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EFFECTS OF ELECTRICAL STIMULATION OF TEMPORAL CORTEX ON VISUAL DISCRIMINATION LEARNING AND RETENTION IN MONKEYS

by

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EFFECTS OF ELECTRICAL STIMULATION OF TEMPORAL CORTEX ON VISUAL DISCRIMINATION LEARNING AND RETENTION IN MONKEYS

INTRODUCTION

The present experiment was designed to make use of the electrophysiological technique of inducing electrically-produced neuronal after-discharges as an analytic tool in the study of the functional role of inferotemporal cortex in visual discrimination behavior. In the large number of previous investigations of this brain-behavior relationship in the monkey, the method of surgical removal of cortical tissue has primarily been employed to interfere with normal brain functioning; here, after a subject recovers from surgery, its performance is measured and compared with that obtained under normal conditions, and the resultant behavioral deficits are generally attributed to the location and extent of the lesion. In addition to the difficulties in the use of ablation methods that limit the interpretation of the experimental resulte, e.g., the resulting secondary degeneration in the thalamus, as well as the extent of pathological tissue damage surrounding the lesion, there are inherent limitations in the ability of the method itself to tease apart the subtle behavioral changes, related to altered neural functioning, in the testing situation. One such inherent difficulty stems from the fact that any lesion-produced phenomena are irreversible, and a subject can never be returned to a normal state to be tested for the results of behavioral changes which occurred in the abnormal state. Because of this limiting feature one cannot efficiently evaluate alterations in a subject's behavior which are due to changes in neural function related to memory processes and the storage of information. In order to determine the way an animal utilizes information it receives when its brain is impaired this animal's behavior must be subsequently analyzed when its brain is again functioning normally. This strong methodological limitation can be overcome by the employment of an alternative physiological technique of inducing localized neuronal afterdischarges in the cerebral cortex-- a technique which Chow (1961) found to block transiently the functioning of specific neural tissue, producing ablation effects that were reversible. This method of behavioral analysis enables each experimental subject to be used as its own control: behavior during a state of temporary cortical impairment can be compared with a subsequent non-impaired state. The effects of such temporary disruptions on the functioning of inferotemporal cortex can be systematically investigated with relation to the learning and retention of behavioral tasks.

Behavioral Deficits Following Inferotemporal Lesions

The crucial importance of the integrity of temporal lobe neocortex for the learning and retention of visually guided tasks in monkeys was pointed out by a series of ablation studies (Blum, et al., 1950; Chow, 1951; Riopelle, et al., 1953) in which only temporal neocortical tissue was extirpated and striate and parastriate cortex were left intact. Initially, Blum, Chow, & Pribram (1950) performed extensive cortical ablations in the parieto-temporo-preoccipital region, which included the striate cortex only minimally (but produced degeneration in the medial portion of the lateral genniculate body as well as in Nucleus Pulvinaris-Lateralis and Nucleus Pulvinaris-Inferior), and found consistent visual deficits on discrimination problems together with less consistent deficits in somesthesis, audition, and gustation. They concluded that the observed behavioral deficits in visual discrimination were not due to primary sensory impairment since one subject with extensive bilateral degeneration in the lateral genniculate, involving the macular portion, readily learned the visual discrimination problems. The authors proposed that the entire parieto-temporo-preoccipital region contained separate foci concerned with discriminative learning in vision and somesthesis. However, since large lesions made only in the temporal lobes of monkeys also produced striking behavioral disturbances, resembling the symptoms of visual agnosia in man (Kluver & Bucy, 1938), it was evident that a specific locus for visually mediated behavior lay somewhere within the temporal lobe. Kluver & Bucy's subjects (1938, 1939) were abnormally reactive rather than unresponsive to all stimuli and were markedly handicapped on form discrimination tests, yet the only sensory deficits found in these animals were slight upper quadrant field defects. In an attempt to confirm whether there exist such specific loci within the temporal lobes as might be responsible for the fisual deficits found to occur after bialteral temporal lesions, Chow (1951) removed the middle temporal gyrus and lateral preoccipital region and found marked deficits on pattern, color, and brightness discriminations, while removal of the temporo-occipital gyrus and ventrolateral preoccipital regions produced no apparent deficits. Lashley(1948), however, found a deficit on a visual conditional reaction after one stage bilateral prestriate ablation, and a recent study by Mishkin (1966), discussed in detail below, points out the significance of prestriate functioning in visually guided behavior.

Further investigations which more specifically related visual deficits to removals of baso-medial temporal cortex (Poirer, 1952) and to lesions in the ventral temporal surface, excluding the hippocampus (Mishkin, 1954) delineated the area selectively related to fisual functions to lie within the inferotemporal convexity which comprises the middle and inferior temporal convolutions. The specificity of the inferotemporal area for the visual deficit has been demonstrated by studies where lesions in the cortex immediately adjacent to, but not included in the inferotemporal area produced impairments in olfactory discrimination (Brown, 1963; Brown et al.,1963), auditory discriminations (Stepien et al., 1960), and taste discriminations (Bagshaw & Pribram, 1953), while the inferotemporal lesion itself was found to have negligible effects on the learning of olfactory (Brown et al., 1963) auditory (Weiskrantz & Mishkin, 1958), and tactual discriminations (Pasik et al., 1958).

In general, inferotemporally ablated monkeys are impaired in situations that involve the learning, retention, and transfer of multi-cue visual tasks (Chow, 1951, 1954; Pribram & Mishkin, 1955; Riopelle et al., 1953) particularly when two or more visual forms or patterns must be differentiated for a rewarded response; however, their behavior is not affected when the solution to a problem involves pressing a single lever or opening a container for food (Ettlinger, 1959). Attentional factors responsible for the deficit were ruled out by Chow and Orbach (1957) who studied visual recognition of colors and patterns in a tachistoscopic situation, and found their performance to be virtually unaffected.

The finding that these animals can still catch flying insects and locate and pull at a fine thread to which a peanut is attached (Mishkin & Pribram, 1954) would indicate that they do not suffer from any severe losses in visual acuity or from debilitating field defects. However, these sensory factors cannot be too readily eliminated since Wilson & Mishkin (1959) found that inferotemporally ablated monkeys were deficient in solving size discrimination problems which depended heavily on visual acuity, and Pasik et al. (1960) found the size of the stimulus to be a critical variable in form discriminations: bilateral inferotemporally lesioned animals showed significant deficits on small visual patterns but none when larger equivalent patterns were presented; however, less postoperative deficit was revealed with small targets if they were presented after criteria had been achieved with larger ones. There is some further support for a direct sensory involvement following inferotemporal ablations in the findings that during successive or simultaneous discrimination problems involving differences in brightness, color, form, pattern, and flicker, the magnitude of the visual deficit varied with the degree of task "difficulty" (Riopelle and Ades, 1953; Riopelle et al., 1953; Chow, 1954b; Mishkin, 1954; Mishkin & Hall, 1955; Pribram & Mishkin, 1955; Orbach & Fantz, 1958; Mishkin & Weiskrantz, 1959), Pasik et al., (1960), however, found that after bitemporal lesions, subjects made more errors on a "go, no-go" discrimination than they did on a more difficult "positional" discrimination, when difficulty was defined in terms of the preoperative learning scores on each problem. The pattern of errors made on the "go, no-go" task suggested that this task measured the animal's ability to inhibit unrewarded responses to successively presented stimuli.

Weiskrantz & Cowey (1963), using a perimetric technique, measured visual acuity pre-and postoperatively in monkeys given bilateral resection of either striate or inferotemporal cortex; in the lateral striate lesioned subjects, where macular vision would be involved, impairments in acuity were shown, the severity of which corresponded to the location and completeness of the lesion. On the other hand, inferotemporal subjects showed no decrease in acuity. However, since the perimetric technique used in this study was not sensitive enough to measure the physiological blind spot, it is likely that the presence of more subtle changes in the visual fields would remain undetected, particularly changes in the peripheral fields, if they resulted from the inferotemporal lesions.

Mishkin & Weiskrantz (1959) found that critical flicker frequency (CFF) in monkeys was impaired by both inferotemporal and lateral occipital lesions, and not by frontal lesions when tested in a "go, no-go" discrimination situation where "flicker-go" and "steady, no-go" trials were presented in a balanced sequence. For all subjects, however, most of the errors made were due to persistent responding in the presence of the steady light. Symmes (1965), however, found no such CFF differences in monkeys with bilateral frontal, inferotemporal, and lateral occipital lesions when half of the subjects had flickering light as positive stimulus and steady light as negative, and half had the reverse conditions. Symmes found that subjects in the "flicker-go" situation decreased their proportion of overresponding during rates close to CFF, while subjects in the "flicker, no-go" situation increased their proportion of overresponding during difficult flicker rates. He concluded that in previous experiments on CFF the majority of errors in the "go, no-go" situation were failures to inhibit responding on the negative trials, and that this tendency could be modified by changing the reward contingencies used in the testing situation.

With regard to the role of inferotemporal cortex in behavioral processes relating to memory and retention of learned habits, Orbach

& Fantz (1958) found that monkeys given extensive overtraining trials preoperatively, showed no retention decrement postoperatively on color, brightness, and pattern discriminations; whereas, when no overtraining was given during acquisition, postoperative retention was drastically impaired. These findings supported Chow's (1942a) earlier observations that in one of two monkeys with temporal ablations, previously learned visual discrimination habits, lost after surgery, were reinstated after further training on other discrimination problems. Taken together, the above observations support Chow's (1952a) conclusion that the temporal neocortex is not a "storehouse of visual memories", since a stable memory trace, in all its complexity, for the learned habit was obviously not obliterated by inferotemporal ablation. This does not, however, rule out the possibility that this cortical area is involved in the neural concommitants of consolidation, whereby recent memory traces are transformed into a stable, long term trace (Konorski, 1961).

Neuronal Relationships

Attempts to distinguish the neural processes which mediate the inferotemporal cortex's direct participation in visual functions have revealed two possible neuronal systems by which impulses may be transmitted from the inferotemporal area to the geniculo-striate complex; viz. via a cortico-cortical, and a thalamo-cortical system. The cortico-cortical system was suggested by both anatomical data (Mettler, 1935a, 1935b; Clark, 1942), and by early strychnine neuronographic studies (Bailey et al., 1944; von Bonin et al., 1944; Pribram & MacLean, 1953). These revealed the existence of cortico-cortical connections leading from the striate area to parastriate and preoccipital areas, and from there to the inferotemporal areas. The striate cortex was found to have no direct connections with the temporal lobes, but fired into area 18 via short axon fibers (Mettler, 1935; Clark, 1931), which in turn transmitted the impulses transcortically to the ventral and posterolateral portions of the temporal lobes. A recent study by Kuypers et al., (1965) of fiber degeneration as the result of cortical lesions suggests that the striate cortex projects to specified parts of a "circumstriate cortical belt" which in turn projects to the caudal two thirds of the inferotemporal area; there are projections from the inferotemporal area back to a portion of this circumstriate belt. Ettlinger's (1959a) finding that monkeys with lesions of one optic tract were impaired in visual discrimination learning only after a contralateral lesion was made in temporal cortex but not after an ipsilateral lesion, suggests that the anatomical pathways responsible for the interaction between visual and temporal areas are restricted to the same hemisphere. Mishkin (1966), after resecting contralateral inferotemporal and striate cortex also found visual discrimination deficits and concluded that crossed striate and inferotemporal areas were of considerable importance in visual discriminations; however, such subjects were able to relearn, with difficulty, previously acquired visual discriminations.

A recent study of Mishkin (1966) in which he used a multiple lesion technique indicates the crucial importance of the functioning of prestriate cortex in the role of inferotemporal involvement in visual discrimination learning. The first stage of Mishkin's ablation procedure consisted of a unilateral inferotemporal resection, followed in the second stage by a contralateral occipital lobectomy. Presuming that in such a preparation there was a cortical interaction between the striate cortex of one hemisphere and the inferotemporal cortex of the other, Mishkin (1966) found that removal of the preoccipital gyrus in either hemisphere had no detectable effect on an animal's visual discrimination performance; however, when the pre occipital gyrus plus the entire cortical area to which the striate cortex projects was removed there resulted a visual discrimination deficit which revealed the necessity of this region as an essential mediator between inferotemporal and striate cortwx. This extensive ablation included the parastriate and preoccipital areas (Brodmann, areas 18, 19; von Bonin, & Bailey, areas OB, OA) including both banks of the lunate sulcus, the surface of the preoccip ital gyrus, the caudal bank of the superior temporal sulcus, the annectant gyri in the depths of the parieto-occipital junction and the banks of the caudal portion of the intraparietal sulcus.

Evidence for a second thalamo-cortical system was provided by Chow (1950) and Whitlock & Nauta(1956), who demonstrated that the anterior temporal cortex receives subcortical fibers from the medial portion of the Nucleus Pulvinaris, and sends fibers back to this nucleus. The Nucleus Pulvinaris, an intrinsic thalamic nucleus (Rose & Woolsey, 1949), receives postsynaptic fibers from the lateral genniculate body in the cat (Bishop & Clare, 1955), and collaterals from the genniculo-striate projections have been postualted by Hassler (1959), in man. In addition, the temporal neocortex sends a projection to the superior colliculus (Whitlock & Nauta, 1956) an important midbrain structure. After total bilateral removal of the temporal lobes in monkey, Bucy & Kluver (1955) reported retrograde cellular degeneration in the posterior tip of the pulvinar as well as degeneration within the medial and lateral portions of this nucleus.

Chow (1952) furnished evidence against the relevance of a critical subcortical-inferotemporal interaction. His finding that the disturbance in visual discrimination learning was not correlated with degrees of retrograde degeneration found in the lateral part of the pulvinar was corroborated by a later study (Chow, 1954) where bilateral medial pulvinar lesions failed to disrupt color and pattern discriminations. However, Chow's pulvinar lesions were never bilaterally complete in any given subject, nor did he report the effects of degeneration of the posterior tip of this nucleus. In another study, Chow (1961) failed to observe visual discrimination deficits by undercuttint the temporal cortex parallel to the surface in order to eliminate all subcortical projection fibers. The visual deficit was present, however, when the temporal cortex was crosshatched to eliminate the intracortical and arcuate fibers. Chow concluded that cortico-cortical pathways were of the primary importance in the interchange of information between the visual and temporal areas. The findings by Rosvold et al. (1958), that visual discrimination learning was not impaired after extensive lesions of the superior colliculus was still additional evidence against the notion of a critical relationship between inferotemporal cortex and subcortical structures.

Recently, electrophysiological evidence has been offered by Spinelli & Pribram (1966) which provides support for a mechanism of neural interaction linking the inferior temporal cortex with the primary visual system. They observed that continuous low level electrical stimulation of monkeys' inferior temporal cortex altered the sensitivity of striate cortical cell aggregates to pairs of light flashes which caused an increased delay of recovery to each flash. This did not imply that inferotemporal control was exerted directly on the cells of the occipital cortex; perhaps subcortical pathways were involved, for in the cat it was found (Battersby & Oesterreich, 1963) that low energy bipolar stimulation of n. pulvinaris-lateralis posterior complex produced an increase in the amplitude of the photic response in primary visual cortex, and reliable photic responses were recorded from those electrode sites in n. pulvinaris lateralis which produced the above effects. Spinelli & Pribram concluded that normally, inferotemporal cortex is instrumental in the maintenance of a given level of complexity of cell firing patterns within occipital cortex, and that inferotemporal impairment would, theoretically, reduce this level of complexity thereby decreasing the number of cell aggregates within the visual cortex, receptive to repeated photic input.

Experimentally Induced Disruption of Normal Electrocortical Activity

In addition to ablation techniques, studies in which neuronal structures are not destroyed, but where ongoing neuro-electrical activity is disrupted, further support the implication of inferotemporal cortex in visual discrimination tasks. Stamm & Pribram (1961), have shown that in monkeys with experimentally induced epileptic foci in bilateral inferotemporal cortex, deficits have been observed on visual pattern discriminations during acquisition, although performance on previously learned tasks was not impaired. Epileptic subjects exhibited maximum impairment during the early phases of training but were able to reduce the behavioral deficit during the course of testing.

Another technique powerful in delineating the neural processes which underly visual learning is that of sub-convulsive electrical stimulation of the cortex. Here each animal can be used as its own control while the effects of electrical interference upon the efficiency of continuous performance can be studied in a systematic fashion with no apparent disrupting motor or reward effects. The behavior of each subject during cortically disrupting stimulation can be compared with the subject's normal behavior after stimulation is terminated. In contrast with the substantial literature on the effects of electrical stimulation of subcortical and limbic structures, only a few reports are available on the behavioral consequences of subconvulsive stimulation of the cerebral cortex during learning. Weiskrantz, Mihailovic and Gross (1960) observed a disruption of previously learned performance on delayed alternation in monkeys during stimulation of prefrontal cortex, and likened the technique of stimulation to one of reversible ablation. Stamm (1961),however, found that the effects of subconvulsive stimulation of the frontal cortex was a function of the degree of prior learning on the delayed alternation task. Such stimulation retarded acquisition but not retention of learned tasks.

A further refinement of the electrical stimulation technique is one where electrical stimulation is used only momentarily to produce an afterdischarge in a restricted cortical area, and the afterdischarge itself provides a means of seriously disrupting the normal transmission of neural impulses. Zuckermann (1959) observed interference with conditioned responses to visual stimuli during the period of after-discharge which followed stimulation of visual cortex in the cat but not after motor cortex or reticular formation were stimulated. Flynn & Wasman (1960) and Flynn et al. (1961), studied the role of the hippocampus on learned and emotional behavior in cats by inducing neuronally disrupting after-discharges in that structure.

The use of neuronal after-discharge technique has its advantages, in that problems associated with widespread cortical disturbance and possible damage, inherent in the direct stimulation technique (Reynolds, 1965) are minimized, and a subject can be returned to a "normal" state with little difficulty. After such cortical disturbance is electrically initiated, the underlying patterning of local neuronal circuits is interfered with due to changes in the normal transmission of neural impulses (Chow, 1961; Flynn et al., 1963), and monitoring cortical activity during the after-discharge would provide a most accurate means of localizing the extent of cortical interference in experiments designed to test the effects of eliminating brain structures which are differentially involved in learning and memory.

The factors primarily involved in an after-discharge are the number of neurons active, their firing rate, and pattern of firing. Kandel & Spencer (1961) indicate that during an afterdischarge initiated by electrical stimulation, cell membrane potentials are synchronized with the EEG in the absence of spikes, but that spikes later appear with the return of polarization. Flynn et al., (1963), differentiate the effects of after-discharges from those of direct stimulation in that the frequency of the afterdischarge varies although the stimulation frequency is fixed, and that during after-discharge intracellular recordings reveal that the depolarization potential can reach a level great enough to inactivate the spike generator; during electrical stimulation this does not ordinarily occur. In addition, Enamoto & Ajmone-Marsan (1959) and Creutzfeldt et al. (1966), point out that there is an extremely high correlation between the EEG and the activity of single nerve cells during after-discharges produced by electrical stimulation.

Chow (1961) used the after-discharge technique to advantage in a study of the effects of bilateral and unilateral, electrically induced, disruption of neuronal circuitry in bilateral lateral temporal cortex during the learning and retention of successive visual pattern discrimination in monkeys. His subjects were first trained on such tasks during bilateral temporal lobe afterdischarges and showed no learning of any problems. They were then given the same visual problem under unilateral after-discharges and reached criterion. Retention tests on previously learned problems demonstrated that bilateral temporal afterdischarges completely interfered with retention, while unilateral after-discharges did not. Bilateral after-discharges induced in hippocampus and occipital cortex did not have any effects on retention scores. Chow's subjects were allowed only a single response, in a "go, no-go" situation, during each after-discharge; they had either to respond when the positive stimulus was presented, or withold a response during the presentation of the negative stimulus in order to receive food.

From the results of Chow's experiment it is difficult to evaluate whether any sort of visual deficit, i.e. a purely sensory deficit or a "higher" visual deficit, was actually produced by the bilateral remporal afterdischarges, or whether the effects of stimulation primarily prevented the subjects to inhibit their responses to the unrewarded stimuli; Chow, himself, reported that in all cases the failure of subjects to acquire or retain the discriminations was due to their reaching for the stimulus object on every trial. Pribram & Mishkin (1955) showed that bilaterally temporal lesioned monkeys performed poorly on form discriminations in a "go, no-go" situation, and when the same 2 stimuli were presented simultaneously and a choice between them was permitted, performance markedly improved. Similar findings by Pasik et al. (1960) have been cited earlier in the present report.

Another difficulty with Chow's procedure was that after each (bilaterally stimulated) subject failed a given problem after 150 trials, it was given the same problem for an additional 60 to 90 trials to criterion with unilateral stimulation. In order to conclude that unilateral stimulation had no effect on acquisition of visual discriminations new problems should have been given to the subjects under the unilateral after-discharge condition. In addition, further acquisition trials with bilateral after-discharges might have revealed that subjects could eventually distinguish between the stimuli.

Chow reported that the after-discharge did not spread from the temporal lobe site of stimulation to other neighboring structures such as hippocampus, lateral genniculate, and occipital cortex; however, he did not discuss the possibility of spread of disturbance to the optic radiations, only several mm. away from the point of stimulation. Moreover, he had no control subjects with which to measure the effects of bilateral after-discharges elicited in the primary visual system itself during the acquisition trials.

The present series of experiments was designed to answer some of these questions, left unexplored in Chow's (1961) afterdischarge study. A testing procedure is employed in which a subject's continuous behavior on a visual discrimination task, rather than single-trial performance, is examined under the effects of bilateral inferotemporal after discharges, and the 2-cue visual pattern problems are presented simultaneously, rather than in a successive, "go, no-go" fashion. In addition, both acquisition and retention are differentially tested under both inferotemporal and lateral occipital after-discharge effects, and behavior on a control spatial reversal task is also examined after inferotemporal stimulation.

EXPERIMENT I

In experiment 1 the effects of inducing a markedly abnormal level of electrical activity in inferotemporal cortex of Macaca Speciosa, through bilaterally implanted electrodes, are observed during the learning of two-cue simultaneous visual discrimination tasks. A technique is used whereby the same subject, serving as its own control, on one day performs at a pattern discrimination task under the effects of stimulation-produced afterdischarges, and on the following day performs on another pattern problem which is matched to the first for difficulty, but administered without electrical stimulation.

Assuming that in all likelihood the abnormal bilateral afterdischarge (and subsequent disturbance in cortical rhythms) reflects a gross disorganization of the neurons beneath the stimulating electrodes, we are then in effect comparing the performance of an animal with an **impaired** inferotemporal cortex on one day with its performance on the following day when the temporal lobes are once again "intact".

To evaluate the aftereffects of bilateral inferotemporal stimulation on an already learned discrimination each subject receives a retention test, given with electrical stimulation, on the day after it attains criterion level performance on any problem. This phase of the investigation is then extended by giving subjects a prolonged series of post-criterial overtraining trials on a single problem under varied daily conditions of either stimulation or no stimulation. EEGs are recorded directly from the cortical stimulation sites during all experimental sessions.

Subjects Three experimentally naive Stumptail monkeys (macaca speciosa) were used. Each subject was housed in an individual cage and maintained throughout the course of the experiment on a daily diet of peanuts, lab chow, and a fresh orange slice.. Vitamin supplements were given bi-weekly.

Apparatus During testing sessions each subject was placed in a restraining chair (Figure 1) arranged so that the monkey's head was in an enclosure, the front of which was constructed of clear plastic with an opening in front of the animal's mouth. One of the subjects' wrists was restrained by a chain and cuff attached to the chair. Each subject performed with the same free hand during all testing sessions. While in the restraining chair, the monkeys were placed before a vertical panel containing two visual display units mounted at the level of their eyes. Each unit was 1 1/2 inches wide and 2 inches high, and had a clear plastic window in front. The display units contained simple geometric patterns which could be projected on screens immediately behind each window. When a monkey pressed on either window the pattern lights were turned off for 5 seconds. For correct responses a dextrose pellet was delivered in the cup beneath the pattern and the cup was illuminated from the rear for 2 seconds. For two-choice simultaneous visual discriminations the rewarded patterns were presented at the left or right side on successive trials according to a pre-programmed Gellermann(1933) sequence; the non-rewarded patterns appeared on the alternate side. An overhead light provided constant illumination throughout each testing session.

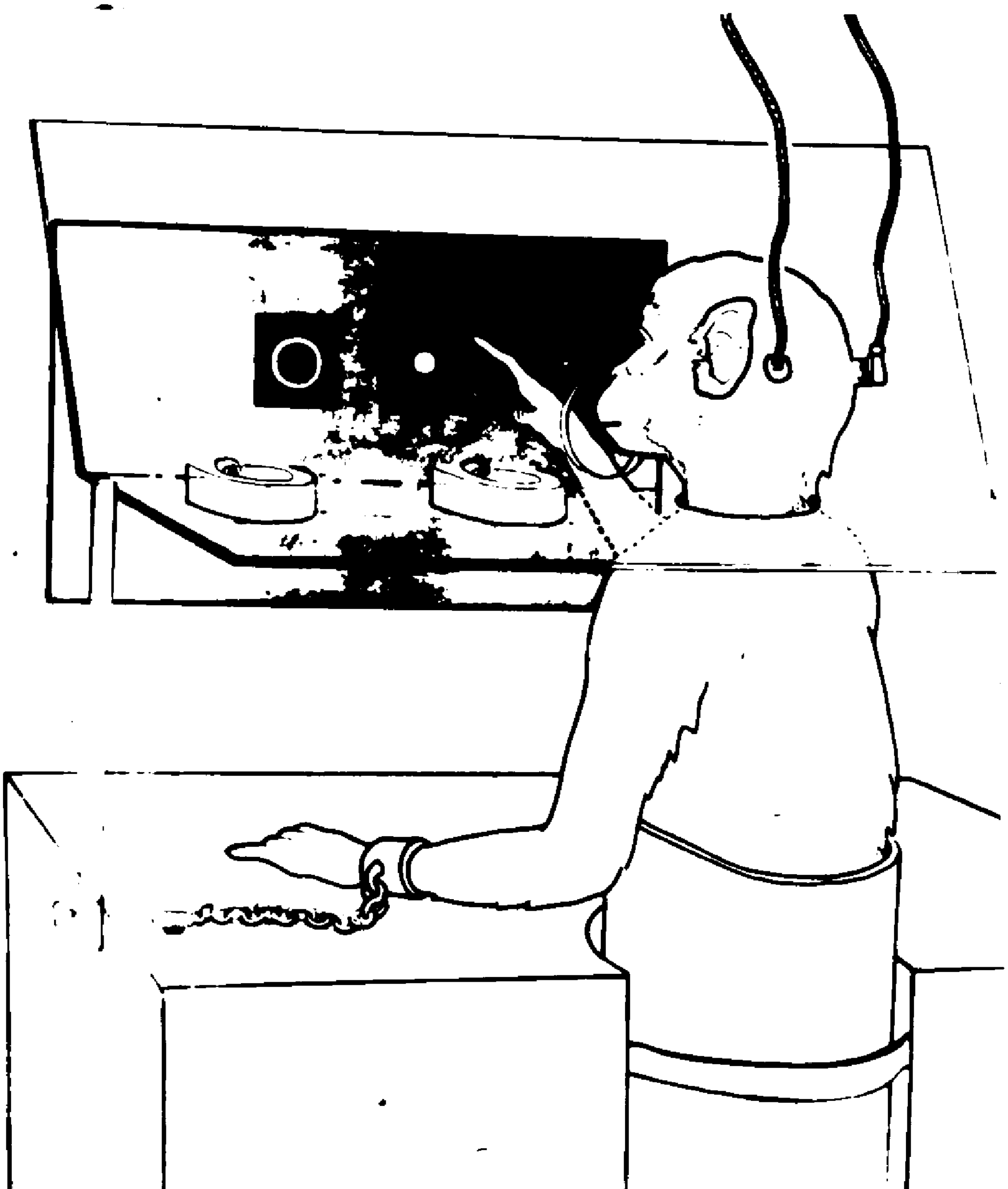

Fig. 1. Monkey seated in restraining chair.

All testing was carried out in an electrically shielded, sound-proofed cubicle and continuous operation of a white noise generator further masked possible external auditory distractions.

Adaptation During adaptation sessions each unoperated animal learned to sit quietly in the restraining chair at the automatic panel, and to press at alternate stimulus patterns for dextrose pellets when a single pattern, a solid white dot on a black background appeared at either window, when the animals reached criterion of 90% correct presses in 100 trials in a single session, electrode assemblies were bilaterally implanted in each monkey.

Electrodes An electrode assembly (Figure 2.1) consisted of a thin flexible pliofilm plastic sheet which held eight stainless steel, insulated, ball tipped wires. Each electrode point is an insulation-free steel sphere of approximately .5mm in diameter. The points were arranged for maximum coverage of the cortical surface beneath the pliofilm with a distance of 6mm between adjacent points. The wires from the spherical tips are brought together in a cable covered with a sheath of polyethylene tubing and soldered to a female miniature Amphenol hexagon connector. The soldered junction is embedded in acryllic dental plastic, and externally coated with several layers of Insl-X insulation material. Heavier stainless steel support wires, soldered to the body of the Amphenol connector are fastened to the subject's skull. Matching male Amphenol connectors with locking clips are used to connect the electrode assembly with the stimulating and recording apparatus.

Surgery Bilateral electrode implantation was performed aseptically in two stages, with a recovery period of two weeks between implants.

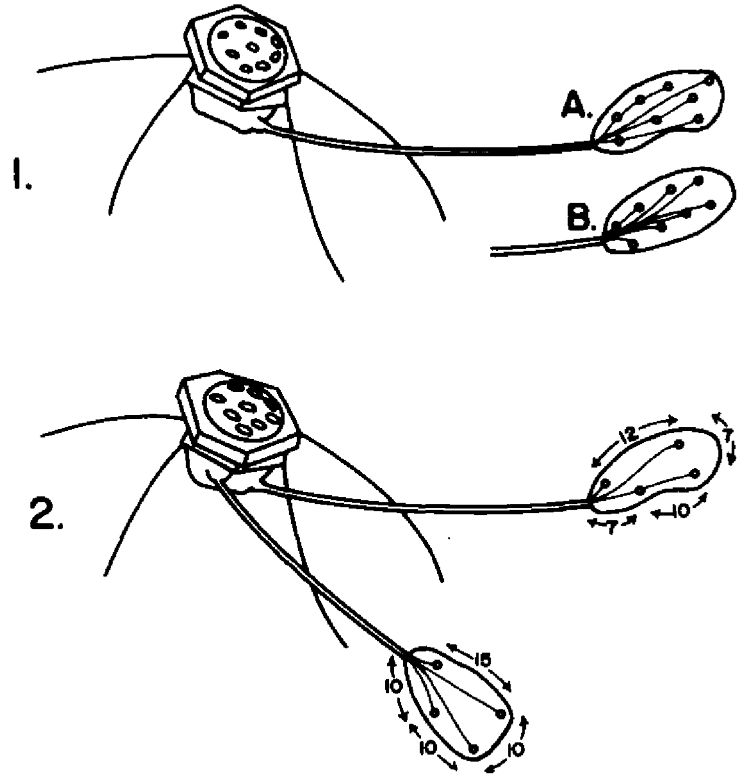

Fig. 2. Sketch of inferotemporal electrode assemblies (top) and combined inferotemporal-occipital assembly (bottom) showing distance in mm. between stimulation points.

The initial implantation was balanced among subjects with regard to placement in left or right hemisphere. During surgery the temporal muscle was cut and the temporal bone was opened dorsal to its junction with the zygoma. After cutting the dura the temporal lobe was gently retracted with small cottonoid patties. An electrode assembly was then inserted between cortex and dura so that its posterior edge was anterior to the vein of L'Abbe, and the ball tips in its medial edge lay over the inferotemporal gyrus. The dura was then closed and the temporal muscle was sutured in layers, permitting the cable to exit. The cable was fastened to the temporal bone, just above the bone opening with stainless steel ligature wire. The amphenot connector, continuous with the cable, was tied to the occipital bone with the attached stainless steel wires.

Electrical stimulation and recording A single Grass S4 stimulator and Stimulus Isolation Unit was used to deliver electrical stimulation to both electrode assemblies implanted in each animal. Switching connections were constructed in a manner which allowed any individual electrode point , or combination of points, to be switched either to the output of the Stimulus Isolation Unit, or to the Grass 12 channel electroencephalograph. The polarity of each point could be selected independently of the others, allowing a wide selection of patterns of current flow in each cortical stimulation area. The stimulating pulse was monitored at all times by a Tektronix dual-beam oscilloscope.

Threshold determinations of the stimulation parameters necessary for the production of after-discharges were carried out by simultaneously stimulationg both hemispheres with a pulse which was gradually increased in steps of 1 to 5 volts. Each step was separated by a 3 to 5 minute recovery interval. The EEG was recorded immediately after a given interval of stimulation. This procedure was carried out over a wide range of electrode combinations in each hemisphere until a minimum number of points in each electrode assembly was found which gave reliable afterdischarges. Optimal stimulation parameters were found to be a 50 c./sec. square wave pulse of 1.0 m. sec. duration, at 20 to 30 volts, applied continuously for 10 seconds. The electrical pulses were delivered through the "biphasic" control setting of the S-4 stimulator and had both negative and positive components which were inherently equal in coulombs if averaged over a sufficient period of time; however, these components were not of the same peak current or voltage.

Preliminary training A series of preliminary training trials was administered to each subject two weeks after the second electrode implantation when EEGs indicated good recovery of cortical tissue from surgical trauma. Each monkey then learned three relatively easy simultaneous visual discrimination problems and became accustomed to performing with connector plugs fastened to their electrodes, although stimulation was never applied. Subjects were given 6 blocks of 15 trials daily until a within-day criterion of 54 rewarded responses in 60 was attained on each problem (90% correct). The 3 adaptation problems were: a) ring vs. dod; b) diamond vs. hourglass; c) red dot vs. yellow dot. After each animal demonstrated its ability to perform at ease in the testing and recording apparatus, stimulation thresholds were determined for cortical after-discharges and testing began.

Procedure In the testing procedure subjects were each given a series of paired visual discrimination problems (see Fig. 3). Each problem was a 2-cue simultaneous pattern discrimination, and one problem of a pair was presented only after electrical stimulation on one day, while the other problem was given on the next day without stimulation. Both problems of the pair were learned alternately to a criterion of 54 correct trials in 60 (90% correct) in a single day's session. The pattern pairs used were equated for difficulty in a previous study (unpublished) where the number of trials to criterion performance on these problems was determined for a group of naive Rhesus monkeys. Figure 3 presents the series of 3 paired tasks learned by subjects #48 and #57. The administration of these tasks was balanced with regard to a) order of presentation; b) problem learned under stimulation vs. non-stimulation; c) initial presentation of stimulated vs. non-stimulated task. #31 was given only 2 of the problem pairs.

In the beginning of a stimulation session the subject sat quietly, facing away from the testing panel while a pretesting EEG was recorded bilaterally. The EEG was switched off and the subject, observed through a one-way window in the testing cubicle, was stimulated while the pulse dimensions were monitored on the CRO. At the end of 10 second stimulation the EEG was immediately switched on, and during the initial fast activity of the induced after-discharge the animal was placed before the stimulus windows and allowed to respond. Responses were directly recorded on the EEG by a signal marker, and also on an Esterline-Angus event recorder which was in operation throughout the experiment. After 15

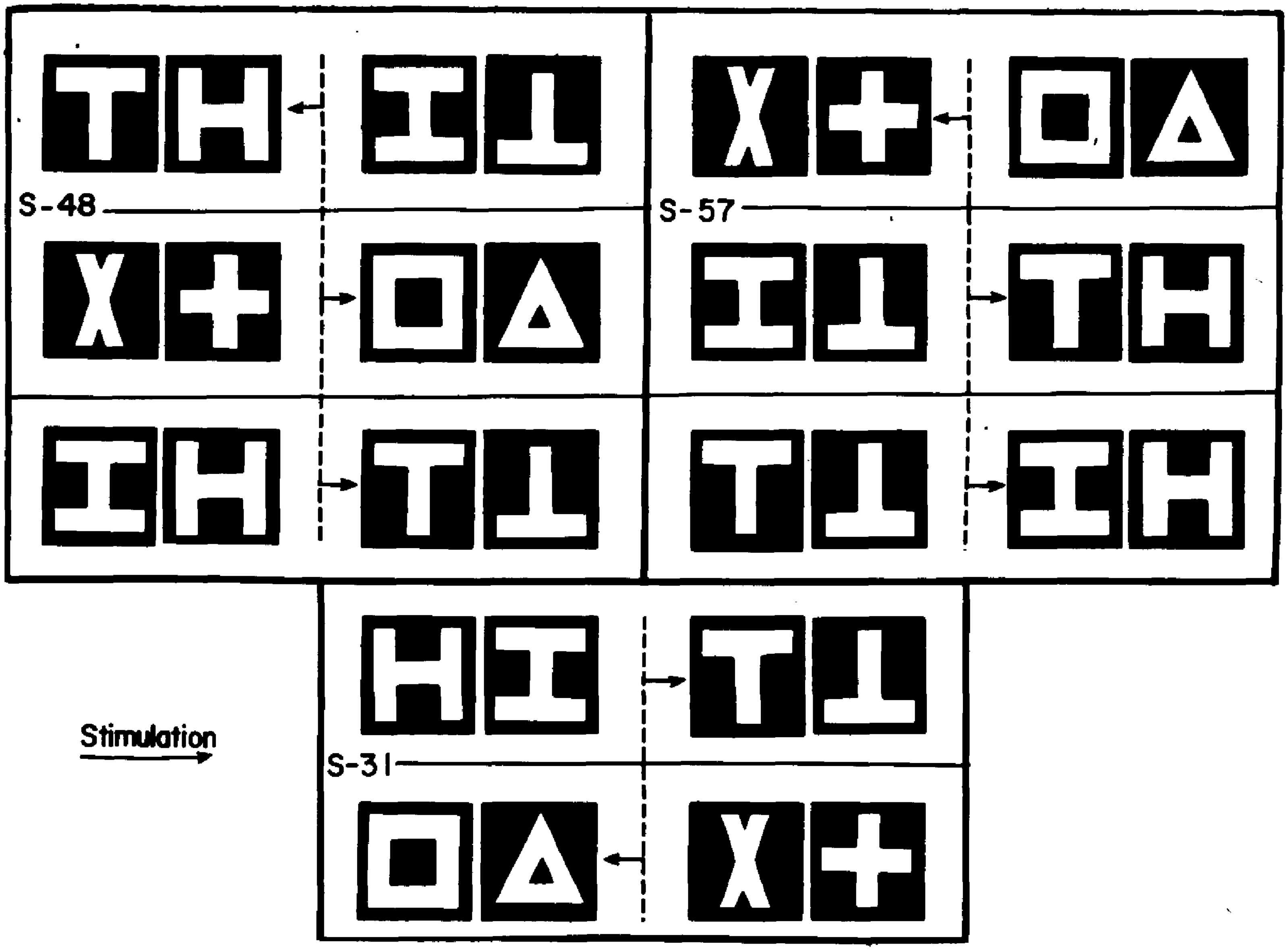

Fig. 3. Paired discrimination problems of Experiment I shown in order of presentation. Left pattern of each problem was rewarded.

trials the animal was turned away from the stimulus windows and sat quietly for 4 minutes. After this rest period the stimulation polarity was reversed for both electrodes and stimulation was again administered. This procedure was repeated for 6 15-trial blocks. During alternate days of non-stimulated testing trials the same procedure was followed with the exception of turning on the Grass stimulator. When the subject attained criterion it was given post-criterial retention trials on that problem on the following day. During the retention session the subject was first allowed to press at the recently learned problem for twenty uninterrupted trials without stimulation. The animal was then turned away from the apparatus, and after a 5 minute waiting period retention testing was carried out in 15 trial blocks under stimulated conditions until a criterion was reached of 54 correct trials in 60 (90% correct).

Subjects #48 and #57 were given a series of 14 daily 90-trial overtraining sessions on the same 2-cue problem which had been previously learned to 90% criterion during the experiment. These subjects each received 8 stimulated overtraining sessions and 6 non-stimulated overtraining sessions in a counterbalanced order.

Results of Experiment 1

Electrode Placements Figure 4 presents photographs of the brains of subjects #48 and #57 with markers delineating the actual placement of recording assemblies on inferotemporal cortex. The ball electrode tips actually used were about .5 times the size of the markers shown. The recording and stimulating points were arranged along the middle and inferotemporal gyri, anterior to the occipito-temporal sulcus, not including the temporal pole.

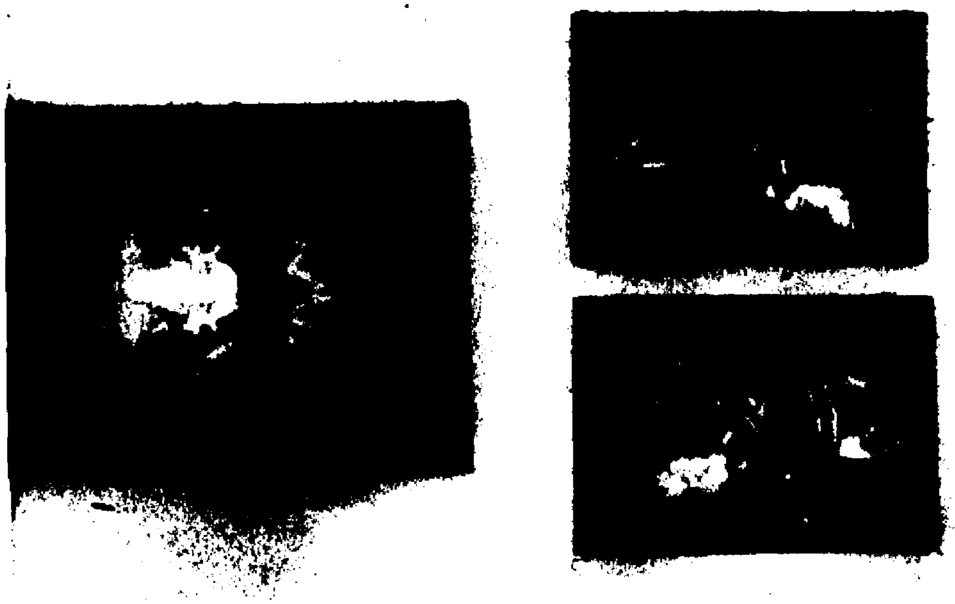

Fig. 4. Photographs of brains of subjects #48 (left) and #57 (right) showing markers to indicate the placement of electrode points.

Characteristics of EEG after-discharges Figure 5 shows a typical post-stimulation temporal lobe EEG for subject #57 taken during a block of 15 training trials. In all subjects there appeared after termination of the biphasic stimulation pulse, the brief build up of a lasting train of high-voltage, 100 to 400 microvolt multiphasic repetitive, 8 to 20 per second discharges which usually persisted from 5 to 15 seconds. This initial bursting occasionally endured for as long as 30 seconds in subject #31. The fast activity terminated suddenly and was often followed by a brief period of electrical inactivity. Intermittent slow wave trains followed at the rateof 1 - 4c./sec. These slow waves persisted throughout the duration of each subject's performance on a block of trials at the testing apparatus. #48 and #57 exhibited consistant bilateral initial fast afterdischarges, while #31 only showed this activity in the left hemisphere. All subjects, however, exhibited the persistent 1 - 4c./sec. activity bilaterally. In Fig. 5, the arrows indicate the subject's response. The pattern presed (left or right stimulus window), and the correct response are designated above the arrow. Figure 6 shows a temporal lobe EEG taken the following day during subject #57's performance on a problem without stimulation. The trains of slow 1 - 4c./sec. waves have subsided and fast temporal lobe activity has been resumed with the occasional presence of isolated slow waves.

Subjects #48 and #57 usually did not begin to press the manipulanda for pellets until the initial bursting of high voltage fast waves terminated. Subject #31 often performed during the initial rapid afterdischarge. As soon as the subjects began to respond to

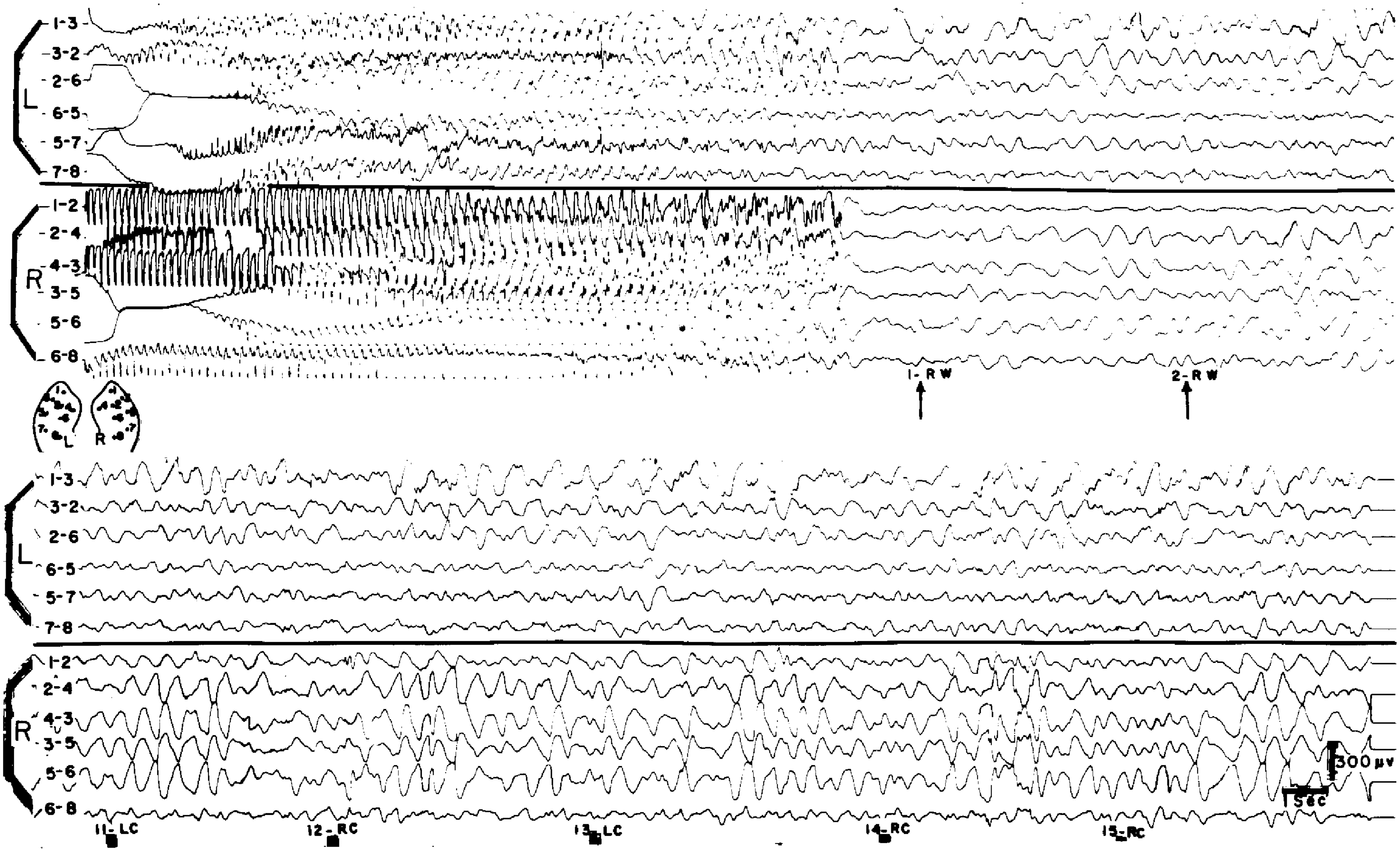

Fig. 5. Typical post stimulation EEG for subject #57. Arrows indicate subject's responses. Letters above arrows indicate the specific responses made: R right press, L left press, C press was rewarded W press was not rewarded.

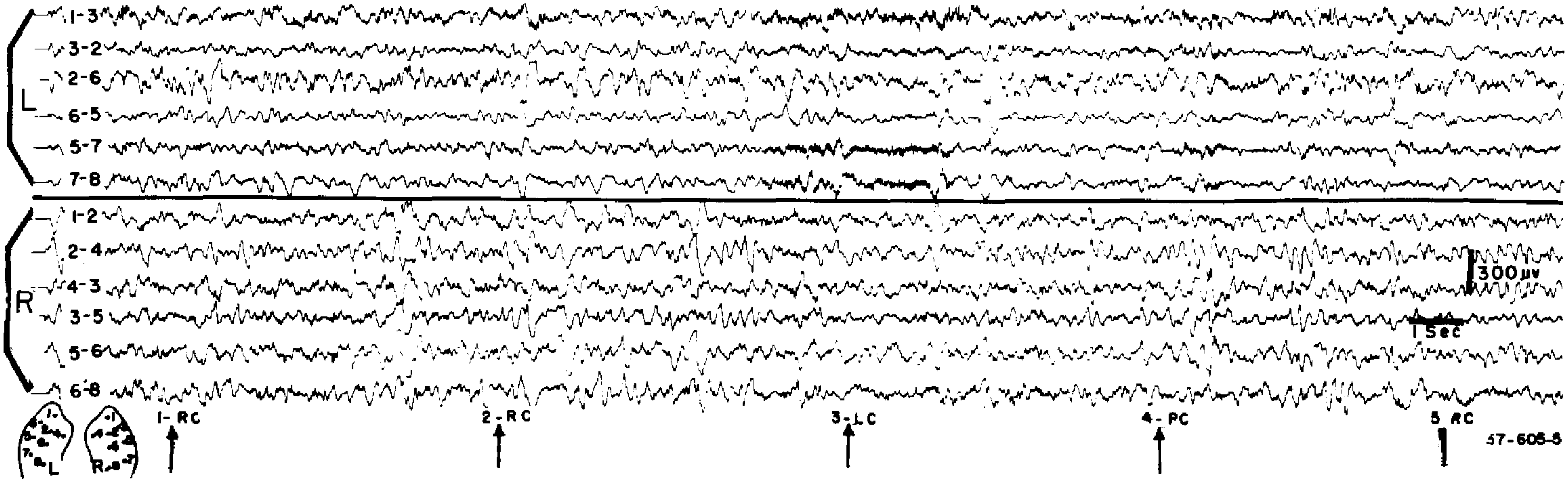

Fig. 6. Temporal lobe EEG for subject #57 recorded the day following a stimulation session. Arrows indicate subject8s responses. Letters above arrows indicate the specific responses made: R right press, L left press C press was rewarded, W press was not rewarded.

the patterns they continued to press regularly with their appearance at the stimulus windows every five seconds. Few presses were made during the time-out period when the patterns were not projected. While the stimulation pulse was administered the subjects sat motionless, stared into space, and occasionally made grasping movements of either hand. These behavioral signs ceased immediately with the termination of the pulse. While the subject in the restraining chair was moved to face the manipulanda no observable abnormal motor signs were present. During this period, when post-stimulation fast, high voltage bursting was recorded subjects would reach for peanuts held before their eyes by the experimenter and ate avidly if allowed to take the food.

Acquisition of visual discrimination Figure 7 shows typical learning curves for each subject on the initial acquisition of tasks after stimulation and non-stimulation. The curves show that retardation in acquisition under stimulation is not due to a prolonged failure to perform above chance level. Rather, subjects responded at a level of performance between 60% and 80% correct during the majority of trials to criterion. Table 1 presents each subject's trials and errors to criterion in acquisition for tasks learned under stimulation and non-stimulation. All subjects consistantly had greater difficulty in learning simultaneous pattern discrimination tasks under stimulation than similar tasks without stimulation. Mean errors made on stimulated problems for subjects #48, #57, and #31 were 168.0, 277.3, and 268.5, respectively. These subjects' mean errors to criterion for paired problems given without stimulation were 36.3, 60.0, and 93.0, respectively. There was never any

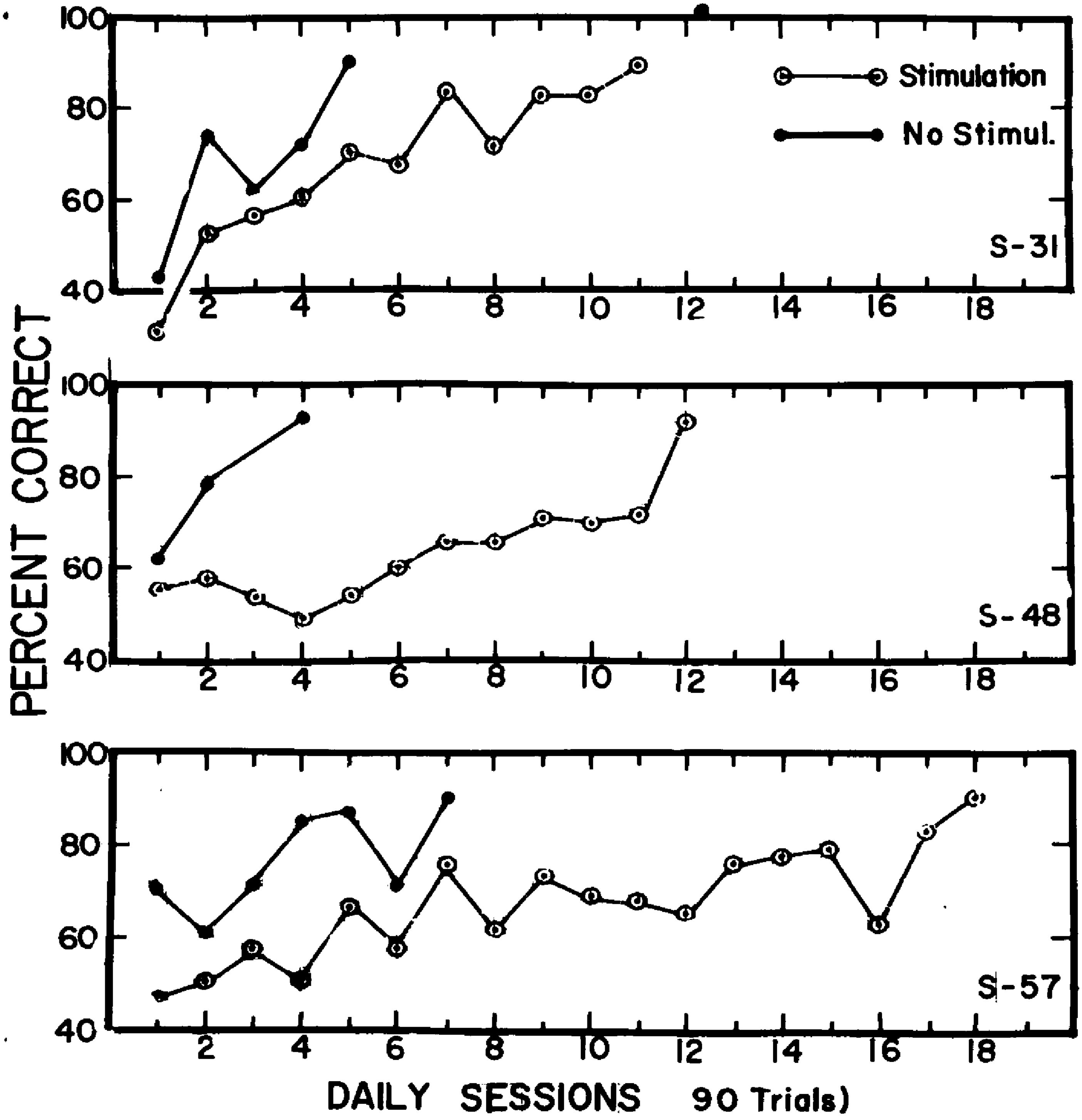

Fig. 7. Typical learning curves for subjects #31, #48, and #57, obtained during sessions with stimulation and without stimulation.

TABLE 1

TRIALS AND ERRORS TO CRITERION IN ACQUISITION OF VISUAL DISCRIMINATION PROBLEMS

Subject	Problem Pair	Stimulated Problem		Non-Stimulated Problem	
		Trials	Errors	Trials	Errors
#48	1	645	291	210	47
	2	1050	390	240	58
	3	510	123	60	4
	Mean	735	268	170	36.3
#57	1	1590	508	690	58
	2	735	213	345	59
	3	555	111	240	63
	Mean	960	277.3	425	60
#31	1	840	314	340	109
	2	600	223	240	77
	Mean	720	268.5	290	93

overlap, for any subject, in the number of trials or errors to criterion under stimulated vs. non-stimulated acquisition conditions.

Retention of visual discriminations When 20 trial retention tests were administered without stimulation all subjects retained previous learning to a 90% criterion on all problems without any additional retraining trials. However, in **Figure** 8 it is observed that when further retention testing was carried out under stimulation conditions subjects required additional retraining trials to again reach criterion of 54 correct in 60 trials (90% correct). Subject #48 had particular difficulty in stimulated retention of learned problems. Analysis of variance of subjects' errors to retraining(Table 2) revealed no significant difference in the number of stimulated retention errors whether or not acquisition was given with or without stimulation ($1/F= 1.25$, df= 4/1, $p>.05$). No significant differences were found in the number of errors made on the first, second, and third problem pairs ($1/F= 1.57$, df= 4/2, $p>.05$), and the Stimulation (in acquisition) X Problem Pair interaction was also insignificant($1/F= 1.22$, df= 4/2, $p>.05$). Figure 8 presents a graphic summary of each subject's performance on all stimulated retention sessions. Shown for each subject is the median percent correct score, determined across all problems, achieved on successive blocks of 15 trials. The first score in each graph is that for non-stimulated retention; the subsequent scores are for stimulated retention trials. Retention scores dropped from 90% and 95% correct during the 20 trial non-stimulated retention testing, to 80% and 83% correct during the subsequent stimulated retention tests. Scores for subjects #57, and #31 rose rapidly to criterion, while those of subject $48 showed a more

TABLE 2

TRIALS AND ERRORS TO STIMULATED RETENTION CRITERION OF VISUAL DISCRIMINATION PROBLEMS*

Subject	Problem Pair	Stimulation in Acquisition		No Stimulation In Acquisition	
		Trials	Errors	Trials	Errors
#48	1	15	5	45	14
	2	60	13	180	64
	3	135	36	30	11
	Mean	70	18	85	29.7
#57	1	0	3	30	12
	2	0	4	0	2
	3	0	4	0	6
	Mean	0	3.7	10	6.7
#31	1	0	5	0	7
	2	0	6	15	7
	Mean	0	5.5	7.5	7

*Final 60 criterial trials are not included

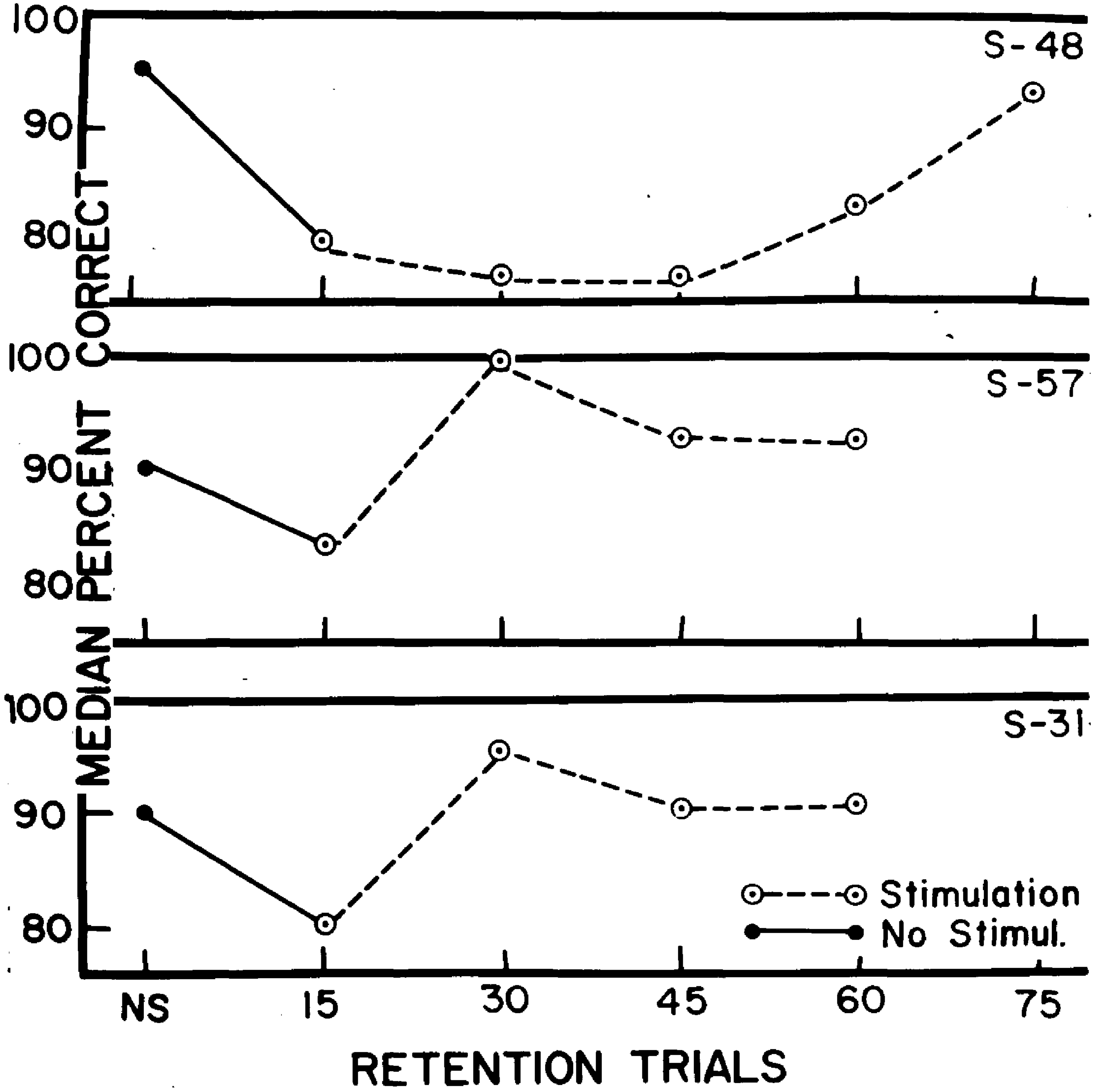

Fig. 8. Median retention scores for subjects #48, #57, #31. Each graph shows the median percent correct score of averaged retention problems for consecutive 15 trial blocks. NS non-stimulated retention trials.

lasting depression.

Effects of overtraining Figure 9 presents daily performance scores in extensive overtraining session plotted for subjects #48 and #57. Regardless of whether overtraining was carried out under stimulation or non-stimulation, scores rarely departed from the 90% correct level during daily sessions. However, within-day variability was slightly greater on stimulated overtraining trials than on non-stimulated trials. For both subjects, on the stimulated testing day which followed four successive days of non-stimulated overtraining no significant depression in scores, below criterion, was observed.

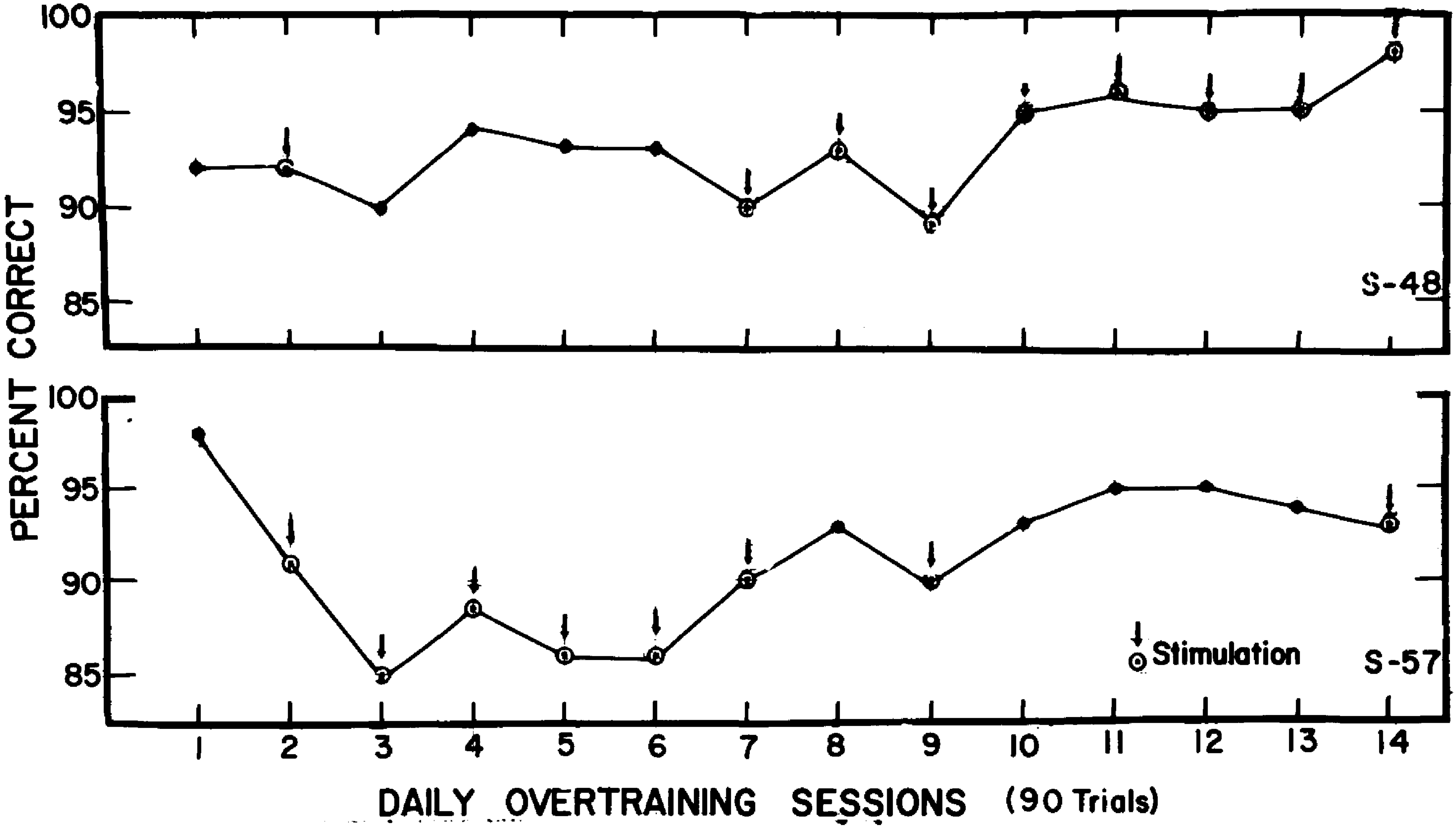

Fig. 9. Daily performance scores in extensive stimulated and non-stimulated overtraining sessions for subjects #48, #57.

EXPERIMENT II

In the present experiment a similar testing and recording procedure as that described in Experiment I was used to differentiate the effects, on visual discrimination learning, of bilateral inferotemporal stimulation from direct stimulation of primary visual (lateral occipital) cortex. Those features of the present experiment which differed from those of Experiment I will be described.

Subjects The subjects were 4 immature, experimentally naive Stumptail monkeys (Macaca Speciosa), housed and maintained in a similar fashion to those used in Experiment I.

Apparatus The testing chair and automatic visual display panel used were identical with those in Experiment I. In the present experiment, however, the hand cuff was only applied during the adaptation period; during this time all subjects learned to press efficiently with a single hand at the stimulus window manipulanda.

Adaptation The initial adaptation procedure used here was the same as that of Experiment I.

Electrodes The type of stimulation-recording cortical electrode used in this experiment was essentially a modification of the electrode described in Experiment I (Figure 2.2), and included the addition of a second assembly of ball tips with cable, soldered to the single Amphenol connector for placement on lateral occipital cortex. In this electrode each pliofilm plastic base held only 4 ball tips. The spacing of electrode points in millimeters is designated in Figure 2.2. The same use of insulation and support wires as described in the previous experiment was employed here.

Surgery Surgery was performed in 2 stages, each stage consisting of ipsilateral electrode placement in inferotemporal and lateral occipital cortex. The initial implantation was balanced among the 4 subjects with respect to placement in either hemisphere. After the inferotemporal assembly was implanted, as described in experiment I, support wires were secured, and the occipital bone was opened. The second electrode assembly was subdurally placed posterior to the lunate sulcus. The two medial ball tips were arranged several millimeters from the midline; the remaining points extended 10mm. laterally. The cable connection from these four points was tied to the occipital bone with stainless steel ligature wire.

Electrical stimulation and recording Two Grass S-4 stimulators and isolation transformers were used to deliver independently controlled electrical impulses to the electrodes in each hemisphere. Switching and polarity-control circuitry were similar to those previously described. The electrical current values for each delivered train of stimulus pulses were calculated by taking all CRO readings across a 1000 ohm resistor in series with each electrode. Stimulation parameter determinations for after-discharge thresholds were made independently for each of the 4 electrode assemblies implanted in a given subject. Selected combinations of points in each assembly were stimulated with a pulse, which, after a 3 to 5 minute recovery interval, was increased in steps of .2mA until a reliable localized afterdischarge was elicited from a given array of points. Because of the qualitative differences in the response to electrical stimulation, separate EEG criteria for afterdischarge were used for inferotemporal and occipital placements. The presence of high amplitude spike or wave trains from occipital cortex after stimulation was terminated, usually of shorter duration than inferotemporal after-discharges, was the accepted indication of neuronal disruption. The final stimulation characteristics used for both inferotemporal and occipital placements were: a 50 cps biphasic*square wave pulse, from 1 to 1.3 m.sec. in duration, delivered bilaterally for 10 seconds. The pulses were staggered between right and left hemispheres by introducing a constant 5 m.sec. delay between the outputs of both S-4 stimulators. The applied stimulation voltages varied from 10 to 25V, current values used ranged from 5 to 10 ma.

Preliminary training Two weeks following the second electrode implantation each subject was given the same series of 8 preliminary 2-cue simultaneous color discrimination problems for adaptaton purposes. These problems were administered without stimulation according to the procedure for testing described in the previous experiment. A correction procedure was applied during training on the first two of these preliminary problems. The sequence of these discriminations learned to 90% criterion (54 correct trials in 60) was: White vs. Green; Red vs. Yellow; Red vs. Green; Red vs. Blue; Blue vs. Green; Yellow vs. White; Black vs. White; White dot vs. White Ring.

Procedure The technique, described in Experiment I, of using 2-cue simultaneous pattern problems, one given with stimulation and one, without, was again used in the present experiment. In the testing situation (Figure 15) each subject was first trained to criterion on two pairs of problems: A vs. B; C vs. D. Bilateral cortical stimulation of only one area (inferotemporal or occipital) was

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* See Experiment 1, Electrical Stimulation and Recording, p. 23.

administered on the alternate problem of each pair. Each subject was then trained to criterion on two additional problems: E vs. F; G vs. H. After-discharges were now elicited from the previously non-stimulated cortical area during performance on alternate problems. A balanced order was used with respect to cortical area stimulated; problem learned under stimulation vs. non stimulation; initial presentation of stimulated vs. non-stimulated problem. The patterns used as discrimination problems are shown schematically in Figure 15. The left pattern of each combination was reinforced with food reward. The order of presentation of problems shown in Figure 15 was modified for subject #85. This animal received problem C vs. D (inferotemporal stimulation) last, due to a loosening of one electrode's support wire which was subsequently repaired. All subjects were given postcriterial retention trials on each problem in the same manner as described in the previous experiment.

The daily testing procedure was identical with that of Experiment I with the exception that subjects were not moved away from the testing panel between blocks of trials when stimulation was administered. During all daily sessions subjects sat facing the manipulanda throughout testing. A stimulation-adjustment procedure was used whereby if the first electrical stimulation of a session produced bilateral after-discharges no adjustment in stimulating current was made; if no afterdischarge was elicited by the stimulation then an increase of .2ma. was made in the stimulating pulses for the next stimulation.

Results of Experiment II

Electrode Placements Post mortem photographs showing electrode placements are presented in Figure 10. In each subject the infero-

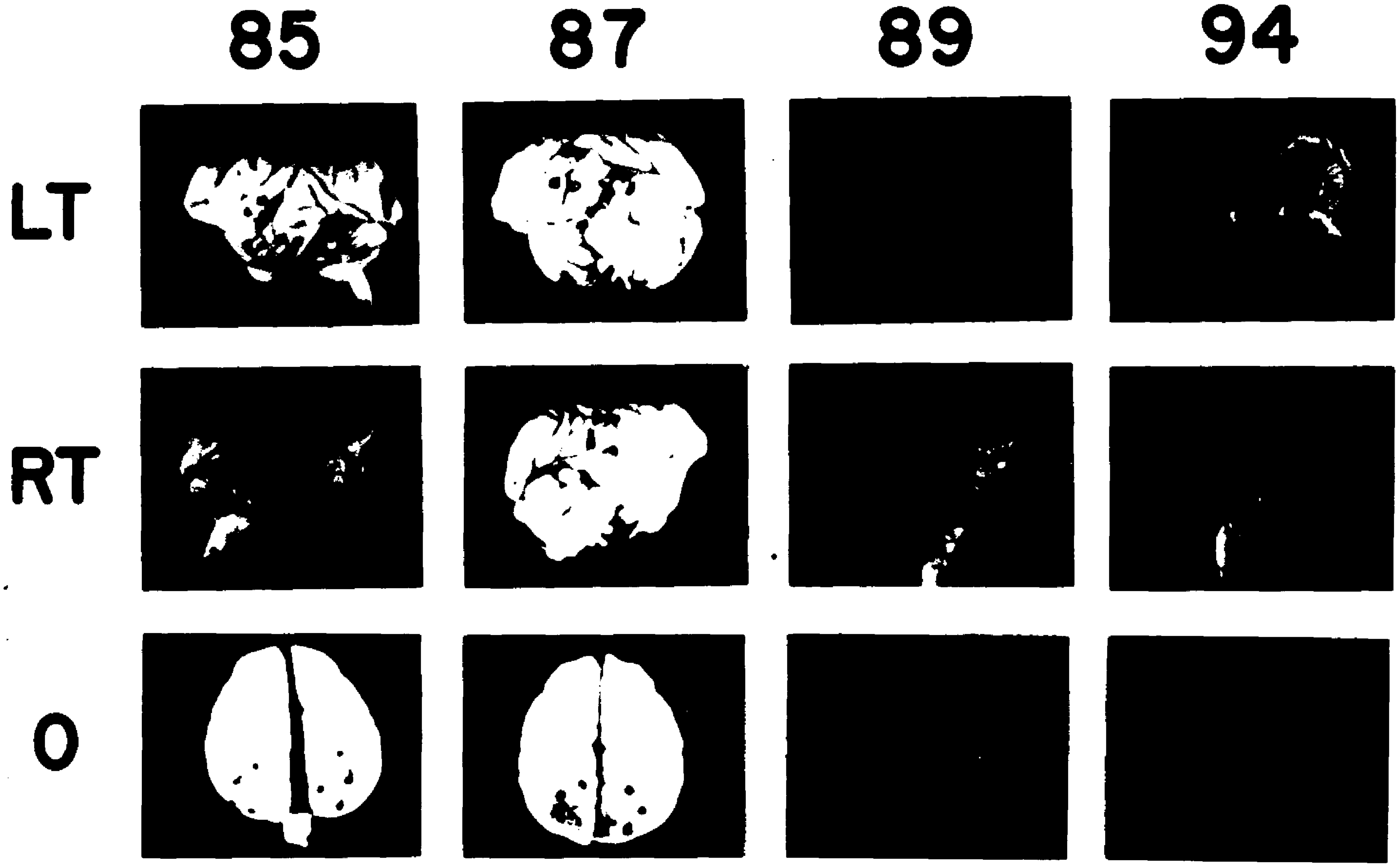


Fig. 10. Post mortem photographs of brains showing markers to indicate the placement of electrode points. LT left temporal, RT right temporal O occipital.

temporal electrode assemblies lay within the cortical area extending from the lower banks of the superior temporal sulcus, ventrally, toward the occipito-temporal sulcus, sparing the temporal pole. A combination of 3 points in each temporal electrode assembly was stimulated with the most ventrally located point situated on the inferotemporal gyrus. In each occipital electrode assembly stimulation was applied to an array of 3 points lying within the macular projection zone. The average daily stimulation current values used with each electrode placement are presented in Table 3 for all subjects.

Characteristics of EEG after-discharges Table 4 shows the percentage of cases for all acquisition stimulation trials in which bilateral and unilateral high voltage, fast, after-discharges were elicited immediately following electrical stimulation of inferotemporal and occipital cortex. Bilateral post-stimulation after-discharges were elicited more frequently by inferotemporal stimulation, and in 2 subjects, #85 and #89, only unilateral occipital afterdischarges were found after occipital stimulation.Except for subject 94,occipital stimulation produced a greater number of instances where after-discharges were absent in the post-stimulation EEG than did inferotemporal stimulation.

Table 5 shows each subject's means and standard deviations for the duration of all local afterdischarges elicited during all acquisition sessions for both inferotemporal and occipital stimulation trials. Inferotemporal stimulation generally produced longer enduring after-discharges when they occurred bilaterally. Variability of duration was also greater for inferotemporal after-discharges.

TABLE 3

AVERAGE DAILY STIMULATION CURRENT VALUES USED WITH IMPLANTED ELECTRODE ASSEMBLIES

Subject	Hemisphere	Locus of cortical stimulation	
		Inferotemporal	Occipital
#85	Left	10 ma.	10 ma.
	Right	9 ma.	9 ma.
#87	Left	9 ma.	10 ma.
	Right	8 ma.	10 ma.
#89	Left	7 ma.	9 ma.
	Right	5 ma.	9 ma.
#94	Left	6 ma.	8 ma.
	Right	6 ma.	8 ma.

TABLE 4

PERCENTAGE OF BILATERAL, UNILATERAL, AND NO AFTER-DISCHARGES ELICITED BY ELECTRICAL STIMULATION DURING ACQUISITION

Stimulation Site	Type of After-discharge	Subject			
		#85	#87	#89	#94
Infero-temporal	Bilateral	25.6	63.7	64.6	26.1
	Unilateral	36.0	26.3	16.4	51.2
	No After-discharge	38.4	10.0	19.0	22.7
Occipital	Bilateral	0.0	11.1	0.0	48.2
	Unilateral	66.4	63.0	60.0	38.9
	No After-discharge	33.6	25.9	40.0	12.9

TABLE 5

MEANS AND STANDARD DEVIATIONS FOR DURATIONS OF AFTER-DISCHARGES (IN SECONDS) DURING ALL ACQUISITION SESSIONS

Stimulation Site	Type of After-discharge		Subject #85	Subject #87	Subject #89	Subject #94
Infero-temporal	Bilateral	$\bar{X}$	28.0	14.6	15.5	15.8
		s	20.5	5.2	5.1	7.7
	Left Unilateral	$\bar{X}$	8.5	9.4	8.5	8.6
		s	3.3	3.9	1.5	4.8
	Right Unilateral	$\bar{X}$	17.5	7.5	9.3	--
		s	10.6	2.7	2.8	--
Occipital	Bilateral	$\bar{X}$	--	11.0	--	14.7
		s	--	1.4	--	5.0
	Left Unilateral	$\bar{X}$	10.0	9.9	--	8.4
		s	2.1	2.6	--	3.5
	Right Unilateral	$\bar{X}$	30.0	--	9.4	3.0
		s	0.1	--	6.4	0.2

The extent of localization of inferotemporal and occipital after-discharges is shown in Table 6, where the laterality and percentage of cases is presented in which a) occipital after-discharges were recorded immediately following bilateral inferotemporal stimulation during acquisition, and b) inferotemporal afterdischarges were recorded after occipital stimulation. The majority of afterdischarges elicited from either cortical area did not spread to the alternate cortical area, however inferotemporal afterdischarges tended to spread bilaterally while occipital after-discharges spread unilaterally.

Figure 11 shows selections from an EEG recorded during a 15 trial acquisition block before, and immediately after bilateral inferotemporal stimulation of subject #89 was terminated. The record shows a typical bilateral localized inferotemporal after-discharge involving little electrical disturbance of ongoing occipital rhythms. The characteristic train of 8 to 20 per second high voltage after-discharge activity terminated suddenly and was followed by slow, dysrhythmic 2 to 4 per second wave trains from inferotemporal cortex which gradually increased in voltage while the subject responded at the testing apparatus. The high voltage slow activity subsided in intensity to some degree during the resting period between 15 trial blocks of testing trials. On the following non-stimulated testing day the high voltage slow wave trains from inferotemporal cortex were no longer present although some isolated 3 to 4 per second slow waves still persisted throughout testing. Table 7 shows the percentage of cases of all acquisition stimulation sessions, for each subject, in which localized unilateral and bilateral high voltage slow wave trains were present after both

TABLE 6

LOCALIZATION OF AFTER-DISCHARGES DURING ACQUISITION

Type of After-discharge	Subject			
	#85	#87	#89	#94

A. Percentage of cases in which bilateral inferotemporal stimulation elicited occipital after-discharges.

Bilateral spread	10.5	12.7	11.4	4.2
Unilateral spread	19.8	20.0	15.2	32.8
No spread	69.7	67.3	73.4	63.0

B. Percentage of cases in which bilateral occipital stimulation elicited inferotemporal after-discharges.

Bilateral spread	0.0	7.4	3.3	37.0
Unilateral spread	10.0	29.6	36.7	27.9
No spread	90.0	63.0	60.0	33.3

TABLE 7

PERCENTAGE OF EEGS IN ACQUISITION SHOWING HIGH VOLTAGE SLOW WAVES AFTER STIMULATION

Stimulation Site	Locus of Slow Waves	Subject			
		#85	#87	#89	#94
Infero-temporal	No Slow Waves	4.7	7.3	1.3	2.5
	Bilateral	64.5	91.8	97.4	97.5
	Unilateral	30.8	0.9	1.3	0.0
Occipital	No Slow Waves	64.0	85.2	60.0	79.6
	Bilateral	10.0	0.0	6.7	3.7
	Unilateral	26.0	14.8	3.3	16.7

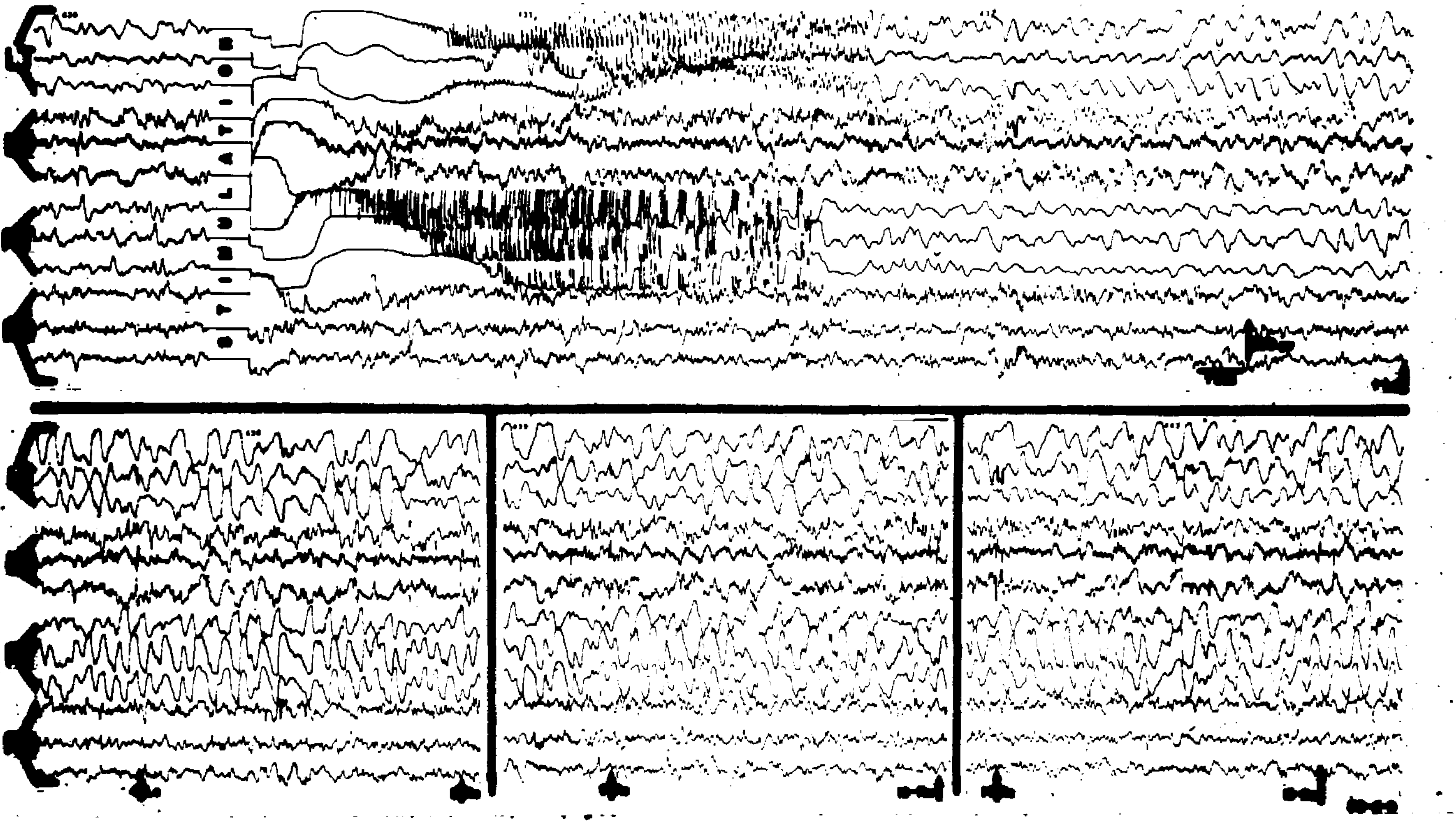


Fig. 11. Typical post inferotemporal stimulation EEG for subject #89. Arrows indicate subject's responses. Numerals indicate trial within 15 trial blocks. L left Press, R right press, C press was rewarded, W press not rewarded, LT left temporal, RT right temporal, LO left occipital, RO right occipital.

loci of stimulation. In the majority of inferotemporal stimulation cases slow activity was produced bilaterally even though the initial fast afterdischarge may have been unilateral or absent. This slow activity rarely spread to occipital cortex.

The subjects generally did not respond at the testing apparatus during the initial inferotemporal fast after-discharge phase of the EEG. At this time they sat quietly, facing the illuminated patterns, and made no attempts to press at the manipulanda until the EEG slow wave phase had begun.

Figure 12 shows an EEG recorded from subject #94 prior to, and immediately following bilateral occipital lobe stimulation during a typical acquisition session. The record shows a bilateral after-discharge characterized by an initial burst of high frequency activity which terminated in a train of 4 per second waves, ended abruptly without the brief period of electrical silence usually present after inferotemporal stimulation. This course of activity was typical of occipital after-discharges although they were, for the most part, unilateral (see Table 4). The high voltage slow activity were largely absent after occipital stimulation (see Table 7) and the EEG returned to pre-stimulation baseline level. During the 10 second interval of occipital stimulation subjects would often gaze upward, reach into the air, and try to pick at or catch some non-existant object. This behavior terminated suddenly with the conclusion of stimulation. Subjects responded to the presentation of pattern stimuli when on-going post-stimulation after-discharges were present in the occipital EEG.

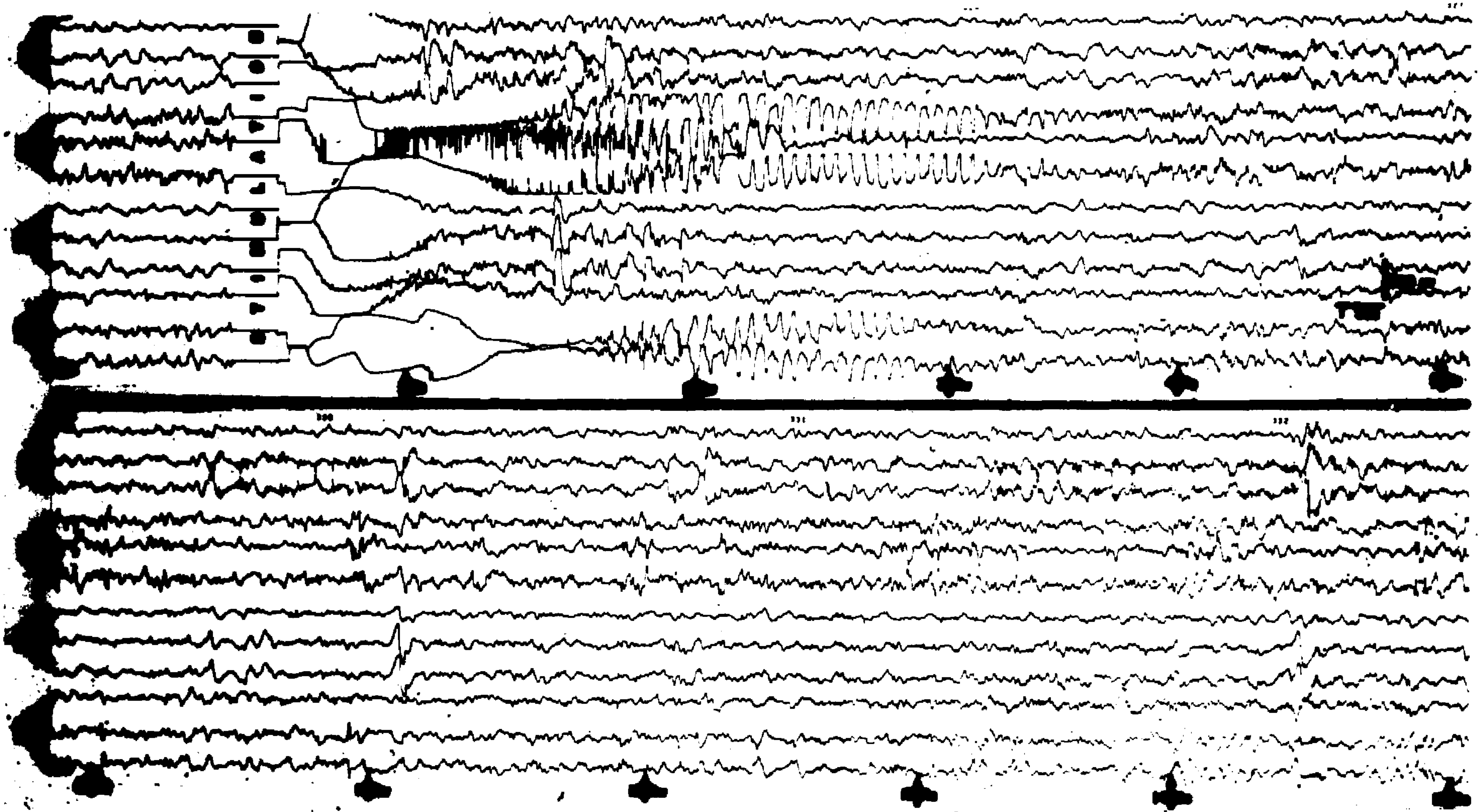


Fig. 12. Typical post occipital stimulation EEG for subject #94. Arrows indicate subject's responses. Numerals indicate trial within 15-trial block. R right press, L left press, C press rewarded, W press non rewarded. LT left temporal, RT right temporal, LO left occipital, RO right occipital.

EEG response to photic stimulation Figure 13a shows an EEG taken shortly after a typical bilateral inferotemporal after-discharge was elicited in subject #94 and the dysrhythmic high voltage slow waves were prominent in the temporal lobe tracings only. A continuously flickering, variable frequency, light source was presented to both the subject's eyes with a Grass Photic Stimulator. The EEG recorded during this period (Fig. 13b) shows that the occipital recording exhibited a continuous frequency specific response to the flickering light source over a wide range of frequencies, while the inferotemporal EEG produced long periods of stabilized 3-4c./sec. rhythmic activity when the external light source flickered at 3c./sec. The inferotemporal EEG resumed its typical dysrhythmic pattern of post-stimulation slow activity when photic stimulation was presented at higher frequencies. Figure 14 shows the EEG recorded from subject 94 just prior to the elicitation of the after-discharge shown in Figure 13a. Here the occipital lobe tracing shows the typical wide range frequency specific response to photic stimulation, but inferotemporal rhythms from non stimulated cortex were not altered by the 3 c./sec. flickering light. Higher photic flash frequencies also failed to elicit any temporal lobe following.

Acquisition of visual discrimination In Figure 15 the number of acquisition trials and errors to criterion are shown for each subject in the order in which the visual discrimination problems were presented under both conditions of electrical stimulation. Analysis of variance of these data yields a significant difference in the number of errors made to criterion under the 2 stimulation and the 2 control conditions (F=11.97, *df* = 3/9, *p*=>.01). Inferotemporal stimulation had an over-

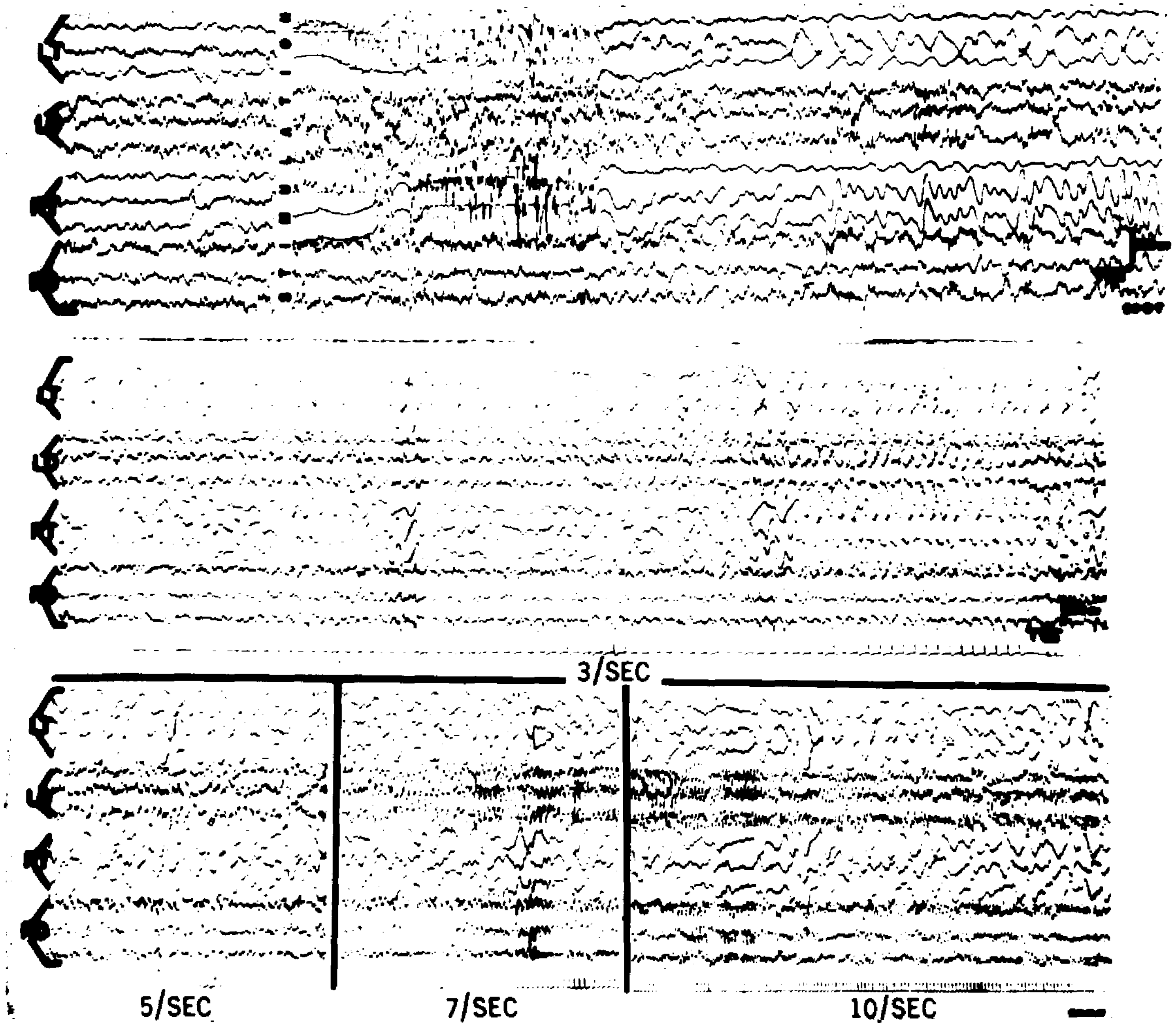


Fig. 13. Post inferotemporal stimulation EEG for subject #94 showing: A. immediate afterdischarge in inferotemporal cortex, B. response to photic stimulation (bottom trace).

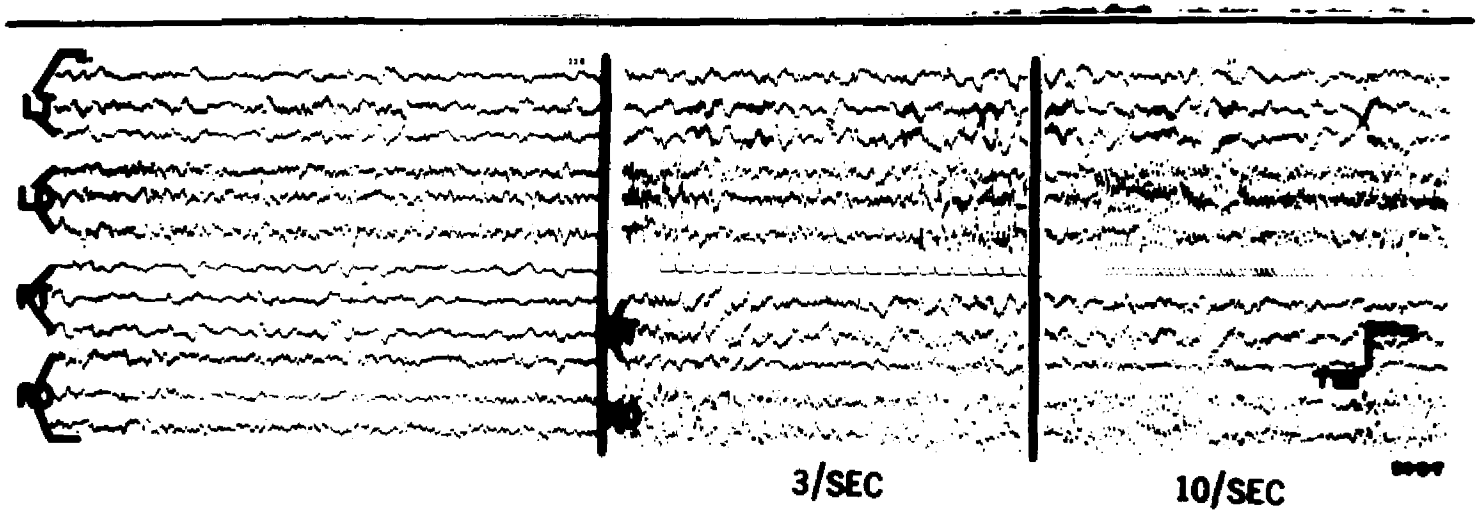
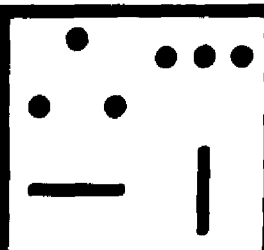
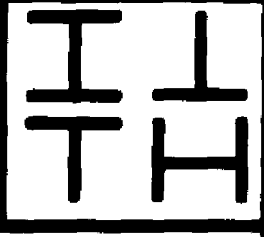
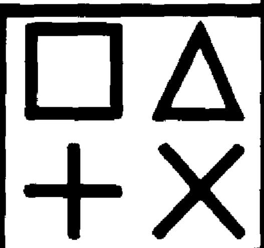
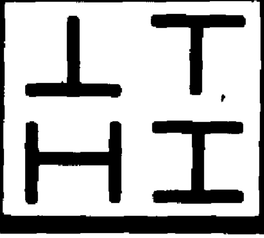


Fig. 14. Normal EEG for subject #94 showing response to photic stimulation (bottom trace). following response is seen in occipital tracings. LT left temporal, RT right temporal, LO left occipital, RO right occipital.

PATTERNS		Monk	89		85		87		94	
			Inferotemporal Stim				Occipital Stim			
A		Pat (1)	/A/	B	A	/B/	/A/	B	A	/B/
		Trial (2)	490	90	480	1890	270	390	465	465
B		Err (3)	153	46	203	687	106	94	131	174
C		Pat	C	/D/	/C/	D	C	/D/	/C/	D
		Trial	270	660	645	210	160	135	315	195
D		Err	76	226	272	126	63	35	99	91
			Occipital Stim				Inferotemporal Stim			
E		Pat	/E/	F	E	/F/	/E/	F	E	/F/
		Trial	195	225	270	270	660	210	135	Fail (4)
F		Err	63	64	103	84	218	65	38	849
G		Pat	G	/H/	/G/	H	G	/H/	/G/	H
		Trial	180	105	360	360	390	765	810	315
H		Err	77	55	119	125	160	311	320	161

(1) /A/ = stimulation; A = nonstimulation

(2) Trials to criterion

(3) Total errors, including criterion trials

(4) Failure after 2250 trials of stimulation (270 trials of nonstimulation to criterion)

Fig. 15. Pattern discrimination problems and results of experiment II.

whelming effect on acquisition scores. There was no significant difference between the number of errors made on the first and second problems which were given to subjects under each stimulation condition (F= 1.30, df = 1/3, p = >.05), and the interaction of Stimulation Condition X Order of Problem was insignificant (F= 1.41, df = 3/9, p= >.05).

Table 8 presents the mean trials and errors made by each subject to attain criterion on paired stimulated and non-stimulated problems, and the overall means for each stimulation group. In contrast with inferotemporal stimulation vs. control, occipital stimulation had little effect on performance. Analysis of variance of mean errors to criterion under occipital stimulation and control discloses no significant difference in the number of errors made (F= 1.99, df= 1/3, p=>.05). A separate analysis of each subject's mean errors to criterion under the 2 non stimulated control conditions reveals no significant differences (F= 1.70, df= 1/3, p=>.05).

Figure 16 graphically summarizes the median total errors made by all subjects on each pair of pattern discriminationproblems with respect to the type of electrical stimulation administered. Inferotemporal stimulation had an overwhelming effect in retarding acquisition regardless of problem pair, while the number of errors made under occipital stimulation on each problem overlapped considerably with those made when no stimulation was administered.

Figure 17 presents individual learning curves of subjects #87 and #89 for the complete sequence of paired visual discrimination problems. All problems are designated alphabetically (see Fig. 15), and according to the cortical area stimulated. An examination of all subjects' individual learning curves for each problem revealed that

TABLE 8

MEAN TRIALS AND ERRORS TO CRITERION IN ACQUISITION

Subject	Problem Given Without Stimulation		Problem Given With Stimulation	
	Trials	Errors	Trials	Errors
Inferotemporal Stimulation				
#85	345.0	164.5	1267.5	479.5
#87	300.0	112.5	712.5	264.5
#89	180.0	61.0	575.0	89.5
#94	225.0	99.5	1530.0	584.5
Mean	262.5	109.4	1021.3	354.5
Occipital Stimulation				
#85	315.0	114.0	315.0	101.5
#87	275.0	78.5	202.5	70.5
#89	202.5	70.5	150.0	59.0
#94	330.0	110.0	390.0	136.5
Mean	280.6	93.5	264.3	91.9

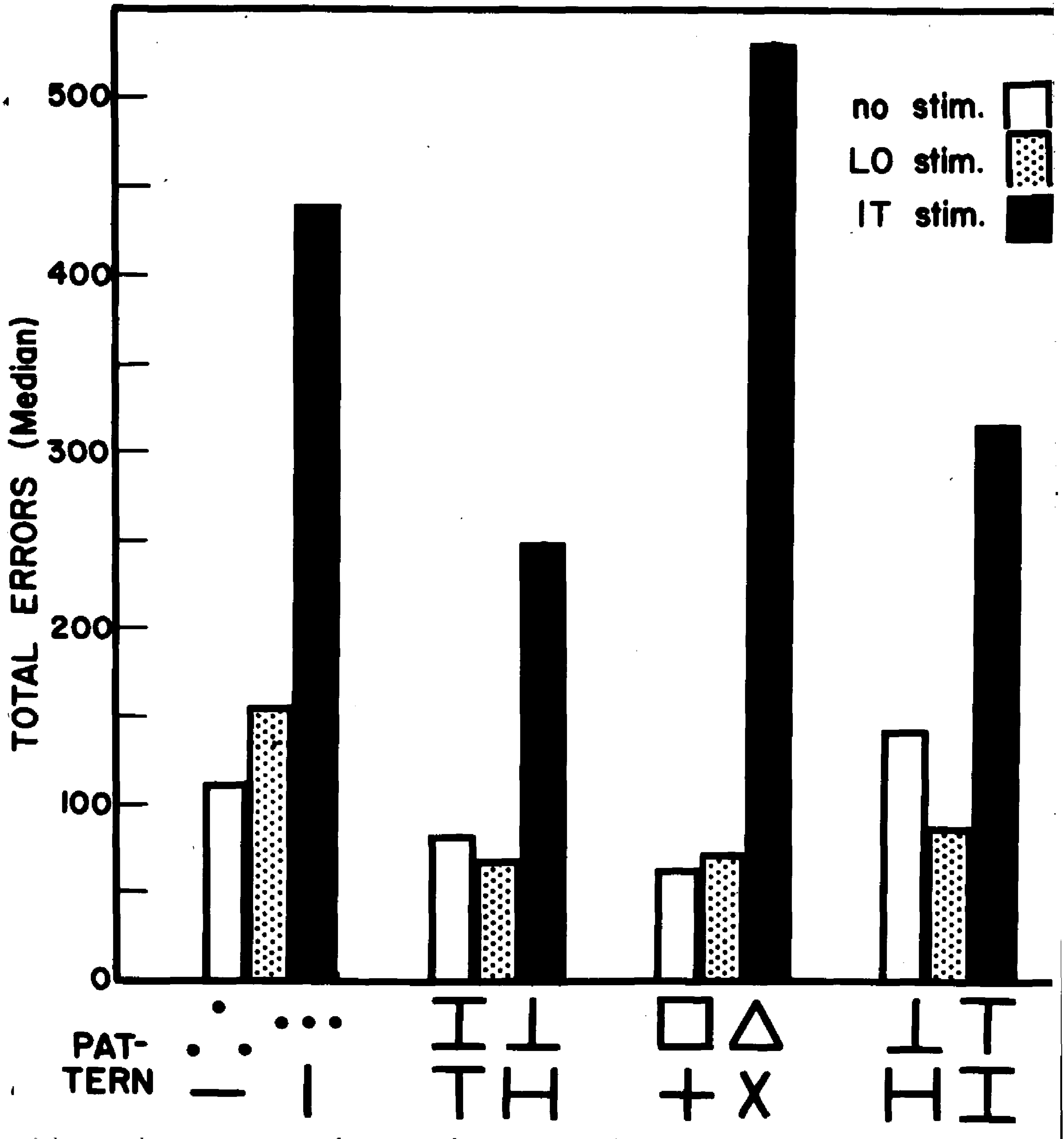


Fig. 16. Median errors to criterion for subjects #85, #87, #89, #94 for all problems in experiment II. Upper pattern of each pair was rewarded.

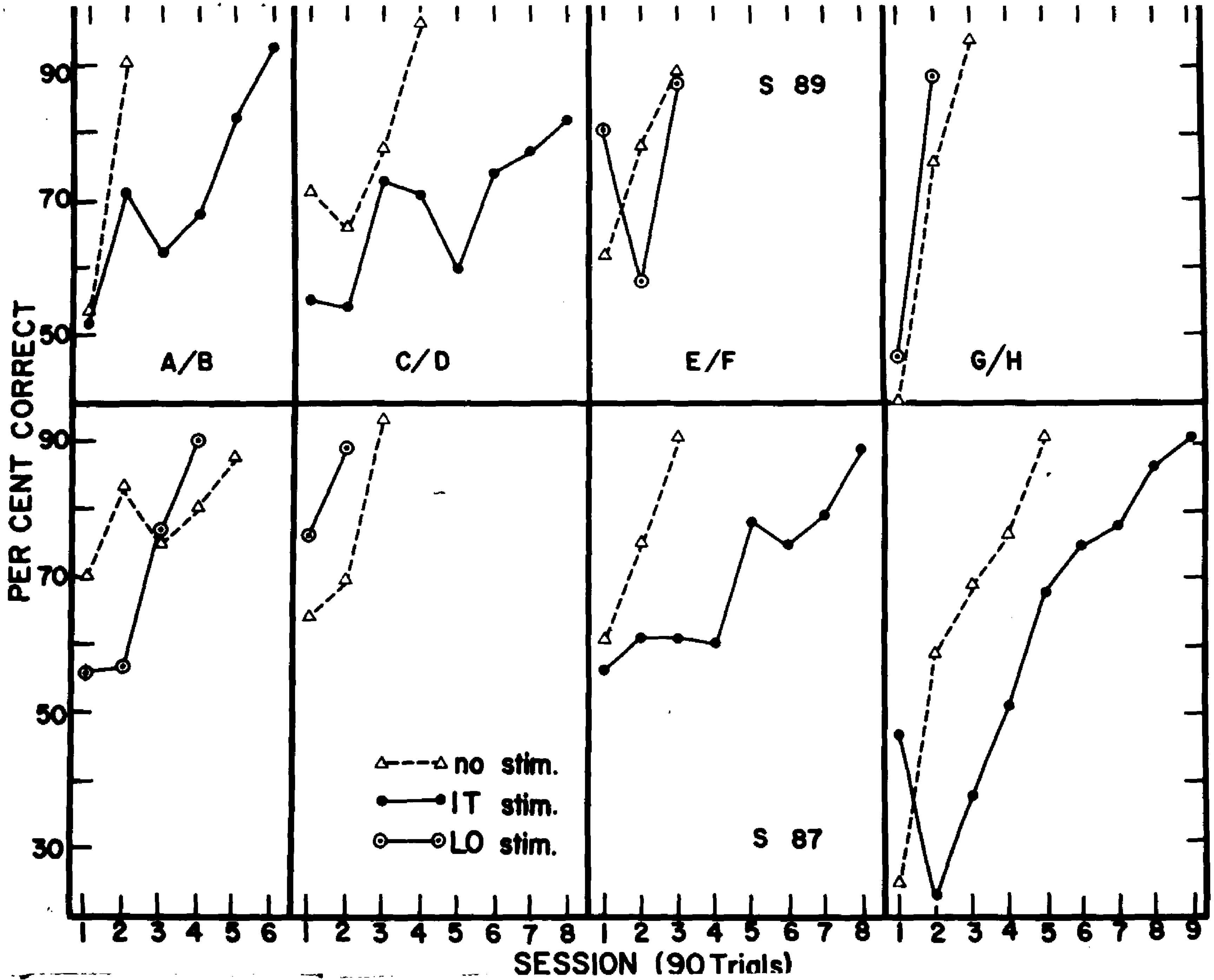


Fig. 17. Learning curves of Subjects #89 and #87 for all problems in experiment II.

the course of acquisition to criterion under occipital stimulation closely resembles acquisition without stimulation. When inferotemporal stimulation was administered learning proceeded gradually; here, subjects were not retarded at chance level but responded between 60% and 80% correct for prolonged periods. This was also true for subject #94 (see Fig. 18) who failed to achieve criterion under inferotemporal stimulation on problem F after 2250 trials and required an additional 270 trials without stimulation to reach criterion. Note that on this subject's first non-stimulated session, after prolonged stimulation testing, on problem F, performance remained at approximately the same level as the preceeding stimulated day. Two subsequent sessions were required to reach criterion. This subject solved the next problem, G, administered with inferotemporal stimulation, in 810 trials.

Problem pair G/H is a partial reversal of pair C/D (see Fig. 15): the positive (food reinforced) stimuli of C/D were the negative stimuli in G/H. Subjects 85, 87, and 94 all initially learned one problem pair of the above partial reversal under occipital stimulation and control non-stimulation, and later on in the course of the experiment they were trained to criterion on the partially reversed problems under inferotemporal stimulation and control. Their learning curves for these problems, presented in Figures 17 and 19 show that when given the partial reversal under inferotemporal stimulation and control, performance was far below chance level during the initial acquisition sessions. These subjects consistently responded to the negative stimuli which were previously reinforced in the partial reversal learned to criterion. This is perhaps indicative of the subjects' ability to differentiate between the patterns early

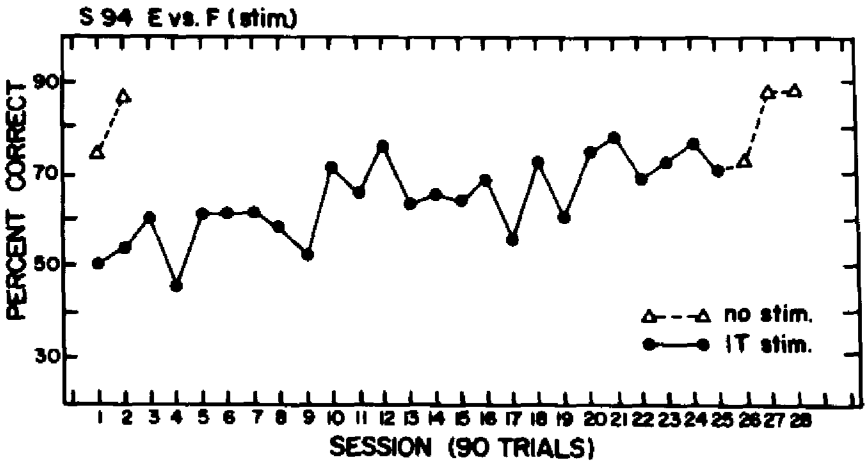


Fig. 18. Learning curves for Subject #94 on problem E and F.

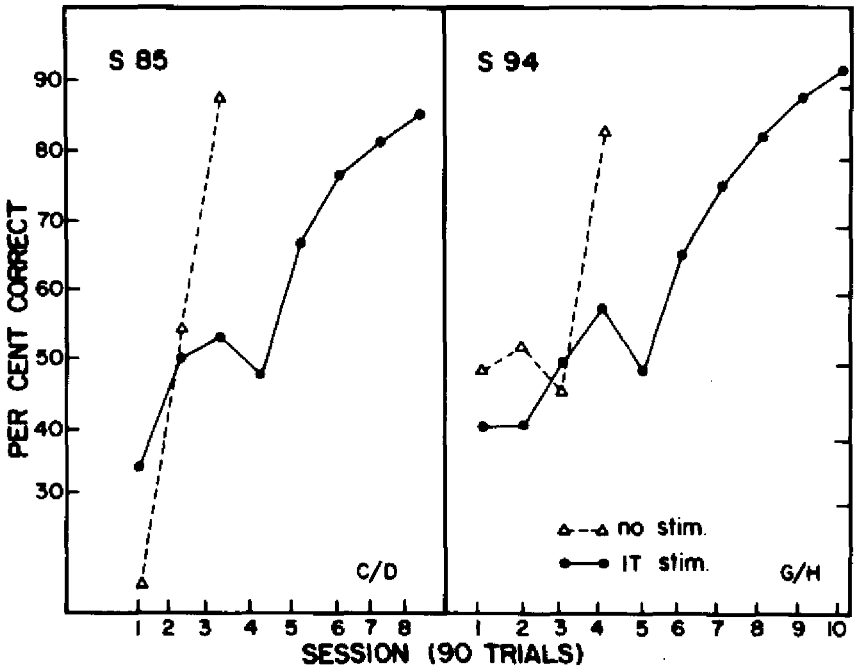


Fig. 19. Learning curves of subjects #85 and #94 on problems C vs D, G vs H. IT stim. problem given with inferotemporal stimulation.

in the course of inferotemporally stimulated acquisition.

Figure 20 is an error analysis for each stimulation and control condition showing the percent of total errors made by all subjects to successive acquisition criteria. The graph shows that when subjects received occipital stimulation and control non stimulation they made the greatest percentage of total errors when performance was at the initial chance level. However, when inferotemporal stimulation was administered, subjects made the largest percentage of errors when performance level was at 61-70% correct. The occipital stimulation group is differentiated from the non-stimulated controls when performance scores were 71-80% correct. Here an increase of total errors was seen in the occipital group, while a decrease appeared in the controls. When performance at 81-90% correct, occipital errors decreased to 13.5%, while control errors increased to 16.7%. A greater percentage of total inferotemporal errors was made at the 81-90% performance level than for the other stimulation groups.

Figure 21 shows standard deviations of daily performance scores for each 90 trial acquisition session, computed for all subjects, and averaged according to performance level (percent correct in 90 trials), for each stimulation and control condition. These results illustrate the similarity of daily performance variability at each level of learning, for all stimulation and control conditions. Note the simultaneous decrease in the variability of <u>all</u> performance when daily scores were 75% correct, and the subsequent increase when scores were 80% correct. Daily variability fell off sharply for all conditions when scores rose above 80% correct.

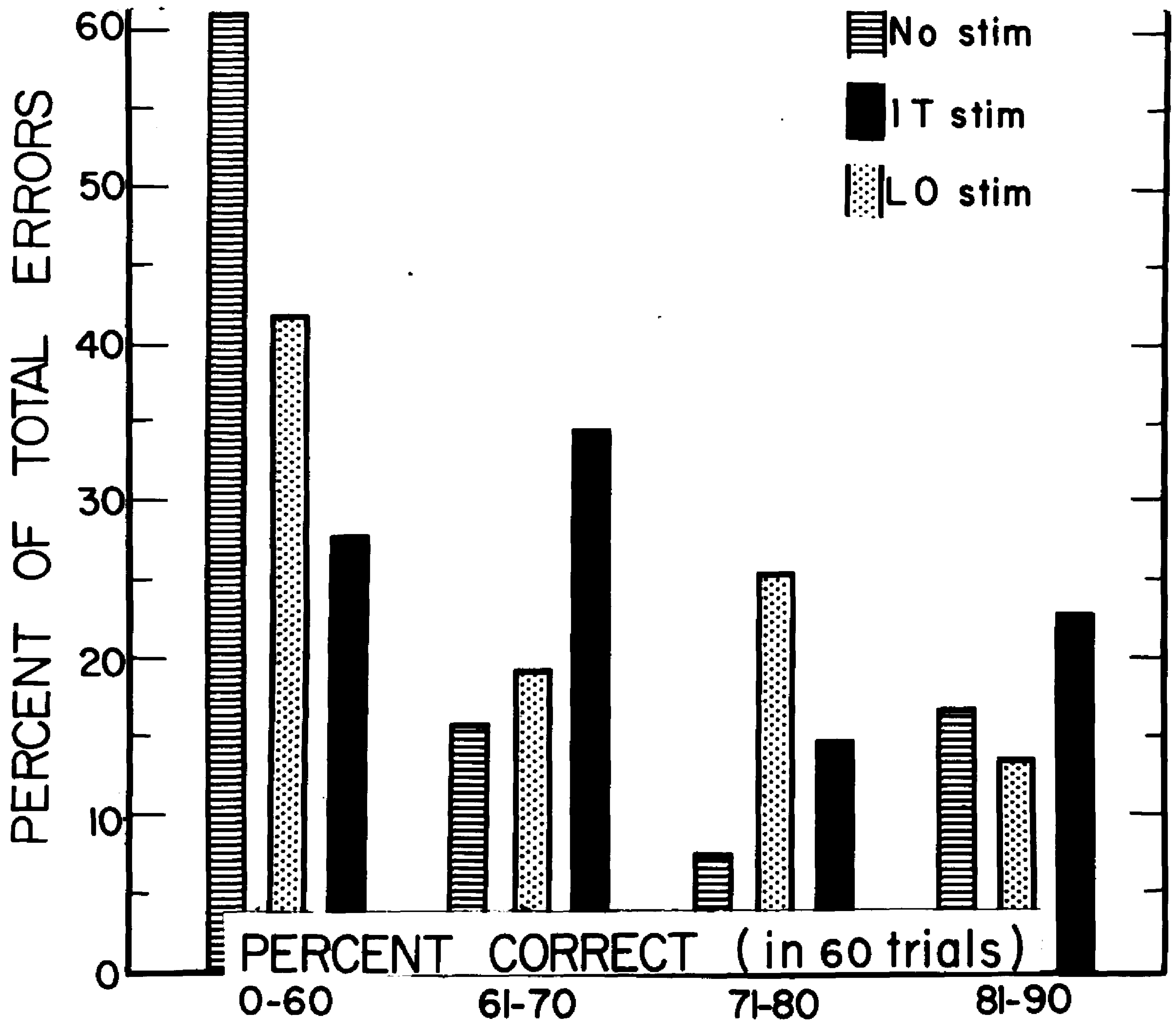


Fig. 20. Percent of total errors made by all subjects to successive criteria in acquisition

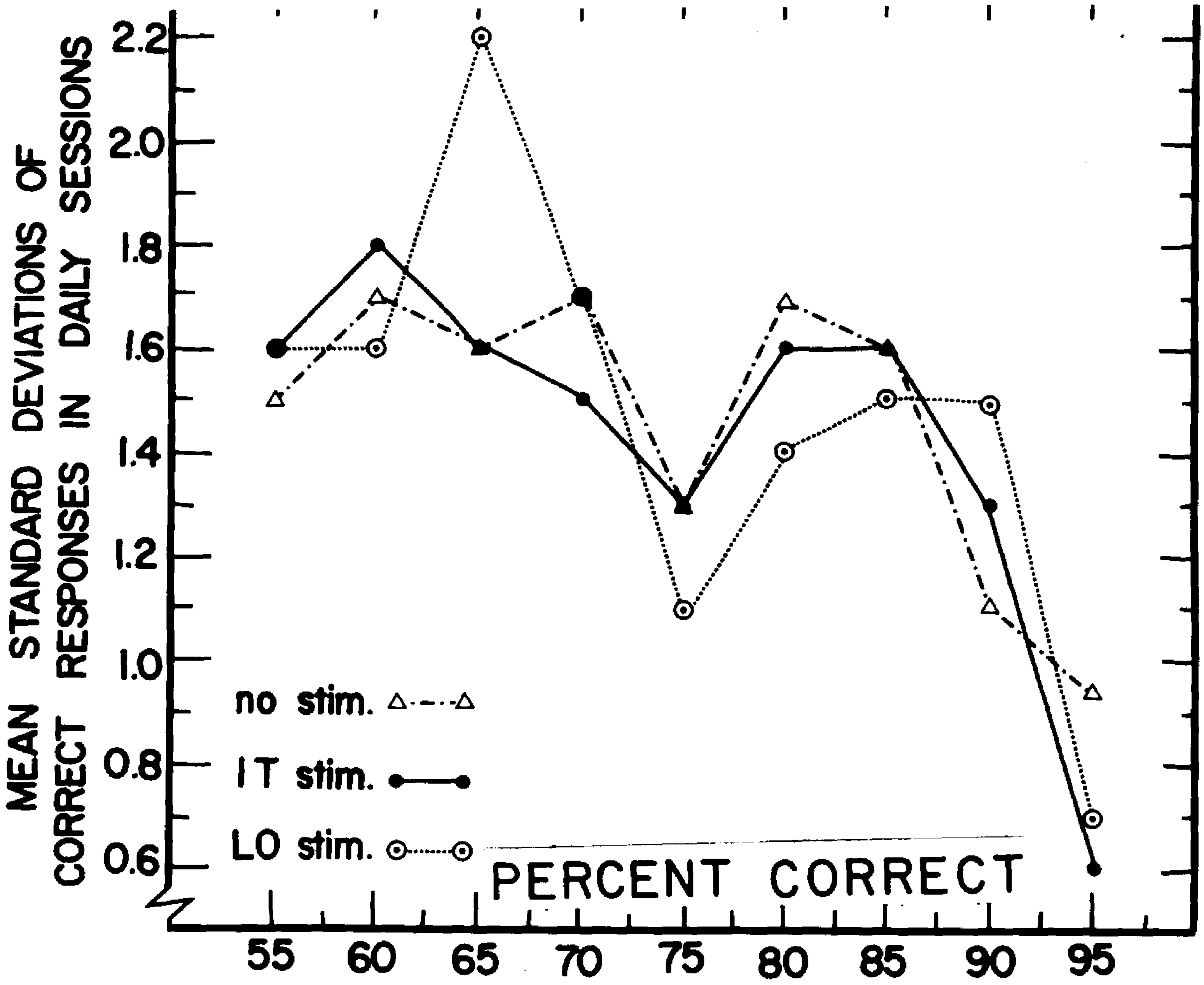


Fig. 21. Standard deviations about daily mean performance scores. IT inferotemporal, LO, lateral occipital.

A determination was made of the extent to which occipital afterdischarges which were elicited by inferotemporal stimulation were a significant factor in the depression of acquisition scores. All performance scores (number of reinforced presses) obtained for each subject on inferotemporally stimulated blocks of 15 trials, were sorted into the following 4 categories which were present in the post stimulation EEGs taken during performance: 1) no spread of afterdischarge; 2) bilateral spread to occipital cortex; 3) unilateral spread to left occipital cortex; 4) unilateral spread to right occipital cortex. Analysis of variance performed on 480 blocks of training trials revealed that there were no significant differences among score means for each EEG category ($F = 1.79$, $\underline{df} = 3/464$, $\underline{p} > .05$). The interaction of Subject X EEG Category was also insignificant ($F = 1.60$, $\underline{df} = 9/464$, $\underline{p} > .05$). A significant difference between Subjects revealed the presence of individual differences ($F = 5.72$, $\underline{df} = 3/464$, $p < .005$).

In order to determine whether the behavioral effects of electrical stimulation were most pronounced during a specific portion of a subject's ensuing block of response trials, each block of 15 responses in acquisition, stimulated and non-stimulated, was partitioned into 5 "initial" trials, 5 "middle" trials, and 5 "final" trials. Scores for each subject (number of reinforced presses to criterion) on all "initial," "middle," and "final" trials were separately talleyed for each problem. A Chi Square analysis of each problem revealed that there were no significant differences between "initial," "middle," and "final" scores ($p > .05$) regardless of the type of stimulation or non-stimulation administered during learning. Summed Chi Square Values obtained for combined data yielded similar results.

Retention of visual discrimination Table 9 presents the mean number of errors made by all subjects on the 20 trial retention test, given without stimulation, which was administered on the day following criterion acquisition of each problem. All subjects made few errors during this phase of testing irrespective of whether initial learning took place with or without either type of cortical stimulation. Also shown here are the mean errors each subject made to criterion on successive blocks of 15 retraining trials given with stimulation. An analysis of variance on these data revealed that subjects did not differ significantly in mean errors made during retraining irrespective of whether original learning occurred under stimulation or non stimulation ($F = 1.94$, $df = 1/3$, $p > .05$), and that there was no significant difference in errors made under inferotemporally stimulated retraining or occipitally stimulated retraining ($F = 1.21$, $df = 3/3$, $p > .05$). The interaction between Acquisition Condition X Retraining Stimulation was also insignificant ($1/F = 18.21$, $df = 3/1$, $p > .05$). In Figure 22 a comparison is made between all subjects' mean performance scores on their final criterion acquisition sessions, and scores obtained on the following day during stimulated retention testing to criterion. Scores are averaged for problems originally learned under each stimulation and paired control condition. After criterion was reached in acquisition, no matter what the stimulation or control condition of original learning, subjects had a mean retention score of 92% on the following day when given 20 non stimulated trials. However, when additional blocks of stimulation trials were given, all scores on the first block of 15 trials dropped below this retention level. When occipital stimulation was given during retention the mean scores on stimulated and control problems

TABLE 9

MEAN ERRORS TO POSTCRITERIAL RETENTION

Subject	Non-stimulated Retention		Stimulated Retention	
	Non-stim. Acquisition	Stim. Acquisition	Non-stim. Acquisition	Stim. Acquisition
Inferotemporal Stimulation				
#85	1.0	2.5	5.5	6.0
#87	2.5	2.0	15.0	7.5
#89	2.0	0.5	3.0	3.0
#94	1.5	2.0	12.0	10.5
Mean	1.8	1.8	8.9	6.8
Occipital Stimulation				
#85	1.0	1.5	1.5	4.0
#87	2.5	1.5	7.0	4.0
#89	0.5	2.0	9.5	3.5
#94	2.5	2.5	7.5	8.0
Mean	1.6	1.9	6.4	4.5

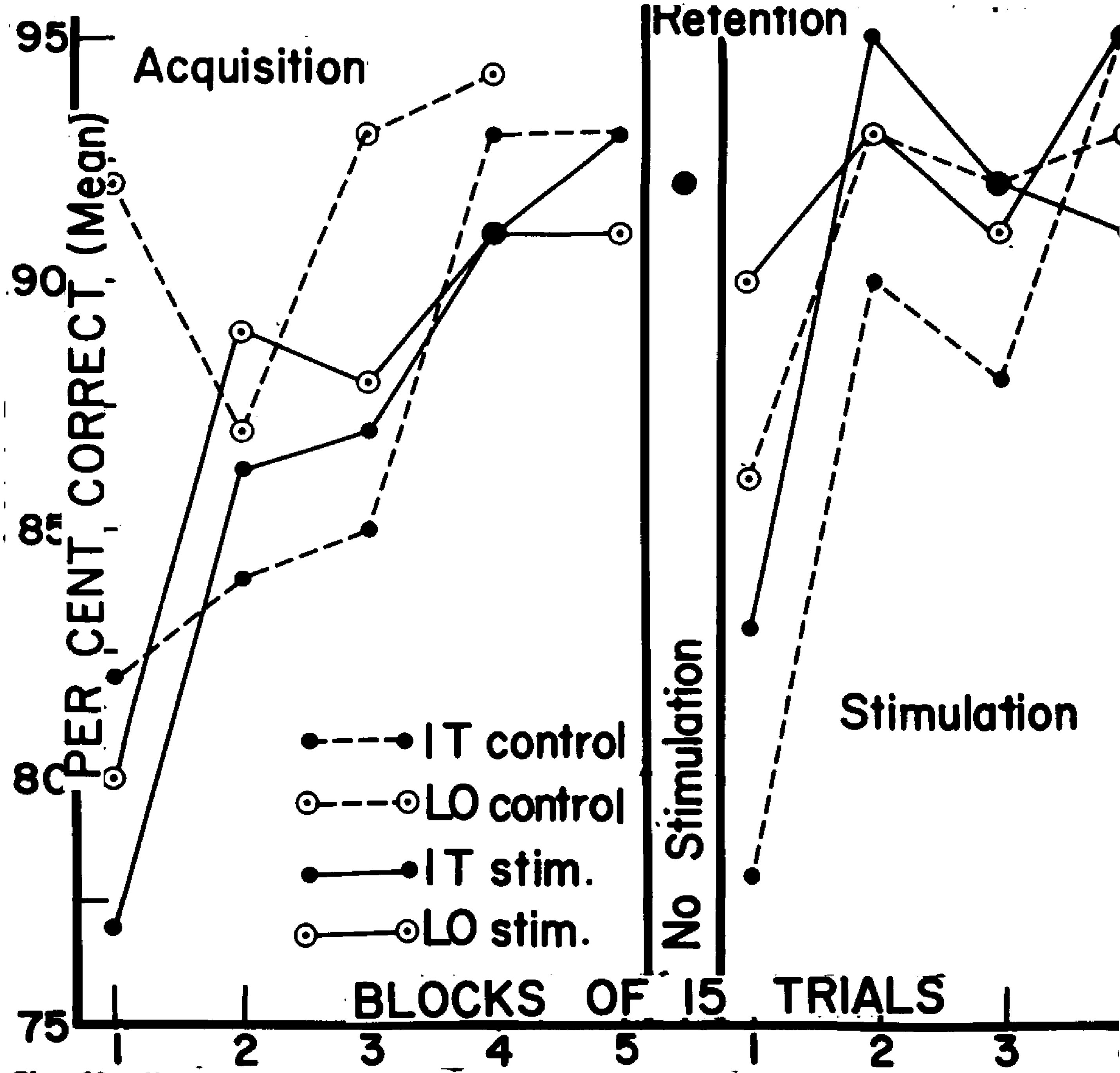


Fig. 22. Mean percent correct scores for all subjects during criterial acquisition trials, and during retention trials. IT inferotemporal, LO lateral occipital.

were 90% and 86% respectively. When inferotemporal stimulation was given during retention the mean scores on problems initially learned under stimulation and control conditions dropped to 83% and 78% respectively.

EXPERIMENT III

The main purpose of Experiment III was to determine the effects of bilateral inferotemporal stimulation, as described in the previous experiment, upon the learning of a series of consecutive spatial reversal problems where subjects are not required to differentiate between complex visual stimuli in order to receive food reinforcement.

Subjects The subjects were the 4 monkeys with implanted electrodes used in Experiment II.

Apparatus The automatic testing apparatus described in the previous experiment was modified so that the same pattern (a white diamond on black background) was projected upon both stimulus windows simultaneously. Dextrose pellets were given to a subject only when it pressed either at the left or right manipulandum, depending upon the switch position set by the experimenter on the external control panel. After a response was made the patterns were automatically switched off for a 5 second time out period.

Electrical stimulation and recording Bilateral after-discharges were elicited from inferotemporal cortex, prior to each block of 15 performance trials, in the same manner as described in the previous experiment. EEGs were taken during the testing trials which immediately followed each stimulation period.

Preliminary training On the day prior to the start of position reversal testing, a determination was made of each subject's "preferred" side at the behavioral apparatus. This was achieved by programming the panel to reinforce all presses made by the subject, observing the side to which the subject first made 10 consecutive presses, and then adjusting the apparatus so that only the "preferred" side was reinforced. The subject responded in blocks of 15 trials, four minutes separated each block, until a criterion was reached of at least 13 reinforced responses made in each of two consecutive blocks of trials (87% correct).

Procedure On the day after preliminary training subjects were retrained to criterion (2 consecutive blocks of 13 correct out of 15 responses) on the "preferred" side, and then had to reverse their responses to the opposite manipulandum to receive dextrose pellets. Reversal testing was then given in 15 trial blocks until the criterion previously specified was reached in the day's session. In subsequent sessions all subjects were first retrained to criterion on the previous day's "reversal" side, and then had to reverse and press for pellets to criterion at the opposite stimulus window. During stimulated reversal sessions pretraining trials to criterion (on the previous day's "reversal" side) were also given under conditions of inferotemporal stimulation.

Each subject was given 3 blocks of 6 daily reversals to criterion. 3 consecutive reversals in each block were administered after bilateral stimulation and 3 were given without stimulation, according to a design balanced among subjects (see Table 10). Upon completion of Block I, all subjects were given 3 reversals to criterion without stimulation after which Blocks II and III were administered. Subjects received a total of 21 reversals, 9 of which were given with stimulation, except for #89 which was discontinued after a total of 18 daily sessions due to a damaged electrode.

Results of Experiment III

Table 10 presents a summary of each subject's total errors to criterion on all pretraining and reversal tasks. Asterisks in the table indicate the sequence in which stimulation was administered during testing. These data are plotted for each subject in Figure 23 as cumulative errors. There appear to be no marked changes in the slope of any of the cumulative error curves when reversals to criterion are given either with or without stimulation. However, a flattening of Subject #89's error curve does occur during the last group of non stimulated reversals, but this may be attributed to the marked increase in error reduction often observed during later learning. Subject #94's pattern of cumulative errors reveals its particular difficulty with the position reversal task, moreso than for the other subjects, regardless of whether or not stimulation was administered.

Table 11 shows the mean errors made by each subject for blocks of 6 pretraining and reversal sessions. During stimulated and non stimulated pretraining all subjects consistently made far fewer errors than they did during reversals. Analysis of variance of this of this pretraining data yields no significant difference between errors made during stimulated and non-stimulated sessions ($F= 4.32$, *df* 1/3, $p>.05$). There were no significant differences between pretraining blocks ($1/F= 6.09$, *df* 6/2, $p>.05$) which indicates that the small number of errors to criterion made by subjects during each block of pretraining sessions was not significantly reduced as training progressed. The Block X Stimulation interaction was also insignificant for pretraining errors ($F= 1.04$, *df*= 2/6, $p>.05$). This result indicates that the high retention level for each learned position reversal was maintained throughout the experiment and was not affected by inferotemporal stimulation.

TABLE 10

SUMMARY TABLE
ERRORS TO CRITERION MADE DURING PRETRAINING AND REVERSAL TRIALS

Block	Reversal	Subject							
		#85		#87		#89		#94	
		Pre.	Rev.	Pre.	Rev.	Pre.	Rev.	Pre.	Rev.
I	1	*4	*17	1	21	*0	*45	4	21
	2	*4	*30	4	24	*1	*11	0	50
	3	*2	* 9	1	17	*1	*21	0	24
	4	7	16	*15	*32	1	20	*2	*33
	5	0	17	*1	*7	0	20	*11	*24
	6	6	10	*6	*22	0	8	*1	*26
	7	1	10	1	5	1	10	1	20
	8	2	22	1	4	2	7	1	15
	9	1	12	2	11	1	7	3	15
II	10	*2	*9	1	11	*4	*10	18	5
	11	*0	*8	1	6	*2	*9	2	14
	12	*0	*8	1	5	*0	*15	3	17
	13	1	4	*0	*9	0	12	*15	*15
	14	2	4	*0	*12	1	3	*21	*19
	15	0	9	*2	*17	0	3	*9	*22
III	16	3	5	2	5	4	3	2	22
	17	2	5	3	12	0	0	4	8
	18	2	3	1	5	1	2	7	9
	19	*5	*2	*1	*4	—	—	*2	*17
	20	*5	*7	*1	*7	—	—	*2	*14
	21	*1	*6	*0	*6	—	—	*2	*11

TABLE 11

MEAN ERRORS PER BLOCK OF 6 PRETRAINING AND REVERSAL SESSIONS

Block	Subject	Stimulation		No Stimulation	
		Pre.	Rev.	Pre.	Rev.
I	#85	3.3	18.7	4.3	11.0
	#87	7.3	20.3	2.0	20.7
	#89	0.7	25.7	1.3	31.7
	#94				
	X̄	4.0	23.1	2.0	19.9
3 Non-Stim. Reversals	#85			1.3	14.7
	#87			1.3	6.6
	#89			1.3	8.0
	#94			1.7	16.7
	X̄			1.4	11.5
II	#85	0.7	8.3	1.0	5.7
	#87	1.3	12.7	1.0	7.3
	#89	2.0	11.3	0.3	6.0
	#94	15.0	18.7	7.7	12.0
	X̄	4.8	12.8	2.5	7.8
III	#85	3.7	5.0	2.6	4.3
	#87	0.7	5.7	2.0	7.3
	#89	--	--	1.7	1.7
	#94	2.0	14.0	4.3	13.0
	X̄	2.1	8.2	2.7	6.6

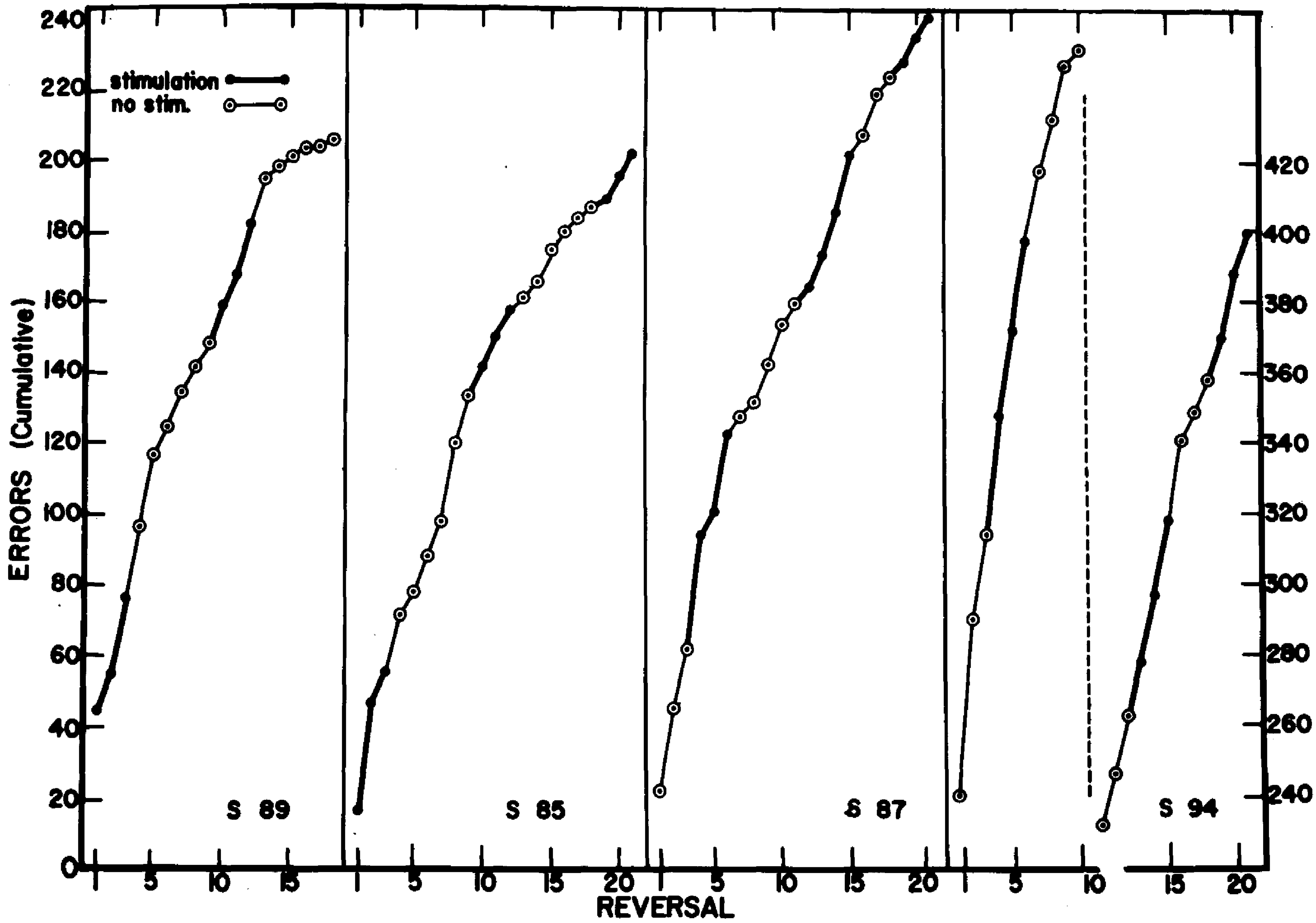


Fig. 23. Cumulative errors to successive spatial reversal criteria made by subjects in experiment III.

Analysis of variance of the reversal data revealed no significant difference in errors to criterion for stimulated vs. non-stimulated sessions ($F = 5.43$, $df = 1/3$, $p > .05$). A highly significant difference was found between blocks of reversal trials ($F = 83.27$, df 2/6, $p < .001$) reflecting the consistant improvement in performance shown by subjects throughout the course of reversal learning. The Block X Stimulation interaction was insignificant ($1/F = 1.48$, $df = 2/6$, $p > .05$); thus, the consistant improvement in performance from block to block was not influenced by stimulation.

Figure 24 presents a graph of all subjects' mean errors to criterion made on their first stimulated reversal compared with mean errors made on their first non-stimulated reversal, errors on their second stimulated reversal compared with errors made on their second non-stimulated reversal, etc., for all reversals (reversal "pairs" 4,5,6 are the three non-stimulated reversals given to all subjects after completion of the first block of 6 reversals). These averaged learning curves reveal that mean errors made during stimulated reversals overlapped with those of non-stimulated reversals during both early and later phases of testing, although subjects generally tended to make more errors when stimulation was applied.

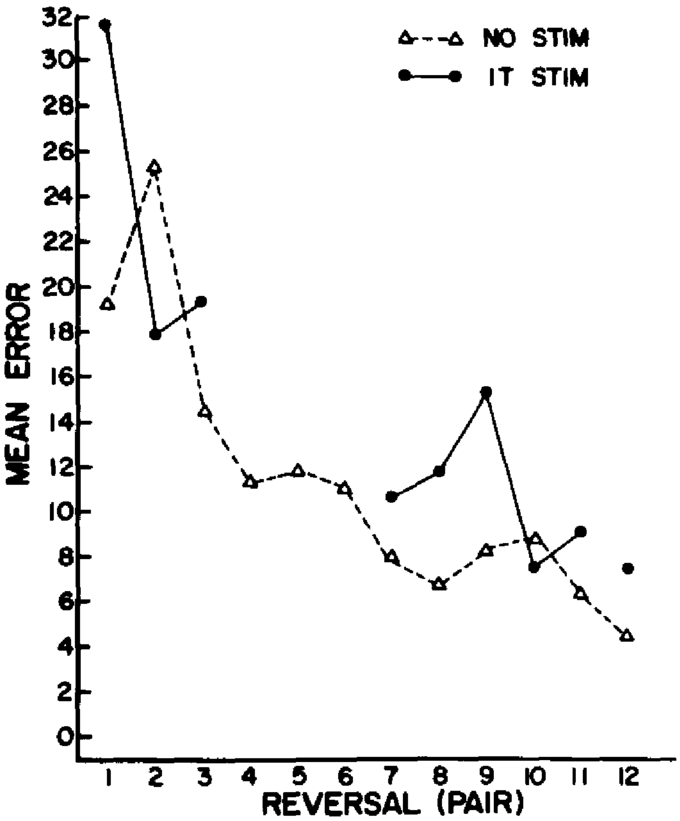


Fig. 24. Mean errors to criterion on all subjects' stimulated and non stimulated spatial reversals. IT inferotemporal stimulation.

DISCUSSION

The results of the present study indicate that the acquisition of 2-cue visual pattern discrimination tasks was significantly retarded in all subjects when ongoing neuronal activity in inferotemporal cortex was manifestly disrupted by prior bilateral electrical stimulation. Acquisition progressed at a markedly higher rate when the subjects performed on similar problems, given without stimulation, on alternate testing sessions. When pulse trains of neuronally disorganizing electrical stimulation were directly applied to bilateral occipital cortex (striate cortex) at a level of current intensity equal to or greater than that used with inferotemporal cortex, no such retardation effects on the acquisition of visual discrimination were observed. The application of either inferotemporal or occipital stimulation during retention of learned visual discriminations had only a slight, transitory effect on performance and the cortical area stimulated made little difference in overall retention scores. During extensive overtraining trials on a previously learned visual discrimination the presence of bilateral inferotemporal after-discharges was found to have no detrimental effects upon performance. When subjects were given an extensive series of position reversal tasks the elicitation of bilateral inferotemporal after-discharges immediately prior to performance was not found to have a significant effect on learning scores; retention of each learned position habit after criterial reversal was also unaffected by bilateral stimulation.

These findings are in agreement with the results of earlier ablation experiments (Chow, 1951; Mishkin & Pribram, 1954; Wilson & Mishkin, 1959) insofar as all subjects exhibited significant deficits in the acquisition of visual discriminations after bilateral disruption of inferotemporal functioning; however, the term "reversible ablation" as used by Chow (1961) to describe the effects of his afterdischarge technique (where bilateral temporal lobe stimulation totally blocked both acquisition and retention of visual discrimination tasks) cannot be readily applied in the same sense to the stimulation technique employed in the present study. Here it was found the the effectiveness of inferotemporal stimulation, in depressing visual discrimination scores, was evidently a function of the degree of prior learning of a particular problem. An isolated exception to these findings was subject #94 who failed to reach acquisition criterion on its first problem given with inferotemporal stimulation after 2250 trials. It did, however, solve the next stimulated problem within 810 trials. It is worthy to note that this subject consistantly required more trials to reach criterion than any other subject on all problems in the experiment. The above findings are in accord with those of Orbach & Fantz (1958), who observed the amount of practice to be a significant factor in determining the effects of inferotemporal resections on visual discrimination; Stamm & Knight (1963) also found that subjects with epileptogenic foci in the inferotemporal areas exhibited maximum impairment on visual discrimination tasks during the earlier phases of learning.

In Chow's (1961) study he allowed his subjects to make only a single response to the discriminanda during the presence of fast frequency afterdischarges, and it appeared that when induced bilaterally, these immediate post stimulation effects were primarily instrumental in producing the observed behavioral deficits. In the present experiment, however, subjects rarely pressed at the stimulus windows during the fast afterdischarge, which was often unilateral, and made almost all of their responses during the presence of bilateral slow waves in the EEG. Moreover it was found that the intensity of disruptive effects of stimulation on performance did not rapidly dissipate with time but was consistent throughout each 15 trial block which required a minimum of 75 seconds for a subject to complete; this was revealed by an analysis of subjects' responses which showed no consistent differences in performance scores within blocks of resppnse trials when each block was subdivided into "early," "middle," and "late" trials with regard to the proximity of the preceeding electrieal stimulation. It is thus likely that the appearance in the inferotemporal post-stimulation EEG of persistent bilateral slow waves was perhaps the most significant effect of stimulation associated with the retardation of visual discrimination learning.

It was clear that during the presence of EEG slow waves, the subjects' behavior did not exhibit any signs of gross disorganization or lack of attentiveness. After pressing at the stimulus windows had commenced during the onset of these waves, subjects continued to press regularly at the appearance of the patterns on the stimulus windows. They were well motivated in retrieving pellets they received, and made few irrelevant presses between trials when the stimuli were not projected.

In the present experiment post stimulation EEGs occasionally revealed a spread of the initial fast inferotemporal after-discharge to occipital cortex; however, an analysis of visual discrimination scores in relation to EEG characteristics showed that no significant changes in performance were present when this spread of after-discharge was either found to occur or did not appear in the EEG. Moreover, approximately 40% of all occipital stimulations elicited fast frequency inferotemporal afterdischarges, without the consequent occurrence of rhythmic slow waves, and were not associated with adverse effects on performance.

Occipital EEG tracings showed no signs of abnormality while subjects performed during the presence of slow waves in inferotemporal cortex, and when variable frequency photic stimulation was administered to a subject during this inferotemporal slow activity, occipital photic following occurred over a wide range of flicker frequencies. In view of Pribram & Spinelli's (1966) finding that inferotemporal stimulation alters the sensitivity of occipital cell aggregates, it is possible that if, in the present experiment, intensive quantitative studies of occipital excitability cycles were carried out, they would reveal alterations in the response to photic stimulation during the presence of inferotemporal slow waves. Interestingly enough, inferotemporal slow waves showed synchronization when photic flashes were presented at 3c/sec. This finding may also reflect a direct inferotemporal interaction with the visual system.

Despite the findings of Cowey & Weiskrantz (1963) and Weiskrantz & Cowey (1963) who when using a limited "perimetric" technique to study visual field defects in monkeys, found that inferior temporal lobe lesions produced no marked alterations in visual fields, it is conceivable that the nature of the visual discrimination deficit observed in the present experiment may be attributable to diffuse disturbances initiated in striate cortex indirectly by electrical disruption of corticofugal connections from the inferotemporal area to n. pulvinaris or superior colliculus, or by sequelae of inferotemporal stimulation acting directly on the optic radiations.

For such direct interference with striate cortical functions to have an extensive detrimental effect on pattern discrimination they would need to be considerably more disorganizing to a subject's visual acuity, or produce more disturbing visual field defects than did direct electrical stimulation of lateral occipital cortex, an area involved in macular vision and particularly concerned with visual acuity. Since, in the present experiment, the inferotemporal stimulation site was located within about 6 mm. from the optic radiations, and no EEG monitoring was carried out directly from the radiations or lateral genniculate body after stimulation, it was possible that inferotemporal stimulation elicited a strongly disruptive influence on occipital cortex via the radiations in orthodromic fashion; this would conceivably produce visual field alterations severe enough to alter the distinctiveness of visual cues available to a subject during pattern discrimination testing. There were, however, indications that inferotemporally stimulated were still able to distinguish between reinforced and non-reinforced pattern stimuli early in the course of testing namely, they responded consistently to the non-reinforced pattern (associated with food reward in a previously learned problem) of a partial stimulus reversal; as training continued with inferotemporal stimulation, these subjects again encountered difficulty in learning the problem to criterion. This observation would suggest that the discrimination deficit was not due solely to overwhelming visual field defects or loss of visual acuity, and would conceivably lend support to an interpretation of the inferotemporal stimulation effects which take into account the differential nature of the reinforcement associated with the complex visual stimuli. One such interpretation would hold that inferotemporal stimulation was instrumental in disrupting neural processes involved in the memory of visual cues so that a subject, after stimulation, had unusual difficulty from trial to trial in associating a particular stimulus pattern with food reward.

Another indication which might suggest that purely visuo-sensory factors were the key element in the pattern discrimination deficit was the finding that inferotemporal stimulation did not result in strong position habits. Normal subjects respond in this fashion when the cue for a response is not clear, or the problems are insoluble. Such position perseverations would result in a subject's responding at a chance level of performance; however, an error analysis revealed that the inferotemporally stimulated subjects made a large majority of their total errors while performing significantly above chance. The similarity in shapes of the learning curves between stimulated and non-stimulated sessions is also indicated in the analysis of subject's variability in scores, which shows no significant difference between groups. Additional evidence is provided by subject #94's gradual attainment of criterion without stimulation after failing to learn after 2250 trials under inferotemporal stimulation. If stimulation had resulted in visuo-sensory disturbances then this subject should have shown a more rapid improvement in performance than actually occurred, particularly since it already had a good deal of experience with the discrimination task from solving 4 previous problems given with occipital and control stimulation, and this subject previously solved the paired inferotemporal control problem in only 135 trials.

Since only poststimulation inferotemporal and occipital EEGs were monitored in the present study, the possibility exists that electrical stimulation induced undetected, widespread seizure discharges in neighboring neural structures such as amygdala, hippocampus or thalamus. A study in monkeys by Segundo et al. (1955), however, demonstrated that propagated seizure technique failed to reveal spread of activity to the basal ganglia, amygdala and rhinencephalic cortex upon stimulation of the second temporal gyrus. Jasper et al. (1952), however, have pointed out that projecting fibers from thalamus to cortex are not always direct and may have widely distributed collaterals which may serve to protect the cells of origin from degeneration.

In the present experiment the findings that subjects were not severely impaired in spatial reversals after inferotemporal stimulation, and that their level of performance on these tasks continuously improved throughout the extensive testing series offers evidence that the amygdala was not detrimentally affected by the parameters of stimulation used. It is known that behavioral deficits related to the amygdaloid system as determined by ablation studies,, involve the performance of tasks, such as spatial reversals and stimulus reversals (where the originally positive and negative stimuli of a simultaneous 2-cue visual discrimination problems is reversed in its reward values), that depend strongly on transfer of training from previous learning (Stamm et al., 1962; Stamm & Knight, 1963; Mahut & Cordeau, 1963; Schwartzbaum & Poulos, 1965). Schwartzbaum & Poulos (1965) indicate that this behavioral deficit of amygdalectomized monkeys is most likely due to a general difficulty such animals have in suppressing their previously rewarded response tendencies. The spatial reversal problem used in the present experiment, however, was not an analogous modality specific control task for visual discrimination as simultaneous tactual, auditory, or olfactory discriminations would have been. Spatial reversals were primarily employed here to determine whether or not inferotemporal stimulation was severely disruptive to a subject's behavior when it was not required to efficiently differentiate between complex visual cues in order to obtain food reward. Additional experiments will have to be carried out to test the effects of such stimulation on non visual sensory discrimination problems.

Further definitive EEG studies will also have to be made concerning the possible spread of inferotemporal after-discharge effects to the hippocampus, a structure which has been implicated in such functions as memory (Adey et al. 1960; 1962), recall Penfield, 1958; Penfield & Milner, 1958), and drive states (Correll, 1957), which are essential for learning. Chow (1961) found no effects on the retention of visual discriminations under bilateral hippocampal afterdischarges, but he did not study acquisition of this task under such stimulation. In the present experiment the absence of striking emotional display by subjects after stimulation such as retching, vocalization, urination and defecation, seen after hippocampal stimulation (Kaada, 1951; Chow, 1961) was our primary indication that this structure was not grossly involved.

The findings that after inferotemporal stimulations all subjects' visual discrimination scores did not repeatedly drop back to chance level but improved gradually until criterion was reached, and that their learning scores attained on days of non stimulated testing were not in the least disrupted by the following days' repeated cortical stimulation would indicate that the neural concommitants of a stable memory trace were not susceptible to the disruptive effects of stimulation. Also supporting this idea is the observation that all subjects showed perfect recall of task solutions on non stimulated retention tests which were administered on the day after criterion was reached on each problem. Stamm (1961) found similar results by electrically stimulating frontal cortex in monkeys during a delayed alternation task. It is likely that the transitory decrement in performance which occurred when retention testing on all problems was resumed under stimulation may have been related to the associative cues connected with the stimulation itself, particularly since the most prominent temporary depression in retention scores were made on the control problems originally learned without stimulation; here it is possible that the sudden presence of stimulation served as a conflicting situational cue which was previously associated with similar food-reinforced pattern stimuli in the paired stimulated-acquisition problem. Such temporary depressions in retention scores were observed following both inferotemporal and occipital stimulation, and, in any event, stimulated retention testing was never severely impaired and transient deficits in performance did not appear during extensive overtraining trials given after inferotemporal stimulation.

Conclusion

In conclusion, there can be little doubt that the inferotemporal area plays a significant role in the integration of complex visual input information with broader behavioral functions of the organism. The question remains as to what relationship actually exists between the functioning of this cortical area and a monkey's behavior on visual discrimination problems. The present experiment revealed that electrical interference with neuronal activity in the vicinity of this cortical region retarded the acquisition of visual discriminations, but not by virtue of any clear cut sensory loss, emotional or gross behavioral disturbance, or by drastically interfering with a subjects ability to isolate and respond to salient elements of the complex visual stimuli. Furthermore, it was also established that the consequences of inferotemporal stimulation did not serve to disrupt a stabilized memory trace once it was formed. In view of these findings, the distinct possibility exists that the observed visual discrimination deficit was brought about by stimulation-produced interference with neural processes within inferotemporal cortex involved with the actual formation of the stable "long term" memory trace . It is, thus, conceivable that the marked, rhythmic, high voltage disturbances elicited by electrical stimulation served to disrupt the ongoing neural events correlated with a subject's storage of trial to trial information regarding the differential reinforcement of the pattern stimuli. Such alteration in the stability of short term memory storage would effectively delay the consolidation of short term memory traces into a stabilized long term trace, thereby retarding a subject's acquisition but not interfering with retention of visual discrimination tasks. Further experimental investigation of this hypothesis would be possible in a procedure whereby electrical disturbances are bilaterally induced in inferotemporal cortex immediately <u>after</u> a subject makes a series of responses to simultaneous visual pattern stimuli. If acquisition of the task were impaired under these conditions, where performance is allowed to occur only in the presence of undisturbed electrocortical activity, one would then be forced to conclude that direct interference with the neural concommitants of memory, related to the reinforced stimulus events, produce the behavioral deficit.

The incorporation of the physiological technique of inducing controlled electrocortical afterdischarges into a behavioral testing routine served well, in the present experiment, as an analytic means of evaluating the role of cortical functioning in discrimination behavior. The use of this method enabled an investigation of the neural correlates of behavior while an alert animal's continuous performance on a task was evaluated; moreover, this experimental technique was found to give reliable, differential results which were related to the generally accepted knowledge of the monkeys' nervous system. The testing method developed in the present experiment could conceivably be applied to a wide range of discrimination problems in the sensory modalities, as well as to other behavioral tests which have been used to study the effects of cortical ablations.

SUMMARY

This investigation is concerned with the function of inferotemporal cortex in acquisition and in retention of visual discrimination tasks. The experimental procedures involved implantation of chronic cortical electrodes and the elicitation of cortical afterdischarges prior to behavioral testing sessions. Monitoring of post stimulation electrocorticograms throughout behavioral testing permitted the determination of correlations between neuronal processes and behavioral impairments.

In the first experiment three monkeys had electrodes implanted bilaterally in inferotemporal cortex. Stimulation parameters were determined for eliciting bilateral inferotemporal afterdischarges. Each monkey was trained on pairs of visual two-cue simultaneous pattern discriminations, with one problem given after the elicitation of afterdischarges, and the other, without electrical stimulation. The results indicate that (1) inferotemporal stimulation severely retards the rate of acquisition but; (2) affects retention of previously learned problems only slightly,as seen by a transient drop in scores after the first postcriterial stimulation; (3) after extensive overtraining, inferotemporal stimulation did not affect retention performance.

In the second experiment the procedure of testing subjects on paired visual discriminations on alternate days was again used. Four monkeys with bilaterally implanted occipital and inferotemporal electrodes were trained on pairs of discriminations of approximately equivalent difficulty. The experimental design was arranged for comparing acquisition rates after inferotemporal stimulation, and occipital stimulation. Inferotemporal stimulation always resulted in retarded acquisition rates compared to non-stimulation conditions, with an average of three

times as many errors under the former condition. There were no differences in errors to criterion for occipital stimulation and the paired non-stimulation condition. Only slight, transient, deficits in retention scores were found after both inferotemporal and occipital stimulation.

In the third experiment the group of four monkeys was trained on a series of successive spatial reversal tasks, after stimulation and without stimulation. No significant behavioral deficits occurred under the former condition.

The detrimental effects of prior inferotemporal stimulation on acquisition cannot be readily attributed to sensory or emotional disturbances. It was concluded that this form of stimulation interfered with consolidation of memory traces but did not interfere with well established memory traces. The stimulation-afterdischarge technique was found to be an efficient method of studying the effects of cortical impairment on behavior.

APPENDIX I

SUMMARY OF ANALYSIS OF VARIANCE ON ERRORS TO RETRAINING IN EXPERIMENT I

Source of Variation	df	MS	Row of Error Term	F	$F_{.05}$
1. Problem (P)	2	104.29	5	1/F = 1.57	19.25
2. Stimulation in Acquisition (A)	1	130.68	6	1/F = 1.25	225.00
3. Subject (S)	2	658.79	--	--	
4. P X A	2	214.85	7	1/F = 1.22	19.25
5. S X P	4	163.34	--	--	
6. S X A	2	45.19	--	--	
7. S X P X A	4	262.72	--	--	
8. Total	17				

APPENDIX II

SUMMARY OF ANALYSIS OF VARIANCE ON ERRORS TO ACQUISITION CRITERION IN EXPERIMENT II

Source of Variation	df	MS	Row of Error term	F	$F_{.05,\ .01}$
1. Problem (P)	1	18145.13	5	1.30	F.05 = 10.13
2. Cortical Stimulation (C)	3	158718.21	6	11.97	F.01 = 6.99
3. Subject (S)	3	34842.71	--	--	
4. P X C	3	20922.37	7	1.41	F.05 = 3.86
5. P X S	3	13940.21	--	--	
6. S X C	9	13253.01	--	--	
7. S X P X C	9	14820.79	--	--	
8. Total	31				

APPENDIX III

1. SUMMARY OF ANALYSIS OF VARIANCE ON MEAN ACQUISITION ERRORS TO CRITERION: OCCIPITAL STIMULATION VS OCCIPITAL CONTROL

Source of Variation	df	MS	Row of Error Term	F	$F_{.05}$
1. Cortical Stimulation (C)	1	586.53	3	1.99	10.13
2. Subject (S)	3	1243.86	3	4.22	9.28
3. Remainder	3	294.78			
4. Total	7				

2. SUMMARY OF ANALYSIS OF VARIANCE ON MEAN ACQUISITION ERRORS TO CRITERION: OCCIPITAL VS INFEROTEMPORAL CONTROL

Source of Variation	df	MS	Row of Error term	F	$F_{.05}$
1. Control Condition (C)	1	693.78	3	1.69	10.13
2. Subject (S)	3	2112.28	3	5.16	9.28
3. Remainder	3	408.87			
4. Total	7				

APPENDIX IV

SUMMARY OF ANALYSIS OF VARIANCE ON SUBJECTS' MEAN SCORES UNDER 4 POST STIMULATION EEG CATEGORIES IN EXPERIMENT II

Source of Variation	df	MS	Row of Error Term	F	$F_{.05}$
1. EEG Category (E)	3	.79	4	1.79	2.61
2. Subject (S)	3	3.83	4	5.72	2.61
3. E X S	9	1.07	4	1.60	1.89
4. Error	464	.67	--	--	
5. Total	479				

APPENDIX V

SUMMARY OF ANALYSIS OF VARIANCE ON ERRORS TO RETRAINING IN EXPERIMENT II

Source of Variation	df	MS	Row of Error Term	F	$F_{.05}$
1. Stimulation in Acquisition (A)	1	13.14	5	1.94	10.13
2. Cortical Locus (C)	1	19.14	6	1.21	9.28
3. Subject (S)	3	27.27	--	--	
4. A X C	1	0.39	7	1/F = 18.21	216.00
5. A X S	3	6.76	--	--	
6. S X C	3	15.81	--	--	
7. S X C X A	3	7.10	--	--	
8. Total	15				

APPENDIX VI

SUMMARY TABLE OF THE ANALYSIS OF "INITIAL,""MIDDLE," AND"FINAL" RESPONSES IN EACH 15 TRIAL BLOCK DURING ACQUISITION IN EXPERIMENT II.

($X^2_{.05}$, df/2 = 5.991)

Subject	Inferotemporal Stimulation		Occipital Stimulation	
	Problem	X^2 (df2)	Problem	X^2 (df2)
#85	A	.023	E	.008
	*B	.065	*F	.499
	*C	.339	*G	.343
	D	.790	H	.414
#87	*E	.333	*A	.073
	F	.444	B	.135
	G	.057	C	.643
	*H	1.328	*D	.394
#89	*A	.073	*E	.325
	B	.135	F	.443
	C	.450	G	.086
	*D	.394	*H	1.327
#94	E	.089	A	.111
	*F	1.559	*B	1.214
	*G	1.425	*C	.269
	H	1.431	D	.159

* Problem learned with stimulation

ALL INFEROTEMPORAL STIMULATION X^2 = 5.216 df= 16
ALL INFEROTEMPORAL CONTROL X^2 = 3.419 df= 16

ALL OCCIPITAL STIMULATION X^2 = 4.446 df= 16
ALL OCCIPITAL CONTROL X^2 = 1.999 df= 16

($X^2_{.05}$, df/16 = 26.296)

APPENDIX VII

SUMMARY OF ANALYSIS OF VARIANCE OF MEAN ERRORS PER BLOCK OF 6 REVERSAL PRETRAINING SESSIONS IN EXPERIMENT III

Source of Variation	df	MS	Row of Error Term	F	$F_{.05}$
1. Block of Pretraining (B)	2	3.07	5	1/F = 6.09	19.33
2. Cortical Stimulation (C)	1	9.38	6	4.32	10.13
3. Subject (S)	3	23.74	--	--	
4. B X C	2	4.75	7	1.04	5.14
5. S X B	6	18.70	--	--	
6. S X C	3	2.17	--	--	
7. S X B X C	6	4.56	--	--	
8. Total	23				

APPENDIX VIII

SUMMARY OF ANALYSIS OF VARIANCE OF MEAN ERRORS PER BLOCK OF 6 REVERSAL SESSIONS IN EXPERIMENT III

Source of Variation	df	MS	Row of Error term	F	$F_{.05, .01}$
1. Block of Reversals(B)	2	442.97	5	83.27	F.001 = 27.0
2. Cortical Stimulation (C)	1	65.34	6	5.43	F.05 = 10.13
3. Subjects (S)	3	125.13	--	--	
4. B X C	2	5.61	7	1/F = 1.48	F.05 = 19.33
5. S X B	5	5.32	--	--	
6. S X C	3	12.03	--	--	
7. S X B X C	6	8.29	--	--	
8. Total	23				

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