DISTURBANCE OF MYOCARDIAL CONTRACTILITY IN STRESS: EFFECT OF ANIMAL'S AGE

A. I. Saulya

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The decline in the principal parameters of myocardial contractility with age, shown to take place in animals [2] and man [3], correlates with an increase in volume of the cardiomyocytes forming the myocardium and a decrease in the relative area of the sarcolemma of these cells. Simultaneously with the age-associated decrease in the amplitude and velocity of contraction, the reactivity of the heart to changes in Ca^{++} concentration in the external fluid, the positive high-frequency inotropic effect, and adrenoreactivity increase [2]. Since these effects are realized through entry of Ca^{++} into the cardiomyocytes, their increased effectiveness may be due to a reduction in power of the sarcolemmal transport systems responsible for removal of Ca^{++} from the cells with age. Excessive entry and accumulation of Ca^{++} in cardiomyocytes also are known to play an important role in the pathogenesis of myocardial lesions during extremal (stress) adrenergic effects [1]. The resistance of the heart muscle to stress injury probably decreases with age, and this may be manifested even before aging has begun: in the transition period from the early stage of ontogeny to the adult state.

The aim of this investigation was to compare depression of myocardial contractility under the influence of emotional-painful stress (EPS) in growing rats aged 1 month and in animals of the same genetic line but aged 6 months.

EXPERIMENTAL METHODS

Experiments were carried out on 40 male Wistar albino rats divided into two age groups: 1) aged 1 month and weighing 95 ± 5 g, 2) aged 6 months and weighing 421 ± 10 g. EPS was induced in about half of the animals of each group by the method in [4] in the course of 6 h.

TABLE 1. Effect of Age and Emotional-Painful Stress on Contractility of the Isolated Papillary Muscle of the Rat Left Ventricle (M ± m)

Freq. of stimulation, Hz	Parameter	Rats aged 1 month		Rats aged 6 months	
		control (10)	stress (9)	control (11)	stress (10)
0,1	Amplitude of contraction, % of initial length	10,45±0,30	7,75±0,25*	4,80±0,19*	1,83±0,11†
	Velocity of contraction, m.u./sec	1,43±0,04	0,88±0,03*	0,65±0,02*	0,19±0,02†
	Velocity of relaxation, m.u./sec	1,34±0,04	0,85±0,03*	0,63±0,02*	0,16±0,02†
1,0	Amplitude of contraction, % of initial length	11,76±0,31	6,82±0,20*	3,08±0,14*	1,49±0,09†
	Velocity of contraction, m.u./sec	1,90±0,04	0,80±0,02*	0,42±0,02*	0,17±0,01†
	Velocity of relaxation, m.u./sec	1,66±0,04	0,75±0,02*	0,40±0,02*	0,14±0,01†
5,0	Amplitude of contraction, % of initial length	10,41±0,30	9,12±0,29*	4,09±0,15*	1,88±0,10†
	Velocity of contraction, m.u./sec	1,82±0,04	1,52±0,03*	0,75±0,02*	0,28±0,01†
	Velocity of relaxation, m.u./sec	1,72±0,04	1,50±0,03*	0,88±0,03*	0,25±0,01†

Legend. *) Difference from control animals aged 1 month significant; †) the same, compared with control animals aged 6 months. Number of animals given in parentheses.

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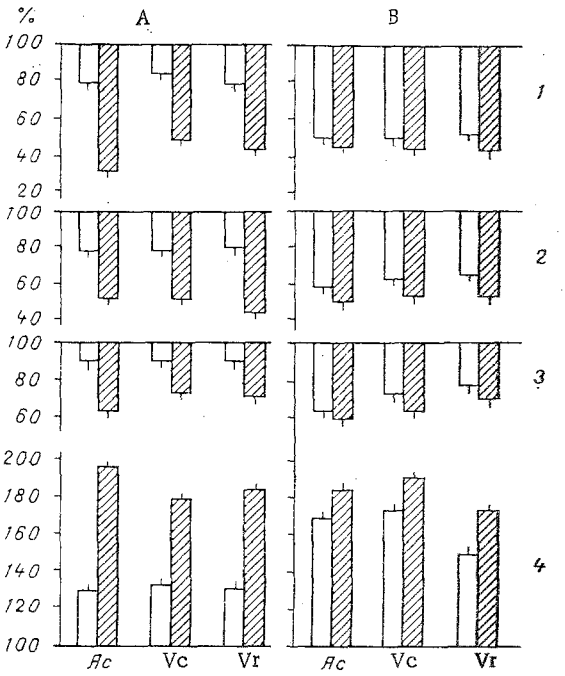

Fig. 1. Effect of age and EPS on response of isolated papillary muscles to changes in H^+, Na^+, and Ca^{++} concentration in surrounding solution. Abscissa: Ac) amplitude of contraction, Vc) velocity of contraction; Vr) velocity of relaxation; ordinate, changes in basic parameters (in % of initial value). Unshaded columns — intact animals, obliquely shaded — animals exposed to stress. A) Young rats, B) adult rats. 1) pH 6.85, 2) NaCl 165 mM, 3) $CaCl_2$ 1.25 mM, 4) $CaCl_2$ 7.5 mM.

Contractility of strips of papillary muscle from the left ventricle was tested 2 h after exposure to EPS by the method in [2]. The amplitude of contraction was expressed as a percentage of the initial length of the muscles and the maximal velocity of contraction and relaxation (the first derivative of the contraction process) was expressed in muscle units per second (m.u./sec).

EXPERIMENTAL RESULTS

In the transition period from early ontogeny to the adult state, which is accompanied by rapid growth of the animal's body and heart, a decline in the basic parameters of contractility was observed even if the frequency of contractions was low (20/min); the amplitude of contraction decreased by 54% and the velocity of contraction and relaxation also were reduced by half in rats aged 6 months compared with those aged 1 month (Table 1). If a progressive increase in frequency of contractions was imposed on the papillary muscles, this age difference in myocardial contractility became particularly marked at a frequency of 60 contractions/min as a result of opposite changes in the heart muscle preparations studied. Short-term imposition of a high frequency of contractions (300/min) caused no significant changes in the basic parameters of myocardial contractility of the young animals, whereas in mature rats the amplitude of myocardial contraction was increased by 33%, and the velocity of contraction and relaxation was about twice that observed at the initial frequency of stable contractions (60/min).

The fact that with an increase in the imposed frequency of contractions below the normal physiological range of values the inotropic properties of the heart muscle of adult animals decline is in agreement with data showing that during growth of the heart the ratio of the surface area of the heart cells to their volume decreases and, consequently, the efficiency of coupling of excitation with contraction, in which an important role is played by

binding and release of Ca^{++} by the sarcolemma [5, 6], may be reduced. This explanation of the mechanism of changes in contractility of the physiologically hypertrophied myocardium is in harmony with the data presented in Fig. 1, which indicate that an increase in the concentration of H^+ and Na^+ ions, i.e., cations competing with Ca^{++} on the sarcolemmal membrane, leads to much greater depression of this function in adult than in young animals.

In fact, extracellular acidosis and excess of sodium in these experiments led to a fall in the amplitude of contraction and in the velocity of contraction and relaxation by 35-40% compared with 18-20% in the myocardium of young animals ($P < 0.05$). This fact may indicate that binding of Ca^{++} in the sarcolemma becomes disturbed with age, and it is more easily displaced than in young animals by competing cations, i.e., by H^+ and Na^+ ions. The fact is that the resistance of the myocardium of adult animals to Ca^{++} deficiency is much less than in young animals (Fig. 1). Actually, with a decrease in the Ca^{++} concentration in the surrounding solution by half the basic parameters of contraction of the papillary muscles of the young animals were virtually unchanged, whereas in adult rats they fell by 25-30% ($P < 0.01$). A threefold increase in the Ca^{++} concentration in the perfusion fluid induced a significant inotropic effect in animals aged 1 month, manifested as an increase in the amplitude and velocity of contraction by 38%, and in the velocity of relaxation by 29%. In rats aged 6 months this positive effect was almost twice as great.

The data in Table 1 and Fig. 1 also indicate that young animals after exposure to EPS develop depression of myocardial contractility, expressed as a decrease in amplitude and velocity of contraction and also the velocity of relaxation by 26-38%. An increase in the frequency of stimulation to 60/min led to a decrease in the basic parameters of myocardial contractility, indicating disappearance of one of the principal features distinguishing the myocardium of animals in this age period: The positive dependence of inotropic effect on rhythm was converted to negative. As a result of these opposite shifts in the inotropic behavior of the myocardium in animals exposed to stress, differences between the intact and experimental animals increased: The amplitude of contraction fell by 42% compared with the control, whereas the velocity of contraction and relaxation fell by 57 and 54%, respectively ($P < 0.01$). Meanwhile, a sufficiently marked decrease in resistance of myocardial contractility to the action of an excess of competitive Ca^{++} ions and a more than twofold increase in the depression of this function usually caused by Ca^{++} deficiency were observed, together with a positive inotropic effect of excess of Ca^{++} of almost the same magnitude. This last fact is in agreement with the higher inotropic effect of the myocardium in young animals exposed to stress, in response to short-term imposition of a frequency of 300 contractions/min.

In the context of this description it is important to note that poststress depression of myocardial contractility is realized to a rather greater degree in adult than in young animals. However, it is very important to note that this takes place against a background of depressed contractility and, as a result, the ultimate contractility of the myocardium of aging animals exposed to stress is reduced to a very low level. For instance, at near-physiological frequency the amplitude of contraction in adult animals exposed to stress was only half of that in intact animals and only one-fifth of that in young animals. This suggests that aging is accompanied by depression of myocardial contractility as a result of the development of age-associated hypertrophy of the heart, and that severe stress may lead to profound depression of this function, which brings it to the limit of the physiological powers of adaptation.

There is also clinical evidence of the important role of stress in impairment of myocardial contractility in relatively young people, with no frank manifestations of aging of their heart.

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