The third model comes the closest to explaining the kinetic properties of MAO and, in particular, the presence of the intermediate plateau on the v versus [S] plots (Fig. 2) and also the observed possibility of separation of mitochondrial MAOs under mild conditions without the use of detergents [6].

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EFFECT OF CHRONIC STIMULATION OF RATS WITH INTACT AND DEAFFERENTED HYPLTHALAMI ON LIPID METABOLISM AND THE ADRENAL CORTEX

V. E. Ryzhenkov, N. S. Sapronov, G. G. Khechinashvili, I. V. Mosina, and T. A. Oletskaya

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Chronic stimulation of rats after a mock operation and rats with deafferented hypothalami leads to a decrease in the total cholesterol concentration in the blood and to the accumulation of triglycerides in the liver. Injection of dexamethasone into rats is accompanied by an increase in the blood cholesterol and triglyceride concentrations and accumulation of triglycerides in the liver. The action of dexamethasone is stronger in animals with a deafferented hypothalamus. The rate of secretion of 11-hydroxycorticosteroids into the adrenal vein was reduced in the latter.

KEY WORDS: *deafferentation of the hypothalamus; cholesterol; triglycerides; 11-hydroxycorticosteroids; dexamethasone.*

Previous investigations have shown that hypophysectomy in rats prevents the increase in the nonesterified fatty acid level in the blood plasma in response to administration of certain drugs with central action or to short-term immobilization of animals [4, 6].

The object of this investigation was to study the effect of prolonged stimulation of rats and deafferentation of the hypothalamus on indices of lipid metabolism and on the state of the adrenal cortex.

N. N. Anichkov Department of Atherosclerosis and Department of Pharmacology, Institute of Experimental Medicine, Academy of Medical Sciences of the USSR, Leningrad.

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TABLE 1. Indices of Lipid Metabolism after Chronic Stimulation of Rats and Injection of Dexamethasone (M ± m)

Groups of animals	Experimental conditions	Number of animals	Blood plasma		Liver	
			cholesterol, mg %	triglycerides, mg %	cholesterol, mg/g	triglycerides, mg/g
Mock operation	Control	15	103±6	67±6	4,5±0,23	6,6±0,55
	Immobilization for 12 days	9	79±4*	73±10	4,3±0,43	12,2±1,46*
	Injection of dexamethasone (0,07 mg/kg daily for 12 days)	6	137±5[a]	126±25*	4,2±0,43	13,4±1,43*
Deafferentation of hypothalamus	Control	14	106±12	83±12	4,1±0,38	6,5±0,70
	Immobilization for 12 days	8	72±4*	73±15	5,0±0,27	14,4±1,72*
	Injection of dexamethasone (0,07 mg/kg daily for 12 days)	6	168±12†	147±17*	4,4±0,43	22,3±2,94†

*) $P < 0.05$ compared with control.
†) $P < 0.05$ compared with animals undergoing mock operation and receiving dexamethasone.

EXPERIMENTAL METHOD

Experiments were carried out on male rats (180-200 g). Deafferentation of the hypothalamus [9] was performed under general anesthesia (amobarbital, 70-75 mg/kg, intraperitoneally). The aim of the operation was to ensure complete isolation of the hypothalamus from nervous influences from higher brain structures while leaving intact connections between the infundibulum of the hypothalamus and the adenohypophysis. In the control animals the deafferentation knife was inserted into brain tissue as far as the base of the skull and withdrawn. The experimental and control (mock operation) rats were kept together at room temperature on a standard diet. The animals were used in the experiments 2 weeks after the operation. They were immobilized by fixation to a frame for 30 min daily (except Sundays) for 12 days. In another series of experiments, the rats received intraperitoneal injections of dexamethasone (0.07 mg/kg) daily for 12 days. The animals were decapitated and their plasma concentrations of total cholesterol [8], triglycerides [11], nonesterified fatty acids [10], and 11-hydroxycorticosteroids (11-HCS) [5] were determined. Some animals were anesthetized and blood flowing from the adrenals was collected in order to determine the rate of 11-HCS secretion. The experimental results were subjected to statistical analysis [1].

EXPERIMENTAL RESULTS

Daily fixation of the rats to a frame led to a decrease in the plasma cholesterol concentration and an increase in the concentration of triglycerides in the liver of the animals both after the mock operation and after deafferentation of the hypothalamus (Table 1). An increase in the weight of the adrenals and in the plasma 11-HCS concentration also was observed and was about equal in the rats of the two groups (Fig. 1). However, the rate of secretion of 11-HCS into the adrenal vein was slower in the deafferented rats than in those undergoing the mock operation.

By contrast with chronic stimulation, injection of dexamethasone into the rats increased the cholesterol and triglyceride levels in the blood plasma. There was a simultaneous increase in the triglyceride content in the liver, especially in the deafferented animals. These changes could evidently be linked with the lipolytic effect of dexamethasone on the adipose tissue, leading to an increase in the supply of nonesterified fatty acids and glycerol into the blood stream followed by an increase in the synthesis of triglycerides in the liver and in their secretion into the blood stream as very-low-density lipoproteins; these lipoproteins are then transformed into low-density, cholesterol-rich lipoproteins. Consequently, 18 h after the end of the dexamethasone injections, the blood nonesterified fatty acid concentra-

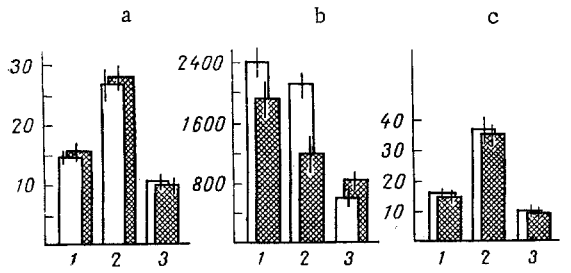

Fig. 1. Weight of adrenals, rate of secretion of 11-HCS into adrenal vein, and their concentration in peripheral blood plasma of animals undergoing mock operation (unshaded columns) and deafferentation (shaded columns); a) weight of adrenals (in mg/100 g body weight); b) rate of secretion of 11-HCS into adrenal vein (in μg/g weight of adrenal/h); c) 11-HCS concentration in peripheral blood plasma (in mg%). 1) Control; 2) chronic immobilization; 3) administration of dexamethasone.

tion in the rats undergoing the mock operation rose to 558.7 ± 48 μeq/liter (390.6 ± 26.3 μeq/liter in the control) and in the deafferented rats to 781.1 ± 70 μeq/liter (control 309.4 ± 27.5 μeq/liter). Since the cholesterol concentration in the liver was unchanged, the increase in its concentration in the blood plasma could be due partly to delay in its excretion. An increase in the blood level of low-density lipoproteins has also been observed in animals even after a single injection of cortisol [3]. In rats undergoing chronic stimulation, the decrease in the plasma cholesterol concentration can evidently be attributed to its more rapid metabolism and (or) excretion.

Despite the reduced rate of 11-HCS secretion in the animals with deafferented hypothalami (especially under conditions of chronic stress), their concentration in the peripheral blood plasma was indistinguishable from that in the animals undergoing the mock operation. This can evidently be explained by depression of 11-HCS metabolism in the deafferented rats.

Chronic stimulation of rats thus has a twofold effect on lipid metabolism: It lowers the blood cholesterol concentration and increases the triglyceride content in the liver. After short-term (1-5 days) electrical stimulation of the hypothalamus, other workers [2] found an increase in the blood cholesterol concentration of rats, followed by a decrease in its level during continued stimulation. Physical exertion (rats running on a treadmill) led to a decrease in the concentrations of cholesterol and total lipids in the blood [7]. These results are in agreement with those of the present experiments showing a decrease in the total cholesterol concentration in the blood of rats undergoing chronic stimulation. It is difficult at present to explain the fact that dexamethasone produced a much greater increase in the level of nonesterified fatty acids and also (in consequence of this) in the accumulation of triglycerides in the liver in the deafferented animals than in those undergoing the mock operation. It can tentatively be suggested that the sensitivity of the adipose tissue to the lipolytic action of dexamethasone is increased in deafferented rats. Meanwhile deafferentation of the hypothalamus has no significant effect on the changes in the indices of lipid metabolism during chronic stimulation of animals.

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