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EFFECT OF THE ANTIOXIDANT IONOL ON FORMATION AND PERSISTENCE OF A DEFENSIVE CONDITIONED REFLEX DURING PEAK EXERCISE

F. Z. Meerson, V. M. Boev, and R. I. Kruglikov

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KEY WORDS: conditioned reflex; peak exercise; antioxidant ionol.

During exposure to extremal environmental factors, including peak exercise, changes take place in the formation, fixation, and recall of temporary connections in untrained animals [1]. It has also been shown that exposure to stress and unusually heavy exercise cause activation of lipid peroxidation (LPO) [3], especially in the brain [2]. It can accordingly be postulated that activation of LPO in the brain is one cause of the disturbance of higher nervous activity during peak exercise and that, correspondingly, administration of inhibitors of LPO (antioxidants) before loading might prevent these disturbances.

To test this hypothesis, the effect of preliminary injection of the LPO inhibitor ionol on the disturbance of formation and preservation of conditioned bilateral avoidance reflexes (BCAR), which usually appear under the influence of peak loading (up to the limit), was studied in the investigation described below.

EXPERIMENTAL METHOD

Experiments were carried out on 120 male Wistar rats weighing about 200 g. In the experiments of series I the animals were divided into four groups: 1) control, 2) daily intraperitoneal injection of ionol in a dose of 20 mg/kg for 3 days, 3) a single session of peak exercise consisting of running on a treadmill at a speed of 16 m/min "to the limit," 4) administration of ionol in the dose indicated above, followed by the same exercise. A defensive BCAR was formed in all the animals in a shuttle box. The conditioned stimulus consisted of a flashing light and after it had acted for 5 min an electric current was applied through the floor of the box. The intervals between combinations measured 0.5-1.5 min. In the first and second training sessions, the interval between which was 7 days, the animals were given

Institute of General Pathology and Pathological Physiology, Academy of Medical Sciences of the USSR, Moscow. Orenburg Medical Institute. Institute of Higher Nervous Activity and Neurophysiology, Academy of Sciences of the USSR, Moscow. (Presented by Academician of the Academy of Medical Sciences of the USSR P. D. Gorizontov.) Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 96, No. 9, pp. 70-71, September, 1983. Original article submitted December 22, 1982.

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TABLE 1. Effect of Ionol on Formation and Preservation of BCAR during Peak Exercise (M ± m)

Conditions of testing	Number of conditioned avoidance responses	
	during first 50 combinations	during second 50 combinations 7 days later
Control (n = 19)	5,63±0,92	18,55±2,00
Ionol (n = 29)	6,33±1,30	20,22±3,30
Peak exercise before training (n = 25)	0,93±0,10*	7,10±1,00*
Ionol + peak exercise (n = 20)	2,00±0,32†	14,92±2,70 †

Legend. *P < 0.01 compared with control, †P < 0.01 compared with peak exercise. n) Number of animals.

TABLE 2. Effect of Ionol on Formation and Recall of Temporary Connections during Peak Exercise (M ± m)

Conditions of testing	Number of conditioned avoidance responses	
	during first 50 combinations	during second 50 combinations 7 days later
Ionol (n = 29)	6,33±1,30	20,22±3,30
Peak exercise after training (n = 15)	5,40±0,77	9,62±1,46
Ionol + peak exercise after training (n = 12)	5,00±0,54	19,10±2,63*

Legend. *P < 0.01 compared with peak exercise. n) Number of animals.

50 combinations of flashes and electric shocks, and the number of avoidances and the number of escapes were recorded. The number of avoidances during the first training session and its increase during a repeat session served as the index of formation and preservation of BCAR. In the animals of groups 3 and 4, BCAR was formed 10 min after the end of exercise.

In series II there were also four groups of animals but the experimental situation differed in that the conditioned reflex was formed in the animals of groups 3 and 4 at the beginning, and peak exercise was undertaken after the end of conditioning. Preservation of BCAR was tested at the same times.

EXPERIMENTAL RESULTS

BCAR after peak exercise was found to be almost impossible to achieve by animals not receiving the antioxidant (Table 1). Moreover, on reconditioning 7 days later the animals of this group gave 7.10 ± 1.00 avoidance responses, i.e., almost as many as by the control animals in the first experimental session. Consequently, in animals not receiving ionol, repetition of conditioned reflex formation after peak exercise essentially constituted the formation of these reflexes afresh. Meanwhile in animals receiving the antioxidant before, 2.00 ± 0.32 conditioned avoidance reactions were observed in the original experiment, i.e., twice as many as in animals not protected by ionol. Testing preservation showed that the number of conditioned avoidance responses was 14.92 ± 2.70.

Preliminary injection of ionol thus prevented considerable disturbances of formation and recall of the conditioned reflex usually observed under the influence of exercise. In these experiments the LPO inhibitor could prevent disturbances of the formation, retention, or recall of the temporary connection equally.

To assess separately the protective effect of ionol on fixation and recall of the temporary connection, in the second series of experiments peak exertion by animals not protected

or protected with ionol was given after conditioning. Retention of BCAR also was tested after 7 days.

The results show that peak exercise, used after direct and successful conditioning of animals not receiving ionol reduced the degree of retention of the reflex by half, whereas in animals protected by the antioxidant, no such disturbance was observed (Table 2). Since the tests were carried out 7 days after exercise it is unlikely that the exercise could have disturbed recall processes. It can accordingly be postulated that the peak exercise "to the limit" disturbs fixation of the temporary connection and that ionol prevents such disturbance. This result is in agreement with the view that activation of LPO does in fact play a role in the disturbances of higher nervous activity associated with peak exercise and it opens up the prospects for prevention of such disturbances by antioxidants.

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DISTURBANCES OF THE SUPPLY OF HIGH-ENERGY COMPOUNDS TO THE BRAIN IN CHRONIC STRESS AND THEIR CORRECTION BY PSYCHOTROPIC DRUGS

V. I. Kresyun

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KEY WORDS: stress; psychotropic drugs; high-energy compounds; brain.

Psychoemotional stress is a basic component of unfavorable situations affecting man. Besides the widely known changes, stress also causes marked disturbances of metabolism of the brain [1, 4, 12], principally its energy metabolism [3, 5]. Correction of emotional stress includes action directed toward many links of the pathogenetic chain of development of stress reactions. A leading place among the pharmacologic agents which regulate the course of stress reactions is occupied by psychotropic drugs, specifically by tranquilizers. However, the molecular mechanisms of the protective effect of tranquilizers in stress have not been adequately studied. There are no clear ideas on the ways of realization of their pharmacologic effects.

The object of this investigation was to study the effect of tranquilizers, derivatives of different chemical groups, on the content of high-energy compounds in the brain structures of animals exposed to chronic stress.

EXPERIMENTAL METHOD

Experiments were carried out on 987 male Wistar rats weighing 220-250 g. Chronic emotional stress was produced in the form of a so-called anxiety neurosis [10] in the writer's modification, consisting of prolonged (2 h daily for 12 days) exposure of the hungry animals (deprived of food for 12 h) to the stressor, and also random alternation of a conflict situation with immobilization of the animals and electrodermal stimulation. The stress-producing action could be intensified by placing the animals in pairs in special transparent cages. Only animals with high and average levels of emotional response on preliminary testing were chosen for the experiment [11]. In this way it was possible to obtain stable changes in the biochemical parameters of the brain corresponding to the level of transition of the stage of stress from the state of compensation to one of decompensation or an excessively catabolic

Department of Pharmacology, N. I. Pirogov Odessa Medical Institute.

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