FUNCTIONAL INTERACTION BETWEEN DETERMINANT AND OTHER FOCI OF EPILEPTIFORM ACTIVITY CREATED BILATERALLY IN THE CORTEX

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Experiments on cats anesthetized with pentobarbital showed that on the creation of a hyperactive focus with a high level of excitation in the orbital or coronary cortex and a series of foci in the opposite neocortex a functional complex is formed, which works to the same program determined by the activity of the hyperactive focus. The latter plays the role of a determinant structure. Depression of activity of the determinant focus by pentobarbital leads to disintegration of the epileptic complex. Division of the rostral portion of the corpus callosum led to disturbance of synchronized operation of the determinant and other foci of epileptic activity. The results confirm the general concept of the role of determinant structures in the activity of the nervous system. KEY WORDS: determinant focus; epileptic complex; strychnine; corpus callosum; ether.

It has been shown [2] that a powerful focus of excitation created by means of strychnine in the cerebral cortex plays the role of a determinant structure [1] which determines the character of activity of other scattered foci of strychnine excitation, potentiates excitation in them, and unites them into a single functional complex and determines the activity of the complex as a whole. This complex could be destroyed by suppression of the determinant focus. Blocking of the other foci constituting the complex, however, had no significant effect on the activity of the complex as a whole. In the investigations mentioned above the determinant and dependent foci were created in the same hemisphere. It was therefore important to discover whether a hyperactive focus created in one hemisphere can possess determinant properties relative to other foci created in the cortex of the opposite hemosphere. It was also interesting to study the role of interhemispheric commissures in functional interaction between determinant and dependent foci forming a complex of epileptic activity.

EXPERIMENTAL METHOD

Acute experiments were carried out on cats. Under pentobarbital anesthesia (25-40 mg/kg, intraperitoneally) the skin and subcutaneous cellular tissue were divided by a midline incision running from the nasal bones to the occiput. The eyes were drained. Through burr-holes in the cranial bones wide access was obtained to different parts of the frontal and temporal zones of the neocortex. Subconvulsive foci were created by application of filter paper (2 mm^2) soaked in a 0.025-0.05% solution of strychnine nitrate, in different parts of the coronary, anterior and posterior sigmoid, and orbital gyri. A focus of powerful epileptiform activity was created by application of 3% solution or a crystal of strychnine to the orbital or coronary gyrus of the opposite hemisphere. The foci were blocked by local application of a 6% solution of pentobarbital. The commissures between the hemispheres were divided by means of a spatula introduced through the longitudinal cerebral fissure. Completeness of division was verified histologically. Activity in the foci was inhibited by ether anesthesia (injection of ether vapor into the jet of inspired air). Brain potentials were recorded by a monopolar method with the reference electrode secured to the nasal bones.

EXPERIMENTAL RESULTS

After application of 0.01-0.1% solutions of strychnine to different parts of the coronary, sigmoid, and orbital or ectosylvian gyri of one hemisphere, strychnine potentials of varied amplitude developed (Fig. 1A, zones 2-4). Each focus generated strychnine discharges asynchronously. The creation of a new and powerful

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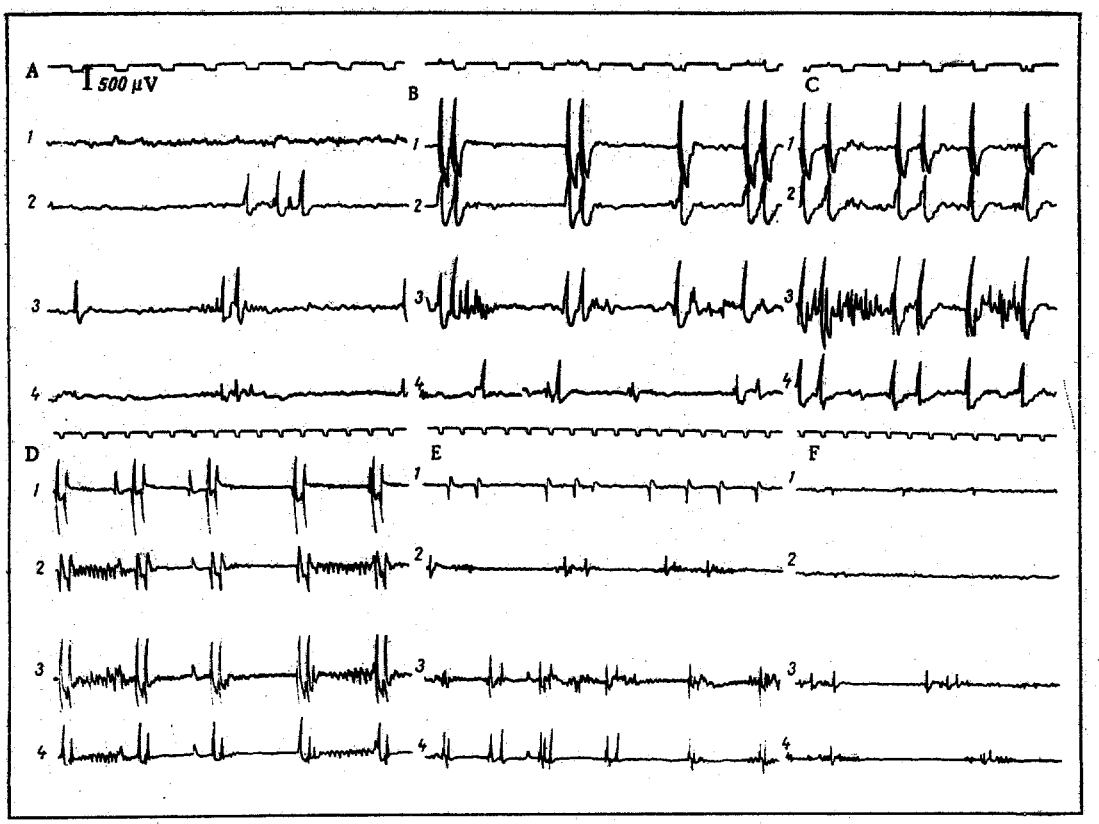

Fig. 1. Role of determinant focus in formation and activity of functional complex of epileptiform activity in cortex of both hemispheres. Experiment No. 1: A) formation of foci of increased excitability in areas 2-4 of left hemisphere by subconvulsive strychnization (0.01% solution); application of strychnine discontinued after appearance of activity. B, C) Formation of determinant focus in zone 1 of right hemisphere by application of 3% solution of strychnine and synchronization of epileptiform activity in all foci. Experiment No. 2: D) 40 min after beginning of formation of determinant focus in zone 1 of left hemisphere, synchronization of spike activity in zones 2-4 of right hemisphere with activity of focus 1. E and F) 15 and 40 min respectively after application of 6% solution of pentobarbital to region of determinant focus in zone 1. 1) Left orbital cortex, 2) right coronary cortex, 3 and 4) anterior and posterior right sigmoid gyri respectively. Calibration: 500 μV, 1 sec.

focus of epileptiform activity in the orbital cortex of the contralateral hemisphere by application of a 3% solution or crystal of strychnine led to an increase in the amplitude and frequency of the strychnine spikes in the subconvulsive foci. As activity increased in the foci in the orbital cortex, synchronization of epileptiform discharges in the subconvulsive foci with discharges of the focus in the orbital cortex was observed. Synchronized discharges appeared first in the focus in the orbital cortex located symmetrically to the powerful (hyperactive) focus (Fig. 1B, zone 2); discharges in nonsymmetrical foci of the coronary and sigmoid gyri still continued to be generated asynchronously during this period (Fig. 1B, zones 3, 4). Synchronization of epileptiform activity developed later in the foci of the coronary and sigmoid gyri. At the height of development of the process generation of discharges in all foci was synchronized with generation of discharges in the hyperactive focus in the orbital cortex. Besides synchronization of epileptiform activity there was a further increase in the amplitude of discharges in the subconvulsive foci (Fig. 1C).

In individual experiments foci of epileptiform activity in cortical zones of the coronary or sigmoid gyri not symmetrical relative to the hyperactive focus were not completely subordinated to the activity of the hyperactive focus and continued to generate asynchronous epileptiform activity. The absence of synchronization (or its substantially later onset) in the sigmoid foci was observed comparatively often when an area of neocortex symmetrical relative to the hyperactive focus was not subjected to preliminary treatment with a weak solution of strychnine, and only discharges transmitted via the corpus callosum from the hyperactive focus in the orbital cortex of the contralateral hemisphere were recorded in this area. This fact suggested that the symmetrical focus plays a definite role in the synchronization of nonsymmetrical foci.

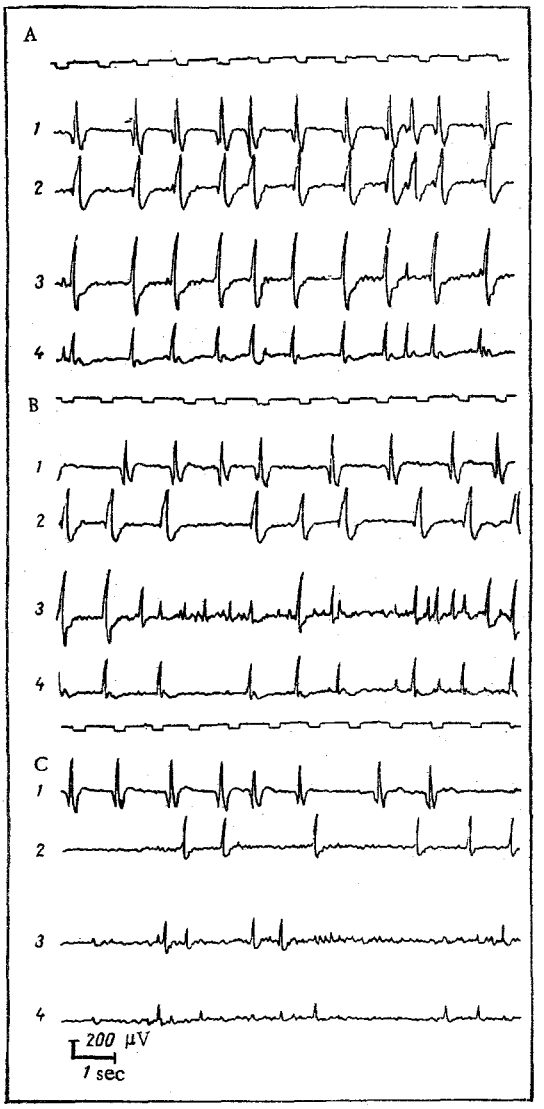

Fig. 2. Effect of division of rostral part of corpus callosum on synchronization of epileptiform activity in complex of foci created in both hemispheres. A) Synchronization of epileptiform activity in zones 2-4 of right hemisphere with activity of determinant focus in zone 1 of left hemisphere. B and C) 5 and 15 min respectively after division of rostral part of corpus callosum. 1 and 2) Left and right coronary gyri respectively; 3 and 4) right posterior and anterior sigmoid gyri respectively. Calibration: 200 μV, 1 sec.

To study whether the hyperactive focus in one hemisphere in fact plays a determinant role with respect to the character of activity of foci in the contralateral hemisphere, experiments were carried out with pharmacological blocking of the determinant focus. After application of filter paper soaked with a 6% solution of pentobarbital to the region of the hyperactive focus in the orbital cortex (at the stage when all foci were working to the same program of synchronized activity) activity in this focus fell sharply after 20-50 sec. During this period synchronized epileptiform discharges continued to be generated in the foci in the contralateral hemisphere. A gradual decrease in amplitude and disturbance of synchronization of appearance of paroxysmal discharges were observed in these foci 5-10 min after application (Fig. 1E). After total suppression of activity in the determinant focus total desynchronization and a decrease and subsequent disappearance of the epileptiform discharges in all foci were observed (Fig. 1F). Application of pentobarbital to the other foci (in the coro-

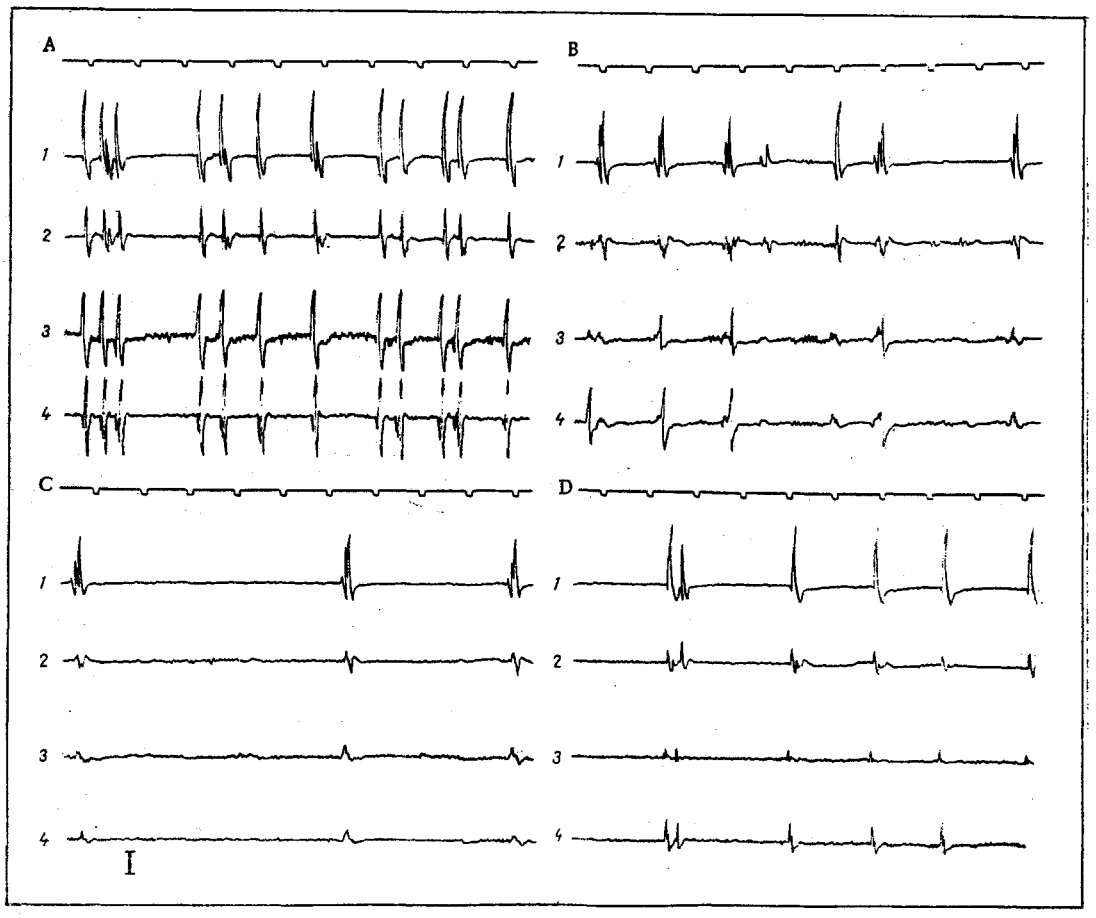

Fig. 3. Effect of inhalation of ether on complex of foci of epileptiform activity created in cortex of both hemispheres. A) Synchronization of epileptiform activity in zones 3 and 4 of one hemisphere, subjected to preliminary strychninization (0.01% solution) and in zone 2, without preliminary strychninization, with activity created by application of 3% solution of strychnine to determinant focus in zone 1 of opposite hemisphere. B and C) State of complex of foci 10 and 12 min respectively after inhalation of ether. D) 5 min after end of inhalation of ether. 1) Left orbital cortex; 2) right orbital cortex; 3) right coronary cortex; 4) right anterior sigmoid gyrus. Calibration: 500 μV, 1 sec.

nary or sigmoid gyri) led to inhibition of activity only in the same focus and the other foci continued to work to the previous program of synchronized activity.

In a separate series of experiments the effect of division of the rostral part of the corpus callosum (genu and rostrum) on functional relations between a hyperactive focus in one hemisphere and dependent foci in the neocortex of the opposite hemisphere was investigated. Division of this part of the corpus callosum at the stage when all foci were working to the same program of synchronized activity (Fig. 2A) led to disturbance of synchronization of the activity of the determinant and dependent foci. For several minutes after division of the corpus callosum synchronized discharges continued to be observed in the dependent foci (Fig. 2B), and this was followed by complete desynchronization and a reduction in the amplitude of the discharges in the dependent foci (Fig. 2C). Epileptic activity in the determinant focus showed no significant change under these circumstances.

In the next series of experiments the effect of inhibition of the cortex by a general anesthetic on the activity of the complex of foci of epileptic activity was studied. The general anesthetic used was ether, whose action is predominatly cortical [3]. During inhalation of ether (at the stage when all foci were working to the same program of synchronized activity) the amplitude and frequency of the epileptiform discharges fell, initially in the dependent foci and later in the determinant focus (Fig. 3). The order of suppression of activity differed in different experiments. If besides the coronary and sigmoid gyri, the zone of the orbital cortex of the opposite hemisphere symmetrical relative to the determinant focus was subjected to preliminary treatment with strychnine, inhibition of epileptiform activity in the focus in this zone of the neocortex took place last, and at a time when the level of activity in the determinant focus was considerably depressed. In cases when weak solu-

tions of strychnine were not applied to the orbital cortex and only epileptiform discharges conducted from the determinant focus in the contralateral orbital cortex were recorded in it, under the influence of ether the dependent focus in the orbital cortex was the first to be suppressed, followed by foci in zones subjected to preliminary strychninization (the sigmoid and coronary gyri). Epileptiform discharges continued to be recorded in the determinant focus at this time and subsequently. After administration of ether ceased epileptiform activity gradually recovered in the dependent foci and the epileptic complex was restored (Fig. 3C). These experiments also revealed the following fact. In some cases after creation of a determinant focus in the orbital cortex the epileptic activity of one of the most distant dependent foci was not completely synchronized with the activity of the determinant focus and it continued to generate some discharges in accordance with its own program. If ether was given under these conditions, the asynchronous activity was the first to be suppressed in this focus, although initially the amplitude of the paroxysmal potentials in that focus could have been greater than the amplitude of the discharges in the determinant and the other dependent foci. In this period in all other foci the epileptiform activity showed no significant change. Stopping the inhalation of ether led to restoration of epileptiform activity in that particular focus within a few minutes.

These experiments thus showed that a focus of powerful epileptiform activity created in the cortex of one hemisphere can play the role of determinant relative to foci in the cortex of the contralateral hemisphere, which become dependent foci. The results are also evidence that the properties of the determinant focus mentioned above, and also the relations between the foci reflect a general rule unconnected with the location of the foci.

The results of the experiments with division of the rostral part of the corpus callosum demonstrate conclusively the important role of direct anatomical pathways of conduction of epileptiform activity in the mechanisms of interaction between the determinant and dependent foci in the formation and activity of a complex of foci of epileptic activity. These findings confirm clinical observations on patients with epilepsy undergoing sagittal division of the corpus callosum and other interhemispheric commissures in order to prevent the interhemispheric generalization of epileptiform discharges [5, 7, 8]. The earlier suppression of epileptic activity in dependent foci during administration of the general anesthetic was evidently due to the fact that their mechanisms of regulation were relatively more intact, fewer neurons were activated [4, 6], and the anesthetic disturbed synaptic conduction from the determinant focus.

On the whole, these experiments confirm on a new model the general concept of the role of determinant structures in the activity of the nervous system and the theory of generator mechanisms of neuropathological syndromes [1].

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