INCREASED LACTIC ACID PRODUCTION BY RESTING SKELETAL MUSCLES DURING VASODILATOR SYMPATHETIC INFLUENCES

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Vasodilatation in skeletal muscles observed during stimulation of the sympathetic chain after administration of dihydroergotoxin or reserpine is accompanied by increased lactic acid production by the skeletal muscle. The activation of metabolism in this case is evidently unconnected with liberation of catecholamines. It is postulated that the increase in lactic acid production reflects the metabolic influence of the sympathetic system.

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The character of the vascular response to humoral stimuli depends on the tissue in which the vessel is situated. For example, the vessels of skeletal muscles, which dilate under the action of acetylcholine, adrenalin, and some other substances, lose this property if they are isolated from the muscle [8, 18-20].

When studying the mechanism of action of adrenalin on blood vessels, Lundholm [16] showed that this substance acts primarily on the smooth muscle of the vessel, increasing its tone, and only secondarily on the metabolism of the striated muscle fiber (in particular, on lactic acid production). The activation of metabolism leads secondarily to vasodilatation.

The ability of the blood vessels of skeletal muscles in situ to respond by vasodilatation is known relative not only to humoral, but also to nervous influences. Stimulation of a certain part of the hypothalamus and of other points of the central nervous system and stimulation of the sympathetic chain against a background of ergotoxin or reserpine are accompanied by dilatation of the blood vessels in skeletal muscles [9, 21, 22].

Are the nueorogenic vasodilator responses in skeletal muscles connected with the influence of the nervous system on metabolism of the muscle fibers? Such influences essentially are already known in the form of the Orbeli–Ginetsinskii phenomenon. This effect consists of an increase in the strength of contraction of muscles during stimulation of the sympathetic chain. The influence of the sympathetic system is evidently not limited to improving the conduction of excitation in the region of the neuromuscular synapse, as some authors consider [14]; influences are also exerted on the state of the muscle fiber itself [2-7]. Rosell and Uvnas [17], and Hyman and co-workers [15] showed that during vasodilator sympathetic effects the oxygen consumption of the muscle and the rate of clearance of some substances by the blood are decreased. However, the hypothesis of the opening of arteriovenous shunts, which was put forward on this basis, has not been confirmed [12].

If excitation of sympathetic fibers is capable of increasing the strength of contraction of the muscle fiber, it can be expected that sympathetic effects will be accompanied by activation of one of the forms of energy metabolism. Since the oxygen consumptions of the muscle and, consequently, its aerobic metabolism are diminished, it must be assumed that unaerobic metabolism is activated.

We have studied the production of lactic acid (the end product of anaerobic metabolism) by muscles during vasodilator sympathetic influences.

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EXPERIMENTAL METHOD

Experiments were carried out on cats anesthetized with ether and urethane. The velocity of the blood flow in the femoral vein was recorded by means of an intervalograph. The sympathetic chain was stimulated at the level of the 4th-5th lumbar segment. In the course of the experiment samples of arterial and venous blood were taken before, during,and, in some cases, after stimulation. The venous blood samples were taken from the femoral vein of the limb in which the sympathetic chain was stimulated. Samples of arterial blood were taken from the carotid artery. Lactic acid was determined by the usual method [1]. Knowing the velocity of blood flow and the arteriovenous difference it was possible to calculate the amount of lactic acid leaving the muscle in a certain time period.

To obtain a vasodilator effect during stimulation of the sympathetic chain, dihydroergotoxin (0.2 mg/kg during the experiment) or reserpine (5 mg/kg on the day before the experiment) was injected into the animal. Venous blood samples were taken at the time of maximal increase in velocity of the blood flow produced by stimulation of the sympathetic chain. In addition, the lactic acid content in the muscle tissue was investigated. Samples were taken from the gastrocnemius muscle. During development of the vasodilator effect, the muscles were immersed in liquid nitrogen. The muscle of the contralateral limb, whose sympathetic chain was not stimulated, was frozen in the same way 1-2 min later.

EXPERIMENTAL RESULTS

Comparison of the arteriovenous difference in lactic acid content in the resting state and during the vasodilator effect, undertaken in 10 experiments, showed that this difference changes only slightly despite a considerable increase in the blood flow velocity (mean values 11.2 mg% at rest and 10.9 mg% stimulation). This means that the quantity of lactic acid isolated from the muscle increased. The mean amount of lactic acid washed from the muscle was 0.385 mg/min under normal conditions and 0.831 mg/min during stimulation. The increase amounted to $210 \pm 19\%$ of the initial level. The results are statistically significant ($P < 0.001$).

This effect was observed regardless of which substance—dihydroergotoxin or reserpine—was injected into the animal to obtain the vasodilator effect.

Was the increased amount of lactic acid removed from the muscle associated with a decrease in its content in the muscle? In eight experiments the lactic acid content in the muscle during development of the vasodilator effect was compared with its content in the muscle on the control (not stimulated) side. The corresponding mean values were 55.3 and 49 mg%. The small increase of $12 \pm 5\%$ is statistically significant ($P < 0.05$). In conjunction with the measurements carried out on the blood, these results demonstrate an increase in lactic acid production by the muscle during the period of the vasodilator effect. In one of his surveys based on unpublished data, Uvnas [22] reported that he also observed an increase in the amount of lactic acid leaving a muscle in the blood during a vasodilator effect produced by stimulation of the hypothalamus. However, he considers that this was the result of the effect of adrenalin secreted by the adrenals. Since in our experiments vasodilatation was obtained by stimulation of the peripheral end of the sympathetic chain in the lumbar region, this interpretation of our results is ruled out.

The observations described indicate that the sympathetic fibers can influence metabolisms of the resting muscle fiber. Comparison of our results with those published in the literature suggests that activavation of anaerobic metabolism and inhibition of aerobic metabolism were observed. Adrenalin and noradrenalin are known to have the power of influencing the energy metabolism of striated and smooth muscles [10, 11]. However, in the present case the mechanism of the effect of metabolism was evidently different and unconnected with catecholamines, for in our experiments an increase in lactic acid production was observed against the background of the action of reserpine, a drug known to abolish catecholamine reserves at the periphery. The state of the blood vessels is known to be intimately connected with metabolism in the tissue in which they are situated [13]. For this reason, the fact that changes in metabolism occur in the skeletal muscle during stimulation of sympathetic fibers suggests that the vasodilator effects in this organ are associated with the influence of the sympathetic system on metabolism of the tissue surrounding the vessels.

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