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ELECTROCORTICOGRAPHIC EFFECTS OF STIMULATION OF POSTERIOR ORBITAL, TEMPORAL AND CINGULATE AREAS OF *MACACA MULATTA**†

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IN A PREVIOUS study, the electrocorticographic effects of electrical stimulation of the anterior cingulate gyrus were described (2). In addition to suppression of strychnine spikes, previously obtained by McCulloch (11) after application of strychnine to the cingulate gyrus, three other effects were noted: suppression of spindles (like suppression of strychnine spikes, this was an ipsilateral effect), flattening of the spontaneous electrocortical activity, and production of a seizure discharge. All these electrocorticographic effects occurred independently of each other and of the motor and respiratory effects of cingulate gyrus stimulation.

Kaada, Pribram and Epstein (8) have recently reviewed anatomical and physiological evidence indicating the functional similarity of the continuous band of tissue which includes the tip of the temporal lobe, the anterior insula, the posterior orbital surface of the frontal lobe, the anterior perforate space, the sub- and pre-callosal areas and the anterior cingulate gyrus. The authors were able to elicit similar vascular and respiratory responses after electrical stimulation of these areas, and they discussed the evidence suggesting that these areas belong functionally to the so-called rhinencephalon. Neuronographic study of these areas has shown them to be interconnected (13). In the course of the neuronographic study a record of the electrocorticographic effects of electrical stimulation was obtained in order to see whether any effects could be elicited and whether these effects bore any resemblance to the electrocorticographic effects of stimulation of the anterior cingulate gyrus. Evidence was sought concerning the functional similarity of these areas with respect to electrographic effects in view of the evidence presented for their functional similarity with respect to vascular and respiratory effects (8).

MATERIALS AND METHODS

Immature macaque monkeys were anesthetized with Dial (0.4 mg./kg., half intramuscularly and half intraperitoneally). The orbital roof and eye, temporal muscle and zy-

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goma were removed. The skull was removed well beyond the midline, exposing one entire hemisphere of the brain. Adequate exposure was facilitated by fixing the head in the proper position. Drying of the exposed brain was prevented by keeping it well coated with mineral oil. Satisfactory excitability of the cortex and easy strychninization were facilitated by the subcutaneous injection of 10–20 cc. of 5 per cent glucose with 5–10 mg. of benzedrine whenever the electrocortical activity appeared to be failing. Benzedrine in this dosage was given at most every hour for four or five doses, but was usually given one to three times in the course of a 15-hour experiment. The results of stimulation reported here are based on findings in four animals, in which it was possible to stimulate the areas in question.

Electrographic records were also obtained in 10 other monkeys and in 8 dogs but no

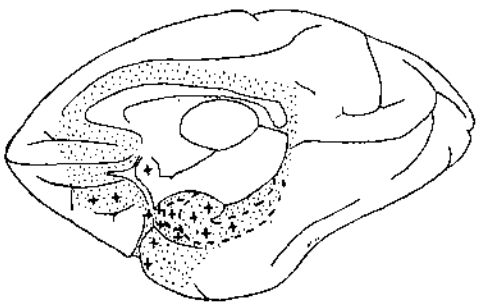

FIG. 1. Crosses (+) indicate points from which spontaneous spikes were recorded electrographically. Stippling indicates areas from which electrocortical recordings were obtained.

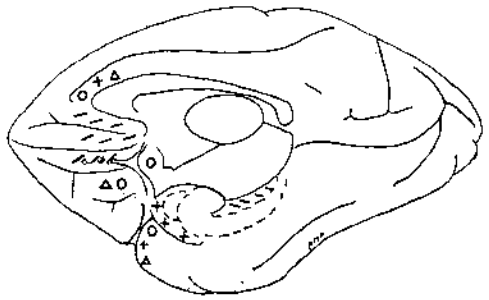

FIG. 2. Symbols indicate areas stimulated. Effects of such stimulation on electrical activity of areas other than that stimulated are designated as follows: △ suppression of spontaneous spikes (see Fig. 1); ◎ suppression of strychnine spikes; + production of seizure discharge; ⌐ no electrocorticographic effect.

stimulation was carried out in these animals. The dogs were operated by a method and for a purpose already reported (3). No benzedrine was given to the dogs.

Strychnine spikes were obtained by the application of a 1 × 2 mm. piece of filter paper soaked in a saturated aqueous solution of strychnine sulphate to the areas noted above. Points stimulated are shown in Figure 2. The cortical area stimulated was always different from that to which strychnine had been applied just previously. A 6-channel Model II Grass electroencephalographic amplifier was used. The electrode holder used was designed by C. Marshall (13). Multi-lead needle electrodes (3) were inserted into the brain in the region of the hippocampus, amygdaloid nucleus and head of the caudate nucleus. After the experiment the needle electrodes were left in place, the brain removed and fixed in formalin, and the position of the recording points determined by sectioning the brain. All records obtained from dogs were made by this technique. Both unipolar and bipolar recordings were made. A square-wave stimulator designed by A. Mauro (to be published) was employed. This stimulator allows independent variation of frequency, pulse duration and intensity. The usual parameters of stimulation were frequency 40 per sec., intensity 2–5 volts, sigma 10, duration 15 seconds. The stimulating electrodes consisted of two silver wires, insulated except at the tips. The tips were separated by a 1–2 mm. distance.

RESULTS

Spontaneous electrocorticographic characteristics. Unelicited spikes (Fig. 1) were frequently recorded simultaneously from the periamygdaloid cortex, temporal pole, and posterior orbital surface of the frontal lobe, or from one of these areas alone. They occurred most frequently from the periamygdaloid

cortex. Spikes, synchronous with these surface spikes, were recorded from needle electrodes in the region of amygdala and the hippocampus.

Electrocorticographic effects of stimulation. These fall into three categories

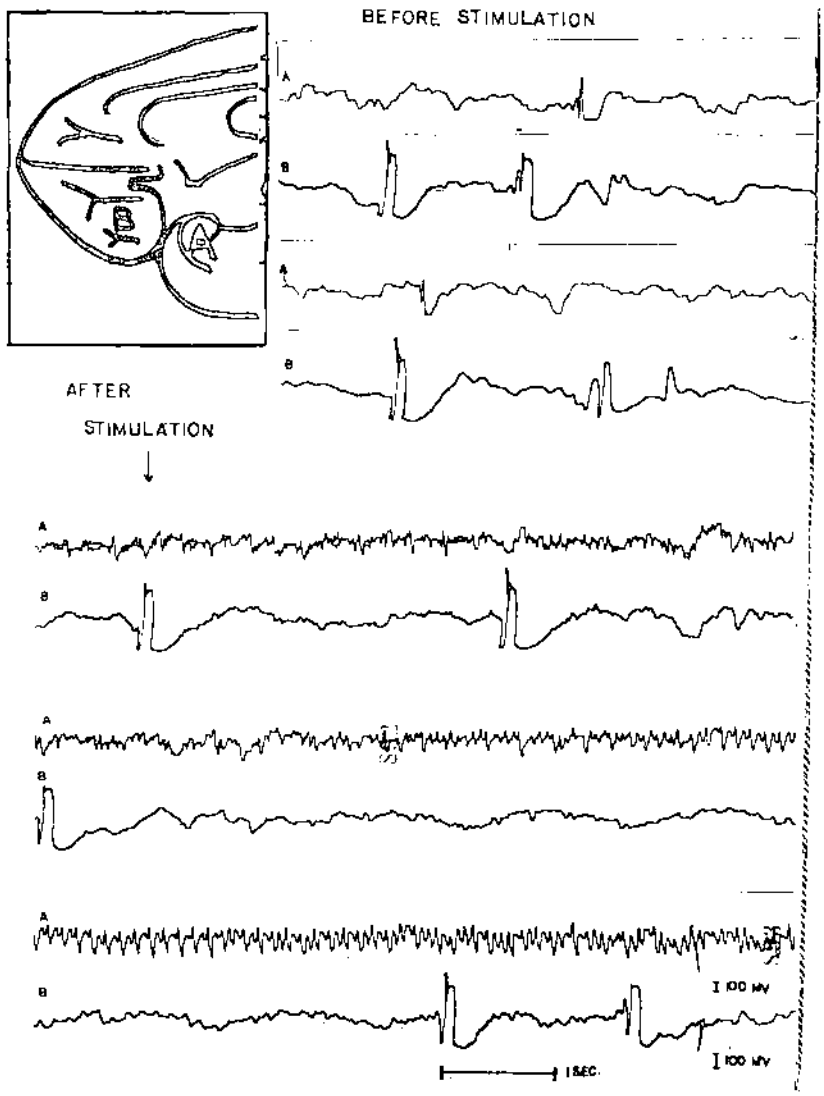

FIG. 3. Electrocorticograph from periamygdaloid cortex (A) and posterior orbital cortex (B). Before stimulation at point A, spontaneous spikes in A and strychnine spikes in B. After stimulation, seizure discharge in A. Strychnine spikes in B are unaffected.

(Fig. 4): (i) elimination of strychnine spikes in areas other than that stimulated; (ii) elimination of unelicited spikes in areas other than that stimulated; (iii) production of a seizure discharge (Fig. 3) without accompanying clinical signs.

Each of the above-mentioned electrocorticographic effects occurred independently of the other effect. Several different effects were sometimes produced by stimulation of the same point, but each effect could and did occur alone. Each of the above electrocorticographic effects was elicited at some time by stimulation of the supracallosal anterior cingulate gyrus and temporal pole. Seizure discharge was elicited more frequently from the

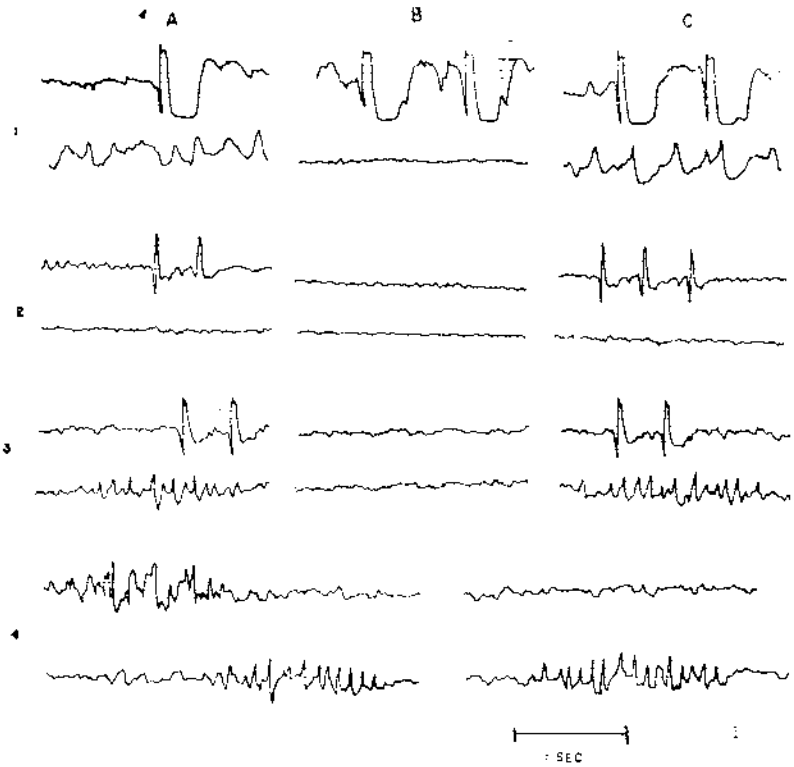

FIG. 4. Electrocorticographic effects of stimulation of posterior orbital, temporal and cingulate areas of *Macaca mulatta*. Column A illustrates electrocorticogram before stimulation, column B 30 sec. after stimulation, and column C 3 min. later. All recordings are obtained from areas other than that stimulated. 1: suppression of spontaneous electrocortical activity (lower line); strychnine spikes recorded from another area are unaffected. 2: simultaneous elimination of spontaneous electrocortical activity and of strychnine spikes. 3: elimination of strychnine spikes (on contralateral hemisphere) and spindles (recorded from ipsilateral hemisphere). 4: elimination of ipsilateral spindles (line 1) with no effect on contralateral spindles.

temporal pole than from the anterior cingulate gyrus, whereas stimulation of the periamygdaloid cortex always provoked a seizure discharge. A seizure discharge produced by stimulation of the periamygdaloid cortex invariably appeared at needle electrodes placed in the region of the amygdala and hippocampus (*cf.* 14, 15). Stimulation of the posterior orbital surface of the frontal lobe eliminated strychnine and spontaneous spikes, but a seizure discharge was not produced by stimulation in this area. Stimulation of the

precallosal and subcallosal areas and of the entorhinal area or hippocampus did not produce electrocorticographic changes in any of these experiments.

Discussion

The functional similarity of the periamygdaloid, temporal polar, posterior, orbital, subcallosal and anterior cingulate cortex with respect to respiratory and blood pressure effects has been demonstrated (8). This similarity also exists with respect to electrocorticographic effects. However, as with vascular and respiratory changes, certain areal differences are observed. Although a seizure discharge is sometimes elicited by stimulation of the anterior cingulate gyrus, it is always elicited by stimulation of the periamygdaloid cortex and somewhat less often by stimulation of the temporal pole. This is the area where unelicited spikes are such a prominent feature of the electrocorticogram.

This observation is consistent with the electroencephalographic observations in patients with psychomotor epilepsy. Jasper and Kershman (5) describe temporal localization "in the hippocampal area" in patients with automatisms, and Gibbs *et al.* (4) emphasize the high incidence of spikes in anterior temporal leads in patients with psychomotor epilepsy. Favorable therapeutic results have been obtained following removal of these spike foci (1, 11). Jasper (6) describes the localization of these spikes at operation at the mesial tip of the temporal lobe and orbital surface of the frontal lobe predominantly, and finds, as do Walker *et al.* (16), that these epileptogenic spikes occur in areas from which seizure discharge and after-discharge can be elicited more readily than from normal cortex.

The presence of unelicited spikes in our monkeys in the same areas as in epileptic humans suggests the possibility that the spikes may not be the sole epileptogenic factor in the epileptic human being and demonstrates the necessity for a search for spikes in these areas in non-epileptic human beings. Jasper (6) describes the high-voltage, slow wave which appears over both frontal areas simultaneously with the basal spike in human epileptic patients, and Gibbs *et al.* (4) state that spread seems to be peculiar to spikes from the anterior temporal area. The slow wave and spread do not occur in the monkeys under the conditions of this experiment and do occur in patients with subcortical pathology without epilepsy (9). Possibly the activation by the basal spike of some subcortical structure is responsible for the clinical and electroencephalographic characteristics of psychomotor seizures. This postulate is consistent with the fact that clinical improvement follows excision of the cortical spike, and that improvement follows temporal lobotomy as well. In such operations, the factor which sets off the subcortical discharge is removed by excision or by interruption of the efferent pathway.

Summary and Conclusions

1. Unelicited spikes were recorded frequently from the periamygdaloid cortex, temporal pole, and posterior orbital areas, and simultaneously at needle electrodes in the region of the amygdala and hippocampus.

2. Electrical stimulation of the periamygdaloid, temporal polar, posterior orbital and anterior cingulate areas produced similar electrocorticographic effects: (*i*) elimination of strychnine spikes in areas other than that stimulated; (ii) elimination of unelicited spikes in areas other than that stimulated; (iii) production of an after-discharge locally and sometimes in areas other than that stimulated.

3. These effects were independent of one another, in that each might occur alone or in any combination with others.

4. Certain areal differences were noted. Stimulation of the anterior supracallosal area and of the temporal pole produced all effects. Stimulation of the periamygdaloid cortex produced a seizure discharge in all trials. Stimulation of the posterior orbital area eliminated strychnine and spontaneous spikes but did not result in a seizure discharge. No effect was produced by stimulation of the pre- or sub-callosal areas.

5. Some implications of these findings with respect to the mechanisms involved in psychomotor epilepsy are discussed.

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