# EFFECT OF ADAPTATION TO AVERAGE ALTITUDES ON ACTIVE AVOIDANCE CONDITIONS AND ITS MAINTENANCE AFTER EMOTIONAL-PAINFUL STRESS

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UDC 612.833.884-06:612.275.1.014.49

KEY WORDS: conditioned reflex; adaptation to mountain climate; emotional-painful stress; amnesia; resistance

The study of mechanisms of the disturbance of integrative brain activity arising during exposure to stress of varied intensity and duration and the development of measures of protection of the body against these disturbances are matters of some urgency [3, 5].

We know that emotional-painful stress (EPS) causes activation of lipid peroxidation (LPO) [5]. This effect also is characteristic of maximal physical exertion [3, 6], giving rise to motor hypoxia and disturbances of higher nervous activity [3]. Preliminary administration of the LPO inhibitor, ionol, prevents disturbances of conditioned reflex formation and reproduction, such as are usually observed under the influence of physical exertion [6]. In the course of adaptation to average altitudes the raised MDA level, observed during EPS [1], is lowered. However, the effect of EPS on maintenance of conditioned reflexes under the conditions of a mountain climate has not hitherto been studied.

The aim of this investigation was to study the course of formation and preservation of a conditioned active avoidance reflex (CAAR) after single or triple exposure to EPS during adaptation at average altitudes (1600 m) in the mountains.

## EXPERIMENTAL METHOD

Experiments were carried out on 58 noninbred male rats weighing 180-240 g, using the bilateral avoidance defensive conditioned reflex (BACR) method. The conditioned stimulus was the ringing of a bell (30 dB), after 5 sec of which an electric shock (36 V) was applied through the floor of the chamber. Intervals between combinations were 0.5-1.5 min [3]. In each experiment, which was repeated daily, the animals were subjected to 15 conditioned stimulations with reinforcement. The effectiveness of training, which lasted 20 days, was assessed by a number of conditioned reflexes formed in the animals of each group after 60, 120, 180, 240, and 300 combinations. EPS was simulated by the method in [4] in the writers' modification (strengthening of the current in order to cause pain). A conflict of afferent excitation was created in the experimental chamber: extroceptive stimuli, namely light from an electric lamp (L, 300 W), the ringing of a bell (B, 60 dB), and electric shocks (E, 60 V), were used as stressors. The aperiodic cycle of presentation of the stimuli, in a standard order (B, L. E, B, L, E + B + L, B + L, L) lasted 8 min. This cycle was repeated several times in the experiments and the total duration of EPS was 120 min. The second and third sessions of exposure to stress were given in the course of 2-3 days. EPS was induced in the rats in the foothills — animals of group 1 (Frunze, altitude 760 m) and in the mountain — animals of groups 2, 3, and 4 (on the shore of Lake Issyk-Kul', altitude 1600 m). Animals of group 2 were kept in the foothills before exposure to stress, whereas rats of group 3 were adapted beforehand to mountain conditions for 1 month. Rats of group 4 were kept in the plains (they were brought in from Moscow by air). After adaptation for 1 month to the foothills (760 m) they also were exposed to stress in the mountain (1600 m). Active avoidance reflexes also were formed in these animals after the third day of their stay in the new situation.

## EXPERIMENTAL RESULTS

A change in the ordinary living environment has a significant effect on avoidance conditioning in the rats (Table 1). CAAR formation was readily achieved during 60 combinations in

Laboratory of Pathophysiology, Institute of Physiology and Experimental Pathology of High Altitudes, Academy of Sciences of the Kirghiz SSR, Frunze. (Presented by Academician of the Academy of Medical Sciences of the USSR G. N. Kryzhanovskii.) Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 103, No. 5, pp. 524-526, May, 1987. Original article submitted May 21, 1986.

 0007-4888/87/0005- 0592$12.50 

TABLE 1. Effect of Adaptation to Mountain Climate on Number of CAAR in Rats (M ± m)

| Group of animals | Experimental conditions | Number of animals | Total number of combinations of conditioned and unconditioned stimuli | | | | |
|---|---|---|---|---|---|---|---|
| | | | 60 | 120 | 180 | 240 | 300 |
| 1 | Foothills, (control) | 15 | 9,7±3,5 | 13,7±2,7 | 34,5±4,6 | 41,7±2,3 | 60,3±2,1 |
| 2 | Foothills, unadapted rats | 14 | 3,2±0,6 | 44,2±10,1* | 57,7±9** | 49,5±3 | 62,2±3,8*** |
| 3 | Foothills, adapted rats | 14 | 6,2±1,5 | 33,7±3,5* | 46,5±1,8*** | 89,5±9,5** | 137,4±8,4** |
| 4 | Plains | 15 | 6,5±1,4 | 50,7±6,7* | 49,5±2,5*** | 68,5±4,3** | 93±7* |

Legend. Number of CARR formed in all experimental rats is shown. Here and in Table 2: *p < 0.01, **p < 0.001, ***p < 0.05.

TABLE 2. Effect of EPS on Maintenance of CAAR under Foothill and Mountain Conditions (M ± m)

| Group of animals | Experimental conditions | $N_1$ | $N_1'$ | $N_{1,3}$ | $N'_{1,3}$ | | |
|---|---|---|---|---|---|---|---|
| | | | | | one session of EPS | two sessions of EPS | three sessions of EPS |
| 1 | Foothills (control) | 7,5±0,2 (6) | 3±0,7* | 6,2±0,2** (5) | 4,1±0,8*** (5) | 2,4±0,6** (5) | 1,7±0,4** (5) |
| 2 | Foothills, unadapted rats | 9,2±1,6 (5) | 3,3±1,2* | 9,2±1,6 (5) | 0 (5) | 0 (5) | 0 (5) |
| 3 | Foothills, adapted rats | 11,8±1,4 (5) | 2,7±1,4* | 13,4±0,8 (5) | 11,5**** | 6,5**** | 0 |
| 4 | Plains | 10±1,6 (5) | 5,7±1,7* | 12,6±1,2 (5) | 6,2±2,6* | 5,5±1,4* | 4±1,7* |

Legend. $N_1$ and $N_{1,3}$) Initial number of CARR before single and multiple exposure to stress, respectively; $N_1'$, $_3$) number number of CAAR realized after single and multiple exposure to stress, respectively. Number of experiments shown in parentheses. ****) Failure of all CAAR in 3 animals.

rats whose living environment was appropriate and constant (group 1.) In rats unadapted to their new conditions of life (group 2) the number of CAAR was less. When the "emergency stage" (the 11th day) of adaptation had ended [1], better parameters of avoidance conditioning were observed (after 120 combinations) in the "newcomers" (group 2) and in the strictly lowland (group 4) rats (Table 1). Previously adapted animals (group 2) occupied an intermediate position as regards the number of CAAR.

Combinations of the conditioned and unconditioned stimuli up to 240 times coincided with the beginning of formation of long-term adaptation in the animals of groups 2 and 4. During this period the number of CARR in rats of group 2 was the same as in the control, whereas in the rats of group 4 the number of CAAR was 1.5 times greater than normal foothill values. Rats of group 3, in which the stage of adaptation had already been completed (53rd day) were characterized by a larger number of CAAR than the normal foothill value and by incomplete adaptation (group 2). The rats of group 3 toward the end of training (after 300 combinations), occupied the first place as regards the number of fixed conditioned reflexes compared with animals of the other groups. In rats from the plains adapted in stages to foothill and mountain conditions, the number of CAAR was greater than in those left in the foothils and in those not previously adapted to mountain conditions.

After the effect of adaptation to mountain conditions on avoidance conditioning has been studied, the effect of exposure to EPS on this parameter was investigated. Experiments showed that the number of CAAR in foothill rats was reduced by half after a single exposure to EPS, and was reduced by more than two-thirds after three exposures (Table 2). In rats of group 2 a single exposure to EPS caused a reduction by two-thirds in the number of CARR, whereas three exposures caused total failure of all conditioned reflexes after each session. The previously adapted rats of group 3, which had the largest number of CAAR in the initial state, preserved one-quarter of them after the first sessions of EPS. After multiple exposure to stress the initial number of CAAR was found in most rats after the first and second sessions, but total absence of CAAR was oberved in all rats after the 3rd session of EPs. Clearly the outcome was

unfavorable — EPS had an inhibitory effect on all conditioned avoidance reflexes, although in the animals of group 2 complete absence of CAAR was observed in all three sessions of EPS (Table 2). Better parameters of conditioned reflexes (their formation and preservation of EPS) were obtained with the lowland rats of group 4 after a single exposure to EPS. Activation of LPO is known to inhibit conditioned reflex formation [6]. Adaptation to an altitude of 1600 m itself follows a stress-like course [10] and initiates moderate activation of LPO by the 30th-40th day of adaptation [2]. In this respect rats adapted in stages to foothill and mountain conditions (groups 4 and 3) were in an advantageous position, for they had sufficient time (50-60 days) for stabilization of the system regulating LPO activity to occur [8]. During this time, LPO products are evidently detoxicated by enzymic (activation of superoxide dismutase and catalase) and nonenzymic (an increase in the concentration of reduced glutathione) mechanisms [9]. Adaptive strengthening of the antioxidant system under mountain climatic conditions is evidently equivalent to the action of exogenous antioxidants, inhibiting the intensification of free-radical reactions in the brain during stress [7]. Prevention of LPO activation on account of a higher level of the antioxidant system evidently lies at the basis of the better state of preservation of CAAR after single and triple exposure to EPS in rats adapted in stages to foothill and mountain conditions and to mountain conditions only.

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