Parameters of Cerebral Energy Metabolism in Rat Breathing Nitrogen- and Argon-Containing Hypoxic Mixtures

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The study explores the effects of oxygen-nitrogen and oxygen-argon hypoxic mixtures (5-6%) on energy metabolism in rats. It is shown that in animals breathing an argon-containing hypoxic mixture oxidative phosphorylation is less affected by acute hypoxia that in animals breathing a nitrogen-containing mixture.

Key Words: *hypoxia; argon; nitrogen*

Inert gases under high barometric pressure exert a pronounced biological effect: an inert-gas narcosis. Moreover, inert gases under normal and elevated pressure are not biologically inert and modulate the rate of fundamental biological processes [2,8], in particular they enhance oxygen consumption by hepatocyte suspension in an Ar/O_2 normoxic media [1]. However, we found no publications on the effect of inert gases in hypoxic mixtures on respiratory enzymes.

It has been previously demonstrated that life span of rats breathing hypoxic oxygen-argon mixture containing 4% oxygen 2-fold longer than that of rats breathing hypoxic nitrogen-oxygen mixture with the same percentage of oxygen.

In the present study we investigated the effect of argon on the respiratory enzymes NADH dehydrogenase (NADH-DH) and succinate dehydrogenase (SDH) in the motor cortex under hypoxic conditions.

MATERIALS AND METHODS

Random-bred albino rats were divided into 4 groups (4 rats per group) and placed to an air-conditioned pressure chamber (35 liters) equipped with a life-support system.

The chamber was then ventilated with hypoxic (7% oxygen) oxygen-argon (group 1) or oxygen-nitrogen (group 2) mixture until oxygen content decreased to 7% and then it was maintained within 5-6%. Group 3 animals breathed air (control). Temperature in the chanber was 19-20°C, content of CO_2 did not exceeded 0.4 kPa. The duration of the experiment was 1 h. Group 4 animals were intact.

All animals were decapitated immediately after the experiment, heads were wrapped in aluminum foil and frozen.

Activity of respiratory enzymes SDH and NADH-DH in the motor cortex was measured using a quantitative histochemical method [5]. The amount of formazan (M) formed by 1 M protein nitrogen for 1 min at 37°C was taken as one unit of enzyme activity and expressed in milliunits (mM) formazan per 1 min. Morphological evaluation of enzyme activity was carried out.

RESULTS

In group 1, SDH and NADH-DH activities after inhalation of an oxygen-argon mixture decreased by 17% in comparison with intact rats (Fig. 1).

In group 2, activities of both enzymes after inhalation of nitrogen-oxygen mixture decreased by 30%,

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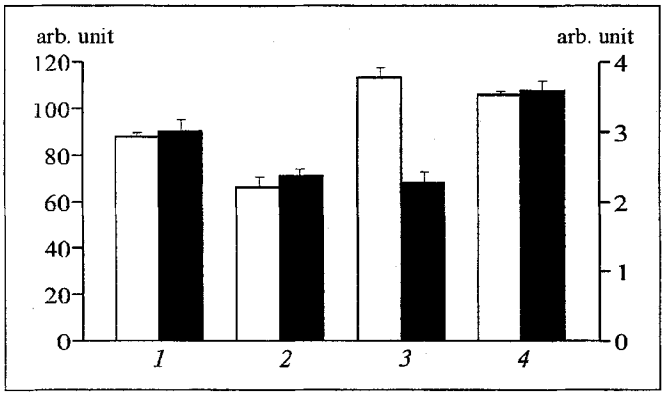

Fig. 1. Succinate dehydrogenase (open bars, left axis) and NADH dehydrogenase activities (shaded bars, right axis) in the cortex of rats exposed to acute hypoxia and breathing oxygen-argon (*1*) and oxygen-nitrogen (*2*) mixtures, control (*3*) and intact rats (*4*).

indicating severe disturbances of energy metabolism. More then 2-fold decrease in SDH and NADH-DH activities renders the process irreversible, since normal tissue respiration in mitochondria of cortical neurons under these conditions becomes impossible [3,4,7].

In group 3 rats (control), SDH activity slightly increased, while NADH-DH activity decreased by 36% in comparison with intact animals. This attests to limitation of NAD-dependent oxidation and impaired cell protection. Under these conditions the cells can transit to highly effective FAD-dependent succinate oxidase oxidation pathway. Activation of this metabolic pathway under conditions of stress was described previously [6].

It can be hypothesized that inhibition of NADH-DH in experimental animals is caused primarily by stress (new environment and the noise of gas purification system), while the decrease in activity of both enzymes in groups 1 and 2 is induced by hypoxia.

Histological examinations showed that the decrease in enzyme activity in group 1 is associated predominantly with glial cells, while in group 2 it occurred primarily in neurons. It is known that reparative capacity of glial cells far surpasses that of neurons.

Thus, the presence of argon in respiratory medium reduces the hypoxia-induced disturbances in oxidative phosphorylation in rat brain.

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