PREVENTION OF STRESS-INDUCED DISTURBANCES OF MYOCARDIAL CONTRACTILITY BY GENTLE ADAPTATION TO SHORT-TERM STRESS

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Preliminary adaptation of animals to repeated short-term stress, in the form of immobilization for 1 h daily for 12-15 days, largely prevents depression of myocardial contractility during long-term stress [2, 3]. It has been suggested that the protective effect of such adaptation is based on increased power of the central and cellular systems of the body which limit the stress reaction, i.e., ultimately on increased efficiency of enzymes forming GABA, endorphins, and enkephalins in the brain, as well as of natural antioxidants, prostaglandins, and adenosine in the effector organs [1]. The protective effect of adaptation to stress in the form which has hitherto been used is incomplete, and this adaptation has its "price," i.e., by itself it depresses the main parameters of myocardial function by 15-20%.

In the present investigation an attempt was made to eliminate the "price" of adaptation by reducing the number of short exposures to stress. The idea was that long-term adaptation to factors of different kinds, including to stress factors, is based on a memory effect and, in particular, brain memory [1], which can often be more effectively realized by repeated exposures at considerable time intervals than by too frequent exposures [4]. Accordingly short exposures to stress were given on alternate days rather than daily, and only six times instead of 12 times.

EXPERIMENTAL METHOD

Male Wistar rats weighing 200-290 g were used. There were four series of experiments: I) control, II) animals exposed to long-term immobilization stress by fixation in the supine position for 6 h, III) animals adapted to short-term stress by repeated fixation in the supine position for 15 min the first time. 45 min the second time, and 60 min on each of the next four times; the rats were exposed to stress of this kind on alternate days; IV) after a course of short-term adaptation the rats were subjected to long-term immobilization stress. Myocardial contractility was studied on the isolated right atrium. The atrium was removed and placed in 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 fixed immovably and the apex of the auricle was attached to the F-50 myograph of the DMP-4B physiograph (Narco Bio-Systems, USA). The atrium contracted spontaneously for 40-50 min, after which it was stretched by stepwise increasing external loads (100 mg) to length l_{max}, at which the atrium developed maximal tension. During stretching at each step of the load the developed tension (T_p), heart rate per minute (F), and extensibility of the atrium, i.e., the increase in its length to response to the applied external load (Δl) were recorded, a Starling curve was plotted, and the intensity of functioning of structures (IFS), the product of developed tension and heart rate, expressed per unit of mass, i.e.,

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

where m is the mass of the atrium, was determined at the plateau of the curve. The dimensionality of IFS is: g force/mg mass · min. The results were subjected to statistical analysis and the significance of differences was determined by Student's test.

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TABLE 1. Effect of Adaptation to Short-Term Stress on Myocardial Contractility during Long-Term Stress

Series of experiments	IFS, $\frac{\text{g force}}{\text{mg mass} \cdot \text{min}}$
I — Control (n=16)	4,04±0,26
II — Stress (n = 8)	1,54±0,39
	$P_{II-I}<0,001$
III — Adaptation (n = 8)	4,84±0,37
	$P_{III-I}<0,05$
I — Adaptation + stress (n = 9)	3,62±0,51
	$P_{IV-III}<0,01$
	$P_{IV-I}<0,2$

Legend. n) Number of animals in series.

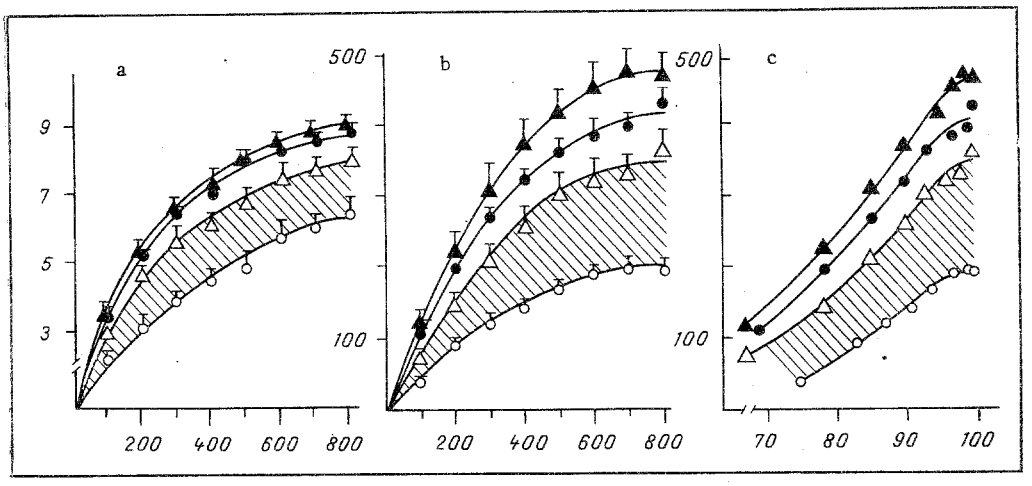

Fig. 1. Effect of gentle adaptation to short-term stress on extensibility and contractility of myocardium during long-term stress. a: Abscissa, resting load (T_r) (in mg); ordinate, increase in length of atrium (Δl) (in mm); b: abscissa, resting load (T_r) (in mg); ordinate, developed tension (T_p) (in mg); c: abscissa, length of atrium (in % of l_{max}, taken as 100); ordinate, developed tension (T_p) (in mg). Filled circles – control, empty circles – stress, filled triangles – adaptation, empty triangles – adaptation + stress.

EXPERIMENTAL RESULTS

The curves in Fig. 1 illustrate the dynamics of parameters of atrial contractility during stretching. Adaptation to repeated stress, in the version which we used, i.e., achieved by comparatively infrequent exposures to stress at long time intervals, was found not to produce depression of any of the measured parameters of myocardial contractility. On the contrary, curves of extensibility and developed tension and Starling curves in adapted animals were a little above the control level.

Just as previously [2, 3] stress induced depression of extensibility and a certain kind of rigidity of the myocardium (Fig. 1a) and also depression of developed tension (Fig. 1b); finally, it induced marked depression of the Starling curve (Fig. 1c). Preliminary adaptation prevented the development of this combination of disturbances of atrial contractility (the shaded zone in Fig. 1). As a result of this protection, extensibility and contractility of the myocardium on the plateau of the Starling curve in adapted animals after stress was much higher than in unadapted animals. The increase for extensibility of the myocardium was 20% and for its developed tension 84%. As a result, all these parameters on the plateau of the Starling curve, for adapted animals after stress, did not differ significantly from the control: Protection was complete.

The question accordingly arises: What is the effect of gentle adaptation on an integral parameter of myocardial contractility such as IFS. It will be clear from Table 1 that stress for 6 h induces a characteristic fall of IFS by 2.5 times. By itself gentle adaptation does not depress this parameter, but prevents its depression arising under the influence of long-term stress.

Hence, by the use of a rational strategy of adaptation to stress, i.e., by reducing the number of exposures and lengthening the time intervals between them, the negative effect of adaptation itself on myocardial contractility can be completely prevented and, at the same time, depression of the contractile function of heart muscle arising during long-term stress can be completely prevented. In other words, the "price" of adaptation to repeated stress, measured in depression of the contractile function of the heart, is not inevitable, complete protection of cardiac contractility against the effects of long-term stress can be achieved through the use of a correct strategy of adaptation without this undesirable effect.

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ADENYLATE CYCLASE ACTIVITY OF THE GASTRIC MUCOSA AND MORPHOLOGICAL CHANGES IN THE GASTROINTESTINAL TRACT IN EXPERIMENTAL DUODENAL ULCERATION FOLLOWED BY TRUNCAL VAGOTOMY

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Duodenal ulcer is a polyetiologic disease whose pathogenesis is based on an imbalance between protective and injurious factors in the stomach and duodenum. Because it is impossible to analyze the role of each factor and their dynamic interaction in the development of the disease completely under clinical conditions, experimental approaches have been used. By now many different methods of inducing duodenal ulcers in animals of different species have been developed [3-5, 7, 10].

In the present investigation a cysteamine model of experimental duodenal ulcer [11] was used with some modifications. A study of the mechanism of action of cysteamine revealed a considerable and significant increase in secretion of hydrochloric acid and pepsin and also an increase in blood levels of gastrin and corticosterone [9]. Disturbances of the microcirculation and edema of the mucosa also develop under these circumstances in different parts of the gastrointestinal tract [6]. Administration of cysteamine thus increases the aggressiveness of the acid-peptic factor and also weakens the protective properties of the duodenal mucosa, phenomena which correspond to a considerable degree to the pathogenesis of this disease.

EXPERIMENTAL METHOD

Experiments were carried out on 40 noninbred male albino rats weighing 160-180 g. The rats were deprived of food for 24 h before receiving cysteamine and kept in special cages preventing coprophagy. Instead

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