The results of the present and previous investigations thus indicate that during the development of neurogenic injuries to the myocardium caused by electrical stimulation of the aortic arch for 3 h considerable disturbances in the energy metabolism of the heart muscle tissue take place. Comparison of the activity of certain enzymes of glycolysis, of the pentose phosphate pathway of carbohydrate oxidation [4], the Krebs' cycle, and the respiratory chain of the mitochondria shows disturbance of the coordinated regulation of energy metabolism, with the ultimate result that oxidative phosphorylation is uncoupled and the synthesis of high-energy compounds is reduced.

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MECHANISM OF FORMATION OF COMPLEXES OF EPILEPTIC ACTIVITY IN THE CEREBRAL CORTEX UNDER THE INFLUENCE OF A DETERMINANT FOCUS

G. N. Kryzhanovskii,* R. F. Makul'kin, A. A. Shandra, and D. V. Boiko

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Experiments on cats anesthetized with pentobarbital showed that when a hyperactive focus with a high level of excitation is formed in the temporal cortex and a series of foci with lower levels of excitation is formed in other parts of the neocortex, a functional complex with coordinated activity is created and is controlled by the activity of the hyperactive focus. The latter plays the role of a determinant structure. Depression of the determinant focus leads to disintegration of the epileptic complex. The nature of the foci is unimportant as regards the realization of these relationships: Both determinant and dependent foci could be created with the aid of strychnine and penicillin, which disturb different types of inhibition. 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; neocortex; strychnine; penicillin.

It has been shown [2] that a powerful focus of excitation created with the aid of strychnine in the cerebral cortex plays the role of determinant structure, determining the character of activity of other discrete foci of strychnine excitation, strengthens excitation in them, unites them into a single functional complex, and determines the behavior of the complex as a whole. This complex can be destroyed by suppression of the determinant focus, whereas blocking the other foci constituting the complex had no significant effect on its behavior.

*Corresponding Member of the Academy of Medical Sciences of the USSR.

Laboratory of General Pathology of the Nervous System, Institute of General Pathology and Pathological Physiology, Academy of Medical Sciences of the USSR, Moscow. Department of Pathological Physiology, N. I. Pirogov Odessa Medical Institute.

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In the experiments cited above a focus with determinant properties was created in the orbitofrontal cortex, which plays an important role in the generalization of paroxysmal activity and performs the functions of a unique trigger system [6, 12, 13]. The next important step was to discover whether a hyperactive focus created in other parts of the neocortex could possess determinant properties. It was also interesting to study relations between the determinant focus and dependent foci created by means of substances disturbing different forms of inhibition.

The object of the present investigation was to study relations between a hyperactive focus located in various parts of the temporal cortex and foci of excitation located in other parts of the neocortex, when both the hyperactive focus and the other foci were created by means of different substances, disturbing different types of inhibition (strychnine and penicillin) [7-11].

EXPERIMENTAL METHOD

Acute experiments were carried out on 22 cats. Under pentobarbital anesthesia (25-30 mg/kg, intraperitoneally) through a mid-line incision from the nasal bones to the occiput the skin and subcutaneous fascia were divided. The eye was drained. Wide access to different parts of the frontal and temporal regions of the neocortex was obtained through burr-holes drilled in the skull. Subconvulsive foci were created by application of a piece of filter paper (2 mm^2) soaked in a 0.025-0.5% solution of the sodium salt of penicillin. These foci were created in different parts of the coronary, anterior and posterior sigmoid, orbital, lateral, and suprasylvian gyri. A powerful focus of paroxysmal activity was created by application of penicillin powder to the anterior, middle ectosylvian, or anterior sylvian gyri. These foci were blocked by local application of 6% pentobarbital solution. To depress activity in the foci, ether anesthesia was used; ether vapor was injected into the stream of inspired air. Brain potentials were derived by a monopolar technique, the indifferent electrode being fixed in the nasal bones. The potentials were recorded on a 4-ÉÉG-3 ink-writing electroencephalograph.

EXPERIMENTAL RESULTS

After application of subconvulsive doses of strychnine to the coronary (zone 2) and posterior (zone 3) and anterior (zone 4) sigmoid gyri, paroxysmal discharges of varied magnitude appeared in these areas, and their amplitude did not exceed 400 μV (Fig. 1A). Each of the foci thus created generated discharges asynchonrously and independently of each other. After the appearance of activity in these foci, the pieces of filter paper with strychnine were removed. At this stage a 3% solution (or crystal) of strychnine was applied to the anterior ectosylvian gyrus (zone 1). Triphasic strychnine discharges with an amplitude reaching 1.0-2.0 mV appeared at this last site of strychninization. In the first stages of formation of the new hyperactive focus, the other foci worked asynchronously; later, as the spikes in the new focus grew larger (zone 1) an increase in the amplitude and frequency of the discharges was observed in the foci in the coronary (zone 2) and sigmoid (zones 3 and 4) gyri. Meanwhile the activity in these foci (zones 2-4) became synchronized with the discharges in the hyperactive focus in the temporal cortex (zone 1). In most experiments synchronous discharges appeared initially in foci in the sigmoid gyri; discharges were still generated asynchronously in the coronary cortex at this period. At the height of development of the process all the foci of excitation discharged synchronously, in accordance with the same program, and a single functional complex was produced (Fig. 1B).

To make sure that it is a hyperactive focus in the temporal cortex that plays the determinant role in the formation of the complex of foci, experiments were carried out with pharmacological depression of the various foci. On application of filter paper soaked in a 6% solution of pentobarbital to the region of the hyperactive focus in the temporal cortex, at the stage when all foci were discharging synchronously in accordance with the same program, within a few minutes a marked decrease was observed in the amplitude of the discharges in this focus. Meanwhile, high-amplitude discharges, frequently synchronized with each other, continued to be generated in the other foci (Fig. 1C). Later, 5-10 min after application of pentobarbital, a marked decrease in amplitude and disturbance of the synchronization of the discharges were observed in all foci (Fig. 1D). Repeated application of a 3% solution or crystal of strychnine (after rinsing to remove pentobarbital) to the anterior ectosylvian gyrus (zone 1) or to other parts of the temporal cortex free from strychnine led to restoration and synchronization of epileptiform discharges in all foci (Fig. 1E). Application of pentobarbital to the foci in the coronary or sigmoid gyri (zones 2-4) led to inhibition of activity only in that particular focus, and the determinant focus and other foci continued to discharge synchronously and in accordance with the same program (Fig. 1F).

In the next series of experiments subconvulsive foci were created by application of a 0.25-0.5% solution of penicillin to the coronary (zone 2) and sigmoid (zones 3 and 4) gyri. Characteristic spike potentials appeared

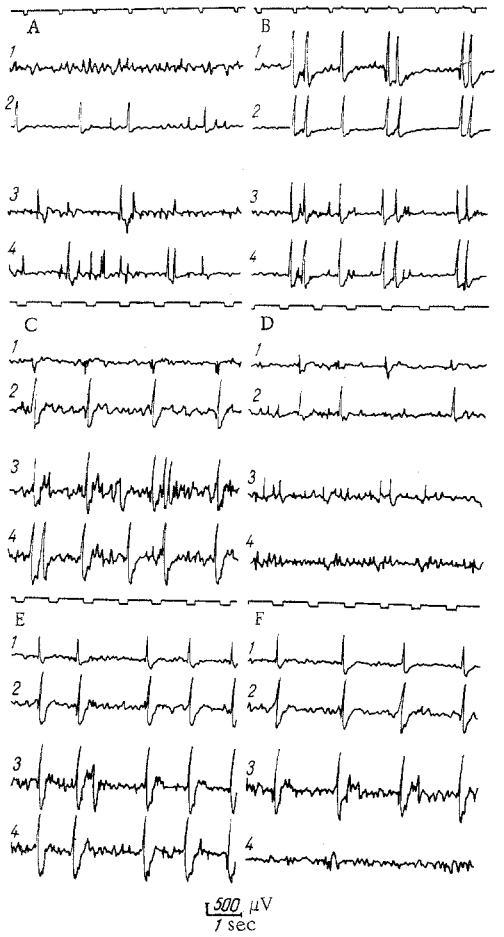

Fig. 1

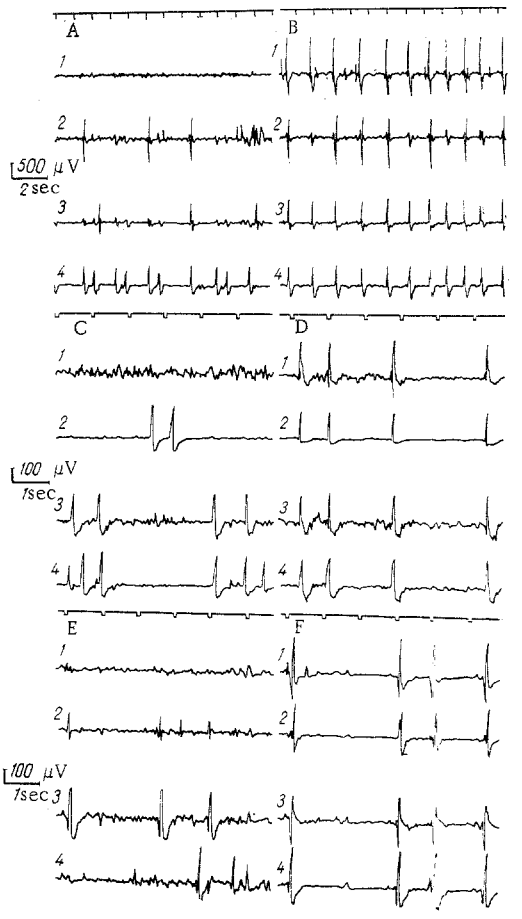

Fig. 2

Fig. 1. Effect of determinant focus created by application of strychnine to temporal cortex on formation and behavior of complex of foci produced by means of strychnine in various parts of neocortex. A) Formation of foci of increased excitability in zones 2-4 by subconvulsive strychninization (0.01% solution); application of strychnine terminated after appearance of activity; B) formation of determinant focus in zone 1 by application of 3% strychnine solution and synchronization of epileptic activity in all foci; C) 1 min, and D) 5 min after application of 6% pentobarbital solution to zone 1, appearance of epileptiform activity in determinant focus and disintegration of complex of foci; E) repeated formation of determinant focus in zone 1 by application of 3% strychnine solution after rinsing to remove pentobarbital, and repeated formation of complex (potentiation and synchronization of epileptiform activity in all foci); F) 5 min after application of 6% pentobarbital solution in zone 4. Depression of dependent focus and preservation of complex of foci of epileptic activity. 1) Anterior ectosylvian gyrus; 2) coronary cortex; 3) anterior and 4) posterior sigmoid gyri. Calibration, 500 μV, time marker 1 sec.

Fig. 2. Functional relations between foci created by means of strychnine and penicillin in different zones of the cerebral cortex. A, B) Experiment No. 1: A) formation of foci of increased excitability in zones 2-4 by application of 0.25% penicillin solution; after appearance of activity, application of penicillin ceased; B) 10 min after formation of determinant focus in zone 1 by application of strychnine crystal, synchronization of epileptic activity in all foci. C, D) Experiment No. 2: C) formation of foci of increased excitability in zones 2-4 by application of 0.025% strychnine solution; D) formation of determinant focus in zone 1 by application of penicillin crystal, synchronization of epileptic activity in all foci. E, F) Experiment No. 3: E) formation of foci of increased excitability in zones 2 and 4 by application of 0.01% strychnine solution and in zone 3 by application of 0.25% penicillin solution; F) formation of determinant focus in zone 1 by application of strychnine crystal and formation of complex of foci of epileptic activity. Remainder of legend as in Fig. 1.

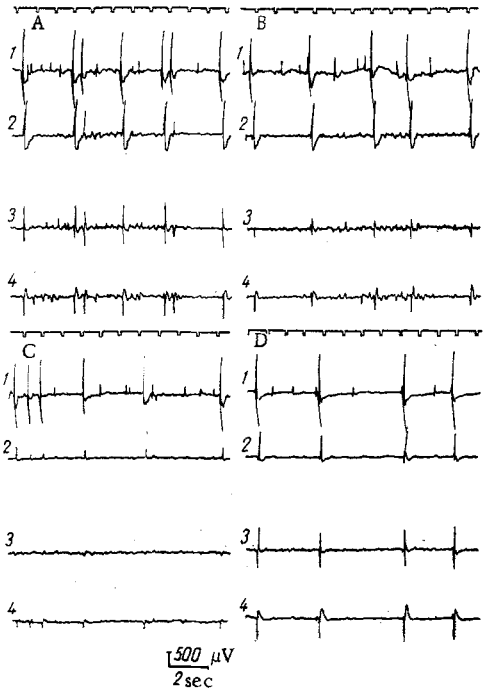

Fig. 3. Effect of inhalation of ether on complex of foci of epileptic activity created in different zones of the cortex by strychnine and penicillin. State of complex before (A), 40 sec after (B), and 5 min after (C) inhalation of ether; D) 8 min after end of inhalation. Determinant focus in zone 1. 1) Anterior ectosylvian gyrus (determinant focus created by application of 3% strychnine solution); 2) anterior sigmoid gyrus (application of 0.01% strychnine solution); posterior sigmoid gyrus (application of 0.25% penicillin solution); 4) coronary gyrus (application of 0.01% strychnine solution). Calibration 500 μV, time marker 2 sec.

at the sites of application (Fig. 2A). After the appearance of activity in these foci the filter paper with penicillin was removed. Discharges were generated asynchronously in these foci and independently of each other. Application of a 3% solution or crystal of strychnine to the temporal cortex led to the appearance of triphasic strychnine potentials at the site of strychninization. Initially the discharges in all foci were generated asynchronously and independently of each other. Later, with an increase in the level of activity in the focus located in the temporal cortex (zone 1), an increase in amplitude and synchronization of the paroxysmal discharges were observed in the coronary and sigmoid gyri. Synchronized discharges appeared initially in the posterior sigmoid gyrus (zone 4) and later in the other foci. A single functional complex consisting of four foci developed, in which the determinant role was played by the determinant focus in the temporal cortex (Fig. 2B).

The next series of experiments was devoted to a study of relations between subconvulsive foci created by strychnine and a hyperactive focus created by penicillin. For this purpose, at the stage when asynchronous discharges were recorded in subconvulsive foci in the coronary and sigmoid gyri (zones 2-4), penicillin powder was applied through filter paper to the anterior ectosylvian gyrus. Application of penicillin caused the appearance of paroxysmal spikes, the maximal amplitude of which reached 1.5-2.0 mV. In the course of formation of this focus the discharges in the other foci became synchronized: at first in the coronary (zone 2) and later in the sigmoid (zones 3 and 4) gyri, and all the foci became united into a single complex (Fig. 2D).

In a separate series of experiments subconvulsive foci in the coronary (zone 2) and posterior sigmoid (zone 4) gyri were produced by application of 0.01% strychnine solution and a focus in the anterior sigmoid

gyrus (zone 3) was produced by application of 0.25% penicillin solution. Under these circumstances asynchronous spike potentials of low amplitude also appeared in all foci (Fig. 2E). The creation of a powerful focus under these conditions by application of a 3% solution or crystal of strychnine to the temporal cortex caused an increase in activity in the foci in the coronary and sigmoid gyri and synchronization of their discharges with those in the determinant focus (Fig. 2F).

In the next series of experiments the effect of anesthetic depression of the cortex on activity of the complex of foci of paroxysmal activity produced by strychnine and penicillin was studied. Ether, which acts mainly on the cerebral cortex [3-5], was used as the anesthetic. A few minutes after administration of the ether (which began at the stage when all foci were working in accordance with the same program of synchronized activity, Fig. 3A), a decrease in the amplitude and frequency of the paroxysmal discharges was observed in the dependent foci, whereas in the determinant focus in the temporal cortex during this period no significant changes were found in the amplitude or frequency of the paroxysmal discharges (Fig. 3B). Depression of paroxysmal activity was more marked initially in foci in the coronary gyrus (zone 2) and, in particular, in the focus in the anterior sigmoid gyrus (zone 3; Fig. 3C). At the stage when paroxysmal activity was almost suppressed in all the dependent foci, it still continued in the determinant focus (Fig. 3C). After the end of ether administration paroxysmal activity remained suppressed for a few minutes longer in the dependant foci (zones 2-4), after which paroxysmal discharges were gradually restored in these foci; the discharges appeared first in the foci in the sigmoid gyri and later in the focus in the coronary cortex (Fig. 3D).

These experiments thus showed that a powerful focus of paroxysmal activity created in different parts of the temporal cortex can play a determinant role. The writers showed previously [2] that a determinant structure can be created in the orbitofrontal cortex. Simultaneous experiments showed that the relations formed between a determinant focus and foci which become dependent reflect a general rule that is unconnected with the location of the foci.

It is an interesting fact that, regardless of the substance used to form the foci of disturbance of inhibition, these foci may become both determinant and dependent. The factor responsible for the determinant properties of the focus is the strength of the excitation it generates. These data confirm one of the basic propositions in the general theory of the role of determinant structures in the activity of the nervous system [1], according to which the mechanism of determination is essentially that a structure of the CNS with a high level of excitation forms an intensive functional volley, which reaches the corresponding zones of the CNS and overpowers the mechanisms whereby these zones regulate their own activity. The experiments also showed that disturbance of different types of inhibition in various parts of the cortex is an important condition for the production of secondary foci of epileptic activity in them under the influence of the determinant focus.

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