EFFECT OF ADAPTATION TO HIGH-ALTITUDE HYPOXIA AND SUBSEQUENT DISADAPTATION ON CONDITIONED REFLEX RETENTION

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After adaptation to high-altitude hypoxia the degree of retention of a conditioned active avoidance reflex is considerably increased. Only half as many combinations of the conditioned and unconditioned stimuli were required to reach the necessary level when the retention of the reflex was tested 24 h after its formation in adapted rats as in the control. This level of adaptation was produced 1 and 5 days after the end of a course of exposures to hypoxia. During disadaptation, the increase in the degree of retention of the reflex which had been achieved disappeared 10 and 27 days after the end of exposure to hypoxia.

KEY WORDS: adaptation to hypoxia; disadaptation; conditioned active avoidance reflex.

Adaptation to high-altitude hypoxia arising as a result of a long stay in the mountains or of exposure in a pressure chamber activates RNA and protein synthesis in the neurons and glial cells of the cortex and underlying regions of the brain [4, 6]. This change is accompanied by an increase in the rate of fixation of temporary connections and the degree of their retention [2, 3, 5], which is in harmony with the view that nucleic acid and protein synthesis plays a decisive role in the consolidation of memory [1, 7, 8]. It was later found that protein synthesis in the brain of animals diminishes rapidly after the end of exposure to hypoxia, and within 6 days it is back to the control level [4]. If the effect of adaptation on conditioned reflex fixation is due to the activation of protein synthesis, it ought not to be manifested after the end of exposure to hypoxia, i.e., during disadaptation.

To test this hypothesis, the effect of adaptation to hypoxia on the formation and retention of a conditioned reflex and the dynamics of disappearance of this effect during disadaptation were studied.

EXPERIMENTAL METHOD

Experiments were carried out on noninbred male rats weighing 250-300 g. Preliminary adaptation to high-altitude hypoxia was created by keeping the rats in a pressure chamber for 5 h daily at an "altitude" of 5500 m. Exposure to hypoxia continued for 40 days. A conditioned active avoidance reflex (CAAR) was formed in four different groups of rats 1, 5, 10, and 27 days after completion of the course of exposures to hypoxia. The CAAR was formed in a Y-shaped maze as avoiding electric shocks by running into the safe, illuminated passage. The reflex was regarded as formed when four of five decisions were correct. Retention of the reflex was tested 24 h after its production by producing it again. The index of retention of the reflex was calculated by the equation: $C = \frac{n_1 - n_2}{n_1} \cdot 100\%$, where n_1 is the number of combinations of the conditioned and unconditioned stimuli required to reach the criterion when forming the reflex, and n_2 the number of combinations required to reach the criterion on testing retention of the reflex. Each of the four groups of previously adapted animals had its own control. However, since there were no differences between the control groups, they could be considered together.

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EXPERIMENTAL RESULTS

At all times studied after completion of the exposure to hypoxia a very small increase in the rate of CAAR formation was observed compared with the control. For instance, the previously adapated animals in all groups required 25-27 combinations of conditioned and unconditioned stimuli to produce the reflex, compared with 31 combinations in the control (Table 1).

The main differences between the previously adapted and control animals appeared when retention of the CAAR was tested 24 h after its formation. To achieve the original level of the criterion during reproduction of the reflex by the control rats 15 combinations were required and their index of retention was 49%. Meanwhile, 1 and 5 days after the end of exposures to hypoxia, the adapted animals required only seven and eight combinations, respectively. The index of retention of the reflex in these two groups was considerably higher than the control, namely 72 and 69%, respectively.

To obtain a more reliable estimate of the effect of adaptation on formation and retention of the CAAR the control animals were divided into two subgroups depending on the number of combinations required to form the conditioned reflex up to the specified criterion. The animals of subgroup 1 (11 rats) required on the average 25 combinations to form the CAAR, i.e., only half that of the adapted rats. The animals of subgroup 2 (nine rats) required 40 combinations to produce the reflex, i.e., 1.5 times as many as the adapted rats, and their index of retention was 71%, i.e., the same as for the adapted animals. In other words, for the same number of combinations during reflex production the degree of retention in the adapted animals was twice as high as in the controls, whereas to obtain the same degree of retention in the control animals as in the adapted rats, the number of combinations during conditioning had to be increased by more than 1.5 times.

The essential fact was that this effect of adaptation was expressed about equally 1 and 5 days after the end of the course of exposures to hypoxia. Later, with an increase in the duration of disadaptation, the degree of retention of the CAAR fell. It follows from Table 1 that 10 and 27 days after the end of exposure to hypoxia, 10 and 13 combinations were now needed to attain the original criterion during repetition of the reflex. The indices of retention were 59 and 53%, respectively, and were virtually indistinguishable from the control.

The considerable increase in the degree of retention of the conditioned reflex achieved as a result of adaptation to hypoxia thus disappeared during disadaptation during roughly the same period of time as the activation of RNA and protein synthesis in the cells of the cerebral cortex [4]. This is in agreement with the view that adaptation to high-altitude hypoxia increases the degree of retention of conditioned reflexes through the activation of nucleic acid and protein synthesis. The problem of what changes in the synapses and in mediator metabolism develops as a result of the activation of protein synthesis and the role of these changes in the increase in the degree of retention of conditioned reflexes discovered during adaptation to hypoxia will be the topic for future research.

TABLE 1. Retention of Conditioned Active Avoidance Reflex during Adaptation to High-Altitude Hypoxia and during Disadaptation

Group and number of animals	Number of combinations to form reflex	Number of combinations to test retention of reflex	Index of retention of reflex, %
1. Control (n = 20)	31±2	15±1	49±5
2. 1 day after end of exposures to hypoxia (n = 10)	27±0,4	7±0,5	72±3
3. 5 days after end of exposures to hypoxia (n = 10)	27±2	8±1	69±5
4. 10 days after end of exposures to hypoxia (n = 10)	25±2	10±1	59±7
5 27 days after end of exposures of hypoxia (n = 10)	27±2	13±2	53±4
P_{1-2}	<0,05	<0,01	<0,01
P_{1-3}	>0,05	<0,01	<0,01
P_{1-4}	<0,05	<0,01	>0,05
P_{1-5}	>0,05	>0,05	>0,05

LITERATURE CITED

1. A. A. Manina, A. V. Rikkl', R. P. Kucherenko, et al., Zh. Vyssh. Nervn. Deyat., No. 2, 363 (1975).
2. F. Z. Meerson, V. A. Isabaeva, A. Z. Ivanshina, et al., Zh. Vyssh. Nervn. Deyat., No. 2, 470 (1971).
3. F. Z. Meerson, V. A. Isabaeva, and A. Z. Ivanshina, Dokl. Akad. Nauk SSSR, 202, 982 (1972).
4. F. Z. Meerson, D. Krants, and T. S. Sadyraliev, Tsitologiya, No. 3, 324 (1973).
5. F. Z. Meerson, R. I. Kruglikov, and E. S. Solomatina, Zh. Vyssh. Nervn. Deyat., No. 5, 1026 (1976).
6. F. Z. Meerson, M.Ya. Maizelis, and V. B. Malkin, Izv. Akad. Nauk SSSR, Ser. Biol., No. 6, 819 (1969).
7. H. Hyden and P. V. Lange, Zh. Évol. Biokhim. Fiziol., 5, No. 2, 145 (1969).
8. J. F. Flood, E. L. Bennet, A. E. Orme, et al., Physiol. Behav., 14, 177 (1975).

EFFECT OF ADAPTATION TO HIGH-ALTITUDE HYPOXIA ON THE MICROCIRCULATION IN THE RAT MESENTERY

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After prolonged adaptation of rats to high-altitude hypoxia (in a pressure chamber at an "altitude" of 6500 m, for 6 h daily for 30-40 days) considerable hyperemia of the intestinal wall and mesentery was observed; the number of functioning capillaries was several times greater than in the control animals but the blood flow in the dilated microvessels was slowed and its structure was disturbed. Besides obvious hemoconcentration in the arteries and veins, hemodilution was observed in the capillaries. Definite hemorheological changes evidently connected with the polycythemia and increased hematocrit index were noted.

KEY WORDS: hypoxia; microcirculation.

Prolonged adaptation to hypoxia affects various structures and functions of the body. Its influence is seen particularly clearly in the blood [1, 3, 6] and circulatory [2, 8, 9] systems. Definite changes have been found also in the structure of the microvascular system, in the endothelial cells of the microvessels [4], and also in the regional circulation in various organs [9].

The object of this investigation was an intravital study of the state of the peripheral circulation and, in particular, of the microcirculation after prolonged keeping of animals in an atmosphere with a reduced oxygen concentration.

EXPERIMENTAL METHOD

Experiments were carried out on 20 noninbred adult male rats divided into two groups: 1) control (10 animals), 2) experimental (hypoxia; 10 rats). The animals of the experimental group were kept for 6 h daily for 35 ± 5 days in a pressure chamber at an "altitude" of 6500 m. A constant composition of the atmosphere in the pressure chamber was maintained by forced ventilation with external atmospheric air. The animals were used for the experiments 16-20 h after the last session. Control animals were kept for the whole of this time in the animal house under ordinary conditions.

Observations on the microcirculation with photographic recording were made on the mesentery of the small intestine by means of an apparatus mounted on the base of an MBI-6 microscope, with a photographic ocular 10× and objectives 10, 20, and 40× (the last two with oil immersion). The mesentery, removed under

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