The new multiparametric method of assessing states of anxiety and phobia in rats, which we have suggested, is simple and is readily available in laboratory practice, it requires no complicated equipment, and yields rapid results.

As our experience of the use of the combined scale shows, this method offers new prospects for the study of the pathogenetic mechanisms of anxiety states and phobias, and also for the preclinical substantiation of the appropriate drugs to correct states of this kind.

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OPPOSITE EFFECTS OF ADAPTATION TO CONTINUOUS AND INTERMITTENT HYPOXIA ON ANTIOXIDATIVE ENZYMES

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Preliminary adaptation to intermittent hypoxia under pressure chamber conditions has a powerful protective effect on the heart and, in particular, it significantly limits ischemic and reperfusion-induced arrhythmias as well as the size of ischemic and adrenergic necrotic lesions [5, 13, 15]. If the antiarrhythmic action of adaptation to intermittent hypoxia is compared with that of adaptation to continuous hypoxia at medium altitudes, both forms of adaptation are found to have a protective effect against ischemic arrhythmias caused by ligation of the coronary artery. Meanwhile their effect on reperfusion arrhythmias arising after removal of the occlusion were found to be opposite in kind: adaptation to intermittent hypoxia protected against reperfusion arrhythmias and abolished fibrillation of the heart and mortality among the animals whereas adaptation to continuous hypoxia, on the other hand, sharply potentiated arrhythmias and increased mortality among the animals [4]. In an attempt to explain the causes of this paradoxical result, attention was paid to the fact that activation of free-radical oxidation plays an important role in

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the pathogenesis of reperfusion arrhythmias [8]. On this basis it has been suggested that during adaptation to continuous hypoxia in the mountains a long stay under conditions of reduced partial pressure of oxygen leads to partial loss of activity of the antioxidant system in accordance with the "disuse atrophy" principle, whereas during adaptation to intermittent hypoxia, every "ascent" in the pressure chamber is followed by a "descent," accompanied by reoxygenation and the appearance of active forms of oxygen. As a result of repeated activations of free-radical oxidation, an adaptive increase in activity of the antioxidative enzymes takes place in vitally important organs.

The aim of this investigation was to test this hypothesis by comparing the content of lipid peroxidation products and activity of antioxidative enzymes in the heart, brain, and liver of animals during adaptation to continuous hypoxia in the mountains and to intermittent hypoxia in a pressure chamber.

EXPERIMENTAL METHOD

Male Wistar rats weighing 200-220 g were subjected to adaptation to continuous hypoxia in the mountains at an altitude of 2100 m above sea level for 30 days. Adaptation took place at a base located in the Caucasian foothills (Terskol District). Adaptation of the same animals to intermittent hypoxia was carried out in a pressure chamber; on the 1st day the pressure corresponded to an altitude of 1000 m above sea level, and each consecutive day the altitude was increased by 1000 m up to 5000 m, The animals were "lifted" to this altitude daily for 6 h for 30 days. Twelve animals were used in each series. Lipid peroxidation was monitored by determining concentrations of products interacting with 2-thiobarbituric acid in the homogenates, by the method in [14]. Superoxide dismutase activity was determined as in [7] and catalase activity as in [8].

EXPERIMENTAL RESULTS

The main results of the investigation are given in Table 1. At least three conclusions can be deduced from Table 1.

First, the content of TBA-active lipid peroxidation products fell in the heart, liver, and brain in the mountains; in the last two of these organs the decrease was significant, whereas in the heart it was only a tendency. The decrease in concentration of lipid peroxidation products thus revealed can be taken as evidence that the intensity of this process actually fell as a result of a long stay with exposure to low pO_2 at a comparatively low altitude. During adaptation to intermittent hypoxia this was not observed in any of the organs studied.

Second, it follows from Table 1 that in all the organs studied catalase and superoxide dismutase activity fell during adaptation to continuous hypoxia. The decrease in catalase activity of the heart was 14%, and that of superoxide dismutase 35%. The corresponding values for the liver were 19 and 31%, and for the brain 13 and 33%. This fact essentially means that during a sufficiently long period of adaptation, even to moderate but intermittent hypoxia, partial disassembly of the antioxidative enzyme systems of the body takes place. From the theoretical point of view this observation is in agreement with the general concept of the structural price of adaptation [3], which implies that long-term adaptation to any environmental factor, leading to an increase in functional capacity of particular systems, for example, an increase in the coronary blood flow and myoglobin level in the heart during adaptation to hypoxia or of the brown adipose tissue during adaptation to cold [1, 9, 10], is often accompanied by atrophy of other systems, not involved in adaptation. On the practical level, this lowering of activity of antioxidative protection of the body during long-term residence at a high altitude may be one explanation of the disadaptation syndrome [6], manifested as feeling unwell and reduced working capacity observed in athletes and tourists after descent from the mountains. It is from this point of view that ways of correcting this syndrome by the use of descent in stages for administration of exogenous antioxidants should be studied.

The third conclusion to be drawn from Table 1 is that of a significant increase in activity of antioxidative enzymes in the organs studied during adaptation to intermittent hypoxia. This is not a new phenomenon – it was found in previous studies [2] but underestimated. Nevertheless, it not only explains many of the protective effects of adaptation to intermittent hypoxia [5, 13, 15], but is also evidence of definite advantages of adaptation to intermittent hypoxia compared with adaptation to continuous hypoxia in the mountains.

TABLE 1. Effect of Continuous and Intermittent Adaptation to Hypoxia on Lipid Peroxidation and Activity of Antioxidative Enzymes in Rat Tissues

Parameter	Control (base)	Continuous hypoxia	Intermittent hypoxia
Heart			
Malonic dialdehyde, mmoles/mg protein	0,68±0,03	0,61±0,04	0,63±0,03
Catalase, mmoles H_2O_2/mg protein/min	162±3	140±2*	176±8*
Superoxide dismutase, U/g protein	640±41	416±36**	712±23*
Liver			
Malonic dialdehyde, mmoles/mg protein	0,77±0,05	0,47±0,03**	0,62±0,04
Catalase, mmoles H_2O_2/mg protein/min	580±10	472±27**	742±29**
Superoxide dismutase, U/g protein	720±30	500±48*	1060±39**
Brain			
Malonic dialdehyde, mmoles/mg protein	1,15±0,05	0,66±0,04*	1,03±0,03
Catalase, mmoles H_2O_2/mg protein/min	325±9	283±8*	410±11**
Superoxide dismutase, U/g protein	1270±12	850±18*	1760±16**

Legend. *$p < 0.05$, **$p < 0.01$ Compared with control.

Recently this type of adaptation to intermittent hypoxia in large multimanned pressure chambers has been successfully used in the treatment of nervous and allergic diseases [12]. Besides other factors, potentiation of the antioxidative protection of the patient may play a role in the mechanism of this therapeutic effect.

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