Coincidence of bursts of discharges of neurons with the negative phase both of the polymorphic Δ waves and of SSC confirms the previous hypothesis [3] that the SSCs are one type of Δ wave, and that synchronization of SSC in all the subcortical formations of the brain tested means that it is possible to distinguish them among the various types of Δ waves. Synchronization of unit activity recorded from the various brain structures during SSC suggests the existence of a single SSC generator.

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EFFECT OF ELECTRICAL STIMULATION OF THE SUPRAOPTIC REGION OF THE HYPOTHALAMUS ON LIPID METABOLISM AND THE DEVELOPMENT OF ATHEROSCLEROSIS

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9:612.826.4.014.424

Electrical stimulation of the supraoptic region of the hypothalamus for 3 weeks in rabbits kept for 3-8 weeks on an atherogenic diet accelerates and intensifies the development of hypercholesteremia and lipoidosis of the coronary arteries and also the metabolic disturbances in the myocardial tissue. These last disturbances are expressed as a fall in the tissue noradrenalin and creatine phosphate concentration and an increase in the inorganic phosphorus and lactic acid concentration.

KEY WORDS: hypothalamus; coronary arteries; electrical stimulation; lipid metabolism; atherosclerosis.

The role of negative psychogenic factors in the development of hyperlipidemia, atherosclerosis, and ischemic heart disease has been noted by a number of workers [2].

In the present investigation the effect of electrical stimulation of the supraoptic region of the hypothalamus on lipid metabolism and of the development of atherosclerosis of the coronary arteries was studied in rabbits receiving cholesterol.

EXPERIMENTAL METHOD

Experiments were carried out on 30 male rabbits weighing 2.8-3.3 kg. Cholesterol (0.5 g/kg body weight) was administered through a tube for 3-8 weeks before the beginning of electrical stimulation of the hypothalamus and in the period of stimulation. Bipolar nichrome electrodes with a tip 120 μ in diameter and with an

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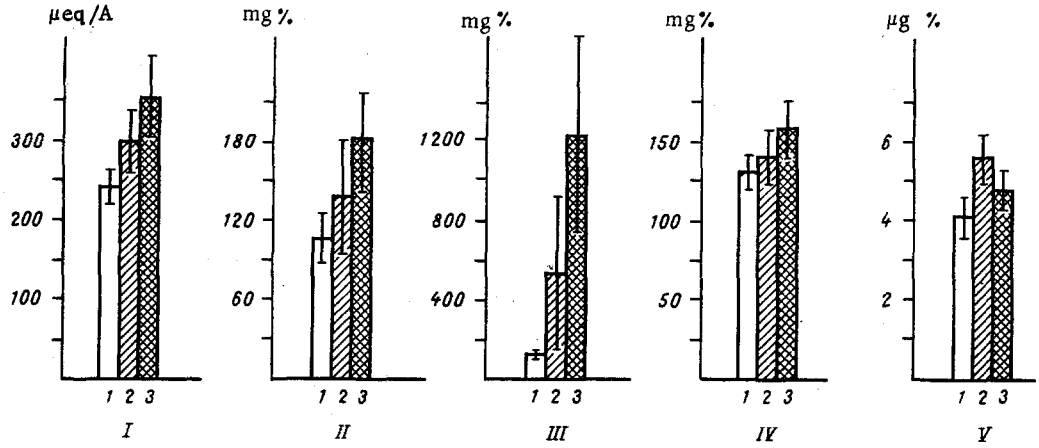

Fig. 1. Blood biochemical indices of rabbits after electrical stimulation of supraoptic region of hypothalamus and cholesterol feeding: I) NEFA; II) triglycerides; III) cholesterol; IV) glucose; V) 11-HCS. 1) Control; 2) rabbits receiving cholesterol for 2 months; 3) electrical stimulation of supraoptic region of hypothalamus for 3 weeks in rabbits receiving cholesterol for 2 months. Each column shows mean results obtained with 4-8 animals. P = 0.05.

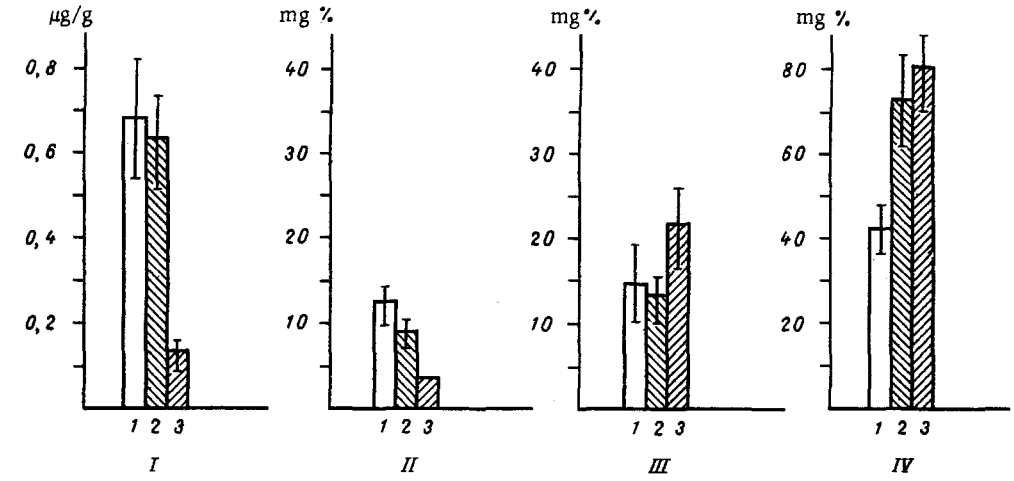

Fig. 2. Biochemical indices of tissue metabolism in heart of rabbits after electrical stimulation and cholesterol feeding. I) Noradrenalin; II) creatine phosphate; III) inorganic phosphate; IV) lactic acid. 1) Control; 2) rabbits receiving cholesterol for 2 months; 3) electrical stimulation of supraoptic region of hypothalamus for 3 weeks in rabbits receiving cholesterol for 2 months. Each column shows mean results obtained with 7-8 animals. P = 0.05.

interelectrode distance of 0.5 mm were implanted into the region of the supraoptic nucleus of the hypothalamus by a stereotaxic technique. Electrical stimulation was applied to the hypothalamus for 1 h daily for 7-25 days. The parameters of stimulation were: 50 Hz, 1.5-2 V, pulse duration 0.1 msec.

The concentrations of total cholesterol [4], triglycerides, nonesterified (free) fatty acids (NEFA), glucose, and 11-hydroxycorticosteroids (11-HCS) were determined in the animals' blood. Blood for testing was taken in the morning before feeding. After the end of the experiments the cholesterol and triglyceride content in the liver and the noradrenalin [3], creatine phosphate [5], inorganic phosphate, and lactic acid content in the heart muscle tissue were determined. The results were subjected to statistical analysis [1]. Heart tissue for microscopic investigation was fixed in 10% neutral formalin and then embedded in celloidin-paraffin.

EXPERIMENTAL RESULTS

Electrical stimulation of the supraoptic region of the hypothalamus for 20 days after preliminary feeding of the rabbits for 2 months with cholesterol led to a significantly greater increase in the plasma cholesterol

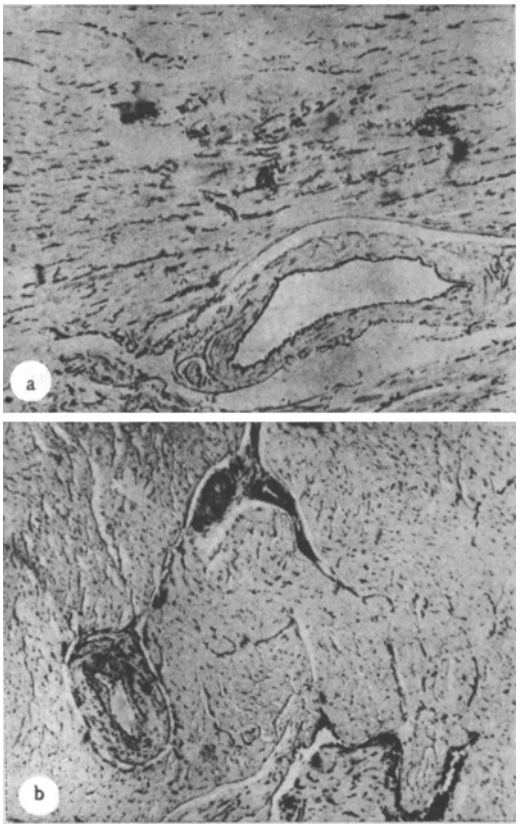

Fig. 3. Myocardium of rabbit subjected for 3 weeks to electrical stimulation of the supraoptic region of hypothalamus and cholesterol feeding for 2 months; a) hypertrophy of wall of intramuscular branch of coronary artery; sharply defined changes in myocardium consisting of destruction and fatty infiltration of muscle fibers; b) stenosing arteriosclerotic plaques and marked hypertrophy of wall in branches of intramuscular arteries of the heart. Stained with Sudan III and hematoxylin; 240×.

concentration and was accompanied by a tendency for the NEFA, glucose, and triglyceride levels to be higher than in animals receiving cholesterol but not subjected to electrical stimulation (Fig. 1). However, in the animals of these groups no significant difference was observed in the concentrations of cholesterol and triglycerides in the liver and 11-HCS in the blood plasma.

An increase in the plasma cholesterol concentration also was found in animals receiving cholesterol for 3 weeks followed by electrical stimulation of the supraoptic region of the hypothalamus for 6 days. Under these experimental conditions the cholesterol concentration increased from 282.0 ± 40.9 (rabbits receiving cholesterol only) to 384.5 ± 48 mg% (animals receiving cholesterol and also stimulated). The serum triglyceride level in the animals receiving cholesterol and stimulated showed a tendency to rise.

The study of the biochemical indices in the heart showed that electrical stimulation of the hypothalamus for 3 weeks combined with an atherogenic diet caused a disturbance of metabolism in the myocardial tissue (Fig. 2). Under these experimental conditions, the concentration of the adrenergic mediator, noradrenalin, was reduced in the rabbits by one-half to two-thirds. The disturbance of the tissue noradrenalin balance was accompanied by changes in energy metabolism, expressed as a decrease in the concentration of creatine phosphate and an increase in the concentration of inorganic phosphate and lactic acid. Metabolic disturbances of a similar character were observed in the myocardial tissue of rabbits receiving cholesterol but not stimulated.

However, it must be emphasized that in the latter case a longer period of cholesterol feeding, not less than 4 months, was required.

Repeated electrical stimulation of the supraoptic region of the hypothalamus for 7-20 days led to marked structural damage to the arteries and veins. Venous congestion, hyperemia of the capillary network, stasis, and hemorrhages were found. In many intramuscular branches of the coronary arteries hypertrophy of the walls was observed, leading to almost total obliteration of the lumen of the vessels. The elastic membrane was fragmented over a wide area. The pathomorphological changes, mainly microfocal in character, were also characteristic of the heart muscles: the structure of the myofibrils was disturbed, regions of fragmentation, degeneration, and necrosis appeared, and at the same time extensive scar changes of a varied degree of maturity appeared in the myocardium. All the structural lesions to the vascular and muscular elements of the heart were more severe in rabbits subjected to a combination of electrical stimulation of the hypothalamus and cholesterol feeding (Fig. 3). Multiple extensive foci of fatty infiltration and disintegration of muscle fibers, with the formation of connective-tissue scars, were observed in the myocardium of these animals. In some cases atherosclerotic plaques were observed not only in the intramuscular branches, but also in the main branches of the coronary arteries. Changes developed in the wall of the aorta in the region of the arch and also in the thoracic portion. This picture was never observed at the same times in rabbits either receiving a high cholesterol diet only or subjected to electrical stimulation of the hypothalamus for 3 weeks only.

The results indicate that stimulation of the supraoptic region of the hypothalamus accelerates the development of pathomorphological and biochemical disturbances in the cardiovascular system in experimental atherosclerosis. This is observed against the background of a comparatively short period of cholesterol feeding of the animals (3 weeks) and is more marked after such feeding for 2 months, when a very considerable increase in the plasma cholesterol concentration is observed compared with the control. It is interesting to compare these observations with those of Gutstein et al. [12], who showed that electrical stimulation of the lateral hypothalamus in rats led to contraction of the endothelial cells of the intima of the coronary arteries, enlargement of the endothelial spaces, and increased permeability of the intima to the components of the plasma. Under the present experimental conditions with stimulation of the supraoptic region, the endothelial spaces of the intima of the coronary vessels also were perhaps enlarged, and the penetration of cholesterol into them was facilitated. The decrease in the concentration of the mediator, noradrenalin, in the rabbits' heart during electrical stimulation of the supraoptic region of the hypothalamus was accompanied by an energy deficiency and by impairment of the nutrition of the heart muscle and coronary arteries. The dystrophic changes in the vessel walls could also undoubtedly promote the development of lipoidosis in them.

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