EFFECT OF ADAPTATION TO HIGH-ALTITUDE HYPOXIA IN EARLY ONTOGENY ON HIGHER NERVOUS ACTIVITY

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UDC 612.825.1-06:612.275.1.017.2-053.3

Newborn male and female Wistar rats were adapted to hypoxia in a pressure chamber. Adaptation began at an "altitude" of 1000 m for 1 h daily, after which the duration and intensity of exposure were gradually increased so that, starting from the 17th day, the animals were adapted to an altitude of 5000 m for 5 h on 5 days a week. After adaptation for two months, a conditioned active avoidance reflex was produced in the animals. In the adapted males a tendency was observed for the reflex to be formed more rapidly and for it to be preserved to a much greater degree than in the control animals. In females adapted to hypoxia under similar conditions no changes were observed in the formation and preservation of the reflex.

KEY WORDS: *Adaptation; hypoxia; conditioned reflexes.*

A fall in the DNA concentration and, consequently, a decrease in the number of cells in the cerebral cortex and hypothalamus [8], have been observed in rats born and reared at an altitude of 3800 m. These findings were confirmed in investigations by other workers [6] and they led some writers [7] to postulate that associative activity in animals reared at a high altitude is comparatively limited. Meanwhile, during adaptation of adult animals to periodic hypoxia in a pressure chamber, RNA and protein synthesis in neurons and glia of the cortex and other parts of the brain is activated [2, 4], and this is accompanied by an increase in the degree of preservation of conditioned reflexes, the more rapid transition from short-term to long-term memory [1], and advantageous changes in the animals' behavior in situations of conflict [5].

It seemed likely that by the use of periodic hypoxia of gradually increasing intensity, even in the early stage of ontogeny when the brain is particularly susceptible to oxygen lack, adaptation accompanied by positive changes in conditioned-reflex activity could be observed.

EXPERIMENTAL METHOD

On the second to third day after birth 30 male and female Wistar rats were placed together with their mothers in a pressure chamber and kept there for 1 h at an "altitude" of 1000 m. During the next 16 days the "altitude" and length of stay of the animals in the pressure chamber were gradually increased, and on the 17th day the rats were kept at an "altitude" of 5000 m for 5 h. Later adaptation was carried out at an "altitude" of 5000 m for 5 h daily 5 days a week for six weeks. The total duration of adaptation was thus 2 months. One month after the beginning of the experiment the males and females were separated and the mother rats removed. Male and female rats born at the same time as the experimental animals and kept in the same animal house, but not subjected to adaptation, were used as the control. The experimental animals did not differ from the control in body weight.

Laboratory of Pathophysiology of the Heart, Institute of General Pathology and Pathophysiology, Academy of Medical Sciences of the USSR, Moscow. (Presented by Academician of the Academy of Medical Sciences of the USSR A. M. Chernukh.) Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 82, No. 8, pp. 902-903, August, 1976. Original article submitted January 16, 1976.

TABLE 1. Effect of Early Adaptation to "High-Altitude" Hypoxia on Formation and Preservation of CAAR

Animals	No. of combinations required for CAAR formation	No. of combinations required for forming CAAR again 24 h later
Males:		
control (n=12)	17,7±3,44	5,5±1,94
experiment (n=12)	12,1±1,00	0,5±0,18
P	>0,05	<0,001
Females:		
control (n=14)	17,9±2,23	7,2±1,90
experiment n=12)	19,7±2,97	5,3±1,36
P	>0,05	>0,05

On the third to fourth day after the end of adaptation to hypoxia the rate of formation and degree of preservation of the defensive conditioned active avoidance reflex (CAAR) were studied in the animals.

To form the CAAR the rats were placed in the initial part of a T-shaped maze, the light was switched on in one passage of the maze and, 5 sec later, a current of 40 V was passed through the floor of the maze. The action of the current was stopped as soon as the animal had run into the illuminated part of the maze; the left and right passages of the maze were illuminated in random order in accordance with Hellerman's table. The criterion of CAAR formation under these conditions was five correct runs in response to five presentations of the photic stimulus. Preservation of the reflex was tested after 24 h.

EXPERIMENTAL RESULTS AND DISCUSSION

The experimental results (Table 1) indicate that in male rats adapted to "high-altitude" hypoxia there was a tendency for the more rapid formation of CAAR. Meanwhile the level of preservation of this reflex in the adapted males was sharply increased. To form the CAAR the second time to the level of the criterion specified in the control animals a mean of 5.5 combinations was necessary, compared with only 0.5 in the adapted rats; the conditioned reflex was virtually reproduced at once. The index of preservation of the formed CAAR, equal to the ratio (in %) of the difference between the number of combinations necessary for the first and second formation of the reflex to the number of combinations required to form the reflex initially, was 68% in the control animals and 95% in the adapted rats. The degree of "forgetting" of the temporary connection during the 24 h after formation of the reflex was 32% control rats but only 5%, i.e., 6 times less, in the adapted rats. These results are in good agreement with the activation of nucleic acid and protein synthesis in the brain during adaptation to high-altitude hypoxia, for in the modern view such synthesis plays a decisive role in the consolidation or fixation of temporary connections responsible for preservation of conditioned reflexes [3, 5].

In the adapted female rats, unlike in the males, no changes were observed in the formation or preservation of conditioned reflexes. This absence of "adaptation benefits" in the females was also found by the writers in connection with the contractile function of the heart: The maximal strength of contractions of the myocardium of the right ventricle and its resistance to prolonged overloading increased in adapted males but was indistinguishable from the control in females. This difference may perhaps be connected with the greater inhibition of secretions of anabolic sex hormones in females than in males under the influence of hypoxia.

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THALAMIC INHIBITION OF LOCOMOTION INDUCED BY MESENCEPHALIC STIMULATION

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UDC 612.76-06-[612.826.4+612.826.5

By stimulation of a region of the thalamus with its center corresponding to Horsley–Clarke coordinates A7, L2, H2, locomotion of the lightly anesthetized cat with an intact brain can be inhibited, whether evoked by stimulation of the subthalamic or of the mesencephalic "locomotor" region.

KEY WORDS: *locomotion; mesencephalon; thalamus.*

In the intact, lightly anesthetized cat locomotion can be induced by stimulation of certain "locomotor" regions of the subthalamus (LRS) [3] or mesencephalon (LRM) [2]. Locomotion evoked by stimulation of LRS can be inhibited by stimulation of nonspecific nuclei of the thalamus (T) [4].

The object of this investigation was to discover whether locomotion evoked from LRM can be suppressed by thalamic stimulation. This problem could not be solved previously because the mechanisms of thalamic inhibition of locomotion evoked from LRS are unknown and the role of LRS in the control of locomotion differs from that of LRM [1, 2, 3].

EXPERIMENTAL METHOD

The cat was anesthetized (with ether in seven, pentobarbital in five experiments) and its head fixed in a stereotaxic apparatus. The animal's limbs were placed on the belt of a treadmill [3]. The dorsal surface of the skull was exposed and two holes drilled in it through which, after incision of the dura, electrodes were inserted into T (Horsley–Clarke coordinates A7, L2, H2), into LRM (P2, L4, HO), and LRS (A8, L2.5, H3) (the centers of the corresponding regions are indicated). In ten experiments electrodes were inserted into all three regions, in two experiments into T and into LRM only. The electrode was inserted perpendicularly into T, but anteriorly at an angle of 40° into LRM in order to avoid the tentorium cerebelli [2, 6]. The electrode was inserted into LRS anteriorly at an angle of 15°. All electrodes were located ipsilaterally. Each electrode consisted of tungsten wire 20 μ in diameter with glass insulation.

Monopolar stimulation with square pulses of negative polarity was used. The duration of each stimulus was 0.5 msec and their frequency 40-80/sec. To evoke locomotion a current (usually 30-100 μA for LRM and 50-150 μA for LRS) inducing walking or slow trotting was applied, and for thalamic stimulation a maximal current (usually 150-250 μA) too low to induce motor responses in the resting animal was used.

Laboratory of Physiology of Movements, Institute for Problems in Information Transmission, Academy of Sciences of the USSR, Moscow. (Presented by Academician V. N. Chernigovskii.) Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 82, No. 8, pp. 903-906, August, 1976. Original article submitted January 30, 1976.