It is interesting to note that, by contrast with previous investigations [2, 4], in which terrilytin had not only lytic properties, but also certain toxic properties, manifested even within the range of effective therapeutic doses, in the present study no side effects were found from the use of much larger doses of terrilytin. In the writer's view, the reason for this is that the solvent used for the terrilytin was not physiological saline but a solution of polyvinylpyrrolidone, which has a marked detoxicating action, has a beneficial effect on the systemic and regional hemodynamics, and restores the disturbed acid-base balance [6, 7].

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SIMULATION OF DETERMINANT AND DEPENDENT FOCI OF EPILEPTIC ACTIVITY IN THE RAT CEREBRAL CORTEX

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Foci of increased activity with independent firing patterns were created by means of weak solutions of strychnine in acute experiments on rats. A hyperactive focus of excitation created by means of concentrated strychnine solutions played the role of determinant structure. Its role was to determine the character of activity of the other epileptogenic foci, to enhance their paroxysmal activity, to combine them into a single functional complex, and to determine the behavior of the whole complex. This complex could be destroyed by suppressing the activity of the determinant focus. Elimination of any of the dependent foci forming the complex did not disturb the complex itself. These investigations confirm, on a new model, the general concept of the role of determinant structure in the activity of the CNS.

KEY WORDS: determinant focus; strychnine; neocortex; epileptic complex.

It was shown previously [2, 3] that a focus of powerful excitation created with the aid of strychnine in the cat cerebral cortex plays the role of determinant structure [1], which determines the character of activity of other scattered foci of excitation, enchances excitation in them, unites them into a single functional complex, and determines the behavior of the complex as a whole. Such a complex of foci can be destroyed by suppressing the activity of the determinant focus. The next step was to discover whether the relations established between the foci are connected with species-specific properties of the morphological and functional organization of the cat's brain.

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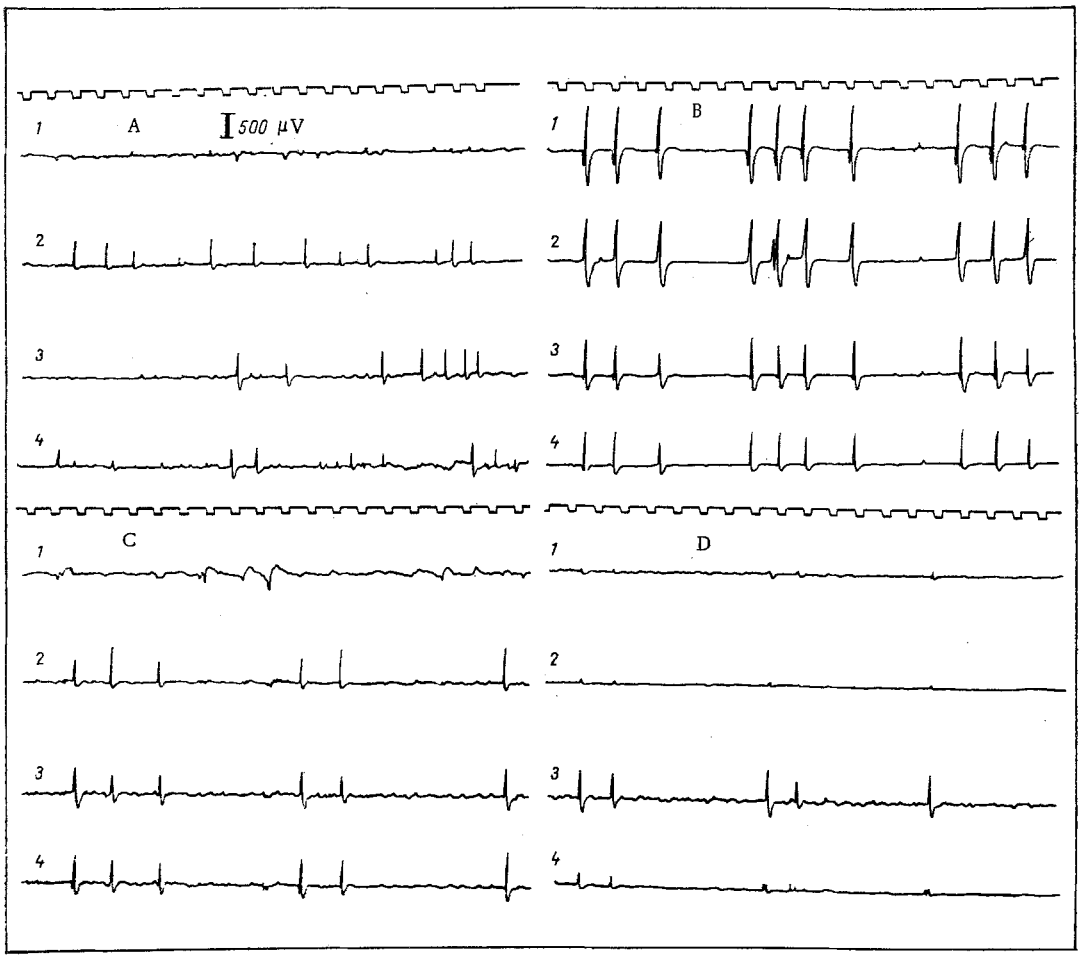

Fig. 1. Role of determinant focus in formation and activity of functional complex of epileptiform activity in rat cerebral cortex. A) Formation of scattered foci of epileptiform activity in areas 2-4 by application of 0.5% strychnine – application of strychnine ended after appearance of activity; B) 15 min after beginning of formation of determinant focus in area 1 of ipsilateral hemisphere by application of 3% strychnine and synchronization of epileptic activity in areas 2-4 with activity of focus 1; C) 8 min after application of 6% pentobarbital to region of determinant focus in area 1, remaining foci continued to generate synchronized epileptic discharges; D) 30 min after application of pentobarbital, further decrease in amplitude and frequency of epileptiform discharges and their disappearance in all foci. Here and in Fig. 2: 1) parietal cortex, 2) sensomotor cortex, 3) occipital cortex, 4) temporal cortex. Calibration: 500 μV, time marker 1 sec.

The object of the present investigation was to study functional relationships between foci with different levels of paroxysmal activity created in the cerebral cortex of the rat, which differs in certain structural and functional respects from that of the cat.

EXPERIMENTAL METHOD

Acute experiments were carried out on albino rats weighing 190-230 g. Under pentobarbital anesthesia (40 mg/kg, intraperitoneally) the skin and subcutaneous areolar tissue were divided by a midline incision from the nasal bones to the occiput. A burrhole in the cranial bones over one hemisphere provided wide access to different parts of the neocortex. The dura in the middle part of the hemisphere was divided by a cruciate incision and its borders were retracted. Before application of strychnine, the area of neocortex was carefully dried with filter paper. Scattered foci of epileptic activity were created by application of filter paper (1-2 mm^2) soaked in 0.1-0.5% solution of strychnine nitrate, in different parts of the sensomotor, visual, and auditory areas of the neocortex (areas 1, 2, 3, 4, 7, 17, and 18 after Krieg [4]). The distance between the foci was 5-10 mm. A focus of powerful epileptiform activity was created by application of filter paper (1-2 mm^2) soaked in strychnine

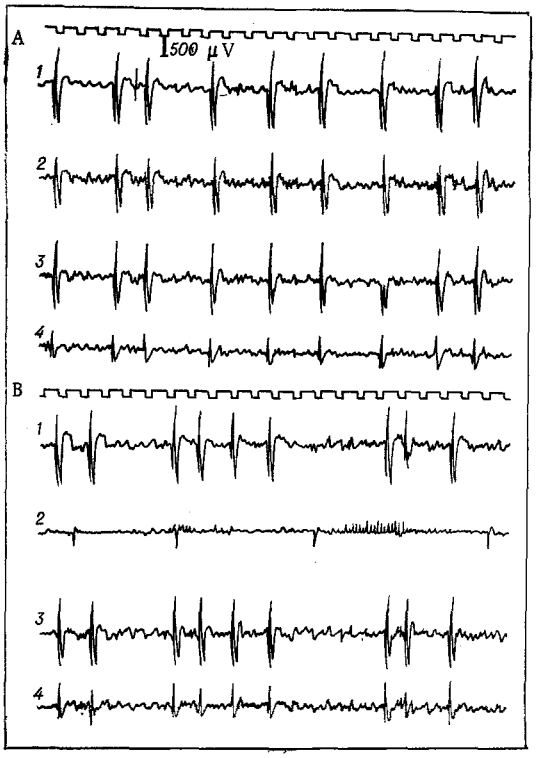

Fig. 2. Behavior of complex of foci after suppression of dependent focus. A) State of foci 20 min after creation of determinant focus in zone 1; B) 15 min after application of 6% pentobarbital to focus in zone 2. Remainder of legend as in Fig. 1.

solution (1-3%) to the parietal or temporal region of the ipsilateral cortex. To prevent diffusion of the strychnine, the region surrounding the electrode was carefully dried and the excess of fluid removed with filter paper. The foci were blocked by local application of filter paper soaked in 6% pentobarbital. The reference electrode was fixed in the nasal bones, and the active electrodes consisted of cotton threads soaked in physiological saline. Potentials were recorded on the 4-ÉÉG-3-ink-writing electroencephalograph.

EXPERIMENTAL RESULTS

A few minutes after application of 0.1-0.5% strychnine solution to different parts of the sensomotor, visual, and auditory areas of the cortex of one hemisphere, strychnine potentials of different sizes appeared, first in the sensomotor, and later in the auditory and visual areas of the neocortex (Fig. 1A; areas 2-4). Epileptiform discharges were recorded asynchronously and independently in each focus. After the appearance of these potentials the paper with strychnine was removed. The creation of a new powerful focus of epileptiform activity under these conditions in the parietal cortex of the ipsilateral hemisphere by application of 3% strychnine solution led to an increase in the amplitude and frequency of the epileptiform discharges in the other foci. Meanwhile synchronization of the epileptiform discharges was observed in the scattered foci with the discharges in the new focus (area 1). Initially synchronization of discharges took place in the foci of strychninization nearest to the new focus. At the height of development of the process, discharge generation in all the foci was completely synchronized with discharge generation in the new focus (Fig. 1B). A single functional complex of epileptic activity consisting of all four foci was thus formed, and the hyperactive focus in area 1 played the organizing and determinant role in it.

In certain experiments the scattered foci of epileptiform activity were not controlled by the activity of the hyperactive focus but continued to generate asynchronous epileptiform activity. The absence of synchronization (or its much later onset) was observed comparatively frequently in foci which generated considerable epileptiform activity and which were more distant than the other foci from the hyperactive focus. Synchronization of the activity of such a focus with that of the hyperactive focus took place at later stages, when activity in the given

focus was reduced and activity of the hyperactive focus was enhanced. In other experiments one of the foci began to generate high epileptiform activity and to produce discharges in its own firing pattern.

To settle the question of whether the hyperactive focus does in fact play the determinant role in the formation of the complex of foci and to establish its mode of operation, experiments were carried out with pharmacological suppression of the epileptiform activity of the determinant and other foci. On application of filter paper soaked in 6% pentobarbital solution to the region of the hyperactive focus in area 1 (at stages when the activity of all foci of the complex was synchronized to the same firing pattern) a considerable decrease in amplitude of the negative wave of the epileptiform discharges was observed in that focus but with preservation of amplitude of their positive wave. During this period, high-amplitude synchronized epileptiform discharges continued to be recorded in the other foci. From 10 to 20 min after application of pentobarbital a gradual decrease in the amplitude and frequency of the discharges was observed in all foci, and each of them began to generate discharges asynchronously and independently. After complete suppression of epileptiform activity in the hyperactive focus complete desynchronization and a decrease and subsequent disappearance of the epileptiform discharges in all the foci were observed (Fig. 1D). If, however, activity was suppressed in any other focus of the complex, the complex as a whole was preserved and the remaining foci continued to discharge in accordance with the previous pattern of synchronized activity (Fig. 2).

The focus of powerful epileptiform activity created in the rat cerebral cortex could thus play a determinant role relative to the other foci of epileptic activity.

At the same time, these experiments also revealed certain distinguishing features. The important role of rigidly preformed cortical connections in the mechanism of functional interaction between foci of excitation and in the formation of complexes of epileptic activity was demonstrated previously [1]. The present investigation confirmed those findings and showed that the stronger the connections between the areas of the neocortex in which the foci are formed, the more rapidly and completely the determinant focus imposes the character of its own activity on the other foci, unites them into a single functional complex, and determines the behavior of the complex as a whole. The experimental results also demonstrate the important role of intensity of the functional volley generated by the determinant focus in the realization of its effects. This is confirmed by the following fact: The combination of scattered foci into a single functional complex and the synchronization of their activity under the influence of the determinant focus were clearly manifested during superficial pentobarbital anesthesia, i.e., when some impairment of synaptic conduction was present. Under those conditions only the most powerful focus, generating intensive excitation, could play the determinant role.

The results also indicate that the properties of the determinant focus established previously [2, 3] and also the relations discovered between the acute epileptogenic foci in the cerebral cortex reflect a general rule and do not depend on species-specific features of the morphological and functional organization of the brain.

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