Effect of Motor Cortex Ablations on Reflex Myoclonus in the Monkey. (20187)

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We have previously reported(1) that ablation of the motor cortex in the cat produces a marked depression of the myoclonic responses of the affected extremities, as elicited by afferent stimulation after administering subconvulsive doses of metrazol. These studies have been extended to the macaque for two purposes: 1. To ascertain if the motor cortex plays a similar role in the myoclonic mechanism in a primate. 2. To be able to more sharply delimit the cortical ablations than was possible in the cat and to avoid implication of non-motor frontal ("pre-frontal") cortex.

Methods. Experiments were performed on 5 mature rhesus monkeys (*Macaca mulatta*). For studies of the reflex myoclonic responses, the animals were anesthetized with pentobarbital (nembutal) 50 mg/kg intraperitoneally. In one experiment, dial 45 mg/kg was used. Electrical activity of the brain was recorded either through phonograph needles embedded in the skull or through wick electrodes placed on the cortex. Electromyograms were recorded from bipolar needle electrodes placed symmetrically in the limb pairs. All records were made by a Grass 8-channel, ink-writing oscillograph. Sub-convulsant doses of metrazol, 5 to 10%, were administered by slow intravenous injection during continuous recording. The physiologic stimulus was a click produced in an earphone by the square-wave output of a Grass stimulator. The usual frequency of repetition of the click was 0.5/sec. Cortical ablations were performed with suction and cautery as follows: 1. Acute ablation of pre-central gyrus of one side—one monkey. 2. Acute ablation of one arm area—one monkey. 3. Chronic ablation of one arm area—2 monkeys. 4. Chronic ablation of one leg area—one monkey. Before performing the limited ablations, the excitable cortex of the pre-central gyrus was identified by stimulation, dial, 40 mg/kg, being used for anesthesia in all except the first preparation. In the chronic preparations, the ablations were performed aseptically and the animals were kept for 6 to 7 weeks, at which time they had attained an essentially static level of recovery of function, and showed only slight awkwardness in movement in the distal portion of the affected extremity. At the end of this period, the animals were prepared for study of the reflex myoclonic responses, as described above.

Results. The results of all experiments were essentially similar. Ablation of the motor cortex, in whole or in part, resulted in complete or partial failure of the affected extremities to participate in the myoclonic response to acoustic stimulation. In the case of the ablation of the whole pre-central gyrus, the affected upper and lower extremities both showed depression of the myoclonic response. With the ablations limited to arm or leg area,

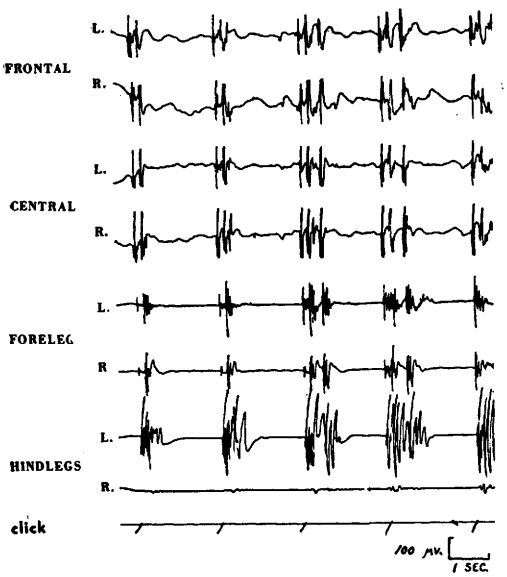

FIG. 1. Ablation of left hind-leg area performed 6 wk previously (lesion shown in Fig. 2). Note the almost complete absence of response of the right hind-leg.

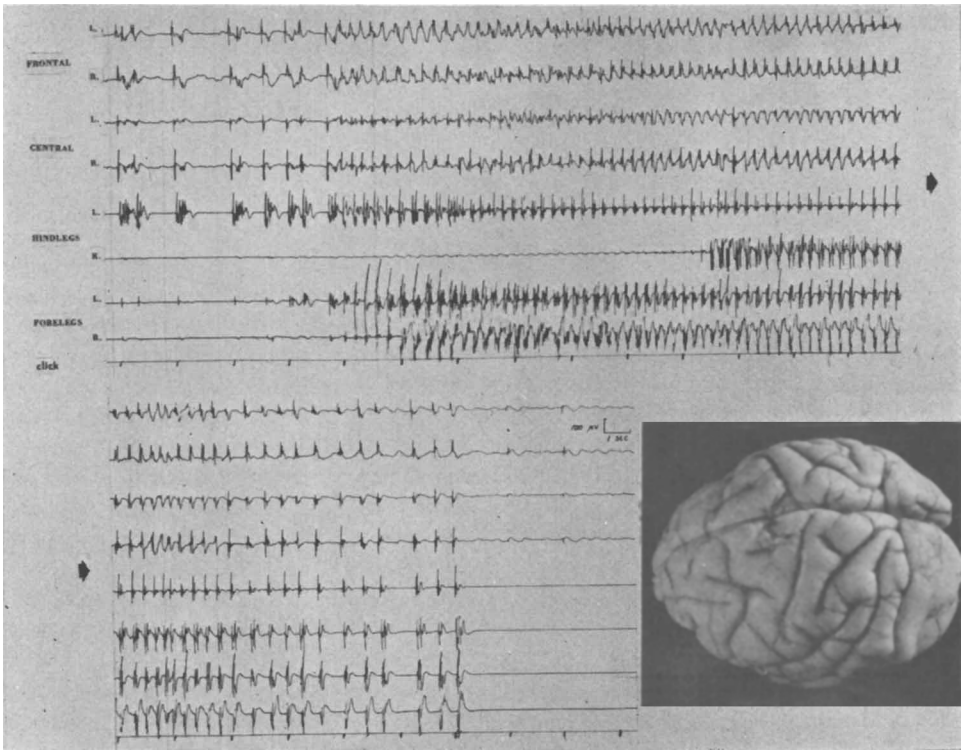

FIG. 2. Same preparation as in Fig. 1. Generalized seizure, with right hind-leg participating, but only after a delay of more than 14 sec.

the single extremity showed depressed response (Fig. 1).

Frequently, the depression was complete, no myoclonic responses of the affected extremity being recorded. On occasion, the depression was only partial, being manifested by a marked asymmetry of response between the two sides. The myoclonic responses of the paretic extremities, when they did appear, also showed a difference in pattern, being confined mostly to the proximal muscles of the limb; there was absence or marked diminution of the finger-flexor movements observed prominently in the normal extremity. In one chronic preparation, stimulation at the time of the acute experiment demonstrated that not all the primary cortical motor representation of the upper extremity had been ablated. Nevertheless, this animal showed marked depression of the myoclonic response, as was demonstrated in the animals with complete ablation.

With increasing dosage of metrazol, grand mal seizures occurred spontaneously or could be induced by repetitive acoustic stimulation. During such seizures, the affected extremities were at first quiescent, but after a variable period, became involved in the seizure activity, sometimes beginning with almost no buildup, almost as if a switch had been thrown (Fig. 2). During a seizure the movements of these extremities showed a difference in pattern similar to that observed during single myoclonic twitches, with diminished finger and toe-flexor activity and with the extensors of the limb more active than the flexors.

Discussion. The findings of depression or absence of the myoclonic response consequent upon limited ablation of motor cortex in the monkey are in accord with those previously reported in the cat with more extensive frontal ablation.

Although not studied in the monkey, it has been demonstrated in the cat that myoclonic responses may still be obtained after bilateral ablation of motor cortex, although there is a great increase in threshold, *i.e.*, considerably more metrazol is required(1). Unilateral

ablation of all cortex except the frontal pole does not influence the responses. Bilateral, but not unilateral, ablation of specific sensory cortex has been reported to abolish these responses(2,3), but evidence has been presented demonstrating that this too represents only a rise in metrazol threshold, involving only the specific sensory system whose cortical representation has been ablated(4). In the case of the motor cortex, with unilateral ablation there is a depression of the response to all forms of stimulus.

It is evident that the motor cortex contributes but is not essential for reflex myoclonus. This infers that in some way the motor cortex exerts a facilitatory action on the neuronal mechanisms involved in the response. Whether this action is exerted at a spinal or supraspinal level is not yet established. Preliminary observations indicate the probability that metrazol has little influence on the spinal mechanisms in the nembutalized cat(5). If this be true, it is evident that the facilitatory influence of the motor cortex is to be attributed to activity at a supraspinal level, through its extrapyramidal projections.

The actual site and mechanism of action of metrazol are unknown. It is of interest that the myoclonic twitch of metrazolized man or animal is primarily a bilateral flexor response. Ablation of the motor cortex markedly diminishes these responses, and the participation of the affected extremity in a generalized seizure is characterized by a relative sparing of extensor mechanisms. The neuronal basis of such specificity of metrazol action is under investigation at the present time.

Summary. 1. Sharply limited ablation of the arm or leg area of the precentral motor cortex in the macaque produces a complete or partial depression of the reflex myoclonic responses of the affected extremities as elicited after subconvulsant metrazol dosage. This occurs in chronic, as well as acute preparations. 2. When responses are present, there is a predominance of extensor muscle activity, with marked diminution of finger- or toe-flexor responses. A similar pattern is observed when generalized seizures are elicited by repetitive acoustic stimulation.

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Estimation of Vi Antibody Employing Erythrocytes Treated with Purified Vi Antigen.* (20188)

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The occurrence of Vi antibody in the sera of individuals harboring typhoid bacilli was first observed by Felix(1,2). Reports from many laboratories have confirmed and generally established this relationship(3-5). Consequently, the presence of Vi agglutinins is now commonly considered to be correlated with the harboring of typhoid bacilli and may serve as a satisfactory means of detecting the carrier state. As a result of its relative simplicity and because it is a more practicable method than the bacteriological examination of stool specimens, the test for Vi antibody has been employed extensively as a screening procedure for the detection of typhoid carriers in large populations. The method enjoying the widest

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