MYOCARDIAL CONTRACILITY DURING REGRESSION OF ADAPTATION TO SHORT-TERM STRESS

F. Z. Meerson and L. S. Katkova

UDC 612.172.014.49:613.863

KEY WORDS: myocardial contractility; stress; adaptation to stress.

As a result of repeated exposure to short-term stress situations adaptation develops and serves to prevent the harmful action of emotional-painful or immobilization stress on the heart, the stomach, and the system of normal killer cells, which play a role in anti-tumor immunity [3-5]. The question of how long this regression of the adaptive increase in resistance to stress injury lasts and how it takes place has not hitherto been studied, although it is of great importance for our understanding of the nature of adaptation of the organism to environmental influences of this kind.

The aim of this investigation was to examine this problem by assessing disturbances of myocardial contractility arising under the influence of prolonged immobilization stress, induced immediately after a course of short (adaptive) exposures to stress and at different times after the end of such a course.

EXPERIMENTAL METHOD

Experiments were carried out on male Wistar rats weighing 220-300 g and they consisted of 10 series: series I) control experiments; II) prolonged immobilization stress produced by fixing the animals in the supine position for 6 h; III) animals exposed daily to short (adaptive) periods of stress by fixation in the same way: On the 1st day the rats were fixed for 15 min, on the 2nd day for 30 min, on the 3rd day for 45 min, and during the next 10 days for 1 h; IV) immediately after a course of adaptive exposures to stress the animals were subjected to prolonged immobilization stress; V) the animals were exposed to the same course of adaptive stress as in the previous series, but were used in the experiments 3 days after the end of adaptation; VI) animals adapted to short exposures to stress were subjected, 3 days after the end of the course, to prolonged immobilization stress, and used in the experiments later; VII) the animals were exposed to adaptive stress and used in the experiments 5 days after the end of the course; VIII) adapted animals, 5 days after the end of the course of adaptation were exposed to prolonged immobilization stress, and used in the experiments later; IX) the animals were used in the experiments 10 days after the end of the course of adaptation; X) adapted animals were exposed to immobilization stress for 6 h 10 days after the end of the course of adaptation.

To assess contractility of the heart muscle the right atrium was excised and placed in a constant temperature bath containing oxygenated Krebs–Henseleit solution (95% O_2, 5% CO_2, pH 7.4, 34°C). Under these circumstances the base of the atrium was fixed immovably, and the apex of the auricle was attached to the F-50 myograph of a DMP-4B Physiograph ("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 at which it developed maximal tension under isometric conditions of contraction (l_{max}). Changes in length of the atrium were recorded by a micrometer as the load was increased by every 100 mg. Extensibility of the atrium was judged from the increase in length (Δl) up to l_{max}. Contracility was judged from the maximal value of developed tension (T_p) under isometric conditions of contraction, and by calculation of the intensity of functioning of structures (IFS), determined as the tension developed by unit mass of myocardium in unit time, and calculated by the equation:

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 D. S. Sarkisov.) Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 98, No. 12, pp. 655-657, December, 1984. Original article submitted November 18, 1983.

0007-4888/84/9812-1625$08.50

TABLE 1. Effect of Preliminary Adaptation to Short Periods of Stress on Resistance of Myocardial Contractility to Prolonged Stress

Parameter	Series of experiments									
	I ($n=17$)	II ($n=9$)	III ($n=10$)	IV ($n=10$)	V ($n=7$)	VI ($n=7$)	VII ($n=7$)	VIII ($n=7$)	IX ($n=7$)	X ($n=8$)
Extensibility (Δl), mm	9,20±0,40	6,58±0,38*	7,74±0,31*	8,2±0,36	7,46±0,32	7,50±0,50	8,21±0,32	8,29±0,36	9,34±0,43	7,49±0,90
Developed tension (T_p), mg	676,0±76,0	318,3±23,3*	511,3±37,40*	522,0±39,2	388,0±67,1*	462,0±50,2	580,0±32,1	556,7±37,8	640,0±40,2	413,3±42,1
Intensity of functioning of structures (IFS), g/mg·min	4,48±0,30	2,34±0,28*	3,0±0,29*	3,6±0,4	2,74±0,36*	3,58±0,50	4,19±0,34	3,96±0,22	3,86±0,40	2,84±0,24**
IC after calcium loading for 5 min, %	98,42±10,0	147,8±21,20*	117,0±10,92	77,0±6,8**	142,3±25,0*	74,7±9,3	90,7±4,7	76,8±8,5	91,7±10,6	78,1±10,5**
IC after hypoxia for 20 min, %	110,5±10,8	169,1±14,70	78,0±9,86*	66,0±6,63*	203,9±12,3	149,7±14,8**	118,5±28,1	82,3±17,1	107,5±19,2	156,2±17,7

Legend. Parameters of contractility determined at l_{max}, i.e., on the plateau of the Starling curve. $P < 0.05$; *) between control and remaining series, **) between "adaptation" and "adaptation + stress" series for each time of adaptation respectively.

$$IFS = \frac{T_p \cdot F}{M},$$

where T_p is the developed tension (in g), F the heart rate in beats/min, and M the weight of the atrium. To assess the atrial response to an excess of calcium the Ca^{++} concentration in the working solution was trebled (to 7.5 mM) for 5 min, and to assess the atrial response to hypoxia, the oxygenated working solution was replaced for 20 min by a nonoxygenated solution. The response to both factors was estimated as the index of contracture (IC) developing under the influence of hypoxia or of excess of calcium. IC is the ratio of resting tension during contracture (T_o) to the developed tension:

$$IC = T_o \Big/ \frac{T_o}{T_p} \cdot 100\,\%.$$

EXPERIMENTAL RESULTS

The main results of all series of experiments are given in Table 1, from which certain basic principles can be distinguished.

The first principle is that the atrial function of animals exposed to prolonged stress was significantly disturbed. Extensibility, estimated as Δl, was reduced in these animals by one-third, and the developed tension and IFS by about half. Resistance of the myocardium to hypoxia and to excess of Ca^{++} also was reduced, and the index of contracture arising in response to these situations was correspondingly by 1.5 times after exposure to stress. These disturbances of myocardial contractility are in agreement with results published previously [1, 3].

The second principle is that adaptation to repeated stress may itself give rise to disturbances of extensibility and contractility of the myocardium, which follow a definite time course after the end of the course of exposures to stress. In fact, extensibility and contractility of the atria taken from animals immediately after a course of short exposure to stress, i.e., from adapted rats, were lower than in the control. However, this effect of repeated exposures to stress was small: as regards extensibility it was 15%, and as regards developed tension and IFS it was 20-30%. Resistance of the atria of the adapted animals to excess of Ca^{++} was not significantly changed, and resistance to hypoxia was increased. Consequently, immediately after the end of the course of short exposures to stress a limited reduction of atrial myocardial contractility was observed, a unique manifestation of what has been called the price of adaptation [2, 3]. Three days after the end of adaptation, the "price" of adaptation was significantly increased relative to the basic parameters of contractility. The developed tension was reduced by half and IFS by 39%. Later (after 5 days) all these disturbances were sharply reduced and ceased to be significant. As a result the extensibility, contractility, and resistance to hypoxia and to excess of Ca^{++} did not differ significantly from the control. Ten days later a tendency appeared for all these parameters to increase. Thus after completion of adaptation to short exposures to stress the function of the heart and its resistance to hypoxia and to excess of calcium changed so that initial

marked depression of these parameters was followed (by the 5th day) by their restoration to the control level.

The third and most important principle is that adaptation to short periods of stress completely prevents disturbance of myocardial contractility due to ordinary prolonged stress. The experimental results are evidence that (Table 1) this prophylactic effect is completely preserved as long as 5 days after the end of the course of adaptive exposures, i.e., under conditions when myocardial contractility of the adapted animals no longer differed from the control. In other words, complete recovery of all parameters of myocardial contractility in animals undergoing a course of short adaptive exposures to stress is in no way accompanied by disappearance of resistance to prolonged stress acquired as a result of such adaptation. This situation arises much later, namely 10 days after the end of the course of short exposures to stress (Table 1).

Consequently, a stage of the process is reached at which the negative effect of adaptation, or its "price," is not manifested at all, whereas its positive effect, namely increased resistance to the harmful action of prolonged stress, is completely preserved. As a result, extensibility of the myocardium, developed tension, and resistance to hypoxia and to excess of calcium after prolonged stress were completely indistinguishable from the control values. This main fact established by this investigation is in agreement with the view that the prophylactic effect of preliminary adaptation to short periods of stress is closely linked with activation of the inhibitory antistress systems of the brain [2, 3] and is therefore preserved for quite a long time.

LITERATURE CITED

1. E. Ya. Vorontsova, M. G. Pshennikova, and F. Z. Meerson, Kardiologiya, No. 11, 68 (1982).
2. F. Z. Meerson, Adaptation, Stress, and Prophylaxis [in Russian], Moscow (1981).
3. F. Z. Meerson, L. S. Katkova, Yu. P. Kozlov, et al., Byull. Éksp. Biol. Med., No. 12, 21 (1983).
4. F. Z. Meerson, L. S. Katkova, and V. V. Malyshev, Kardiologiya (1983), in press.
5. F. Z. Meerson, G. T. Sukhikh, L. S. Katkova, et al., Dokl. Akad. Nauk SSSR, (1983), in press.

HEMODYNAMIC AND MOTOR DISTURBANCES OF THE GASTROINTESTINAL TRACT IN INTRAMURAL ISCHEMIA

Z. M. Sigal, Yu. V. Makotchenko, A. P. Kravchuk, and P. A. Pletnev

UDC 616.33/.34-005.4-092.9-07:616.33/.34-009.1

KEY WORDS: motor activity; hemodynamics; pulsomotorgraphy; angiotensometry; intramural ischemia.

Motor and hemodynamic disturbances in the hollow abdominal organs lie at the basis of intramural ischemia and are responsible for viability of the stomach and intestine. These two important functions are nowadays beginning to be considered in conjunction with each other, having regard to their mutual interaction in hollow organs [1, 6, 7, 9]. The anatomical substrate for this interaction is the intimate arrangement of the principle collector of the intramural blood flow in the submucosa with the subjacent muscular coat. The main drawback to the investigations mentioned above is the use of different methods of determining the motor and hemodynamic parameters of the wall of hollow organs. The indirect nature of the methods of determining the intramural hemodynamics [2, 3, 8] and the traumatic nature of methods of investigation of motor function, which affect the reliability of the results, must also be borne in mind. In the investigation described below motor and hemodynamic para-

Department of Operative Surgery and Topographic Anatomy, Izhevsk Medical Institute.

(Presented by Academician of the Academy of Medical Sciences of the USSR G. N. Kryzhanovskii.) Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 98, No. 12, pp. 657-659, December, 1984. Original article submitted May 28, 1984.