EFFECT OF BILATERAL AVOIDANCE CONDITIONING ON BRAIN LIPID COMPOSITION IN RATS

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Lipids play an important role in the function of membranes, for they determine their viscosity, the state of their receptors and ionic channels, and the activity of membrane-bound enzymes [9]. It has been shown that the lipid component of synaptosomes is a modulator of activity of the serotoninergic system [2]. Differences in the lipid composition of the brain have recently been demonstrated in mice selected on the basis of different brain weight and differing in their learning ability [1]. One of the most important processes leading to modification of the lipid component of membrane is free-radical lipid peroxidation (LPO), changes in the intensity of which accompany many changes in brain function [1, 2, 4, 8].

The aim of this investigation was to study the state of LPO and of the brain lipid composition during training.

EXPERIMENTAL METHOD

Experiments were carried out on 42 noninbred male albino rats weighing 150-200 g. Bilateral avoidance conditioning (AC) was conducted in a shuttle box. The conditioned stimulus was a flashing light, and after it had acted for 5 sec an electric current of individually chosen strength was applied to the floor of the box. The duration of AC was 30 min. Animals performing five or more conditioned avoidance responses in succession were taken as trained (TR). Animals failing this test constituted the group of untrained rats (UTR). The active control (C) group comprised rats receiving the same number of conditioned and unconditioned stimuli, but not in combination.

The rats were decapitated after the end of training and the concentration of LPO products reacting with 2-thiobarbituric acid [13], conjugated dienes [7], and superoxide dismutase activity [12] were determined in homogenates of the cerebral cortex and hippocampus. The concentration of Schiff's bases in brain lipid extracts was determined as in [10] and the lipid composition of the extracts was determined by thin-layer chromatography [14].

EXPERIMENTAL RESULTS

The results are given in Table 1. Changes observed in the C group reflect the action of acute stress (electric shocks, flashes). Changes in the intensity of LPO, activation of scavenging of superoxide radicals, lowering of the cholesterol level, phospholipid accumulation, and changes in the phospholipid spectrum, discovered in this group, were identical with those found previously in the initial phase of stress caused by painful electrical stimulation and by immobilization [5, 6]. The LPO level was low in rats receiving combinations of electric shock and flashes, but the intensity of superoxide radical scavenging was high. According to all the parameters studied in rats of the TR group the degree of inhibition of LPO and of activation of superoxide radical scavenging was higher than in the UTR group. Phospholipid accumulation also was more marked in rats of the TR group.

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TABLE 1. Changes in Parameters of LPO and Lipid Composition in Cerebral Cortex and Hippocampus of Rats during Avoidance Conditioning (in % of corresponding parameters for passive control group) ($M \pm m$)

Parameter	C (10)	TR (7)	UTR (15)
TBA-active products (cortex)	53,4±1,4	16,1±3,4	45,3±2,5
	$p_1<0,01$	$p_{1,2}<0,01$	$p_{1,3}<0,01$
TBA-active products (hippocampus)	53,7±0,9	18,3±5,2	48,1±3,0
	$p_1<0,01$	$p_{1,2}<0,01$	$p_{1,3}<0,01$
Conjugated dienes (cortex)	49,4±5,0	42,2±9,8	70,4±3,2
	$p_1<0,01$	$p_1<0,01$	$p_1<0,01$, $p_{2,3}<0,05$
Conjugated dienes (hippocampus)	46,8±3,1	45,1±8,4	66,7±3,0
	$p_1<0,01$	$p_1<0,01$	$p_1<0,01$, $p_{2,3}<0,05$
Schiff's bases (cortex)	72,4±0,5	48,7±1,9	60,9±2,0
	$p_1<0,01$	$p_{1,2}<0,01$	$p_1<0,01$, $p_{2,3}<0,05$
Scavenging of superoxide radicals (cortex)	288,0±10,0	237,8±16,1	184,8±13,1
	$p_1<0,01$	$p_1<0,01$, $p_2<0,05$	$p_{1,2}<0,01$
Scavenging of superoxide radicals (hippocampus)	266,9±12,4	224,1±7,4	169,5±9,4
	$p_1<0,01$	$p_1<0,01$, $p_2<0,05$	$p_{1,2}<0,01$, $p_3<0,05$
Chlolesterol	86,7±3,3	152,4±6,3	147,4±5,6
	$p_1<0,01$	$p_{1,2}<0,01$	$p_{1,2}<0,01$
Phospholipids	116,8±1,5	133,7±4,3	111,3±3,3
	$p_1<0,01$	$p_1<0,01$, $p_2<0,05$	$p_1<0,01$, $p_3<0,05$
Cholesterol/phospholipids	74,1±3,3	115,2±1,0	114,0±4,3
	$p_1<0,01$	$p_1<0,01$, $p_2<0,05$	$p_1<0,5$, $p_2<0,01$, $p_3<0,05$
Sphingomyelin	118,6±2,4	111,9±3,1	105,4±2,1
	$p_1<0,01$	$p_1<0,01$, $p_2<0,05$	$p_2<0,01$, $p_3<0,05$
Phosphatiylcholine	84,2±1,1	88,2±1,8	90,6±2,8
	$p_1<0,01$	$p_1<0,01$, $p_2>0,5$	$p_1<0,01$
Phosphatidylethanolamine	87,3±2,2	83,5±0,6	110,0±0,5
	$p_1<0,01$	$p_1<0,01$	$p_{1,2,3}<0,01$
Phosphatidylserine	76,9±0,7	87,4±0,8	82,1±1,9
	$p_1<0,01$	$p_1<0,01$, $p_2<0,05$	$p_1<0,01$
Phosphatidylinositol	128,1±2,1	135,4±1,6	124,9±3,1
	$p_1<0,01$	$p_1<0,01$, $p_2<0,5$	$p_1<0,01$, $p_3<0,05$
Cardiolipin	123,7±1,4	147,1±1,2	83,5±1,2
	$p_1<0,01$	$p_{1,2}<0,01$	$p_{1,2,3}<0,01$

Legend. p_1, p_2, p_3) significance of differences from passive control, active control, and trained groups, respectively. Number of experiments shown in parentheses.

*) Data on lipid composition given only for lipid extracts of cerebral cortex.

The fact that cholesterol accumulated in the brain of rats subjected to combined stimulation by flashes and electric shock, unlike in the C group in which the cholesterol level was depressed, deserves particular attention. Lowering of the cholesterol level was observed previously in models of acute stress [5, 6]. Cholesterol accumulation accompanied by depression of LPO cannot be unequivocally explained by the existing theory of free-radical regulation of metabolism [3].]

The cholesterol/phospholipids ratio was higher in the TR and UTR groups than in either the passive or the active control groups. Individual differences in the cholesterol/phospholipids ratio were exceedingly small in all the groups tested (the difference between the extreme values was by 1.06 times) except the UTR group (in which the difference was 1.82 times). Changes in the phospholipid concentration as a rule were in the same direction in the C, TR, and UTR groups, with the exception of changes in the phosphatidylethanolamine and cardiolipin levels in the UTR group than in the C group is noteworthy.

The main distinguishing feature of the brain lipid composition of the TR and UTR animals is the considerable accumulation of cholesterol in the brain (the cholesterol concentration was 1.5 times higher than in the passive control and 1.7-1.8 times higher than in the active control). The specificity of this phenomenon for the brain of animals exposed to combinations of stimuli is confirmed by the opposite direction of changes in the cholesterol concentration on the C group, which received the same stimuli but not in combination, and also by the fact that in cases described hitherto, involving inhibition of LPO, the cholesterol level in the brain was lowered [3, 5, 6].

Since changes in lipid composition found in brain homogenates are as a rule repeated fully in synaptosomal fractions, it can be postulated that during exposure to combinations of photic and electrical stimuli the cholesterol level rises in the synaptic membranes of the brain also, and this may lead to changes in their structural and functional state.

Further research is required in order to determine whether the combination of inhibition of LPO and cholesterol accumulation is a specific phenomenon accompanying learning processes.

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MODULATING ACTION OF ESTRADIOL ON NORADRENALIN SENSITIVITY OF SINGLE HYPOTHALAMIC PREOPTIC AREA NEURONS

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The current view in the literature that estradiol (EST) plays an important role in triggering the preovulatory wave of luteinizing hormone (LH) and subsequent ovulation is based on the results of experiments in which estrogens were injected into the bloodstream [6, 8] or crystalline EST was implanted into various hypothalamic structures [7]. The actual triggering mechanism has been shown to be realized at the level of the preoptic area of the hypothalamus (PA), as the center regulating pituitary gonadotropic function [4, 11]. Characteristically, elevation of the blood estrogen level precedes the development of the preovulatory wave of LH [9, 10]. However, the mechanism of action of estrogens on the level of the cyclic center is not yet completely clear. This effect of sex steroids is evidently formed by several functional mechanisms, among which an important place is occupied by a change in the character of action of neurotransmitters of the monoamine series, under the influence of estrogens. Previously, when studying the sensitivity of neurons of PA to noradrenalin (NA) in the course of the estrous cycle in rats, we

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