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EFFECT OF EMOTIONAL-PAINFUL STRESS ON CONTRACTILITY OF THE HYPERTROPHIED MYOCARDIUM

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Compensatory hyperfunction and subsequent development of hypertrophy of the myocardium constitute the chief factor of compensation in heart diseases, hypertension, and other diseases of the circulatory system. However, after hypertrophy of the myocardium has reached a certain limit, it leads to a decrease in the functional capacity of the heart, which may go on to heart failure [1, 3]. Clinical experience shows that the breakdown of compensation in patients with marked hypertrophy of the heart is often due to infections, toxic conditions and, in particular, prolonged stress situations, which have themselves been shown capable of causing marked depression of contractility of the previously intact heart [5].

However, the question of how long-existing hypertrophy of the myocardium affects its resistance to stress-induced injury and, in particular, the degree of stress-induced depression of contractility, has not previously been studied.

The aims of this investigation were, first, to assess in more detail the contractility of the hypertrophied myocardium and study the effect of cations competing with Ca^{++} for its binding sites on cardiomyocyte membranes on contractility and, second, to discover how hypertrophy developing previously as the result of an experimental heart lesion affects resistance of myocardial contractility to injury by stress.

EXPERIMENTAL METHOD

Experiments were carried out on male Wistar albino rats weighing 150-170 g, divided into two groups. Rats of the main group were anesthesized with ether and their aorta constricted by application of a steel spring to its subdiaphragmatic segment by the method in [2]. A mock operation was performed on the control animals. Six months after the operation each group was divided into two subgroups; rats of subgroup 1 were subjected to emotional-painful stress (EPS), whereas rats of subgroup 2 remained intact.

EPS was produced by the method in [6] with exposure of 6 h. Contractility of strips of myocardium was studied 2 h after the end of exposure to stress, and also in intact animals, by the method described previously [5], the only difference being that the investigation was conducted only on strips of papillary muscle with an area of cross section under 1 mm^2 in which, according to data in the literature [1] hypoxia is not observed in the interior of the preparations.

The weight of the heart was determined by separate weighing [9], and showed that at the end of constriction of the aorta for 6 months the weight had increased to 1362 ± 10 mg com-

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TABLE 1. Effect of EPS on Contractility of Strips of Papillary Muscle of Hypertrophied Left Ventricle of Rats (M ± m)

Frequency, Hz	Parameter	Control (11)	Stress (9)	Hypertrophy (11)	Hypertrophy + stress (10)
0,3	Amplitude of contraction	3,85±0,21	1,86±0,10*	2,61±0,19*	1,04±0,08**
	Velocity of contraction	0.45±0,02	0,24±0,01*	0,32±0,01*	0,10±0,01**
	Velocity of relaxation	0,43±0,02	0,23±0,01*	0,28±0,01*	0,09±0,01**
1	Amplitude of contraction	3,08±0,18	1.49±0,09*	2,56±0,18	0,95±0,07**
	Velocity of contraction	0,42±0,02	0,17±0,01*	0,26±0,01*	0,09±0,01**
	Velocity of relaxation	0,41±0,02	0,14±0,01*	0,20±0,01*	0,08±0,01**
5	Amplitude of contraction	4,09±0,27	2,41±0,13*	2,66±0,15*	1,11±0,10**
	Velocity of contraction	0,75±0,02	0,33±0,01*	0,30±0,01*	0,13±0,01**
	Velocity of relaxation	0,88±0,02	0,35±0,01*	0,26±0,01*	0,12±0,01**

Legend. Amplitude of contraction shown in percent of initial length, velocity of contraction and relaxation in muscle units/min. *) Difference from control significant, **) difference from corresponding values during hypertrophy significant.

TABLE 2. Effect of EPS on Resistance of Contractility of Hypertrophied Myocardium to Competitors of Ca^{++} and Its Deficiency in the Surrounding Solution (M ± m)

Experimental conditions	pH		NaCl concentration, mM		$CaCl_2$ concentration, mM	
	7,40	6,85	136	165	2,50	1,25
Control(11)	3,08±0,21	1,63±0,10* (—47%)	3,12±0,20	1,86±0,12* (—40%)	3,15±0,21	2,11±0,1* (—33%)
Stress (9)	1,12±0,10*	0,47±0,04* (—58%)	1,58±0,11*	0,69±0,05* (—56%)	1,41±0,11**	0,48±0,03* (—66%)
Hypertrophy (11)	2,56±0,19	0,74±0,07* (—71%)	2,62±0,18	0,65±0,05* (—75%)	2,52±0,15**	0,53±0,04* (—79%)
Hypertrophy + stress (10)	0,95±0,08**	0,17±0,01* (—82%)	1,05±0,10*	0,13±0,01* (—87%)	0,96±0,07**	0,12±0,01** (—88%)

Legend. *) Changes in amplitude of contraction differ significantly from initial value, **) the same relative to control.

pared with 951 ± 10 mg in the control ($P < 0.01$). Hypertrophy of the heart was due mainly to an increase in weight of the left ventricle (by 50%), and to a lesser degree in weight of the right ventricle (by 24%).

EXPERIMENTAL RESULTS

The data in Tables 1 and 2 reflect the principal results of the investigation and enable the effect of the hypertrophied heart, of EPS, and of a combination of both factors on myocardial contractility to be estimated separately. Compensatory hypertrophy of the myocardium itself, even with a low frequency of contraction (60/min), was found to be accompanied by a fall in the principal parameters of contractility (Table 1). The amplitude of contraction was reduced by 17% and the velocity of contraction and relaxation by about half compared with that observed in the control. During short-term imposition of a progressive rise in the frequency of contraction on the papillary muscles tested, this disturbance of contractility, which is a feature of the hypertrophied myocardium, increased and, when the frequency was 300 contractions/min, the amplitude of contraction of the hypertrophied papillary muscles was reduced by 35% and the velocity of contraction and relaxation by about two-thirds compared with the control.

The fact that with an increase in frequency of bound contractions failure of the hypertrophied myocardium became more evident is in agreement with data showing that during the development of hypertrophy the relative area of the sarcolemma and the ratio of area of the sarcolemma to weight of a cardiomyocyte decreased [3, 7]. Consequently, the effectiveness of coupling of excitation with contraction, in which an important role is played by binding and liberation of Ca^{++} in the sarcolemma [8], may be reduced. This interpretation of the mechanism of disturbances of contractility of the hypertrophied myocardium is supported by data showing that an increase in concentration of H^+ or Na^+ cations, competing with Ca^{++} for the sarcolemmal membrane, as well as a decrease in the Ca^{++} concentration in the surrounding

solution, led to much greater depression of contractility of the hypertrophied myocardium than of the myocardium of control animals.

These data are in agreement with the view expressed previously that it is the ability of the membrane apparatus of the cardiomyocytes to bind and transport Ca^{++} that plays an important role in the depression of contractility of the hypertrophied myocardium. This shift may play an essential role in the onset of failure of the hypertrophied heart, for it reduces its resistance to tachycardia, acidosis, and disturbance of the cationic balance.

The results also indicate that after exposure to EPS, depression of myocardial contractility develops in the control, and is expressed as a reduction in the amplitude and velocity of contraction and also in the velocity of relaxation by 50-60%. At the same time a tendency was observed for resistance of contractility of the heart to decrease under the influence of an excess of ions competing with Ca^{++}, and for the usual depression of contractility induced by Ca^{++} deficiency to be doubled in magnitude. Similar changes have previously been described for the myocardium of animals exposed to EPS, and are due to injury to the cardiomyocyte membrane observed under the influence of stress [4].

It is essential to note in the present context that this poststress depression of contractility is realized against the background of contractility that is depressed on account of pre-existing hypertrophy, and, consequently, the resultant contractility of the hypertrophied myocardium of animals exposed to stress is depressed to a very low level, such as is never observed either in the control or during pure hypertrophy.

It can be postulated that during marked hypertrophy exposure to severe stress leads to profound depression of the principal parameters of myocardial contractility which is sufficient to bring it to the borderline of heart failure. It is from this standpoint that we must assess clinical experience that points to the important role of stress in the development of circulatory failure in patients with a hypertrophied heart.

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