6-hydroxydopamine. Meanwhile there are reports in the literature that the hyperthermic effect of PG can be weakened by injection of α-adrenoblockers [10, 11], atropine [5], and serotonin antagonists [10] into the ventricles or into hypothalamic structures.

According to the results of the present experiments PG-hyperthermia is effectively prevented by hemicholinium-3. However, this substance is reported to have a marked action on membranes and, for that reason, the effect observed evidently cannot be explained purely in terms of the anticholinergic action of the drug.

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EFFECT OF ETHIMIZOLE ON RNA-SYNTHESIZING ACTIVITY OF RAT BRAIN CELL NUCLEI DURING LEARNING

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KEY WORDS: ethimizole; RNA synthesis; cerebral cortex; hippocampus; rats; irradiation.

Activation of the genetic apparatus of nerve cells may be the trigger factor in induction of synthesis of macromolecules (RNA and polypeptides) which participate in learning and memory processes [2, 6]. One of the most important indicators of activity of the genetic apparatus of cells is the RNA-polymerase activity of the nuclei, characterizing the level of chromatin transcription.

The object of this investigation was to study the effect of ethimizole (bis-1-ethylimidazole-4,5-dicarboxylic acid bis-methylamide), which increases the intensity of memory processes in man and animals [1, 4, 5], on RNA synthesis in isolated nuclei of the cerebral cortex and hippocampus during the formation and consolidation of conditioned reflexes in rats.

EXPERIMENTAL METHOD

Experiments were carried out on 155 male Wistar rats weighing 180-200 g. In the experiments of series I the animals were taught to solve a problem of conditioned active avoidance

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TABLE 1. Incorporation of ^{3}H-UTP (in cpm/mg DNA) into Acid-Insoluble Fraction of Isolated Cell Nuclei from Cerebral Cortex and Hippocampus of Rats during Learning

Group of animals	Number of animals	Experimental conditions	Cortex	Hippocampus	%	Ratio of activity cerebral cortex/hippocampus
1	60	Control (untrained)	599 598*	299 596*	100	2,0
2	10	Trained (CAA + physiological saline)	367 125*	280 625	93,7	1,3
3	10	Trained (CAA + (ethimizole)	371 714*	867 400†	289,5	0,4
4	25	Trained (RSSAFR + physiological saline)	377 000	362 000	120,8	1,0
5	25	Trained (RSSAFR + ethimizole)	277 000	497 000†	169,9	0,5
6	25	Untrained animals + ethimizole	372 000	413 000†	137,9	0,8

*P < 0.01.
†P < 0.001.

(CAA) of a painful electric shock in a Y-maze in response to light. CAA was formed in the course of four days, at the rate of one series of 10 tests daily. The criterion of learning was 80% of correct responses on the 4th day of training. In the experiments of series II the rats were taught a response of spontaneous spatial alternation of food reinforcement (RSSAFR) in a complex maze designed by A. M. Kotin and V. D. Savel'ev. Training took place for 10 min daily for 8 days. The criterion of learning was 10 correct findings of food in particular branches of the maze in the course of 10 min. Ethimizole (1.5 μg/kg) and physiological saline (control) were injected intraperitoneally in both series of experiments daily 30 min before training. The animals were decapitated 90 min after completion of the last series of training. Isolated cell nuclei from the cerebral cortex and hippocampus of the rats were obtained at 4°C by a modified method [12]. The purity of the nuclei was verified microscopically by staining them with toluidine blue. The RNA-synthesizing activity of the nuclei [9] was estimated and DNA [7] and protein [11] were determined.

EXPERIMENTAL RESULTS

It will be clear from Table 1 that training in CAA and RSSAFR was accompanied by a significant fall in incorporation of ^{3}H-UTP, the labeled precursor of RNA synthesis, into the TCA-insoluble fraction of the cell nuclei in the cerebral cortex and by an increase in RNA synthesis in the hippocampus during learning with positive reinforcement (Table 1, group 4). Under these circumstances the ratio of RNA-polymerase activity in the cerebral cortex to that of the hippocampus fell from 2.0 in the control to 1.3-1.0 after learning. Preliminary injection of ethimizole, a compound which accelerates trace consolidation and increases the duration of preservation of a habit [5], increased the uptake of labeled UTP in the hippocampus by 70-190% and considerably reduced the ratio of RNA-polymerase activity in the cerebral cortex to that in the hippocampus. Control injections of ethimizole for 8 days, unaccompanied by training, caused a less marked increase in RNA synthesis in the hippocampus (by 38%) and lowered its level in the cortex.

The results are in agreement with those of experiments [8, 10] in which an increase in RNA synthesis also was found in the hippocampal neurons during training, evidence of the important role of activation of the genetic apparatus in the brain structure under the influence of physiological and pharmacological agents. This suggests that ethimizole activates

the genetic apparatus of nerve cells, in particular of the hippocampus, and this contributes to the fixation and subsequent consolidation of the conditioned reflexes. This hypothesis is in agreement with data in the literature [3] according to which ethimizole produces dilatation of the cisterns of the endoplasmic reticulum and intensifies protein synthesis on the ribosomes.

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EFFECT OF HIRUDIN—THROMBIN AND PHENYLMETHYLSULFONYL—THROMBIN PREPARATIONS ON SOME BLOOD CLOTTING CHARACTERISTICS

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KEY WORDS: thrombin; anticlotting system; phenylmethylsulfonyl—thrombin; hirudin—thrombin; receptors.

The reflex act of the anticlotting system (ACS) of the blood is known to begin with excitation of chemoreceptors of the vascular system under the influence of thrombin [9]. This is shown by the results of experiments in which the humorally isolated kidney and carotid sinus of rabbits and the carotid sinus and carotid labyrinth of frogs were perfused with thrombin. Prethrombin-1, a product of proteolysis of prothrombin by thrombin or plasmin, which possesses neither clotting nor esterase activity, can also induce excitation of the ACS during perfusion of the frog's carotid labyrinth [6, 11].

Activation of the ACS is due to direct interaction of thrombin with receptors in the vessel wall. It has been shown that thrombin can specifically bind with membrane receptors of the endothelial cells of the umbilical vein [12]. Binding of thrombin with receptors stimulates a response of liberation of prostacyclin from the endothelial cells. This reaction requires integrity of the catalytic region of the active center of the enzyme, for diisopropylphosphothrombin (DP-thrombin), although it binds with endothelial receptors, does not induce liberation of prostacyclin [12].

In most investigations mechanisms of interaction of thrombin with its specific receptors on platelets have been studied. The initial degree of interaction of thrombin with the receptor protein of the platelets is its binding with the reactive site of the receptor [14]. However, binding of thrombin with the receptor is an essential but insufficient condition for

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