EFFECT OF MODULATED SHF ELECTROMAGNETIC FIELDS ON CALMODULIN LEVELS IN BRAIN STRUCTURES

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Quantitative reactions of the CNS to the biological action of electromagnetic fields (EMF) depend on the frequency band, the time of irradiation, and the duration of exposure. Two approaches to this problem can be distinguished by analysis of existing views on the nature of the biological effects of the EMF: the first is based on the leading role of energy interactions, the second is linked with the study of the possible informational interactions of EMF with elements of the biological system. Research into the effect of low-intensity shf fields, modulated within the frequency band of bioelectrical rhythms, is particularly interesting. It has been shown that threshold intensities of such shf radiation are much lower than those characteristic of pulsed or, more especially, of continuous radiations [1-3, 5]. The index of absorption of an shf-signal by nerve tissue increases if the modulation frequency falls within the spectrum of intrinsic rhythmic activity of the brain, which is accompanied by changes in the intracellular Ca^{2+} concentration [2, 6]. Radiations of this type may have a selective effect on regulatory functions of the CNS. These and other data have led to the conclusion that the efficacy of modulated low-intensity (with energy flux density – EFD – below 10 $\mu W/cm^2$) shf fields is evidently connected with activation of biological amplification mechanisms and is based on the ability of the biological system to respond selectively to parameters of EMF such as the "space–time" code or the pattern of modulation. Activation of calcium-dependent reactions, with analysis of the intracellular regulatory protein, calmodulin, can be identified as a fundamental mechanism of biological amplification.

The aim of this investigation was to determine the effect of a modulated low-intensity field on calmodulin levels in different brain structures.

EXPERIMENTAL METHOD

The experimental model for irradiation of animals with a weak (under 10 $\mu W/cm^2$) pulse-modulated shf field consisted of a control system unit (CSU), based on the "Ékstrema-1" hybrid computer, and including function and special function generators of the modulating signal shaping unit (MSSU), and an action unit (AU), incorporating a G4-V7A generator and P6-23A horn-type antenna (Fig. 1). Modulation took place in accordance with a natural law revealed by a mathematical model, based on application of the theory of nonlinear pendulums and of resonance phenomena to biocontrol processes [4]. Experiments were carried out on 30 male albino rats weighing 180-200 g. Animals of group 1 were irradiated in accordance with the "2V4" modulation program, those of group 2 on a "2V8" modulation program, and animals of group 3 served as the control. After irradiation the animals were decapitated and the cerebral cortex, hippocampus, and hypothalamus quickly removed. Calmodulin was extracted from the brain tissue by homogenization in Tris-HCl buffer, pH 7.8, containing 2 mM $MgSO_4$ and 1 mM EGTA [7, 8]. The homogenized tissue was heated for 5 min at 90°C. After cooling in a mixture of acetone + dry ice the samples were centrifuged at 5000 rpm for 30 min. The calmodulin level in the supernatant was determined by radioimmunassay using kits from "DRG-International" (USA). The results were analyzed by parametric and nonparametric statistical tests.

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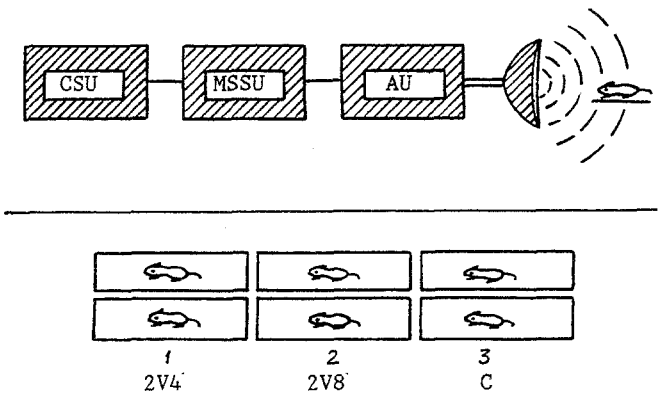

Fig. 1. Diagram of experimental apparatus for irradiating animals with a modulated shf field: 1) irradiation under 2V4, 2) 2V8 conditions, 3) control; CSU) control system unit, MSSU) modulating signal shaping unit; AU) action unit.

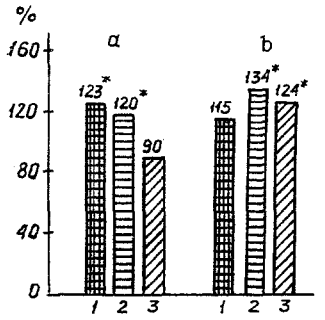

Fig. 2. Calmodulin levels in rat brain structures during exposure to modulated shf field. Ordinate: calmodulin level (in %); abscissa: a) calmodulin level in cortex (1), hippocampus (2), and hypothalamus (3), with exposure to modulated shf field on 2V4 program; b) the same, 2V8 program. *$p \leq 0.05$ Compared with control group.

EXPERIMENTAL RESULTS

Under normal conditions the calmodulin level in intact animals was 491 ± 78 ng/ml in the cerebral cortex, 463 ± 29 ng/ml in the hypothalamus, and 412 ± 70 ng/ml in the hippocampus. Meanwhile. exposure to an shf field modulated on a "2V4" program led to a significant increase in the calmodulin level in the hippocampus (by 34%, $p \leq 0.05$) and hypothalamus (by 24%, $p \leq 0.05$). Irradiation of the animals with an shf field with "2V8" type of modulation was accompanied by a significant increase in calmodulin level in the sensomotor cortex (by 23%, $p \leq 0.05$) and hippocampus (by 20%, $p \leq 0.05$) and by lowering of its level in the hypothalamus (Fig. 2). Consequently, the modulated shf field had a marked effect on calcium-dependent processes taking place with the participation of calmodulin. Moreover, the "2V4" program simultaneously raised the calmodulin level both in the hypothalamus – the center for autonomic regulation and emotional behavior, and also in the hippocampus, a structure playing an active role in the realization of mechanisms of long-term memory. Conversely, the "2V8" program reduced activity of calcium-dependent mechanisms somewhat in hypothalamic structures, but increased their activity in the hippocampus and sensomotor cortex, which is directly connected with integrative activity of the brain.

The principles of information processing in the CNS are based on mechanisms that are universal for all parts of the brain, and based on processes changing the excitability of the neurons. These universal mechanisms regulating intracellular activity include the system of secondary messengers, to which the calcium–calmodulin complex belongs. Calmodulin-dependent phosphorylation and dephosphorylation of membrane and cytosol proteins in the nervous system lead to a change in the characteristics of the neuronal membranes and in relations between individual structural components of the cell. Taken as a whole, these processes enable regulation of the functions of the CNS by calmodulin to take place. It has been shown, for instance, that calmodulin can modify synaptic transmission [7], by its action on mediator biosynthesis (as has been shown for catecholamines and serotonin), mediator secretion, and sensitivity of receptors to neurotransmitters.

Our experiments showed that a low-intensity modulating shf field has a marked influence on calmodulin levels in brain structures, and that the character of this effect is determined by the conditions of modulation. Our results confirm the previous view that the efficacy of low-intensity modulated shf fields is associated with activation of biological amplification mechanisms. Deliberate interference with calmodulin levels in brain structures by means of shf fields may provide a new and nonpharmacologic approach to the correction of nervous and mental disturbances, emotional activity, and memory.

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ACTIVATION OF ATP-SENSITIVE K^+ CHANNELS OF CARDIOMYOCYTES BY ENDOGENOUS CARDIOPEPTIDES

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Among the various biologically active substances, ever-increasing interest is being displayed in compounds of peptide nature, with cardiotropic effects [9]. Endogenous cardiopeptides obtained by extraction from myocardium constitute a new group of these compounds. Despite the varied manifestations of their action on heart muscle, as experimental and clinical studies have shown [14], the molecular and cellular mechanisms of the physiological activity of endogeneous cardiopeptides still remain unexplained. There is evidence of a direct action of these peptides on activity of K^+ channels in nonmyocardial cells [6, 8, 12], but no attempt has been made to verify the presence of such effects of peptides from the heart on K^+ channels of cardiomyocytes.

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