THE EFFECT OF GLUTAMINIC ACID ON CERTAIN METABOLIC PROCESSES IN ANOXIA AND DURING PHYSICAL WORK

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We have shown in previous papers [2, 3] that the administration of glutaminic acid to animals in anoxia stimulates their oxygen demand. The hypothesis was put forward that this effect, in these conditions, is dependent on the more intensive inclusion of incompletely oxidized metabolic products in the oxidation cycle of the three-carbon acids.

In order to test the reliability of this hypothesis, we investigated the effect of glutaminic acid on the content of incompletely oxidized metabolic products in the blood (oxygen debt), on the blood sugar and lactic acid contents and on the lactic acid and glycogen contents of the liver. The adenosinetriphosphate (ATP) content of the liver, skeletal muscle and brain was also determined. Experiments were carried out on animals kept in a gaseous environment deficient in oxygen. Under these circumstances an accumulation of incompletely oxidized metabolic products and of lactic acid is known to be observed in the body, and there is a considerable utilization of the glycogen reserves and of high-energy compounds [6-11, 13, 14, 16].

EXPERIMENTAL METHOD

Experiments were performed on adult white rats. In order to ensure approximately equal glycogen contents in the liver and muscles of the experimental animals, the rats used were preliminarily starved for 24-30 hours, and were given subcutaneous injections of glucose, in a dose of 5 mg/ g body weight, 1½ hours before the experiment. One of the animals (experimental) was injected 30 minutes later with sodium glutamate (1 mg/ g body weight), and both rats were then kept for 2 hours in a specially constructed apparatus ensuring a stable oxygen content of the inspired gaseous mixture (10-12 %) and absorption of the expired carbon dioxide. The animals were then quickly decapitated; after exsanguination, their tissues were frozen in liquid nitrogen and subjected to biochemical investigation. In this series 13 experiments were carried out on 26 animals. The results obtained were subjected to statistical analysis.

EXPERIMENTAL RESULTS

According to the results obtained (Table 1), the administration of sodium glutamate to animals kept in a lowered partial pressure of oxygen led to a considerable decrease in the level of incompletely oxidized products (by 36.3 %) and of lactic acid (by 30.3 %) in the blood, by comparison with their concentration in control animals. There was also an appreciable fall in the lactic acid content of the muscles (by 23.2 %). So far as the glycogen content of the tissues was concerned, this was only slightly changed in the skeletal muscles and remained at a high level in the liver. In the cardiac muscle of the experimental animals the glycogen level was also much higher than in the control animals (by 52 %). The ATP content of the experimental animals was higher than that of the controls, especially in the brain tissue (by 61 %).

TABLE 2

The Effect od Administration of Glutaminic Acid on the Metabolic Indices during Swimming (mean values, in mg%, of 20 experiments)

Indices	Swimming for 15 minutes			Swimming for 1 hour		
	Control	Experiment	difference, %	Control	Experiment	difference, %
BLOOD						
Sugar	112±3,4	129±2,3	+15	106,2±5,12	121,7±5,3	—15
Incompletely oxidized products (oxygen debt)	123,2±5,96	99,5±5,38	—19	147±4,97	109±3,3	—25
Lactic acid	75,0±1,3	59,0±1,38	—21	61,4±2,7	49,6±1,6	—19
SKELETAL MUSCLE						
Glycogen	394±15,6	479±9,3	+21	307±11,4	372±12	+23
Lactic acid	230,4±9,9	174,6±3,89	—24	191,7±4,06	165,5±6,35	—16
LIVER						
Glycogen	1115±78,6	1178±77,6	+6	794±42,9	861±32,5	+8

Note: Apart from the liver glycogen, the changes in the other indices were statistically significant.

It will be seen from the results in Table 2 that, in the rats receiving preliminary injections of sodium glutamate, after 15 minutes' swimming the content of incompletely oxidized products in the blood was less than in the control animals by 19.3%, and after swimming for 1 hour by 25.4%; the lactic acid concentrations were 21.4 % and 19.3 % less respectively. The blood sugar levels of the experimental animals were also slightly higher.

A lower lactic acid concentration was also found in the skeletal muscles of the experimental animals: after swimming for 15 minutes by 24.2 % and after 1 hour by 16%. The glycogen content of the muscles and liver of the rats receiving sodium glutamate remained at a higher level: in the muscles after swimming for 15 minutes by 21%, after one hour by 23%; in spite of the fact that the difference between the values of the glycogen content of the liver of the experimental and control rats was not statistically significant, a tendency was shown for the glycogen content in the experimental animals to remain at a higher level.

The results of these experiments thus show that during intensive physical work, the preliminary injection of sodium glutamate brings about better utilization of intermediate products of metabolism and maintenance of the carbohydrate reserves of the animal. These findings were, in fact, similar to those which we obtained in the anoxia experiments.

As long ago as in 1936 it was shown [18] that glutaminic acid supports the respiration of brain sections, suppreses anaerobic glycolysis [19] and maintains aerobic glycolysis. This is associated with the fact that glutaminic acid also plays an important role in the oxidation cycle of the three-carbon acids [1].

In experiments on the mitochondria of the heart [17], it was shown that each member of the cycle readily oxidizes pyruvate. The work of M. F. Gulyi et al. [5] has shown that administration of one of the components of the cycle — citric acid — to rabbits with alloxan diabetes and to human patients with glycosuria lowers the hyperglycemia and the glycosuria, the ketonuria and the polyuria. It has further been shown that, during fatiguing work, citric acid leads to smaller changes in the metabolism of purines and ATP of the working muscle of the rabbit, and also halts the excretion of purines in the urine in man [4]. These findings demonstrate that when oxidative processes are diminished in the body, they may to some extent be restored by administration of citric acid.

It can be seen from our experiments that glutaminic acid also possesses an analogous action and that during intensive physical work, disturbances also take place in the three-carbon acid cycle which may,

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In connection with these findings, we thought it of interest to investigate the effect of sodium glutamate on the concentrations of the above -mentioned constituents of the blood and tissues during intensive physical work, and in particular in rats during swimming. According to reports in the literature [12, 15], under these circumstances a considerable increase takes place in the lactic acid content of the blood and muscles, with a fall in the glycogen content of the muscle tissue, i.e., biochemical changes closely resembling those observed during anoxia.

TABLE 1

The Effect of Administration of Glutaminic Acid on the Metabolic Indices during Anoxia (mean values, in mg %, of 13 experiments)

Indices	Control	Experiment	Difference, in %	Statistical oxygen significance
BLOOD				
Sugar	93,5±2,79	107±2,79	+14	Significant
Incompletely oxidized products (oxygen debt)	152±7,6	107,2±8,44	—36,3	»
Lactic acid	38,0±2,2	26,5±1,85	—30,3	»
SKELETAL MUSCLES				
Glycogen	474,5±20	504,6±17,5	+6%	Not significant
Lactic acid	169,4±9,75	130,1±8,7	—23,2	Significant
ATP	29,0±1,42	32,0±1,37	+10,2	Not significant
LIVER				
Glycogen	1097±66	1367±65	+24,6	Significant
ATP	12,3±0,19	15,9±0,19	+29	»
BRAIN				
ATP	15,4±1,26	22,2±1,58	+61	»
HEART MUSCLE				
Glycogen	544±25,4	808±29	+52	»

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Experiments were carried out on adult white rats of the same sex and weight. As in the previous series of investigations, 4 animals were starved for 24-30 hours and then injected subsutaneously with glucose solution (5 mg/ g body weight). Sodium glutamate was injected 30 minutes later (1 mg/ g body weight) into 2 experimental rats, and the rats were placed after one hour in water at a temperature of 35-36°. After swimming for 15 minutes the rats were sacrificed. In another series of experiments the animals were sacrificed after swimming for one hour. In all, 20 experiments were performed. The results were subjected to statistical analysis.

evidently, be compensated by the administration of this amino acids. The concrete mechanism of this effect requires further investigation.

The higher glycogen content in the liver and heart muscle and ATP content of the tissue of the brain of the animals receiving glutaminic acid, which we observed in our experiments, emphasizes yet again the power of this amino acid to normalize the metabolism, by virtue of the more intensive inclusion of incompletely oxidized products of metabolism in the aerobic phase of oxidation. This action of glutaminic acid is shown particularly clearly in tissues which are most sensitive to oxygen deficiency (brain, heart muscle and liver).

SUMMARY

The effect of administration of glutaminic acid on the content of incompletely oxidized metabolic products (oxygen debt), lactic acid, glycogen and adenosinetriphosphate was studied in anoxia, as well as after physical exertion (swimming). It was established that glutaminic acid promotes the reduction of the blood level of incompletely oxidized metabolites and of lactic acid, decreases their accumulation in the muscles, maintains the glycogen content of the liver and especially of the cardiac muscle, as well as the concentration of adenosinetriphosphate in the brain at a higher level. In experiments with swimming it was demonstrated that preliminary administration of glutaminic acid promotes a lesser accumulation of incompletely oxidized products and lactic acid in the blood and decreases the glycogen utilization in the muscles. A suggestion is made that this effect is due to stimulation of the oxidative processes by glutaminic acid at the expense of more intense involvement of the incompletely oxidized metabolites in the tricarboxylic cycle.

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