EFFECT OF HIGH-ALTITUDE TRAINING ON INTENSITY OF PROTEIN SYNTHESIS IN THE BRAIN AND RESISTANCE OF ANIMALS TO CONVULSANT FACTORS

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During interrupted training of rats for high-altitude hypoxia, protein synthesis is stimulated, and the RNA content rises in the cerebral cortex. At the same time the resistance of the animals to convulsant factors is increased.

The writers have shown previously that the synthesis of nucleic acids and proteins in the myocardium is stimulated in animals undergoing training for hypoxia, and that this leads to hypertrophy of the heart and to increased resistance of the heart to acute overloading [1].

TABLE 1. Dynamics of Incorporation of Methionine-S^{35} into Rat Brain Proteins and Concentration of Nucleic Acids in Cortex during Training for High-Altitude Hypoxia

Time after beginning of training (in days)	Investigations*	Intensity of methionine incorporation (in $\frac{\text{pulses/min/g protein}}{\text{pulses/min/g body weight}}$)			DNA concentration (in μg/100 mg fresh tissue)	RNA concentration (in μg)
		cortex	medulla	hypothalamus		
10	Control	1,41±0,017	1,51±0,014	1,52±0,122	9,8	14,8
	Experiment	1,92±0,041	2,28±0,173	1,92±0,170	9,4	16,5±0,33
	P	<0,02	<0,01	>0,05		>0,2
20	Control	0,97±0,118	1,14±0,183	1,10±0,168	9,1	13,7±0,40
	Experiment	1,46±0,094	1,57±0,065	1,44±0,059	10,0	18,5±0,16
	P	<0,01	0,05	>0,05		<0,001
40	Control	0,82±0,146	1,11±0,26	1,25±0,21	8,9	14,6±0,20
	Experiment	1,49±0,228	1,61±0,186	1,84±0,256	10,1	21,9±1,01
	P	<0,05	>0,1	>0,1		<0,001
Training stopped 50	Control	1,01±0,06	0,91±0,133	1,18±0,105	9,7	14,6±0,40
	Experiment	1,41±0,112	1,09±0,148	1,35±0,107	9,8	17,6±0,37
	P	<0,01	>0,2	>0,2		<0,01
80	Control	1,33±0,245	1,32±0,289	1,49±0,080	9,6	15,4±0,20
	Experiment	1,59±0,197	1,27±0,088	1,29±0,136	9,5	16,0±0,30
	P	<0,2	>0,5	>0,2		>0,2

*Control series includes 4 rats, experimental series 8.

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TABLE 2. Effect of Preliminary Training for Hypoxia on Course of Epileptiform Convulsions Induced by Leptazol

	Number of animals	Latent period (in sec)		Number of fits	Duration of convulsions (in sec)
		from injection of leptazol to appearance of first spasms	from injection of leptazol until beginning of convulsions		
Control	13	89±10,7	160±18	2,2±0,42	83±24,3
Training for hypoxia (20 days)	7	171±18	259±54	1,6±0,03	17±3
P		<0,01	>0,1	>0,2	<0,02

TABLE 3. Effect of Training for Hypoxia on Course of Audiogenic Convulsions

Times of training (in days)	Number of animals			Duration of convulsions (in sec)
	total	showing inhibition of motor excitation (2 waves)	developing convulsions	
Initial state	10	2	10	57,0±14,3
10	10	6	7	16,9±4,4
20	10	4	7	12,6±3,4
30	9	4	5	31,2±5,2
40	9	5	4	19,0±1,7

Considering the importance of activation of nucleic acid and protein synthesis in training to increase resistance to high-altitude hypoxia, protein synthesis and the content of nucleic acids were studied in the brains of animals undergoing such training, and the resistance of the animals to convulsant factors was determined.

EXPERIMENTAL METHOD

Female Wistar rats weighing 130-150 g were kept in a pressure chamber for 6 h daily. During the first 7 days the oxygen pressure in the chamber was gradually lowered to the equivalent of an altitude of 2000 to 7500 m, and thereafter until the 40th day the rats were kept at an "altitude" of 7500 m. Experiments on the animals began 18 h after their last "ascent" in the pressure chamber. The intensity of incorporation of methionine-S^{35} into protein in the cerebral cortex, brain stem, and hypothalamus was determined 10, 20, and 40 days after the beginning of training, and also 10 and 40 days after its end. The isotope was injected (activity 12 μCi) 3 h before decapitation. The concentrations of RNA and DNA in the cortex were determined by the method of Schmidt and Thannhauser at the same times of training. Leptazol (70 mg/kg body weight) and audiogenic stimulation were used as the convulsant factors.

EXPERIMENTAL RESULTS

Ten days after the beginning of training the incorporation of methionine-S^{35} into cortical proteins was increased by 36%, into the medulla by 51%, and into the hypothalamus by 27% (Table 1). Later, protein synthesis in the cortex and hypothalamus continued to increase in intensity, while in the medulla, on the other hand, its intensity decreased. On the 20th and 40th days of training, the most intensive protein synthesis was observed, accordingly, in the cortex, where the incorporation of methionine-S^{35} was increased by 50 and 82%, respectively, compared with increases of 38 and 45% in the medulla and 31 and 47% in the hypothalamus.

After the completion of training, protein synthesis in all parts of the brain gradually declines: after 10 days the intensity of incorporation of methionine-S^{35} in the cerebral cortex was increased by only 40%, in the medulla by 20%, and in the hypothalamus by 15%. After 40 days, activation of synthesis persisted only in the cortex.

In the late stages of training, when the animals' resistance to hypoxia was increased, a considerable and gradually progressive activation of protein synthesis was thus observed in all the investigated parts of the brain, most marked in the cortex. After the end of training, synthesis gradually declined, remaining at the highest level in the cortex.

The RNA concentration in the cerebral cortex rose during training parallel to the increase in intensity of protein synthesis: after 10 days it was increased by 14%, after 20 days by 35%, and after 40 days by 51%. After the end of training the RNA concentration also fell, parallel to the decrease in intensity of protein

synthesis: after 10 days it was still raised by 20%, but after 40 days it was not significantly different from normal. The DNA concentration in the cortex remained almost unchanged at all stages of training.

Consequently, during training for high-altitude hypoxia, protein synthesis in the brain is stimulated, and the concentration of RNA in the brain rises, while after the ending of training these indices decline again.

Investigation of the effects of training for hypoxia on the convulsant action of leptazol showed (Table 2) that for 20 days after training the latent period of convulsions was considerably lengthened, while the duration of the paroxysmal period was shortened.

After 40 days of training for hypoxia, 4 of the 10 animals did not develop convulsions after receiving injections of convulsant doses of leptazol.

Similar results were obtained with pure-line rats*, in 100% of which audiogenic stimulation evoked motor excitation and clonicotonic convulsions. During training for hypoxia, the animals became more resistant to audiogenic stimulation: the course of the convulsions became milder, their duration was shortened, inhibition of motor excitation appeared (2 waves), and the number of animals not responding by convulsions to prolonged audiogenic stimulation was increased (Table 3).

These investigations thus demonstrated that during training for high-altitude hypoxia progressive activation of protein synthesis and an increase in the RNA concentration take place in the cerebral cortex, and the resistance of the animals to the action of convulsant factors is increased. Further investigations will be undertaken in order to study the mechanism of and connection between these phenomena.

LITERATURE CITED

1. F. Z. Meerson, M. Ya. Maizelis, V. B. Malkin, et al., Dokl. Akad. Nauk SSSR, 184, No. 2, 500 (1969).

* Line KM was bred in the Department of Physiology, Moscow University.