Experimental Epilepsy After Rostral Reticular Formation Excision*

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Contemporary studies dealing with the genesis of epilepsy have focused considerable attention on subcortical structures, and the concept of "subcortical epilepsy" or "centrencephalic epilepsy" has become so firmly rooted that these terms are now familiar clinical expressions. Nevertheless, clinical and laboratory evidence to date has failed to affirm or deny a subcortical mechanism in epilepsy.

Knowledge of the physiological activity of subcortical centers has accumulated rapidly since the pioneer studies of Moruzzi and Magoun0 and Jasper.24,25 Abundant data have confirmed the existence of a multisynaptic brain stem system, the reticular formation, with rostral projections to the basal diencephalon (the ascending reticular activating system or ARAS), and diencephalic projections to the cerebral cortex (the diffuse thalamic projection system or DTPS). Stimulation of this system in the intact animal is followed by arousal and desynchronization of the electroencephalographic recording (EEG). Lesions of the reticular formation produce the reverse, namely, depression of awareness and synchronization of the EEG.

Since subcortical, or centrencephalic, epilepsy is associated with sudden loss of consciousness and hypersynchronization of the EEG, many questions arise regarding the role of the reticular formation. The experiment reported herein was designed to examine the consequences of partial or complete isolation of an entire cerebral hemisphere from reticulo-cortical input. Unilateral enucleation of the mesial thalamus (10 monkeys) and unilateral lesions consisting of hemisection of the midbrain tegmentum (8 Rhesus monkeys) were created singly or in combination with a split-brain lesion in which the corpus callosum and midline commissures were divided.45 Anatomical separation of the two hemispheres was undertaken in the latter cases to remove crossed as well as ipsilateral reticular input to one cerebral hemisphere. EEG patterns were then recorded from the operative side ("the isolated hemisphere") and compared with those recorded from the non-operative side ("the intact hemisphere"). Information regarding the threshold of spontaneous and drug-induced convulsive phenomena was provided by clinical observations of chronic animals.

Method

Eighteen healthy Rhesus monkeys weighing 4 to 8 lbs. were used in the study. Anesthesia for the chronic preparations consisted of pentobarbital sodium administered through an intravenous drip controlled by the anesthetist. In acute procedures, animals were anesthetized briefly with open-drop ether, intubated, and attached to the Palmer respirator. The craniotomy and cutdown wounds were generously infiltrated with 1 per cent procaine and the animals were positioned comfortably on the operating table. Succinylcholine was then delivered by a slow intravenous drip, sustaining the intended muscular paralysis for the duration of surgery. The animals were physiologically monitored by means of electrocardiogram (EKG) and arterial blood pressure tracings, and corticograms were recorded with Jasper cortical electrodes connected to the Ofner 8-channel transistorized electroencephalograph. In chronic cases, permanent dural electrodes were fixed firmly into the replaced bone plate. Prior to sacrifice, acute and chronic preparations were injected with intravenous sodium fluorescein and examined under Wood’s light. None of the animals reported showed any deposit of dye in the brain suggestive of cerebrovascular compromise.

1. Lesions of the Diencephalon. In 10 animals, thalamic lesions were created singly or in com-
bination with the split-brain lesion. Employing microdissection tools and the Zeiss dissecting microscope, unilateral enucleation of the thalamus (thalamectomy) was accomplished by means of the transcallosal microdissection technique.37

The 3rd ventricle was entered in all cases through a midline incision of the corpus callosum. The lateral walls of the 3rd ventricle are formed on each side by the thalamus and are sheer, convex, and connected by a massa intermediaria in 90 per cent of the cases. The foramen of Monro marks the rostral limits of the thalamus and is identified by locating the outpouching of choroid plexus which resides in the foraminal orifice and pulsates in and out with diastole and systole. Coursing through the foramen of Monro is the thalamostriate vein; this vessel runs in the groove between the caudate nucleus and the thalamus, and marks the anterolateral limits of the thalamus. The vessel is an essential landmark for thalamectomy.

From a point just behind the thalamostriate vein, the thalamus was removed in a rostrocaudal direction by applying low suction through the capillary micropipette. Lateral dissection in these cases was halted approximately 6 mm. from the midline to spare the lateral thalamic nuclei and internal capsule. Complete unilateral thalamectomy usually requires removal of 9-10 mm. of tissue. Although inferior landmarks were few, and the depth of each lesion necessarily varied, dissection was kept safely above the floor of the 3rd ventricle to spare the hypothalamic nuclei. Caudal dissection was continued to the orifice of the aqueduct of Sylvius and was concluded just rostral to this landmark.

In animals in which unilateral thalamectomy was combined with the split-brain lesion, attention was redirected to the midline and the following structures were divided in order: the anterior callosum and genu; anterior commissure and lamina terminalis; massa intermedia; posterior callosum and splenium; and the habenular, hippocampal, and posterior commissures. The optic chiasm and floor of the 3rd ventricle were purposely left intact and not violated by surgical manipulation.

2. Lesions of the Mesencephalon. A number of animals were subjected to hemisection of the midbrain tegmentum, alone or in combination with the split-brain lesion. The brain stem was approached by the supratentorial route, and access to the superior colliculus was gained by retraction of the occipital pole. At ×15 magnification and with microsuction tools, an avascular hemisection was created as far medially as the aqueduct of Sylvius and inferiorto the level of the basis pedunculi. The lesions, therefore, spared the pyramidal outflow tracts, while dividing all ascending and descending pathways of the tectum and tegmentum on one side.

Chronic animals were recapitulated with bone plates containing 12 dural electrodes, and the electrodes were brought out in 2 trails from the left and right posterior cervical areas. The animals were seated in monkey chairs and placed on regular diets immediately.

The consequences of surgery were studied in 18 animals with the following lesions: acute hemisection of the midbrain tegmentum (4), acute hemisection of the midbrain tegmentum combined with the split-brain lesion (4), acute unilateral thalamectomy combined with the split-brain lesion (2), chronic unilateral thalamectomy combined with the split-brain lesion (4), chronic unilateral thalamectomy (2), and chronic bilateral thalamectomy (2).

Clinical Findings

Wherever possible, the surgical lesions were clinically assessed. The study of acute animals, under the influence of succinylcholine, provided little or no useful information. Chronic monkeys, however, displayed interesting neurological findings.

Chronic Unilateral Thalamectomy Preparations. The 2 animals subjected to unilateral thalamectomy had a contralateral agnosia which persisted, with only slight improvement, for as long as they were studied (9 months). In addition, they usually ignored the side of the body opposite to the lesion, while manual tasks, feeding, and defense responses were confined to the ipsilateral extremities. Despite repeated testing, however, no sensory loss to pin or touch, rigidity, ataxia, paresis, or reflexive changes were found in the contralateral limbs. There seemed to be an homonymous hemianopsia on the "ignorant side," but all other findings in the neurological and general physical examinations were normal.

Of particular interest were the consequences of Metrazol (pentylene-tetrazol) administration on the 5th postoperative day. During slow infusion of the drug in convulsant dosage, both animals responded with adventitious movements in the upper extremity contralateral to thalamectomy. These consisted of fine clonic jerks beginning in the thumb flexors and abductors and spreading after 5-10 seconds to the wrist and elbow. One animal, in addition, displayed dorsiflexion jerks of the contralateral ankle synchronous with those at the wrist and elbow.