Effect of Adaptation to Moderate Physical Loads on the Increased Resistance of the Isolated Heart to Ischemia and Reperfusion

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Adaptation to physical loads elicits pronounced anti-ischemic and antireperfusion effects on the isolated heart. By the 20th min of total ischemia contracture in the hearts of adapted animals is much less than that in the control group. During reperfusion of hearts from adapted animals the degree of restoration of the contractile force was 6-fold higher, contracture was lesser, and the total period of tachycardia and fibrillation were 3-fold shorter than in the control.

Key Words: *adaptation; physical load; isolated heart; ischemia; reperfusion, resistance*

Repeated moderate physical loads lead to adaptation of the organism, not only increasing its resistance to large physical loads [5] but also providing a broad-spectrum protection, for example, against hypobaric hypoxia [1,2], toxins [1], and ionizing radiation [7]. However, adaptation to physical loads has the most potent effect on the resistance of the cardiovascular system to damaging factors. It markedly increases the myocardial resistance to ischemia [9,13], limits the necrosis zone [12], and prevents disorders in cardiac rhythm and contractility during experimental stenosis of the aorta [3] and in severe emotional-pain stress [4]. In attempting to elucidate the mechanisms of the cardioprotective effect of adaptation to physical loads, one should remember that such adaptation leads to the activation of the central stress-limiting systems [5] and reduces the responses of the sympathico-adrenal and hypophyseal-adrenocortical systems to stress [10,17]. In addition to these neurohumoral alterations, adaptation to physical loads is accompanied by activation of local mechanisms at the level of the heart: the coronary flow [12] and myoglobin concentration [8] increase, which results in augmentation of the oxygen uptake by the myocardium. The increased number of mitochondria [14] and heightened activity of mitochondrial cytochrome oxidase [16] add power to the myocardial energy systems, and the activity of antioxidant enzymes also increases [15]. The increase in the capacity of the sarcoplasmic reticulum [11] stimulates Ca^{2+} transport. The direction of the adaptation shifts occurring in the heart implies that its protection is provided not only by the central neurohumoral mechanisms but also by local mechanisms, which are activated in the heart itself. The significance of these local shifts for increasing cardiac resistance to physical loads remains open to discussion. In order to resolve this problem it is necessary to find out whether the anti-ischemic effect of adaptation to physical loads elicited at the level of the whole organism is preserved in the isolated heart, where the influence of the central neurohumoral mechanisms is eliminated.

Our objective was to assess the effect of adaptation to moderate periodic physical loads on heart damage caused by total ischemia and reperfusion.

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MATERIALS AND METHODS

Experiments were performed on male Wistar rats weighing 250-300 g. The animals were adapted to physical loads (swimming) during a 45-day period in winter. During the first week the swimming sessions were lengthened from 15 to 30 min. During the second week they were prolonged to 60 min per day, and then 1 h was added every day. The water temperature was 32°C.

The cardioprotective effect was assessed on isolated hearts perfused after Langendorff. The rats were given intraperitoneal injections of heparin (2000 U/kg) and nembutal (50 mg/kg). The hearts were excised and placed in a reperfusion system with the standard Krebs-Henseleit solution. The mechanical activity of the isolated hearts was assessed with a TD-112S isotonic sensor (Nihon Kohden) and recorded together with the electrocardiogram on an RM-6000 polygraph (Nihon Kohden). For modeling of the ischemic and reperfusion damage the coronary flow was arrested for 20 min, after which the reperfused hearts were observed for 15 min. The damage to the isolated heart caused by ischemia and reperfusion was assessed according to the suppression of the contraction amplitude, contracture, and cardiac rhythm disorders. The damage to the sarcolemma was assessed spectrophotometrically by measuring the creatine kinase activity in the outflow solution. The cardioprotective effect was estimated from the degree of prevention of ischemia-reperfusion damage.

The results were analyzed using Student's *t* test.

RESULTS

The curves in Fig. 1 illustrate the response of control and adapted hearts to ischemia and reperfusion. A 20-min ischemia led to pronounced contracture in the control, which was equal 1.35± ±0.31 mm. In the adapted animals heart contracture at the 20th min of ischemia was 0.11±0.03 mm (Fig. 1, *a*), which is considerably lower than in the control. Prior to ischemia the contraction amplitude was the same in control and experimental animals; whereas after 5 min of ischemia it was equal to zero in both groups (Fig. 1, *b*). Thus, adaptation to physical loads exhibits a pronounced anticontracture effect in total ischemia.

The hearts of adapted animals were characterized by a markedly increased resistance to reperfusion damage. By the 5th min of reperfusion the amplitude of heart contractions in these animals was 6-fold higher than in the control. By the 15th min, in the control group it was 0.20±0.12 mm, the degree of recovery being 7.2%, while in adapted animals it was 5.6-fold higher than in the control, the degree of recovery being 42%. It can be seen from the figure that the accelerated postischemic recovery of contraction amplitude in adapted animals is due to lower contracture.

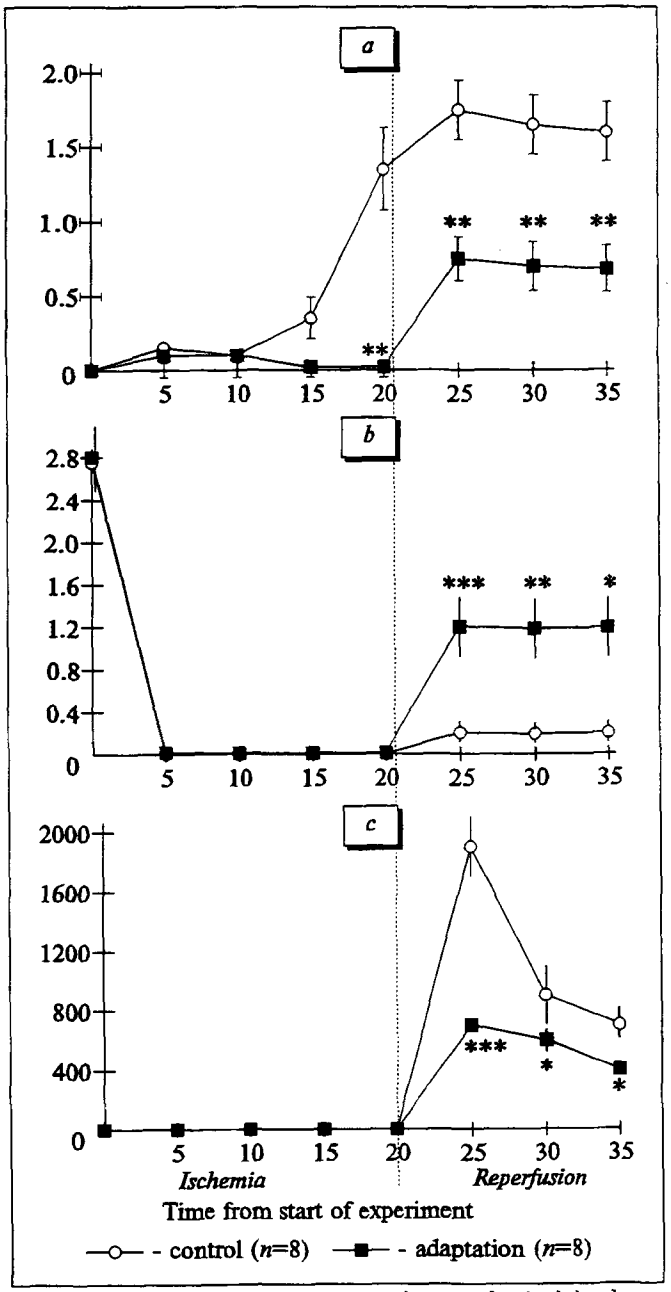

Fig. 1. Effect of adaptation to moderate physical loads on contracture, contraction amplitude, and creatine kinase content in the perfusate of isolated rat heart during ischemia–reperfusion. Ordinate: *a*) contracture of the apical–basal heart shortening, mm; *b*) contraction amplitude for apical–basal heart shortening, mm; *c*) creatine kinase content in the perfusate, IE/min/g heart weight. One, two, and three asterisks indicate values significantly different from the control at $p<0.05$, $p<0.01$, and $p<0.001$, respectively.

During reperfusion, the anticontracture effect of adaptation to a physical load was accompanied by an antiarrhythmic effect: the total duration of tachycardia and ventricular fibrillation calculated per heart in the control group was 6.8±2.2 min, whereas in adapted animals it was only 1.8±1.7 min. Fibrillation was observed in 5 out of 8 hearts in the control group but only in one heart out 8 hearts in adapted rats ($p<0.05$).

The curves in Fig. 1, *c* show that adaptation to physical loads provides direct protection of the heart against the reperfusion-induced damage, judging from the creatine kinase content in the perfusate. By the 5th min of reperfusion, the enzyme activity in the control group and in adapted animals was 1871±211 and 657±45 IU/min/mg heart weight, respectively.

Thus, adaptation to physical loads has pronounced anticontracture, antiarrhythmic, and membrane-protecting effects and undoubtedly protects the isolated heart against ischemic and reperfusion damage. It can be concluded that the protective effect of adaptation to physical loads is realized not only at the level of the whole organism but also at the organ (heart) level. Consequently, for such adaptation the activation of local mechanisms (stimulation of the myocardial energy supply [14,16] and of the antioxidant [15] and Ca^{2+} transporting systems [11]) plays an important role in protecting the organism against ischemia-reperfusion damage.

When considering the role of local mechanisms in the protection of adapted hearts, one should take note of recent findings that heat stress proteins of the HSP70 family are accumulated during adaptation to repeated stressors. These proteins serve as a foundation for the generalized phenomenon of adaptational stabilization of cell structures, i.e., increased cell resistance in the heart, liver, and other organs to the direct influence of damaging factors [6]. It has been shown that during adaptation to stress the accumulation of HSP70 and adaptational stabilization are fundamental for protecting the heart against reperfusion damage [6]. Since the stress reaction is a necessary component in the adaptation to various factors, it is reasonable to assume that activation of HSP70 synthesis and adaptational stabilization of cell structures play a role in adaptation to a great number of environmental factors and, particularly, in the adaptation to a physical load (in this case the significance of the stress reaction has been proved [5]). This hypothesis requires further experimental evidence.

Our findings confirm the important role played by the activation of local mechanisms in cardiac protection during adaptation to physical loads, which is the most widespread variant of adaptation employed in medicine, sports, aviation, and space programs.

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