound image is produced by the brain stem, perhaps at the level of the superior olivary nuclei, where input from the two ears first converges. Although the brain stem is *necessary* for the perception of the location of a sound, it does not follow that it is *sufficient*. It is well established that auditory cortex is necessary for the perception of auditory location (Mas-

terton and Diamond 1964), and it may be that the interaural intensity disparity, although sufficient to produce a lateralized image in normal monkeys, failed to produce a lateralized image in these animals.

The second assumption is that the brain stem, in particular the superior olivary nucleus, was functioning normally in these animals. Although there do not seem to be any major descending connections between auditory cortex and the superior olivary nuclei (Harrison and Howe 1975), the possibility exists that removal of cortex could affect the chain of descending influence on the lower brain stem and disrupt the normal processing of locus cues. If so, then normal neuronal responses to a binaural sound might be disrupted at the level of the brain stem after cortical lesions.

However, regardless of whether a hemisphere is concerned primarily with the contralateral ear or contralateral hemifield, the fact remains that an animal with a unilateral auditory cortex lesion would not be expected to be insensitive to sounds arising in the contralateral hemifield as long as they were of sufficient intensity to reach the opposite ear.

The analysis of the psychophysical functions and the results of the binaural test thus indicate that the hearing loss most closely resembles a sensory deficit such as that arising from direct damage to the ear alone. Indeed, because of this similarity the question arises as to whether the deficit was due to some change in peripheral function. Although this question cannot be conclusively answered at this time, it should be noted that auditory brain stem response latency-intensity functions performed on these monkeys after bilateral ablation (which resulted in a large permanent hearing loss) indicated that they had normal peripheral auditory sensitivity (Hood and Heffner 1989). This finding suggests that the observed hearing loss was not because of any change in cochlear functioning, which might result from disruption of the descending influence of the cortex, nor to accidental damage to the ear itself.

Analysis of the hearing loss

VARIATION IN HEARING LOSS WITH FREQUENCY. The question arises as to whether there is any systematic variation in the hearing loss with frequency. Examination of the audiograms (Figs. 7, 9–11) reveals no obvious pattern, as the maximum hearing loss could occur at low frequencies (*M-214*), in the midrange (*M-337*), or at high frequencies (*M-207*). The only observable pattern is that the lower one-half of the audiogram (63 Hz to ~1 kHz) is in most cases less affected than higher frequencies, an effect that has been noted to occur after bilateral auditory cortex lesions (Heffner and Heffner 1986, 1989b).

The fact that the hearing loss varied greatly from one frequency to the next is curious. Auditory cortex is tonotopically organized, and unilateral ablation of a cortical zone representing a restricted band of frequencies has been shown to affect the localization of sound in the contralateral hemifield, whereas complete lesions totally abolish the ability to localize sound in the contralateral hemifield (Jenkins et al. 1982, 1984). Thus, although partial lesions might be expected to affect the hearing of some frequencies while sparing others, the lesions in this study are, to the best of our knowledge, reasonably complete and would be expected to affect all frequencies equally.

A possible explanation of such "frequency sparing" may lie in the representation of the ears in the cortex. The prevailing view is that both ears are represented in each hemisphere, with the contralateral ear represented more strongly (a view that is supported by the present study). It is the bilateral representation, however, that accounts for the fact that the hearing loss after a unilateral lesion is much less severe than that following a bilateral lesion—the intact hemisphere being able to mediate the detection of sound in the ear contralateral to the lesion. However, it is conceivable that the degree of bilateral representation of an ear could vary with frequency. If so, then the uneven effect of the lesions across frequency could be the result of some frequencies being more strongly represented in the ipsilateral hemisphere than others.

RELATION OF HEARING LOSS TO LESION SIZE. Previous studies of the effect of bilateral auditory cortex lesions have indicated that the size and location of a lesion determines the severity of a bilateral hearing loss. Bilateral lesions that include the entire superior temporal gyrus result in a larger hearing loss than do subtotal lesions (cf. Heffner and Heffner 1986, 1989b). Bilateral lesions restricted to the primary and secondary auditory areas result in a smaller hearing loss, as do lesions of the superior temporal gyrus ventral to these areas. However, lesions of the caudal tip of the superior temporal gyrus have little, if any, effect on thresholds.

Although there was little variation in the size and placement of the lesions, the lesion in one monkey, *M-267*, spared more of the superior temporal gyrus rostrally. This animal also had the smallest hearing loss, an observation that supports the idea that the rostral portion of the superior temporal gyrus has auditory functions.

Relevance to human unilateral temporal lobe lesions

Before generalizing the present results to humans, it is important to note that the effect of cortical ablation on hearing varies between species. Total ablation of neocortex has no effect on absolute thresholds in opossums (Ravizza and Masterton 1972), whereas auditory cortex ablation in cats and ferrets results in only small elevations in threshold (Cranford and Igarishi 1977; Kavanagh and Kelly 1988). As a result, it is necessary to use caution in generalizing the results of one species to another.

There are, however, major functional as well as anatomic and physiological similarities between the brains of humans and macaques that suggest that the present results may have significance for humans. Of particular relevance is the fact that bilateral ablation of auditory cortex in macaques and humans results in a hearing loss in both ears, i.e., cortical deafness (for a review, see Heffner and Heffner 1986). As a result, it would be expected that unilateral auditory cortex lesions would also have the same effect in both species.

Although a large number of human unilateral temporal lobe cases have been studied, very little has been written concerning the effect of such lesions on absolute thresholds. The main exception has been the study by Karp and his colleagues, which found a statistically significant contralateral hearing loss in hemiplegic patients (1969). However, the general view has been that although unilateral

temporal lobe lesions may result in a hearing loss, the loss is usually not substantial and may not be permanent (e.g., Chandler and Sedge 1987; Jerger et al. 1969).

The lack of attention given to the contralateral hearing loss in humans is understandable in view of the magnitude of the deficit and the effect of lesion size. In the present study our animals received large auditory cortex lesions, and we occasionally observed threshold shifts of ≤68 dB, but most initial shifts were <40 dB. Furthermore, the animals showed rapid recovery, and within a few weeks the shifts had dropped to <30 dB. Because we had recent preoperative audiograms on each animal, we were able to detect shifts of <5 dB. However, such an opportunity is rare in the clinic.

In the case of human patients, lesions may spare part of auditory cortex, with the result that any hearing loss is likely to be small and recovery more complete. Furthermore, the patients are often elderly and may have hearing losses unrelated to their lesions. Because recent premorbid audiograms are virtually nonexistent, small changes in threshold are not detectable. Finally, because the emphasis is often on determining whether a patient should be considered "disabled," deviations from normal hearing levels are not considered significant unless they exceed 26 dB, and hearing losses of 27–40 dB are labeled as "mild" (Downs 1976). Thus a hearing loss of the magnitude seen in monkeys would probably not be considered worthy of note in a typical human patient.

In conclusion, unilateral cortical damage has been linked in humans to contralateral hearing loss. That this phenomenon has not been well studied is probably because of the difficulties involved in detecting small hearing losses and then associating them with cortical lesions. Because it is well established that bilateral auditory cortex damage results in cortical deafness in both humans and monkeys, it seems reasonable to expect that unilateral damage to auditory cortex in humans also results in a contralateral hearing loss similar to that observed in monkeys.

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REFERENCES

CHANDLER, D. AND SEDGE, R. K. Pure-tone sensitivity and speech recognition findings following head injury. *Semin. Hear.* 8: 241–251, 1987.

CRANFORD, J. L. AND IGARISHI, M. Effects of auditory cortex lesions on temporal summation in cats. *Brain Res.* 136: 559–564, 1977.

DOWNS, M. P. The handicap of deafness. In: *Hearing Disorders,* edited by J. L. Northern. Boston, MA: Little, Brown, 1976, p. 195–206.

FERRIER, D. The Croonian Lecture. Experiments on the brain of monkeys (2nd ser.). *Philos. Trans. R. Soc. Lond. B Biol. Sci.* 165: 433–488, 1876.

FINGER, S., LEVERE, T. E., ALMLI, C. R., AND STEIN, D. G. (Editors) *Brain Injury and Recovery.* New York: Plenum, 1988.

GALABURDA, A. M. AND PANDYA, D. N. The intrinsic architectonic and connectional organization of the superior region of the rhesus monkey. *J. Comp. Neurol.* 221: 169–184, 1983.

GLENDENNING, K. K. AND MASTERTON, R. B. Acoustic chiasm: efferent projections of the lateral superior olive. *J. Neurosci.* 3: 1521–1537, 1983.

HARRISON, J. M. AND HOWE, M. E. Anatomy of the descending auditory system (mammalian). In: *Handbook of Sensory Physiology. Auditory System,* edited by W. D. Keidel and W. D. Neff. New York: Springer-Verlag, 1975, vol. V, pt. 1, p. 363–388.

HAYS, W. L. *Statistics for Psychologists.* New York: Holt, Rinehart, & Winston, 1963.

HEFFNER, H. E. AND HEFFNER, R. S. Hearing loss in Japanese macaques following bilateral auditory cortex lesions. *J. Neurophysiol.* 55: 256–271, 1986.

HEFFNER, H. E. AND HEFFNER, R. S. Cortical deafness cannot account for the inability of Japanese macaques to discriminate species-specific sounds. *Brain Lang.* 36: 275–285, 1989a.

HEFFNER, H. E. AND HEFFNER, R. S. Effect of restricted cortical lesions on absolute thresholds and aphasia-like deficits in Japanese macaques. *Behav. Neurosci.* 103: 158–169, 1989b.

HOOD, L. J. AND HEFFNER, H. E. Auditory evoked potentials in normal and lesioned Japanese macaques. *Abstr. Assoc. Res. Otolaryngol. Twelfth Midwinter Research Meeting, St. Petersburg Beach, FL,* 1989, p. 26–27.

HOUBEN, D. AND GOUREVITCH, G. Auditory lateralization in monkeys: an examination of two cues serving directional hearing. *J. Acoust. Soc. Am.* 66: 1057–1063, 1979.

JENKINS, W. M. AND MASTERTON, R. B. Sound localization: effects of unilateral lesions in central auditory system. *J. Neurophysiol.* 47: 987–1016, 1982.

JENKINS, W. M. AND MERZENICH, M. M. Role of cat primary auditory cortex for sound-localization behavior. *J. Neurophysiol.* 52: 819–847, 1984.

JERGER, J., WEIKERS, N. J., SHARBROUGH III, F. W., AND JERGER, S. Bilateral lesions of the temporal lobe: a case study. *Acta Oto-Laryngol.* 258, *Suppl:* 1–51, 1969.

KARP, E., BELMONT, I., AND BIRCH, H. G. Unilateral hearing loss in hemiplegic patients. *J. Nerv. Ment. Dis.* 148: 83–86, 1969.

KAVANAGH, G. L. AND KELLY, J. B. Hearing in the ferret (*Mustela putorius*): effects of primary auditory cortical lesions on thresholds for pure tone detection. *J. Neurophysiol.* 60: 879–888, 1988.

MASTERTON, R. B. AND BERKLEY, M. A. Brain function: changing ideas on the role of sensory, motor, and association cortex in behavior. *Annu. Rev. Psychol.* 25: 277–312, 1974.

MASTERTON, R. B. AND DIAMOND, I. T. Effects of auditory cortex ablation on discrimination of small binaural time differences. *J. Neurophysiol.* 27: 15–36, 1964.

MASTERTON, R. B. AND GRANGER, E. M. Role of the acoustic striae in hearing: contribution of dorsal and intermediate striae to detection of noises and tones. *J. Neurophysiol.* 60: 1841–1860, 1988.

MERZENICH, M. M. AND BRUGGE, J. F. Representation of the cochlear partition on the superior temporal plane of the macaque monkey. *Brain Res.* 50: 275–296, 1973.

MESULAM, M.-M. AND PANDYA, D. N. The projections of the medial geniculate complex within the sylvian fissure of the rhesus monkey. *Brain Res.* 60: 315–333, 1973.

MIDDLEBROOKS, J. C. AND PETTIGREW, J. D. Functional classes of neurons in primary auditory cortex of the cat distinguished by sensitivity to sound location. *J. Neurosci.* 1: 107–120, 1981.

PANDYA, D. N. AND SANIDES, F. Architectonic parcellation of the temporal operculum in rhesus monkey and its projection pattern. *Z. Anat. Entwicklungsgesch.* 139: 127–161, 1973.

PHILLIPS, D. P. AND GATES, G. R. Representation of the two ears in the auditory cortex: a re-examination. *Int. J. Neurosci.* 16: 41–46, 1982.

RAVIZZA, R. J. AND MASTERTON, B. Contribution of neocortex to sound localization in opossum (*Didelphis virginiana*). *J. Neurophysiol.* 35: 344–356, 1972.

WOOLSEY, C. N. Tonotopic organization of the auditory cortex. In: *Physiology of the Auditory System,* edited by M. B. Sachs. Baltimore, MD: National Educational Consultants, 1972, p. 271–282.

WOOLSEY, C. N. AND WALZL, E. M. Cortical auditory area of *Macaca mulatta* and its relation to the second somatic sensory area (Sm II). In: *Cortical Sensory Organization: Multiple Auditory Areas,* edited by C. N. Woolsey. Clifton, NJ: Humana, 1982, vol. 3, p. 231–256.