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SOME ASPECTS OF EXPERIMENTAL PSYCHOSURGERY*

The Effect of Scarring Frontal Cortex on Complex Behavior

KARL H. PRIBRAM, M.D.

The application of cerebral surgery to illness in which there is no obvious gross and localizable disease of the brain is increasing. It becomes therefore of the utmost importance to track down the precise function of the neural structures involved by this surgery. It has commonly been assumed that the deficits in performance resulting from tumor, trauma or infarct give an accurate picture of the functions of the parts of the cerebral hemispheres involved. This assumption has value in neurological diagnosis; it has, however, proved insufficient when the surgeon is faced with the problem of utilizing cortical excision or undercutting for the treatment of diseases such as mental illness or epilepsy. With this in mind, an experimental analysis of the mechanisms by which cerebral lesions produce symptoms has been undertaken.

The symptoms associated with cerebral lesions must not necessarily be due to the disruption of the anatomical basis for function. It is possible that they result from interference with the normal patterning of neuronal discharge (Penfield).² In order to evaluate the role of the latter possibility as regards frontal lobe lesions, cortical scarring was produced with aluminum hydroxide cream (Kopcloff, et al.).¹ The animals used were part of a more extensive study comparing the effects of ablation, leukotomy and scarring of various subdivisions of the frontal lobe. One protocol is presented in detail as a basis for briefer comparison of the results in other animals.

An immature *Chacina* baboon (Baboon E), playful and friendly, learned after 70 trials, to perform a visual color discrimination to a criterion of 20 errorless trials. Successful performance consisted in always choosing the red box of a red-green pair, opening it for a peanut reward therein. She took 450 trials at 10 seconds delay to reach an 89% level of performance on 150 consecutive trials in a delayed response situation. Performance on this test consisted in choosing between two apparently identical closed boxes, one of which contained a peanut which had been placed in it ten seconds previously within view of the animal. An opaque screen was lowered between animal and test object during the 10 second interval. A correct choice permitted the animal to open the box and take out the peanut. Neurological and electroencephalographic observation prior to operation showed no abnormality.

Under intraperitoneal sodium amytal anesthesia a full osteoplastic calvarium flap was turned on the left temporal muscle. The dura was opened bilaterally, exposing the cortex anterior to the central fissure. Five silver discs approximately 1 mm. in diameter (electroencephalographic scalp electrodes) filled with aluminum hydroxide paste were then placed over each

* From the Laboratory of Physiology, Yale University School of Medicine, New Haven, Connecticut. Supported by grant from the Veterans Administration to Yale University.

frontal lobe—one over the superior limb of the arcuate sulcus; four anterior to the arcuate sulcus, two of which were placed above and two below the sulcus principalis. The dura was closed tightly over them, the flap replaced and muscle and scalp closed. Observations were begun as soon as the animal was about in her cage—approximately four hours after operation. Post-operatively the animal seemed somewhat less active, was less inclined to approach and play with the observer and failed to perform above chance on either test (100 trials, discrimination; 150 trials delayed response) for two weeks. For another week (150 trials) she continued chance performance on delayed response but after 60 trials reached criterion (20 errorless trials) on visual discrimination. By the end of the first postoperative month (450 trials), however, the animal had again reached criterion (85% on 150 consecutive trials) in the delayed response situation. She also resumed her lively, friendly, preoperative personality. This level of performance was maintained during the next 2 months. During the third postoperative month, however, she was observed to run around in circles to the right whenever excited. In the following weeks the running became more and more rapid. Finally, 12 weeks postoperatively, the running culminated in a Jacksonian seizure. Her head and trunk were twisted to the right, then her right arm showed clonic convulsive movements which spread to the rest of the body within a few seconds. Chomping jaw movements, drooling, urination and defecation accompanied the seizure. All activity was interrupted and the animal was unresponsive during the seizure which lasted approximately 3 minutes. Following this episode, similar Jacksonian seizures, always beginning with circular running to the right were observed to occur spontaneously and could be induced by tantalizing with food or by threatening the animal with a stick. During this period test performance gradually fell—to 80% on 150 consecutive trials in the first fortnight of the fourth postoperative month and to 64% (150 trials) in the second fortnight. By the fifth postoperative month, performance was chance in the delayed response situation although in the discrimination 90% performance on 100 consecutive trials was still possible. Throughout this period a progressively increasing ataxia with intention tremor was observed in the test situation. This became so disabling six months postoperatively that formal testing had to be discontinued. Neurological examination at this time showed bilateral hyperreflexia and increased resistance to passive movements of the extremities, somewhat greater on the right than on the left. There was a marked nystagmus on lateral gaze to either side.

Electroencephalograms taken under amytal anesthesia at monthly intervals showed abnormal four per second slow activity over both frontal regions on all records. Beginning in the third postoperative month spikes were occasionally superimposed on the slow waves but were not synchronous on the two sides. The slow activity became greater in amplitude at this time, the whole record becoming more "pathological" in appearance.

Autopsy revealed no abnormality save that in the frontal region of the cerebral hemispheres. The brain was serially sectioned (25 μ —every 20th saved) and stained with thionine. The aluminum hydroxide cream discs had outlined round areas in the frontal cortex which were compressed and had lost the laminar arrangement of nerve cells. Throughout and around the

margins of each of these areas was a moderate amount of glial proliferation. The cortex surrounding each lesion stained poorly with thionine for as far as two mm. although no chromatolysis, pyknosis or other abnormality was apparent. Serial analysis of the thalamus failed to reveal any cellular abnormality. The cerebellum was grossly and histologically normal.

Two other immature female baboons were trained and prepared in a similar manner except that in one (Baboon C) the aluminum hydroxide cream discs were all placed anterior to the arcuate sulcus while in the other (Baboon H) the discs were placed above and within the limbs of the arcuate sulcus but not over the frontal polar cortex. These animals failed to show the spontaneous and permanent deterioration described for Baboon E. Baboon C showed such deterioration after the intravenous administration of metrazol in the fourth postoperative month which caused a generalized seizure at the time of administration and a spontaneous seizure about two hours later. The latter resembled the circular running fits described for Baboon E. In spite of this she performed at the 80% level (30 trials) during the subsequent test. The following two days' trials brought performance up to 86% on 100 consecutive trials. The following week, however, performance was down to 75% on 150 consecutive trials and two weeks following the injection performance was chance on 150 trials. During this period she began to be less active and friendly, appeared dull though distractible, performance being interrupted by any extraneous noise. This deteriorated behavior persisted for the next three months. A period of two months was then allowed to elapse before testing was resumed. After approximately one hundred trials a 95% level of performance was attained on 150 consecutive trials. Another attempt was made to induce the deteriorated behavior with metrazol. Again there was no drop in performance immediately. However, performance dropped to 83% on the subsequent 150 trials given in the next two weeks. Following this the animal became highly distractible and unmanageable in the test situation, attempting to destroy the apparatus rather than test. Whenever a few trials were accomplished random scores were obtained. This behavior persisted for a month at the end of which time the animal was sacrificed. EEG abnormality was not as gross as in the case of Baboon E and no spikes were seen at any time. Pathological examination showed only a difference in locus of lesion between Baboon C and Baboon E.

Baboon H showed a period of spontaneous deterioration in the fourth postoperative month. Seizures similar to those described for Baboon E occurred. They could also be brought on by excessive stimulation of the animal. During this month performance of delayed response fell from 90% to 64% on successive series of 150 consecutive trials. However, at the end of this time performance returned to above 85% and seizures were no longer observed. During the sixth postoperative month a series of metrazol injections resulted in only temporary (lasting one week—150 consecutive trials) diminution of performance level (to 66%). However, a control animal with no lesion showed no such fluctuation in performance even though twice as much metrazol had to be administered in order to produce generalized convulsive seizures. In spite of the generally high level of performance shown by Baboon H, EEG has continually shown marked slow activity over the frontal regions (4-6 per second) with occasionally super-

imposed spiking. This animal also became combative, destructive and distractible in the test situation but is still under observation so final outcome and pathological analysis must be deferred.

These experiments demonstrate that marked impairment of performance may result from a lesion which causes only minimal damage to the anatomical organization of the cerebral cortex. In these animals electrographic abnormalities were present. However, no specific relation between type and severity of change in electroencephalogram and change in behavior was obtained, possibly because of the use of anesthesia during electrographic examinations, the rarity with which they were made and the fact that direct cortical recording was not possible. Nevertheless, it is most likely that the symptoms produced by these lesions can be attributed to interference with the normal patterning of neuronal discharge. Experimental analysis of what constitutes such "normal patterning" must now be obtained before further investigation of interference factors will become meaningful. However, the evidence presented emphasizes the importance of scar-minimizing techniques in cerebral surgery even when applied to the so-called "silent" areas.

Comparison of the results presented here with those of leukotomy or ablation reported elsewhere³ is also illuminating. After lobotomy or restricted ablations of the areas involved by scar in this study a four to six month period of deficit in performance resulted which could be overcome by training. When scar minimizing technique was used no irreversible or unpredictable performance deficit has occurred. Following such ablations, therefore, a more stable cerebral organization results which in the long run seems to be more adaptive for the organism than that produced by scar.

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