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DISCRIMINATION OF ELECTRICAL STIMULI ON LATERAL AND MEDIAL STRIATE CORTEX IN *MACACA MULATTA*

by

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INTRODUCTION

Brain Stimulation as a Conditional Stimulus: Acquisition and Generalization

Electrical stimulation of circumscribed brain loci has frequently been employed to investigate the neural substrate of learning. In order to determine cortical and subcortical mechanisms participating in learning processes, many investigators have by-passed the peripheral sensory pathways by using brain stimulation as a conditional stimulus (CS). Electrical stimulation has certain advantages over environmental stimulation in that stimulation of known form, frequency, and intensity can be administered directly to specific loci. In contrast, impulses initiated at the receptor which result from "adequate" stimulation reach the brain in extremely complex and undetermined temporal and spatial patterns.

Electrical stimulation of the brain was first used as a CS by Loucks (1938) who conditioned dogs to salivate or move a limb using the classical method. The unconditional stimuli (US) were acid or food in the mouth for the former response and electric shock of the leg for the latter. The CS was faradic stimulation of striate and para-peristriate cortex. Current applied to all investigated sites proved effective as a CS.

Subsequent experiments, employing instrumental techniques, have extended these results to many other cortical and subcortical areas in both the cat and the monkey. The literature on cats will be reviewed first. In an early study, Doty, Rutledge, and Larsen (1956) trained cats to respond to cortical stimulation with a forelimb flexion to avoid shock. Stimulation within all major cortical areas acquired CS properties (criterion = 15 avoidance responses out of 25 trials). Successful conditioning was obtained by stimulating the marginal, postlateral, middle suprasylvian, and middle and posterior ectosylvian gyri.

Since the electrodes were in proximity of meningeal and vascular tissue, the possibility remained that stimulation of the receptors of these structures was the key factor in the observed conditioning. For this reason control studies were performed. Trigeminal neurotomies denervating the meningeal and vascular areas in the vicinity of the electrodes had no effect on the conditioned response (CR). In addition galvanic skin responses usually accompanying meningeal and vascular stimulation were most often absent in conditioned animals.

In a later study (Doty and Rutledge, 1959), cats were trained to avoid shock by responding to a signal which consisted of cortical stimulation for some animals and a light or tone for others. After the cats reached criterion of learning (15 avoidances out of 25 trials) tests for generalization were initiated. The US was continued throughout the test trials. Generalization was considered to have occurred "if the animal made several CR's to the test modality during the first session of its application and attained a performance of 15 CR's for 25 presentations in about one-fourth the number of trials for initial learning" (p. 429). In some cases, not fulfilling these requirements, generalization was considered equivocally present or absent on the basis of the subject's entire protocol, including the interpretation of partial avoidance responses, i.e., foot movements not resulting in shock avoidance, and galvanic skin responses to the CS. Using these criteria, the following results were obtained: (1) An adequate stimulus (light or sound) usually "generalized" to the other adequate stimulus. (2) Adequate stimuli usually "generalized" to cortical stimulation. (3) Cortical stimulation (all but one of 13 placements were on the marginal gyrus) "generalized" about half the time to adequate stimulation (both light and sound). (4) Stimulation of points homotopic to the trained areas usually "generalized." (5) Stimulation of heterotopic points "generalized" about fifty percent of the time.

The fact that generalization was seen to occur quite frequently may well have been a function of the method employed. In contrast to Doty's use of the term, generalization is usually reserved for those procedures in which reinforcement contingencies are associated with the original CS only. Thus in 14 reference experiments concerning the generalization of a CS cited by Kimble (1963), none associated reinforcement with responses made to stimuli other than to the original CS. Grandine and Harlow (1948) have stated that if responses to test stimuli are reinforced then "responses...could be influenced by learning, and strictly considered, are not measures of generalization alone" (p. 333). Doty himself states that because test stimuli, as well as the training stimulus, signalled shock, "it might...be best to refer to the outcome in these earlier experiments as 'transfer of training' rather than 'generalization'" (1965, p. 631). Transfer of training here is being used to describe the relatively rapid acquisition of a <u>reinforced</u> response to one stimulus after initial training to another. On the other hand, generalization refers to CR's made to the second stimulus <u>without</u> any intervening reinforcement. Determination of generalization then usually involves an extinction procedure where no reinforcement is associated with responses made to the test stimulus.

Essentially what was demonstrated in the study of Doty and Rutledge (1959) was that learning the CS properties of one type of stimulation aided the animal in learning the CS properties of another. For example, after learning that light signalled shock, the cats more readily learned that tone signalled shock, although technically, no generalization was shown to have occurred. The substantial amount of reported generalization may be attributed to this point.

A more recent experiment (Nielson, Knight, and Porter, 1962) which investigated subcortical CS's, substantiates the contention that transfer of training is indeed more readily obtainable between diverse brain loci than is generalization. Shock avoidance responses were conditioned to stimulation of various subcortical areas. After a criterion level was attained (15/25 avoidance responses), generalization trials were presented without reinforcement by stimulating different brain loci. Generalization from one locus to another was rare, occurring only between 2 levels of the lateral lemniscus, and to a lesser extent from the superior colliculus and centre median nucleus to the mesencephalic reticulum. In contrast, the savings scores (trials to criterion for the original CS minus trials to criterion for the second CS) showed that transfer of training from one locus to another was common. In other words, after learning in a particular number of trials that stimulation of one site signalled shock, subjects learned quickly that a second site signalled shock. The transfer of training shown here parallels the results of Doty and Rutledge (1959).

No mention of homotopic generalization was made. In this study, only one cat (KLOD) was equipped to receive stimulation in one area during training and in its homotopic area during the test for generalization. Other electrodes were also present in this preparation, and it is not possible to determine whether this particular combination was employed.

Recently, however, homotopic generalization in certain subcortical structures has been demonstrated (Buchwald, Romero-Siera, Hull, and Wakefield, 1967). For one group of cats, subcortical stimulation signified that a bar-press would result in food reward. For a second group the absence of stimulation signified that the response would result in reward. Training loci included the caudate nucleus and the ventrolateral nucleus of the thalamus. For both groups (positive and negative cue training), homotopic generalization occurred for animals initially trained to either caudate or ventrolateral nucleus stimulation. No generalization was seen to other sites, either cortical or subcortical.

In contrast to the 2 previously mentioned studies, no positive transfer of training was demonstrated in any of the locations tested (hippocampus, thalamus, anterior limbic cortex, and nucleus entopenduncularis). In fact, no learning in the new training sites could be demonstrated even after presenting 3 times the number of trials required for initial learning. That it was possible for stimulation of these sites to acquire CS properties was shown either by the authors (unpublished data) or by Nielson, Knight, and Porter (1962). However, the stimulus frequency employed in their experiment was only 3/sec, far below the 30-300/sec range employed by Nielson, et al., and may have differed (no information presented) from the frequencies employed in their own unpublished work. In brief, those sites showing such extreme negative transfer may require a higher frequency of stimulation in order for conditioning to occur.

Electrical stimulation of the brain has been employed as a CS more recently in monkeys. Using a simple avoidance technique, Doty (1963) demonstrated that stimulation of widespread areas of the monkey brain can serve as a CS. He also demonstrated that homotopic generalization to striate and precentral cortex followed training of the contralateral striate and precentral areas respectively, whereas no heterotopic generalization was observed.

In a later study, Doty (1965) trained monkeys to discriminate between stimulation at 2 different loci. Upon stimulation at one site, the animal was trained to press a plate with its face, mouth, or tongue to obtain food. Upon stimulation at the other site, the animal was trained to press a hand lever to avoid shock. Stimulation of widespread cortical and subcortical areas proved effective CS's for both response-reward contingencies. After conditioning, unreinforced tests for generalization were conducted at loci where stimulation had never been associated with either response. Since the monkeys were treated differently, it is convenient to discuss them separately.

For one monkey, stimulation of the right superior frontal cortex was the signal for the shock-avoidance response, while stimulation of the left striate cortex was the signal for the food-reward response. During tests of generalization, stimulation of ipsi- and contralateral striate areas resulted in the food-reward response. No response resulted from parietal or temporal stimulation.

In another monkey, the food-reward response was trained to right striate cortex stimulation. The shock-avoidance CS was first applied to the right frontal arcuate cortex, and later, after no generalization was observed to stimulation of the left optic radiations, to this latter site. Subsequent testing of the right optic tract, the right lateral geniculate, and the right brachium of the superior colliculus resulted in the shock-avoidance response (presumably because of the previous left optic radiation training). At the same time, stimulation of left striate cortex evoked the food response. No response resulted from stimulation of the right prestriate areas.

In general, if an electrical stimulus was employed as a CS at one striate cortex site, then stimulation of other sites on striate cortex also resulted in the response without any intervening reinforcement.

That generalization occurs between striate cortices was confirmed utilizing a somewhat different method (Schuckman and Battersby, 1966). One brain locus was used for training, a discrimination being made on the basis of frequency in a go--no-go format. At one frequency of stimulation, a leg-flexion was necessary to avoid shock. At another frequency, shock was avoided if the response was not made. Three animals were tested for generalization.

One monkey, trained to discriminate the 2 different frequencies on left orbital frontal cortex, did not generalize to right orbital frontal, left rolandic, occipital, or right internal capsule stimulation. A second monkey, trained to right corpus striatum stimulation, did not generalize to right arcuate, right occipital, right temporal, or right internal capsule stimulation.

The only instance of generalization obtained in this experiment was in a monkey which generalized from right striate cortex stimulation to the homotopic point on the left. Generalization did not occur to stimulation of the right rolandic cortex, the left caudate nucleus, or the left corpus striatum.

Generalization of a striate cortex CS to contralateral striate cortex stimulation was demonstrated in another study which employed a simple shock-avoidance situation (Schuckman, 1966). The one monkey used was over-trained by requiring 90 percent avoidance responses for 5 consecutive days. No generalization occurred to stimuli of the contralateral frontal cortex.

If electrical stimulation of one area of striate cortex is used as a CS, stimulation of any other regions of striate cortex is apt to elicit the conditional response. So far stimulation of these latter areas appears to elicit the conditional response to a similar extent regardless of their distance from the site of original training. Doty has noted "the nearly total equivalence obtained between points in area 17 of macaques" (Doty, 1969, p. 306). However, no systematic study has been made on this point, and more sensitive techniques may reveal that the distance between the original site of training and a second site of stimulation is a relevant factor in the elicitation of the conditional response by stimulation of the latter site. For example, the responses resulting from striate cortex stimulation farther from the locus of original training may be increasingly more extinguishable, i.e., a decremental monotonic relation may exist as a function of interstimulus distance. Continued unreinforced trials of the untrained locations along with interspersed reinforced trials at the training site may result in extinction of all but the sites closest to the training site. Alternatively, there may be no differences in response strengths between any points within striate cortex.

Anatomy Underlying Cerebral Generalization

Since generalization occurs between different areas of striate cortex, some pathways must be operating to convey information from one striate area to another. The pathways conveying information contralaterally have received more attention than those conveying information ipsilaterally. Considerable data regarding mechanisms of transcortical transfer of information has been acquired via the split-brain preparation which, in studies of the visual system, involves the longitudinal sectioning of the optic chiasm and corpus callosum, and possibly other commissural pathways (Sperry, 1961). When one eye is occluded in these preparations, the stimuli are introduced directly into one hemisphere only (at least in terms of the classical visual system).

In an early experiment (Sperry, Stamm, and Miner, 1956), split-brain cats (chiasm and corpus callosum sectioned in the mid-sagital plane.) were trained monocularly to choose 1 of 2 simple patterns to obtain a food reward. After a criterion level of performance was attained, the contralateral hemisphere was trained by shifting the eye patch to the previously trained eye. The learning curves obtained with the first and second eye revealed that prior training to one hemisphere had no effect on the other, i.e., as many trials were needed for the cat to learn the problem using the second eye as it did using the first. Since interocular transfer in a chiasm-sectioned cat with an intact corpus callosum does occur (Myers, 1955), it can be argued that it was the interruption of the corpus callosum which prevented the interhemispheric transfer of the discrimination.

Studies in the monkey also indicate the importance of the cerebral commissures in interhemispheric transfer. Sperry (1958) showed that animals with mid-sagital sections of the corpus callosum, optic chiasm, and hippocampal and anterior commissures failed to transfer color, pattern, three-dimensional shape, size, and brightness discrimination problems.

Although the integrity of the cerebral commissures appears important in the interhemispheric transfer of discrimination problems, there are certain conditions under which transfer occurs despite the extensive disruption of these fibers. These exceptions appear to reflect both the nature of the discrimination problem and the nature of the reinforcement. Accordingly, sectioning of the corpus callosum and the optic chiasm in cats resulted in the absence of interhemispheric transfer of a near-threshold brightness discrimination (Meikle, 1960), but had no effect on the transfer of a problem of gross brightness discrimination (Meikle and Sechzer, 1960). Similar preparations showed no transfer of a pattern discrimination task when food was used as reinforcement, but did demonstrate transfer when shock-avoidance motivation was employed (Sechzer, 1964).

Since the interhemispheric transfer of a number of discrimination tasks are dependent upon an intact corpus callosum, it might be suggested that homotopic generalization of a cortically applied CS may also depend on an intact callosal system. Data acquired thus far do not confirm such a contention.

Using cats, Doty and Rutledge (1959) found that a pre-training section of the posterior 3/4 of the corpus callosum plus a section of the hippocampal commissure did not prevent the transfer of a shock-avoidance task from a point on one middle ectosylvian gyrus to the homotopic point on the other. In monkeys with divisions of the corpus callosum and psalterium, Doty (1966) demonstrated that a frequency discrimination problem (2/sec = food-reward response; 10/sec = shock-avoidance response) learned at one occipital locus, can generalize to stimulation applied to the homotopic point. In 2 monkeys with additional sectioning of the anterior commissure, no homotopic generalization was observed (Doty, 1967). Since no animal underwent sectioning of the anterior commissure alone, it cannot be determined whether this structure is necessary or merely sufficient in the mediation of homotopic generalization. In any case these studies suggest that homotopic generalization is at least partly mediated by part or all of the cerebral commissures.

Recently electrophysiological studies have suggested a subcortical mechanism related to the homotopic generalization of a cortically applied CS. In an experiment by Rutledge (1965), 7 cats were trained and overtrained to flex a foot upon suprasylvian stimulation in order to avoid foot shock. Three control cats received comparable amounts of suprasylvian stimulation but no foot shock was employed. Subsequently, the animals were anesthetized with chloralose in the acute stage of the study, wherein interhemispheric delayed responses (IDR, a long latency, noncallosal response initiated at one cortical locus and recorded from a homotopic site) were measured.

In the conditioned cats the IDR was enhanced if the stimulation used to evoke it was the CS and recording was done from the homotopic point. In other words, if the right suprasylvian gyrus was used in training, the IDR would be of greater magnitude if the acute stimulation were applied also to the right suprasylvian gyrus and recording was done from the left suprasylvian gyrus. Stimulation in the opposite direction, i.e., from "naive" to trained cortex, resulted in IDR's comparable to those of control animals. Since control animals showed no enhancement, mere electrical stimulation during the training stage was apparently not responsible for the IDR enhancement recorded from the "naive" cortex in the trained animals. It should also be noted that the enhanced IDR's obtained from the "naive" cortex did not reflect an acquired increase in responsiveness to all forms of input since evoked potentials to photic and auditory stimulation and the transcallosal potentials were similar from side to side.

These findings demonstrate that a particular electrographic change in the IDR occurs at a point homotopic to the site of CS administration. Since anatomical and physiological techniques (Rutledge and Kennedy, 1960; 1961) suggest that the IDR is mediated by structures within the posterior diencephalon and mesencephalic reticular formation, the previous study suggests that the homotopic generalization of a cerebral CS may be at least partially mediated by these subcortical centers.

Although not addressed to generalization, a study by Rutledge and Doty (1962) suggests that ipsilateral generalization may be mediated by subcortical mechanisms. Cats were trained to avoid shock when an electrical CS was applied to either marginal gyrus. Following training, the 2 stimulated areas were surgically isolated from some of the adjacent areas in 2 ways. One trained area was undercut in order to sever vertical connections with lower brain structures while the contralateral area was incompletely circumsected and thus isolated from most of the neighboring cortex by a U-shaped incision 4 or 5 mm deep (a full circumsection results in cortical degeneration). Stimulation of the U-cut cortex was significantly more effective in eliciting the preoperatively trained response than was stimulation on the undercut cortex. In fact, only 2 out of 10 cats with undercut cortex showed any signs of post-operative recall of training although they all eventually relarned the task (never, however, to the preoperative level) after many training trials.

According to the authors, "the results show unequivocally the subcortical rather than transcortical projections are the most important for effective elaboration of a cortically applied electrical CS" (p. 489). Although cerebral generalization is not mentioned, these findings together with those implicating brain-stem structures in interhemispheric transfer, suggest a possible subcortical mechanism in ipsilateral generalization.

Striate Cortex and the Field of Vision

On the lateral aspect of the brain of *Macaca mulatta*, the striate cortex has its anterior border 1 to 2 mm posterior to the lunate sulcus, and its ventral border the same distance dorsal to the inferior occipital sulcus. It extends posteriorly to and around the occipital pole and continues anteriorly, where it surrounds the ventral and dorsal branches of the calcarine fissure. A major portion of striate cortex at this point becomes buried within all branches of the fissure (Bonin and Bailey, 1947). The position of striate cortex on the brain of man is similar. In man, however, striate cortex does not project onto the lateral surface but is intimately associated with the calcarine fissure on the mesial aspect of the brain (Crosby, Humphrey, and Lauer, 1962).

During this century, much attention has been focused on the relationship between striate cortex and the retina. Prior to World War I, 2 general theories relating the retina to the brain prevailed (see Klüver, 1927). One theory, espoused chiefly by Henschen (1924), postulated that, at all links of the visual system including the visual cortex, there exists a point-to-point correspondence. An area on the retina is represented by corresponding neural elements of the optic nerve, chiasm, lateral geniculate body, radiations, and visual cortex. The retinal image was considered to be faithfully projected with its spatial relationships intact onto the cortex. Consequently, Henschen used the term cortical retina to designate the anatomical and functional relationship between the photoreceptor cells of the retina and the neurons of the visual cortex.

The other view postulated a diffuse, relatively non-localized correspondence between the retina and the brain. Those adhering to this view rejected the idea of a cortical retina and a strict point-to-point representation of the retina in the cortex. The leader of this diffuse concept was Constantine V. Monakow. According to Klüver, most neurologists and ophalmologists before World War I favored the cortical retina concept.

During and after the War, many studies investigating the relationship between cranial injuries and visual field defects were reported which reinforced the cortical retina concept. In the studies of Holmes and Lister (1916) and Holmes (1918), the locus and extent of lesions were deduced primarily from an examination of external skull injuries. Although this method could yield only approximate clues at best, and post-mortem investigations of the damaged brains were rare, certain conclusions were reached. The upper half of the visual field is represented in striate cortex ventral to the calcarine fissure while the lower half of the visual field is subserved by cortex dorsal to the fissure. The foveal area is projected on the occipital pole while the more peripheral areas are projected progressively more anteriorly. The vertical axes are represented in the dorsal and ventral margins of striate cortex, whereas the areas closer to the horizontal axes are projected onto the walls and floor of the calcarine fissure.

Holmes employed primarily stationary white targets in his studies. However, when the patient was tested with a colored target, a deficiency in color recognition was often encountered in the area immediately surrounding the region of total blindness. This condition was considered to be not a loss of color vision *per se*, but a reduction of general visual function, since a white object presented to the same retinal area was seen as indefinite and unclear.

Holmes noted also that the presence of a moving object may be detected in areas where the same object if stationery would not be perceived. In addition, faster or more abrupt movement led to the report of an object in areas where slow movements did not. It is important to note that Holmes considered the perception of motion in an otherwise "blind" area and the inability to detect color in an otherwise "spared" area as the result of incomplete destruction of that cortical matter responsible for the perception of the affected part of the visual field.

According to Holmes, a "clean" lesion should leave a totally blind area surrounded by a normal visual field. If the assumption used to explain the differential disturbances of various areas of the visual field, i.e., incompleteness of lesion, had not been made, the theory of a strict cortical retina would have been abandoned in favor of some alternate concept. The theory demands that those areas subserved by cortex outside the destroyed cortex be normal, and the area subserved by the destroyed cortex be completely anopic (even to moving stimuli).

In mapping visual field defects, Holmes states that the defect caused by occipital injury may not appear congruous for both eyes. He attributes this condition to artifactual circumstances such as lack of attention, fatique, and the fluctuations of chance. If the visual cortex represents the visual field, then damage to an area of cortex should result in the loss of an area of visual field regardless of which eye is tested. In attributing incongruous defects to artifacts, Holmes avoids having to reconcile their existence with the concept of the cortical retina.

These studies, involving occipital injuries of World War I, seemed to have reinforced the pre-existing cortical retina bias (Klüver, 1927). As Henschen (1924) stated, "the doctrine of projection has been victorious in all instances; there exists a 'cortical retina.' All those facts settle forever the doctrine of a complete projection, point by point, in all details...each retinal point has its cortical point, there exists a constant correspondence" (quoted in Kluver, 1927, p. 318).

The topological projection concept demands that (1) the area of visual field subserved by the destroyed cortex should be affected completely and (2) no other area should be affected. Recent clinical studies, however, have emphasized that different methods of testing yield different results in the delimitation of a scotoma within the visual field. These studies show that the perimetrically blind areas may possess residual function. An elevated critical flicker frequency within the "spared" visual field of patients with striate cortical damage was reported by Battersby (1951). In another study, a second stimulus presented in a "spared" area resulted in the disappearance of an original stimulus presented to a different part of the spared area (Bender and Furlow, 1945). Local color adaptation was found to occur much faster in the "spared" areas of the visual field of patients with homonymous scotomata than in normals (Bay, 1953). Bay stated that "size, shape, even the type of field defect depends largely on the stimulus employed for the examination and, therefore, are not significant for the extention and location of the cerebral lesion; thus the theory of strict retino-cortical correspondence has led to a wrong assumption" (p. 532).

Residual vision in a perimetrically blind area of the visual field also causes some trouble for the point-to-point theory. Movement may be perceived within the scotoma (Riddock, 1917). Light may also be seen under conditions of dark adaptation (Krieger and Bender, 1951). These studies are at odds with a cortical retina concept since the concept demands an absolute scotoma in that area of the visual field which is projected onto the destroyed cortex.

A recent study (Brindley and Lewin, 1968) correlating the subjective location of a phosphene with the locus of stimulation of striate cortex, while supporting to some extent the point-to-point theory, creates an additional problem. Thirty-nine electrodes were placed on the right striate cortex of a blind patient. Upon stimulation of sites close to the occipital pole, the subject reported a white object about the size of a star in the macular region. Further anterior, where stimulation yielded phosphenes farther into the periphery, phosphenes were elongated like grains of rice held at arm's length. Most anterior, stimulation resulted in more nebulous images still farther in the periphery. The cortical map conformed to the missile wound studies previously mentioned.

An unexpected finding was that, at higher currents, a second phosphene appeared for 12 of the sites. The high-threshold map resembled the low-threshold map inverted about the horizontal meridian. If the low-threshold phosphene was between 10 and 12 o'clock, the high-threshold phosphene would be between 6 and 8 o'clock. This latter finding cannot be derived from a strict point-to-point theory of the cortical retina.

The resolving power of striate cortex was also investigated in this study. It was found that if 2 electrode sites separated by only 2.4 mm were stimulated in succession within 0.2 and 2.0 sec, they were seen as different. If a longer time interval passed between the presentations, no discriminations were made, i.e., the 2 were indistinguishable.

The topological relationship between the visual field and striate cortex in the monkey is similar to that found in man. In a study by Talbot and Marshall (1941), a punctate beam of light was focused onto the retina of a monkey's mechanically immobilized eye. Maximal evoked potentials were recorded from different cortical areas depending on the retinal area activated by the photic stimulus. A cortical map was constructed which revealed the most anterior aspect of lateral striate cortex to be concerned with foveal vision. A shift to peripheral vision occurred posteriorly until at the occipital pole maximal evoked potentials resulted from targets 9 deg from the fixation point.

In addition, it was shown that the amount of striate cortex activated by stimulation was dependent upon where in the field the stimulus was presented. At the fovea 1 deg of visual angle occupied 30 mm of cortex whereas the same angle 5 deg from the fixation point occupied 3.3 mm of cortex.

In terms of its implications for the concept of the cortical retina, Marshall and Talbot (1942) stated that "The anatomical conception of one-to-one projection of the retina on to the cortex then, may be regarded as functionally correct in so far as the maintenance of spatial relations is concerned. But quantitatively the unit paths near central vision should now be conceived, not as lines but as expanding cylinders whose ends bear an area ration of 1 : 10,000 and a cellular ration of perhaps 1 : 100" (pp. 134-5).

Because Talbot and Marshall employed only surface electrodes a large portion of striate cortex was inaccessible and thus unexplored. It was not until 1961 when Daniel and Whitteridge used depth electrodes that a more thorough investigation of striate cortex was made. Confirming the previous study, these investigators showed that foveal targets evoked maximal activity from anterior lateral striate cortex 1-2 mm posterior to the lunate sulcus. As the target was moved into the peripheral field, loci closer to the occipital pole were activated until at 9 deg the target excited the cortex around the pole. As the target was moved further into the peripheral field the maximal evoked potentials were recorded via depth electrodes from progressively more anterior aspects of cortex associated with the calcarine fissure. In addition, the farther these targets were presented from the horizontal meridian, the more lateral was the evoked potential within the buried calcarine cortex.

Like Talbot and Marshall, Daniel and Whitteridge found a greater area of cortical participation for foveal stimulation as opposed to peripheral stimulation. At 0, 5, and 60 deg from the point of fixation 1 deg of visual angle was subserved by 6.0, 2.0, and 0.1 mm of cortex. This decrement in cortical participation as a function of angular distance from the fixation point occurred regardless of whether the target was on the horizontal, vertical, or an intermediate meridian.

Since no data are available which correlate visual acuity with distance from the fixation point in monkeys, the magnification factor cannot yet be precisely related to acuity. Daniel and Whitteridge, however, assembled their data on magnification in the monkey together with human visual acuity data (Weymouth, 1958) to show that magnification in monkeys and acuity in man fall off in a more or less similar fashion. They therefore assumed that the acuity changes within the visual field were, at least, partially determined by the differences in the amount of cortex activated by stimuli of equal size presented in different areas of the field.

Both the magnification factor and the topological organization shown in gross physiological studies have been confirmed by anatomical methods. Polyak (1933) observed circumscribed areas of degeneration in the lateral geniculate body of monkeys which resulted from the destruction of delimited areas of striate cortex. By combining his data with those showing the topological relationship between the retina and lateral geniculate body (Brouwer and Zeeman, 1926), Polyak (1957) was able to demonstrate a relationship between the retina and cortex which was congruent to that revealed by the physiological studies of Talbot and Marshall (1941).

In summary, the clinical and experimental studies suggest that the visual system does show some point-to-point organization. This topological correspondence can best be observed clinically by simple perimetric testing of visual field defects. However, with the increased usage of different methods of testing, a more complicated picture arises. It has been shown that the perimetrically "intact" areas are not normal, and perimetrically "blind" areas are not necessarily completely insensitive.

These results cast some doubt on a point-to-point theory since that area of the visual field which is mediated by destroyed cortex should be completely blind, while the area of the visual field mediated by spared cortex should be normal.

Experiments employing stimulation and recording techniques have in general supported the concept of some type of correspondence between points in the visual field and points on striate cortex. The magnification factor and the high-threshold inverted map of Brindley and Lewin (1968), however, discourages the acceptance of a strict point-to-point correspondence.

The following section will consider the cortical retina concept in conjunction with the findings of those studies employing direct striate cortex stimulation as a CS.

STATEMENT OF THE PROBLEM

Clinical, anatomical, and electrophysiological studies have all indicated some type of topological relationship between the visual field and striate cortex. In general, the greater the distance between striate cortical loci, the farther apart will be the points in the visual field they subserve.

In summarizing the generalization studies employing electrical stimulation as a CS, Doty (1969) emphasized "the nearly total equivalence obtained between points in Area 17 of macaque" (p. 306). Test stimuli administered to widespread areas of striate cortex have resulted in the same responses as those resulting from training site stimulation. Response probability likewise appeared unaffected by the distance between the sites. The cortical retina appears irrelevant in the determination of the equivalence of electrical stimuli applied to striate cortex.

The observed equivalence may reflect experiments not specifically designed to reveal differences in response strengths associated with inter-stimulus distances. The previous experiments on the generalization of an electrical stimulus on cerebral cortex can each be divided into 2 stages. The first involved presentation of only the CS, whereas the second stage presented only test stimuli. Thus there was negligible opportunity for temporal comparison of the training and test stimuli. A different technique, affording such comparisons, may, however, reveal a relationship between response strength and inter-stimulus distance. Using a discrimination paradigm which allows for the frequent temporal juxtaposition of of training and test stimuli, the present experiment will determine:

1. The rapidity of extinction for electrode sites placed at successive distances from the original site of training on the

same hemisphere.

2. The rapidity of extinction for electrode sites placed at successive distances from the point homotopic to the site of original training on the contralateral hemisphere.
3. Whether the gradients from lateral striate and medial striate cortex differ, thereby indicating cortical differences related to foveal and peripheral vision, respectively.

METHOD

Subjects and Implantations

1. Subjects. Six male monkeys (Macaca mulatta) weighing between 2.9 and 3.4 kg were used in the experiment.

2. Electrodes. Electrodes (all cortical) were made of .01 in tungsten wire balled with mercury at one end, and soldered to 30 gauge Alpha wire leads at the other. Two types of electrode units were employed, one consisting of 2 the other of 5 linearly arranged electrodes. In both electrode combinations, electrodes were sandwiched together between 2 layers of onionskin paper with vinyl enamel being used as the adhesive, insulating, and waterproofing medium (Stoner-Mudge Packaging Coating Material, Number S-986-015). The electrodes tips were carefully scraped of insulation and protruded slightly from the sandwich. Electrode tips were 2.8 mm apart.

3. Operation. The monkey was anesthetized with Ip Nembutal (30 mg per kg) with supplementary doses administered intramuscularly as required. The operation was performed under sterile conditions. The monkey was placed in a stereotaxic apparatus and a midline incision was made from just above nasion to beneath the lambdoid suture. After reflecting muscles and connective tissue and exposing the skull, holes were trephined and enlarged with rongeurs. An incision through the dura and arachnoid membranes allowed for the electrode units to be slipped onto the brain surface.

The Alpha wire exited from the skull openings which were packed with Gelfoam and covered with a layer of dental acrylic in order to secure the electrodes in place.

Several stainless steel screws were screwed into the skull, 3 of which were wired together as a "diffuse bone indifferent" electrode. Leads from all electrodes were soldered to a female Cannon subminiature plug (ITT Cannon DB-25S-C7). With the plug on top, the entire assembly was covered with a mound of acrylic cement. The skin was drawn around the mound and sutured. Local and systemic antibiotics were administered postoperatively.

Each subject received at least 1 bipolar electrode unit and 2 5-electrode banks. The bipolar electrodes were placed on the frontal, temporal, and/or parietal lobes of both cerebral hemispheres. An attempt was made in 3 monkeys to place the 5-electrode units bilaterally on the lateral surfaces of striate cortex. In 3 other subjects, an attempt was made to place the units bilaterally on the mesial surfaces of striate cortex. For each animal, the electrode banks were placed as homotopically as possible.

Apparatus

During training and testing, the monkey was seated in a restraining chair and enclosed in a sound attenuated Lehigh Valley chamber equipped with a one-way viewing window. A blower circulated air and masked extraneous sounds. A steel lever 5 cm wide protruded 3 cm from a panel located in front of the monkey to his right. A Lehigh Valley pellet dispenser delivered Ciba Nutrient Pellets (190 mg) into a small chute located directly in front of the monkey.

A Grass Stimulator (Model S4) connected in series with a Grass Stimulus Isolation Unit (Model SIU 4678) and a Grass Constant Current Unit (Model CCU 1A) supplied the electric stimuli to the brain. Electrodes were selected via 2 rotary switches. Current was monitored using a Dumont Cathode-Ray Oscillograph (Type 306H) to measure the voltage drop across a known resistance (100 ohms) in series with the stimulating circuit. Stimulus and reinforcement contingencies were programed via a BRS Electronics system.

Procedure

After a post-operative recovery period of about two weeks, the monkey was placed in the restraining chair. Resistances between electrode combinations to be used were ascertained. While the monkey was in full view of 2 observers, thresholds for motor responses were determined for the same electrode combinations. The stimulus was a 2-sec train of 100 pulses per sec (pulse duration = 0.3 ms). Subsequent current was delivered at 90 percent of the threshold current for the motor response.

The animal was trained to press a bar for reward only during brain stimulation. At varying intervals, ranging from 20-60 sec, brain stimulation, utilizing the above parameters, was delivered. This training stimulus always involved the 2 most anterior or posterior electrodes in 1 of the 5-electrode units on striate cortex.

A response made between stimulations recycled the inter-trial inverval and initiated a 4-sec noxious tone. Fifty stimulations were presented per session. Criterion performance was 90 percent responses during stimulation and no more than 10 inter-trial responses for each of 5 successive sessions.

During testing for spatial discrimination, sites other than the original training sites were stimulated (test sites). Inter-trial intervals were unchanged. "Naive" sites generally included at least 1 in extra-striate cortex and 7 in striate cortex. Stimulation of each test site occurred in random order twice per session. Bar-presses during these presentations were not rewarded. The total number of test stimulations was matched by an equal number of randomly intermixed presentations of the training stimulus. Responses during stimulations of the training site were rewarded. This procedure was continued until no responses were made to any test stimulus during an entire session (i.e., perfect spatial discrimination).

The monkey was then tested for polarity reversal discrimination at the training site. In this procedure, the subject was stimulated at the training site both with the electrode polarity previously employed (during which a response would be reinforced) and with an equal number of randomly intermixed reversed polarity stimulations (during which a response would not be reinforced). The procedure was continued until no responses were made to the reversed polarity stimulation for 3 successive presentations with 100 percent responses to interspersed training stimulation.

After completion of all training and testing, the subjects were sacrificed and perfused (via heart or carotid artery) with saline followed by 10 percent formalin. The brains were removed and placed in formalin. Striate cortex placements were confirmed by cutting through the cortex at the electrode sites and visualizing the stripe of Gennari.

RESULTS AND COMMENTS

General Remarks

Although the specific electrode placements for each subject will be illustrated below, certain general characteristics can be stated. The lateral striate cortex electrodes were aligned roughly parallel to the inferior occipital sulcus, midway between this landmark and the longitudinal fissure. The medial striate cortex electrode banks were oriented parallel to and between the superior branch of the calcarine fissure and the parietal-occipital fissure. Compression of cortex adjacent to the electrode banks, occuring in some subjects, appeared the only alterations associated with the implantations.

The intensities of the stimuli necessary to elicit unconditional responses for each electrode pair in the lateral and medial cortex subjects are listed in Tables I and II respectively. The current magnitudes resemble those of Schuckman (1966) and Schuckman and Battersby (1966) who used pial surface electrodes, but are about one hundred times greater than current intensities used by Doty (1965) whose electrodes were inserted in the cortex. The use of pial electrodes may explain the high threshold values.

Spatial Discrimination

Lateral Striate Cortex Group. Fig 1 shows the percentage of bar-presses made by Subject 1L in response to stimulation of each site examined during testing. Complete discrimination between all test sites and the training site occurred at session 10, and the figure is based on the response percentages to stimulation at each site for all 10 sessions (20

TABLE I

UNCONDITIONAL RESPONSES, THRESHOLD CURRENTS, AND RESISTANCES FOR ALL SITES IN LATERAL STRIATE CORTEX

Subject	Site	Resistance (K-ohms)	Threshold for Unconditional Response (ma)	Unconditional Response
S-1L	-3,4L*	85	11.0	Right eye blink
	-5,6L	25	18.0	Eyes Right
	-6,7L	20	13.0	" "
	-7,8L	14	27.0	" "
	-8,9L	15	13.0	" "
	-10,11R	20	7.0	Eyes Left
	-11,12R	26	13.0	" "
	-12,13R	20	8.0	" "
	-13,21R	15	8.0	" "
	-16,17R	20	13.0	Head Left
S-5L	-1,2L	50	3.0	Right Foot Twitch
	-3,4L	30	24.0	Eyes Right
	-4,5L	30	24.0	" "
	-5,6L	20	25.0	" "
	-6,7L	35	28.0	" "
	-8,9R	20	28.0	Eyes Left
	-9,10R	18	24.0	" "
	-10,11R	15	22.0	" "
	-11,12R	15	25.0	" "
	-14,15R	25	3.0	Left Hand Twitch
S-7L	-1,2L	100	2.0	Right Foot Twitch
	-4,5L	50	18.0	Eyes Right
	-5,6L	100	12.0	" "
	-6,7L	75	23.0	" "
	-7,8L	100	18.0	" "
	-15,16R	50	20.0	Eyes Left
	-16,17R	50	18.0	" "
	-17,18R	50	17.0	" "
	-18,19R	50	18.0	" "

* - = cathode, L = left, R = right

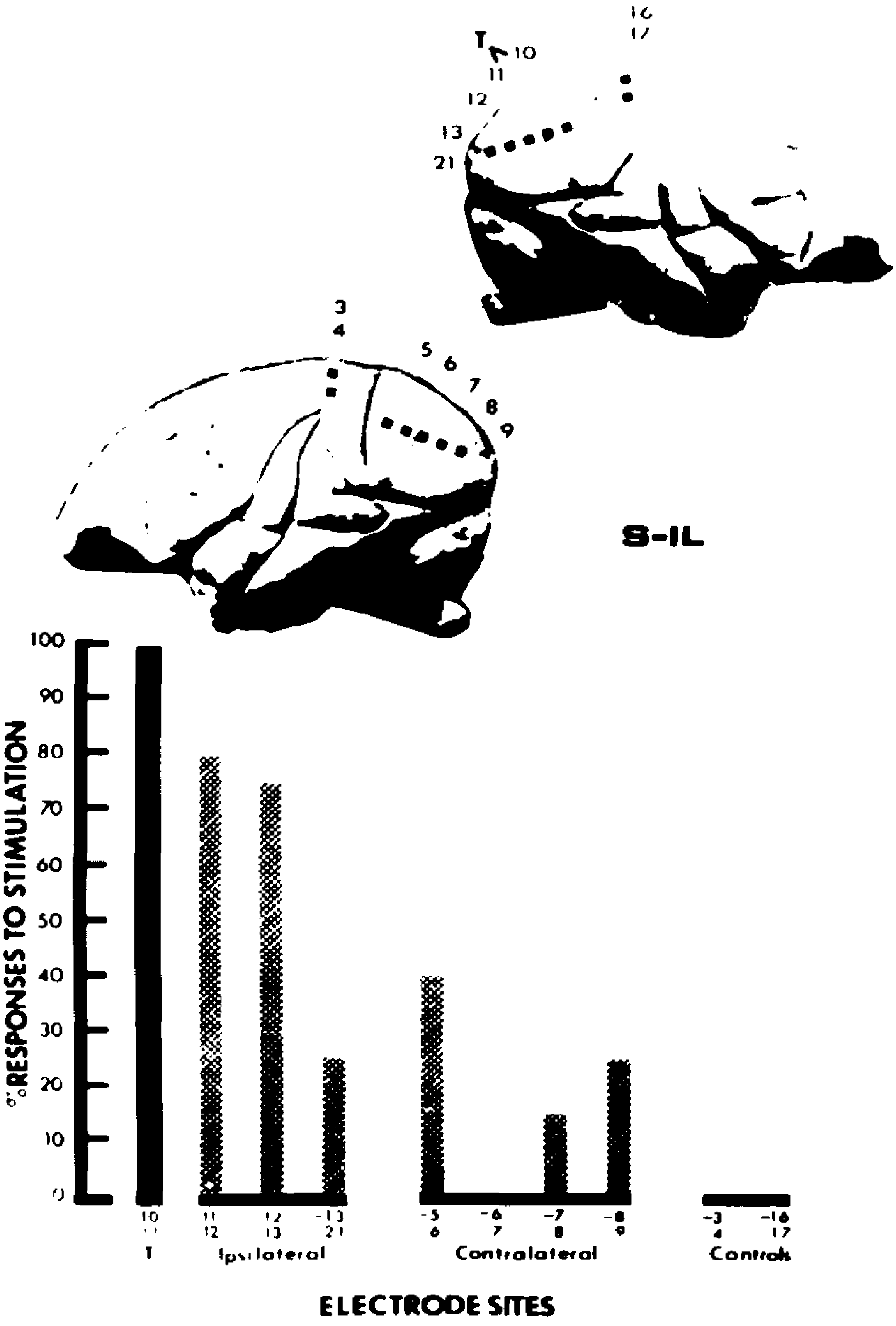
TABLE II

UNCONDITIONAL RESPONSES, THRESHOLD CURRENTS, AND RESISTANCES FOR ALL SITES IN MEDIAL STRIATE CORTEX

Subject	Site	Resistance (K-ohms)	Threshold for Unconditional Response (ma)	Unconditional Response
S-6M	-1,2L*	70	7.0	Eyes, Head Right
	-3,4L	40	20.0	Eyes Right
	-4,5L	35	23.0	" "
	-5,6L	35	20.0	" "
	-6,7L	30	32.0	" "
	-14,15R	40	11.0	Eyes, Head Left
	-16,17R	40	35.0	Eyes, Left, Downward
	-17,18R	30	33.0	" " "
	-18,19R	30	24.0	" " "
	-19,20R	40	12.0	" " "
S-8M	-1,2L	40	2.5	Right Foot Extension
	-14,15R	50	15.5	Eyes, Left, Downward
	-15,16R	50	15.5	" " "
	-16,17R	30	15.5	" " "
	-17,18R	40	15.5	" " "
S-9M	-1,2L	65	2.0	Head Right
	-3,4L	65	1.0	Right Leg Flexion
	-5,6L	27	17.0	Eyes, Right, Downward
	-6,7L	30	19.0	" " "
	-7,9L	30	21.0	" " "
	-9,11L	25	23.0	" " "
	-17,18R	50	6.0	Eyes, Left, Downward
	-18,19R	35	6.0	" " "
	-19,20R	27	23.0	" " "
	-20,21R	30	23.0	" " "
	-14,15R	75	2.0	Head Left

* - = cathode, L = left, R = right

Fig 1. Percentage of responses made by S-1L to stimulation of the training site and test sites during testing. Electrode placements are shown on the brain diagram. The training site (T) is indicated on the bar graph in black. The negative sign (-) indicates the cathode on each electrode pair. The figure is based on the response percentages for 10 sessions (20 stimulations per test locus and 180 stimulations of the training site).


16
17
T
10
11
12
13
21
3
4
5
6
7
8
9
S-IL
%RESPONSES TO STIMULATION
0
10
20
30
40
50
60
70
80
90
100
10
11
T
11
12
12
13
-13
21
Ipsilateral
-5
6
-6
7
-7
8
-8
9
Contralateral
-3
4
-16
17
Controls
ELECTRODE SITES

stimulations per test locus and 180 stimulations of the training locus).

The figure shows a response gradient on the ipsilateral side, response percentages decreasing as a function of distance from the training site. Although the response decrement was small for the closest sites, there was a marked decrease in response frequency at the furthest ipsilateral striate cortex locus. No pattern was apparent on the contralateral side, although the highest responding site was the site "most" homotopic to the training site. However, it fell considerably below the 2 highest ipsilateral response frequencies. Why stimulation of site -6,7 resulted in no responses was not discernable upon gross inspection of the brain or electrodes. Since both electrodes 6 and 7 were effective in combination with other electrodes (5 and 8 respectively), the viability of each was proven, although the possibility of a short circuit between them cannot be eliminated. No responses were made to parietal stimulation of either hemisphere.

In Fig 2, the 10 sessions are broken down into the first and second group of 5 sessions. This figure reveals that for the first 5 sessions, on ipsilateral striate cortex, complete lack of differentiation occurred in the 2 sites closest to the training site while stimulation of the furthest site was responded to at a 50 percent level. In contrast, the second 5 sessions revealed a considerably steeper gradient. On the contralateral side, although moderate response percentages occurred for the first 5 sessions, only 1 response occurred during the second 5 sessions.

For Subject 5L, complete discrimination between the training site and the test sites occurred at session 11. The percentage of responses to stimulation of each site is shown in Fig 3. Each test site percentage

Fig 2. Percentage of responses made by S-1L to stimulation of the training site and test sites stimulated during first 5 and second 5 sessions. See Fig 1 for explanation of symbols.

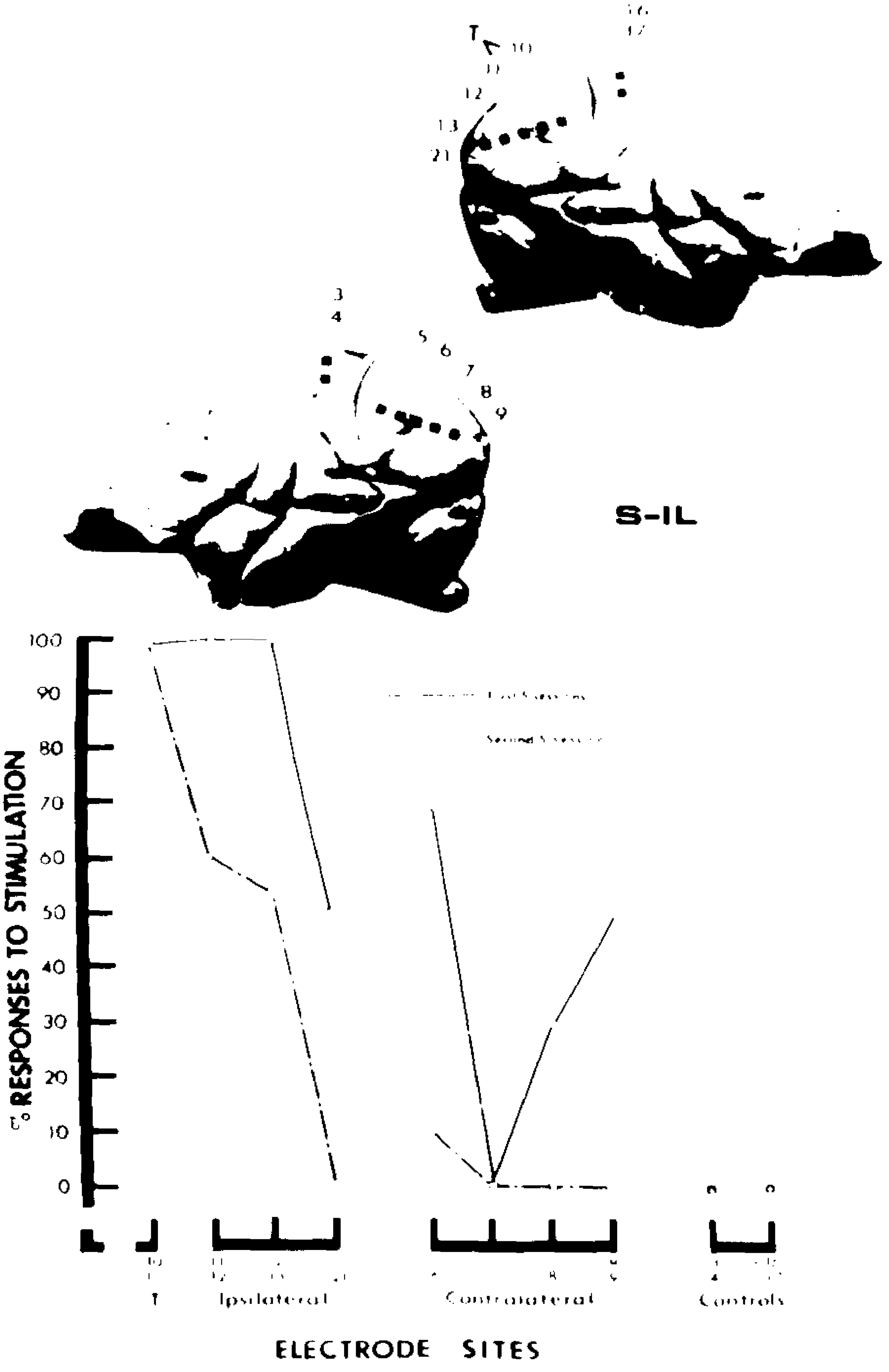
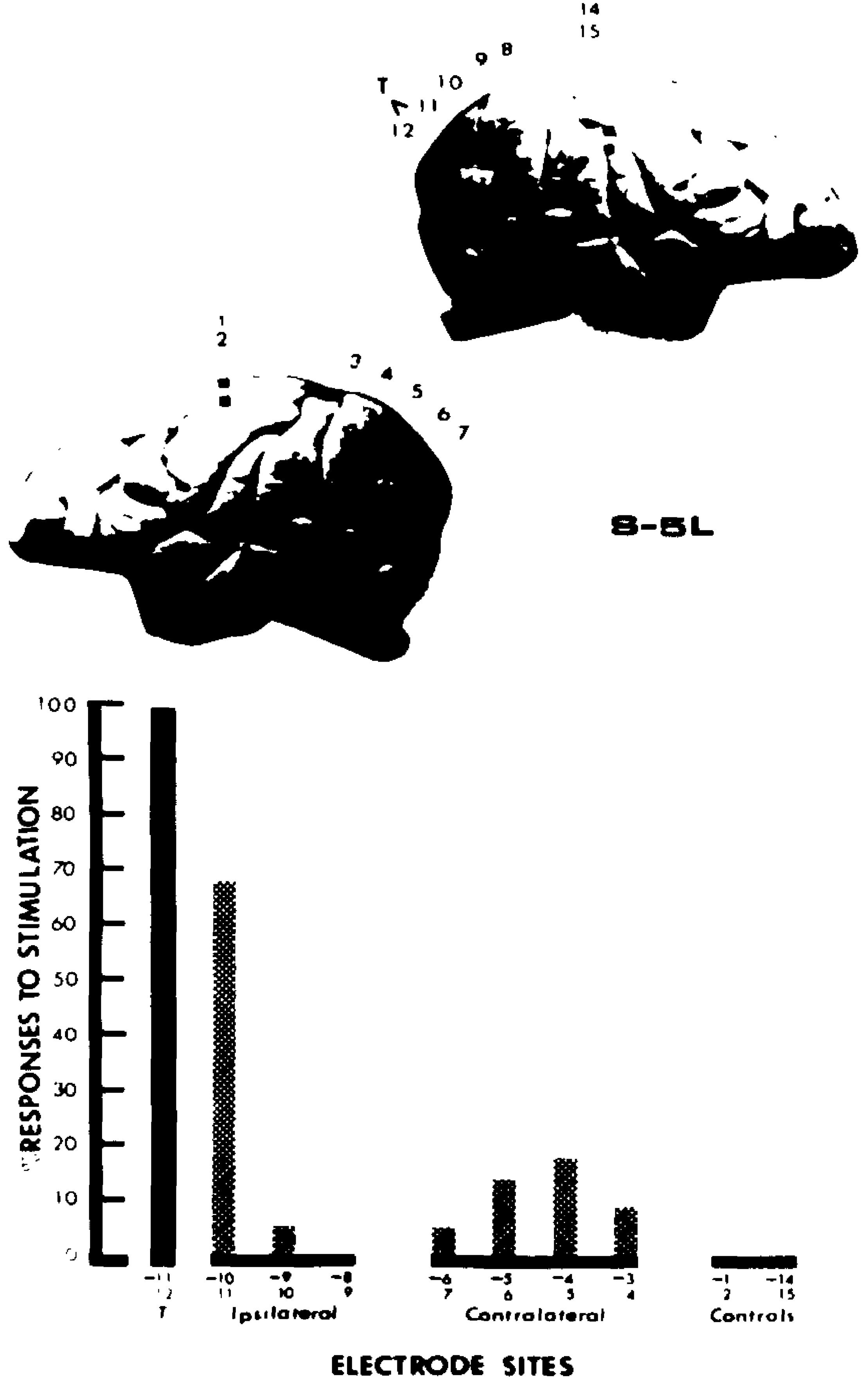

S-IL
T
10
11
12
13
21
16
17
3
4
5
6
7
8
9
% RESPONSES TO STIMULATION
0
10
20
30
40
50
60
70
80
90
100
First Sessions
Second Sessions
T
Ipsilateral
Contralateral
Controls
ELECTRODE SITES

Fig 3. Percentage of responses made by S-5L to stimulation of the training site and test sites during testing. The figure is based on 11 sessions (22 stimulations per test site and 198 stimulations of training site). See Fig 1 for explanation of symbols.


14
15
9 8
T 10
11
12
1
2
3 4 5 6 7
8-5L
RESPONSES TO STIMULATION
100
90
80
70
60
50
40
30
20
10
0
−11
12
T
−10
11
−9
10
−8
9
Ipsilateral
−6
7
−5
6
−4
5
−3
4
Contralateral
−1
2
−14
15
Controls
ELECTRODE SITES

is based on 22 stimulations, while the training site received 198 stimulations. As can be seen from the figure, a rather steep response gradient occurred ipsilaterally as a function of training-testing site distance. Stimulation of the furthest ipsilateral site resulted in no response.

Responses to stimulation of the contralateral striate cortex were low in comparison to all other animals. The contralateral gradient shown in Fig 3 indicates that response frequency was lowest at the point "most" homotopic to the training site (-6,7). The stimulation of parietal sites on either hemisphere yielded no responses.

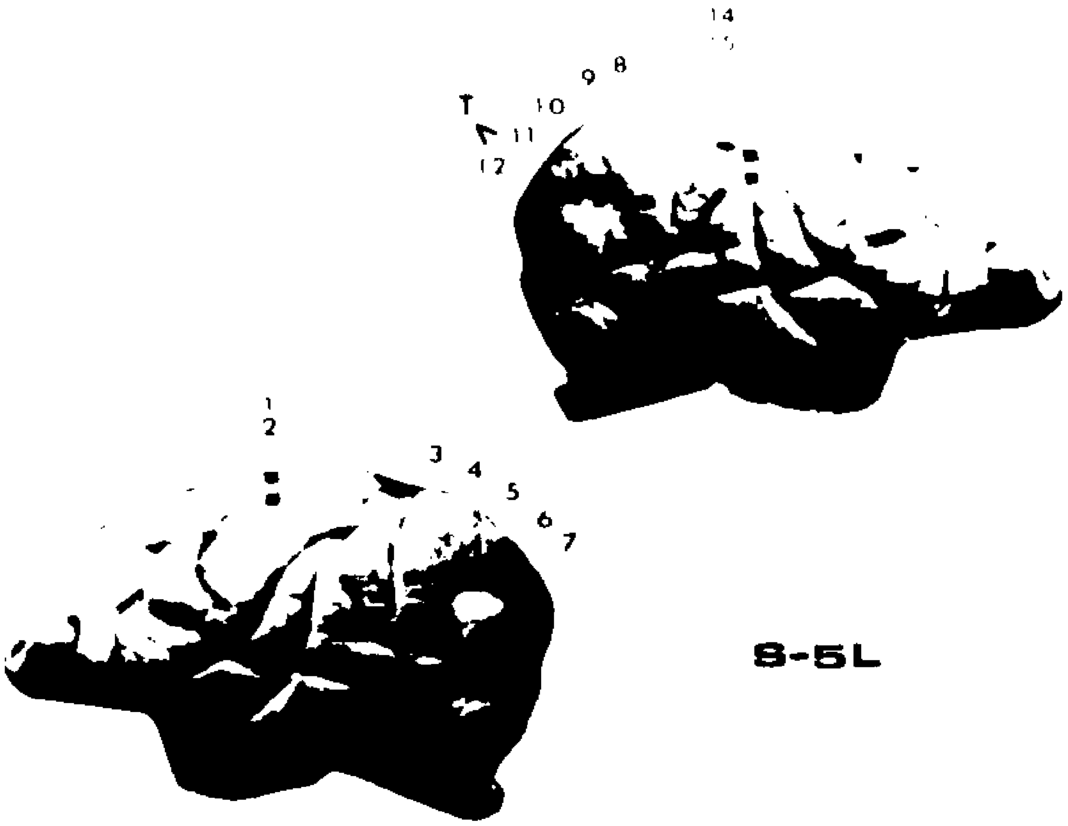
In Fig 4, the same data are graphed into the first 5, second 5, and last session. An elimination of responses to all stimulation except the site adjacent to the training site occurred by session 6. During session 11, no responses were made to stimulation of any test site.

The percentage of responses for S-7L for each stimulated site during the 7 sessions necessary for complete discrimination to occur is seen in Fig 5. The figure is based upon 14 stimulations per test locus and 112 stimulations of the training locus. The 2 electrodes furthest from the training site were on para-peristriate cortex, too far anterior to be on striate cortex. As can be seen, the response frequencies for these sites were both minimal.

On the side contralateral to training, the most anterior electrode contacted peristriate cortex. A gradient appeared which peaked at the sites "most" homotopic to the training site. There were no responses to stimulation of the parietal site.

It can be seen from Fig 6, which graphs the data into the first 5

Fig 4. Percentages of responses made by S-5L to stimulation of the training site and test sites during first 5, second 5, and last session. See Fig 1 for explanation of symbols.


14
T
10
9
8
11
12
1
2
3
4
5
6
7

S-5L

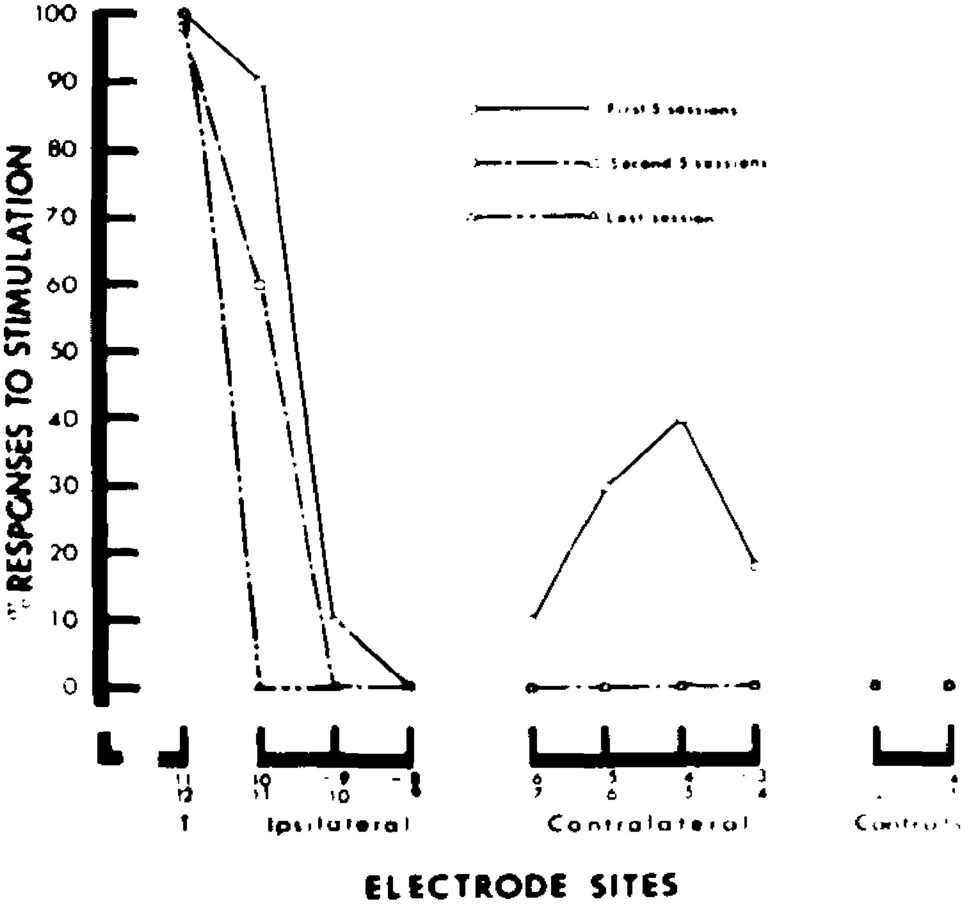
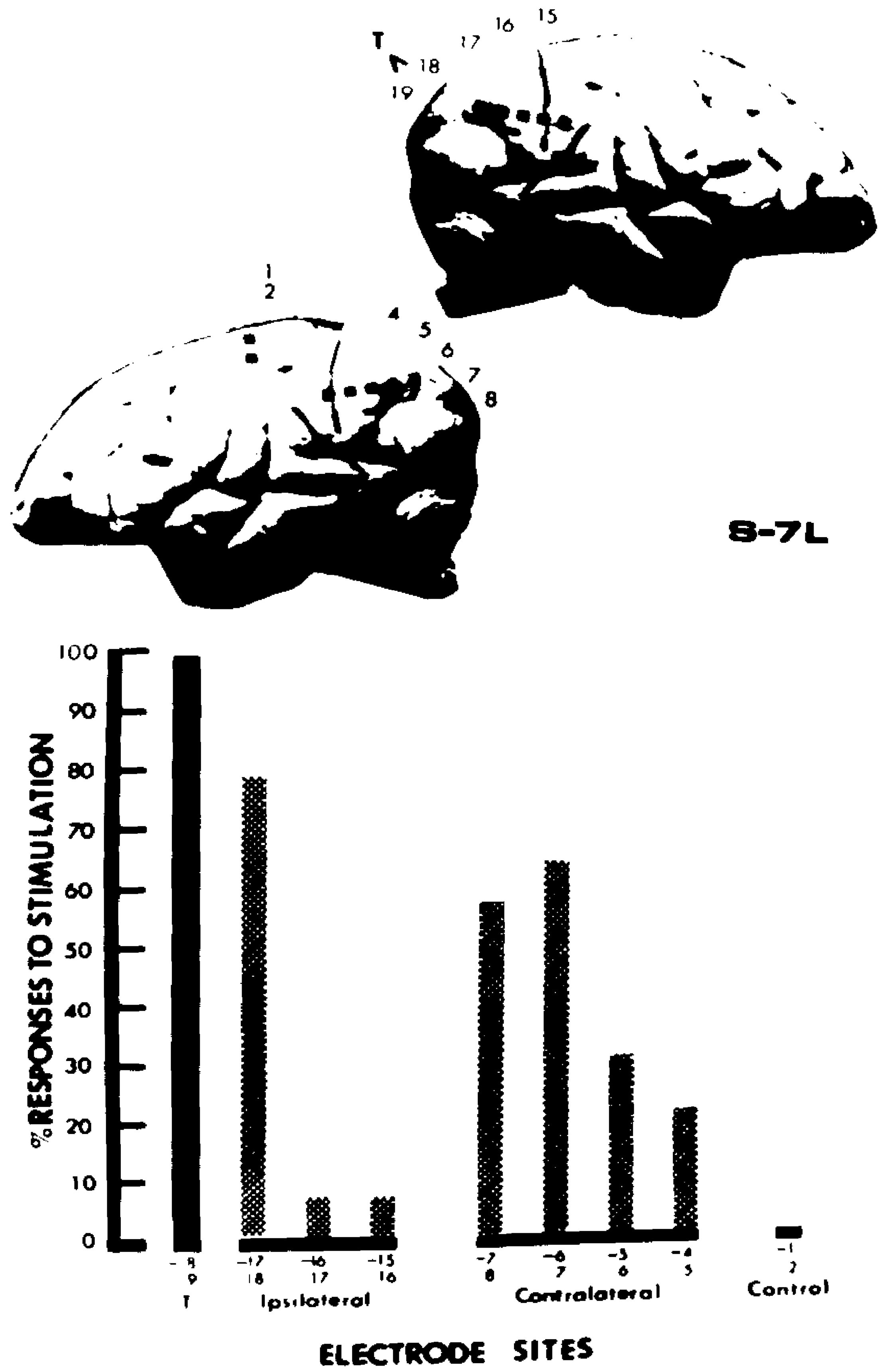
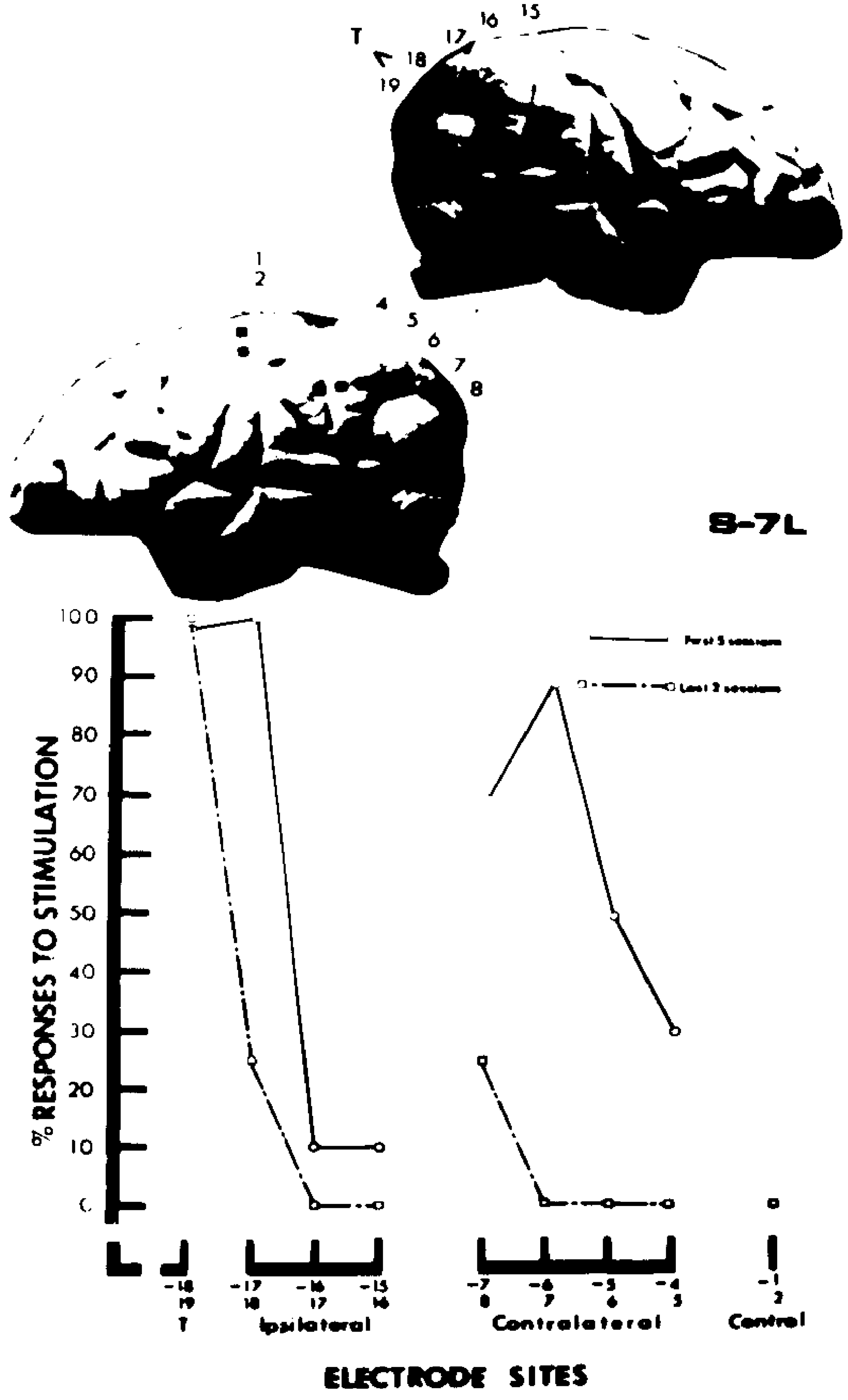

% RESPONSES TO STIMULATION
100
90
80
70
60
50
40
30
20
10
0
First 5 sessions
Second 5 sessions
Last session
11
12
1
10
11
9
10
8
Ipsilateral
6
7
5
6
4
5
3
4
Contralateral
Controls
ELECTRODE SITES

Fig 5. Percentage of responses made by S-7L to stimulation of the training site and test sites during testing. The figure is based on the response percentages for 7 sessions (14 stimulations per test locus and 112 stimulations of the training site). See Fig 1 for explanation of symbols.


T
1
2
4
5
6
7
8
15
16
17
18
19
% RESPONSES TO STIMULATION
0
10
20
30
40
50
60
70
80
90
100
-8
9
T
-17
18
-16
17
-15
16
Ipsilateral
-7
8
-6
7
-5
6
-4
5
Contralateral
-1
2
Control
ELECTRODE SITES

8-7L

Fig 6. Percentage of responses made by S-7L to stimulation of the training site and test sites during first 5 and last 2 sessions. See Figure 1 for explanation of symbols.


T
19
18
17
16
15
1
2
4
5
6
7
8
8-7L
% RESPONSES TO STIMULATION
100
90
80
70
60
50
40
30
20
10
0
First 5 sessions
Last 2 sessions
-18
19
T
-17
18
-16
17
-15
16
Ipsilateral
-7
8
-6
7
-5
6
-4
5
Contralateral
-1
2
Control
ELECTRODE SITES

and last 2 sessions, that discrimination between the training site and the test sites increased as a result of the testing experience. By session 7, only stimulation of the training site yielded a response.

Medial Striate Group. Eighteen sessions were necessary for Subject 6M to completely discriminate between the test sites and the training site (36 stimulations per test locus and 324 stimulations of the training locus). It can be seen from Fig 7 that no gradient occurred ipsilaterally. Contralaterally, highest response frequencies resulted from stimulation of sites closest to the area homotopic to the training site. No responses were made to frontal stimulation.

The data, graphed for successive groups of 5, 5, 5, and 3 sessions, appear in Fig 8. With few exceptions, there was a general tendency for increased discrimination to progress as a function of testing sessions both ipsilaterally and contralaterally. By the eighteenth session there was complete discrimination between the training and testing sites.

Fig 9 presents the data of S-8M for each test site and the training site for the 14 sessions necessary for complete discrimination to occur (28 stimulations per test locus and 112 stimulations of the training locus). The contralateral bank of electrodes was not used since no unconditional responses could be elicited from its electrodes. No ipsilateral gradient can be observed. Contralateral frontal stimulation elicited no responses. Inspection of Fig 10, which presents the data for the first 5, second 5, and last 4 sessions shows that partial discrimination between the training site and the test sites did not occur until the last 4 sessions. Complete discrimination occurred by session 14.

The percentage of bar-presses made by Subject 9M in response to all

Fig 7. Percentage of responses made by S-6M to stimulation of the training site and test sites during testing. The figure is based on response percentages for 18 sessions (36 stimulations per test locus and 324 stimulations of the training site). Control electrodes were placed about a centimeter more lateral than pictured on brain. See Figure 1 for explanation of symbols.


T
3
4
5
6
7
1
2
14
15
16
17
18
19
20
S-6M

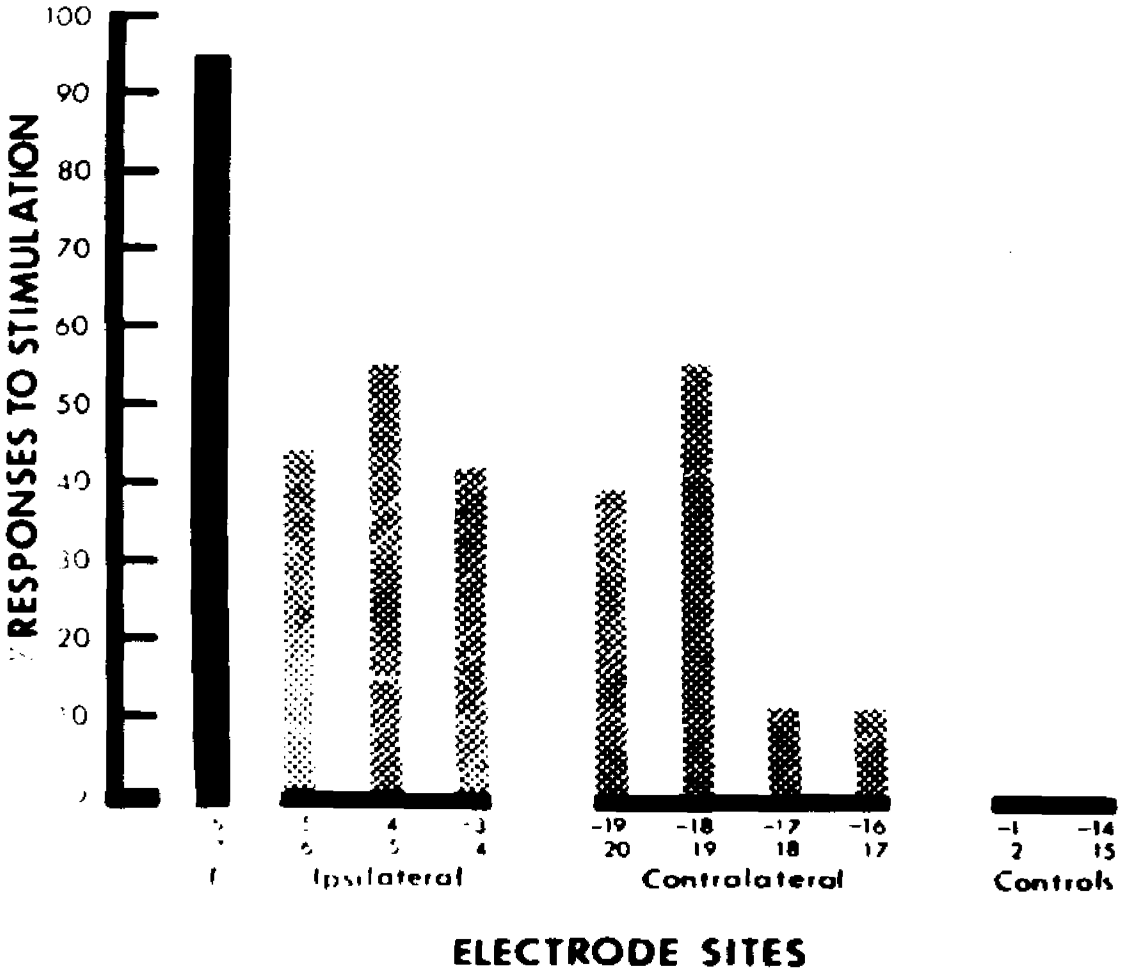

RESPONSES TO STIMULATION
100
90
80
70
60
50
40
30
20
10
0
T
5 6
4 5
-3 4
Ipsilateral
-19 20
-18 19
-17 18
-16 17
Contralateral
-1 2
-14 15
Controls
ELECTRODE SITES

Fig 8. Percentage of responses made by S-6M to stimulation of the training site and test sites during first 5, second 5, third 5, and last 3 sessions. Control electrodes were placed about a centimeter more lateral than pictured on brain. See Fig 1 for explanation of symbols.

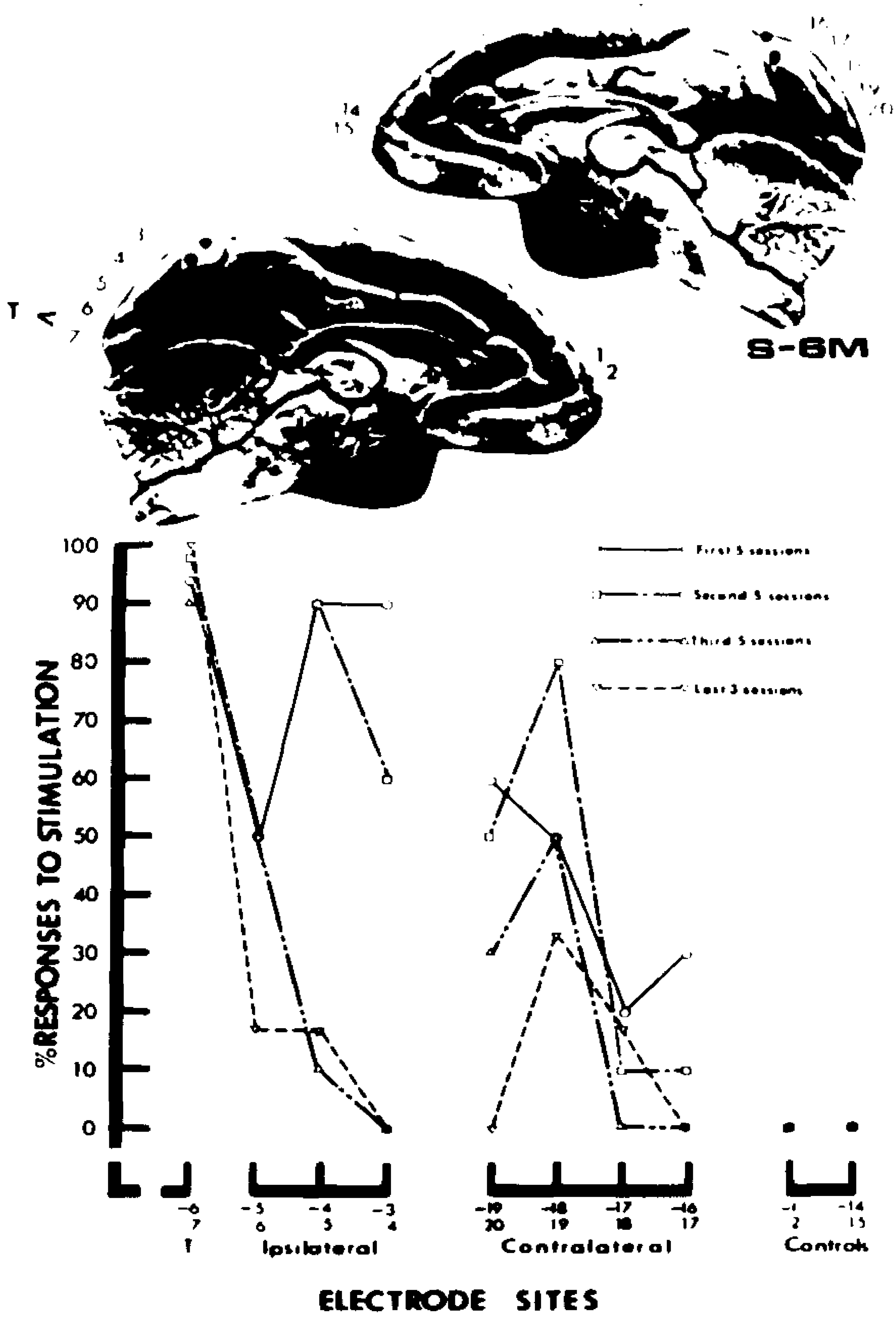

14
15
16
17
18
19
20
3
4
5
6
7
T
1
2
S-6M
100
90
80
70
60
50
40
30
20
10
0
%RESPONSES TO STIMULATION
First 5 sessions
Second 5 sessions
Third 5 sessions
Last 3 sessions
-6
7
T
-5
6
-4
5
-3
4
Ipsilateral
-19
20
-18
19
-17
18
-16
17
Contralateral
-1
2
-14
15
Controls
ELECTRODE SITES

Fig 9. Percentage of responses made by S-8M to stimulation of the training site and test sites during testing. The figure is based on the response percentages for 14 sessions (28 stimulations per test locus and 112 stimulations of the training site). Control electrodes were placed about a centimeter more lateral than pictured on brain. See Fig 1 for explanation of symbols.

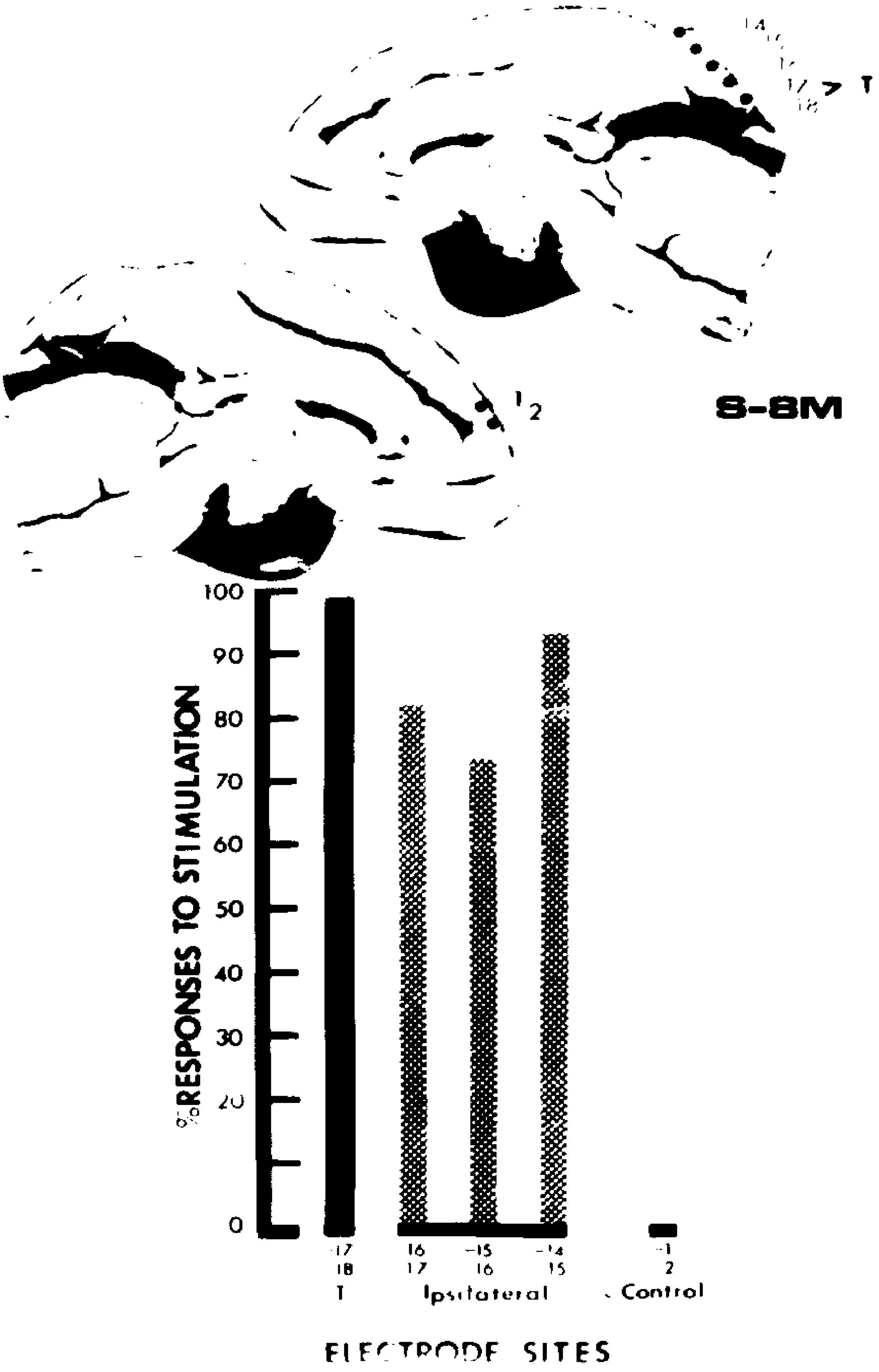
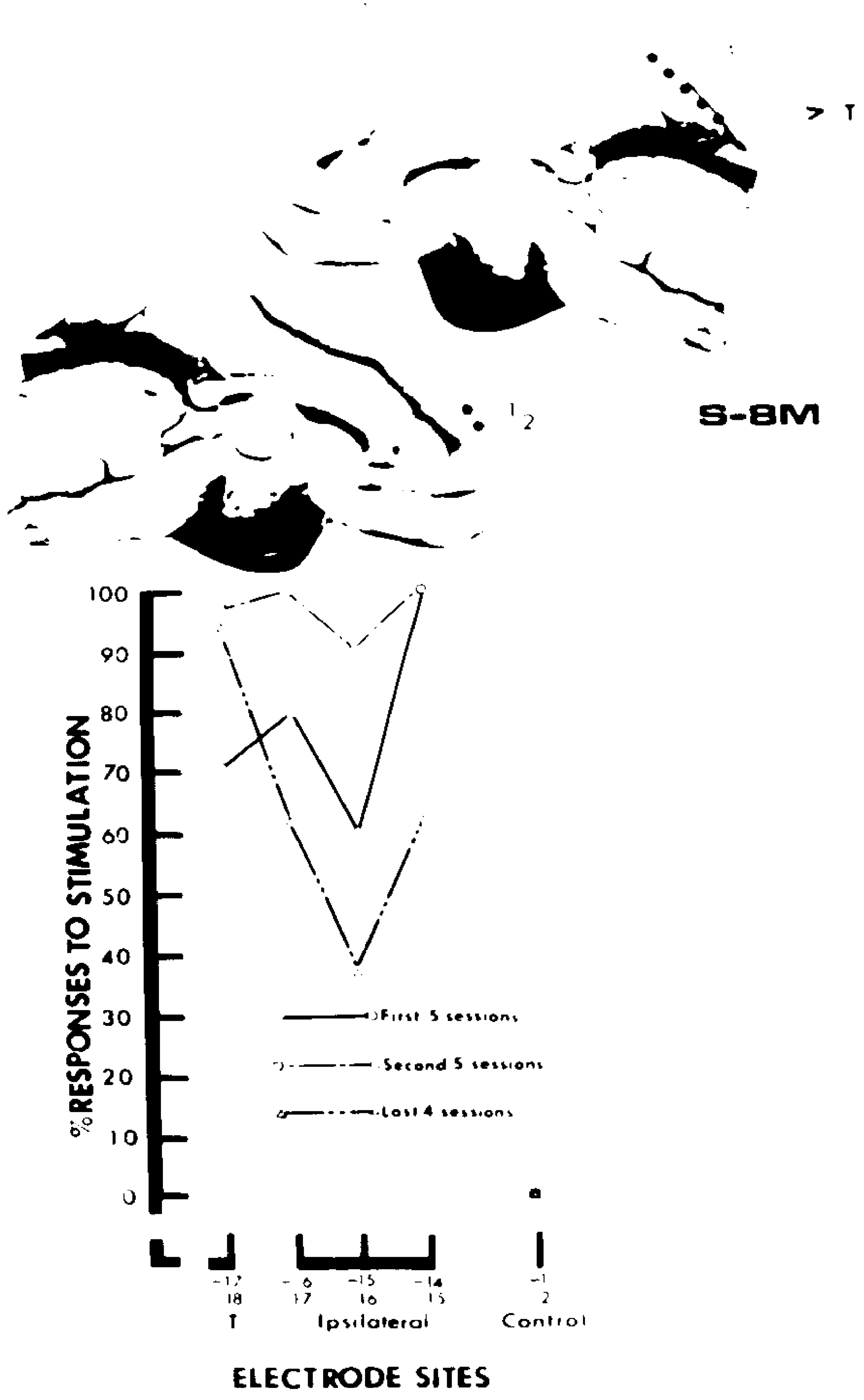

14
15
16
17
18
T
1
2
S-8M
% RESPONSES TO STIMULATION
100
90
80
70
60
50
40
30
20
0
17
18
T
16
17
15
16
14
15
Ipsilateral
1
2
Control
ELECTRODE SITES

Fig 10. Percentage of responses made by S-8M to stimulation of the training site and test sites during first 5, second 5, and last 4 sessions. Control electrodes were placed about a centimeter more lateral than pictured on brain. See Fig 1 for explanation of symbols.


S-8M
> T
1
2
% RESPONSES TO STIMULATION
100
90
80
70
60
50
40
30
20
10
0
First 5 sessions
Second 5 sessions
Last 4 sessions
-17
18
T
-6
17
-15
16
-14
15
Ipsilateral
-1
2
Control
ELECTRODE SITES

sites stimulated during testing is presented in Fig 11. Twenty-two sessions were required for complete discrimination to occur (44 stimulations per test locus and 440 stimulations of the training locus). No gradient occurred, ipsilaterally.

On the contralateral side the highest response frequencies occurred at the sites "most" anatomically homotopic to the training site. These frequencies exceeded the highest ipsilateral response frequency. Only 1 response was made to extra-striate cortex stimulation.

Fig 12, indicating the data from the first 5, second 5, third 5, fourth 5, and last 2 sessions, shows increased discrimination as a function of sessions in almost every instance. By session 22, only stimulation at the training site resulted in responses.

Comparisons of the Lateral and Medial Striate Cortex Groups. Figure 13 shows the mean percentage responses at ipsilateral striate cortex sites for the first 10 sessions in 2 lateral and 3 medial preparations. Subject 7L was not included in the figure since 2 of its electrodes on the training bank were on prestriate cortex. For the lateral group, each test site point in the figure is based upon 40 stimulations, while the training site point is based on 360 stimulations. For the medial group, each test site point is based upon 60 stimulations, while the training site point is based on 440 presentations. In lateral striate cortex, response frequency decreased as a function of distance from the training site. In contrast, the response frequencies resulting from test stimulation of the medial striate cortex sites fell into a virtually flat configuration. Response frequencies of the test sites were not inversely related to their distance from the training site.

Fig 11. Percentage of responses made by S-9M to stimulation of the training site and test sites during testing. The figure is based on the response percentages for 22 sessions (44 stimulations per test locus and 440 stimulations of the training site). Control electrodes were placed about a centimeter more lateral than pictured on brain. See Fig 1 for explanation of symbols.


14
15
18
21
1
2
S-9M

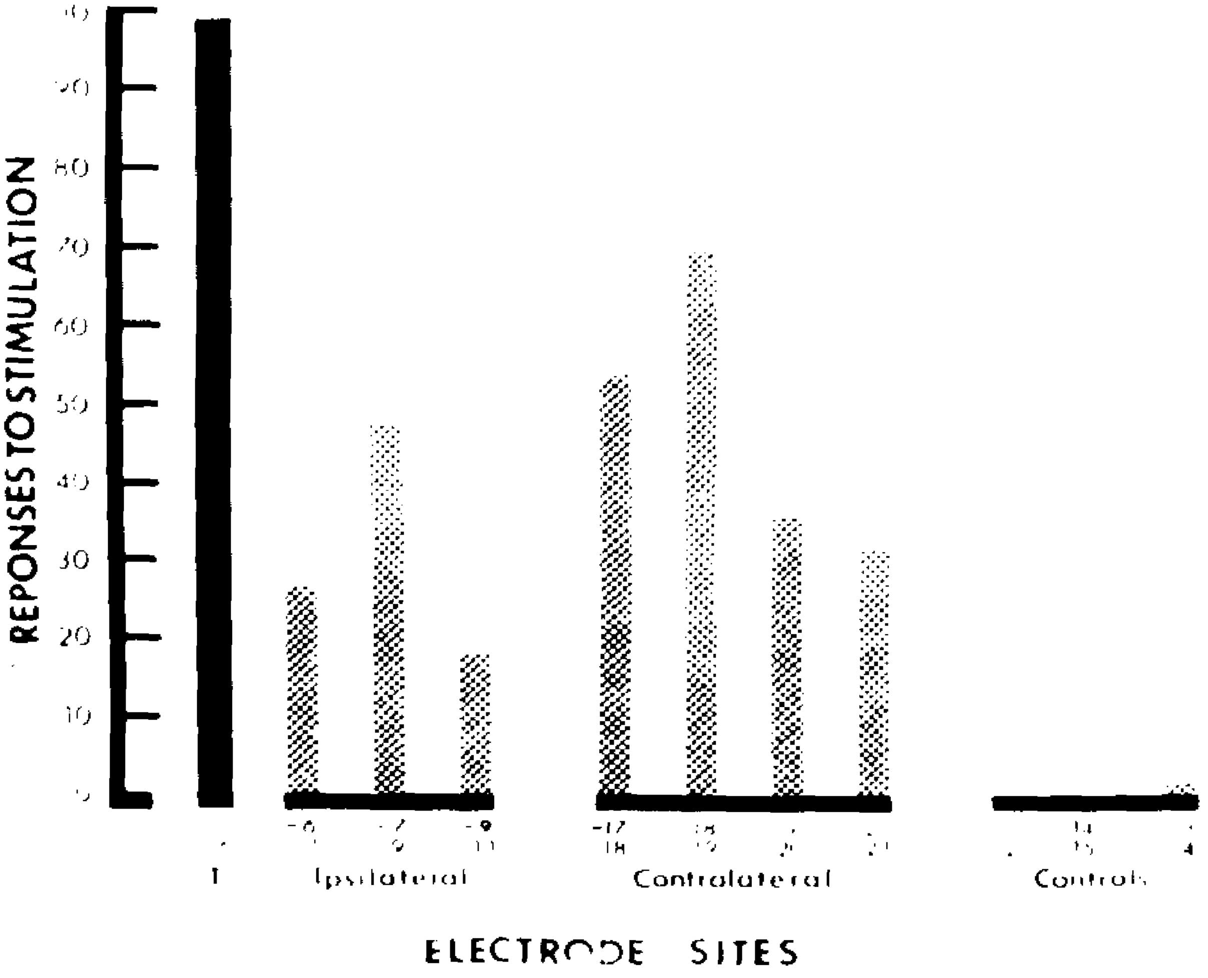

REPONSES TO STIMULATION
10
20
30
40
50
60
70
80
90
-6
-7
9
-9
11
-17
18
18
21
14
15
4
1
Ipsilateral
Contralateral
Controls
ELECTRODE SITES

Fig 12. Percentage of responses made by S-9M to stimulation of the training site and test sites during first 5, second 5, third 5, fourth 5, and last 2 sessions. Control electrodes were placed about a centimeter more lateral than pictured on brain. See Fig 1 for explanation of symbols.


17
18
19
20
21
14
15
T
5
6
7
9
11
3 4
1 2
S-9M

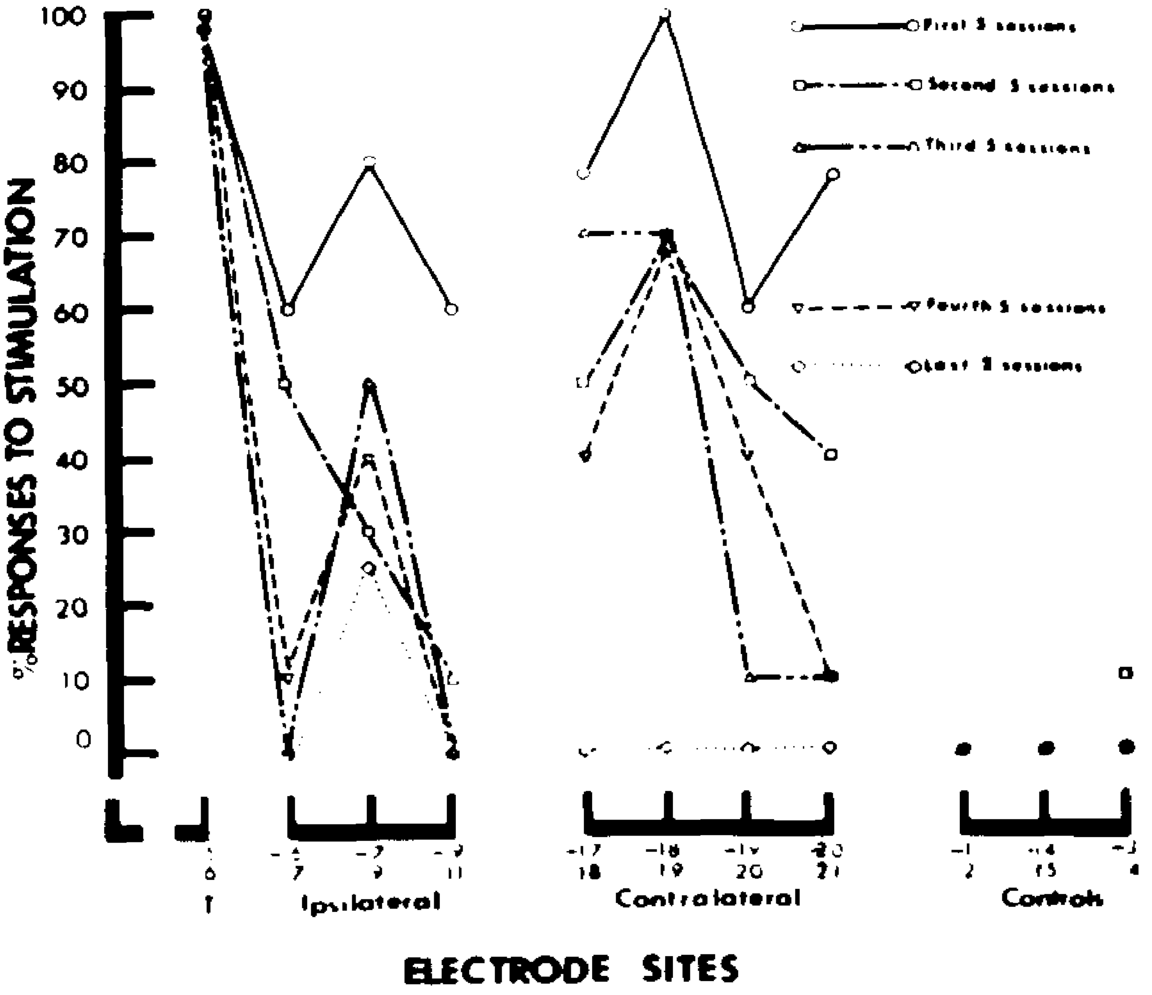
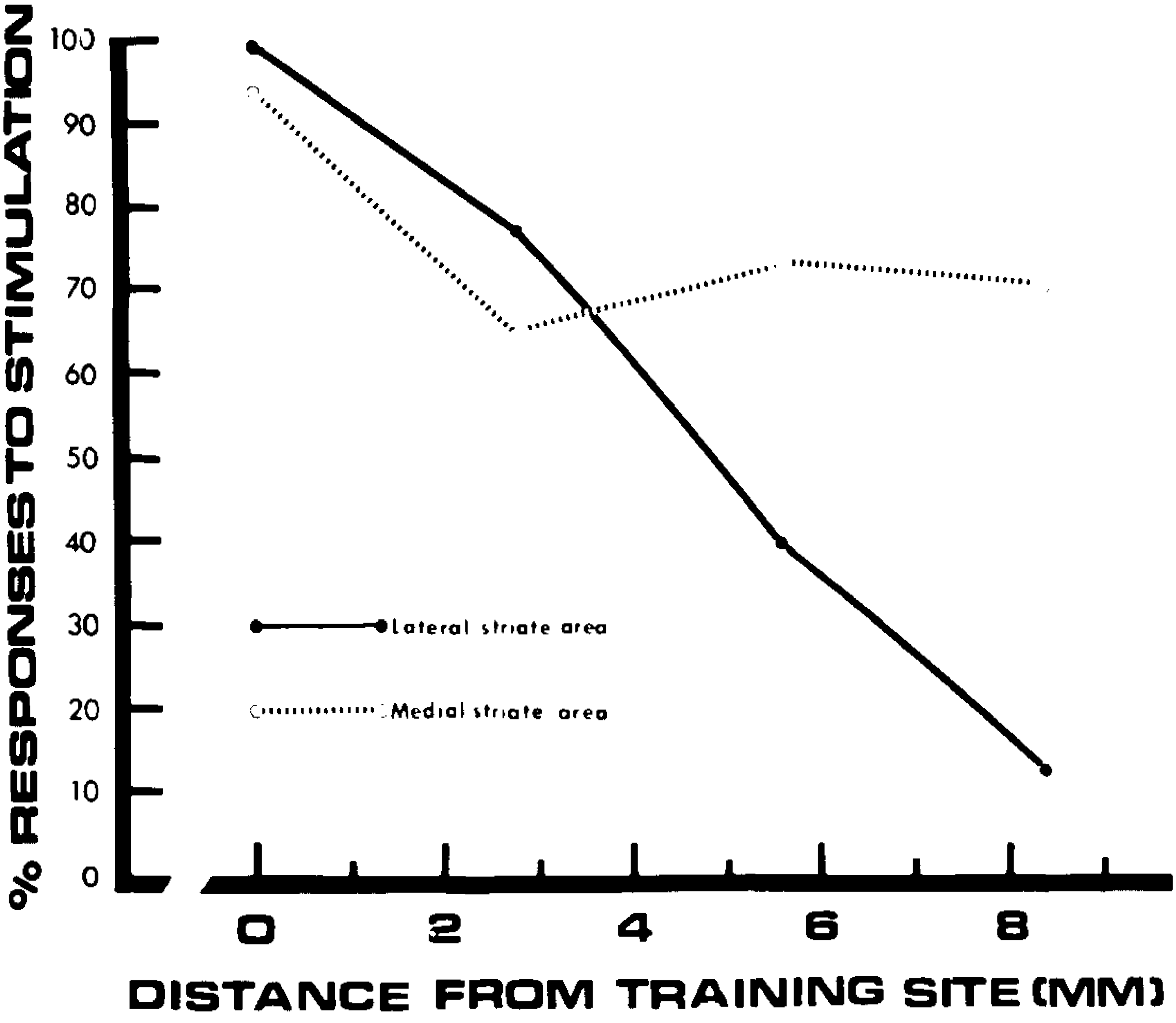

% RESPONSES TO STIMULATION
100
90
80
70
60
50
40
30
20
10
0
First 5 sessions
Second 5 sessions
Third 5 sessions
Fourth 5 sessions
Last 5 sessions
6
T
-4 7
-7 9
-9 11
Ipsilateral
-17 18
-18 19
-19 20
-20 21
Contralateral
-1 2
-14 15
-3 4
Controls
ELECTRODE SITES

Fig 13. Mean percentages of responses at ipsilateral striate sites for the first 10 sessions in 2 lateral and 3 medial subjects. For the lateral group, each test site point is based upon 40 stimulations, while the training site point is based on 360 stimulations. For the medial group, each test site point is based upon 60 stimulations, while the training site point is based on 440 stimulus presentations.


% RESPONSES TO STIMULATION
100
90
80
70
60
50
40
30
20
10
0
0
2
4
6
8
DISTANCE FROM TRAINING SITE (MM)
Lateral striate area
Medial striate area

Differences between the 2 groups were also seen in the number of sessions required for complete discrimination to occur between the training site and the test sites. Table III shows the number of sessions necessary for total discrimination to occur for each subject as well as the group means and standard deviations. The means of the lateral and medial striate cortex groups are significantly different ($t = 3.34$, $p < .05$, $df = 4$).

Discrimination between the training stimulus and test stimuli of the contralateral hemisphere was greater in the lateral than in the medial cortex preparations. In the 2 applicable (bilaterally equipped) medial cortex animals, the highest contralateral test site frequencies were either equal to (S-6M) or greater than (S-9M) the highest ipsilateral test site frequency. In all lateral striate cortex preparations, the greatest contralateral response frequency always fell below the greatest ipsilateral frequency.

Polarity Discrimination

The number of random pairings of training and reversed polarity stimulations necessary for polarity discrimination to occur at the training site is shown in Table IV for both groups of animals. Since S-8M never made the discrimination even after 300 pairings, this number represents an arbitrary point of termination, and thus the S.D. for the medial group is underestimated. Because of this and because of the heterogeneity of variance between groups, a t-test could not be employed as a test for statistical differences between the 2 groups. A Mann-Whitney U test was applied and showed the differences between the groups to be statistically significant ($p = .05$, $U = 0$).

TABLE III

NUMBER OF SESSIONS FOR COMPLETE DISCRIMINATION BETWEEN TRAINING AND TESTING SITES

Lateral Striate Cortex Group		Medial Striate Cortex Group	
Subject	Sessions	Subject	Sessions
S-1L	10	S-6M	18
S-5L	11	S-8M	14
S-7L	7	S-9M	22
Mean	9.33	Mean	18.00
S.D.	1.70	S.D.	3.26

TABLE IV

NUMBER OF RANDOM PAIRINGS OF NORMAL AND REVERSE POLARITY STIMULATIONS NECESSARY FOR POLARITY DISCRIMINATION

Lateral Striate Cortex Group		Medial Striate Cortex Group	
Subject	Trials	Subject	Trials
S-1L	0	S-6M	28
S-5L	0	S-8M	300
S-7L	1	S-9M	74
Mean	.33	**Mean**	134.00
S.D.	.46	S.D.	118.87

DISCUSSION

Several findings of the present study tend to differentiate functionally the lateral and medial areas of the striate cortex: (1) Within lateral striate cortex, the speed with which a discrimination was established between stimulation of the training site and an ipsilateral test site was directly related to the distance between the sites, whereas, within medial striate cortex no such relationship was observed between the time required to establish a discrimination and inter-stimulus distance; (2) In order to attain perfect discrimination, i.e., a session in which no responses were made to any test stimulus, medial striate cortex subjects required twice as many sessions as lateral striate cortex animals; (3) Polarity discrimination required significantly more comparisons of polarity directions for the medial than for the lateral striate cortex subjects; (4) Only animals with medial striate cortex electrodes demonstrated contralateral response frequencies equal to or greater than maximal ipsilateral response frequencies.

The following additional findings, on the other hand, were common to both groups of subjects: (5) Within both cortical areas, discrimination between training and test stimuli increased as a function of the continued differential reinforcement of responses to the two types of stimuli; (6) In 4 out of the 5 subjects with viable bilateral striate cortex electrodes, maximal response frequencies on the contralateral hemisphere occurred at those sites most nearly homotopic to the training site; (7) After conditional stimulus training on either striate cortex area, virtually no responses were made during stimulation of frontal, parietal, or temporal cortex.

The total discrimination between stimulation of striate and non-visual cortex confirms the data of previous generalization studies employing electrical stimulation as a conditional stimulus (Doty, 1965; Doty, 1966; Schuckman, 1966; Schuckman and Battersby, 1966). It is of interest to note that the largest shift in response percentages between adjacent sites (71.5 percent) occurred at the transition from striate to prestriate cortex (S-7L). The largest shift in response percentages between adjacent sites within striate cortex was 63.7 percent (S-5L). This is compatible with the finding of Doty (1969) that a habit learned with striate cortex stimulation as the CS generalizes to prestriate stimulation at a moderately reduced level. Since striate and prestriate cortex are anatomically and physiologically related (Polyak, 1957; Cowey, 1964), such an intermediate equivalence might be expected. It is impossible to determine at this time whether responses made in this area after striate cortex training reflects any functional similarities between the 2 areas or is merely a result of current spread.

Of all the contralateral test sites, those most anatomically homotopic to the training site generally showed the greatest response frequencies. This was true of all 5 subjects bilaterally equipped with striate cortex electrodes except S-5L. Regarding this preparation, it may very well be that points seen as anatomically homotopic may not necessarily be physiologically homotopic. In addition, slight differences in electrode contact may serve to produce different stimulus effects at 2 truly homotopic points.

The finding that only animals with medial striate cortex electrodes demonstrated contralateral response percentages equal to or greater than maximal ipsilateral response frequencies is interesting in view of the cortical representation of the visual field (Daniel and Whitteridge, 1961; Talbot and Marshall, 1941). The lateral striate electrodes excited those points on striate cortex which were associated with the horizontal meridian. The training sites for the 3 lateral striate cortex preparations subserved points in the visual field about 2 (S-1L), 8 (S-5L), and 6 (S-7L) deg from the fovea on the horizontal meridian. Their respective homotopic electrodes on the contralateral hemisphere subserved points of equivalent eccentricities in the opposite hemifield. Stimulation of these test sites thus produced phosphenes about 4, 16, and 12 deg respectively from the phosphenes produced by stimulation of the training sites. The medial striate cortex electrodes, running parallel and in proximity to the border of area 18, subserved the vertical meridian. The training site subserved areas of the field just to one side of the vertical meridian, while its homotopic testing site subserved an area of field just to the other side of the meridian. The 2 phosphenes produced by stimulation of these sites are much closer than those produced by stimulation of homotopic sites on lateral striate cortex. The proximity of phosphenes produced by stimulation of homotopic areas in medial striate cortex along with the tendency for these peripheral phosphenes to possess less distinct borders may have accounted for the relatively high percentage of responses to stimulation of test sites approximately homotopic to the training sites.

Within lateral striate cortex, the finding that response probability is related to the distance between the training site and the test site differs from previous results obtained within a generalization paradigm. In reviewing the earlier findings, Doty (1969) stressed the "nearly total equivalence obtained between points in area 17 of macaque" (p. 306).

Test stimuli applied to various areas of striate cortex have appeared to result in the same responses as those resulting from stimulation of the original training site. Response probability likewise seemed unaffected by the distance between the training and test site. The cortical retinal map revealed by anatomical, clinical, and physiological studies appears irrelevant in the determination of the functional equivalence of 2 striate cortex stimuli. The gradients exhibited by the lateral striate cortex animals in the present study, however, do relate to the cortical retina since the spatial separation between 2 stimuli on striate cortex is an important variable in determining to what extent the 2 stimuli will result in the same response frequencies.

The apparent equivalence observed in the previous studies probably resulted from testing techniques not specifically designed to reveal differences in response strengths associated with the spatial separation of the stimuli. While the previous studies used a generalization paradigm to determine to what extent stimuli applied to various areas of cortex would have equivalent effects, the present study employed a discrimination paradigm to the same end. Test stimuli in this case were thus presented in close temporal proximity to the presentation of the training stimulus. This frequent opportunity for comparison between the stimuli, along with the reinforcement contingencies they represented (responses rewarded during the training stimulus but not during the test stimuli) was probably crucial in demonstrating the role of inter-stimulus distance in determining the functional equivalence of 2 cortical stimuli. Lending validity to this suggestion is the finding that response differences produced by training and test stimulation increased as a function of discrimination training. At the beginning of testing, there was less discrimination between stimulation of the different sites than in the later blocks of sessions where strong discrimination was demonstrated. In other words, as discrimination training continued, response frequencies during test stimuli decreased. Since no such training was involved in previous studies, this differentiation never developed.

The gradients obtained in the lateral subjects stand in sharp contrast to the pattern found in the medial striate cortex group where no correlation between stimulus discrimination and inter-stimulus distance was observed. It should be emphasized that the similar response-producing capacity demonstrated by all test site stimuli on medial striate cortex does not necessarily mean that these sites subserve the same locus within the visual field. It will be recalled from the study of Brindley and Levin (1968) that close phosphenes occupying different areas within the visual field could not be discriminated if more than 2 sec elapsed between the 2 phosphene-producing stimuli. In the present study, at least 20 sec elapsed between stimulus presentations. A shorter inter-trial interval may have revealed a medial striate cortex gradient resembling that found in lateral striate cortex. In any case, with equal testing procedures, no differences in response percentages appeared between test sites on medial striate cortex, whereas test site response percentages on lateral striate cortex formed a gradient as a function of the distance between the training and test sites.

A second finding also indicated lateral striate cortex superiority in spatial discrimination. Although complete discrimination between the training site and the test sites eventually occurred in both lateral and medial striate cortex areas, significantly fewer sessions were required in the former than in the latter area.

The greatest differences between the medial and lateral striate cortex preparations appeared in their capacity to discriminate polarity reversals at the training site. However, polarity reversal discrimination can be viewed as a special case of spatial discrimination. Mihailovic and Delgado (1956) unipolarly stimulated various cortical and subcortical sites in unanesthetized monkeys and found that cathodal stimulation (stimulating electrode negative) was more effective in producing neural activity resulting in an overt response than anodal stimulation. Thresholds obtained for skeletal muscle or autonomic responses were always lower for cathodal stimulation. Thus in the present experiment when the stimulating current is reversed at the training site in relation to the original training direction, the point of maximal excitation occurs 2.8 mm (the interelectrode distance) from the original area of maximal excitation. This spatial difference in maximal excitation was easily discriminated by lateral striate preparations, but was considerably more difficult for the medial striate cortex subjects. In fact, S-8M, after several hundred trials, was still responding to the unreinforced polarity.

At the phenomenological level, the superiority of lateral striate cortex for spatial discrimination can be viewed in conjunction with a finding of Brindley and Lewin (1968). In contrast to the sharply delimited phosphenes reported by their blind subject upon stimulation of the foveal region of striate cortex, stimulation of the peripheral region of striate cortex resulted in phosphenes having no definite shape and indistinct borders. Here then is a subjective correlate of the differences in spatial discrimination observed between lateral and medial striate cortex.

Another phenomenological explanation for the differences between the 2 preparations involves the magnification factor, defined by Daniel and Whitteridge (1961) as millimeters of striate cortex concerned with 1 deg of visual field. These authors determined the magnification factor to be maximal at the fovea, where 1 deg of visual field was subserved by 6 mm of cortex, and to fall off abruptly 10 deg into the periphery, where 1 deg of field was subserved by only 1 mm of cortex. Further equivalent advances into the peripheral field were associated with only small changes in magnification (See Daniel and Whitteridge, 1961, p.212, for the exact function). The greatest change in magnification occurs, then, on the lateral area of striate cortex where the 5 lateral striate cortex electrodes were located. One mm of cortex under the most anterior electrode subserved only about 10 mm of field, while 1 mm of cortex under the most posterior electrode subserved about 30 mm of visual field.

This means that direct excitation of equal amounts of lateral striate cortex produces phosphenes of considerably different sizes. In contrast, the magnification factor associated with medial striate cortex is to a great extent constant from one electrode site to another, and thus the phosphenes resulting from their excitation tend to be of equal size, making discrimination more difficult.

At the physiological and anatomical level, the differences between the 2 areas may have resulted from (1) inherent differences between the 2 striate cortex areas themselves, (2) inherent differences between the projections of the 2 striate cortex areas, and/or (3) differential experiences of the 2 areas in problems of spatial discrimination. These alternatives which, of course, are not mutually exclusive, will be clarified and elaborated in the following sections.

1. Inherent Differences within Striate Cortex. Several attempts have been made to parcellate striate cortex into discrete subareas on the basis of various criteria. In terms of thickness, small differences have been consistently reported between the peripheral and central regions. Solnitzky and Harman (1946) examined transverse sections of primate brains stained with thionin. Each section included both regions of striate cortex so that any differences observed could not be associated with differential treatment of the specimens. It was found that in all diurnal primates included in the study, the lateral area of striate cortex (subserving central vision) was thicker than the medial area of striate cortex (subserving peripheral vision). The central/peripheral thickness ratio ranged between 1.29 and 1.51, the ratio reported for Macaca mulatta being 1.45. Other investigators have obtained similar results. Cowey (1964) and Lashley and Clark (1946) have reported ratios for Macaca mulatta of 1.34 and 1.17 respectively, although, in the former study, where more than one hemisphere was involved, the thickness differences were not significant. Beck (1934) also observed the central region to be thicker than the peripheral region of striate cortex.

If such differences in thickness are real, it might be reasonable to associate these differences with the discrepancy in performance of the medial and lateral striate cortex groups. Cowey (1964), however, states that such differences in thickness are probably the result of differences between the planes of the sections of the 2 cortical areas. Orbach (1959) similarly viewed the angle of the cortical cut to be a contaminating factor which contributes to the apparent differences in cortical thicknesses.

Even if differences in thicknesses do differentiate the 2 cortical areas, these differences may have no functional significance. In reference to the apparently thinner cortex within the calcarine fissure, i.e., where most of the peripheral field is subserved, Lashley states that "the thinning of cortex within sulci is a rather general characteristic and is of very doubtful functional significance" (p. 277).

Besides their investigation of differential thicknesses of the 2 areas, Solnitzky and Harman also examined the cytoarchitectonics of the striate cortex of various primates, and observed differences between the peripheral and central sector in <u>Macaca</u> <u>mulatta</u>. In addition to their finding that each of the 6 layers of striate cortex is thicker within the central region, they also reported structural differences between each layer in the central sector and its counterpart layer in the peripheral sector.

Lashley and Clark (1946) disputed these contentions. In their extensive study on the cytoarchitectonics of both <u>Ateles</u> and <u>Macaca</u> <u>mulatta</u>, these authors concluded that "no valid evidence for the existence of structural or functional subdivisions of the striate area other than those resulting from the topographic projection of the retina, has been presented" (p. 278). The differences, if any, between the 2 areas of striate cortex appear to be rather slight, escaping the trained eye of a number of neuroanatomists besides Lashley and Clark (Bonin, 1942; Brodmann, 1905, 1925; Vogt and Vogt, 1919).

Whether any of these occasionally observed structural differences account for the large differences in spatial and polarity discrimination observed between the lateral and medial straite cortex preparations cannot be ascertained at present.

2. Inherent Differences between the Projections of the 2 Striate Areas. In a recent study by Kuypers, Szwarcbart, Mishkin, and Rosvold (1965), lesions were made at various cortical sites in *Macaca mulatta*. From 11 to 14 days post-operatively the animals were sacrificed and perfused with formalin. Transverse brain sections were prepared and impregnated with silver according to the Nauta-Gygax technique. Lateral striate cortex lesions in 3 monkeys resulted in degeneration within the striate area immediately adjacent to the lesion and within a cortical belt corresponding to Brodmann's areas 18 and 19 (parastriate and peristriate cortex respectively). No medial striate cortex lesions were attempted.

It was determined in other preparations that lesions made in the para-peristriate area (prestriate area) resulted in degeneration mainly in the vicinity of the arcuate sulcus and the caudal 2/3 of the inferior convexity of the temporal lobe. This latter area was shown to send fibers back to the para-peristriate belt as well as to the prefrontal area.

According to Kuypers *et al*. (1965), the para-peristriate inferotemporal connections are of significant functional importance. They suggest that it is by virtue of these fibers that inferotemporal cortex fulfills its function in visual pattern discrimination. The finding that these fibers project to the caudal 2/3 of the inferotemporal cortex along with the additional findings of Brown (1963), Mishkin (1954), and Mishkin and Pribram (1954) that the same 2/3 are concerned with normal pattern discrimination, supports this contention.

It appears that the neural impulses resulting from stimuli at the retina do not terminate upon reaching striate cortex, but are continued through an extensive network of extra-striatal cortical tissue. Thus, direct electrical stimulation of striate cortex involves not only those neurons within close proximity of the electrodes, but also other neurons spread widely over the cortical mantle.

Important for the interpretation of the present study, and in particular for the results demonstrating medial-lateral striate cortex differences in discrimination, are the additional findings showing differences in the quantity of projections of these 2 striate cortex areas to extra-striate cortex. Working primarily with the squirrel monkey, Saimiri sciureus, under barbiturate anesthesia or following a midpontine pretrigeminal decerebration, Cowey (1964) was able to record prestriate electrical responses to punctate photic stimulation and to electrical stimulation of striate cortex. The prestriate evoked potential to light occurred about eight to fifteen msec after the onset of the early surface-positive wave on striate cortex. Although the prestriate response could be evoked by a full-field stimulus, it was more prominent to discrete stimulation presented centrally. Stimuli lying more than 5 deg from the fovea proved completely ineffective. A prestriate cortical retina was demonstrated for central vision which resembled a mirror image of the striate cortical retina. Since unilateral extirpation of striate cortex abolished the prestriate evoked potential to light on the lesioned side, the prestriate response must have been mediated via striate cortex and not by some subcortical mechanism.

The topological relationship between striate and prestriate cortex was also shown by direct stimulation of striate cortical loci (0.1 msec, 2-4 volts). Confirming the results obtained from photic stimulation, electrical stimulation of the medial striate cortex (subserving peripheral vision) yielded essentially negative results. Small potentials resulting from striate cortex stimulation of relatively high voltages (6 volts) were recorded from prestriate cortex in only 2 of 8 attempts.

Most important in terms of the present discussion are the complementary findings that stimulation of the peripheral retina and stimulation of medial striate cortex (peripheral region) resulted in negligible prestriate responses. According to Cowey, these findings may indicate that "the connection between striate and prestriate cortex is well developed in the cortical area concerned with foveal vision, but not elsewhere" (p. 390). Perhaps it is the extensive projection system from lateral striate cortex to extra-striate cortex that accounts for differences in discrimination capacity observed between medial and lateral striate cortex preparations. The greater quantity of neural excitation resulting from the stimulation of lateral striate cortex may be responsible for the capacity for discriminating spatial differences observed in lateral striate animals.

It should be noted that not all investigations of striate-prestriate cortical connections have yielded positive results. Jasper, Ajmone-Marsan, and Stoll (1952) failed to produce after-discharges in prestriate cortex upon repetitive electrical stimulation of striate cortex although such stimulation of the latter area did result in activation of subcortical structures (see below). Negative findings were also reported by von Bonin, Garol, and McCulloch (1942) who applied a strychnine solution to striate cortex and were able to detect electrical changes only from the narrow, parastriate area of prestriate cortex.

Besides the possible differences in cortico-cortical pathways associated with the lateral and medial striate cortex, there are extensive neural projections from striate cortex to subcortical centers which may have had a role in the observed differences between the lateral and medial striate cortex preparations. Jasper, et al., found that repetitive stimulation of striate cortex resulted in a localized after-discharge in a portion of the lateral geniculate body, the lateral area of the pulvinar, and the superior colliculus and its surrounding area. Although the authors state that these after-discharges are not conducted antidromically, Granit (1962) stated, in reference to this study, that antidromic stimulation was a possible contaminating factor. Any differences between these and other subcortical projections of the lateral and medial striate cortex, whether ortho- or antidromic, could have been critical in determining the differences between the spatial discrimination capacities of the 2 preparations observed in the present study. Differences in the subcortical projections can, in fact, be inferred from the eye movements resulting from stimulation of the 2 areas. Stimulation of 80 percent of the medial striate cortex sites resulted in oblique eye movements, whereas stimulation of the lateral sites always resulted in horizontal movements.

Although no definitive conclusion can be reached concerning the role of extra-striate cortex and subcortical systems in determining the behavioral differences observed, it must be noted that striate cortex stimulation has widespread effects on a variety of neural structures. To conclude that any one of these structures was responsible for the differences in spatial discrimination is premature at this point.

3. Differences between Lateral and Medial Striate Cortex Resulting from Differential Experience in Spatial Discrimination. This hypothesis states that at birth, the capacity for spatial discrimination of striate cortex excitation, either photically or electrically induced, is equal for both lateral and medial striate cortex. Discrimination between activ-

ation of adjacent sites A and B on medial striate cortex will occur with the same facility as the discrimination of comparable sites A' and B' on lateral striate cortex. (If the present experiment were performed on monkeys at this stage of development, no differences should be revealed between the 2 cortical areas since the "experience" of the 2 areas would have been equal.)

Central vision would be employed for problems of spatial discrimination at this early stage of development because of the extensive built-in magnification of the foveal region of the retina. Employing the visual system subserving the fovea at this stage results in the involvement of more, not "better" cortex. In other words, at this stage of development it is quantity, not quality of cortex which fully accounts for the differences between foveal and peripheral vision.

According to the hypothesis, with continued exposure to problems of spatial discrimination solely on the basis of differential magnification, lateral striate cortex will become intrinsically more capable of mediating these problems than medial striate cortex. In the present experiment, for example, where inter-electrode distances were held constant in both striate cortex areas, subjects discriminating electrical stimuli on lateral striate cortex showed a greater proficiency than those subjects required to discriminate between similar stimuli on medial striate cortex.

Whether, in fact, any morphological, physiological, or biochemical differences occur between the 2 areas as a function of differential experience is as yet unknown. A number of studies have shown that differential visual experience between animals does result in internal differences in their respective cortices. In an experiment by Valverde (1967), a group of mice were reared in total darkness from birth until just over three weeks of age. Histological examination of striate cortex of these animals, as compared to light-reared subjects, revealed a decrease in the number of spines on the apical dendrites of layer IV pyramidal cells. Light deprivation had no such effect upon area temporalis prima.

A less extreme form of stimulus variation in which all subjects received light stimulation was employed by Bennett, Diamond, Krech, and Rosenzweig (1964). In this study, rats were reared in 2 different environments from 25 through 105 days of life. One group consisted of rats reared singly in quiet, dimly lit cages (Isolated Control, IC). The other group (Environmental Complexity and Training, ECT) was composed of rats reared 10 to 12 in a cage equipped with an assortment of "toys". They were handled daily and given some training in a standardized maze. After 80 days of differential rearing, the animals were sacrificed and various anatomical and biochemical measures were obtained. Total cortex, and in particular, visual cortex, was found to be significantly heavier in the ECT group. Acetylcholinesterase activity paralleled these differences in weight. Control experiments demonstrated that neither differences in locomotion nor social contact was responsible for the observed results. Holloway (1966) has shown that increased dendritic branching also occurs in the visual cortices of ECT rats, possibly accounting for the other anatomical and biochemical observations.

Thus subtle differences in experience can affect visual cortex. Of course, the studies cited involved 2 groups of animals, each group reared in a different environment. The proposed hypothesis, however, is concerned with differential experiences within the same organism, or more specifically, is concerned with differences between the experience of central and peripheral regions of the visual system. A relevant question to consider is whether the differences between medial and lateral striate cortex observed in the normal monkey would also be seen in monkeys deprived of light from birth. If, in these animals, medial and lateral striate cortex demonstrate similar capacities for spatial discrimination, the "differential experience" hypothesis will have received strong support.

Irrespective of what factor or factors are responsible for the differences observed between the 2 preparations, the differences themselves appear real. The capacity for discriminating stimuli applied to striate cortex is dependent on the particular striate cortex area receiving stimulation. Not all areas of striate cortex are equipotential in their capacity to discriminate spatial differences, and this lack of equipotentiality seems related to visual function.

The major results of the present study, i.e., differences between the 2 sectors in their ipsilateral gradients, their rate of polarity discrimination, and the number of sessions required for perfect discrimination to occur, can be given a non-spatial explanation. It can be argued that these differences reflect an unequal capacity for stimulus intensity discrimination at the training site. Responses to current induced at a test site may have resulted from the spread of current to cells activated during training site stimulation. An increase in distance between a stimulated test site and the training site would result in a decrease of current density at the training site. Discrimination could thus be made on the basis of the magnitude of neural activity at the training site produced by test site stimulation.

Even if all responses to test site stimulation resulted from indirect excitation of the training site, and all subsequent discrimination was due to the capacity to discriminate levels of excitation at this latter site, the observed differences between the 2 sectors still exist. The superiority of lateral over medial striate cortex, whether based upon spatial or intensity factors, reflects some underlying structural differences between the 2 areas.

The study of Brindley and Lewin (1968), however, strongly suggests that the stimuli employed in the present study are discriminated on the basis of spatial differences. Stimulation of a given point on striate cortex in a blind subject produced a phosphene at a particular region of the visual field. Even stimuli as close together as 2.4 mm on striate cortex resulted in 2 distinct phosphenes regardless of whether high or low current intensities were used. Apparently in spite of the lateral spread of current, the spatial characteristics of phosphenes are maintained.

Since the brain can be considered as a modified volume conductor, current will also spread vertically into subadjacent white matter, the optic radiations. Because of both differences in their place of origin in the lateral geniculate nucleus and in their final cortical destination (Polyak, 1957), these afferent fibers were differentially oriented with regard to the electrical stimuli used in the present experiment. This factor might account for the differences observed between the lateral and medial striate cortex subjects. If this interpretation is valid, then striate cortex, far from being crucial, merely served as a conductor of electricity from electrodes to white matter.

Two factors, taken collectively, argue against such an interpretation. Although striate cortex is relatively thin cortex, its thickness --

1.07 to 1.43 mm as measured by Cowey (1964) -- is sufficient to allow for a moderate decrement in current density at the cortical-subcortical juncture. Current density in the present experiment at the cortical surface adjacent to the stimulating electrode was greater than current density 1.07 to 1.43 mm beneath the surface (Ochs, 1965). The second factor relates to a finding of Doty (1966) that comparable stimulus intensities for both striate cortex and underlying white matter were required to maintain a conditioned response. Since thresholds at these 2 loci were similar, and since the cortical matter received current of greater density, it follows that the significant neural excitation was primarily cortical.

Using the methods employed in the present study, it may be fruitful to examine various regions of the brain to determine if they differ in their capacity to discriminate spatial differences. For instance, will differences in discrimination gradients be revealed between sensory and association areas, or between cortical and subcortical stations within the same sense modality? Will the differences observed between the foveal and peripheral regions of striate cortex also be revealed in comparing the hand and thoracic region of somatosensory cortex? Since the speed of polarity discrimination appears related to the discrimination of spatial differences, perhaps the former technique, being more convenient, would suffice in differentiating various regions of the central nervous system.

In conclusion, the foveal and peripheral regions of striate cortex appear to share several common characteristics. The discrimination between stimuli in both cortical areas increases as a function of exposure to the stimuli. Stimulation of the sites most homotopic to the training site produces more responses than any other contralateral stimulation.

These similarities, however, should be viewed along with the observed differences which in general indicate lateral striate cortex superiority in tasks of spatial discrimination.

SUMMARY

Monkeys were trained to bar-press upon stimulation of a given striate cortical locus (training site). After reaching criterion, test stimuli at other cortical loci were intermixed with the original training stimulus. Responses during the test stimuli were unreinforced while responses to stimulation of the training site continued to be rewarded. After no responses were made to test stimulation, polarity discrimination training was introduced at the training site. Responses to the original current direction were reinforced while responses to opposite current direction went unrewarded.

Two groups of subjects were used: one group was equipped with a bank of 5 linearly arranged striate cortex electrodes on each hemisphere, while the other group was similarly furnished with electrodes on medial striate cortex. Bipolar parietal and frontal electrodes were implanted in both groups.

Several findings tended to differentiate functionally the lateral and medial areas of striate cortex: (1) Within lateral striate cortex, the speed with which a discrimination was established between stimulation of the training site and an ipsilateral test site was directly related to the distance between the sites, whereas, within medial striate cortex no relationship was observed between the time required to establish a discrimination and interstimulus distance; (2) In order to attain perfect discrimination, i.e., a session in which no responses were made to any test stimulus, medial striate cortex subjects required twice as many sessions as lateral striate cortex animals; (3) Polarity discrimination required significantly more comparisons of polarity directions for the

medial striate than for the lateral striate cortex subjects; (4) Only animals with medial striate cortex electrodes demonstrated contralateral response frequencies equal to or greater than maximal ipsilateral response frequencies.

The following additional findings, on the other hand, were common to both groups of subjects: (5) Within both cortical sectors, discrimination between training and test stimuli increased as a function of exposure to the stimuli; (6) In 4 out of 5 subjects with viable bilateral striate cortex electrodes, maximal response frequencies on the contralateral hemisphere occurred at those sites most nearly homotopic to the training site; (7) After conditional stimulus training on either striate cortex sector, virtually no responses were made during stimulation of frontal or parietal cortex.

These findings indicate that although both sectors of striate cortex share certain functional characteristics, differences between them exist which are reflected in the greater capacity of the lateral sector to discriminate spatial differences. Various anatomical and physiological explanations were offered to account for such differences.

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