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Effect of Eiconol Enriched with ω-3 Polyunsaturated Fatty Acids on Rat Behavior and Alcohol Motivation

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We evaluated the effect of eiconol containing polyunsaturated fatty acids on the behavior and alcohol motivation in rats. Administration of eiconol for 10 days to alcoholized rats against the background of ethanol deprivation produced a sustained suppression of alcohol motivation and corrected deprivation-specific behavior.

Key Words: *eiconol; polyunsaturated fatty acids; behavior; alcohol motivation; rats*

Eiconol is a complex of essential polyunsaturated fatty acids (PUFA) of the ω-3 and ω-6 families (in a ratio of 8:1, approximating the optimal ratio for humans) and vitamins A, D, and E. This preparation produced by Trinita company is widely used for prevention and therapy of many cardiovascular diseases. Recent studies revealed the effect of eiconol on learning and memory in humans. It was also shown that eiconol increased the number of correct responses and decreased the number of incorrect responses in a sensorimotor test [2]. However, this was paralleled by an increase in the number of delayed reactions, presumably due to potentiation of the cognitive component of the decision making process.

Similar results were obtained in animal experiments. Daily intraperitoneal injection of α-linolenic and linoleic acids, the major active components of eiconol, to rats for 3-4 weeks considerably increased the number of correct responses in the Morris water maze [11]. On the other hand, long-term α-linoleic acid deficiency in mice impaired learning and reduced the duration of stay in open plus-maze arms, which indicated enhanced anxiety of experimental animals [4].

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The effects of PUFA on animal behavior and emotional status were also described. M. Raygada *et al.* [9] showed that the progeny of mice maintained on ω-6 PUFA-enriched diets during pregnancy was much more active in the open field test, more aggressive in the resident-intruder test, and showed shortened immobilization in the forced swimming test in comparison with progeny of females fed standard diets.

PUFA determine cell membrane fluidity, which, according to some reports, can modulate cognitive processes [6,10,11]. Moreover, low content of α-linolenic acid in mouse ration changes phospholipid fatty acid composition mainly in the cerebral frontal cortex and striatum, while addition of deficient phospholipids restored the neuronal membrane composition in all examined structures of the brain except the frontal cortex [4,7].

Some scientists explain behavioral disorders and impaired learning in rodents kept on a PUFA-deficient diet by modulation of the dopamine- and serotoninergic systems [3,5] playing the leading role in the formation of alcohol motivation [1]. Moreover, ω-3 PUFA modify neurotransmission in rat frontal cortex [5,7].

We investigated the effects of preparations enriched with ω-3 fatty acids on the behavior and alcohol motivation in albino rats.

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MATERIALS AND METHODS

Male albino rats (250-300 g) were divided into 4 groups: groups 1 and 2 consisted of intact rats; group 3 and 4 rats were alcoholized for 4 months.

Group 2 and 4 rats received eiconol (0.45 g/rat) for 10 days (groups 1 and 3 served as the control). The animals were daily put into individual cages, each experimental rat received rye bread with eiconol. Alcoholized rats (experimental and control) were deprived of ethanol for this period. Behavioral tests were carried out before and after eiconol treatment.

Behavioral testing was carried out using a RODEO automated device for evaluation of motor, orientation, and exploratory activity and an elevated plus-maze for evaluation of the anxiety level. For each parameter the difference (Δ) between the first and second testing was estimated.

After the second testing all rats were put into individual cages under conditions of free choice between 15% ethanol and water for evaluation of alcohol motivation. Mean daily ethanol and water consumption was recorded throughout the observation period. In groups 1 and 2 the effect of eiconol on the formation of alcohol motivation was studied and in alcoholized rats changes in alcohol motivation after deprivation and eiconol treatment were evaluated.

RESULTS

In group 1, testing repeated after 10 days showed only minor changes in rat behavior in an elevated plus-maze (Fig. 1, *a*). Only the duration of freezing slightly increased (Fig. 2), which can be regarded as adaptation to experimental conditions.

In alcoholized controls (group 3) alcohol deprivation increased all parameters, in particular, the time spent in open arms ($p<0.05$ *vs.* group 1, Fig. 1, *a*). The duration of freezing in the maze is the most demonstrative parameter in this respect (Fig. 2). In native controls, the mean Δ for this parameter was 55 sec, while in alcoholized controls it decreased by 17 sec ($p<0.05$ *vs.* group 1) indicating increased anxiety of alcoholized rats during alcohol deprivation. In alcoholized rats treated with eiconol during deprivation (group 4), the time spent in open arms differed significantly from that in group 3 ($p<0.05$, Fig. 1, *b*) and approximated the value in native controls. The dura-

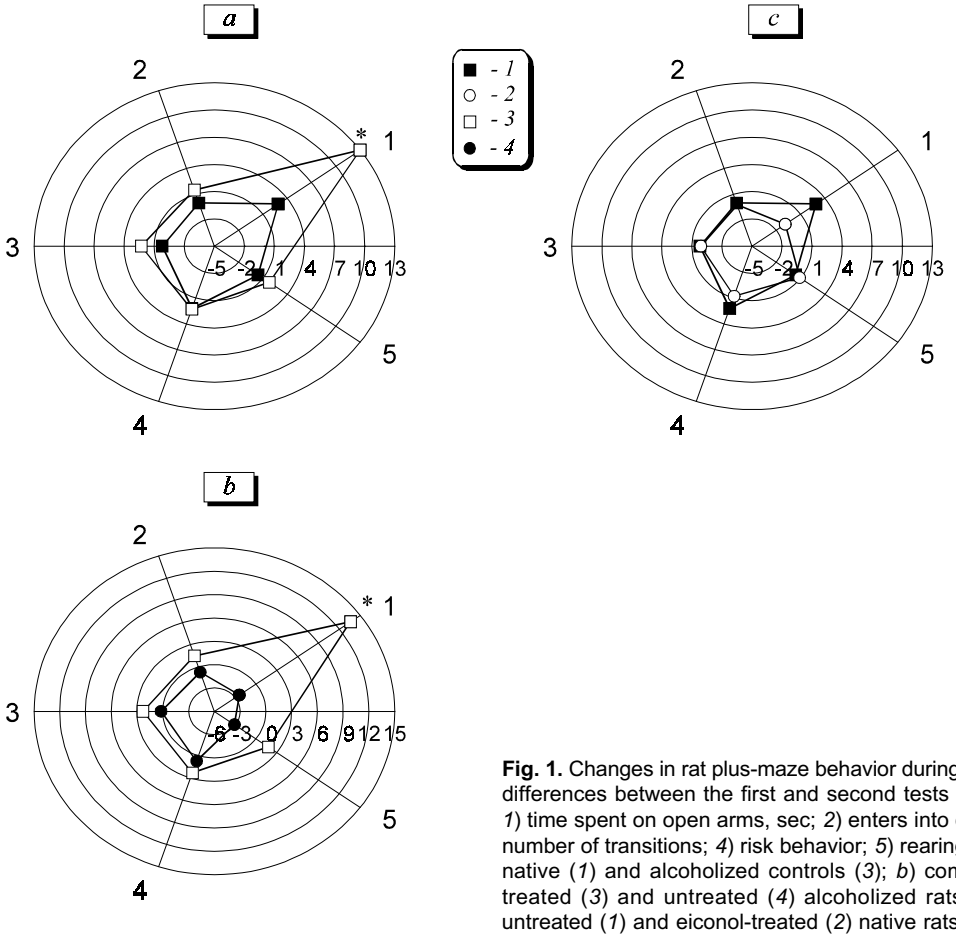

Fig. 1. Changes in rat plus-maze behavior during second testing. The differences between the first and second tests are plotted on axes: *1*) time spent on open arms, sec; *2*) enters into closed arms; *3*) total number of transitions; *4*) risk behavior; *5*) rearings. *a*) comparison of native (*1*) and alcoholized controls (*3*); *b*) comparison of eiconol-treated (*3*) and untreated (*4*) alcoholized rats; *c*) comparison of untreated (*1*) and eiconol-treated (*2*) native rats. *$p<0.05$ significant differences between compared groups.

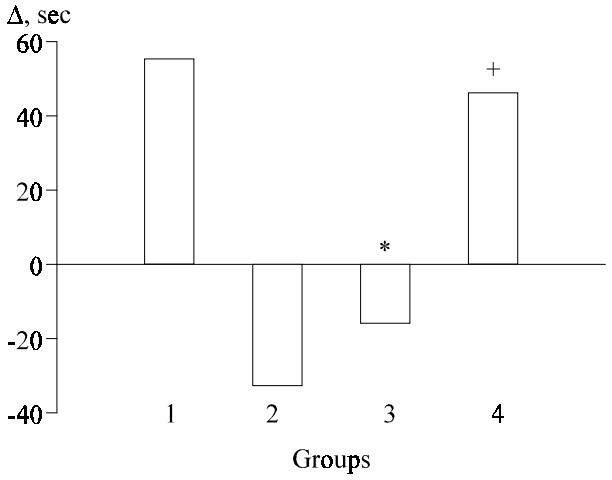

Fig. 2. Changes in freezing time in a plus-maze during the second test. $p<0.05$: *compared to group 1, +compared to group 3.

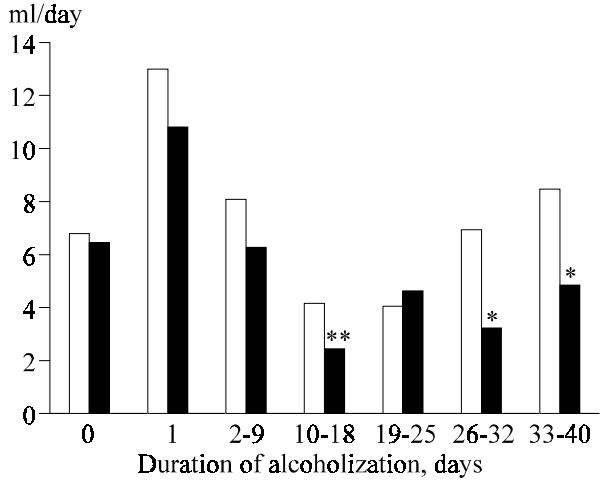

Fig. 3. Consumption of 15% ethanol by alcoholized rats. Light bars: controls; dark bars: eiconol-treated rats. 0) before eiconol treatment. *$p<0.05$, **$p<0.05$ compared to the control.

tion of freezing in group 4 increased like in native controls (Fig. 2). The duration of freezing in alcoholized rats treated and not with eiconol differed significantly ($p<0.05$).

Differences in the open field behavior in the RODEO setup were less pronounced, but similarly directed. The corrective effect of eiconol on alcoholized rats in this test manifested mainly in a decreased number of explored holes compared to that in alcoholized controls.

Hence, eiconol corrected changes in the behavior of alcoholized rats caused by alcohol deprivation, probably due to compensation for PUFA deficit provoked by chronic ethanol consumption [6]. This assumption is confirmed by the fact that eiconol had no effect on the behavior of native rats (group 2). Shortening of the immobilization time in the elevated plus-maze compared to native controls was insignificant (Fig. 2). Other parameters of plus-maze behavior and motor and exploratory activity in the RODEO test remained unchanged (Fig. 1, *c*).

Consumption of 15% ethanol by native control rats and eiconol-treated rats under conditions of free choice was virtually the same, therefore eiconol had no effect on the formation of alcohol motivation in non-alcoholized rats. The volumes of consumed water were also the same.

Evaluation of the effect of eiconol on alcohol motivation in alcoholized rats showed that the volumes of consumed ethanol in these two groups before the experiment were virtually the same (Fig. 3). On day 1 of deprivation, alcohol consumption usually increased. In our experiments ethanol consumption in the control group on day 1 increased 1.9 times. In rats receiving eiconol during deprivation ethanol consumption also increased, but to a lesser extent (86% of the control). Ethanol consumption in experimental rats was decreased throughout the observation period (40 days). These differences were significant on days 10-18 ($p<0.05$) and, especially, on days 26-40 ($p<0.005$) of alcoholization.

These data indicate that eiconol reduced alcohol motivation and corrects the behavior of alcoholized rats during ethanol deprivation. The effect of PUFA on rat behavior can be explained by the formation of compounds similar to the recently discovered anandamine, cannabinoid endogenous receptor ligand [8].

The efficiency of eiconol in decreasing alcohol motivation in humans requires special investigation, the more so as this drug is recommended for wide use.

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