Changes in the Lipid Composition of Blood Plasma and Liver in Rats Induced by Severe Psychic Trauma

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The concentration of high-density lipoprotein cholesterol and triglycerides in rat serum sharply decreased after psychic trauma caused by life hazard. The content of these substances remained unchanged for not less than 1 week after trauma. The concentration of high-density lipoprotein cholesterol was low, while serum content of triglycerides increased 6 weeks after trauma. The concentration of high-density lipoprotein cholesterol significantly decreased after repeated psychic trauma. These changes were accompanied by a sharp increase in the concentration of triglycerides in the serum. Total cholesterol concentration in the liver decreased under these conditions.

Key Words: *psychic trauma; cholesterol; triglycerides; high-density lipoprotein cholesterol*

Psychic stress often causes nervous and mental diseases, including reactive depression and post-traumatic stress disorders (PTSD). Prolonged psychological stress and exposure to adverse psychic or social factors led to disturbances in lipid metabolism and development of atherosclerosis in humans.

The influence of stress factors promotes mobilization of lipids from fat depots, increases plasma level of lipids, but decreases their content in the liver and kidneys [2]. Stress is associated with the release of pituitary-adrenocortical hormones. This system is exposed to inadequate load during stress [3]. Much attention was paid to studying the relationship between cortisol, epinephrine, and norepinephrine, disturbances in metabolism of serum lipids and lipoproteins, and development of cardiovascular diseases [1,5,9]. The relationship exists between the concentration of hormones and lipids, mood, mental state, and temper [4,6,8,10].

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Emotional disorders in most adequate animal models are induced by stress. Most models of pathological states imply physical contact with stress factors. Little is known about the influence of psychic trauma (no physical experience of acute negative emotions) on psychophysiological parameters of animals. It should be emphasized that psychic trauma underlies the pathogenesis of depressions and PTSD in humans. We proposed the model of psychic stress caused by life hazard and followed by a depressive state in animals. This model most adequately reproduces the etiology of PTSD. Here we studied the effect of acute psychic stress on behavioral characteristics and lipid composition of the serum and liver in experimental animals (rats).

MATERIALS AND METHODS

Experiments were performed on male outbred albino rats. Psychic trauma was induced by stress. The animals were divided into groups (n=20-25). After 18-h starvation they were placed in a terrarium with Indian python. One rat died, and the other experienced death of a partner. We recorded

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locomotor activity, sniffing behavior, movements at the site, vertical rearing postures, grooming, and freezing. The rats were removed from the terrarium. Animal behavior was studied in the forced swimming test on days 3-5 after stress to evaluate the severity of depression [7]. For biochemical study, serum and liver samples were taken 30 min and 1, 2, and 6 weeks after stress.

The consequences of single stress were studied in several series. In series I, 25 rats were placed in the terrarium. The blood and liver from 12 animals were assayed immediately after stress (and 13 samples were taken from the experiment described below). Tissue samples from other animals were examined 1 week after stress. Series II involved 20 animals. Biochemical study was conducted 2 (8 rats) and 6 weeks after stress (7 rats).

The consequences of repeated psychic trauma were studied in 3 series. Blood tests were performed after single and twice and trice repeated psychic trauma. Repeated psychic trauma was induced 3 times at a 1-week interval. The blood was sampled 30 min and 7 days after removal of rats from the terrarium. The blood of rats exposed to twice repeated psychic trauma was also examined 4 weeks after stress. Serum concentrations of cholesterol (CH), triglycerides (TG), and high-density lipoprotein CH (HDL CH) were measured in a Chem Well analyzer (Awareness Technology). The concentrations of CH and TG in rat liver were measured after extraction on an AA-2 analyzer (Technicon). Intact rats served as the control in behavioral and biochemical tests. The results were analyzed using Statgraphics software.

RESULTS

The rats exhibited atypical behavior in the terrarium (freezing, interrupted grooming, *etc*.). Some animals moved agitatedly about the terrarium. Most rats were gathered together into a bunch. The form of this bunch changed constantly due to creeping of other animals. Defecation rate in experimental rats was much higher than in control animals maintained in a box of similar size.

The time of immobility in the forced swimming test significantly increased, while the time of passive swimming significantly decreased after trauma. Long-term periods of immobility were intermitted by short-term episodes of vigorous activity. Prolonged immobility (behavioral despair) is typical of depressive states [9]. The decrease in the time of passive swimming (economically advantageous behavior under these conditions) and episodes of activity probably reflect high depressiveness.

The concentrations of HDL CH and TG decreased by 74 and 63%, respectively, after single psychic trauma ($p<0.01$, Table 1). Total CH content in the serum and liver remained unchanged. TG concentration slightly decreased in the liver. The coefficient of atherogenicity increased by several times. Similar changes in the serum were observed 1 week after psychic trauma. Serum lipids returned to normal 2 weeks after trauma. Lipid content in the liver little changed. Changes in the content of TG in the serum and liver and decrease in the concentration of HDL CH were observed again 6 weeks after trauma ($p<0.05$).

Figure 1 shows the effect of repeated psychic stress on lipid content in rat serum. The concentration of HDL CH underwent wave-like changes. Immediately after the second stress exposure (1 week after the first stress exposure), the concentration of HDL CH was also below the control level, but surpassed the value observed after the first stress exposure. Immediately after the third stress exposure, the concentration of HDL CH was intermediate to the levels observed after the first and second stress exposure (decrease by 58%). One month after the third stress exposure, the concentra-

TABLE 1. Lipid Content in Blood Plasma and Liver of Rats after Single Psychic Stress ($M \pm m$)

Group	Concentration of substance in the serum, mg/dl					Concentration of substance in the liver, mg/g	
	CH	TG	HDL CH	HDL CH, %	K_{ather}	CH	TG
Control (n=20)	68±7	30±6	27.4±3.1	40	1.5	4.0±0.3	36±4
Immediately after stress (n=25)	70±8	11±2*	7.2±0.8*	10	9.0	3.5±0.5	22±5
1 week after stress (n=12)	74±8	15±4*	8.4±0.8*	11	8.2	4.4±0.5	14±2*
2 weeks after stress (n=8)	70±9	21±4	24±2.1	34	1.9	4.9±0.6	28±2
6 weeks after stress (n=7)	65±7	62±3*	21.3±1.7*	32	2.1	3.3±0.2*	15±3*

Note. K_{ather}, coefficient of atherogenicity. *$p<0.05$ compared to the control.

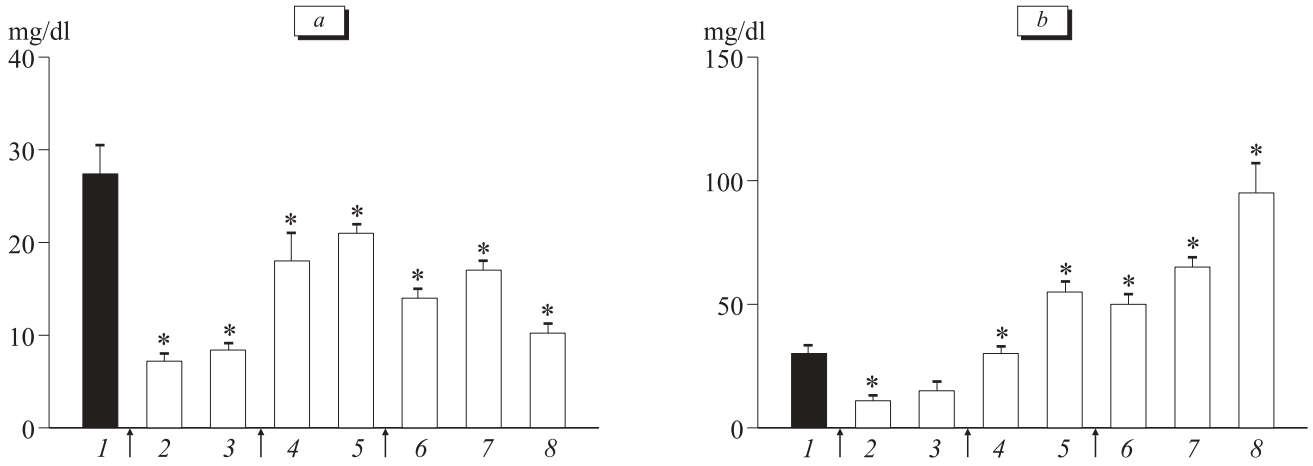

Fig. 1. Serum concentrations of HDL cholesterol (*a*) and triglycerides (*b*) in male rats after repeated psychic trauma (arrows). Control (*n*=40, *1*); immediately after the first stress exposure (*n*=13, *2*); 1 week after the first stress exposure (*n*=11, *3*); immediately after the second stress exposure (*n*=9, *4*); 1 week after the second stress exposure (*n*=10, *5*); immediately after the third stress exposure (*n*=8, *6*); 1 week after the third stress exposure (*n*=8, *7*); 4 weeks after the third stress exposure (*n*=8, *8*). **p*<0.05 compared to the control.

tion of HDL CH was lower than immediately after the third stress exposure. Serum TG content progressively increased after each stress exposure. After the third stress exposure, TG content 3-fold surpassed the control.

The concentrations of total CH and HDL CH in the serum decreased by 28 and 63%, respectively, 1 month after the third stress exposure. CH concentration in the liver decreased by 30%. Serum TG content increased 3-fold. Our results suggest that repeated psychic trauma is accompanied by permanent changes in lipid metabolism. Despite adaptation of animals, changes in lipid composition of the serum and liver persisted for ≥1 month after treatment.

The proposed model of psychic trauma causes a variety of emotional reactions in rats, including anxiety, fear, terror, and freezing. Depressive manifestations in the posttraumatic period are etiologically and symptomatically similar to human depression.

The observed biochemical changes indicate that even single psychic stress of life hazard modifies lipid composition of the serum and liver. Repeated psychic stress is accompanied by permanent changes in lipid metabolism. They primarily manifested in a decrease in serum HDL CH concentration.

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