SOME PECULIARITIES OF METABOLISM IN THE BRAIN TISSUE DURING CLINICAL DEATH IN DEEP HYPOTHERMIA IN CERTAIN HIBERNATING AND NONHIBERNATING ANIMALS

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Investigating the processes of metabolism in the brain during the period of clinical death, we paid special attention to the dynamics of the changes in the system of high energy phosphates—creatine phosphate (cp), adenosine triphosphate (ATP), adenosine diphosphate (ADP), and adenosine monophosphate (AMP),— and the products of anaerobic metabolism, primarily lactic acid. In contrast to a number of authors who conducted investigations on dogs [6], we conducted comparative experiments on the rat and gopher (Citellus citellus, summer season), in order to establish whether there is any pronounced increased resistance of the gopher to the state of clinical death [2] in connection with some peculiarities of the brain metabolism of these animals under conditions of anoxia and the absence of circulation.

EXPERIMENTAL

The animals were chilled by the method that we have described — a combination of hypoxia and hypercapnia [2]. In addition to a study of the brain metabolism during clinical death at a body temperature of 0°C i.e., under conditions of complete stoppage of the heart and respiration, we conducted a series of experiments on animals during various degrees of hypothermia under conditions of acute asphyxia, induced by total clamping of a preliminarily prepared trachea; moreover, the brain tissue was investigated after the stoppage of respiration. The animals were killed by immersing the head in liquid air at definite moments of clinical death or after stoppage of respiration. The brain tissue, pulverized in liquid air, was investigated. For the determination of ATP, ADP, AMP, and lactic acid we used enzymatic methods and the corresponding test preparations. CP was determined according to the method of Alekseeva [1], ATP, ADP, and AMP, according to the method of Thorn et al. [6]; the lactate content was determined on the basis of the data described in the literature [5], according to the prescription of the firm that produces the test preparations (Boeringer and Sons, Manheim).

RESULTS

Figure 1 presents the results of experiments on rats at a body temperature of 15° under conditions of asphyxia, caused by clamping of the trachea. Cp disappears most rapidly from the brain tissue; this occurs in a period of 10 min after stoppage of respiration. The ATP concentration decreases considerably more slowly; it fell sharply after stoppage of the respiratory movements, but remained at a relatively low residual level. The curve of ADP is of a two-phase character: an increase during the period of agonal respiratory movements, and then a decrease and return to the initial level. The AMP concentration increases from the very beginning, moreover, especially sharply during the second descending phase of lowering of the ADP level. The lactic acid level rises to a maximum (approximately 15 μmoles/g).

The change in the enumerated biochemical parameters was also investigated at 4 temperature levels, beginning with normal body temperature and ending with 0°. It was found that the general features of the dynamics

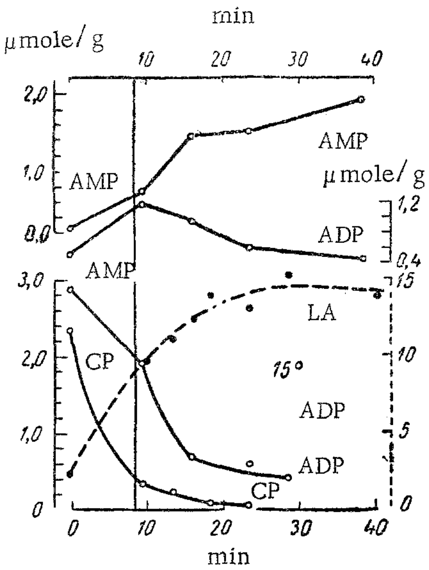

Fig. 1. Dynamics of the changes in the concentration of high-energy phosphates and lactic acid in the rat brain under conditions of acute anoxia at a body temperature of 15°. Each point is an average of data obtained on 5 animals. The vertical line denotes the moment of stoppage of the respiratory movements; the time is counted from the moment of clamping of trachea. The initial point on each curve shows the concentration measured in rats with the same body temperature, but without clamping of the trachea. On the right-hand ordinate—lactic acid concentration.

of the changes in the system of high-energy phosphates and lactate are not specific for hypothermia of 15° (see Fig. 1). However, a lower body temperature (as a result of the slowness of metabolic processes) makes it possible to better follow the changes that occur, and the basic peculiarities of the dynamics are more clearly revealed.

In a comparison of the data obtained with the results of experiments on gophers, a great difference is detected. Figure 2a presents data pertaining to CP, which were obtained in experiments at a body temperature of the animals of 15°. It is quite evident that the CP concentration in the gopher is reduced considerably more slowly than in rats, even after stoppage of the respiratory movements. We should mention also that the period of agonal respiration in the gopher lasts considerably longer. The same results are also noted with respect to ATP (Fig. 2b).

The amount of lactic acid increases more rapidly and reaches a considerably greater value in the gopher than in the rat. From Fig. 3 it is evident that immediately after the stoppage of respiration, its amount in the gopher is considerably greater than that in the rat, and, on the contrary, the amount of AMP is considerably lower in the gopher. This is even more pronounced at the thirtieth minute after stoppage of respiration. The difference in the amounts of ATP and CP in these two species of animals was negligible (during the periods elapsed from the moment of stoppage of the agonal respiratory movements). It should be considered that these movements, as we have already noted, continue considerably longer after clamping of the trachea in the gopher than in the rat.

It is known that under conditions of a normal oxygen supply at a body temperature of 15°, the gopher consumes oxygen considerably more intensively than does the rat [4]. Nonetheless, the data obtained under conditions of severe anoxia indicate greater resistance of the gopher, which thus cannot be explained by the lower level of the general oxidative metabolism and is undoubtedly a result of a definite specificity of the anaerobic processes in the tissues of this animal.

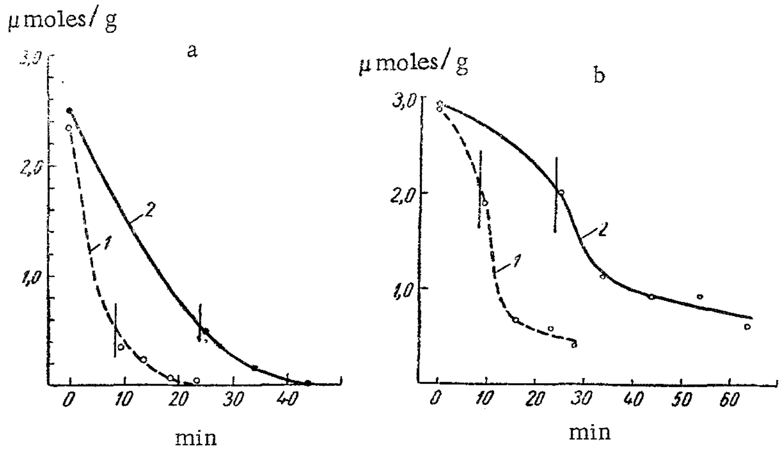

Fig. 2. Change in the concentration of CP (a) and ATP (b) after clamping of the trachea in the brain of the rat and gopher at a body temperature of 15°. Each point represents an average of three experiments. The vertical lines denote the moment of the last inspiration.

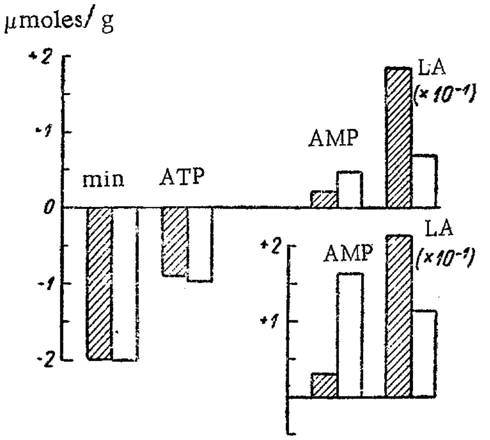

Fig. 3. Changes in the concentration of high-energy phosphates and lactic acid in the brain of the rat and gopher during the first minute (top) and in a period of 30 minutes (bottom) after clamping of the trachea at a body temperature of 15° with respect to the initial level (measured at the same body temperature, but in animals without clamping of the trachea). The lactic acid concentration shown in the figure is 10 times lower than the values found. Light columns) rat; shaded) gopher.

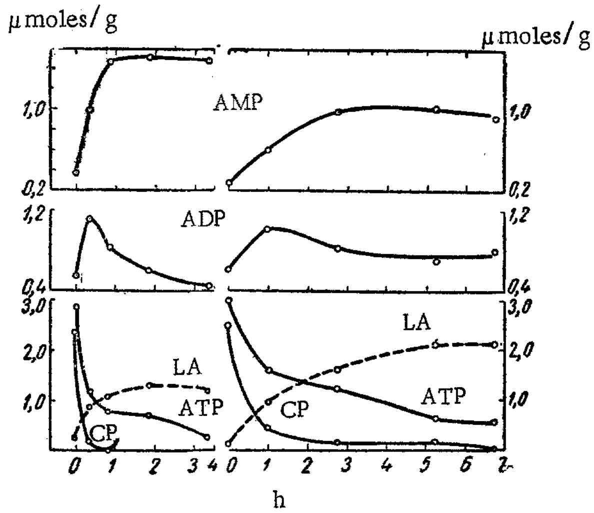

Fig. 4. Changes in the concentration of high-energy phosphates, AMP, and lactic acid (LA) in the brain of the rat (left) and gopher (right) during clinical death at a body temperature of 0°. Each point average value of 3 to 8 experiments. The initial values were measured at a body temperature of 15° before the beginning of cooling to 0°, when respiration and circulation had stopped.

Figure 4 presents the results of experiments with a rat and a gopher in a state of clinical death at body temperature of 0°. There is not only a stoppage of respiration, but also the absence of blood cirulation. From Fig. 4 it is evident that the amount of high-energy phosphates (CP, ATP, and ADP) in the gopher varies more slowly, and the final amounts of the individual metabolites differ from those in the rat. The amount of lactic acid in the gopher is almost twice as great as that in the rat, while the increase in the amount of AMP is considerably less pronounced in the gopher.

The data obtained indicate that the brain tissue of the gopher is capable of more effective utilization of the anaerobic energy resources than that of the rat. That might explain, if only partially, the pronounced increase in the resistance of the gopher to anoxia and its ability to stay for a longer period of time in the state of reversible clinical death during deep hypothermia.

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