BEHAVIORAL AND BIOCHEMICAL CHARACTERISTICS OF RATS PREFERRING ETHANOL OR WATER

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KEY WORDS: ethanol; RNA synthesis; irradiation.

The study of function of the genetic apparatus of nerve cells in experimental alcoholism has so far been confined chiefly to the study of the effect of acute and chronic administration of ethanol on protein content and metabolism in nucleic acids. Meanwhile there is virtually no information in the literature on RNA and protein biosynthesis in the brain of animals with free choice as regards consumption mainly of ethanol or water [8]. Considering that learning and memory processes are largely determined by the intensity of RNA synthesis in specific brain structures [1, 4], it was decided to study the relationship between learning ability of rats preferring ethanol or water and the level of RNA-synthesizing activity of brain cell nuclei.

EXPERIMENTAL METHOD

Experiments were carried out on 109 noninbred male rats weighing 200 ± 20 g, divided into three groups [9]: 1) animals preferring ethanol, 2) animals of the intermediate group, 3) animals preferring water. Two to 3 months after selection of the animals they were taught a conditioned active avoidance reflex (CAAR) of electrical stimulation in a Y-maze or a spatial alternation of food reinforcement response (SAFRR) in a complex maze. CAAR formation was undertaken for 5 days every week, with one series daily, consisting of 10 tests. The criterion of learning was 50% of correct responses on the 5th day of training. During SAFRR formation the rats were taught to take food alternately (pieces of cheese weighing 0.15-0.20 g) in two different passages of the maze. The criterion of learning was obtaining 10 correct responses (finding food with the shortest length of transit between passages in which the reinforcement was given, in the course of 10 min).

RNA-synthesizing activity of cell nuclei from cortical gray matter of the animals was determined 1 month after selection by measuring incorporation of ^{3}[H]uridine triphosphate (UTP) as described previously [10]. The DNA content in the nuclei (70-80% of nuclei in the isolated fractions were nuclei of neurons) was measured by the method in [11]. In each experiment cerebral cortex from three rats was used. The numerical results were subjected to statistical analysis by Student's test at $P \leq 0.05$.

EXPERIMENTAL RESULTS

A significant decrease in the number of correct responses was found in the rats of group 1 on the 3rd, 4th, and 5th days of training in CAAR compared with animals of groups 2 and 3 (Fig. 1). Conversely, the speed and effectiveness of training in SAFRR in the complex maze were greater in the animals of group 1 than in rats preferring water (Fig. 2). In this particular case the mean duration of training was 7.0 ± 1.08 and 10.0 ± 1.11 days respectively ($P < 0.05$).

Comparison of the intensity of [^{3}H]-UTP incorporation into cell nuclei of the cerebral cortex of the animals of group 1 (ethanol accounted for over 50% of the total fluid consumption), animals of group 2 (ethanol about 30% of the total), and animals of group 3 (ethanol under 10% of total consumption), no significant differences were found between groups. How-

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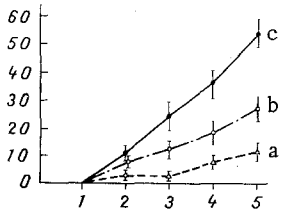

Fig. 1

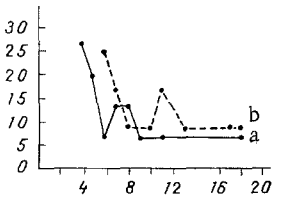

Fig. 2

Fig. 1. Speed of learning CAAR by rats. Abscissa, duration of learning (in days); ordinate, number of correct responses (in %): a) rats of group 1, b) group 2, c) group 3.

Fig. 2. Ability of rats to learn SAFRR in complex maze. Abcissa, duration of learning (in days); ordinate, percentage of animals achieving criterion of learning: a) rats of group 1, b) of group 3.

TABLE 1. Incorporation of [^{3}H]Uridine Triphosphate into Cerebral Cortical Cell Nuclei of Rats (M ± m; P = 0.05)

Parameter	Group of animals		
	ethanol consumption over 80%	2-	ethanol consumption under 10%
No. of expts.	7	5	7
Level of incorp. of label, cpm/mg/DNA	792 454±54 844*	524 381±38 347**	844 646±18 008

Legend. *P < 0.05, **P < 0.01 compared with animals of group 3. Cerebral cortex from three rats used in each experiment.

ever, in rats whose ethanol consumption was more than 80% of the total a much lower level of incorporation of label was observed than in the animals of groups 2 and 3 (Table 1).

The main parameter characteristic of animals preferring ethanol, namely a low blood ethanol level, did not depend on ethanol consumption and was discovered before selection [8]. It is unlikely that these results were attributable to ethanol consumption in the course of selection, for the experiments were carried out 1-3 months after selection. Besides increased ability to utilize alcohol, animals preferring ethanol also are less sensitive to it; in the opinion of some workers, this is connected with structural and functional features of the brain cell membranes [12, 14]. In particular, acetylcholinesterase activity is lower in the brain of rats preferring ethanol, and their serotonin level is higher [15]. Experiments [5-7] have demonstrated the effect of acetylcholine, of acetylcholinesterase inhibitors, and of acetylcholine receptor blockade on the content and synthesis of RNA in brain cells. This effect may differ in different brain structures, depending on the concentration of neurotransmitter, the season of the year, and the batch of animals [7]. Since accumulation fo cyclic GMP and of Ca^{++} ions in the cell is linked with acetylcholine, the initial level of these factors, depending on the animal's physiological state, may perhaps determine the direction of the acetylcholine effect.

A no less interesting fact is the change in monoamine levels in rats preferring ethanol [2]. A predominant increase in the serotonin concentration and some decrease in the noradrenalin concentration in the brain were observed. The latter fact provides a satisfactory explanation of the results of this investigation from the standpoint of Gromova's hypothesis [3], according to which reciprocal relations exist between serotoninergic and noradrenergic brain systems in the consolidation of information. The present experiments showed that learning with positive reinforcement is accompanied by elevation of the brain serotonin level, by contrast with lowering of the catecholamine levels. Opposite relationships were observed in the case of learning with negative reinforcement.

The altered behavior of animals preferring ethanol is thus evidently based on disturbed interaction between mediator and genetic structures of brain cells.

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ENDOCRINE AND METABOLIC MECHANISMS OF THE PATHOLOGICAL SYNDROME INDUCED BY HOMOLOGOUS GLIAL TISSUE ANTIGENS IN MONKEYS

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Exposure to immunoneurophysiological factors (using antigens of brain origin of different kinds or antisera against them) may lead to significant changes in functions of the CNS. An original model has been developed at the Institute of Pathological Physiology, Medical Faculty, Belgrade University, in which antigens of glial tissue of homologous monkey brain are used as the antigenic stimulus [11]. Immunization with these antigens led to the development of a pathological syndrome including disturbances of CNS functions (changes in the animals' behavior, ability to form new and reproduce old conditioned reflexes, and so on), as well as endocrine disturbances, expressed as depression of thyroid function [4-6, 13].

The aim of the present investigation was to continue the study of some endocrine and metabolic mechanisms of development of this syndrome, including parameters of function of the hypothalamo-hypophyseo-adrenocortical and hypothalamo-hypophyseo-thyroid systems (HHACS and HHTS respectively), and also parameters of serum protein metabolism, investigated in immunized and unimmunized animals at rest and exposed to stress.

EXPERIMENTAL METHOD

Experiments were carried out on six monkeys (*Macaca mulatta*) of both sexes, divided into two equal groups. The animals of group 1 were immunized with complex glial antigen in the form of an emulsion prepared from 0.5 ml of glial tissue homogenate from an animal of the same blood group. 0.25 ml of Freund's complete adjuvant (from "Difco," USA), and 0.21 ml of "Areacel A" mineral oil (from "Serva," West Germany), which was injected intramuscularly in four separate doses with intervals of 1 week (total dose of protein injected about 50 mg).

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