Increased Resistance to Heat Shock of Isolated Hearts from Rats Adapted to Moderate Physical Exercise

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Hearts isolated from rats adapted to physical activity through moderate regular exercise (swimming) were more resistant to heat shock than hearts from unadapted controls. Thus, 15-min perfusion of control hearts with a solution heated to 42°C significantly depressed contraction amplitudes and caused a contracture amounting to 36% of the initial contraction amplitude, as well as increased release of creatine kinase into the perfusate. In the hearts from adapted rats, contraction amplitude was, on average, 2.3-fold greater and the contracture 3.2 times less marked than in the control animals; the test and control hearts did not differ significantly in the release of creatine kinase.

Key Words: *adaptation to physical exercise; isolated heart; heat shock; resistance*

The adaptation of animals to physical work through the repeated performance of moderately strenuous exercise has been shown to make them more tolerant not only of heavy physical loads [4] but also of altitude hypoxia [1,2], poisons [1], and even of ionizing radiation [6]. With reference to the heart, it has been established that periodic exposure to physical exercise makes the myocardium more resistant to injurious factors, primarily ischemia [7,8]. Moreover, hearts isolated from adapted animals display enhanced resistance to such insults as ischemia and subsequent reperfusion [3]. This indicates that, apart from alterations in neurohumoral regulation, an important role in affording protection to the heart of an adapted animal is played by mechanisms originating at the level of the heart itself. When considering these local mechanisms, it is appropriate to note that hearts isolated from animals adapted to stress and showing increased tolerance to postischemic reperfusion have also been found to exhibit higher heat resistance and the accumulation of considerable amounts of heat-shock proteins (hsp70) [5]. These proteins can boost the resistance of cells to injurious factors by disrupting abnormal protein-protein interactions [9], and it has been shown that the event underlying the activation of their synthesis during adaptation to stress is a manifold increase, determined by the stress reaction, in the concentration of catecholamines and corticosteroids acting on target organs [5]. Since the stress reaction is known to be an essential component of adaptation not only to stress but also to physical exercise [4], hsp70 are likely to accumulate in the myocardium during the adaptation to the latter and play a large role in protecting the heart.

The present study was undertaken to check this possibility by evaluating the effect of adaptation to moderate periodic physical exercise on the resistance of isolated hearts to the damaging action of heat shock, given that hsp70 accumulation in tissues has been shown to be an indirect physiological measure of increased heat resistance of the corresponding organ [10].

MATERIALS AND METHODS

The experiment was staged on male Wistar rats weighing 250-300 g. They were adapted to physical exercise for 45 days by swimming at 32°C: swimming time was progressively increased from 15

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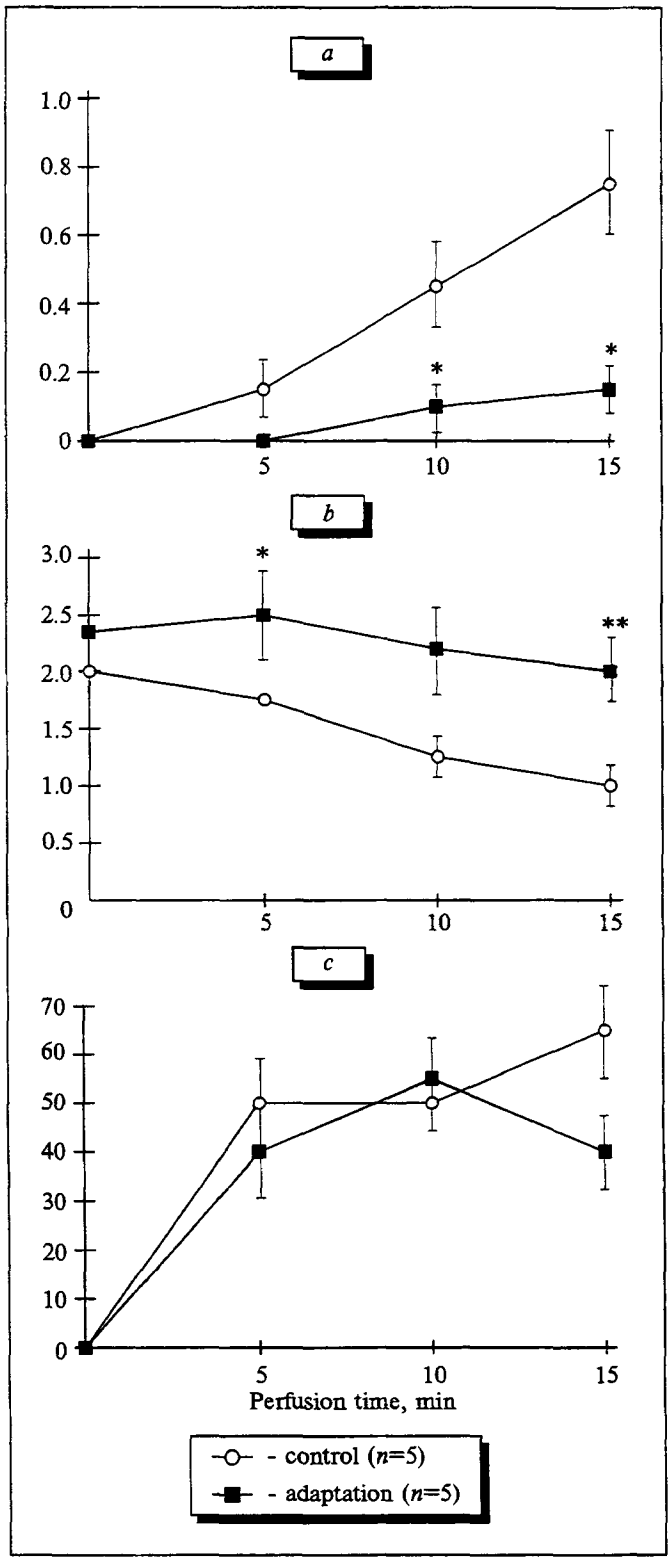

Fig. 1. Effects of adaptation to physical exercise on the contracture and contraction amplitude of isolated rat hearts and on the release of creatine kinase into their perfusate at 42°C. Ordinate: *a*) contracture of apicobasal heart shortening, mm; *b*) contraction amplitude of apicobasal heart shortening, mm; *c*) release of creatine kinase, IU/min/g heart weight. $^{*}p<0.05$, $^{**}p<0.01$ in comparison with hearts from control (unadapted) rats.

to 30 min per day in the first week and to 60 min in the second, after which it remained unchanged at 60 min per day.

The cardioprotective effect was evaluated on isolated hearts perfused by Langendorff's method. The rats were heparinized (2000 units/kg intraperitoneally), anesthetized with Nembutal (50 mg/kg intraperitoneally), and then thoracotomized to remove the heart, which was placed in a perfusion system containing the standard Krebs-Henseleit solution. Mechanical activity of the isolated heart was evaluated using a TD-112S isotonic sensor (Nihon Kohden). Mechanical activity and the electrocardiogram were recorded with modules of an RM-6000 polygraph (Nihon Kohden). Heat shock in the isolated heart was produced by raising the perfusion solution's temperature from 37° to 42°C, after which perfusion was continued for 15 min. The severity of damage to the isolated heart was assessed by the depression of the contraction amplitude and by the degree of contracture; damage to the sarcolemma was assessed spectrophotometrically by the activity of creatine kinase released into the solution from the heart. The protective effect of adaptation was judged by the extent to which these damaging effects were lessened. The accumulation of hsp70 in the myocardium was evaluated indirectly from values of physiological parameters characterizing increased thermotolerance of the heart. Hearts from unadapted rats served as controls.

Statistical differences between the test and control hearts were evaluated by Student's *t* test.

RESULTS

The 15-min perfusion of control hearts with the solution heated to 42°C considerably depressed the contraction amplitude, caused a strong contracture (to 36% of the initial contraction amplitude), and resulted in increased release of creatine kinase into the perfusate (Fig. 1). As shown in the figure, the adaptation to physical exercise significantly limited the depression of the contraction amplitude and the development of contracture: by minute 15 of perfusion with the hot solution, the hearts from adaptated rats were contracting with an amplitude that was 2.3-fold greater than in the control hearts, while their contracture was 3.2 times lower. The difference in the release of creatine kinase was insignificant (Fig. 1).

It is of special note that an increase in thermotolerance was shown only by hearts of rats exposed to a series of swimming sessions and never by those taken from animals exposed to a single session; in other words, the increased thermotolerance developed as a result of adaptation.

Thus, as this study shows, adaptation to physical exercise, in addition to making the heart more resistant to ischemia and reperfusion [3], can also boost its resistance to heat. Since increased heat resistance may depend on the accumulation of hsp70 [9,10], our present results are consistent with the hypothesis that hsp70 may accumulate in the myocardium and that one of the mechanisms responsible for increasing heart resistance may be associated with activated synthesis of these proteins and their protective properties.

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