RELATIONS BETWEEN THE "DISPATCH" AND "DESTINATION" STATIONS DURING FORMATION OF PATHOLOGICAL REACTIONS

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KEY WORDS: "dispatch station" and "destination station"; epileptiform reactions.

The concept of the role of determinant structures in activity of the nervous system is of great importance to the understanding of the mechanisms of development of CNS pathology [3, 4]. Initial (dispatch) and final components of pathological reactions, or what Ukhtomskii [6] calls the dispatch stations and destination stations, play a role in the formation of pathology in the nervous system. During the development of neuropathological syndromes the dispatch station becomes determinant, in other words, it determines the fate of a particular pathological manifestation [4]. The object of this investigation was to study changes in the CNS arising in the presence of certain relations between brain structures forming dispatch and destination stations in animals with epileptiform reactions.

EXPERIMENTAL METHODS

Experiments were carried out on 12 rabbits weighing 3-3.5 kg with electrodes implanted chronically into the cortex (sensomotor, temporal, and occipital regions) and deep structures of the brain (dorsal part of the hippocampus, caudate nucleus, corpus callosum, and medial parts of the thalamus). The method was fully described by the writer previously [5]. The dispatch station was created in the sensomotor cortex by electrical stimulation with an alternating current (frequency 50 Hz, pulse duration 1 msec, duration of stimulation 10 sec). In one series of experiments subthreshold values of current (50 μA) were used, in another series threshold values (150-200 μA), including behavioral reactions and changes in electrical activity of seizure type. Stimulation was applied through bipolar electrodes implanted into the sensomotor cortex. The destination station was the sensomotor cortex symmetrically opposite to the stimulated region. In some experiments it was subjected to micropolarization (MP) by a current of 0.05-0.4 μA. MP was applied through the same electrodes as those used to record electrical activity. Anodal and cathodal MP were used, during which one electrode (active) was located in the sensomotor cortex, the other (indifferent) in the frontal bone. The duration of the experiment was 30-50 min. Electrical activity of the cortex and deep brain structures, respiration, and the animals' movements were recorded.

EXPERIMENTAL RESULTS

In the experiments of series I the possibility that chronic epileptiform changes could be induced in the ECG and in the animals' behavior purely by unilateral electrical stimulation of the sensomotor cortex with a current of threshold values was studied. Threshold electrical stimulation always caused the appearance of epileptiform waves in the structure actually stimulated, but sometimes also in the symmetrically opposite region and in other brain structures studied. Electrographic changes were accompanied by response movements of the head, limbs, and whole body. On subsequent days the epileptiform changes were no longer preserved. Repetitive stimulation on alternate days for 10-14 days, once or twice in each experiment, with a current of threshold value led neither to chronic EEG changes nor to motor disturbances.

In the experiments of series II, besides unilateral threshold stimulation of the sensomotor cortex (dispatch station), MP was applied to the symmetrical region of the opposite

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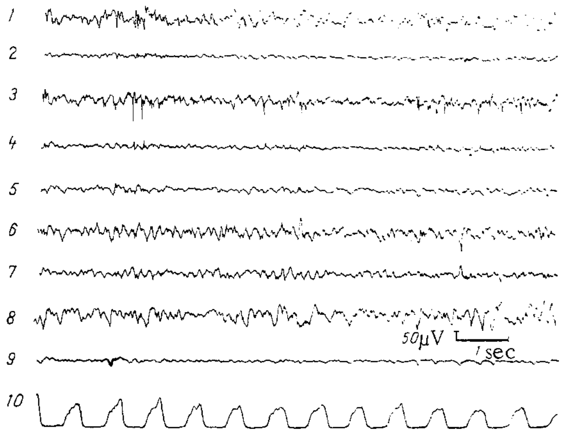

Fig. 1. EEG and subcortical electrical activity of rabbit 5 days after ending electrical stimulation of left sensomotor cortex (50 μA, 1 msec, 50 Hz): pointed waves and spikes present mainly in left sensomotor cortex. 1, 2) Right sensomotor cortex, 3, 4) left sensomotor cortex; 5) corpus callosum; 6, 7) left dorsal hippocampus; 8) right dorsal hippocampus; 9) movements of right forelimb; 10) respiratory movements. 1, 3, 5, 6, 8) Monopolar derivations; 2, 4, 7, 9, 10) bipolar derivations.

cortex (destination station). During MP neither consolidation of the reactions which we induced nor their conversion into chronic was observed.

In the experiments of series III subthreshold stimulation of the sensomotor cortex was used. Stimulation was applied once or twice during an experiment. During the first 5 days in response to electrical stimulation no EEG changes were observed. Starting with the 6th-10th day, immediately after the first electrical stimulation pointed waves and spikes appeared in the stimulated structure, and respiration deepened and sometimes quickened. These changes could arise subsequently without stimulation and they lasted 1-2 weeks (Fig. 1). The spontaneous appearance of epileptiform seizures was observed during this period. The most typical of them were characterized by the development of high-amplitude α-waves, α-like waves, and θ-waves in the EEG of the sensomotor cortex of both hemispheres and, in some animals, in electrical activity of the deep brain structures also, followed by death of the animal (Fig. 2).

Further application of subthreshold stimulation did not lead to potentiation or stabilization of the pathological changes which were formed. The EEG during this period showed the development of spindles of synchronized α-waves in all structures. Epileptiform activity was not exhibited against this background.

In the experiments of series IV, in order to consolidate the epileptiform changes arising during subthreshold stimulation, MP was applied to the sensomotor cortex opposite to the side of stimulation. A direct current was applied continuously for 30-50 min. No difference in principle was found between the action of anode or cathode. Under these conditions the gradual formation of involuntary motor responses (hyperkinesias) was observed in all the animals. Initially the EEG changed. In most structures fast waves began to predominate. On the 5th-6th day of the experiments the first response movements of the forelimbs appeared, and later they were joined by twitching of the hind limbs. The motor responses took place against a background of stable high-amplitude waves with a frequency of 5-7/sec in the dorsal hippocampus (Fig. 3). Hyperkinesias appeared initially only during the combined action of stimulation and polarization. Later they could be produced by a conditioned reflex mechanism to the experimental situation. Stable hyperkinesias lasted 3-4 weeks and then gradually disappeared.

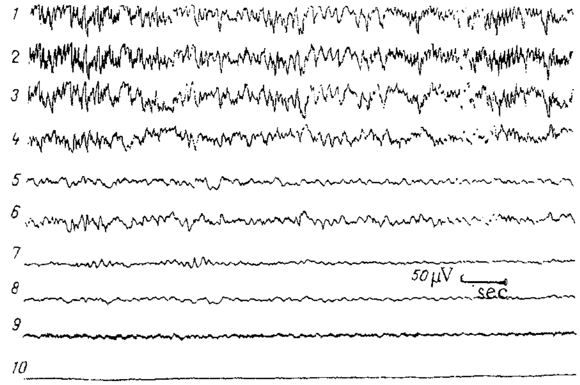

Fig. 2. EEG and subcortical electrical activity of a rabbit nine days after discontinuing electrical stimulation of left sensomotor cortex: predominance of high-amplitude waves in sensomotor cortex of both hemispheres. 1, 2) Right sensomotor cortex; 3, 4) left sensomotor cortex; 5) corpus callosum; 6, 7) right caudate nucleus; 8, 9) left caudate nucleus; 10) movements of right forelimb. 1, 3, 6, 8) Monopolar derivations; 2, 4, 5, 7, 9, 10) bipolar derivations.

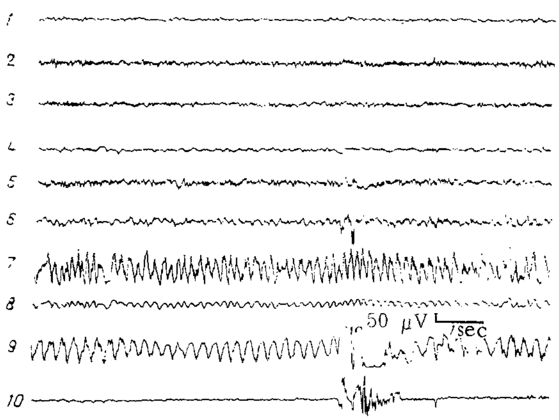

Fig. 3. EEG and subcortical electrical activity of a rabbit before, during, and after spasms of right forelimb. Development of synchronized θ-waves in dorsal hippocampus. 1, 2) Right sensomotor cortex; 3, 4) left sensomotor cortex; 5, 6) right medial thalamus; 7, 8) right dorsal hippocampus; 9) respiratory movements; 10) movements of right forelimb. 1, 3, 5, 7) Monopolar derivations; 2, 4, 6, 8-10) bipolar derivations.

The different series of experiments with electrical stimulation and MP showed that, depending on the procedure and its strength, different kinds of epileptiform reactions could be observed — seizures and hyperkinesias.

Repeated electrical stimulation of the sensomotor cortex by a current of threshold value did not lead to chronic changes in the EEG or in the animals' behavior. The dispatch station formed under these conditions evidently becomes only a temporary, unstable excitation generator. As the investigations of Kryzhanovskii [4] have shown, a dispatch station can become determinant only under certain conditions.

The writer's previous experiments with application of MP to the sensomotor cortex of one hemisphere and threshold stimulation of the opposite cortex showed that combined stimulation of this kind likewise could not raise the level of excitation in the dispatch station to a sufficiently high degree to become determinant. Only as a result of subthreshold stimulation of the dispatch station did chronic changes develop in the CNS. They can evidently be explained by gradual summation of excitation in the sensomotor cortex. The appearance of a "flare-up" in these cases is regarded by many workers [7, 8] as a result of a change in the functional state of the cerebral cortex.

Stable chronic hyperkinesias could be obtained in animals subjected to a combination of subthreshold stimulation and MP. Investigations [1, 2] have shown that MP of the brain accelerates the formation and fixation of motor responses during learning, and subsequently these responses were preserved for a long time and could be reproduced by MP alone. The appearance of stable hyperkinesias in the case of direct action on the dispatch and destination stations can evidently be regarded as the result of functioning of a determinant dispatch station, characterized by a certain strength of excitation, and of the creation of a relatively stable pathological system, as defined by Kryzhanovskii [4].

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EFFECT OF HYPERACTIVATION OF THE LOCUS COERULEUS ON RHYTHM OF THE INTACT AND REACTIVELY CHANGED HEART

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The locus coeruleus (LC), the principle nucleus of the dorsal noradrenergic pathway, is known to be closely connected with various formations of the nervous system, including structures participating in regulation of the circulation [3, 6, 8]. Preliminary coagulation of LC has been shown to considerably reduce disturbances of the cardiac rhythm in acute myocardial ischemia. It has been suggested that in this form of pathology LC may acquire the role of a hyperactive determinant structure [1].

Accordingly, in the present investigation the character of rhythmic activity of the intact heart and of a reactively changed heart was studied during electrical stimulation of LC with the creation of a generator of pathologically enhanced excitation (GPEE) in it [1].

EXPERIMENTAL METHOD

Experiments were carried out on 86 noninbred male rats weighing 200-240 g anesthetized with pentobarbital sodium (25 mg/kg) and artificially ventilated (succinylcholine 0.2 mg/kg).

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