EFFECT OF GLUTAMIC ACID AND HYPOXIA ON TRANSAMINASE ACTIVITY IN THE BLOOD AND TISSUES

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Experiments on adult rats showed that administration of glutamic acid (1 mg/g) increases the activity of alanine- and aspartate-aminotransferases in liver and thyroid homogenates under normal and hypoxic conditions (raising to an altitude of 8000 M for 1 h). The serum level of enzyme activity was not affected by glutamic acid. Hypoxia increased the activity of both transaminases in the blood serum only.

Recent work has shown that tissue transaminase activity is dependent on hormonal influences, notably on the state of thyroid function [1, 15, 16]. The aminotransferases play an important role also in thyroxin production [8, 11, 12, 14]. It can be assumed that the recently discovered [4] stimulating effect of glutamic acid on thyroid function during hypoxia is effected through a change in aminotransferase activity.

The present investigation was undertaken to investigate the validity of this hypothesis, bearing in mind the marked affinity of glutamic acid for pyridoxal phosphate [3, 17] and the activating effect of the latter compound on the apoenzyme of the glutamate transferases [7].

EXPERIMENTAL METHOD

Experiments were carried out on adult male rats divided into four groups with 8-12 animals in each group. Two groups of rats were kept at normal atmospheric pressure, the others under hypoxic conditions in a pressure chamber at the equivalent of an altitude of 8000 m for 1 h. The experimental groups of rats received a subcutaneous injection of neutralized glutamic acid in a dose of 1 mg/g body weight 30 min before introduction into the pressure chamber. The control animals received an equivalent volume of physiological saline at the same time. The rats were sacrificed by decapitation 1.5 h after injection of the solutions or immediately after removal from the pressure chamber. Activities of alanine-aminotransferase (2.6.1.2) and aspartate-amino transferase (2.6.1.1) were determined in the blood serum and in liver and thyroid homogenates by Paskhina's method [6] and expressed in μmoles pyruvate/min/g tissue.

EXPERIMENTAL RESULTS AND DISCUSSION

The highest transaminase activity in intact rats was found in the liver (Table 1). The results of determination of the enzyme activity in the tissues and blood of the healthy rats corresponded approximately to those given in the literature [5, 13].

Injection of glutamic acid into rats under normal conditions did not affect the serum transaminase activity but significantly increased the activity of both transaminases in the liver and thyroid gland. Exposure to hypoxia for 1 h substantially increased the activity of both transaminases in the serum only ($P < 0.05$), while in the tissues the activity showed only a slight change by comparison with the intact

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TABLE 1. Effect of Glutamic Acid on Aminotransferase Activity of Blood, Liver, and Thyroid Gland under Normal and Hypoxic Conditions [in μmoles pyruvate/g (ml)/min]

Experimental conditions	Index	Alanine-aminotransferase						Aspartate-aminotransferase					
		serum		liver		thyroid gland		serum		liver		thyroid gland	
		control	expt.	control	expt.	control	expt.	control	expt.	control	expt.	control	expt.
Normal	M ± m	0,040 0,004	0,039 0,002	6,87 1,20	10,78 1,03	0,68 0,06	0,92 0,09	0,037 0,003	0,047 0,004	12,40 1,26	17,87 0,53	3,67 0,34	4,76 0,42
	Difference from control (in %)	−2,5		+56,9		+35,3		+27,0		+44,1		+29,7	
	p	>0,5		<0,05		<0,05		>0,05		<0,001		<0,05	
Hypoxic	M ± m	0,051 0,003	0,062 0,005	7,25 0,50	10,90 1,14	0,81 0,06	1,09 0,17	0,050 0,002	0,059 0,003	12,27 0,91	17,82 0,71	4,11 0,20	5,57 0,70
	Difference from control (in %)	+21,6		+50,4		+34,6		+18,0		+45,2		+35,5	
	p	>0,05		<0,001		>0,05		<0,05		<0,001		<0,05	

animals (Table 1). In the modern view [2, 18], hypoxia, like other nonspecific stimuli, increases the permeability of cell membranes, thus raising the blood enzyme concentration.

When the rats were given glutamic acid before being placed in the pressure chamber, hypoxia led to a significant increase in the activity of both transaminases in the liver. The activity of the enzymes in the serum and thyroid gland also was increased by glutamic acid, but the increase was significant only in the case of aspartate-aminotransferase.

The increase in transaminase activity in the liver and thyroid gland discovered after injection of glutamic acid under both normal and hypoxic conditions could be attributed to the character of metabolism of this amino acid. Glutamic acid and its deamination product, α-ketoglutaric acid, are known to be active partners of aminotransferases. The additional injection of a large quantity of glutamic acid as substrate therefore led to an increase in transaminase activity. A similar substrate-induced increase in aspartate-aminotransferase activity under the influence of oxaloacetic acid was observed by Hohls [10] in experiments on chickens, in vitro as well as in vivo.

The observed stimulant effect of glutamic acid on tissue transaminase activity explains to some extent its ability to improve oxidative processes and to stimulate thyroid function, especially during hypoxia. By taking part in a transamination reaction, glutamic acid reduces the concentration of oxaloacetate, a powerful inhibitor of succinate dehydrogenase [19, 20]. By abolishing the inhibition of this important enzyme of the tricarboxylic acid cycle, glutamic acid thus stimulated oxidative processes and strengthened the tissue compensatory mechanisms during exposure to hypoxia.

The stimulant effect of glutamic acid on transaminase activity in the thyroid gland also helps to explain the specific effect of this amino acid on hormone formation. Improvement of oxidative processes in the thyroid gland is of great importance to the formation of thyroid hormones. On the one hand, the increase in transaminase activity in the thyroid may itself be a factor promoting thyroxin production. The transamination of diiodotyrosine with α-ketoglutarate is known to be a specific reaction for the thyroid gland [11], for it is inhibited by α-thyroxin and activated by thyrotropic hormone. The pyridoxal phosphate-dependent formation of triiodothyronine and thyroxin from less highly iodinated precursors in the subcellular fractions of the thyroid gland has been observed by several workers [8, 12]. It can accordingly be concluded that an increase in aminotransferase activity is one of the mechanisms whereby glutamic acid stimulates thyroid function.

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