EFFECT OF EMOTIONAL PAIN-INDUCED STRESS ON REACTIVITY OF HEART MUSCLE TO CHANGES IN CALCIUM CONCENTRATION

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The effect of changes in the Ca^{++} concentration in the perfusion fluid on function of the isolated heart of control rats and of rats exposed to emotional pain-induced stress (EPS) was studied. EPS was shown to cause a sharp increase in the intensity of the response of the animals' heart to a change in Ca^{++} concentration in the perfusion fluid: depression of the contractile function in response to a decrease in Ca^{++} concentration and an increase in the basic parameters of the contractile function in response to an increase in Ca^{++} concentration after EPS were considerably more marked than in the control. It is suggested that the increased dependence of the heart of animals subjected to EPS is the result of damage to membrane Ca^{++} transport mechanisms in the myocardial cells.

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

Emotional stress plays an important role in the etiology of diseases of the circulation [4]. However, the mechanism whereby high concentrations of corticosteroids and catecholamines realize their harmful action on the heart during stress is not yet clear in many respects. It has recently been shown that marked activation of lipid peroxidation [2] and labilization of lysosomes [3] develop in the heart muscle during emotional pain-induced stress (EPI). On this basis it has been postulated that lipid hydroperoxides and proteolytic enzymes liberated from lysosomes damage myocardial cell membranes and may disturb Ca^{++} transport [1].

To test this hypothesis experiments on the isolated heart are of great importance, because the disturbances of function of such a heart, removed from an animal after exposure to stress, can only depend on relatively long-lasting disturbances of structure and metabolism. The object of the present investigation was to study how exposure to EPS affects the ability of the heart to adapt itself to changes in Ca^{++} concentration in the perfusion solution and, on that basis, to obtain a closer understanding of the effect of EPS on Ca^{++} transport in heart muscle.

EXPERIMENTAL METHOD

Male Wistar rats weighing 250 g were used. Ten animals were exposed to EPS and ten acted as controls. EPS was produced as the so-called anxiety neurosis by the method of Desiderator et al. [5]. The stress situation lasted 6 h, and the heart was removed from the animals, under urethane anesthesia, 2 h later. The hearts of animals not exposed to EPS served as the control.

The contractile function and oxygen consumption of the working heart was studied by the method of Neely et al. [6]. The heart was perfused with Krebs–Henseleit solution saturated with a mixture of 96% O_2 and 4% CO_2 at 37°C; the heart rate was spontaneous and the filling pressure was 10 mm Hg. The intra-aortic pressure was recorded by means of an electromanometer; the stroke volume, cardiac output, and coronary blood flow also were determined and the partial pressure of oxygen in the perfusion fluid was measured by means of a Clark's oxygen electrode.

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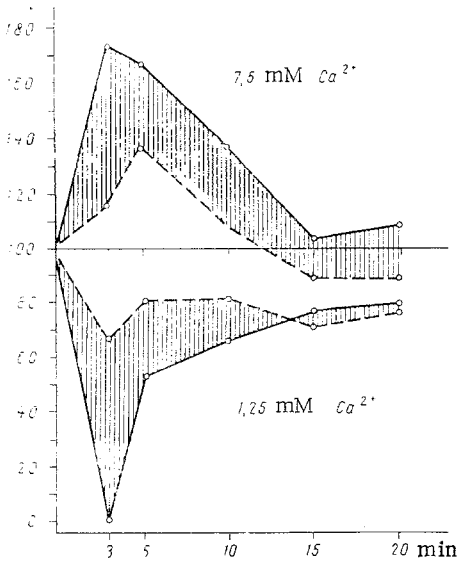

Fig. 1. Course of responses of isolated working heart of control animals (broken line) and of animals exposed to EPS (continuous line) to changes in Ca^{++} concentration in perfusion solution. Bottom part of figure shows response to a decrease in Ca^{++} concentration from 2.5 to 7.5 mM. Ordinate, stroke volume (in % of initial before change in Ca^{++} concentration); abscissa, time (in min) after change in Ca^{++} concentration. Shaded zone indicates effect of EPS.

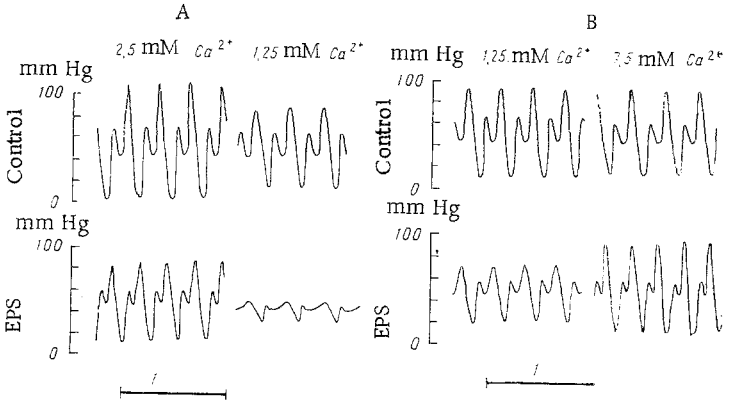

Fig. 2. Effect of decrease (A) and increase (B) in Ca^{++} concentration in perfusion fluid on pressure developed in aorta of isolated working heart of control animals and of animals exposed to EPS.

On the basis of the results the external work done by the heart, oxygen consumption, and efficiency of oxygen utilization were calculated by the usual equations.

EXPERIMENTAL RESULTS

The stroke volume and systolic pressure developed by the heart of animals exposed to EPS was found to be reduced by 10-20% and, as a result of that, the external work done by these hearts under steady-state conditions was reduced by one-third. The oxygen consumption was the same as in the control and the efficiency of the hearts showed a corresponding decrease by one-third.

The main result of the experiment was a sharp increase in the response of the heart of animals exposed to EPS to a change in the Ca^{++} concentration in the perfusion solution.

With a decrease in the Ca^{++} concentration in the perfusion fluid from 2.5 to 12.5 mM the maximal response decrease of stroke volume of the isolated hearts of the control animals was under 40%, whereas the stroke volume of the hearts of animals exposed to EPS was reduced to 0, i.e., by 100% (Fig. 1). With a subsequent increase in Ca^{++} concentration from 1.25 to 7.5 mM the response increase in stroke volume of the control was 20-40%, whereas for the hearts of animals exposed to EPS it was 80%. These changes were well-marked during the first 3-5 min after a change in the Ca^{++} concentration, but later the function of the heart in both series gradually returned to its initial level on account of adaptation of the ion transport mechanisms.

The curves in Fig. 2 show the same phenomenon – the influence of exposure to EPS on reactivity of the isolated heart to changes in the Ca^{++} concentration as reflected in aortic pressure curves. Clearly 3 min after the Ca^{++} concentration was lowered from 2.5 to 12.5 mM the systolic pressure in the control fell by about 20 mm Hg, whereas the heart of the animal exposed to EPS responded to the same decrease in Ca^{++} concentration by a very great fall of systolic pressure. Figure 2B shows that 3 min after a fivefold increase in the Ca^{++} concentration (from 1.25 to 7.5 mM) the systolic pressure developed by the heart of an animal exposed to EPS increased much more than in the control.

There is thus no doubt that after stress, changes develop in the heart muscle of animals which sharply increase the dependence of the contractile function of the heart on the Ca^{++} concentration in the perfusion fluid. When this fact is assessed it must be remembered that the response of the muscle to a change in the external Ca^{++} concentration depends on the power of the mechanisms for transport of this cation. For instance, the well-developed system of the sarcoplasmic reticulum (SPR) in skeletal muscle ensures that nearly all the Ca^{++} which leaves the cisterns of the SPR during the action potential, and which causes contraction of the myofibrils, later returns to the tubules of the SPR. As a result of this 100% Ca^{++} recycling the skeletal muscle can contract for several hours in a solution without Ca^{++}. The power of the mechanisms of Ca^{++} transport located in the SPR and sarcolemma of mammalian heart muscle cells is not so great; recycling does not reach 100%, and accordingly the heart stops beating in a solution without Ca^{++} after performing a few scores of contractions. Finally the SPR in a frog's heart is very poorly developed and after removal of Ca^{++} from the solution the heart stops instantly [7].

These findings suggest that the increasing dependence of the heart of animals subjected to EPS on the external Ca^{++} concentration is the result of injury to membrane Ca^{++} transport mechanisms in the myocardial cells – a result of reduced ability of the sarcolemmal and sarcoplasmic membranes to assimilate and accumulate Ca^{++}.

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