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Impact of Acute Hypoxia on the Fatty-Acid Composition and Lipid Peroxidation in Liver Microsomal Membranes and Blood Plasma of Rats with Low and High Resistance to Oxygen Deficiency

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Within populations of animals there exist intraspecific differences in the resistance to hypoxia that are determined by the totality of genotypic and phenotypic properties possessed by the organism [4,15]. These differences manifest themselves at the organismic and organic as well as tissue levels [5,11]. The importance of research into the mechanisms by which a high resistance to oxygen deficiency is assured stems from the fact that hypoxia is a major factor in the pathogenesis of all pulmonary and cardiovascular diseases and is usually the immediate cause of death under extremely adverse conditions.

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The purpose of this study was to examine how acute hypoxia affects the fattyacid composition and lipid peroxidation (LPO) in liver microsomal membranes and blood plasma of animals differing in their resistance to oxygen deficiency.

MATERIALS AND METHODS

The experiments were conducted on 120 male Wistar rats weighing 190-220 g. Their resistance to hypoxia was assessed by noting the time at which the first agonal inspiration occurred during elevation to an "altitude" of 11,500 m at a rate of 50 m/sec in a pressure chamber [4]. The animals were then divided into four groups: group 1 comprised low-resistance intact animals (LR control); group 2, high-resistance intact animals (HR

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control); and groups 3 and 4, LR and HR test rats, respectively, which were later exposed to acute hypoxia. This was produced by elevating the rats to an "altitude" of 9000 m, at which they remained for 2 h. Immediately thereafter the rats were decapitated. The liver microsomal fraction was obtained by differential centrifugation [2]. The fatty-acid composition of the lipid fraction, extracted by the method of Folch *et al.* [10], was determined in the liver microsomes as well as in the blood plasma. Samples for gas chromatography, for which a Chrom-4 chromatograph was used, were prepared as described previously [8]. The activity of spontaneous and NADPH-dependent LPO in the microsomes was assessed by the formation of malonic dialdehyde (MDA). Total lipids in blood plasma samples were determined using a standard reagent kit (Lachema); MDA [7] and corticosterone concentrations were estimated by radioimmunoassay. Microsomal protein was determined by Lowry's method [12]. The results were treated statistically by Student's *t* test.

RESULTS

No differences in the fatty-acid composition of microsomal membranes were detected between the LR and HR control groups (Table 1). In response to acute hypobaric hypoxia there occurred marked increases in total unsaturated fatty acids in the microsomal lipids of LR rats mainly as a result of increases in arachidonic acid, and in myristic, pentadecanoic, and palmitoleic acids in those of HR rats without any alteration in the concentration of arachidonic acid. The microsomal concentration of MDA formed in the reactions of spontaneous and NADPH-dependent LPO was higher by 58% and 27%, respectively, in the LR group

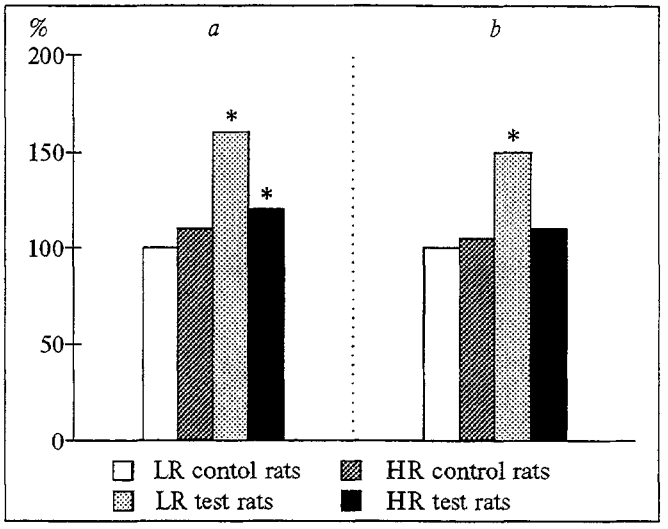

Fig. 1. Effect of acute hypoxia on spontaneous (*a*) and NADPH-dependent LPO (*b*) in low-resistance (LR) and high-resistance (HR) rats.

and by 25% and 10%, respectively, in the HR group (Fig. 1) than in the unexposed controls.

Determination of total plasma lipids indicated substantial differences in the level of lipid metabolism between the LR and HR control groups (Table 2). Thus, the content of total lipids in the latter group was twice that in the former. Also, the LR rats had significantly lower concentrations of pentadecanoic and oleic acids but higher concentrations of linoleic acid than the HR animals. On the other hand, these two groups did not differ significantly in the plasma level of MDA. Acute hypobaric hypoxia did not alter either the content of total plasma lipids, their fatty-acid composition, or MDA concentration in the LR rats but raised total lipids 3.8-fold over the control level in the HR rats, which also had higher levels of these lipids than the LR rats exposed to hypoxia. In addition, the hypoxia-exposed HR rats showed lower concentrations of palmitoleic acid and significantly higher arachidonic

TABLE 1. Effect of Acute Hypobaric Hypoxia on the Fatty-Acid Composition of Liver Microsomal Membrane Lipids in Low-Resistance (LR) and High-Resistance (HR) Rats ($n=7$ to 12). The values are percentages (means±SEM)

Fatty acid (FA)	LR control rats	HR control rats	LR test rats	LR test rats
C14:0	0.11±0.01	0.14±0.03	0.19±0.02*	0.28±0.04**
C15:0	0.08±0.01	0.10±0.01	0.11±0.02	0.20±0.04**
C16:0	16.9±1.2	18.3±1.5	14.8±1.1	18.5±1.3
C16:1	1.7±0.1	2.3±0.3	2.3±0.8	4.1±0.6**
C18:0	23.6±0.6	22.1±1.4	21.8±0.9	22.0±1.9
C18:1	12.8±0.5	12.6±1.3	13.3±0.5	15.5±1.1
C18:2	15.9±0.5	15.6±1.0	15.7±0.5	15.1±0.9
C20:4	25.8±1.2	25.6±1.1	31.4±0.9*	23.4±0.9
Total sat. FA	41.8±1.2	40.6±2.3	36.9±1.9*	41.0±2.4
Total unsat. FA	58.2±1.2	59.4±2.3	63.1±1.9*	59.0±2.4
Sat. index	0.72	0.68	0.58	0.69

Note. Here and in Table 2: *significant difference from the LR control group; **significant difference from the HR control group ($p<0.05$).

TABLE 2. Effect of Acute Hypobaric Hypoxia on the Fatty-Acid Composition of Total Blood Plasma Lipids in Low-Resistance (LR) and High-Resistance (HR) Rats (n=7 to 12). The values are percentages (means±SEM)

Fatty acid (FA)	LR control rats	HR control rats	LR test rats	LR test rats
C14:0	0.30±0.10	0.53±0.18	0.33±0.13	0.26±0.10
C15:0	0.12±0.03	0.28±0.07*	0.14±0.05	0.07±0.008**
C16:0	21.3±1.1	20.7±1.5	18.9±0.6	19.0±2.1
C16:1	6.7±0.5	8.5±0.8	6.6±0.4	5.3±0.8**
C18:0	11.8±0.5	12.5±0.4	12.7±0.6	11.5±0.9
C18:1	17.3±0.9	22.2±2.4	17.7±1.4	19.8±0.7
C18:2	26.1±2.4	20.4±1.0*	25.7±1.9	20.2±1.1
C20:4	16.0±1.3	16.2±1.5	15.3±1.3	23.4±2.5**
Total sat. FA	33.4±1.0	33.9±1.7	31.9±1.0	30.9±1.5
Total unsat. FA	66.6±1.0	66.1±1.7	68.1±1.0	69.1±1.5
Sat. index	0.50	0.51	0.47	0.45

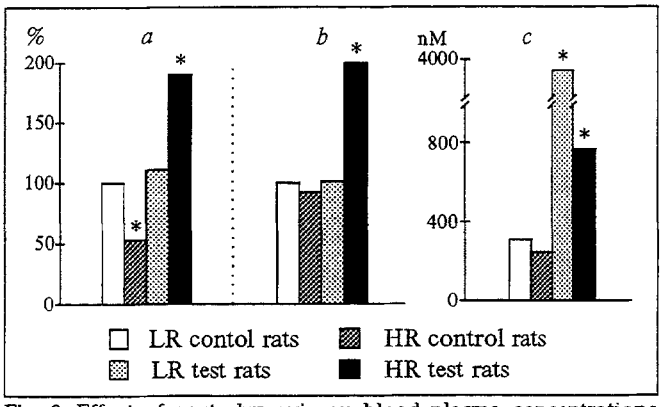

Fig. 2. Effect of acute hypoxia on blood plasma concentrations of total lipids (*a*), malonic dialdehyde (*b*), and corticosterone (*c*) in LR and HR rats.

acid concentrations than the HR controls (Table 2). The plasma level of MDA in the HR rats in response to the acute hypoxia increased 2.1-fold (Fig. 2).

These findings point to the existence of intraspecific differences in responses to oxygen deficiency. In LR rats, the observed rise of arachidonic acid in the microsomal membranes as a mechanism of adaptation to acute hypoxia (aimed at imparting particular liquid properties to the membrane bilayer in order to ensure optimal functioning of membrane-associated enzymes [1]) may be interpreted as an undesirable phenomenon because the metabolic products of arachidonic acid such as prostaglandins and leukotrienes promote hypoxia [9,13]. The LR animals also exhibited a hyperreaction of the adrenal system, as was indicated by a 13.8-fold increase in the plasma corticosterone concentration compared to only a 3-fold increase in the HR rats (Fig. 2). The excess corticosterone in LR rats appears to be one of the reasons for the lowered resistance of their microsomal membranes to the damaging action of NADPH-dependent LPO, given that steroid hormones are capable of altering the hydrophobic characteristics of microsomal membranes [6]. In the hypoxia-exposed HR rats, the arachidonic acid level remained unchanged in the microsomal membranes, but the overall pool of this acid increased as a result of its rise in the total plasma lipids. This latter response appears to raise the level of prostacycline, which possesses antihypoxic properties [14].

In summary, acute hypobaric hypoxia elicits differential responses from the lipid component of the hepatic endoplasmic reticulum membranes and from blood plasma lipids depending on the initial (prehypoxia) resistance of the animal to oxygen deficiency.

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