compared with nuclei of the posterior group and with the parafascicular complex is evidently associated with activation of a certain proportion of the tactile fibers which enter in the composition of the alveolar nerve. The medial zones of the thalamus receive afferent impulses along fibers with higher thresholds [3, 9] than projection fibers, and this evidently explains the greater degree of depression of nociceptive EP after EAP in precisely those zones of the thalamus.

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EFFECT OF ACTH$_{4-7}$ AND LYSINE-VASOPRESSIN ON ACTIVITY OF A GENERATOR OF PATHOLOGICALLY ENHANCED EXCITATION

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Generators of pathologically enhanced excitation (PEE) are one of the most general pathogenetic mechanisms of different forms of pathology of the CNS [5]. The special features of their activity and, in particular, their ability to maintain activity for a long time indicate that PEE generators can be regarded as a unique form of pathological memory [5]. A similar view has also been expressed on foci of epileptic activity [3], which can be regarded as a special form of PEE generator. Consequently the study of behavior of generators and their relations to substances affecting different types and manifestations of memory is of particular interest. It was shown previously that an "extinct" and clinically silent PEE generator can be reactivated by suboccipital injection of a synthetic hexapeptide of definite structure [9].

In the investigation described below the effect of ACTH fragment ACTH$_{4-7}$ (synthesized in the Institute of Molecular Genetics, Academy of Sciences of the USSR, by M. A. Ponomareva-Stepnaya and V. N. Nezovibat'ko) and of lysine-vasopressin (obtained from Serva, West Germany), which play a definite role in consolidation processes in physiological memory [2, 16], on activity of PEE generators was studied.

EXPERIMENTAL METHOD

Experiments were carried out on noninbred albino rats weighing 200-220 g. The PEE generator was formed by the method described previously [5, 8] in the anterior horns of the lumbosacral segments of the spinal cord by means of tetanus toxin (TT), which disturbs different types of inhibition [5, 10, 13-15]. TT was injected in a dose of 1/25 MLD (for rats of the above weight) into the leg and thigh muscles of the left hind limb, from which, as special investigations

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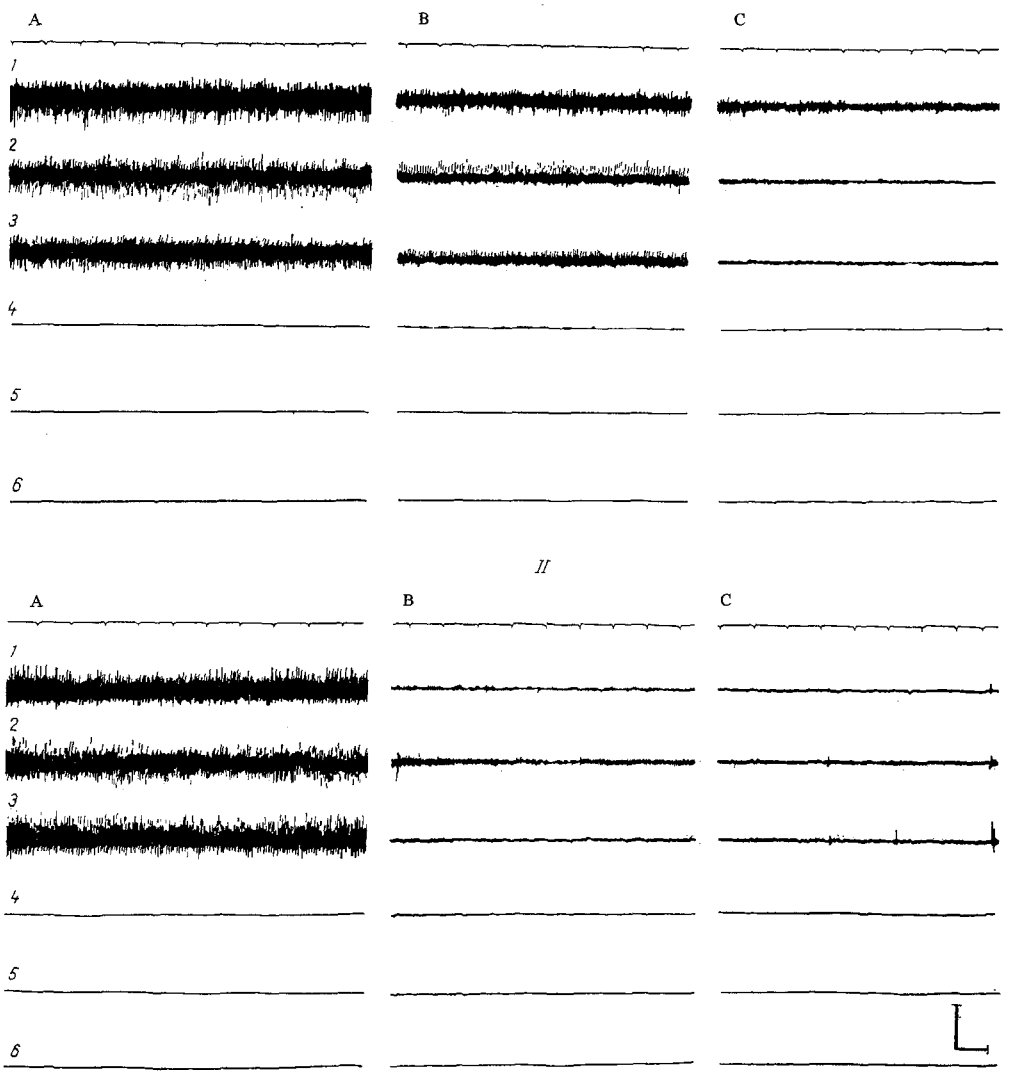

Fig. 1. Electrical activity of hind-limb muscles of animals receiving $ACTH_{4-7}$ (I) and control animals (II) following formation of PEE generator in lumbosacral segment of spinal cord. A) EA of muscles 3 days after injection of TT into left gastrocnemius muscle, B) 28 days, C) 34 days after injection. Recordings from: 1) gastrocnemius muscle; 2) anterior muscles of leg; 3) posterior group of thigh muscles of left hind limb; 4) gastrocnemius muscle; 5) anterior leg muscles; 6) posterior group of thigh muscles of right hind limb. Calibration: 250 μV, 1 sec.

have shown [5], it travels along the motor fibers of the sciatic nerve to the anterior horns of the lumbosacral segments. The effects of the generator thus formed were manifested clinically as enhanced electrical activity (EA) in the muscles of the corresponding hind limb and hypertonus of these muscles. Signs of increased muscle (extensor) tone could be clearly detected clinically and electromyographically 72 h after the injection of TT. Animals with equal degrees of increase in background EA in the muscles and an identical clinical picture of muscular hypertonus were selected in pairs in the experimental and control groups. Starting from this period, animals were given subcutaneous injections of 100 μg/kg $ACTH_{4-7}$ twice a day for 3 days (experiments of series I on 18 rats) and corresponding injections of lysine-vasopressin (series II on 15 rats). The 24 rats of the control group received injections of the same volume of physiological saline at the same times. Clinical features of muscular hypertonus were recorded from the time of its appearance until its disappearance, and EA was recorded in the muscles of both hind limbs. EA was recorded on a Nihon Kohden RM-86M polygraph for 36 days (maximal period of observation), every 2-3 days.

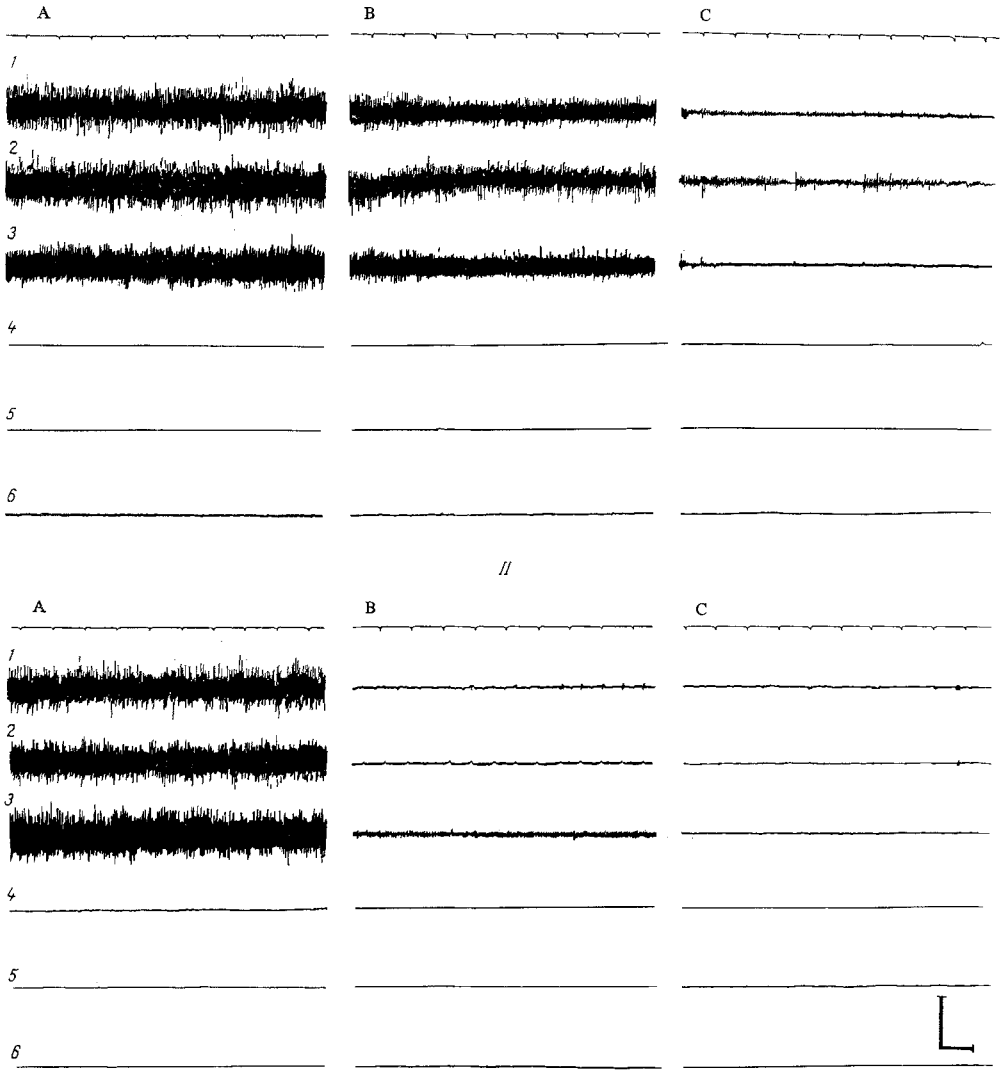

Fig. 2. Electrical activity of hind limb muscles of animals receiving lysine-vasopressin (I) and control animals (II) after formation of PEE generator in lumbosacral segments of spinal cord. Legend as in Fig. 1.

EXPERIMENTAL RESULTS

As already stated, 3 days after the injection of TT the animals developed the characteristic picture of muscular hypertonus (rigidity of the muscles) on the side of injection of TT and increased EA, in the form of prolonged and intensive bursts of asynchronous high-amplitude potentials (Fig. 1, I, A: 1-3 and II, A: 1-3; Fig. 2, I, A: 1-3 and II, A: 1-3). About 14-16 days later the muscular hypertonus began to weaken. In the animals of the control group, by the end of the 4th week (26-28 days after injection of TT) neither clinical nor electromyographic signs of increased muscle tone could be observed (Fig. 1, II, B: 1-3; Fig. 2, II, B: 1-3). This picture of clinical recovery was observed in virtually all the control animals.

In the animals of the experimental group, in both series I (receiving $ACTH_{4-7}$) and series II (receiving lysine-vasopressin) of experiments, toward the end of the 4th week signs of muscular hypertonus were still present, in the form of clumsiness and trailing of the limb during movement, and the rat supported itself not on the whole foot, but only on the tips of the toes. In the muscles of that particular limb increased background EA of asynchronous type was recorded (Fig. 1, I, B: 1-3; Fig. 2, I, B: 1-3). Not until the end of the 5th week (33-36 days) did these signs disappear (Fig. 1, I, C: 1-3; Fig. 2, I, C: 1-3).

The results of these experiments show that $ACTH_{4-7}$ and lysine-vasopressin lengthened the period of activity of the PEE generator by 5-7 days.

Previous investigations [1, 2, 16-18] have shown that $ACTH_{4-7}$ and lysine-vasopressin affect processes of formation of avoidance reflexes and on the increase in the duration of persistence of these reflexes. It has been suggested that $ACTH_{4-7}$, unlike lysine-vasopressin, raises the level of the animals' attention, thereby stimulating learning, rather than acting on consolidation and long preservation of memory.

A particular feature of the results of these experiments is that $ACTH_{4-7}$ and lysine-vasopressin exhibited their action not on physiological processes of memory and learning, but on a pathological functional organization, namely PEE generators, which are based on neuron populations with inadequate inhibitory mechanisms and with activated positive connections [7]. The original view, that PEE generators can be regarded as a unique form of pathological memory, was thus confirmed. In connection with the facts described above, the use of PEE generators as models with which to study the common features and differences in mechanisms of physiological and pathological memory is interesting. Another distinguishing feature of the results of this investigation is that the PEE generator in the experimental animals was located in the spinal cord and, consequently, the effects of $ACTH_{4-7}$ and of lysine-vasopressin were realized at the spinal level. Of course this does not mean that the supraspinal levels of the CNS have no role to play in the mechanism of this phenomenon. This problem must be specially investigated. For example, it was shown previously that after decortication the muscular hypertonus due to a PEE generator formed with the aid of TT lasts much longer in decorticated animals, especially in the case of hypertonus of the forelimb muscles [5]. The similarity between the effects of $ACTH_{4-7}$ and of lysine-vasopressin under the conditions specified should also be noted. The reason may perhaps be that these peptides potentiate processes which facilitate conduction through synapses during the repeated passage of impulses [2], which takes place in the neuron population forming the generator.

These investigations confirm the earlier hypothesis that peptides participate in the course of pathological processes in the CNS, on their role as modulators of the state of pathological systems which can exert a stabilizing and destabilizing effect on pathological systems, and that they can induce certain states of the CNS [6, 7]. These views are in agreement with the data and conclusions of other workers [4, 11, 12].

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