POSTDENERVATION ATROPHY OF THE MYOCARDIUM

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In experiments on dogs a tendency toward a decrease in weight of the ventricles and in the thickness of their walls was observed 18 days after vago-sympathetic denervation of the heart. A significant decrease in diameter and area of cross section of the muscle fibers of the ventricular myocardium and in the volume of the nuclei of the muscle cells was found.

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We have previously shown that prolonged pharmacological parasympathetic block by means of atropine and banthine bromide causes a moderate decrease in weight of the heart in rats, with a decrease in thickness of the ventricular walls and an increase in number of fibers with small cross section compared with controls [1, 2, 11]. Pharmacological blocking of vagal influences also largely prevented the onset of hypertrophy of the heart caused by prolonged physical exertion in the form of swimming [2]. We explained these facts by exclusion of vagal influences on processes of resynthesis in the heart muscle. Although generally speaking we obtained identical results during application of two different types of parasympathicolytic drugs, we nevertheless could not completely rule out the possibility that these preparations have a nonspecific toxic action on the myocardium.

In the present investigation we therefore studied the after-effects of surgical denervation of the heart.

EXPERIMENTAL METHOD

Observations were made on 34 male dogs (mean weight 17 kg), half of which were used as controls. Selective surgical denervation of the heart as described by Černý and Oláh [4] was carried out on 17 dogs. This method consists of removal of all the supracardial nerves leaving the two stellate ganglia and the vago-sympathetic trunks, and participating in the innervation of the heart through the pretracheal plexus. The vagus nerve trunk remained intact, preventing the onset of degenerative changes in other organs supplied by the vagus nerves. A detailed account of the method is given elsewhere [3]. The effectiveness of cardiac denervation was verified by electrical stimulation of nerve trunks and by the atropine test [5].

The animals were sacrificed 18 days after denervation of the heart. The hearts were weighed after separation from the aorta at a point 1 cm from its junction with the left ventricle, and after separation from the plumonary artery immediately beyond the bifurcation. The thickness of the ventricular walls was measured at the same place in each case (margo acutus and margo obtusus). The hearts of 8 control and 8 experimental animals were investigated histologically. Material was taken from the right papillary muscle of the right ventricle at the border between the middle and apical thirds, perpendicularly to the long axis of the muscles.

The samples of material were fixed in neutral 10% formalin and embedded in paraffin wax. Sections were cut to a thickness of 8 μ and stained with hematoxylin-eosin. The sections were placed in a Zeiss microprojector and with a magnification of 1650x the outlines of 100 fibers in each section were traced. The area of cross section of the fiber was calculated from the longitudinal and transverse measurements of the fiber using the formula for area of an ellipse. To represent the results graphically, we used Hintsche's method [9], in which individual classes of values of the area are plotted along the abscissa on a logarithmic scale and their frequency in percent along the ordinate. The symbol k/2 denotes the mean area of section of muscle fibers of the control animals, K/4 its half value, and K twice the mean value.

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TABLE 1. Quantitative Characteristics of Morphological Changes After Denervation of the Heart, M ± m

Group of animals	Weight of heart (in g)	Relative weight of heart	Thickness of ventricular walls (in mm)		Area of cross section of ventricular muscle fibers (in μ^2)	
			left	right	left	right
Control	117.7 ± 3.024	7.35 ± 0.185	11.9 ± 0.287	6.1 ± 0.270	16.56 ± 0.535	16.20 ± 0.630
Experimental	114.0 ± 5.158	6.42 ± 0.224	11.0 ± 0.326	5.5 ± 0.214	13.10 ± 0.314	13.38 ± 0.673
Percent of change	− 3.14	− 12.6	− 7.64	− 9.68	− 20.89	− 17.40

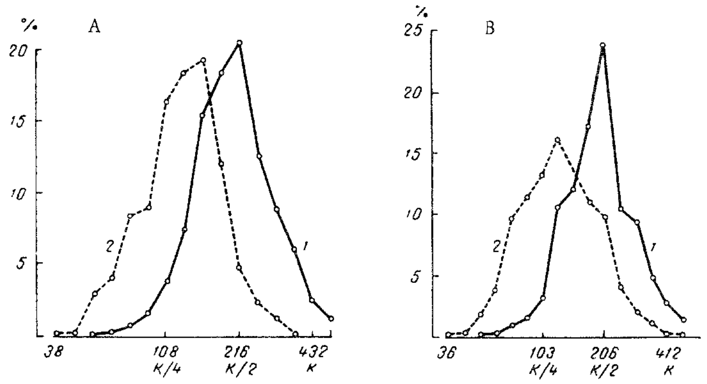

Fig. 1. Curves of distribution of areas of cross section of muscle fibers in left (A) and right (B) ventricles. 1) Control; 2) experimental animals. Abscissa, area of cross section of fibers (in μ^2); ordinate, number of fibers (in percent).

Other histological sections were stained with Heidenhain's hematoxylin. Under a total magnification of 2,880 × the outlines of 100 nuclei in each section were traced. Using the formula for an ellipsoid of rotation, their volume was calculated from the longitudinal and transverse dimensions of their outlines. The results were recorded graphically as described above.

EXPERIMENTAL RESULTS AND DISCUSSION

The absolute and relative weight of the denervated heart had a tendency to decrease, although the difference between the control and experimental groups was not statistically significant. The same tendency was shown by changes in the thickness of the walls of the cardiac ventricles. The mean transverse diameter of the muscle fibers (Table 1) fell significantly ($P < 0.001$). The decrease in thickness of the fibers and denervation of the heart was seen more clearly still when their cross-sectional areas were investigated. It is clear from Fig. 1 that in animals with vago-sympathetic denervation of the heart the number of thinner fibers increased.

After denervation of the heart the nuclei of the ventricular muscle cells also decreased ($P < 0.001$; Fig. 2).

After surgical vago-sympathetic denervation of the heart we thus observed the same phenomenon as after pharmacological parasympathetic blocking, resembling simple postdenervation atrophy of skeletal muscle in Tower's classification [12]. The most convincing results were those obtained by investigation of the areas of cross section of the fibers, independent of the presence of fatty or connective tissue [10]. The fact that no linear relationship could be established between the decrease in thickness of the muscle fibers and the decrease in thickness of the ventricular walls is presumably explained on the basis that after denervation of the heart the content of intracellular fluid falls (on the average by 9%), while extracellular fluid accumulates. These changes are partly responsible for the decrease in volume of muscle fibers after denervation of the heart.

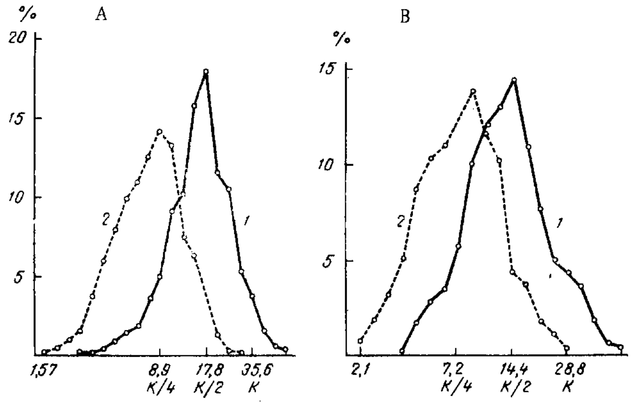

Fig. 2. Curves of distribution of volume of nuclei of heart muscle cells. Abscissa, volume (in μ^2). Remainder of legend as in Fig. 1.

Besides typical morphological changes, changes in protein metabolism also participate in denervation atrophy of skeletal muscle [6, 8, 13]. Investigation of the denervated myocardium showed that the total protein content fell by only 2.8%, the actomyosin content fell by 3.65%, while the content of stromal proteins remained unchanged. Hence, in the stage after denervation which we studied, the decrease in protein content in the muscle fiber did not play an essential role in the decrease in volume of the fibers.

After denervation of skeletal muscle the nuclei of the muscle cells either shrink and break up or swell, and sometimes undergo lysis [7]. After denervation of the heart we observed only the first type of change in the nuclei, i.e., shrinking. The DNA content did not fall after denervation but, on the contrary, it rose slightly (by 6.99% in the muscle of the left ventricle and by 10.14% in the muscle of the right ventricle). This means that the decrease in nuclear volume took place as a result of condensation of chromatin, as was confirmed by investigation of the ultrastructure of the denervated myocardium [3].

In contrast to DNA, the RNA content fell after denervation of the heart, with a corresponding increase in the DNA/RNA ratio. The pycnotic nuclei with condensed chromatin represent a certain stage of denervation of the nucleus. This fact, like the observed decrease in content of RNA, which plays an essential role in synthesis of the protein molecule, shows that after vago-sympathetic denervation of the heart persisting for a considerable time, true postdenervation atrophy of the myocardium may develop. This state is characterized not only by quantitative, but also by qualitative changes in the histological structure of the muscle fibers arising as a result of the disturbance of protein resynthesis.

The results described confirm the view that the nervous system plays an important role in the regulation of processes maintaining the adequate mass of the heart muscle.

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