Some Characteristics of the Proteinase—Inhibitor Systems in Adaptive Response to Strenuous Exercise

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In rats, adaptation to strenuous exercise was accompanied by phasic changes in the activities of the kallikrein-kinin system, elastase-like proteinases, and proteinase inhibitors, and total antioxidant activity in the serum, myocardium, liver, and cerebral cortex. After 30-min physical exercises, activity of the kallikrein-kinin system decreased in the serum and increased in tissue with parallel activation of elastase-like proteinases in the myocardium and cerebral cortex. After 3-h exercises the activity of the kallikrein-kinin system showed some indications of exhaustion, especially in the myocardium and cerebral cortex. Activities of elastase-like proteinases tended to normal due to activation of α_1-proteinase inhibitor and normalization of total antioxidant activity.

Key Words: *physical exercise; stress; kinin system; elastase; adaptation*

Depending on the intensity, physical exercises can be either a stressor or a training factor, if no overload is allowed during their performance. Swimming with a load is often used as a model of stress-inducing physical exercises. Swimming for 3 h was found to induce adaptive changes associated with genome activation in the cerebral cortex, which is considered to provide a basis for enhancement of the CNS functional potential [3,6]. Activation of the kallikrein-kinin system (KKS) observed within the same period after exercise [2] contributes to the stress-limiting mechanisms by stimulating microcirculation and prostaglandin release, which diminishes the effects of catecholamines [5, 14,17]. On the other hand, excessive activation of KKS and enhanced peroxidation of membrane lipids can labilize lysosomal enzymes [5, 15], such as elastase and other proteinases possessing powerful destructive activity. On other hand, destruction can be reduced by proteinase inhibitors and the antioxidant system [5,13].

The objectives of this study were to investigate some characteristics of the proteinase—inhibitor systems and to assess the intensity of lipid peroxidation (LPO), antioxidant activity (AOA), and tissue content of nucleic acids during adaptive responses to physical exercise.

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MATERIALS AND METHODS

Experiments were carried out on 36 inbred male rats weighing 250-300 g. The rats were subjected to intense physical exercises, i.e. swimming with a load (6% of body weight) fixed to the tail [3].

The animals were divided into 3 groups: 1) control (n=15); 2) 30-min swimming (n=6); 3) 3-h swimming (n=15). The state of KKS was assessed by kallikrein activity and serum content of prekallikrein [1]. Activities of elastase [15] and proteinase inhibitors (α_1-proteinase inhibitor and α_2-macroglobulin) [7], as well as the activity of the antioxidant system [4] were determined in the serum and myocardium, cerebral cortex, and liver homogenates. Tissue content of nucleic acids was measured [10]. In the liver, we additionally measured LPO activity [9] and protein content by the biuret method. Blood content of 11-hydroxycorticosteroids was determined as an indicator of stress [8]. The data were analyzed statistically using Student's t test.

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RESULTS

After 30-min swimming, the rats of group 2 exhibited severe fatigue with peripheral vasospasm, significant elevation (by 2.5-fold, $p<0.001$) of serum 11-hydroxycorticosteroids and inhibition of the KKS system. Kallikrein activity was reduced by 80%, while prekallikrein activity did not differ from the control and α_2-macroglobulin activity tended to decrease (Fig. 1). Serum elastase inhibitor activity was almost unaffected. At the same time, tissue activities of elastase-like proteinases sharply increased. In particular, in the myocardium and cerebral cortex, elastase activity increased by 117% and 56%, respectively, while in the liver it only tended to increase. Tissue activity of α_1-proteinase inhibitor did not differ from the control (Fig. 1).

The state of the KKS was assessed by tissue activity of α_2-macroglobulin, the main kallikrein inhibitor. In the myocardium, its level increased by 49%, while in the cerebral cortex it only tended to increase. Total AOA in the myocardium decreased by 20%; it slightly increased in the cerebral cortex, and slightly decreased in the liver. No significant changes in the content of nucleic acids were found in the myocardium and cerebral cortex, while DNA content in the liver decreased by 64% ($p<0.001$) and that of RNA increased by 40% ($p<0.05$).

These data show that the immediate response to 30-min physical exercise includes a complex of adaptive changes with the predominant microcirculatory component, which induces blood redistribution in such a way that working muscles, myocardium, and cerebral cortex have an additional blood supply at the expense of vasospasm in the liver, kidneys, and skin. Simultaneous vasodilatation occurs in intensely working organs due to enhanced activity of local metabolic factors, including tissue kinins. The enhanced activity of α_2-macroglobulins in the myocardium and cortex suggests KKS activation in these tissues with consequent increase in vascular permeability [12].

According to Meerson's classification, this response represents an "immediate" and imperfect adaptation [6]. Reduced AOA and enhanced activity of elastase-like proteinases suggest labilization of cell membranes and the development of destructive processes in the myocardium. In the cerebral cortex destructive changes are less pronounced due to higher capacity of its antioxidant system compared to other tissues [11]. The decrease in the liver DNA content can be attributed to vasospasm-induced decrease in total metabolic activity, rather than to destructive processes. At the same time, the increased content of liver RNA is a good prognostic sign indicating the possibility of activation of biosynthetic processes during adaptation.

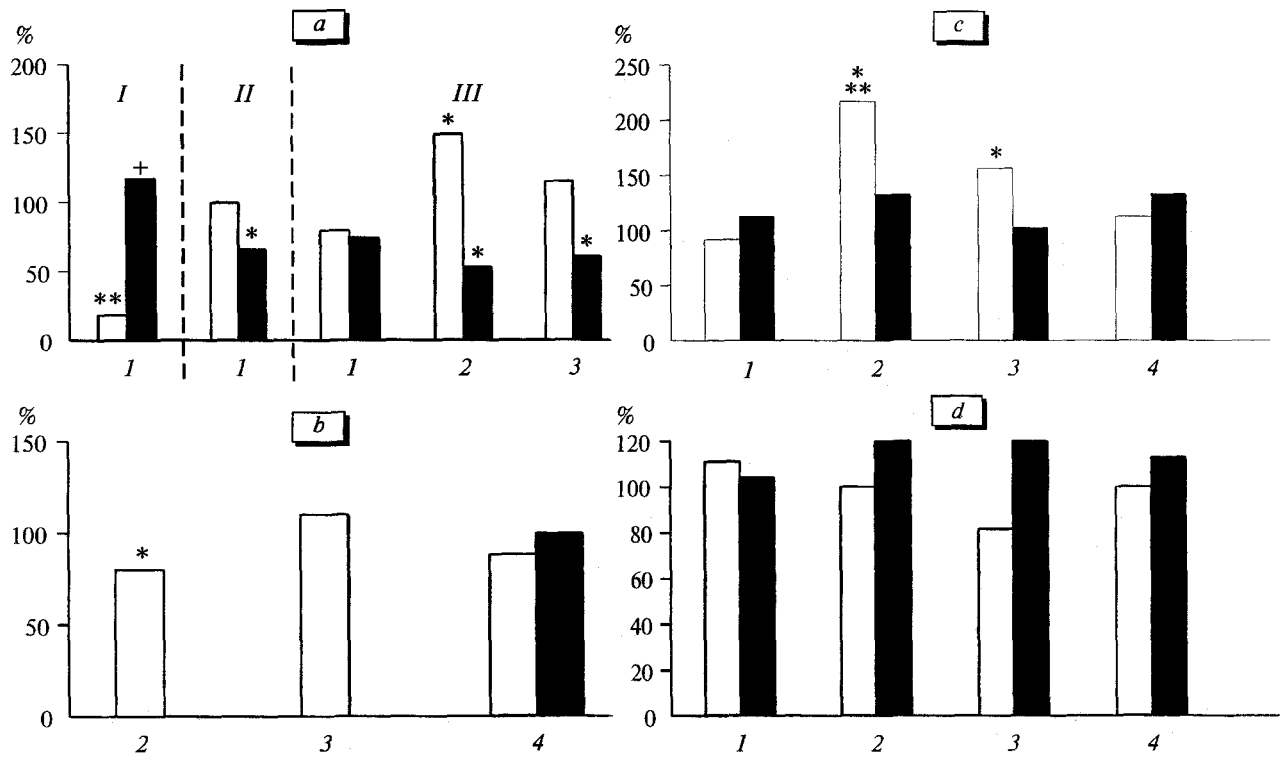

Fig. 1. The state of the kallikrein-kinin system (*a*) and antioxidant (*b*), elastase (*c*), and α_1-proteinase (*d*) activities in rats after 30-min (open bars) and 3-h (filled bars) strenous physical exercise. Kallikrein activity (*I*); prekallikrein content (*II*); α_2-macroglobulin activity (*III*) in serum (*1*), myocardium (*2*), cerebral cortex (*3*), and liver (*4*). $p<0.05$; $^{**}p<0.01$; $^{***}p<0.001$ in comparison with the control (100%); $^{+}p<0.05$ in comparison with 30-min swimming.

After 3-h swimming, the content of 11-hydroxycorticosteroids tended to normal. The serum KKS was activated: kallikrein activity was slightly higher than in the control and 6.5-fold higher than that after 30-min swimming. The content of prekallikrein decreased by 40%. Serum activity of α_2-macroglobulins tended to decrease, while its tissue activity decreased significantly (by 47% in the myocardium and by 39% in the cerebral cortex). Elastase activity changed insignificantly in the serum, remained elevated in the myocardium and liver (by 30 and 34%, respectively), and returned to normal in the cerebral cortex. The antiproteinase potential (α_1-proteinase inhibitor) tended to increase (by 13-20%) in all tissues. In the myocardium, the content of nucleic acids changed insignificantly; while in the cerebral cortex and liver it tended to increase. In the liver, the protein content tended to increase, LPO intensity decreased by 40% ($p<0.05$), and AOA remained at the control level.

Activation of serum KKS after 3-h strenuous physical exercises can be considered as a compensatory reaction, which provides vasodilatation and enhancement of vascular permeability after vasospasm observed after 30-min swimming. According to some reports [5,14,17], stress-induced activation of the KKS increases phospholipase A_2 and C activities. This promotes the release of arachidonic acid from membrane phospholipids and stimulates the synthesis of prostaglandins restricting stress-reaction. At the same time, the decrease in α_2-macroglobulin activity in the serum and tissues suggests its intense utilization in proteolytic processes [12] and intense function of KKS, which can stimulate labilization of cell membranes. The increased tissue activity of α_1-proteinase inhibitor which blocks elastase, provides optimal condition for restriction of destructive processes. From these data it can be concluded that the destructive processes in the brain were arrested, while biosynthetic processes were intensified, as evidenced by a slightly elevated content of nucleic acid. Normalization of AOA, inhibition LPO, and the increase in DNA and protein contents suggest activation of biosynthetic in the liver. However, high elastase activity suggests some insufficiency of the compensatory processes in the liver, where the α_1-proteinase inhibitor is produced. In the myocardium, despite the increased activity of α_1-proteinase inhibitor, elastase activity was maintained at a high level, which implies higher vulnerability of the myocardium to this stress in comparison with the cerebral cortex.

Thus, we observed an inhibition of the KKS in the blood and its activation in the myocardium and cerebral cortex 30 min after strenuous physical exercise, which can be considered as compensatory and adaptive microcirculatory changes. Activity of elastase-like enzymes in the myocardium and cerebral cortex is sharply increased. After 3-h exercise, the KKS in all tissues is activated and shows some signs of exhaustion, while activity of elastase-like proteinases tends to normal due to high antielastase activity and normalized AOA. It should be emphasized that these compensatory shifts are still insufficient to completely prevent the destructive processes in the myocardium, liver, and other tissues.

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