EFFECT OF PAIN-INDUCED EMOTIONAL STRESS ON THE CONTRACTILE FUNCTION OF HEART MUSCLE AND ITS SENSITIVITY TO NORADRENALIN

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The effect of pain-induced emotional stress (PIES) on the contractile function of rat papillary muscle removed 2 h after the end of exposure to stress was studied. The velocity and amplitude of contraction and also the velocity of relaxation of the myocardium of animals exposed to PIES were reduced by more than 40%, whereas the positive inotropic effect of a high frequency of contraction was reduced by 75-86% and adrenergic reactivity was reduced about by half, although the maximal effort developed during isometric contraction was unchanged. It is suggested that during PIES a disturbance develops in the calcium transport system in the membranes and in the sarcolemmal adrenoreceptor—adenylate cyclase system.

KEY WORDS: stress; contractile function of the heart; calcium transport.

The role of emotional stress in the etiology of heart disease is generally familiar. Actually during exposure to stress disturbances of the cardiac rhythm [1, 2] and labilization of the contractile function of the heart have been found. However, no detailed study of the contractile function of heart muscle after the end of exposure to stress has yet been undertaken. Meanwhile, experiments on isolated papillary muscle under conditions when the myocardium is isolated from the regulatory effects of the rest of the body revealed disturbances of contractile function that can only be attributed to long-term disturbances of structure and metabolism remaining in the myocardium after stress. Accordingly the object of the present investigation was to study the effect of exposure to pain-induced emotional stress (PIES) on the contractile function of papillary muscles removed from the animal after the end of exposure to stress and on their sensitivity to noradrenalin.

METHODS

Experiments were carried out on male Wistar rats, ten of which were exposed to PIES and ten of which acted as control.

PIES was produced in the form of an anxiety neurosis by the method of Desiderato et al. [3]. The stress situation lasted 6 h, and 2 h later the animals were killed under urethane anesthesia; control animals not exposed to PIES were killed at the same time.

The contractile function of the lateral papillary muscle of the left ventricle was studied by a modified Sonnenblick's method [4], which was described in detail previously [5].

RESULTS AND DISCUSSION

As Table 1 shows, the maximal velocity and amplitude of isotonic contraction of the papillary muscle of animals exposed to PIES were reduced by about 40%, and the velocity of relaxation was reduced commensurately. By contrast with these parameters, the maximal effort developed by the muscle during isometric contraction was not significantly changed under the influence of PIES. Isometric contraction is known to be associated with a much greater ATP utilization and oxygen consumption than isotonic contraction. The fact that stress did not affect the maximal effort developed during such contraction suggests that depression of the velocity of contraction and relaxation under the influence of PIES was the result of an energy deficiency. In the current view, this depression could be the result either of lowering

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TABLE 1. Disturbances of Contraction and Relaxation of Papillary Heart Muscle After PIES

Parameter	Control	PIES (n = 12)	Difference, %	P
Optimal resting load, g/mm²	0,29±0,02	0,22±0,01	—24	<0,01
Maximal amplitude of contraction corresponding to optimal resting load, % of initial length	8,44±1,10	5,12±1,10	—40	<0,05
Maximal velocity of contraction, unit muscle length/sec	1,30±0,21	0,78±0,16	—40	>0,1
Contraction time, mm/sec	111±7,50	100±4,28	—11	n.s.
Maximal velocity of relaxation, units muscle length/sec	0,92±0,16	0,57±0,11	—39	>0,1
Relaxation index, sec⁻¹	10,08±1,22	10,05±0,83		
Maximal effort during isometric contraction, g/mm²	0,76±0,19	0,68±0,07	—11	n.s.

Legend. n.s.) Not significant.

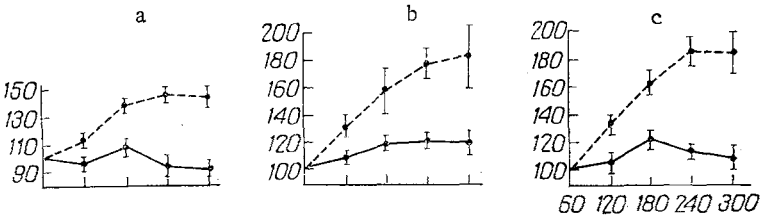

Fig. 1. Effect of exposure to PIES on positive intotropic effect of a high frequency of contraction imposed on the papillary muscle. a) Velocity of contraction, b) amplitude of contractions; c) velocity of relaxation. Ordinate, values of these parameters in % of initial value; abscissa, imposed frequency of contractions per minute. Here and in Fig. 2, broken line represents control animals, continuous line animals exposed to PIES.

of myofibrillary ATPase activity or of a disturbance of membrane calcium transport. Results obtained when a high frequency of contraction was imposed on the papillary muscle give indirect support to the possibility of a disturbance of calcium transport after PIES.

The curves in Fig. 1 show that the papillary muscle in the control responded to imposition of a high frequency of contraction by a marked positive inotropic effect: When the frequency was increased from 60 to the highest imposable frequency of 300 contractions/min the velocity and amplitude of isotonic contraction increased by 65-80% whereas the velocity of relaxation increased by 85%. The papillary muscle of animals exposed to PIES, at the same frequency of contraction, showed an increase in these indices by 10-20% and its inotropic effect was reduced by 75-86%. When this considerable decrease in the positive inotropic effect of a high frequency in the heart muscle of animals exposed to PIES is assessed, the mechanism of this effect must be borne in mind. An increase in the frequency of contractions is known to increase the inflow of Ca^{++} into the myocardial cells and its accumulation in the membranes structures of the sarcoplasmic reticulum and sarcolemma. As a result, with each successive excitation more Ca^{++} enters the myoplasm, the number of actomyosin cross-linkages in the myofibrils increases, and a positive inotropic effect develops [6]. Consequently, the disturbance of the realization of this effect in animals exposed to PIES can more probably be explained on the grounds that PIES cause a disturbance of the uptake of calcium and its accumulation in the membranes of the sarcoplasmic reticulum and sarcolemma.

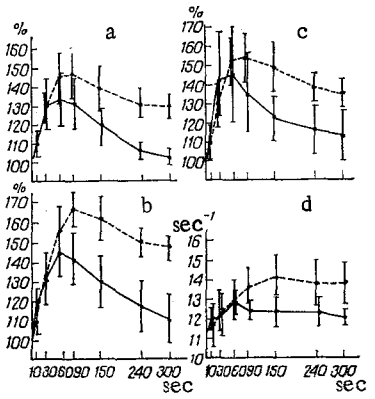

Fig. 2. Effect of PIES on sensitivity of papillary muscle to noradrenalin. a) Amplitude of contraction; b) velocity of contraction; c) velocity of relaxation; d) relaxation index. Ordinate) values of these parameters expressed in % of initial value; abscissa) time after administration of noradrenalin (in sec). Remainder of legend as in Fig. 1.

The effect of PIES on the membrane of the myocardial cell can evidently be explained also by another fact which was discovered during the study of the contractile function of the papillary muscle, namely a decrease in its sensitivity to noradrenalin. The curves in Fig. 2 show that the papillary muscle of the control animals responded to injection of 10^{-6} M noradrenalin into the perfusion fluid by a considerable increase in the velocity and amplitude of contraction and by an even greater increase in the velocity of relaxation. There was a corresponding increase in the relaxation index, the ratio between the velocity of relaxation and the amplitude of contraction. The positive inotropic and relaxing effect of noradrenalin on the papillary muscles of animals exposed to PIES were significantly reduced. After exposure to stress a marked decrease in the sensitivity of the heart muscle to noradrenalin was thus observed.

The positive inotropic effect of noradrenalin is known to take place because this mediator, acting on the adrenoreceptor, activates the adenylate cyclase system located in the sarcolemma, and the cyclic AMP, formed as a result in increased quantity, activates both calcium transport and the formation of actomyosin cross-linkages in the myofibrils [7]. This means that one of the possible causes of the decrease in sensitivity to noradrenalin is a disturbance of the function of the adrenoreceptor—adenylate cyclase system located in the sarcolemmal membrane.

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