D-18

19

ELECTRICAL RESPONSES TO ACOUSTIC CLICKS IN MONKEY: EXTENT OF NEOCORTEX ACTIVATED[1]

KARL H. PRIBRAM, BURTON S. ROSNER, AND WALTER A. ROSENBLITH

*Department of Neurophysiology, Institute of Living, Hartford, Conn.; Department of
Psychology, Yale University, New Haven, Conn.; and the Research Laboratory of
Electronics, Massachusetts Institute of Technology, Cambridge, Mass.*

THE POSTERIOR HALF of the cortex of the supratemporal plane in the monkey has been related to the auditory system by anatomical and electrophysiological techniques (2, 11, 15, 20). One investigation has indicated that the posterior insula also is activated by stimulation of the auditory system (25, 27). Because of the inaccessibility of the supratemporal plane, experimenters usually resect the inferior portions of the frontal and parietal lobe in order to expose the cortex of the inferior bank of the sylvian fissure. In recent experiments on the cortex of the operculum, insula, and supratemporal plane, the customary resection was abandoned and the sylvian fissure was opened by gentle dissection and retracted by packing (16). The present study was undertaken in order to utilize this procedure in a reinvestigation of the extent of the cortex of monkey activated by acoustic stimulation. The unexplained difference in size between the relatively large area of "auditory cortex" in rodent and carnivore and the comparable area in primate suggested that this new research might prove fruitful.

Maps may vary with (i) the dimension of the stimulus or (ii) the criteria of response. For the stimulus, clicks were chosen because they evoke the most nearly consistent electroneural response and appear to activate the cortex extensively. With electrical responses the experimenters must determine which aspects of the responses are to be employed in mapping the cortex. (Since the techniques chosen were used to measure the activity of large populations of responding elements, all-or-none measurements could be made only when "all" and "none" were delimited.) In this study the effect of acoustic clicks of *various* intensities on the electrical activity of the neocortex of the monkey was mapped in terms of *various* criteria. The resulting congruence and incongruence of maps provides topics for discussion.

MATERIALS AND METHODS

Seven preadolescent rhesus (*Macaca*) and mangabey (*Cercocebus*) monkeys were the subjects of these experiments. Both cerebral hemispheres of each monkey were used. The

anesthetic was Dial, administered intraperitoneally in an initial dose of 0.7 cc./kg. body weight, and supplemented with 0.2–0.4 cc. as needed to maintain a relatively flat baseline potential recorded from the cortex. The animals were kept warm (rectal temperature between 35.5 and 37 C.) by a heating pad. Fluid and salt balance was maintained by subcutaneous injection of normal saline solution; penicillin was administered intramuscularly whenever the experiment lasted more than 12 hours.

Three types of surgical procedure were employed. (i) In two experiments the lateral surface of the cerebral hemispheres was exposed and recordings were made, first through the intact dura, and then from the pial surface which was kept moist. (ii) In most of the experiments, the banks of the sylvian fissure were gently separated immediately after the dura was opened; between recordings, the exposure of the supratemporal plane, insula, and operculum was maintained by packing the opened fissure with cotton; during recordings, cotton wicks prevented the accumulation of cerebrospinal fluid in the dependent parts of the exposure. (iii) In one monkey, procedure (ii) was followed by subpial resection of the supratemporal plane and superior temporal gyrus, and the recording from the insula, operculum, and parietal surface was resumed. A similar resection was carried out aseptically six weeks prior to the electrophysiological experiment on three other hemispheres (two monkeys). At the time of the acute procedure no additional cortical dissection was performed. In four animals peripheral responses were recorded from an electrode in the cerebellopontine angle (18).

Control procedures included: (i) recording from the peripheral monitoring electrode, (ii) cutting the eighth nerve, (iii) determining the effect of tactile stimulation on the cortical response, both before and after eighth nerve section, and (iv) resection of the supratemporal cortex. The procedure for controlling and delivering the acoustic stimulus has been described elsewhere in detail (19). When electrical square pulses of 0.1 msec. duration are delivered to PDR-10 (Permoflux) earphones brief acoustic pulses ("clicks") are generated. Flexible plastic tubes lead the stimuli to the monkey's external meatus. The intensity of these stimuli is controllable by attenuators. The recording electrode was a platinum wire #34. Maps were made with unipolar recording, the indifferent electrode placed in several different scalp positions. When abrupt potential changes appeared, electrode placements were checked with bipolar recording. The amplifier, oscilloscope, and recording camera are the same as those described by Rosenzweig and Rosenblith (19). At each electrode placement 10–20 consecutive records were taken. The amplitudes and latencies of the major deflections were measured and the median values were mapped. The median was chosen as a representative measure of central tendency in distributions that include extreme values.

After each cortical resection, the brains were fixed (formalin), dehydrated in alcohols, imbedded in celloidin and sectioned serially. Representative cross-sections and reconstructions are presented. In addition, thalamic degeneration was analyzed and charted for the chronic preparations.
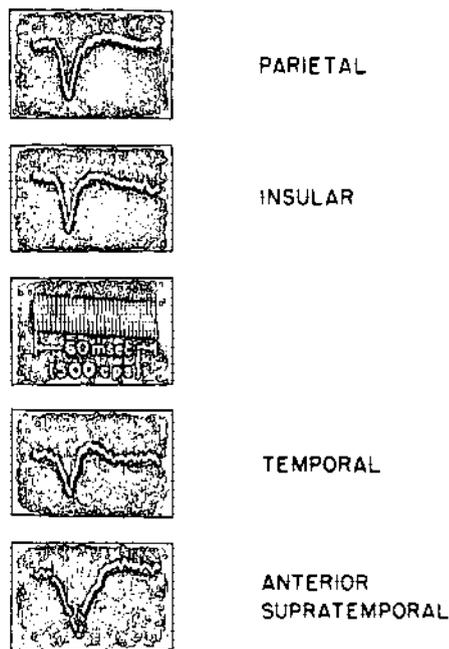
RESULTS

Figure 1 shows the potential changes evoked by acoustic clicks recorded at various cortical locations. These recordings were obtained with unipolar electrodes. When bipolar electrodes were used with one electrode on the non-responsive cortex, the amplitude of the response was slightly reduced; latencies appeared to remain the same. When bipolar recordings were made with both electrodes on adjacent responsive cortical points, the experimenters observed no potential deflection on the oscilloscope face.

Figure 2 shows two maps made with our most intense click stimuli (approximately 70 db above human threshold). The criterion of response employed was the presence of any consistently detectable potential change recorded with a unipolar electrode. Two additional maps, made without opening the sylvian fissure, are shown in Fig 3. These maps indicate the variability in the extent of response among the animals. This variability in the loca-

tion at which definite responses could be elicited appeared to have no correlation with depth of anesthesia, although the barely detectable responses (triangles) disappeared when anesthesia was deepened. When Bremer (5) mapped the extent of the cat's cortex responsive to acoustic stimulation,

RESPONSES TO CLICKS FROM VARIOUS LOCATIONS ON MONKEY CORTEX

PARIETAL

INSULAR

TEMPORAL

ANTERIOR SUPRATEMPORAL

M-103
1/19/52

Fig. 1. Oscilloscope tracings of responses to acoustic clicks from parietal, insular, temporal and anterior supratemporal locations (M103—1/19/52).

he found a similar sharpening in the boundary of the area responsive under anesthesia. In his experiments, however, definite responses were evoked from approximately the same extent of cortex in both anesthetized and unanesthetized preparations. On the other hand, the extent of the area activated does depend on the general condition of the animal, especially body temperature. Whenever the rectal temperature of the monkey dropped below 35°C. we observed a definite constriction in the extent of cortex activated.

Thresholds were determined at approximately 12 of the 60 "definite" points mapped. No difference in threshold intensity was found among cortical points. When the animals were in good condition this threshold was approximately the same as man's. Tunturi (22) has reported a difference in the effect on the cortical response of dog of stimulating the ipsilateral and contralateral ears. In the present experiment little difference would be observed in the extent of activated area, regardless of which ear was stimulated (Fig. 3). The definite precentral responses found occasionally in several animals (Fig. 2), were evoked only by contralateral stimulation.

An attempt was made to map the amplitude of the initial abrupt potential deflection. However, because amplitude is so sensitive to differences in the level of anesthesia, the contact and impedance of the electrode, the general state of the animal, and the length of exposure of the cortex, the values obtained over the course of an experiment were not comparable. In general the amplitudes recorded from the supratemporal plane, the insula, and the superior temporal convolution were greater than those recorded from the operculum and parietal surfaces.

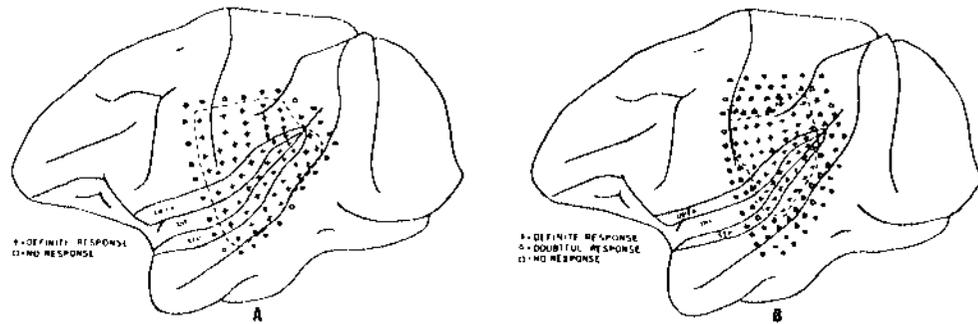Latency measures were more nearly consistent. As Fig. 4 shows, the

Fig. 2. Extent of cortex from which observable potential deflections were recorded in two monkeys. 2A: M103—1/19/52, 2B: M105—4/26/52. Sylvian fissure is diagrammatically opened to show supratemporal plane (STP); insula (INS); operculum (OPR). See also Fig. 3. "Doubtful" responses were characterized by small deflections and broadened wave forms.
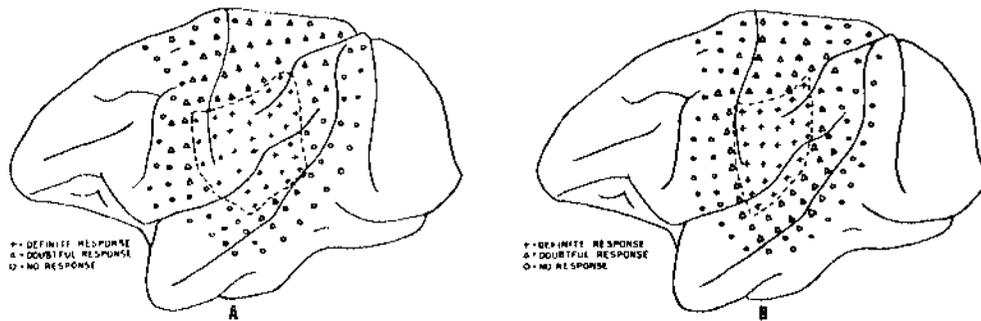

Fig. 3. Extent of cortex activated by stimulation of contralateral (3A) and ipsilateral (3B) ears. Both maps were made from same hemisphere (M104—4/5/52) before opening sylvian fissure. After separation of banks of fissure, extent of responsive cortex on supratemporal plane, insula, and operculum was essentially the same as that shown in Fig. 2.

median latencies of the onset and peak of the first major deflection yield useful indices of cortical activation.

Figure 5 and Table 1 give the results of the acute and chronic ablations of the supratemporal plane and superior temporal gyrus. After acute resec-
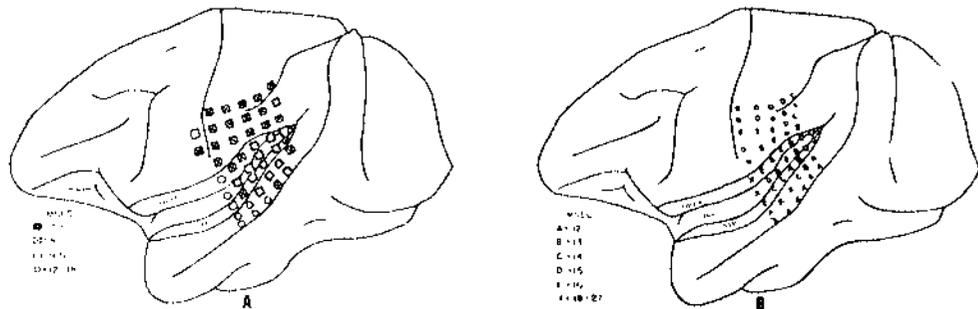

Fig. 4. Latency measures recorded from neocortex after acoustic click stimulation (M103--1/19/52). A. initial latencies: filled square =7.5 msec.; crossed square =8.5 msec.; open square =9.5 msec.; circle =12 to 18 msec. B. latency of first positive peak (see Fig. 1). A =12 msec.; B =13 msec.; C =14 msec.; D =15 msec.; E =16 msec.; X =18–27 msec. All latencies are based on the medians of 20 consecutive oscillographic tracings for each point.
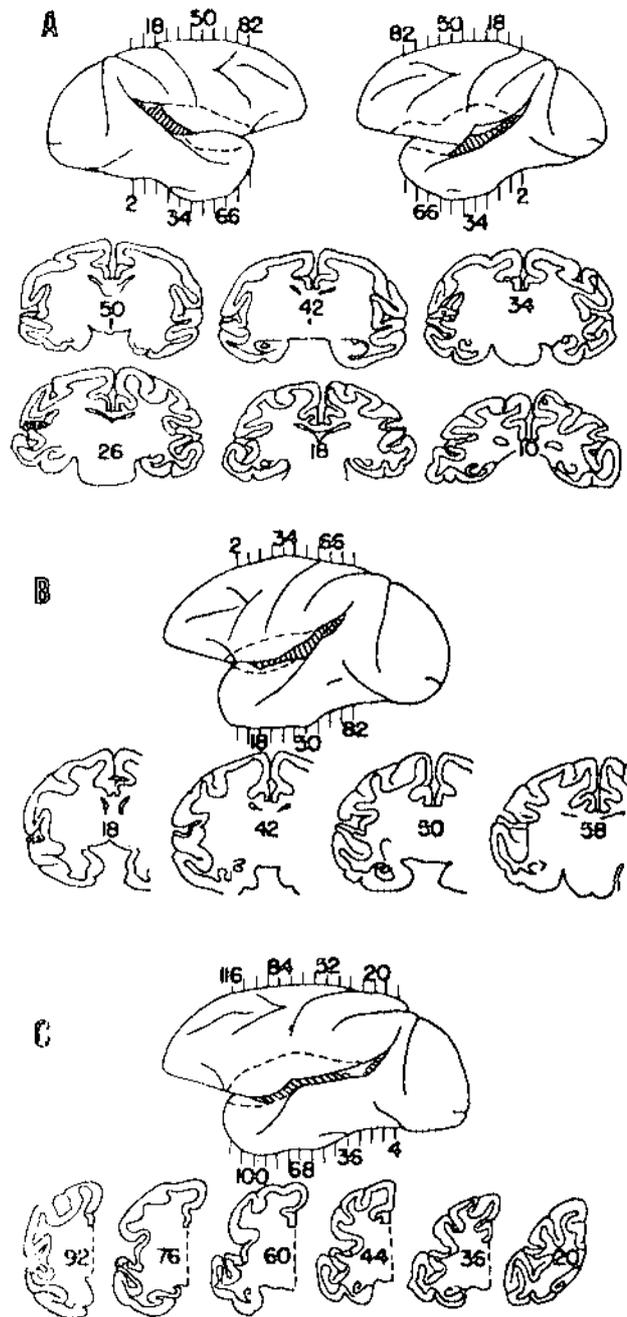
FIG. 5. Reconstructions and cross-sections of brains of animals with resections of supratemporal plane and superior temporal gyrus. *A*. M107: bilateral chronic preparation. *B*. M106: unilateral chronic preparation. *C*. M103: acute preparation. Numbers indicate cross-sections. Lesion is indicated in black on cross-section, by striations in reconstruction. Black areas in reconstructions indicate that underlying island cortex as well as cortex of supratemporal plane and superior temporal gyrus were damaged.

Table 1. Extent of thalamic degeneration in monkeys M107 and M106

	M107 left	M107 right	M106
Microcellular part of medial geniculate:[*]			
Anterior sections	Complete	Complete	Complete
Middle sections	Complete	Ventral tip spared	Complete
Posterior sections	Incomplete: cell loss, gliosis, and pyknosis	Intact	Incomplete: cell loss, gliosis, and pyknosis
Pulvinar:			
Medial	Patch in central portion posteriorly	Patch in central portion posteriorly	None
Lateral	Patch in medial portion posteriorly	Patch in medial portion posteriorly	None

[*] The magnocellular portion of the medial geniculate nucleus remained intact in all preparations.

tion, no immediate change in the electrical response was recorded from the remaining cortex. When time for degeneration of the medial geniculate nucleus of the thalamus had elapsed, however, no cortical responses to acoustic clicks were evoked in the hemisphere containing the lesion. The responses of the other hemisphere of the same animal remained intact (M106). In control experiments the peripheral "monitoring" electrode recorded responses to acoustic clicks and the cortical electrode recorded responses to tactile stimulation from parietal areas no longer activated by acoustic clicks.

DISCUSSION

We have found a larger extent of neocortex to be activated by acoustic clicks than has been heretofore reported. This is explained (at least partly) by the fact that resecting the inferior portion of the frontal and parietal lobes made it impossible for previous experimenters to map completely. The extent of "auditory" cortex found in the primate thus appears roughly comparable to the area that has been found in infraprimate mammals. Within the extent of cortex delimited by our techniques, organization depends on the criterion of response. As we have pointed out, when different criteria and/or stimulus conditions are used, different maps may result. Using electrical stimulation of the cochlea, Woolsey described an Auditory Area I and an Auditory Area II in monkey (27). A similar division (of the "primary" area) has been described for the carnivore by Tunturi (21) and by Woolsey and Walzl (26, 28). On the other hand, Ades (1) and Bremer (5) have described a "secondary" area of response on the basis of differences in the latency of onset of the response. Figure 4 shows that in the monkey, also, one portion of the responsive cortex is differentiated from the rest by extremely long initial latencies. This area covers the anterior part of the responsive cortex of the superior temporal gyrus and the anterior margin of the responsive area of the supratemporal plane, insula, and operculum. Bremer found that in the cat resection of the "primary" area, or section

between the "primary" and the "secondary" areas, destroyed the responsiveness of the "secondary" area (5). He suggests therefore that the "secondary" area is activated via the "primary"; this suggestion is supported by the longer latencies of the responses of "secondary" areas.

A third subdivision of cortex activated by acoustic stimulation has been described for carnivores by Mickle and Ades (13) and Tunturi (22, 23). This area and a part of the area that is activated by tactile stimuli overlap. On the basis of this overlap and anatomical (10, 14) and neuronographic (12,16) homologies between carnivore and primate, we suggest that the extent of parietal cortex activated by acoustic clicks in our experiments corresponds to this third subdivision. This hypothesis is substantiated by the short initial latency found for responses in this subdivision in both carnivore (22) and primate.

The pathways by which responses to acoustic signals reach this third area are not established. Anatomical and electrophysiological studies have established the projection of the medial geniculate nucleus to portions of the supratemporal plane in monkey (3, 4, 8, 15, 24). Resection of the supratemporal plane leads to almost complete degeneration of the microcellular portion of this nucleus. Resection of the inferior portion of the parietal lobe results, not in the degeneration of the medial geniculate nucleus, but in the degeneration of the posterior portion of the ventral nucleus and the pulvinar (4, 6, 8, 9, 24). Possibly responses to acoustic stimuli are relayed via these nuclei. The results of our ablation studies suggest an alternative explanation. Since responses disappeared when sufficient time had elapsed for retrograde thalamic degeneration to occur, but not when the medial geniculate nucleus remained intact, it is likely that collateral fibers ending in the parietal cortex branch off the main projection from the geniculate to the supratemporal plane. From the smaller amplitudes and slightly longer (approximately 1 msec.) latencies of the parietal response, we infer the collaterals to be less densely distributed and of smaller diameter than the fibers of the main projection. Findings in support of these inferences and the presentation of similar evidence for other afferent systems would necessitate modification of the present conceptions (based on retrograde degeneration techniques) of the extent of thalamocortical systems (17). Such reformulation would provide an anatomical base for the finding that a wider extent of cortex is activated by electrical and sensory stimuli than would be predicted from current anatomical knowledge.

SUMMARY

1. The extent of neocortex from which an electrical response could be evoked by acoustic clicks was mapped in seven monkeys.

2. Although it had been customary to resect the inferior portion of the frontal and parietal lobes to gain access to the supratemporal plane, in the present experiments the banks of the sylvian fissure were gently separated.

3. A larger extent of neocortex of monkey was activated by acoustic

clicks than has hitherto been described. The responsive area comprises the posterior supratemporal plane, the posterior superior temporal gyrus, the posterior insula, the parietal operculum, the anterior half of the inferior parietal operculum, and both banks of the anterior half of the intraparietal fissure and the inferior half of the central fissure. The extent of cortex activated was essentially the same whether intense or threshold stimuli were used. Stimuli delivered to ipsilateral and contralateral ears evoked responses at approximately the same cortical locations.

4. The latency of onset of the initial positive deflection delimits a subdivision of "auditory" cortex. This subdivision is a band reaching along the anterior margin of the responsive area on the supratemporal plane, insula, and operculum. The initial latencies are considerably longer in this area (from 12 to 18 msec.) than in the rest of the responsive cortex (7.5–9.5 msec.). This long latency area can be inferred to be homologous with a similar area in the cat (called "secondary" by Ades [1] and Bremer [5]).

5. It is well established that responses to acoustic signals are relayed through the medial geniculate nucleus of the thalamus to the cortex of the posterior supratemporal plane. Resection of the supratemporal cortex did not change the parietal response to acoustic clicks in acute preparations. When such resection antedated the electrophysiological experiment sufficiently to allow retrograde degeneration of the microcellular portion of the medial geniculate body, all neocortical responses on the side of the involved nucleus disappeared. These results suggest that the electrical response to acoustic clicks recorded from the parietal cortex is mediated by collaterals which branch from the main projection and connect the medial geniculate nucleus with the cortex of the supratemporal plane. This inference, if supported and extended to other systems, would provide an anatomical base for electrophysiological findings; at present the area of cortex afferently connected to the periphery is wider than can be demonstrated by the technique of retrograde thalamic degeneration.

REFERENCES

1. ADES, H. W. A secondary acoustic area in the cerebral cortex. *J. Neurophysiol.*, 1943, *6:* 59–63.
2. ADES, H. W. AND FELDER, R. E. The acoustic area of the monkey (*Macaca mulatta*). *J. Neurophysiol.*, 1942, *5:* 49–54.
3. ADES, H. W. AND FELDER, R. E. The acoustic projection system: a comparative study. *J. Neurophysiol.*, 1945, *8:* 463–470.
4. BLUM, J. S., CHOW, K. L., AND PRIBRAM, K. H. A behavioral analysis of the parieto-temporo-preoccipital cortex. *J. comp. Neurol.*, 1950, *93:* 53–100.
5. BREMER, F. Les aires auditives de l'écorce cérébrale. Cours International D'Audiologie Clinique, 1952.
6. CHOW, K. L. A retrograde cell degeneration study of the cortical projection field of the pulvinar in the monkey. *J. comp. Neurol.*, 1950, *93:* 313–340.
7. CLARK, W. E. LEGROS. An experimental study of thalamic connections in the rat. *Philos. Trans.*, 1932, *222:* 1–28.
8. CLARK, W. E. LEGROS AND BOGGON, R. H. The thalamic connections of the parietal and frontal lobes of the brain in the monkey. *Philos. Trans.*, 1935, *224:* 313–359.
9. CLARK, W. E. LEGROS AND NORTHFIELD, D. W. C. The cortical projection of the pulvinar in the macaque monkey. *Brain*, 1937, *60:* 126–142.

10. KAPPERS, C. U. ÄRIENS, HUBER, G. C., AND CROSBY, E. C.   *The comparative anatomy of the nervous system of vertebrates, including man*. New York, Macmillan, 1936, 2 vols.
11. LICKLIDER, J. C. R. AND KRYTER, K. D.   Frequency-localization in the auditory cortex of the monkey. *Fed. Proc.*, 1942, *1*: 51.
12. MacLEAN, P. D. AND PRIBRAM, K. H.   A neuronographic analysis of the medial and basal cerebral cortex comparing cat and monkey. I. Cat. *J. Neurophysiol.*, 1953, *16*: 312–323.
13. MICKLE, W. A. AND ADES, W. H.   Cortical projections of postural impulses. *Fed. Proc.*, 1951, *10*: 92.
14. PAPEZ, J. W.   *Comparative neurology*. New York, Thomas Y. Crowell Co., 1929, 518 pp.
15. POLYAK, S.   *Main afferent fiber systems of the cerebral cortex in primates*. Berkeley, Univ. of Calif. Press, 1932, 370 pp.
16. PRIBRAM, K. H. AND MacLEAN, P. D.   A neuronographic analysis of the medial and basal cerebral cortex comparing cat and monkey. II. Monkey. *J. Neurophysiol.*, 1953, *16*: 324–340.
17. ROSE, J. E. AND WOOLSEY, C. N.   The relations of thalamic connections, cellular structure and evocable electrical activity in the auditory region of the cat. *J. comp. Neurol.*, 1949, *91*: 441–466.
18. ROSENBLITH, W. A., PRIBRAM, K. H., AND ROSNER, B. S.   Electrical responses to clicks recorded from eighth nerve locations in monkey. (In preparation).
19. ROSENZWEIG, M. R. AND ROSENBLITH, W. A.   Responses to successive auditory stimuli at the cochlea and at the auditory cortex. *Psychol. Monogr.*, 1953, *67*: 1–26.
20. SUGAR, O., FRENCH, J. D., AND CHUSID, J. G.   Corticocortical connections of the superior surface of the temporal operculum in the monkey (*Macaca mulatta*). *J. Neurophysiol.*, 1948, *11*: 175–184.
21. TUNTURI, A. R.   Audio frequency localization in the acoustic cortex of the dog. *Amer. J. Physiol.*, 1944, *141*: 397–403.
22. TUNTURI, A. R.   Further afferent connections to the acoustic cortex of the dog. *Amer. J. Physiol.*, 1945, *144*: 389–394.
23. TUNTURI, A. R.   Physiological determination of the boundary of the acoustic area in the cerebral cortex of the dog. *Amer. J. Physiol.*, 1950, *160*: 395–401.
24. WALKER, A. E.   *The primate thalamus*. Chicago. Univ. of Chicago Press, 1938, xxiii, 321 pp.
25. WALZL, E. M.   Representation of the cochlea in the cerebral cortex. *Laryngoscope*, St Louis, 1947, *57*: 778–787.
26. WALZL, E. M. AND WOOLSEY, C. N.   Effects of cochlear lesions on click responses in the auditory cortex of the cat. *Johns Hopk. Hosp. Bull.*, 1946, *79*: 309–319.
27. WOOLSEY, C. N.   Patterns of sensory representation in the cerebral cortex. *Fed. Proc.* 1947, *6*: 437–441.
28. WOOLSEY, C. N. AND WALZL, E. M.   Topical projection of nerve fibers from local regions of the cochlea of the cerebral cortex of the cat. *Johns Hopk. Hosp. Bull.*, 1942, *71*: 315–344.