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EFFECTS OF EPILEPTOGENIC LESIONS OF INFEROTEMPORAL CORTEX ON LEARNING AND RETENTION IN MONKEYS[1]

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In a previous investigation (Stamm & Pribram, 1960) chronic epileptoid discharges were induced in lateral frontal cortex of monkeys by the technique of alumina cream implantation. Monkeys which had learned an alternation problem *before* placement of the irritative material showed no appreciable retention deficit after the onset of epileptoid discharges. Other monkeys which started training *after* the onset of focal discharges from frontal cortex learned the alternation task at markedly slower rates than did their controls, but they were not deficient in the acquisition of a visual discrimination problem. In another investigation Kraft, Obrist, and Pribram (1960) found that monkeys with epileptogenic lesions in striate cortex were deficient in the acquisition of visual discrimination problems but not in learning the alternation task. These results suggest that focal epileptoid discharges from isocortex result in a learning deficit but not in impairment of memory. Moreover, the deficit is restricted to those tasks which, on the basis of ablation studies, are functional correlates of the discharging cortical structures.

Investigations employing the technique of cortical ablation have delineated the inferotemporal structures as important to the acquisition and the retention of visual discrimination tasks (Pribram, 1954; Wilson & Mishkin, 1959). On the basis of the previous findings we may hypothesize that epileptoid discharges from inferotemporal cortex would retard the learning of visual discriminations but would not disrupt the memory for these tasks. This hypothesis is examined in the present experiment.

Method

Subjects and Apparatus

Twelve immature, experimentally naive rhesus monkeys were used. They were tested in a portable cage placed in a plywood enclosure. In front of the monkey was a testing tray consisting of two rectangular boxes 12 in. apart, each covered by a slide which the monkey could push to obtain a half peanut. A sliding opaque panel could be interposed between the monkey and the testing tray, and a sliding one-way-vision screen concealed *E* from *S*'s view.

The following tasks were used:

Delayed alternation. The two food cups were covered by unpainted aluminum slides.

Pattern discrimination. Each of the slides used to cover the two food cups had a yellow pattern painted on black background. The rewarded pattern formed a cross and the unrewarded one the sides of a square, all lines being 4½ cm. long and 1 cm. wide.

Object discrimination. A black, dome-shaped wooden block (rewarded) and a white triangular block, each 7 cm. wide at the base and 17 cm. high, were used to cover two food wells, set 12 in. apart. The *S*s pushed the objects aside to expose the food wells.

Procedure

Surgery. This was performed aseptically under Nembutal anesthesia. Commercial Amphojel, boiled to the consistency of a thick paste, was packed in silver disks, 9 mm. in diameter. The disks were placed bilaterally over inferotemporal cortex, consisting of portions of inferior temporal, fusiform, and hippocampal gyri. Three disks were placed on each side. The dura was closed by sutures over the disks, and the overlying muscle and skin were sutured in layers.

EEG recordings. Electroencephalographic recordings were taken from all experimental animals preoperatively and then at monthly intervals. During these recordings the monkey was placed supinely in a tight wooden box and scalp electrodes (wound clips) were attached over selected cortical areas. The *S*s were in a quiet, electrically shielded room and EEGs were obtained while they were awake or during natural sleep. An Offner six-channel Dynograph recorder was used. In some animals metrazol activation was obtained during preoperative and postoperative recordings by repeated intramuscular injections of graded dosages of the drug.

Anatomy. After termination of testing the experimental animals were sacrificed, the metal disks were removed, and the brains were processed according to procedures previously described (Mishkin, 1954).

Training. During preliminary training *S*s learned to jump into the testing cage, to pick peanuts from the food wells, and finally to push back blank covers. During formal testing 50 trials per day were given to each animal. On the discrimination tasks the rewarded cues were presented at the left or the right position on successive trials according to a chance sequence. On the alternation task both boxes were baited on the first (free) trial of each session, and on subsequent trials the peanut was placed in the cup opposite the one which had been previously rewarded. A correct response

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was scored if S shifted to the opposite cup after obtaining a reward. After an error response the reward remained in the same cup for subsequent responses until it was retrieved by the monkey. Training continued on a given task until S performed at the *learning criterion* of 90 correct responses in 10 consecutive blocks of 10 trials each.

Experimental Design

The following groups of monkeys were tested:

Learning Group. Each of four monkeys began testing after its EEG showed clear-cut patterns of paroxysmal discharges from one or more temporal electrodes. The *Ss* were trained to criterion successively on pattern discrimination, object discrimination, and delayed alternation. They were then retrained to criterion on the pattern discrimination.

Control Group. Six unoperated monkeys (Normal Group) were trained to criterion on pattern discrimination. Two additional monkeys started testing on this task one week after implantation of the alumina cream.

Retention Group. Four *Ss* from the Normal Group were given retention tests on pattern discrimination at intervals of three weeks. On each series they were tested until they responded at the *retention criterion* of 45 correct responses in 5 consecutive blocks of 10 trials each. One week after the second retention series alumina cream was implanted on inferotemporal cortex. A total of eight retention series was given.

Results

Anatomy

At the time of sacrifice the metal disks were encapsulated by connective tissue. The location of the disks and the appearance of the brain of one S, after removal of overlying tissues, are shown in Figure 1. The appearance of cortex and scar tissue corresponded to that reported previously (Stamm & Pribram, 1960).

When thalami were examined for retrograde degeneration, some of the brains showed small areas of gliosis in the ventral portions of the *nucleus pulvinaris posterior*. In other brains thalamic degeneration could not be ascertained, and in no instance was it as extensive as in brains which had undergone ablations of inferotemporal cortex.

Electroencephalography

The 10 operated animals gave essentially normal electroencephalograms throughout the first 7 postoperative weeks. Recordings showing paroxysmal discharges were first obtained 8 to 14 weeks after implantation, with a median interval of 10 weeks. These discharges, originating from one or both hemispheres, were always recorded by electrodes over

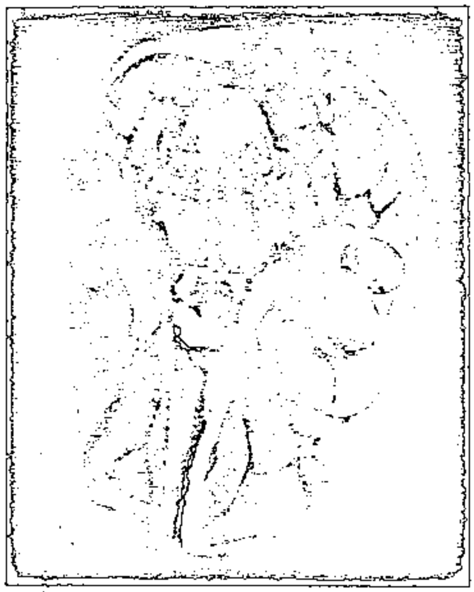

FIG. 1. Photograph of brain (medial view) of S 499 after perfusion and removal of dura.

temporal cortex and generally were observed during the normal waking state. Two *Ss* required small doses of metrazole (3 mg/kg body weight) to initiate these discharges. Focal discharges from temporal cortex were seen in all subsequent recordings until the animals were sacrificed.

Figure 2 shows a sample of a record taken 11 weeks postoperatively. Paroxysmal spike discharges are seen from electrodes over the left anterior and posterior temporal cortex. These discharges are not clearly reflected on the right side, which, as seen by other portions of the EEG, discharged independently. This record indicates a discharging focus from left temporal cortex.

Behavioral Testing

Learning. The six unoperated *Ss* attained the learning criterion on the pattern discrimination after 180 to 340 trials (Mdn., 215). The epileptoid *Ss* showed a range of 750 to 1,340 trials (Mdn., 1,025). The two monkeys which started training one week after implantation of alumina cream responded at the criterional level after 200 and 260 trials, respectively, thus showing no appreciable learning deficit as a consequence of the operation.

The task of choosing between two large

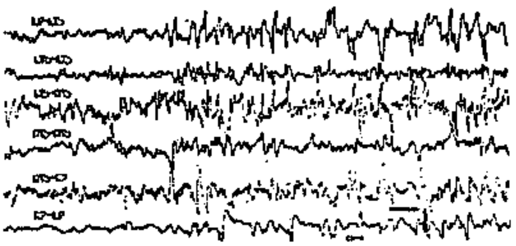

FIG. 2. Sample of EEG of *S* 511 taken 11 weeks after implantation. (Bipolar scalp recordings between electrode locations indicated: *L*, left hemisphere; *R*, right hemisphere; *F*, frontal; *Ta*, anterior temporal; *Tp*, posterior temporal. Calibration: horizontal line, 1 sec.; vertical line, 100 µv.)

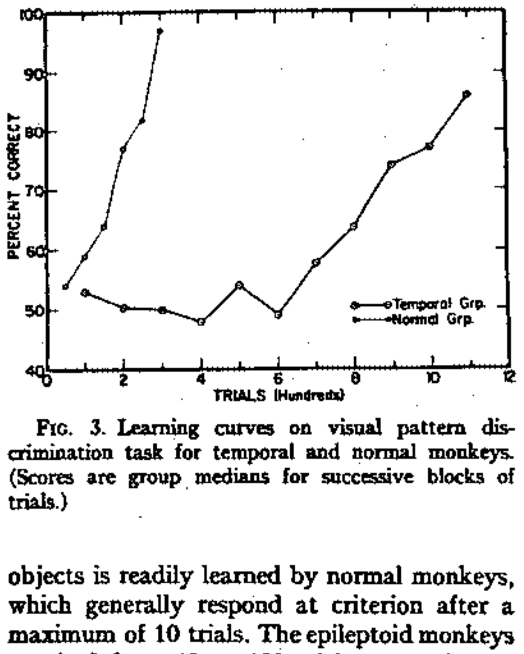

FIG. 3. Learning curves on visual pattern discrimination task for temporal and normal monkeys. (Scores are group medians for successive blocks of trials.)

objects is readily learned by normal monkeys, which generally respond at criterion after a maximum of 10 trials. The epileptoid monkeys required from 40 to 130 trials to attain criterion, an indication of marked learning deficit. On the alternation task, however, the learning scores of 60 to 350 trials for this group are within the limits obtained for normal monkeys.

The difference between the normal and the epileptoid monkeys in learning the pattern discrimination is illustrated by Figure 3. The normal group responded at chance level for the first 50 trials and then improved its scores at an approximately linear rate of 20% increase per 100 trials. The epileptoid group, however, responded near chance for about 600 trials and then gradually improved at the approximately linear rate of 7% increase per 100 trials. Thus, retardation in learning is apparent in this group throughout the course of training, and during the period of improvement in performance the group's learning rate is only about a third that of normal animals.

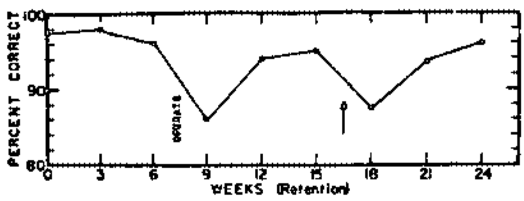

FIG. 4. Retention scores on pattern discrimination on tests at 3-week intervals. (Implantation of alumina cream is indicated by "operate"; epileptoid discharges were first seen during week indicated by arrow.)

Retention. Figure 4 represents the median percentage of correct responses during the first block of 50 trials on each retention series for the pattern discrimination. On the first preoperative test, which was given three weeks after the end of the learning series, the monkeys obtained almost perfect retention scores. On the first postoperative series each *S* performed somewhat more poorly than it had preoperatively, and the group obtained a median of 9.0 errors. Two *S*s responded at criterion during the first 50 trials, while the others required 30 additional trials. The retention curve rose on the two subsequent series, when all *S*s again performed at criterion during the first 50 trials. A second slight drop in scores is seen after the onset of epileptoid discharges, when the group obtained a median of 6.2 errors and *S*s required a maximum of 20 trials to criterion. On the subsequent postepileptic series the scores returned to the normal range, and all *S*s responded at criterion during the first 50 trials of each of the last two retention series.

When the epileptoid monkeys in the Learning Group were tested on retention of the pattern discrimination, three *S*s performed at criterion during the first 100 trials and only *S* 512 required 50 additional trials. These data indicate that the animals' memory for the first task was not markedly impaired by training on the two intervening tasks nor by recurrent epileptoid discharges.

Discussion

The experimental monkeys with discharging foci from inferotemporal cortex achieved criterional performance on the visual pattern discrimination, but they required 4.7 times as many training trials as did their controls. This deficit in learning rate is similar in magnitude to the deficit obtained by monkeys with epileptoid discharges from frontal cortex on delayed alternation (Stamm & Pribram, 1960). The average learning rate for the controls in that experiment was approximately four times the rate for the epileptoid group.

The epileptoid monkeys may also be compared with monkeys trained on pattern discriminations after bilateral ablation of inferotemporal cortex (Wilson & Mishkin, 1959). These monkeys made 5.2 times as many errors as the normal controls. In the present experiment the temporal epileptoid animals made 4.7 times as many errors as their controls in attaining the criterion on pattern discrimination. These analyses suggest that in the *learning* of new tasks the behavioral consequences of epileptoid discharges are comparable to the effects of cortical ablations.

During the series of periodic retention tests on the pattern discrimination, small decrements in the scores of correct responses were seen immediately after the operation and also after the onset of epileptoid discharges. However, the retention curve dropped at most to only a few percentage points below the 90% criterion, and on the subsequent tests all experimental monkeys again responded at their pre-epileptoid level. Similar results were obtained with the frontal epileptoid animals on retention tests of the alternation task.

It is therefore concluded that on retention tests of previously learned tasks, the performance of monkeys with epileptoid discharges from frontal or temporal cortex is essentially indistinguishable from the behavior of normal animals. These findings are in marked contrast with the results from ablation experiments (Pribram, 1954), which show marked disruption of preoperatively learned behavior as the consequence of cortical resection, with performance scores remaining near chance level during extensive postoperative testing.

The technique of alumina cream implantation has consistently produced focal epileptoid discharges as seen in EEG recordings. By this method the effects of cortical lesions on acquisition of new tasks have been dissociated from the effects on performance of previously learned tasks. The converse does not appear to occur; whatever disrupts an acquired performance also retards its rate of acquisition. Thus, the conclusion can be tentatively reached that the engram, once formed, is resistant to interferences that may be sufficient to impair its formation.

The investigations presented thus far have been restricted to epileptogenic foci from isocortical structures—striate (Kraft et al., 1960), lateral frontal (Stamm & Pribram, 1960), and inferotemporal cortex. Other studies have pointed to the medial and basal forebrain and to the brain-stem core as critically important to certain aspects of the memory process. Precise definition of differences in function and of the relationships between these and the isocortical processes detailed in the present report remain open for experimental exploration.

Summary

Experimental epileptoid discharges were induced in rhesus monkeys by bilateral subdural placement of aluminum hydroxide cream over inferotemporal cortex. Scalp electroencephalograms were taken preoperatively and then at monthly intervals. Focal paroxysmal discharges, originating from temporal cortex, were first seen 8 to 14 weeks after implantation and persisted throughout the experiment.

The monkeys were first trained on a visual pattern discrimination, then object discrimination, and, finally, delayed alternation. The epileptoid animals were markedly inferior to normal animals on the first two tasks but performed within normal limits on the alternation task.

Four of the normal monkeys were given two retention tests on the pattern discrimination at an interval of three weeks, then implanted with alumina cream and retested six times at three-week intervals. Their retention curve showed slight drops immediately after operation and again after the onset of epileptoid discharges, but was normal on all other series.

The epileptoid group's deficit in learning rate on the pattern discrimination was found to be similar in magnitude to the learning deficit on an alternation task of frontally epileptoid animals and also comparable to the learning deficit on pattern discrimination of monkeys with inferotemporal ablations. The memory for previously learned tasks, however, was not impaired by epileptoid discharges from frontal or from inferotemporal cortex. It is concluded that an epileptogenic focus in isocortex, established by alumina cream implantation, interferes with the efficient learning of a task but not with the memory for that task. Furthermore, the learning deficit is selective for those tasks which, on the basis of ablation experiments, have been related to the cortical locus under investigation.

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