THE EFFECT OF GLUTAMIC ACID ON THE OXYGEN DEMAND OF ANIMALS IN A STATE OF ANOXIA

A.M. Genkin and N.A. Udintsev

From the Department of Biochemistry (Head – Prof. S.A. Brailovskii)

of the Sverdlovsk Medical Institute (Director – Prof. A.F. Zverev)

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According to numerous reports in the literature [3], the addition of glutamic acid to pulp and extracts of various tissues increases their oxygen demand. However, there is little reference in the literature to the problem of the effect of administration of glutaminic acid on the oxygen demand of the animal as a whole.

Nevertheless, in recent years glutamic acid and its salts have become quite extensively used in the treatment of the most varied diseases, some of which are undoubtedly accompanied by some degree of anoxia, for example, cerebral vascular disorders in the newborn [1, 5], cardiac failure in adults [10], the state of clinical death [6, 7], and so on.

In connection with these findings it is useful to investigate the effect of glutamic acid on the oxygen demand of animals when the inspired air is normal or is deficient in oxygen.

EXPERIMENTAL METHOD

Experiments were performed on young white rats. For measuring the oxygen demand a specially constructed apparatus was used which ensured absorption of the expired carbon dioxide, constancy of a predetermined concentration of oxygen and control over its demand for any required period of time. Construction of the apparatus al-

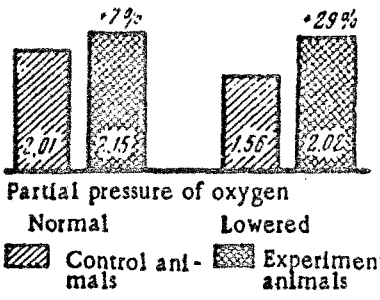

Fig. 1. The effect of administration of sodium glutamate on the oxygen demand of rats (mean results) in ml of oxygen per g body weight per hour.

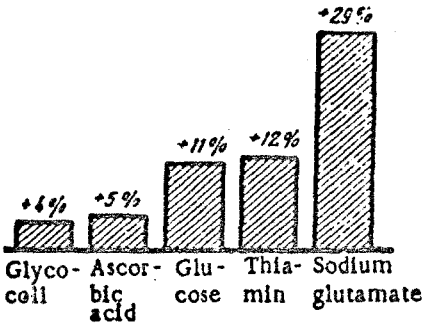

Fig. 2. The effect of administration of various compounds on the oxygen demand of rats (mean results). The values are given in percentage increase of oxygen demand (in ml of oxygen per g body weight per hour) of the experimental animals compared to the controls.

lows simultaneous observations to be carried out on two rats kept under identical experimental conditions but isolated from each other.

Two starving rats were placed in the apparatus for 1½ hours to become accustomed to the conditions of the experiment. Next, for a period of one hour their oxygen demand was determined every five minutes. After this, the system was filled with a mixture of nitrogen (78%) and oxygen (12%), and under these conditions the oxygen demand was again determined in the same way for a further hour. Next, one of the rats was injected subcutaneously with sodium glutamate (1 mg per 1 g body weight) in 5% solution. The control rat was injected with the same volume of physiological saline. Afterwards the oxygen demand under conditions of anoxia was again determined for a period of 2-4 hours.

By way of control observations a series of experiments was performed in which the effect of sodium glutamate on the oxygen demand of rats could be examined with a normal partial pressure of oxygen.

EXPERIMENTAL RESULTS

When the partial pressure of oxygen in the inspired air is normal the injection of sodium glutamate into rats causes no perceptible change in their oxygen demand in comparison with rats not given glutamate. In similar experiments when the oxygen content of the inspired air was reduced, the oxygen demand was very greatly increased after injection of glutamate. Its increase during a two-hour experiment amounted to 29% on the average over its value in control animals (Figure 1).

If, instead of glutamate, the same dose of glycocoll or glucose, or ascorbic acid (20 mg) or thiamine (1 mg) was injected into rats kept in an anoxic state, only a slight increase in the oxygen demand compared with control animals was produced (Figure 2).

Sodium glutamate thus possesses the specific property of considerably increasing the oxygen demand of animals kept in a state of anoxia.

It is not yet possible to give a complete analysis of the mechanism by which glutamic acid stimulates oxidative processes during anoxia. It may be that glutamic acid acts by increasing the synthesis of hemoglobin from pyrrolidonecarbonic acid [8], and we consider that a leading part in this process is played by activation of the reactions of the tricarboxylic acid cycle.

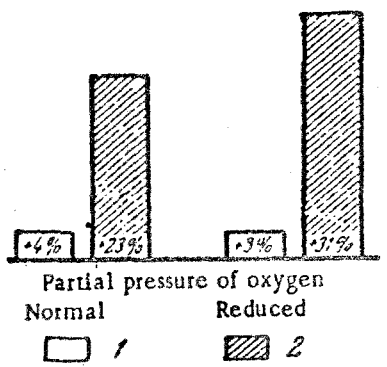

Fig. 3. The effect of injection of lactic and glutamic acid on the oxygen demand of rats (mean results). Values given in percentages of increase of oxygen demand (in ml per g body weight per hour) of the experimental animals over the controls: 1) injection of lactic acid; 2) injection of lactic and glutamic acids together.

Injection of glutamic acid into an animal is known to lead to an increase in the α-ketoglutaric acid content of the tissues and blood [9, 11]. This compound, undergoing further oxidation to succinic and other dicarboxylic acids, results in an increase in the oxalacetic acid concentration, which creates favorable conditions for involving lactic acid and other incompletely oxidized products in the tricarboxylic acid cycle. This is confirmed by the findings of Braunshtein and Kritsman [2, 4] that glutamic acid leads to a decrease in the lactic acid content during aerobiosis. It was to be expected that injection of glutamic acid, with a normal partial pressure of oxygen and with not too great a concentration of incompletely oxidized products, in particular lactic acid, would not have led to a significant increase in the oxygen demand, as in fact took place (see Figure 1).

In anoxic conditions the content of lactic acid and other incompletely oxidized products in the animal tissues increases sharply, and therefore the injection of glutamic acid must facilitate their complete oxidation, thereby leading to an increase in the oxygen demand.

In order to test the correctness of this hypothesis a series of experiments was performed to examine the oxygen demand of rats after preliminary injections of lactic and glutamic acid.

It was found that injection of lactic acid did not cause any increase in the oxygen demand during normal partial pressure of oxygen or anoxia. Injection of lactic acid together with glutamic acid led to

a considerable increase in the oxygen demand, more pronounced during anoxia (Figure 3).

Thus, the results of this series of experiments show that glutamic acid stimulates the oxidation processes not only in tissue pulp and extracts, but also in the intact animal.

The results of the experiments which we have described give reason to suppose that stimulation of the oxygen demand by glutamic acid during anoxia is undoubtedly due to the increased involvement of incompletely oxidized metabolic products in the oxidation cycle of the tricarboxylic acids.

SUMMARY

The effect of subcutaneous introduction of glutamic acid on the oxygen intake of rats was investigated in conditions of normal and decreased (12%) content of oxygen in inhaled air. It was established that the introduction of glutamic acid in normal partial oxygen pressure causes only insignificant increase of its intake (by 6%). In condition of hypoxia it is increased by 29%. On the basis of experiments it is suggested that the stimulating effect of glutamic acid is the result of its ability to introduce the products of metabolism which are not fully oxidized into the oxidative cycle of tricarboxylic acids.

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