ACTIVATION OF BRAIN AND KIDNEY Na,K-ATPase IN RATS DURING ADAPTATION TO COLD

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During interrupted and prolonged (16 weeks) adaptation of rats to cold the Na,K-ATPase activity in their brain and kidneys is increased by 50-100% with no change in the affinity of the enzyme for ATP. It is suggested that an increase in the power of the triiodothyronine (T_3)-dependent sodium pump in the kidneys and of the T_3-independent sodium pump in the brain resulting from adaptation enables heat production to be increased during cooling of the animal.

KEY WORDS: adaptation; cold; Na,K-ATPase; brain; kidney.

The increase in the oxygen consumption of the diaphragm [1], liver [10], and brown fat [5] in cold-adapted animals has been shown to be ouabain-dependent, and hence connected with the functioning of Na,K-ATPase. There is also indirect evidence of the important role of the sodium pump in the regulation of heat production during adaptation to cold. In this case ouabain inhibits the effects of hormones responsible for temperature homeostasis in the course of adaptation: noradrenalin and triiodothyronine (T_3) in the brown fat and liver [4, 6, 7] activation of biosynthesis of the enzyme under the influence of T_3 [8], and correlation between activity of the enzyme and tissue respiration following administration of T_3 to thyroidectomized animals [7].

Direct evidence in support of the participation of Na,K-ATPase in the regulation of thermogenesis could be activation of the enzyme during adaptation to cold. To find out if this occurs, activity of T_3-dependent Na,K-ATPase in the kidneys and of T_3-independent Na,K-ATPase in the brain was determined in rats during adaptation to cold.

EXPERIMENTAL METHOD

Experiments were carried out on male albino rats weighing about 200 g at the beginning of adaptation. The animals were kept at 0-5°C for 6 h daily, 6 days a week for 16 weeks. The isolation medium for the brain contained 0.25M sucrose and 1 mM EDTA, pH 7.4; for the kidneys 0.1% Na deoxycholate was added. The homogenate was centrifuged at 12,000g for 20 min and ATPase activity was determined in the supernatant. The incubation medium (1 ml) contained (in millimoles): NaCl 100, KCl 20, $MgCl_2$ 5, EDTA 1, Tris-HCl 50, ATP 2 μg; protein 30-40 μg, pH 7.4. Activity of the enzyme was calculated from the difference between the increase in phosphate in samples without ouabain and in the presence of 0.1 mM ouabain. Inorganic phosphorus was determined by the method of Rathbun and Betlach and protein by Lowry's method.

TABLE 1. Effect of Adaptation to Cold on Activity of Na,K-ATPase and Mg-ATPase (in μmoles P_i/mg protein/h)

Group of animals	Kidney (M ± m)		Brain (M ± m)	
	Na,K-ATPase	Mg-ATPase	Na,K-ATPase	Mg-ATPase
Control (n = 6)	1,07±0,16	14,6±1,21	1,33±0,18	5,28±0,68
Adaptation for 16 weeks (n = 10)	2,03±0,36	15,3±1,47	2,08±0,16	5,09±0,4
P	<0,01	<0,1	<0,02	<0,1

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EXPERIMENTAL RESULTS

The experimental results show that adaptation to cold is accompanied by a gradual increase in activity of Na,K-ATPase in the brain until the 12th week, when it was increased by 80%, and that it remained at a high level until the 16th week. Activity of the enzyme in the kidneys also was increased by 90% towards the 16th week of adaptation. Activity of Mg-ATPase in the brain and kidneys was unchanged throughout the experiment (Table 1).

Since synthesis of Na,K-ATPase in the kidneys is activated by T_3 [8], this suggests that activation of the kidney enzyme is due to an increase in the number of its molecules on account of chronic hyperfunction of the thyroid gland. The gradual and considerable rise in Na,K-ATPase activity in the brain during adaptation to cold which, as the observation showed, was not accompanied by any change in the affinity of the enzyme for ATP, suggests that this phenomenon also develops on account of activation of enzyme biosynthesis.

The increase in the power of the T_3-dependent sodium pump in the kidneys and of the T_3-independent sodium pump in the brain indicates the universal character of this adaptive mechanism and goes a long way toward removing the objection to the view that Na,K-ATPase participates in the regulation of heat production [8]. In the present writers' opinion, activation of Na,K-ATPase induced by hormones responsible for temperature homeostasis (T_3 and noradrenalin) leads to an increase in the phosphate potential of the cell and to stimulation of oxidative phosphorylation in the mitochondria. Since the efficiency of oxidative phosphorylation and of the ion pumps does not exceed 50% [2], activation of Na,K-ATPase and the associated activation of oxidative phosphorylation may lead to a considerable increase in heat production when the ambient temperature is lowered.

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