COMBINED EFFECT OF A MAGNETIC FIELD AND ANTIOXIDANTS ON EPILEPTOGENIC FOCI IN THE RABBIT HIPPOCAMPUS

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In the last decades there has been a sharp increase in the number of systems whose operation is accompanied by the generation of magnetic fields (MF) with varied spatiotemporal characteristics that can affect the human body. The mechanism of the effect of these MF on biological objects and ways of preventing them have not been adequately studied, and for that reason intensive research in this field is necessary.

It has been shown [5, 6] that MF potentiate activity of experimental epileptogenic foci (EF) created in the rabbit hippocampus. Analysis of data in the literature [3, 8] suggested [6] that this effect is connected with the onset of a state similar to hypoxia in the animal under the influence of MF.

The object of this investigation was to test this hypothesis and to assess the possibility of pharmacologic correction of the adverse effect of MF on EF.

EXPERIMENTAL METHODS

Chronic experiments were carried out on 37 rabbits, divided into six groups (control group — 10 animals, experimental groups — from four to seven rabbits). Chemical electrodes were implanted into the left and right sides of the dorsal hippocampus of all animals, so that EF could be created in them by injecting 0.001 ml of a solution containing 100 Units penicillin into these structures. Foci of hypersynchronized activity were created in each rabbit six times, with an interval of 3 days between them, in the left and right hemisphere alternately. Electrical activity of the brain was recorded by means of an electroencephalograph for 120 min after creation of the EF. Its activity was assessed by counting the number of interictal epileptiform discharges (IED) and estimating electrographic correlates of fits (ECF) during every 10 min of the experiment. Data for all rabbits of one group were averaged and the ratio between the number of IED or ECF obtained in response to the second and third injections of antibiotic into the hippocampus and the corresponding values recorded during the first creation of EF in these structures was determined for each 10-min interval. The results were analyzed by computer, using the Wilcoxon—Mann—Whitney nonparametric U test.

The results of experiments in which an EF was created in the rabbits but no other procedures were carried out (group 1), served as the control. Rabbits of group 2 were placed for 1 h before creation of EF with their head in a horizontal MF with induction of 60 mT, and exposure to the field continued until the end of the experiment. Animals of group 3 received a subcutaneous injection of gutimin (guanylthiourea) in a dose of 50 mg/kg 1 h before the experiment. Rabbits of group 4 were exposed to MF and also injected with gutimin. Animals of group 5 were given an intramuscular injection of sodium hydroxybutyrate (GHBA) in a dose of 25 mg/kg 15 min before creation of EF. Rabbits of group 6 received an injection of GHBA and were placed in the MF under the same conditions as group 2.

EXPERIMENTAL RESULTS

The action of MF on the rabbits of group 2 caused a sharp increase in their epileptiform activity compared with the control (Fig. 1). Under the influence of MF, states simi-

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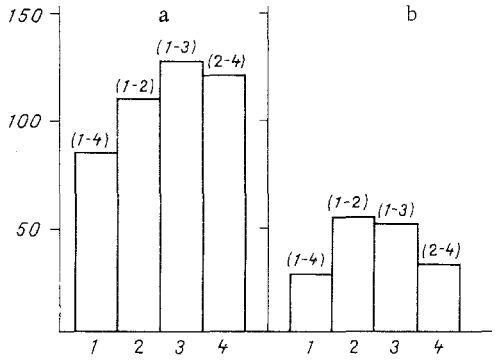

Fig. 1. Effect of MF (2, 6), gutimin (3, 7), and a combination of gutimin and MF (4, 8) on activity of experimental EF in the rabbit hippocampus. Abscissa, group of animals; ordinate, number of IED (a) and ECF (b) during second and third injections of penicillin (in % of number to first injection into rabbit hippocampus). Numbers above columns indicate statistically significant differences between groups ($0.001 \leqslant P \leqslant 0.05$).

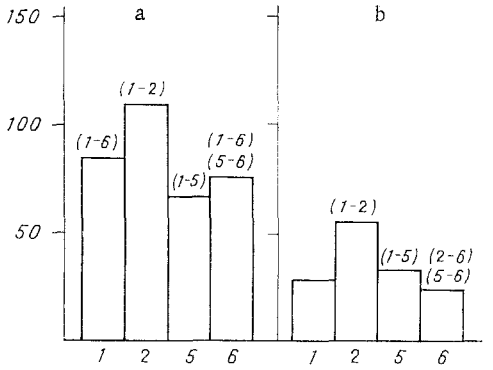

Fig. 2. Effect of MF, GHBA, and a combination of GHBA and MF on activity of experimental EF in rabbit hippocampus. Legend as to Fig. 1.

lar to hypoxic are known to arise in the tissues [3]. Since hypoxia is one of the etiologic factors of epilepsy [4], potentiation of the activity of EF in the rabbits of this group seems natural. Animals of group 3 responded to injection of gutimin (Fig. 1) like the rabbits of group 2, by an increase in the number of IED and ECF. Gutimin belongs to the antioxidant class, whose mechanism of action is realized through a change in metabolism at the cellular level. By activating glycolysis, in particular it improves the energy supply to the tissues [1], and under normoxic conditions this probably leads to potentiation of the activity of EF because of an increase in the energy resources of the cells taking part in IED and ECF formation. Combined treatment of the rabbits of group 4 with gutimin and MF reduced the number of ECF compared with their number in group 2 (exposure to MF only) and in group 3 (gutimin only), but the number of IED was less than in the animals of group 3 and greater than the number of IED in group 2 (Fig. 1). It must be pointed out that the two parameters remained appreciably higher than their control values. The fact that summation of the provoking action of the two factors on activity of EF did not take place in the experiments with combined exposure to MF and gutimin can be explained as follows: the MF, acting on mitochondria, causes inhibition of cell respiration [9], with consequent tissue changes characteristic of mild hypoxia. Gutimin, however, which maintains the energy supply of the cells and inhibits the lipolysis which arises in hypoxic states, neutralizes the aftereffect of MF. However, compensation is only partial, for gutimin does not affect the

primary mechanism of the harmful action of MF, i.e., it does not act directly on the respiratory chain or on individual dehydrogenases, but neutralizes only some of the later consequences of the disturbance of cell respiration (activation of lipolysis, damage to membranes of cells and organelles, and so on) [1]. Meanwhile MF, which inhibits processes of respiration, evidently does not allow gutimin to exhibit its energizing action on the neurons to the full extent, and reduces the intensity of its provocative effect on EF.

After injection of GHBA, which also belongs to the group of antihypoxic agents (group 5), the characteristics of activity of EF were close to those in the control (Fig. 2). The absence of any significant provocation of epileptiform activity under the influence of GHBA (by contrast with gutimin) can probably be explained on the grounds that it has not only an antihypoxic, but also a depriming, general anesthetic action [2], which can block provocation of activity of EF. After combined exposure of the animals of group 6 to MF and GHBA, not only was activity of EF not potentiated, as in the rabbits of group 2 under the influence of MF alone, but it was actually depressed compared with the control (Fig. 2). Unlike gutimin, GHBA is known to stimulate dehydrogenase activity and processes of tissue respiration and oxidative phosphorylation, and to alter the permeability of mitochondrial membranes for oxidation substrates [7]. Considering that MF also affects mitochondrical functions, it is logical to suggest that GHBA and MF have opposite actions on the same structures and processes, so that their influence are mutually compensatory (group 6). The anticonvulsant action of GHBA enables the compound to depress the pathological activity of EF further, even compared with the control.

The results thus show that GHBA is a highly effective agent for pharmacologic correction of the provocative action of MF on hypersynchronized activity of brain neurons.

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