Blood Corticosterone and Resistance to Hypoxia during Operant Conditioning and Development of Learned Helplessness

A. V. Toloknov, O. V. Vvedenskaya, T. D. Bol'shakova, A. F. Bunyatyan, N. K. Khitrov, and V. P. Fisenko

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Operant conditioning under conditions of uncertain behavioral environment was accompanied by a significant elevation of blood corticosterone, high exploratory activity, and increased resistance to hypoxia. The blood content of corticosterone and exploratory activity significantly decreased in rats developing learned helplessness, but their resistance to hypoxia increased in comparison with that during learning.

Key Words: *learning; learned helplessness; corticosterone; resistance to hypoxia*

Under conditions of environmental uncertainty [5] the process of learning is attended by high emotional strain and intense exploratory activity [10,12]. Increasing uncertainty about the environment and, therefore, increasing difficulty in escaping negative experience, e. g. pain, intensifies emotional state of anxiety (EAS) and can result in the development of a neurotic state of learned helplessness (LH). LH is characterized by low exploratory activity, non-responsiveness to conditioned and unconditioned stimuli, including nociceptive, and autonomic and trophic disorders [5,11]. ESA is considered as an essential component of learning; its attenuation by anxiolytics can impair learning and stimulate the development of LH [7]. LH is a form of higher nervous activity disturbance; isolation from stress stimuli reduces energy expenditure and promotes functional recovery of brain neurons [9].

Stress is accompanied by an increased production of glucocorticosteroids and blood content of glucocorticosteroids can serve as a measure of general strain. The high activity of brain neurons requires a high energy expenditure, while non-responsiveness (anesthesia, craniohypothermia, torpid stage of shock) reduces oxygen and energy demands [9]. In this connection we analyzed the level of blood corticosterone and resistance to severe hypoxia in rats during efficient learning and the development of LH under conditions of high environmental uncertainty.

I. M. Sechenov Moscow Medical Academy, Moscow

MATERIALS AND METHODS

Experiments were carried out on outbred male albino rats weighing 250-300 g. Animals were trained bar-pressing to avoid electric stimulation of paws through the grid floor after presentation of a conditioned light stimulus [5]. The probability of occasional performance was low and unfavorable for learning, which increased the level of environmental uncertainty [5].

To assess the dynamics of exploratory activity (EA), the time of conditioning was divided into 5 equal periods and the number of operant reactions per cycle for each period was determined. Thus, EA was measured by the number of operant reactions per cycle (the time of conditioned stimulation and interstimulus interval).

In group 1 (control), blood corticosterone was measured on day 1 immediately before training, in group 2 — immediately after the first session of training; in group 3 — before the last session; in group 4 — immediately after training in conditioned

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rats; in group 5 — after the final session of training in rats with LH. Blood was taken from the caudal vein, the content of corticosterone was determined by radiometry without extraction using transcortine as a competitive ligand [1]. Resistance to hypoxia was assessed after "lifting" to an altitude of 10,000 m for 12 min in a Komovski apparatus. The time after the start of "ascent" to the appearance of periodic breathing and the time of respiratory arrest were measured. The resistance to hypoxia was tested 24 h after the final session of training. The learning was considered to be successful if the number of correct responses to conditioned stimuli significantly exceeded the *a priori* level of their occasional performance [3].

RESULTS

The first session of operant conditioning induced a pronounced stress-response: the plasma content of corticosterone 7-fold surpassed the control (Fig. 1) probably due to initially high environmental uncertainty (2-sec interval between the conditioned stimuli), which in combination with frequent electroshocks led to the development of a conflict situation: the animal was unable to avoid painful stimuli and to establish association between the conditioned stimulus and negative reinforcement. After acquisition of the conditioned reflex (approximately after 3-5 days of training) the content of corticosterone decreased compared to the first session but 3-fold surpassed the initial level (group 3). At the same time, at a given probability of stochastic correct responses some animals were unable to learn [5]. Some rats pressed the lever without conditioned stimuli less frequently than others. They also showed general hypokinesia, decreased EA, hypothermia, loss of body weight, trophic skin lesions, and other signs of neurosis typical of LH [11]. After the final training session (after 5-8 days) the blood content of corticosterone in these animals, although exceeding the initial value, was significantly lower than in successful learners.

In successfully trained rats, the resistance to acute hypoxia was significantly higher than in controls (Fig. 2): periodic breathing and respiratory arrest occurred by 15 and 13% later, respectively, than in the control group. In rats with LH these indices were higher than in successfully trained and significantly higher than in controls.

We showed that animals with LH exhibited significantly lower EA than conditioned rats (Fig. 3), especially in the initial (*I* and *II*) and final (*V*) periods of learning. Earlier, EA dependence on the intensity of conditioned stimulus and probability of reinforcement was shown [6]. Under conditions of high environmental uncertainty, a decrease in the reinforce-

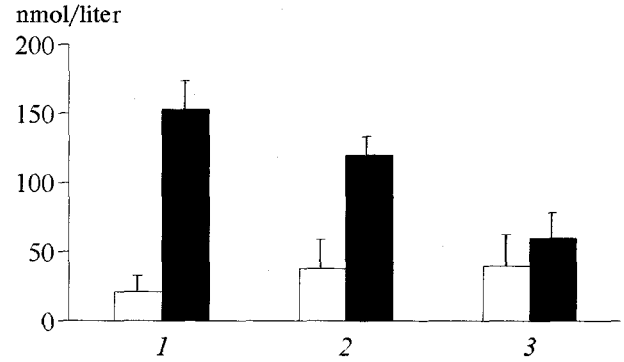

Fig. 1. Plasma concentration of corticosterone during learning and development of learned helplessness in rats. *1)* first session; *2)* final session of conditioning; *3)* final session of conditioning (development of learned helplessness). Open and filled bars correspond to corticosterone concentration in the control and after conditioning, respectively.

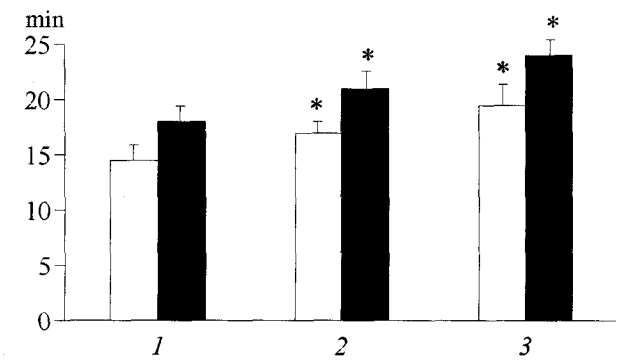

Fig. 2. Resistance to acute hypoxia in rats after conditioning and development of learned helplessness. *1)* control; *2)* resistance to hypoxia in conditioned rats; *3)* resistance to hypoxia in rats with learned helplessness. Open bars correspond to onset of periodic breathing occurrence, filled bars are the time of respiratory arrest. Ordinate: time after the start of "ascent". *$p<0.05$ in comparison with the control.

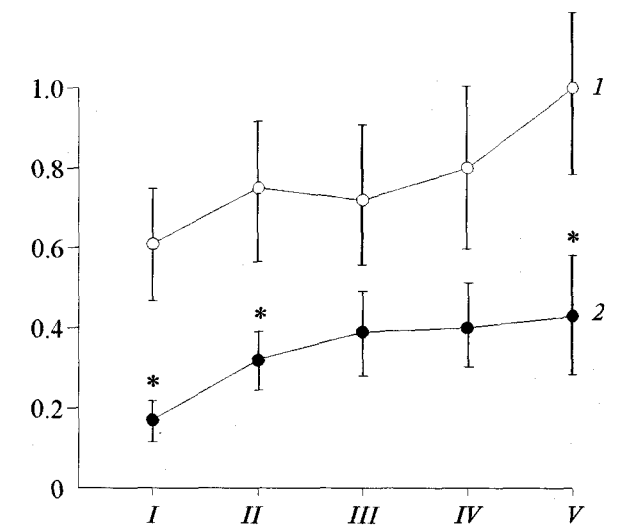

Fig. 3. Exploratory activity in rats with conditioned reflex (*1*) and learned helplessness (*2*) in different periods of learning (*I-V*). Ordinate: number of operant reactions per cycle. *$p<0.05$ in comparison with the conditioned rats.

ment probability from 100 to 25% inhibited EA [4], while weakening of the conditioned stimulus enhanced it [6].

Under conditions of considerable environmental uncertainty EA seems to depend on many factors differently modulating the level of anxiety. As shown previously, both attenuation of anxiety induced by anxiolytic buspirone [7] and its strengthening by the low probability of reinforcement, suppressed EA and impairs learning. It is likely that an optimal level of anxiety and appropriate EA are necessary for effective learning. An excessive stress in the initial period of learning and early exhaustion of stress-realizing systems or early activation of stress-limiting systems can contribute to learning disturbances and the development of LH. This conclusion is based on the fact that in animals with LH, the non-responsiveness to different stimuli and reduced EA manifested themselves against the background of a 2-fold lower corticosterone concentration in comparison with conditioned rats with high orienting and exploratory activities. With respect to the resistance to severe hypoxia LH did not differ from other states with minimal activity of central neurons. It can be suggested that animals are unable to actively adapt to an environment with high uncertainty of vital stimuli. When stress-realizing mechanisms are exhausted, these animals adapt passively by isolation from different stimuli. This strategy reduces energy expenditure and increases the resistance to stress. General hypokinesia and hypothermia accompanying LH contribute to the development of such resistance.

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