EFFECT OF INJURY TO THE ZONE OF THE MEDIAL FOREBRAIN BUNDLE AND PREOPTIC REGION ON ACTIVITY OF AN EPILEPTIFORM FOCUS INDUCED BY PENICILLIN (ON THE PHENOMENON OF THE HYPERACTIVE DETERMINANT DISPATCH STATION)

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Experiments on cats showed that injury to the medial forebrain bundle (MFB) and also partly to the preoptic region on the side of application of penicillin to the cerebral cortex (middle suprasylvian gyrus) causes depression of paroxysmal activity (spike potentials) in the penicillin focus, and also in a secondary "mirror" focus arising in the symmetrical zone of the opposite cortex. Injury to MFB on the side of the "mirror" focus causes depression of paroxysmal spike potentials only in that focus and does not affect activity in the primary epileptiform focus. The effects described are examined from the standpoint of views regarding the role of the determinant dispatch station (DDS) in the activity of the CNS: A primary epileptiform focus is a hyperactive DDS which induces the appearance of secondary foci, supports them, and determines the character of their activity. The results of the investigation suggests a role for MFB in the modulation of cortical epileptiform activity.

KEY WORDS: "penicillin" epileptiform focus; medial forebrain bundle; preoptic region; hyperactive determinant dispatch station; cerebral cortex.

The motivation for these investigations was ideas regarding the role of the determinant dispatch station (DDS) in the activity of the nervous system [1-5]. The DDS is a CNS structure which determines the character of activity of both parts of the CNS to which the functional volley formed by it is addressed; in this connection the DDS determines the behavior of the whole system which it activates. Hyperactive DDS arising when inhibitory processes in the population of neurons forming them are disturbed function as generators of pathologically enhanced excitation [3, 10, 14, 15] and induce the appearance of corresponding neuropathological syndromes [5-12]. It was shown previously [13] that an epileptiform focus arising in the cerebral cortex in response to the application of strychnine is an example of a hyperactive DDS; the latter induces a "mirror" focus in the opposite hemisphere and determines the character of its activity. Injury to the ipsilateral medial forebrain bundle (MFB) has been shown to depress both the hyperactive DDS and the "mirror" focus; at the same time, injury to MFB on the side of the "mirror" focus leads to inhibition of activity in the "mirror" focus only and has no effect on this activity in DDS. Strychnine disturbs mainly glycine postsynaptic inhibition [19, 20, 24].

It was considered important to discover whether the effects mentioned above can be reproduced by the use of substances disturbing other types of inhibition. In this investigation penicillin, which disturbs inhibition induced by GABA, was used [17, 18, 20-23].

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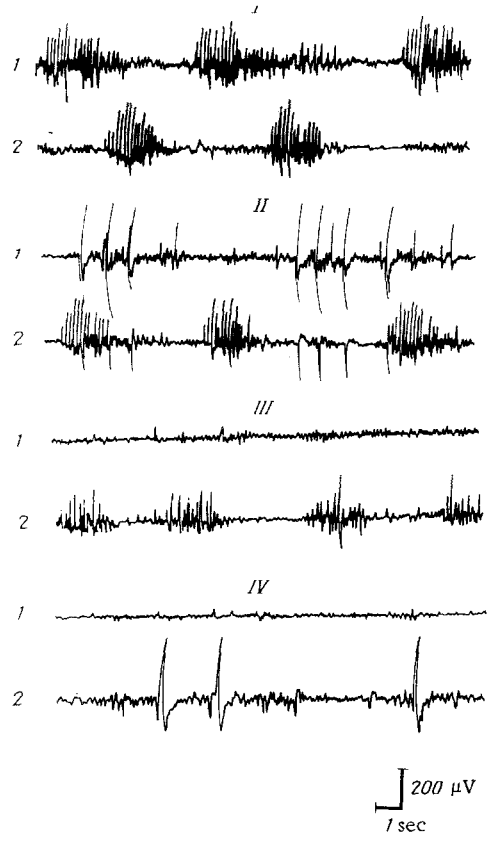

Fig. 1

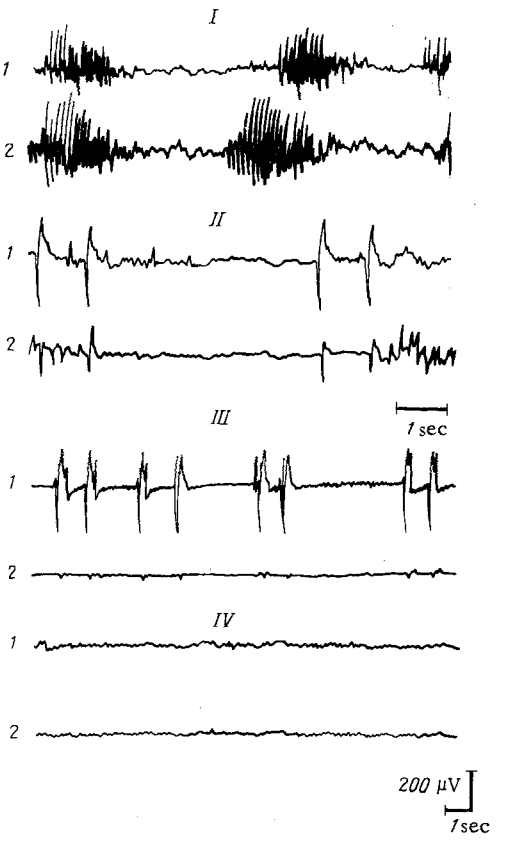

Fig. 2

Fig. 1. Appearance of primary and secondary foci of excitation during local poisoning of cerebral cortex by penicillin and effect of injury to MFB on side of primary focus on them. Primary "penicillin" focus formed in right hemisphere (middle suprasylvian gyrus). In all records: 1) right ECoG (region of application of penicillin); 2) left ECoG (symmetrically opposite region). I) ECoG before application of penicillin; II) paroxysmal spike activity after application of penicillin; III) disappearance of paroxysmal spike activity after injury to MFB on side of primary focus; IV) appearance of paroxysmal spike activity after application of penicillin to cortex of left hemisphere (on side of future secondary focus).

Fig. 2. Appearance of primary and secondary foci of excitation during local poisoning of cerebral cortex by penicillin and effect of injury to MFB on side of secondary focus on them. III) Disappearance of paroxysmal spike activity in secondary focus after ipsilateral injury to MFB; IV) disappearance of paroxysmal spike activity in primary focus after injury to MFB on side of that focus. Remainder of legend as in Fig. 1.

EXPERIMENTAL METHOD

Experiments were carried out on 15 cats anesthesized with pentobarbital (25 mg/kg intraperitoneally). The hemispheres were first exposed and the dura opened. A hyperactive DDS was created in the cortex of one hemisphere (middle suprasylvian gyrus) by application of penicillin powder through a piece of filter paper (2 × 2 mm) soaked in Ringer's solution. The piece of paper was left on the cortex throughout the experiments. The electrocorticogram (ECoG) was recorded in the region of application of penicillin and at the symmetrical points of the opposite hemisphere, by means of an ink-writing electroencephalograph. Derivation of the potentials was monopolar. The reference electrode was placed in the nasal bones. The region of MFB was injured under visual control from the basal surface of the brain by means of a galvanocautery. In some experiments coagulation was carried out in the zone of MFB (Fr 10, L 3, H −5), using a stereotaxic technique, and also in the zone of the preoptic region (Fr 13-14, L 3, H −4.5), taking coordinates from the atlas of Jasper and Ajmone-Marsan [25]. At the end of the experiment the animal's brain was fixed in 10% neutral formalin; sections 50 μ thick were cut on a freezing microtome and stained with hematoxylin and eosin. The same atlas was used to identify the zones of injury [25].

EXPERIMENTAL RESULTS

Application of penicillin to the association cortex (middle suprasylvian gyrus) caused inhibition of barbiturate spindles and the appearance of paroxysmal "penicillin" spikes (Fig. 1, II, 1), the maximal amplitude of which in some cases reached 1-1.5 mV. Soon after, a "mirror" focus with paroxysmal spike activity appeared in the symmetrical region of the opposite hemisphere (Fig. 1, II, 2). After stabilization of the character of electrical activity, MFB was injured unilaterally or bilaterally.

Injury to MFB on the side of the primary focus (the zone of penicillin application) caused a sharp decrease in amplitude (by 30-50 times) of the penicillin spikes or their virtually complete suppression (Fig. 1, III, 1). With a high degree of amplification, besides the β and γ waves remaining on the ECoG, solitary epileptic spikes of low amplitude also were recorded. After suppression of the penicillin spikes, further application of penicillin did not cause the appearance of spike potentials. Suppression of the penicillin spikes continued throughout the experiments (period of observation 4 h). Simultaneously with depression of spike potentials in the primary penicillin focus, spikes also disappeared in the secondary "mirror" focus (Fig. 1, III, 2). Only the induced spike activity disappeared under these circumstances, and bursts of barbiturate spindles were recorded substantially unchanged, or they could even be enhanced. Application of penicillin to the region of the mirror focus caused the formation of a fresh focus of increased activity, similar in character to the primary focus (Fig. 1, IV, 2). Injury to MFB on the side of the secondary "mirror" focus led to depression of activity of the secondary focus only (Fig. 2, III, 2) and did not affect the character of activity in the primary focus (Fig. 2, III, 1). Only further injury to MFB on the side of the primary focus led to the depression of its activity (Fig. 2, IV, 1).

Local application of penicillin to the cerebral cortex thus caused the appearance of a focus of pathologically increased epileptic activity which behaved as a determinant – a hyperactive DDS; this focus induced the appearance of a secondary "mirror" focus and determined the character of its activity. Abolition of the DDS led to abolition of the focus; characteristically, under these circumstances only the induced paroxysmal activity (spikes) disappeared in the secondary focus, and its intrinsic activity (barbiturate spindles, β and γ activity) still remained. This fact emphasizes the total dependence of the secondary focus on the DDS and the determinant role of the latter in the induction of activity of structures connected with it. Depression of spike potentials in the secondary focus after injury to MFB on the same side did not affect the character of activity of the DDS. Relations of the same type between DDS and the secondary focus were observed in a previous study in which DDS was produced by the application of strychnine to the cortex [13]. These results are evidence that the relations observed reflect a general rule.

The results of these investigations emphasize the importance of establishment of true DDS (determinants) if several hyperactive epileptiform foci are present. Although under chronic pathological conditions, when connections between DDS and the secondary foci are of long duration, the latter may acquire some degree of independence and may themselves become a DDS; nevertheless, the establishment of the primary DDS may have important pathogenic significance.

Depression of a hyperactive focus in the cortex after injury to the medial forebrain bundle may be connected with blocking of facilitatory influences spreading along MFB. Furthermore, considering the generator nature of epileptiform activity, it can be accepted that the phenomenon described above is also due to the blocking of inhibitory mechanisms capable of depressing generator activity, for a weakening of the inflow of excitatory stimulation by itself does not lead to abolition of the generator [7].

It is an interesting fact that depression of generator activity following injury to MFB occurs when the generator arises when inhibitory mechanisms are disturbed either by strychnine [13] or by penicillin, i.e., when different types of inhibition are disturbed. It can be postulated on the basis of these results that the MFB system participates in the modulation of epileptogenic activity. This hypothesis is also confirmed by the provocation of epileptic fits [16] observed during stimulation of the frontal cortex, with which MFB is connected, and by evidence of the role of this region of the cortex in epileptic activity [26].

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KINETICS OF CORNEAL FLUORESCENCE IN EXPERIMENTAL KERATITIS

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It was shown by means of a method of scanning photometry, suggested by the writers, that in rabbits with experimental keratitis the response in the zone of a corneal burn consists of three phases: an increase in fluorescein absorption in the reactive stage, loss of ability to absorb fluorescein in the degenerative stage, and a second increase in absorption in the regenerative stage. These phasic changes can be used for the diagnosis of keratitis and for an objective evaluation of its clinical course.

KEY WORDS: inflammation; trophic changes; fluorescence.

It has now been shown that the local signs of an inflammatory process and the corresponding changes in reactivity of the body are due, in particular, to a complex response of the connective tissue [1, 8]. The connective tissue is known to perform supportive and trophic functions in relation to the parenchyma [2, 9] not only under normal conditions, but also during the development of inflammation. However, the dynamics of the

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