Following the immobilization, highly significant positive correlations in GR activity were found between virtually all of the brain structures examined: amygdala-cortex ($p<0.003$), hypothalamus-midbrain ($p<0.015$), cortex-hypothalamus ($p<0.005$), and midbrain-cortex ($p<0.02$). None of these correlations was observed in the control. Uniform changes in all structures in the activity of an enzyme that restores the cellular reserves of glutathione may, on the one hand, be associated with the general mechanisms regulating the activity of that enzyme and, on the other hand, may reflect the enhanced detoxification, in the early phases of ES, of free-radical products of the circulation of neurotransmitter and other metabolites.

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Characteristics of Iron Metabolism and State of the Transferrin-Ceruloplasmin System in Rats with Varying Resistance to Hypoxia

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Studies of the functional differences between animals with high and low resistance to hypoxia (HR and LR) are ongoing. It is known that unadapted animals with a high natural resistance to hypoxia demonstrate a higher lability of succinate dehydrogenase, cytochrome oxidase, ATPases, as well as of glutamic acid-dependent enzymes catalyzing α-glutarate production [1,3].

The above specificity of the functional properties of enzymes in animals highly tolerant of hypoxia

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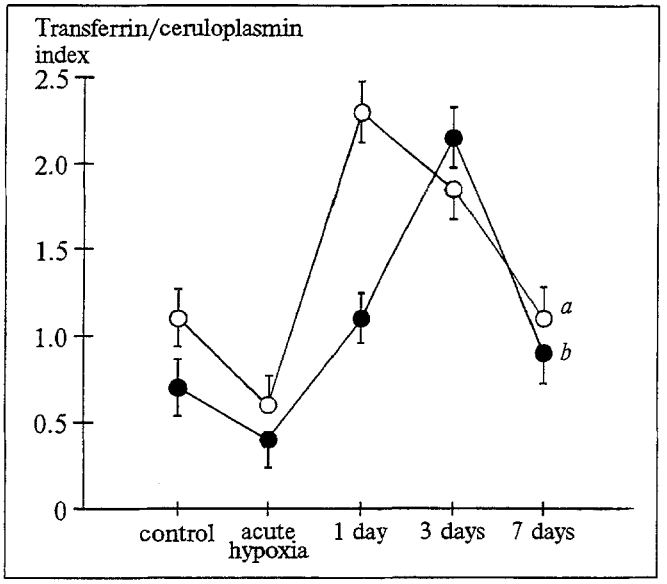

Fig. 1. Dynamics of transferrin–ceruloplasmin index in rats with high (*a*) and low (*b*) resistance to hypoxia during posthypoxic period.

enables their tissues in time to shift to a more beneficial erythron-mediated pathway of oxygen utilization and transport [1,6]. The iron and transferrin-ceruloplasmin (Tr/Cer) system are the substrates that largely determine the lability of this pathway. They are actively utilized during the process of heme synthesis and determine the pro- and antioxidant potential of the blood.

The specific features of iron and ceruloplasmin metabolism during hypoxia are still to be studied in relation to the individual resistance of animals to hypoxia.

The aim of the present study was to investigate the specific features of the main indices of iron metabolism and the state of the Tr/Cer system in LR and HR rats during the period of recovery after acute hypobaric hypoxia.

MATERIALS AND METHODS

The experiments were carried out on male Wistar rats weighing 170-200 g. The animals were divided into HR and LR groups after Berezovskii [1]. Acute hypoxia (AH) was simulated by "raising" the animals to an altitude of 9,000 m in a pressure chamber (2-h exposure). Blood was taken from the caudal vein before hypoxia, directly after the "decsent", and on days 1, 3, and 7 of the posthypoxic period. Intact animals served as the control.

The serum concentration of iron (SI), the total (TIBC) and latent iron binding capacity (LIBC) of the serum, and the percentage of iron saturation (PIS) were measured by the bathophenanthroline method with the aid of Bio-La-Test-Fe kits (Lachema). The level of transferrin was assessed from LIBC [2]. The ceruloplasmin concentration was determined by Ravin's method modified by Ten [5]. The results were processed using Student's t test.

RESULTS

As shown in Table 1, the level of all parameters of iron metabolism studied (excepting PIS) in HR and LR rats was approximately egual before hypoxia. The difference between PIS of HR and LR rats proved statistically reliable ($p<0.05$); a lower level of this index was discovered in LR rats, probably indicating a lesser amount of "reserved" iron. The Tr/Cer ratio was reliably higher in LR rats in comparison with this index in Hr animals, due to a higher Tr concentration; this may attest to a predominant prooxidant potential of the serum in this group of animals.

Directly after AH, the level of SI did not undergo any significant changes in either LR or HR animals compared with the controls. One to three days later, in the posthypoxic period a drop of SI was revealed in HR rats as against the control; in LR animals, a reliable decrease of SI was found only on day 3 after AH. The recovery of SI to the initial level was observed on the 7th day of the posthypoxic period in LR and HR rats.

Under the influence of AH, TIBC and LIBC proved more labile: directly after the influence, independently of the animals' resistance to AH, the concentration of iron-bound and iron-free iron-transporting protein transferrin was markedly (35.6% in HR rats and 57.1% in LR rats) lower than in the control. On days 1 and 3 after AH, a sharp increase of TIBC was detected in LR and HR rats as compared with the intact animals. The increase of both indices was maximal in LR animals on the 1st day of the posthypoxic period, whereas TIBC and LIBC peaked on the 3rd day of posthypoxic period in HR rats; on day 3, TIBC was markedly higher in HR rats than in LR animals. In both HR and LR rats, TIBC and LIBC normalized on day 7 after AH. Analysis of the PIS values provides evidence that the dynamics of this parameter is similar in LR and HR rats: directly after hypoxia, a reliable increase of PIS was observed, apparently due to a decrease in the total and reserve iron-binding capacity of Tr and for an unchanged level of SI. On the 1st day of the posthypoxic period, PIS decreased 3-fold and 2.8-fold in HR and LR animals, respectively. PIS proved to be lowest on the 3rd day of the posthypoxic period in both HR and LR rats, this being consistent with the times of the maximum rise of TIBC and LIBC discovered by us and with the time of maximal ac-

TABLE 1. Indexes of Iron Metabolism and Ceruloplasmin Content During Period of Recovery after Acute Hypobaric Hypoxia in HR and LR rats ($M \pm m$, $n = 7-11$)

Index	Group	Control	Acute Hypoxia	Posthypoxic period, days		
				1	3	7
SI, μM	HR	37.2±3.5	33.7±1.5	21.4±1.5*	25.3±1.3*	30.7±1.9
	LR	32.0±1.9	26.1±1.6	28.1±1.4	24.4±2.2*	34.1±3.1
p		>0.5	<0.05	<0.05	>0.5	>0.5
TIBC, μM	HR	87.3±6.0	56.0±2.3*	111.4=7.48	158.4±6.78	92.8±3.4
	LR	95.9±2.8	46.4±6.4	137.7±14.7*	132.1±9.2*	104.3±8.8
p		>0.5	>0.5	>0.5	<0.05	>0.5
LIBC, μM	HR	50.1±4.5	22.4±1.6*	90.0±6.3*	133.1±0.6*	70.2±6.3
	LR	64.0±3.8	20.3±2.8*	109.5±12.0*	107.6±8.6*	62.2±5.0
p		<0.05	>0.5	>0.5	<0.05	>0.5
PIS, %	HR	42.6±2.9	60.1±4.0*	19.2±1.3*	16.0±1.3*	33.1±2.6*
	LR	33.3±1.9	56.3±7.7*	20.4±2.2*	18.5±1.3*	32.7±2.6
p		<0.05	>0.5	>0.5	>0.5	>0.5
Ceruloplasmin, mg%	HR	61.4±3.7	45.0±6.5*	46.4±1.7*	56.4±5.5	56.7±3.6
	LR	56.3±2.8	36.4±4.5*	85.9±13.9*	74.6±5.3	60.9±2.8
p		>0.5	>0.5	<0.05	<0.05	<0.5

Note. *p*: reliability of differences between HR and LR groups; asterisk indicates significant differences vs. the corresponding control ($p<0.05$).

tivity of erythropoesis responding to hypoxic stress in rats, as reported in the literature [4,7]. In HR and LR animals, PIS decreased by a factor of 2.6 and 1.8, respectively, this being evidence of diminishing iron reserves and a developing iron deficiency on day 3 after AH. On the 7th day of the posthypoxic period, PIS was brought back to the initial level in HR and LR rats.

Analysis of the ceruloplasmin concentration suggests that AH leads to a diminution of this index in LR and HR animals, no differences of its values being revealed depending upon the animals' tolerance of hypoxia. On the 1st and 3rd day of the posthypoxic period, the ceruloplasmin concentration rose in both LR and HR rats. The concentration of this protein peaked on day 1 after AH in HR rats and on day 3 in LR animals. A noteworthy fact is that during the 1st to 3rd day of the posthypoxic period, the increase of the ceruloplasmin level in HR rats was more pronounced than in LR rats. On the 7th day, a normalization of this index was observed in both groups.

An important feature of the state of the Tr/Cer system is a decrease of its quantitative characteristics and a predominance of the ceruloplasmin level, evidently due to a more active utilization of transferrin during acute hypoxia. The prevalence of the antioxidant potential of the blood serum over the prooxidant potential may be regarded as a compensatory response of the organism to acute hypoxia directly after exposure. On the 1st day of the posthypoxic period, a significant increase of the Tr/Cer index was encountered in both LR and HR rats (Fig. 1). It is important that on day 1 after AH, the Tr/Cer index of HR animals, due to the concomitant rise of the concentrations of both proteins, virtually did not differ from that in intact animals, whereas in LR rats this index was twice as high as in the control. This was evidence of a predominance of the prooxidant potential of the blood serum over the antioxidant potential in LR animals.

The shift revealed in the state of the Tr/Cer system of HR animals is explained by a marked intensification of transferrin synthesis in the liver of HR rats, whereas in LR animals this shift may largely be associated with an insufficient level of ceruloplasmin synthesis. Normalization of the Tr/Cer indexes was observed in both LR and HR rats on the 7th day of the posthypoxic period.

Thus, regardless of the degree of resistance to hypoxia, AH leads to similar changes in the iron metabolism and in the state of the Tr/Cer system. Directly after acute hypoxia, a drop of all the indices of the iron transport reserve and of ceruloplasmin is observed. A stimulating effect of acute hypoxia on the synthesis of transferrin and ceruloplasmin, most strongly marked on the 3rd day of the posthypoxic period, was revealed in the animals highly resistant to hypoxia.

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