EFFECT OF STRESS ON EXTENSIBILITY AND CONTRACTILITY OF THE MYOCARDIUM

M. G. Pshennikova, E. Ya. Vorontsova, and F. Z. Meerson

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KEY WORDS: atrium; emotional-painful stress; myocardium.

Animals exposed to emotional-painful stress (EPS) develop disturbances of myocardial contractility, expressed as a decrease in the intraventricular pressure which can be developed in the intact organism [7], a decrease in the stroke volume and pressure developed by the isolated heart [8], and depression of the force and rate of contraction of isolation papillary muscle [3]. However, changes in the mechanisms of self-regulation of heart muscle which may lie at the basis of these disturbances have not hitherto been investigated. It was accordingly decided to study the effect of stress on extensibility of the myocardium and performance of the Starling mechanism in experiments on the isolated rat atrium.

EXPERIMENTAL METHOD

Male Wistar rats weighing 200 ± 7 g were used. EPS was produced once only, in the form of an "anxiety neurosis" [10], lasting 6 h. The rats were decapitated 2 h after the end of EPS, the right atrium was isolated and transferred to a constant-temperature bath containing oxygenated Krebs–Henseleit solution (95% O_2, 5% CO_2, pH 7.4, 34°C) so that the base of the atrium was rigidly fixed and the apex of the auricle was attached to a F50 Physiograph DMP-4B myograph (Narco Biosystems, USA). The atrium contracted spontaneously for 40-50 min, after which it was gradually stretched by means of a weight to the length (l_{max}) at which it developed maximal systolic tension while contracting under isometric conditions. Changes in length of the atrium were recorded by a micrometer as the stretching load was increased by every 100 mg. The weight which corresponded to l_{max} was called the maximal resting load (max T_r). The experiment showed that the weight and initial length of the atria of rats exposed to EPS were 24 ± 0.7 mg and 8.9 ± 0.3 mm respectively and that they did not differ significantly from those in the control (25 ± 0.5 mg and 9.2 ± 0.2 mm).

Extensibility of the atrium was judged from the resting load–length curve, i.e., from the amount of increase in length during stretching to l_{max}, and also from l_{max} itself. Atrial contractility was judged from the maximal value of systolic tension developed (T) during isometric contraction, from the resting load–developed tension curve, from the length–developed tension curve (Starling curve), and also from the efficiency of realization of the Starling mechanism in the course of stretching ($\Delta T/\Delta l$), which describes the increase in T for every millimeter increase in length of the atrium during stretching. Statistical analysis of the results was carried out by Student's test.

EXPERIMENTAL RESULTS

Although the initial length and weight did not differ significantly from the control, the atria of rats exposed to EPS had reduced extensibility and reduced contractility. Figure 1A, for instance, shows that the specific increase in length of the atrium for every 100 mg increase in load was about 33-50% less in rats exposed to EPS than in the control, and that to stretch the atrium by 50% of its initial length in these rats a load of 500 mg had to be applied, i.e., a load 2.5 times greater than in the control (200 mg). Ultimately l_{max} in rats exposed to EPS amounted to 13.8 ± 0.4 mm (compared with 16.7 ± 0.5 mm in the control), i.e., it was 20% less ($P < 0.05$).

It will be clear from Fig. 1B that the atria of rats exposed to EPS developed a systolic tension during stretching that was about 50% less than in the control, and as a result the

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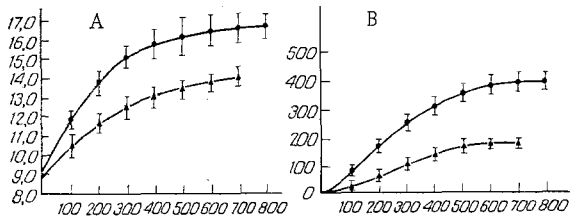

Fig. 1. Effect of EPS on resting load—length (A) and resting load—developed tension (B) curves for rat's right atrium. Abscissa, resting load, (in mg); ordinate: A) length of atrium (in mm), B) developed systolic tension (in mg). Here and in Fig. 2, circles denote control, triangles — EPS.

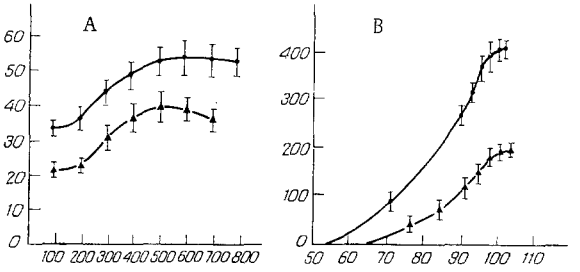

Fig. 2. Effect of EPS on realization of Starling mechanism in right atrial myocardium of rat. A: abscissa, resting load (in mg); ordinate, $\Delta T/\Delta l$ (in mg/mm); B: abscissa, length of atrium (in percent of l_{max}, taken as 100%); ordinate, systolic tension developed (in mg).

maximal value of this parameter was 190 ± 4 mg in these animals compared with 402 ± 30.9 mg in the control, i.e., it was reduced by more than half ($P < 0.001$). Considering the information given above, it will be evident that one cause of poststress depression of atrial contractility was a decrease in atrial extensibility, limiting realization of the Starling mechanism. However, as the curves in Fig. 2A show, the reduction in the contractility of the atrial myocardium in stress was also due to the fact that in response to every millimeter of increase in length in rats exposed to stress the atria were able to develop a smaller tension than in the control. This value of the efficiency of the Starling mechanism was reduced after stress by 30-40% compared with the control (Fig. 2A). As a result, the Starling curve for the atria of rats exposed to stress was shifted downward and to the right (Fig. 2B), a characteristic feature of depression of myocardial contractility.

The two basic facts discovered by this investigation, namely a decrease in extensibility of the atria and a decrease in the efficiency of realization of the Starling mechanism, are evidence that one of the chief causes of disturbance of contractility of the heart in animals exposed to stress is a disturbance of the mechanisms of self-regulation of the heart. A decrease in extensibility of heart muscle limits the optimal increase in length of the sarcomeres of the cardiomyocytes in diastole; in conjuction with a reduction in the specific increase in tension capable of being developed per unit length, i.e., with a reduction in the efficiency of the Starling mechanism, this phenomen leads to a decrease in the pumping function of the heart.

On the basis of modern views regarding the mechanism of myocardial contraction it can be postulated that the cause of this disturbance of the mechanisms of self-regulation of contractility of heart muscle after stress is an increase in the number of residual actomyosin cross-linkages remaining after completion of relaxation and, as a result of this, a reduction in the number of free active centers on the protofibrils capable of forming new cross-linkages during contraction [5, 13]. A increase in number of residual cross-linkages limits the extensibility of the myocardium, whereas a decrease in the number of active centers limits the formation of new cross-linkages and, consequently, the amount of tension which the heart muscle can develop. Two processes play the decisive role in disconnection of the cross-linkages and the relaxation process of the myocardium as a whole: first, the timely supply of ATP to the myofibrils, formed during oxidative phosphorylation and glycolysis and transported to the contractile mechanism by means of the creatine kinase system [9] and, second, removal

of Ca^{++} from the myofibrils by mechanisms of ion transport located in the sarcoplasmic reticulum and sarcolemma [11-13]. Activation of lipid peroxidation in the myocardium [4, 8] and injury by products of this oxidation to the Ca^{++}-transporting mechanism of the sarcoplasmic reticulum [2] and mitochondrial membranes [1] and sarcolemma in the cardiomyocytes, and also a decrease in the glycogen concentration in the myocardium [6] have been found in EPS. This suggests that in the poststress period processes of Ca^{++} transport and the energy supply to the contractile mechanism are disturbed in the cardiomyocytes. As a result, the number of residual actomysin cross-linkages increases, the number of active centers on the protofibrils is reduced, and the reduction of extensibility of the atria and of the systolic tension capable of being developed by them, which was revealed by the present experiments, arises.

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In vivo HEMATOCRIT STUDY IN THE MICROCIRCULATORY SYSTEM BEFORE AND AFTER DEXTRAN INJECTION

V. K. Khugaeva and P. N. Aleksandrov

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The rheologic properties of the blood and, in particular, its viscosity depend to a large extent on the hematocrit index. This index has hitherto been determined in mixed or venous blood by centrifugation in glass capillary tubes. Under these conditions the hematocrit index is usually overestimated because of changes in size of the erythrocytes, between which a layer of plasma always remains. Meanwhile, the hematocrit index is widely used to determine the circulating blood volume and during treatment with blood substitutes. Knowledge of the precise values of the hematocrit index is thus very important not only for practical medicine but also for the construction of a correct mathematical model of the circulation. Yet information on the level of the hematocrit index in different parts of the cardiovascular system is very limited in amount and contradictory in nature [4, 9, 11]. Investigations of the hematocrit index in microvessels have recently been published [5, 8-10].

The object of this investigation was to study the hematocrit index *in vivo* in microvessels before and after injection of polyglucin, a widely used Soviet dextran preparation.

Laboratory of Hemorheology and Pathophysiology of the Circulation, Institute of General Pathology and Pathological Physiology, Academy of Medical Sciences of the USSR, Moscow. (Presented by Academician of the Academy of Medical Sciences of the USSR A. M. Chernukh [deceased].)

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