EFFECT OF MICROPOLARIZATION OF FOCAL AND EXTRAFOCAL BRAIN STRUCTURES ON EXPERIMENTAL EPILEPSY

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The effect of micropolarization (MP) with a current of 0.05-0.75 μA on epileptogenic foci produced by injection of 500 and 1000 units of penicillin solution into the motor cortex was investigated in chronic experiments on rabbits. A single MP of extrafocal structures (corpus callosum, caudate nucleus) and of the region of the focus was shown to inhibit the development of paroxysmal responses. Repeated MP of the region of the focus had the opposite effect. The effects observed can probably be explained not only by the specific role of the structures studied in the processes of formation and spread of excitation, and by their initial functional state, but also by the dependence of the activity of these structures on the conditions of MP.
KEY WORDS: epileptiform seizures; penicillin; micropolarization; inhibitory and facilitatory effects.

On the basis of clinical observations [1, 2] a role of memory has been postulated in the mechanisms of nervous diseases characterized by their particular persistence (epilepsy, hyperkinesia, neurosis, etc.). Investigation of the formation and suppression of pathological responses in experimental models can reveal the role of long-term memory in these processes and ways of active intervention in the pathogenetic mechanisms of persistent pathological states. A convenient model for the study of acute epileptogenesis is the penicillin model of epilepsy [6, 10]. As was shown previously [3, 4, 7], micropolarization (MP) of certain brain structures also effectively influences trace processes and memory.

The object of the present investigation was, accordingly, to study the effect of MP of certain cortical (motor, temporal, and visual regions) and deep brain structures (corpus callosum and caudate nucleus) on epileptogenic foci produced by intracortical injection of penicillin.

EXPERIMENTAL METHOD

The investigation was carried out on six rabbits with electrodes permanently implanted into the cortex (motor, temporal, and visual regions) and deep structures (the rostral zones of the corpus callosum, dorsal hippocampus, medial zones of the thalamus, putamen, caudate nucleus).

Electrodes were inserted into the cortex to a distance of 1 mm from the surface of the dura. The electrodes were introduced into deep structures in accordance with stereotaxic coordinates from an atlas of the rabbit brain [9].

Electrical activity was derived mainly by bipolar electrodes made from stainless steel. The thickness of the bipolar electrode in its Fluoroplast [Teflon] insulation was 200-250 μ. The distance between the electrode tips was 1-1.5 mm and the length of the uninsulated end of the electrode 0.5 mm. In the course of the experiment the animal was kept in a hammock or cage.

Acute epileptogenic foci were formed by intracortical injection of the sodium salt of penicillin in doses of 500 and 1000 units, dissolved in 0.02 ml of bidistilled water, through a cannula specially inserted into the motor cortex on the left side.

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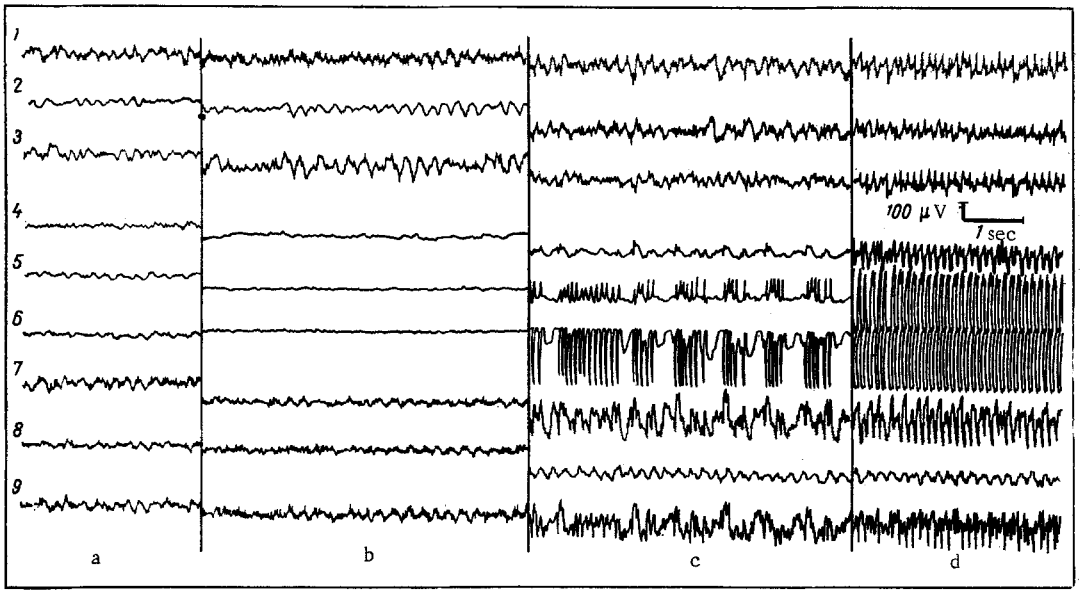

Fig. 1. Dynamics of EEG and ESCoG of rabbit during development of epileptiform fit caused by injection of 500 units penicillin into left motor cortex. a) Spontaneous EEG and ESCoG; b) EEG and ESCoG 3 sec after injection of penicillin; c) development of tonicoclonic discharges in region of focus; d) generalized tonic discharges spread to all brain structures. 1, 2) Right motor cortex; 3) right visual cortex; 4, 5, 6) left motor cortex; 7, 8) left temporal cortex; 9) corpus callosum. Recording in derivations 1, 3, 4, 5, and 7 monopolar; otherwise bipolar.

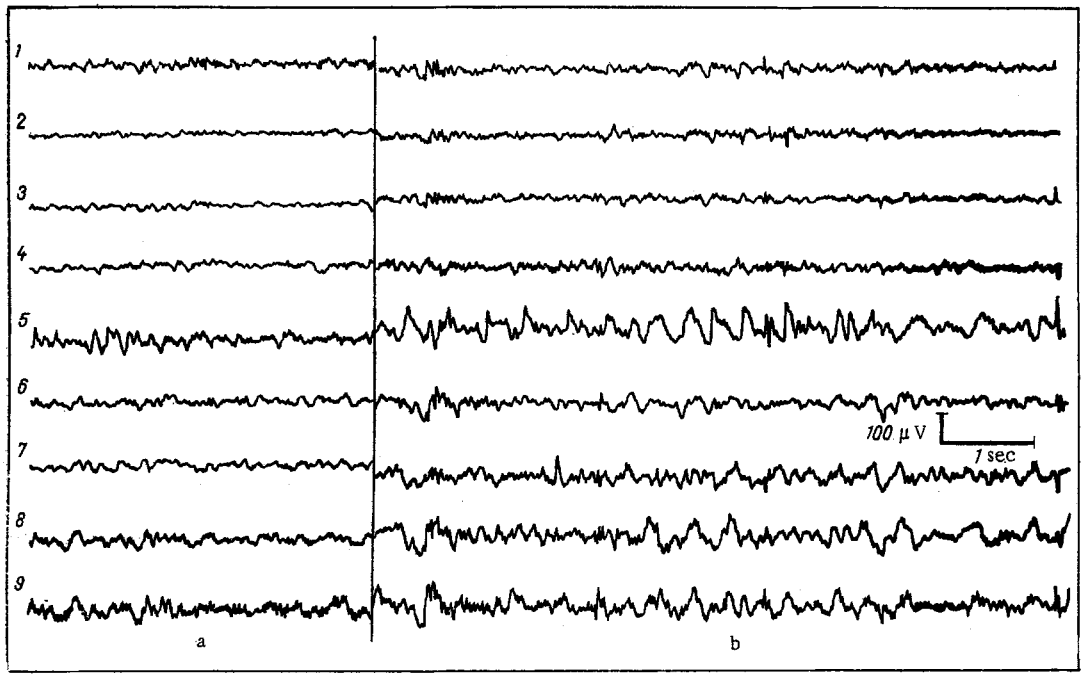

Fig. 2. EEG and ESCoG of rabbit. a) Before injection of 500 units penicillin, after MP (direct current 0.2 μA, 30 min) of region of focus, in left motor cortex; b) 20 sec after injection of penicillin. 1, 2) Right motor cortex; 3, 4) left motor cortex; 5) right temporal cortex; 6) left temporal cortex; 7) right medial thalamus; 8, 9) left caudate nucleus (body). Monopolar recording in derivations 1, 3, 5, and 8; otherwise bipolar.

A battery-powered polarizer assembled to a high-resistance bridge circuit (4-8 mΩ) was used for MP. Different types of polarization were used: bipolar and monopolar – either anodal or cathodal. A direct current of 0.05-0.75 μA was used for MP.

The animals were killed after the experiments had ended and the brain was removed for histological examination to determine the location of the electrodes.

EXPERIMENTAL RESULTS

The character of the electrographic and motor responses was determined by the dose of penicillin. A dose of 250 units caused only electrographic changes, consisting of single spikes, in the zone of injection. Injection of 500 and 1000 units led to the gradual development of changes in the animal's brain electrical activity and behavior.

In typical cases 2-240 sec after injection of penicillin a decrease in amplitude of the waves was observed mainly in the region of the focus, namely the motor cortex (Fig. 1b). Next, single monophasic spikes appeared both in the focus and in the mirror focus in the symmetrically opposite region. Spikes were recorded in all derivations 1-2 min later and were biphasic and polyphasic in character. Their amplitude reached 200-500 μV. The spikes sometimes formed spike–wave complexes with a frequency of 4-6/sec and they spread to all structures of the brain. After 3-6 min grouping of the spikes and the formation of tonicoclonic and tonic electrographic seizure responses were observed (Fig. 1c, d). In the region of the focus the amplitude of the spikes reached a maximum, namely 250-300 μV. Periods of bursts of paroxysmal activity alternated with periods of rest, during which electrical activity was asynchronous and its amplitude depressed. Bursts of paroxysmal activity were repeated many times in the course of 1-2 h.

Rhythmic twitching of the eyelids and the muscles of the mouth, neck, and limbs, and involuntary rotations of the head and trunk as a rule toward the side opposite to the activated hemisphere corresponded to the generalized electrographic changes. The motor responses took place against the background of tonic electrographic epileptiform manifestations (Fig. 1d).

To study the action of certain cortical and deep structures in the mechanism of function of the epileptogenic foci series of experiments were carried out with MP of the motor, temporal, and visual regions of the cortex, the corpus callosum, and caudate nucleus.

A single preliminary MP of the left motor cortex with a current of 0.05-0.35 μA for 25-35 min prevented the development of the paroxysmal responses which develop as a rule easily in response to injection of penicillin into that same region of the cortex, or sharply reduced them. Bipolar and monopolar polarization, when the motor area was the cathode, were effective. The subsequent injection of penicillin led to the development of two types of pathological changes.

1. Epileptiform electrographic responses were characterized by the appearance of single spikes of low amplitude, which were recorded for several minutes, in the region of the focus or the symmetrically opposite region. The amplitude of the potentials recorded in other structures was increased (Fig. 2b). The motor responses included weak rotations of the head (of orienting type) and infrequent contractions of the muscles of mastication.

2. The epileptiform bioelectrical activity was more generalized. Spikes appeared in all derivations and could be of high amplitude (up to 400 μV). However, compared with seizures evoked by penicillin in the absence of MP their amplitude was smaller and the waves themselves were less marked and less variable. The motor responses of the head, trunk, and limbs were weaker. All seizures were of short duration (not exceeding 0.5-1 h).

Repeated MP of the region of the focus with a current of 0.05-0.35 μA for 30 min daily for 3-5 days gave the opposite result. Injection of penicillin after repeated MP to the region of the focus caused a rapid development of very strong epileptiform electrographic and motor responses. Periods of paroxysmal activity were very long, whereas the intervals between paroxysms were shortened.

Preliminary MP of the corpus callosum or caudate nucleus with a current of 0.25-0.30 μA for 25-30 min prevented the development of seizures in response to injection of 500 and 1000 units of penicillin or weakened them. Under the influence of MP the paroxysmal electrographic changes and motor responses were weak in intensity.

The MP of the focus, the mirror focus, or any cortical or deep structure of those listed above, after development of the electrographic and motor responses did not change the character of the seizure. Increasing the polarizing current to 0.5-0.75 μA led to a decrease in the amplitude of the principal spikes in the polarized structure and to suppression of the fast and slow forms of activity in it.

Even in one experiment the function of the epileptogenic focus can be represented as a complex system of pathological excitation spreading to many brain structures. This system can be influenced by certain cortical and deep structures of the brain.

The inhibitory and facilitatory effects formed by MP can evidently be explained not only by the "specific" role of the structures studied in the formation and spread of excitation, but also by the presence of definite dependence of the activity of these structures on the conditions of MP [5]. On the other hand, it was observed that the regulatory effect of MP depends on differences in the original functional state of the brain structures as a whole chosen for polarization. For instance, MP of the motor cortex before provocation of a focus in that same region facilitates the suppression of pathological activity. The application of a direct current actually during a seizure is ineffective because the functional state of the brain under those conditions is sharply modified by the epileptogenic agent.

Facts such as these, evidence of differences in the role of the structures in the course of the pathological responses and of the variability of the functional role of the same structure in the system of pathological excitation, have been described by the writer previously in the case of another model of pathological responses, namely hyperkinesia [8]. They show not only that some of the central mechanisms lying at the basis of epileptiform seizures and hyperkinesia are common to both, but also that micropolarization can effectively control the variously formed systems of pathological excitation.

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