Pharmacological Correction of SHF Radiation-Induced Disturbances in Learning and Memory

I. N. Krylov, V. V. Yasnetzov, A. S. Dukhanin, and Yu. P. Pal'tsev.

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Publications on the effect of electromagnetic superhigh frequency (SHF) radiation on learning and memory processes are scant and contradictory [3]. This fact, together with the widespread use of SHF-equipment in different fields of science and engineering (radio communications, TV, radar, radiospectroscopy, radioastronomy, etc.), suggest the need for a direct investigation of this problem.

The aim of the present study was to elucidate the neurochemical mechanisms responsible for SHF-induced disturbances in learning and memory processes, as well as to investigate the possibility of pharmacological correction of these disorders.

MATERIALS AND METHODS

The experiments were carried out on male Wistar rats weighing 180-200g. The rats were trained in the passive avoidance response (PAR) and immediately thereafter were subjected to SHF radiation (12.6 cm, 2375 MHz, 1 mW/cm^2, 1h). The parameters of SHF radiation were constantly monitored. During the irradiation, rats in individual cages made of radiotransparent materials were placed inside a screened chamber in an uniform electromagnetic field. The animals of the control groups underwent conditioning, followed by a false irradiation. For radioreceptor analysis, rats were decapitated, the brain was removed rapidly in the cold, and the cortex, brain stem, and cerebellum were isolated [8]. The cell membrane fraction from the indicated regions were separated after Simantov and Shyder [9]. ^{14}C-GABA, ^{3}H-flunitrazepam and ^{3}H-quinuclidinylbenzylate were used as ligands for the GABA-, benzodiazepin- (BD) and M-cholinoreceptors, respectively. The following binding characteristics were assessed: the maximal number of binding sites (B_{max}) and the equilibrium dissociation constant (K_d). In separate experiments the following drugs were intraperitoneally injected: naloxone (1 mg/kg), piracetam (100 mg/kg), and oxiracetam (10 mg/kg).

RESULTS

Behavioral experiments revealed that SHF radiation caused retrograde amnesia in rats, manifested as a reduction of PAR retention after irradiation (see Fig. 1). Naloxone, a multi-purpose opioid receptor blocker, when intraperitoneally injected (1 mg/kg) 50 min prior to conditioning and following irradiation, significantly ($p<0.05$) weakened the amnestic effect of SHF radiation. Consequently, it may be assumed that the endogenous opioid system is involved in the genesis of the radiation-induced retrograde amnesia.

Department of Pharmacology, Research Laboratory of Hydrobiont Bioactive Compounds, Ministry of Health of Russia; Department of Molecular Pharmacology and Radiobiology, Russian State Medical University, Moscow. (Presented by P. V. Sergeev, Member of the Russian Academy of Medical Sciences)

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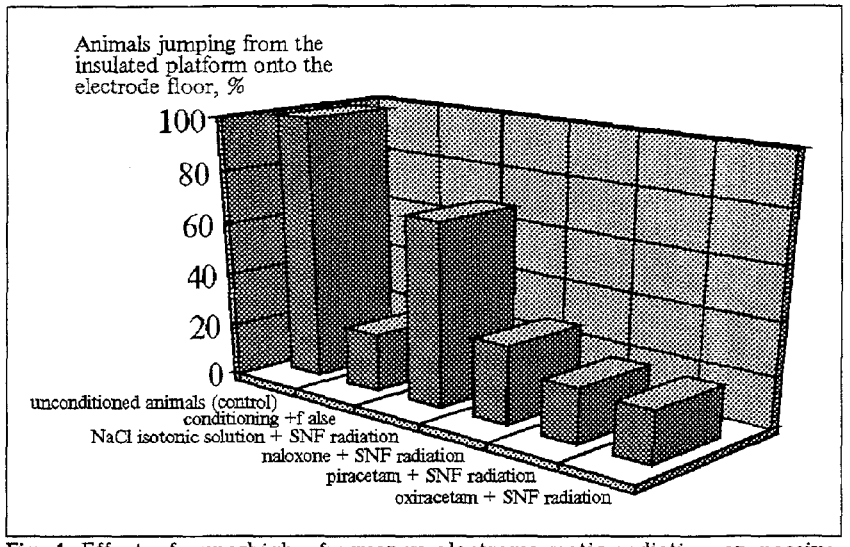

Fig. 1. Effect of superhigh-frequency electromagnetic radiation on passive avoidance response conditioning in rats.

The radioreceptor analysis in vitro showed a reduction of the BD-receptor concentration in the cerebellum from 75 fmol/mg in the control to 44 fmol/mg after irradiation, as well as a decreased capacity of the GABA receptors in synaptic membranes separated from the cortex and cerebellum (the reduction of B_{max} value for ^{14}C-GABA was 31 and 35% in irradiated and control animals, respectively); the number of M-cholinoreceptors in the cortex was increased by 31%. Moreover, SHF irradiation altered the coupling of GABA and BD receptors in the synaptic membranes of the cortex. To determine this, the specific binding of ^{3}H-flunitrazepam in the presence of 10^{-5} M GABA was assessed. The addition of 10^{-5} M GABA to the medium led to a reliable enhancement of the BD-receptor affinity to ^{3}H-flunitrazepam. The number of specific binding sites was unchanged. The GABA-induced increase in the binding affinity of BD receptors in the synaptic membranes was considerably less pronounced in treated rats compared to the control animals.

The involvement of opioidergic, benzodiazepin, GABA, and cholinergic components in the amnestic effect of SHF radiation, together with the impaired coupling between the GABA- and BD-receptor systems in the cortex, opens up prospects for pharmacological correction of the amnestic effect of SHF radiation. Evidently, the agents chosen should be those which act via the indicated pathways. Of the drugs currently used, the relatively new class of psychotropic agents, the pyrrolidone-derived nootropics (piracetam, oxiracetam, etc), best satisfy these requirements. Despite the fact that the mechanisms of action of nootropic agents are not completely understood, an important role of the cholinergic system [10], as well as the involvement of the benzodiazepin component have been established [2,6]; there are also some data (albeit contradictory) on the involvement of the GABA-ergic system [1,7]. Previously we demonstrated the involvement of the opioidergic component in the nootropic activity of piracetam and oxiracetam [4]. In this connection, the next series of experiments was undertaken to evaluate the effect of piracetam and oxiracetam on SHF radiation-induced amnesia.

The results presented in Fig. 1 show that 100 mg/kg piracetam and 10 mg/kg oxiracetam, intraperitoneally injected, prevented the development of radiation-induced amnesia.

Thus, the experiments showed the efficacy of the nootropics piracetam and oxiracetam as drugs for pharmacological correction of learning and memory disturbances induced by SHF radiation.

TABLE 1. Parameters of Specific Binding of ^{3}H-Flunitrazepam (I), ^{14}C-GABA (II), and ^{3}H-Quinuclidinylbenzylate (III) to Synaptical Membranes in Different Structures of Rat Brain

Brain regions	I		II		III	
	Kd	Bmax	Kd	Bmax	Kd	Bmax
			Control			
Cortex	9±1	0.066±0.008	17±3	3.9±0.3	4.0±0.3	0.91±0.06
Brain stem	16±3	0.019±0.004	42±6	0.35±0.03	6.2±0.4	0.26±0.05
Cerebellum	14±3	0.075±0.009	10±1	8.8±0.6	7.0±1.0	0.12±0.01
			SHF radiation			
Cortex	11±2	0.053±0.009	21±3	2.7±0.1*	4.2±0.3	1.32±0.05*
Brain stem	19±5	0.013±0.002	50±6	0.37±0.04	5.3±0.5	0.29±0.04
Cerebellum	12±3	0.044±0.006	15±2	5.7±0.4*	8.0±2.0	0.11±0.01

Note: Kd – equilibrium dissociation constant of ligand-receptor complex (nM), Bmax – maximal concentration of binding sites (nmol/mg protein); asterisk means significant differences from the control ($p<0.05$).

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Evaluation of the Antipyretic Effect of Psychotropic Agents and Their Influence on the Fever-Lowering Effect of Acupuncture

M. V. Nezhentsev and S. I. Aleksandrov

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At present, strenuous efforts are being directed toward the development of new therapeutic approaches as an alternative to the antipyretic and hypothermic drugs traditionally used to treat fever [6,9,10]. Despite the beneficial centuries-old application of acupuncture (AP) for fever reduction, no scientific explanation for this phenomenon has been found [3, 14]. In clinical observation, the antipyretic effect of AP in different hyperpyrexias turns out to be pronounced but short-lived [7,11,13]. It is thus desirable to seek new ways for prolonging and enhancing the antipyretic effect of AP by combining with pharmacological agents [1,4,5].

Department of Pharmacology , Pediatric Medical Institute, St.Petersburg.
(Presented by P. V. Sergeev, Member of the Russian Academy of Medical Sciences)

The aim of the present study was to investigate the effect of several psychotropic drugs on the antipyretic effect of AP.

MATERIALS AND METHODS

The experiments were carried out on 36 male Chinchilla rabbits weighing 2.5-3.5 kg. Pyrogenal (1 μg/kg) was injected intravenously for fever induction [8]. AP was performed at the shao-shan (P-11) and shan-yan (GI-1) point analogs 45 min after the start point for 30-45 sec [12]. The rectal temperature was measured with a TET-C-11 thermometer every 15 min for 6 h, inserting the probe 8 cm into the rectum.

Each set of experiments was performed on 9 animals. The control group consisted of animals on which AP was performed outside the points studied or in which AP was combined with physiological

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