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STRUCTURAL CHANGES IN THE RAT MYOCARDIUM DURING ADAPTATION TO MOUNTAIN HYPOXIA

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Changes in weight indices for different parts of the heart, the area of cross sections of the myocytes, and vascularization of the myocardium during adaptation to hypoxia were studied in experiments on rats exposed to high-altitude hypoxia (3200 m above sea level). The morphological manifestation of compensatory and adaptive reactions of the rat heart to hypoxia is an increase in its weight, chiefly on account of hypertrophy of the myocardium of the right ventricle. Increasing hypertrophy of the myocardium is accompanied by the corresponding increase in its vascularization.

KEY WORDS: myocardium; hypoxia; morphometry.

The effect of mountain conditions on man and animals is a subject that increasingly attracts the attention of research workers. Even a short stay under conditions of high-altitude hypoxia in the mountains evokes a response primarily of the cardiovascular system [2, 4, 10, 12]. However, all the extensive evidence so far available is concerned mainly with functional manifestations of adaptation of the cardiovascular system to hypoxia [1, 13, 14]. There are few data on the structural manifestations of adaptation of the system. Among the most important morphological criteria of adaptation to hypoxia are hypertrophy of the myocardium of the right ventricle and an increase in the blood supply to the tissues. However, information on the dynamics of development of hypertrophy and vascularization of the hypertrophied myocardium is frequently contradictory [8, 11].

The object of this investigation was to study the dynamics of weight indices of the heart, the area of cross section of the myocytes, and vascularization of the myocardium during adaptation of animals to mountain hypoxia.

EXPERIMENTAL METHOD

Noninbred male rats weighing 200-250 g were used. The control consisted of 16 animals killed in the city of Frunze (760 m above sea level). The experimental rats (75 animals) were taken up to Tyuya-Ashu Pass, at an altitude of 3200 m above sea level in the mountains of Kirghizia. The duration of the experiment was counted as the number of days of exposure of the rats to mountain hypoxia. Tests were carried out on the 1st, 3rd, 7th, 15th, 30th, and 45th days. To determine the weight indices of the heart, the heart was weighed by Müller's method in Il'in's modification [5] separately in six rats at each of the above-mentioned times of the experiment. The absolute weight of the heart, the weight of the right and left ventricles and septum, and the cardiac and ventricular indices were determined. The numerical results were expressed per 100 g body weight. The area of cross section of 100 muscle fibers from the right and left ventricles of each rat was determined in the same animals in histological sections cut after embedding in paraffin wax by the method of direct microplanimetry. The area of the arterial microcirculatory system was measured in frozen sections cut from rat hearts perfused with an aqueous solution of ink (six rats at each time of the experiment). The area of the myocardial vessels in the right and left ventricles was calculated in 10 fields of vision as a percentage of the total area of the myocardium. The method of direct microplanimetry, with the aid of a microprojector, was used for this investigation. The numerical data were subjected to statistical analysis. The coefficient of correlation was calculated by the method of squares.

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TABLE 1. Weight Indices of Rat Heart at Different Times of Exposure to Mountain Hypoxia

Day of experiment	Weight, mg/100 g body weight, of				Index	
	heart	right ventricle	left ventricle	septum	cardiac	ventricular
Control	350,8±21,5	76,0±7,67	136,8±6,28	113,0±10,22	0,0035	0,46
1st	359,0±4,6	77,3±7,5	142,0±8,3	103,0±8,6	0,0035	0,62
3rd	363,0±14,6	84,2±3,7	158,0±13,2	93,3±5,3	0,0036	0,54
7th	451,0±4,8	98,6±3,1	148,0±5,2	119,0±4,8	0,0044	0,67
15th	399,0±6,4	112,0±2,8	143,3±2,6	100,0±3,6	0,0040	0,78
30th	429,0±24,1	125,3±8,2	172,0±9,3	95,2±7,8	0,0043	0,70
45th	417,0±10,7	128,0±3,6	160,2±5,5	100,5±9,1	0,0044	0,72

TABLE 2. Indices of Area of Vascularization of Rat Myocardium at Various Times of Exposure to Mountain Hypoxia

Day of experiment	Right ventricle		Left ventricle	
	area of blood vessels, %	area of myocardium, %	area of blood vessels, %	area of myocardium, %
Control	21,0±1,58	79,0±1,58	21,5±1,7	78,5±1,7
1st	23,2±1,53	76,8±1,53	22,9±1,35	77,1±1,35
3rd	35,3±1,84	64,7±1,84	33,4±1,05	66,6±1,05
7th	37,0±1,03	63,0±1,03	35,6±2,3	64,4±2,3
15th	42,6±1,41	57,4±1,41	30,7±1,08	69,3±1,08
30th	45,4±0,96	54,6±0,96	43,6±2,04	56,4±2,04
45th	46,8±1,44	53,2±1,44	43,2±1,96	56,8±1,96

EXPERIMENTAL RESULTS

The results of separate weighing of the rats' hearts are given in Table 1. They show that after the first days of the animals' exposure to mountain conditions there was an increase in the absolute weight of the heart. The absolute weight of the hearts was significantly increased until the 7th day. Later it fell somewhat, and starting with the 30th day of the experiment and continuing until its end it became stabilized at a new level, higher than that in the control. The results of separate weighing show that changes in the weight of the heart were due to hypertrophy of the myocardium of the left and, in particular, of the right ventricles: An increase in the absolute weight of the right ventricle was observed constantly at all times of the experiment. For all values $P < 0.001$. Correlation between the weights of the heart and the myocardium of the right ventricle was strongly positive ($r = 0.76$). The absolute weight of the myocardium of the left ventricle showed cyclic changes. It increased during the first three days of the experiment and again after the 30th and 45th days. The absolute weight of the septum of the rat heart at different times of the experiment varied, sometimes being higher, sometimes lower than the control. However, differences between these indices were not statistically significant.

The cardiac and ventricular indices were higher at all times of the experiment than in the control, and their actual values fluctuated. The differences between most values of the cardiac and ventricular indices and the control was statistically significant. Correlation between the ventricular and cardiac indices was strongly positive ($r = 0.58$). This is evidence of hypertrophy predominantly of the right ventricle as the factor causing the increase in weight of the heart.

The area of cross section of myocytes of the right ventricle increased with an increase in the duration of exposure of the animals to mountain conditions. For instance, whereas the mean area of cross section of a myocyte in the control rats was 121 μm^2, on the 3rd day of the experiment it increased to 123.6 μm^2, by the 15th day to 139.8 μm^2, and by the 45th day, to a maximum of 142.2 μm^2. The difference between these values and the control is statistically significant ($P < 0.001$).

The area of cross section of the muscle fibers of the left ventricle increased during the first three days of the experiment and again on the 30th and 45th days (129.3 and 123.5 μm^2 respectively).

The area of cross section of the myocytes showed strong positive correlation with the weight of the myocardium and, in particular, the weight of the right ventricle, concerning the presence of true working hypertrophy of the myocardium of the right ventricle.

The dynamics of changes in the area of the arterial component of the microcirculatory system in the rat myocardium is shown in Table 2. Clearly at all times of the experiment the area of the blood vessels was greater than in the control. In the right ventricle the area of the vessels accounted on average for $21 \pm 1.58\%$ of the total area of the myocardium in the control, on the 3rd day of exposure of the animals to mountain conditions the ratio was increased to 35.3%, and at subsequent times of the experiment an increase in area of the vessels was observed until the 45th day, when they accounted for 46.8% of the total area ($P < 0.001$). Strong positive correlation was found between the weight indices of the myocardium of the right ventricle and the area of its blood vessels ($r = 0.87$).

The area of the arterial component of the microcirculatory system in the myocardium of the left ventricle showed cyclic changes in the course of the experiment, either rising or falling. However, no clear correlation was found between the area of the blood vessels of the left ventricle and its weight ($r = 0.36$).

As the experimental results showed, after the first few days of the animals' exposure to mountain conditions, compensatory and adaptive mechanisms of adaptation of the circulatory system began to operate. A structural manifestation of the adaptive reactions was the increase in weight of the heart because of hypertrophy of the left and, in particular, of the right ventricle. Hypertrophy of the myocardium of the right ventricle was due to pulmonary hypertension, which is observed in hypoxia [6, 9]. Parallel with the increasing hypertrophy of the myocardium of the right ventricle, its vascularization also increased. This was shown by the increase in area of the arterial components of the microcirculatory system. In accordance with the views of Anestiadi and Russu [3] and of Meerson [8], these changes are evidence of structural manifestations of adaptive reactions of the myocardium.

A similar pattern also was observed in the myocardium of the left ventricle. However, correlation analysis of the weight indices, area of cross section of the myocytes, and vascularization of the myocardium of the left ventricle indicates that structural manifestation of adaptive reactions follow a cyclic course in it: The corresponding parameters are sometimes increased (1st-7th day of the experiment), sometimes reduced (7th-15th day). Starting with the 30th-45th day of the experiment, indices such as the absolute weight of the left ventricle, the area of cross section of its myocytes, and the area of its blood vessels became stabilized at a higher level than the control. These data indicate that the structural manifestations of adaptive reactions of the myocardium to hypoxia are characterized by a series of successive changes, as Mirrakhimov and Yusupova [6] have shown.

Possibly as a result of a special kind of changes in the hemodynamics of the pulmonary circulation and alveolar hypoxemia other regular mechanisms of compensation, which determine differences between the adaptive reactions of structural components of the myocardium of the left and right ventricles to mountain hypoxia, are brought to light [7, 14].

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