BIOCHEMICAL AND ELECTRON-MICROSCOPIC CHARACTERISTICS OF MITOCHONDRIA OF THE DOG'S HEART IN HYPOKINESIA

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During exposure of dogs to hypokinesia for 15 days a marked decrease was found in the concentration of high-polymer RNA in mitochondria from the myocardium of the left and right ventricles. Hypokinesia is followed by a decrease in the ability of the mitochondria to incorporate C^{14}-labeled amino acids. Electron-microscopic investigation of the ventricular mitochondria after hypokinesia for 15 days reveals slight damage to mitochondria of general type, while mitochondria of muscular type are well preserved.

The harmful action of limited mobility on man and animals has been known for a long time. However, the mechanisms lying at the basis of progressive disuse atrophy of the entire muscular system and, in particular, of the myocardium, have received inadequate study. Metabolic processes in the myocardium during severe limitation of its physiological function are undoubtedly changed at "all levels of regulation of the myocardium, but principally at the cellular and molecular levels" [5].

The object of the investigation described below was to study changes in the concentration and composition of high-polymer RNA and changes in the ability to incorporate radioactive amino acids in vitro observed in an isolated fraction of mitochondria from the left and right ventricles and to compare these indices with the morphological structure of the mitochondria in hypokinesia.

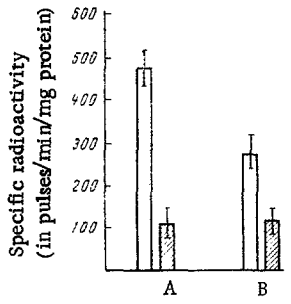

Fig. 1. Specific radioactivity of mitochondria from left (A) and right (B) ventricles. Unshaded columns – control; shaded columns – hypokinesia.

EXPERIMENTAL METHOD

Experiments were carried out on 12 dogs weighing 15-18 kg. Hypokinesia was produced by secure

TABLE 1. Concentration of High-Polymer RNA in Mitochondria from Different Parts of Dog's Heart after Hypokinesia (in μg RNA/mg mitochondrial protein)

Group of animals	Left ventricle	Right ventricle	P
Control	5,3 ±0,102	3,69±0,209	<0,001
Hypokinesia	2,61±0,37	2,68±0,165	<0,01

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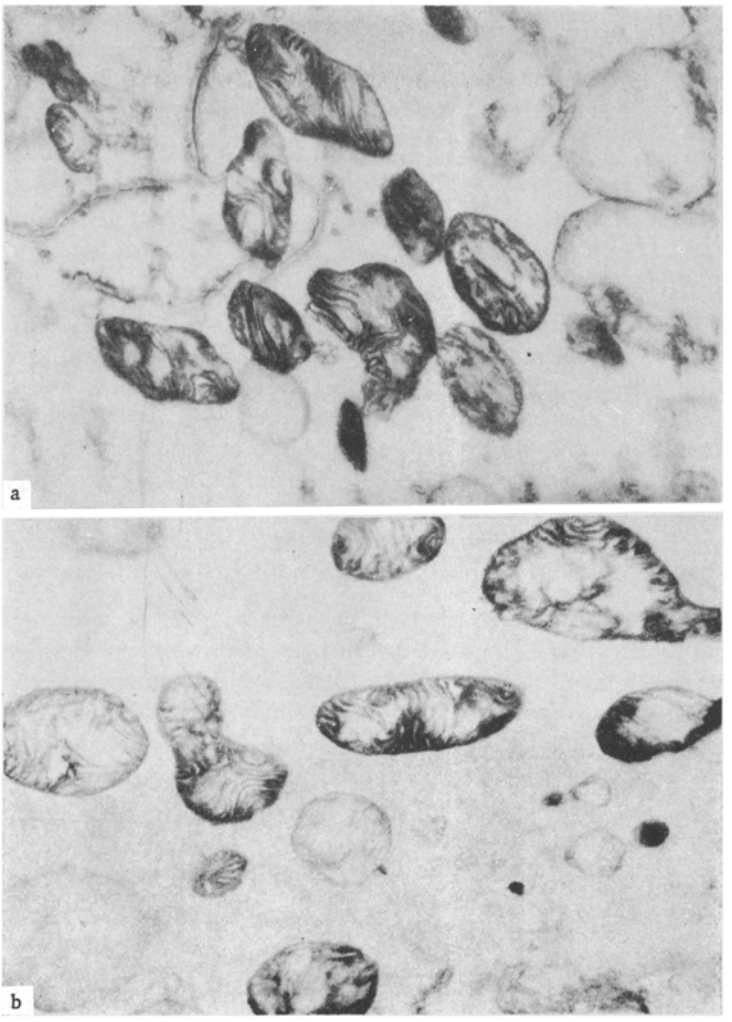

Fig. 2. Mitochondria from left (a) and right (b) ventricles of a dog following hypokinesia (25,000 ×).

fixation by application of soft splints, or plaster of paris slabs and bandages under morphine anesthesia, ensuring a state of total immobility. The animals' position corresponded to a state of physical rest (lying in the prone position). To prevent the development of pressure sores, the plaster cast was lined with cotton wool. The animals remained securely fixed for 15 days, after which the plaster cast was removed under morphine–hexobarbital anesthesia, after which thoracotomy was performed and the heart quickly extracted. Methods of obtaining a pure fraction of mitochondria, of isolation of high-polymer RNA from it, determination of its concentration and composition, and determination of the mixture of C^{14}-labeled amino acid* in proteins of the mitochondrial fraction of the myocardium in vitro, and methods of electron-microscopic control have been described previously [1, 3].

EXPERIMENTAL RESULTS

The animals were divided into two groups: controls, kept under normal conditions in the animal house, and animals subjected to hypokinesia.

Immobilization of the animals for 15 days led to a decrease of 27-30% in the absolute weight of the heart. A marked decrease in the number of mitochondria was found in the left and right ventricles; this decrease, calculated relative to dry weight, was 20-25%.

The concentration of high-polymer RNA in mitochondria from myocardium of the left ventricle of dogs exposed to hypokinesia was reduced by 50.8%, and in the mitochondria of the right ventricle by 27.5% (Table 1).

*Proline, valine, arginine, serine, threonine.

Hypokinesia led not only to a sharp decrease in the concentration of high-polymer RNA, but also to changes in its nucleotide composition. These were particularly marked in RNA from mitochondria of the left ventricle. For instance, the base ratio (G+C/A+U) was shifted toward the GC-type: 1.25 ±0.071 in the control animals and 1.37 ±0.01 in the immobilized animals. This change in the base ratio was evidently due to the fact that mitochondria of muscular type, whose RNA is most strongly of the GC-type, [3] were predominant in the myocardium.

The specific activity of mitochondrial protein from the left ventricle of intact dogs and of dogs exposed to hypokinesia was 475 and 113 pulses/min/mg protein, respectively, and the corresponding figures for mitochondria of the right ventricle were 274 and 112.5 pulses/min/mg protein (Fig. 1).

On electron micrographs, specimens of mitochondria from the left ventricle of animals exposed to hypokinesia appear mainly as mitochondria of muscular type, with their structure in most cases well preserved (Fig. 2a). In some mitochondria clearing of the matrix is observed and the orderly arrangement of the cristae is less clear. Only a few ordinary mitochondria with short, tubular cristae were present, and they were slightly modified. The electron-microscopic picture of mitochondria from the right ventricle (Fig. 2b) was basically the same, except that fewer mitochondria of muscular type were present in the specimen. In these mitochondria the matrix occupied a larger area, and the arrangement of the cristae was slightly abnormal, but the limiting membrane was intact (electron micrographs of mitochondria from the heart of intact animals have been published by the writers previously [3]).

Hypokinesia for two weeks thus leads to slight disturbances of the structure of the myocardial mitochondria, manifested mainly as destruction of mitochondria of the general type while those of muscular type remain intact. Diminution of the contractile function of the myocardium as a result of hypokinesia also depresses protein synthesis in the myocardial mitochondria. Temporary deprivation of motor activity depresses the contractile function of the animals' heart, and also, consequently, reduces the degree of wear and tear on its cell structures. The need for synthesis of specialized proteins, providing the myocardium with the materials required for its contractile function, is reduced, so that the decrease in intensity of synthesis of protein and RNA observed in the mitochondria conforms to modern views regarding the dependence of synthesis of protein and nucleic acids on the level of physiological cell function [4].

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