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HISTOTOPOGRAPHY OF SOME METABOLIC PROCESSES IN THE HEART

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The localization of the principal metabolic processes in the heart of untrained, trained, and overtrained rats in a state of relative rest and in untrained rats exposed to single and repeated physical exertion was investigated histochemically. Processes of glycogenolysis and glycolysis in the myocardium were found to be more active in the subendocardial layers, whereas oxidation of fatty acids and ketone bodies was more active in the subepicardial layers. The reverse relationships were found in the myocardium of trained and overtrained rats. The role of the subepicardial layers of the myocardium in the maintenance of cardiac function in response to a sharp increase in the intensity of its activity is demonstrated.
KEY WORDS: *myocardium; metabolic pathways; topography; physical exertion.*

After many years of histochemical investigation of the heart it has been concluded that different parts of the myocardium differ in the intensity and direction of their metabolism [3, 4]. Various enzyme processes and their substrates have been shown to be located principally in the subepicardial or subendocardial zones of the myocardium [2, 7, 8]. However, no systematic study of the topography of the principal metabolic processes in the heart in different functional states has hitherto been undertaken. This was the object of the present investigation, which was based on the assumption that this approach could shed some light on the fine mechanisms of adaptation of the heart to the conditions of its activity.

EXPERIMENTAL METHOD

Male Wistar rats weighing 180-200 g were studied. All the physical loads consisted of swimming in water at 30°C by the animal carrying a weight amounting to 2.5% of its body weight. Animals exposed to physical exertion once only were decapitated in the "running in" period (the first 7 min of swimming), the period of stationary work (90 min) and the period of fatigue (the time of sacrifice was determined individually within the period from 180 to 240 min of swimming). In the rest period the rats were decapitated 24 and 48 h after the end of exertion. Some animals were subjected to repeated exertion after a rest of 24 and 48 h, and they were decapitated at the same stages of the second exertion as during the first.

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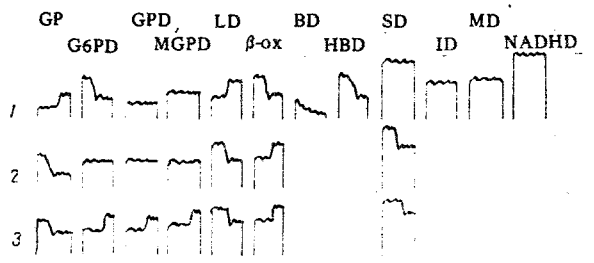

Fig. 1. Distribution of products of enzymic reactions along thickness of wall of left ventricle of untrained (1), trained (2), and overtrained (3) rats in stage of relative rest. Schematized curves here and in Figs. 2 and 3 obtained on IFO-451 microphotometer. Subepicardial layers of myocardium shown in curves on left.

Some animals were trained for 11 days; on the first day the duration of swimming was 20 min, and this was increased every day by 15 min. Overtrained animals have been trained by the above-mentioned scheme until they ceased to carry out the work as planned. This was usually observed on the 19th day. In the last two series of experiments the rats were killed 24 h after the last training session. At each stage of these experiments 10 rats were killed; in addition, 10 untrained rats in a state of relative rest were decapitated.

Activity of the following enzymes was studied in frontal frozen 7-μ sections through the heart: glycogen phosphorylase (GP) by Takeuchi's method [1], glucose-6-phosphate dehydrogenase (G6PD), cytoplasmic α-glycerophosphate (GPD), lactate (LD), β-hydroxybutyrate (HBD), isocitrate (ID) and malate (MD) dehydrogenases by the method of Hess et al. [1], succinate (SD) and NADH (NADHP) dehydrogenases by the method of Quaglino and Hayhoe [9], activity of β-oxidation of fatty acids (β-ox), and butyryl-CoA-dehydrogenase (BD) by the method of Yazvikov et al. [6], and mitochondrial α-glycerophosphate dehydrogenase (MGPD) by Nartsissov's method [3]. The distribution of the products of enzymic reactions along the thickness of the walls of the chambers of the heart was recorded by means of the IFO-451 microphotometer.

EXPERIMENTAL RESULTS

Data on the topography of enzymes in the wall of the left ventricle are given below. It should be pointed out that in nearly every case the topography of the enzymes in the walls of the other chambers of the heart was indistinguishable from that in the wall of the left ventricle. The only exception was the myocardium of the right ventricle of untrained rats at rest.

As is clear from Fig. 1, section 1 the intensity of the reaction of GP and LD was greater in the subendocardial layers but the intensity of the reaction for G6PD, β-ox, BD, and HBD was greater in the subepicardial zones. The intensity of the other reactions was about equal throughout the thickness of the wall. Consequently, in the myocardium of untrained animals in a state of rest the processes of glycogenolysis and glycolysis, on the one hand, and of oxidation of fatty acids and ketone bodies, on the other hand, are territorially distinct. The same result was found in the myocardium of trained (Fig. 1, section 2) and overtrained (Fig. 1, section 3) rats, but in these animals these processes of carbohydrate metabolism were more active in the subepicardial layers and oxidation of fatty acids was more active in the subendocardial layers; this result was evidently connected with adaptation of the organ to physical exertion. Meanwhile in the heart of the trained rats (Fig. 1, section 2) the intensity of reactions for G6PD, GPD, and MGPD was about the same throughout the thickness of the wall, and in the heart of the overtrained rats it was higher in the subendocardial layers (Fig. 1, section 3); this result probably reflects changes in the intracardiac regulation of metabolism in the overtrained organ.

During the "running in" period of single physical exertion (Fig. 2, section 1) most enzymes (except GP, G6PD, GPD, and SD) were more active in the subepicardial layers. In the

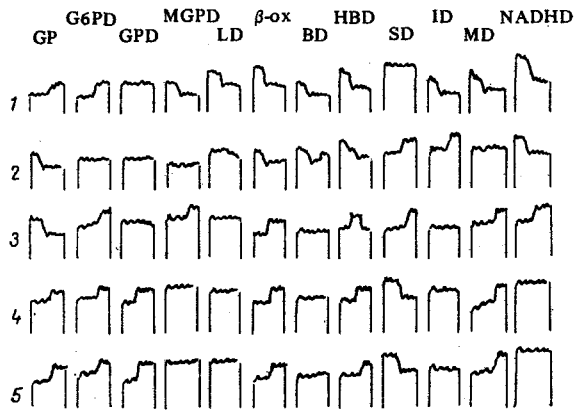

Fig. 2

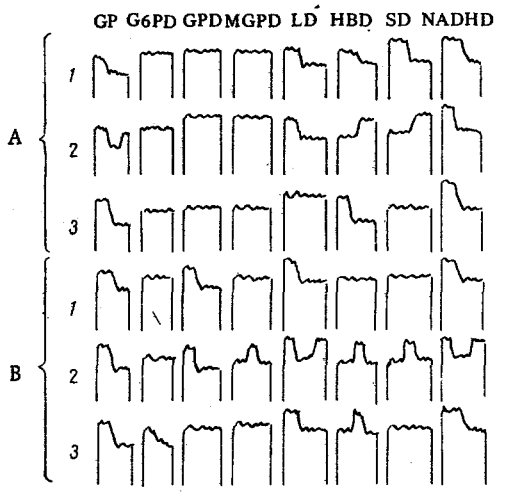

Fig. 3

Fig. 2. Distribution of enzymic reaction products along thickness of wall of left ventricle of untrained rats in "running in" period (1), period of stationary work (2), and period of fatigue (3) during single physical exertion and after resting for 24 h (4) and 48 h (5) thereafter.

Fig. 3. Distribution of enzymic reaction products along the thickness of wall of left ventricle at stages of repeated exertion after resting for 24 h (A) and (48) h (B) after first exertion. Remainder of legend as in Fig. 2.

period of stationary work relocation of the enzymic reactions took place (Fig. 2, section 2); in the subepicardial layers as before, however, higher activity of oxidation of fatty acids was observed, but the reactions of glycogenolysis and glycolysis in these zones also were activated. In the period of fatigue (Fig. 2, section 3) most of the enzymic reactions studied were more active in the subendocardial layers, whereas processes of glycogenolysis were more active in the subepicardial layers. In the course of repeated physical exertion a relocation of the principal metabolic processes thus takes place in the heart (maximal activity of glycogenolysis in the subepicardial layers, maximal activity of oxidation of fatty acids in the subendocardial layers), as is characteristic of the trained heart at rest. This change evidently reflects short-term adaptation of cardiac metabolism to work under conditions of physical exertion, and this is later consolidated as a long-term mechanism. It is also an interesting fact that during the "running in" period metabolism of the subepicardial layers of the myocardium is activated, in the period of stationary work these layers are no longer distinguishable by their metabolic activity, and in the period of fatigue the highest activity of most enzymes was observed in the subendocardial layers. The impression was obtained that this dynamics is not accidental. To test this hypothesis experiments were carried out with repeated exertion after resting for 24 and 48 h after the first exertion, when most enzymic reactions were more intensive in the subendocardial layers of the myocardium (Fig. 2: sections 4 and 5).

Activation of the absolute majority of the reactions studied in the subepicardial layers of the myocardium was in fact observed in the "running in" period of repeated exertion (Fig. 3). The equalization of activity of various enzymes along the thickness of the wall (GPD and G6PD in Fig. 3A, section 1 and G6PD and HPD in Fig. 3B, section 1) can be explained not by a decrease in the intensity of the reactions in the subendocardial layers, but by their activation in the subepicardial layers. In the period of stationary work relocation of the enzymic reactions is observed, whereas in the period of fatigue during repeated exertion activation of the enzymes in the subendocardial layers could not be demonstrated (Fig. 3).

In response to a sharp intensification of cardiac activity, such as takes place at the beginning of physical exertion, activation of metabolism is observed in the subepicardial layers of the myocardium, which evidently play the leading role in the maintenance of cardiac activity in this situation.

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CHANGES IN ULTRASTRUCTURAL SYNAPTOARCHITECTONICS CAUSED BY ENDOTOXIN

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The ultrastructure of the synapses of the sensomotor cortex in dogs was studied in response to intravenous injection of typhoid endotoxin. The most marked changes were observed in the dendritic apparatus of the neurons. Activation in cortical structures was associated with an increase in the number of functioning synapses and reorganization of interneuronal connections. The extent of the contacting membranes and the number of synaptic vesicles were increased, and the contents of the dense-core vesicles were liberated. Depression was associated with degenerative changes in the synapses.

KEY WORDS: *endotoxin; neurons; synapses.*

Intravenous injection of filtrates of intestinal microorganisms and of typhoid endotoxin lead within the space of 1 h to the appearance of a powerful discharge of impulses in some nerve fibers with an increase in the amplitude and frequency of the spikes [2]. In the sensomotor cortex a considerable increase of bioelectrical activity is observed and precedes the development of characteristic morphological changes [3, 4]. However, a closer electron-microscopic analysis revealed irreversible changes in some internal organs (lungs, liver, kidney) as early as 30-60 min after injection of endotoxin [5, 6]. It was therefore interesting to study the ultrastructural changes in the CNS responsible for the development of electrophysiological phenomena observed previously.

This paper describes the results of electron-microscopic observations on the state of nerve cells and synapses in the sensomotor cortex of dogs after injection of endotoxin.

EXPERIMENTAL METHOD

Experiments were carried out on 10 adult mongrel dogs weighing 8-17 kg into which *Salmonella typhi* endotoxin (lipopolysaccharide) was injected intravenously in a dose of 5 mg/kg. Physiological saline was injected into three control animals. The animals were decapitated 1 h after the injection and pieces of the sensomotor cortex were fixed in glutaraldehyde, made up in phosphate buffer, and postfixed in OsO_4 solution. The material was

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