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MARCIA S. KRAFT,[2] WALTER D. OBRIST,[3] AND KARL H. PRIBRAM[4]
Institute of Living, Hartford, Connecticut

Reprinted from:
COMPARATIVE and PHYSIOLOGICAL PSYCHOLOGY
Volume 53 February 1960 Number 1

Journal of Comparative and Physiological Psychology
Vol. 53, No. 1, 1960

THE EFFECT OF IRRITATIVE LESIONS OF THE STRIATE CORTEX ON LEARNING OF VISUAL DISCRIMINATIONS IN MONKEYS[1]

MARCIA S. KRAFT,[2] WALTER D. OBRIST,[3] AND KARL H. PRIBRAM[4]

Institute of Living, Hartford, Connecticut

There is abundant evidence that the solution of complex visual tasks remains remarkably unimpaired by damage to the occipital cerebral cortex provided a small portion is left intact. Lashley (1939) found that rats were able to retain preoperatively learned discriminations of geometric figures after extensive bilateral lesions of the striate cortex in which only a remnant of the projection area was spared. Similar results have been obtained by Settlage (1939) in monkeys. Wilson and Mishkin (1959) observed that monkeys were able to learn new painted-pattern discriminations following extirpation of large areas of the striate cortex. The performance of these animals was only slightly inferior to that of normal controls.

In the experiments cited, tissue was removed by subpial suction, a technique that minimizes scar formation, necrosis, and vascular anomalies. Hebb and Penfield (1940) and Penfield (1952) have suggested that pathological tissue, especially scar formation, may cause more irritation and disruption of neural function than the clean removal of tissue alone. The present study was undertaken to determine whether irritative lesions in the striate cortex can produce an impairment of visually guided behavior that is not produced by simple ablation. To achieve this, the alumina cream method (Kopeloff, Kopeloff, & Pacella, 1947) was used to create a chronic epileptogenic focus.

Alumina cream had previously been applied to the striate cortex by Henry and Pribram (1954) and to the prestriate area by Chow and Obrist (1954). No deficits were obtained for the *retention* of preoperatively learned visual discriminations, in spite of electroencephalographic evidence of active foci. However, in a preliminary unpublished study, Pribram found that such lesions do impair visual learning. The present experiment extends this work by testing the effects of striate irritative lesions on the original *learning* of a visual task.

METHOD

Four experimentally unsophisticated, preadolescent monkeys (*Macaca mulatta*) served as *Ss*. Surgery was performed under pentobarbital anesthesia with aseptic technique. A bone flap exposed the occipital portion of the brain bilaterally. Six silver discs (EEG scalp electrodes) were filled with sterilized aluminum hydroxide cream (Amphojel) and placed on the occipital cerebral surface, three over each hemisphere. Two of the animals (Nos. 362 and 369) were reopened after six months because they failed to develop electroencephalographic abnormalities. The second operation consisted of injecting a total of approximately .2 cc. of aluminum hydroxide in droplets into the occipital cortical layer of each hemisphere. This method has been shown to produce electrographic changes somewhat more rapidly and more consistently than surface application (Chusid, Pacella, Kopeloff, & Kopeloff, 1951).

The electroencephalogram (EEG) served as the criterion for the development of an "irritative" lesion. Recordings were made preoperatively, and at monthly intervals following surgery. The animal was placed supinely in a tight wooden box, as described elsewhere (Kennard & Nims, 1942). Needle electrodes were inserted bilaterally into the scalp over the frontal, parietal, occipital, and temporal areas. Both unipolar (ear reference) and bipolar tracings were obtained on a Model III-D Grass Electroencephalograph. Recording was done mostly at night in order to facilitate natural sleep, a condition favorable for the production of epileptic discharges. On two occasions the animals were given repeated small doses of metrazol intramuscularly until seizure patterns developed (20 mg. every 10 to 15 min.). It had previously been demonstrated that metrazol will activate EEG foci produced by alumina cream lesions (Johnson & Walker, 1952).

The EEGs were evaluated for the presence or absence of epileptic patterns (Pacella, Kopeloff, & Kopeloff, 1948). Care was taken to distinguish between the "paroxysmal activity" of normal sleep (Kennard, 1956) and genuine seizure discharges, which also occur frequently during sleep. The former are bilaterally synchronous sharp waves from the central and anterior regions, resembling the light sleep pattern of humans, but of sharper configuration. Epileptic discharges, on the other hand, consist of repetitive spikes of short duration (20 to 50 msec.), maximum over the alumina cream lesion, and usually occurring unilaterally. A distinction was also made between the normal EEG response to metrazol, which is generalized, and the epileptic response, consisting of a focus near the lesion.

[1] Submitted by M. S. Kraft in partial fulfillment of the requirements for the M.D. degree, Yale University School of Medicine.

[2] Now at the University of Southern California School of Medicine, Los Angeles.

[3] Now at Duke University School of Medicine.

[4] Now at Stanford University Medical School.

Visual discrimination tests were begun when the EEG gave evidence of an epileptogenic focus. In two of the animals (Nos. 362 and 369), testing was started between two and three months after the second operation (intracortical injection), at which time the EEG revealed spontaneous focal seizure discharges. In the two monkeys with surface implantation only, testing was begun when the EEG showed a focal epileptic response to metrazol, 10 months postoperatively. The latter animals (Nos. 346 and 367) never developed spontaneous EEG abnormalities.

The main behavioral test was the learning of a painted pattern discrimination (yellow plus sign vs. yellow square), presented in a Wisconsin General Test Apparatus. This consisted of a sliding tray upon which there were two boxes 12 in. apart that could be concealed from the animal by lowering an opaque screen. The lids of these boxes had the respective cues painted on them, and were randomly changed so that the plus sign (positive stimulus) appeared on either the left or right. A noncorrection technique was used in which the animal found a peanut in the box when the appropriate choice was made, but received no reward when an error was committed. Fifty trials a day were performed six days a week, until the criterion was reached of 90 correct responses out of 100 consecutive trials.

Since Harlow (1945) has shown that three-dimensional stimulus objects are less difficult to discriminate than patterns, it seemed desirable to determine the effect of the lesions on such an easy task. The discriminanda consisted of a black pyramid, 17 cm. high, and a white dome-shaped object, 10 cm. high. In order to rule out the factor of differences in total luminus flux, the test was repeated with the same objects after they were both painted black and equated in size (30 cm.²).

The possibility always exists that an observed deficit may be due to a general impairment of learning ability that is not limited to the specific function in question. A spatial alternation problem was administered to evaluate such a possibility. This was performed on the same apparatus, using unpainted lids. A peanut was placed alternately on the left and right, the animal being permitted to correct an error before the position was changed.

Five mature, unoperated monkeys served as normal controls. These animals all had had previous test experience with spatial problems, but not with visual discriminations. On this occasion, both painted patterns and three-dimensional objects were administered. Additional control data have previously been reported (Pribram, 1954) for 44 untrained, unoperated monkeys on the same painted pattern discimination.

After testing was completed, the experimental animals were sacrificed. The brains were fixed and cut into 50-μ coronal sections, every twentieth one being stained with thionine. The locations of the lesions were reconstructed from the stained cross sections, and both the cortex and thalamus were examined histologically.

Results

Anatomical Findings

Gross examination of the brains revealed encapsulation of the alumina cream discs by connective tissue. In three of the animals there was no evidence of pathology, except for scarring and thinning of the cortex underlying the discs. The fourth monkey (No. 362) had, in addition, a small hematoma over the left parietal lobe.

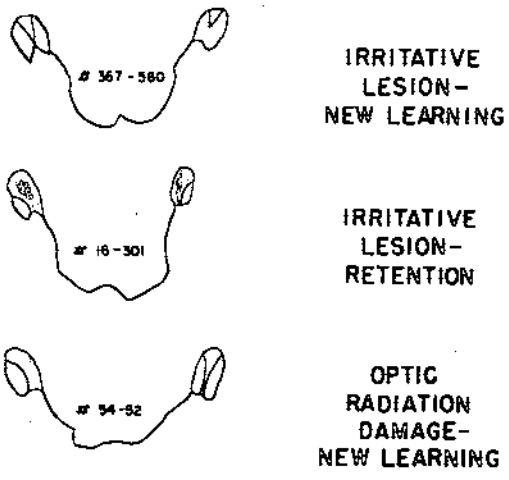

FIG. 1. Actual tracings representative of the amount of lateral geniculate degeneration in three different experiments. *Top:* Monkey No. 367 from the present study. *Middle:* Irritative lesion of striate cortex associated with no deficit in retention of visual discriminations. *Bottom:* Optic radiation damage from an occipito-parietal resection associated with no deficit in learning visual discriminations (315 trials to criterion).

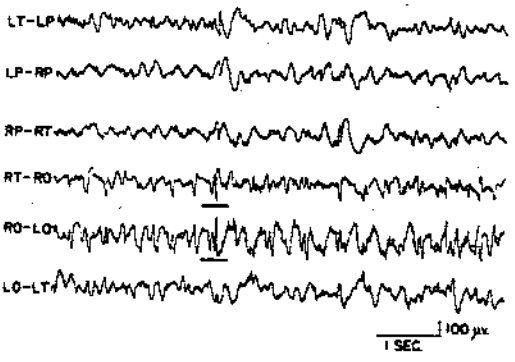

FIG. 2. Example of focal spikes (underlined) from the right occipital area of Monkey No. 367, 10 months postoperatively, following a subconvulsive dose of metrazol. *L*, Left; *R*, Right; *T*, Temporal; *P*, Parietal; *O*, Occipital.

Areas of retrograde degeneration were found in the thalami of all animals. However, only about an eighth of the total mass of the lateral geniculate nucleus was involved in each case. Figure 1 illustrates the small amount of genic-

ulate degeneration observed (upper drawing). A comparison is made with animals from other studies which showed more extensive degeneration accompanied by minimal impairment of learning or retention. It is argued that the large learning deficits obtained in the present study cannot be attributed to thalamic degeneration.

Electroencephalography

All animals had normal preoperative EEGs and normal routine tracings for six months following surface implantation of alumina cream. One monkey (No. 367) gave a focal response to metrazol three months postoperatively, but behavioral testing was postponed with the hope that a spontaneous abnormality would develop. The first spontaneous epileptic patterns appeared in Monkeys 362 and 369 two and three months, respectively, after their second operation (intracortical injection).

Monkey 362 gave an abnormal EEG in association with focal seizures. These started with clonic movements of the right arm and face, followed by involvement of the right lower extremity, at times spilling into a generalized tonic-clonic convulsion. Interseizure tracings revealed repetitive spike discharges from the left occipital area and an amplitude asymmetry of background activity over the parietal region. Neurologically, this monkey showed past-pointing to the left and impaired visual acuity for very small objects, although there was no demonstrable visual field defect. Monkey 369 also had repetitive EEG spiking over the left occipital area, plus a right occipital delta focus. This was not accompanied by clinical signs.

Spontaneous electrical activity of the two monkeys with surface implantation only (Nos. 346 and 367) remained normal throughout the experiment. However, metrazol in subconvulsive doses produced definite focal occipital spiking 10 months postoperatively in both animals. Figure 2 is an example of occipital spiking after 110 mg. of metrazol in small intramuscular doses (Monkey 367). The underlined spikes show a phase reversal about the right occipital electrode.

Behavioral Testing

With the exception of Monkey 362, described above, none of the monkeys had convulsions or detectable disturbances in visual acuity and depth perception. All four animals revealed normal visual fields, eye movements, and object recognition upon gross examination.

TABLE 1

TEST PERFORMANCE OF OPERATED AND CONTROL MONKEYS

Animal No.	Trials to Criterion[a]		
	Painted Pattern Discrimination	Object Discrimination	Spatial Alternation
Operates:			
362	1,900 (failed)	76	285
369	1,900 (failed)	83	143
346	1,300 (failed)	55	95
367	1,300 (failed)	46	108
Controls:			
375	549	0	Not Attempted
376	559	5	
379	825	0	
387	405	7	
388	946	0	

[a] The criterion was 90 correct out of 100 consecutive trials. Figures do not include criterional trials.

Table 1 presents the results on three learning tasks. The two reoperated animals (Nos. 362 and 369) gave chance performance on the painted pattern discrimination after 1,900 trials, at which time testing was discontinued. The other two monkeys were carried to 1,300 trials without evidence of learning. In contrast, all five control animals learned the discrimination in an average of 657 trials. The latter figure is high when compared with that previously reported—an average of 375 trials for the same problem (Pribram, 1954). The discrepancy may be attributable to interference from prior training on spatial problems in the present control group.

With respect to large object discrimination, the experimental animals showed evidence of learning, but were markedly inferior to the normal controls. As shown in Table 1, the operates took from 46 to 83 trials, while the normal monkeys learned the problem almost immediately. The experimental group retained the habit when the stimuli were equated for brightness and size. This suggests that the original object discrimination was probably more dependent on differences in form than upon differences in total luminous flux.

Table 1 also gives the results of the spatial alternation test for the experimental group. The average number of trials required was 158, which is within the normal range of performance. This indicates that the monkeys were quite capable of learning a task which did not involve visual discrimination.

Discussion

The results indicate that irritative lesions are capable of producing disturbances in problem-solving behavior, which is consistent with earlier investigations on the frontal lobe (Pribram: 1951, 1955; Pribram, Kruger, Robinson, & Berman, 1955). Specifically, it was found that monkeys with alumina cream lesions in the occipital area have greater difficulty learning visual discriminations than normal controls. This confirms the preliminary findings of Pribram (unpublished), who studied two monkeys following intracortical injection of alumina cream in the occipital area. These animals also presented EEG evidence of epilepsy, and failed to learn a painted pattern discrimination in 880 and 1,000 trials.

The general hypothesis that irritative lesions may produce more disruption of function than the clean removal of tissue (Hebb & Penfield, 1940; Penfield, 1952) is supported by the present findings. The animals studied here had much greater difficulty learning a painted pattern discrimination than did monkeys which had had extensive bilateral removals of striate cortex (Wilson & Mishkin, 1959). It might be inferred that irritative lesions cause an electrophysiological disruption of the entire occipital cortex, whereas partial ablation leaves certain areas intact that continue to function normally. Morrell, Roberts, and Jasper (1956) obtained similar differences between alumina cream lesions and cortical ablation with respect to EEG conditioning in monkeys. Discharging lesions in the primary sensory areas interfered markedly with conditioning of photic responses to light, sound, and tactile stimuli. However, excision of the irritative focus, with consequent removal of large areas of cortex, permitted the easy establishment of conditioned responses. These authors also found that alumina cream selectively disturbed conditioned responses involving the particular sense modality represented at the locus of the lesion. In the experiment reported here, the lesions disrupted visual discrimination learning, but did not interfere with the learning of spatial alternation. It would appear that the nature of the dysfunction depends upon where the alumina cream is placed. Experiments are now underway to test its effects on behavior when applied to other parts of the cortex.

The inability of monkeys to *learn* a visual discrimination after alumina cream application to the striate area is in striking contrast to their capacity to *retain* preoperatively learned discriminations following either striate (Henry & Pribram, 1954) or prestriate (Chow & Obrist, 1954) irritative lesions. This suggests that the occipital cortex is not the locus of "memory traces" for visual discrimination, but that it is somehow essential for the original acquisition of the habit. The distinction between learning and remembering warrants emphasis. Riopelle and Ades (1953) have noted differential effects of ablation (prestriate and temporal areas) upon the learning and retention of difficult visual problems, e.g., mirror image patterns. Since monkeys in the present study were able to learn an easy object discrimination, the question arises whether the factor of difficulty is relevant to differences between learning and retention. In any event, the possibility that separable neurological mechanisms are involved invites further experimentation.

The mechanism underlying the impairment of visual discrimination learning by alumina cream lesions is obscure. One might speculate that irritative lesions are continuously discharging and thus distort the pattern of incoming impulses in the cortex. Kooi and Hovey (1957) have shown that epileptic discharges in the human EEG are associated with repeated transient disturbances of mental test performance. The desirability of recording EEGs simultaneously with behavioral tests has been stressed by Morrell et al. (1956). Unfortunately, this was not done in the present experiment, so it is impossible to evaluate the momentary effects of epileptic discharges on learning performance. The fact that two of the monkeys never had spontaneous seizure patterns, but showed EEG disturbances only under metrazol, argues against a temporal relationship between abnormal electrical activity

and behavioral impairment. Nevertheless, this remains a possibility that deserves careful empirical study. Since scalp recordings are notably deficient in picking up epileptic discharges, a negative EEG does not necessarily mean the quiescence of a lesion (Henry & Kruger, 1955). The spread of potentials to adjacent cortical or subcortical areas may also be of considerable significance. Studies with chronically implanted electrodes are needed to answer these specific questions before investigating other possible mechanisms.

Summary

Aluminum hydroxide discs were implanted bilaterally on the striate cortex of four monkeys. Six months later two of the animals had additional aluminum hydroxide injected intracortically in the same area. Electroencephalograms were recorded preoperatively and at monthly intervals following surgery, with metrazol activation on two occasions. When the EEGs showed evidence of epileptic discharges, behavioral tests of learning were administered. These consisted of (*a*) a painted pattern discrimination, (*b*) a large object discrimination, and (*c*) a spatial alternation test.

The two monkeys with both types of alumina cream application developed spontaneous epileptic patterns in their EEGs. One of them had focal seizures. The other two animals continued to have normal spontaneous EEGs, but gave focal epileptic patterns in response to metrazol.

All four experimental animals failed to learn the painted pattern discrimination in 1,300 to 1,900 trials. Five unoperated normal controls learned it in 405 to 946 trials. The large object discrimination was learned by the operates in 46 to 83 trials, and in 7 trials or less by the controls. The experimental animals learned the spatial alternation problem in an average of 158 trials, which is within normal limits.

It was concluded that aluminum hydroxide lesions in the occipital cortex impair the ability of monkeys to learn visual discriminations, but do not affect their capacity for all types of learning. The deficits obtained were more severe than those reported for extirpations covering a similar area of occipital cortex. This suggests that irritative lesions can produce a greater disruption of function than that produced by the removal of tissue.

The results are complementary to previous findings which indicate that retention of visual discriminations is not impaired by alumina cream lesions in striate and adjacent cortex. The fact that the learning of such discriminations is disturbed by these lesions suggests that the neural mechanisms of learning and of remembering are separable.

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(Received January 23, 1959)