Effect of Tactivin on Functional Disturbances in Avoidance Reaction in Rats

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Translated from *Byulleten' Eksperimental'noi Biologii i Meditsiny*, Vol. 147, No. 1, pp. 75-77, January, 2009
Original article submitted July 10, 2008

Experiments on outbred albino rats showed that tactivin (thymic polypeptide preparation) reduced functional disturbances in active avoidance reaction induced by extra electric current exposure violating the established relationships between the stimuli, reaction, and its result. The preparation provided high level of avoidance reaction after its violation. New effects of immunocorrective agent tactivin were detected. It not only restored the disordered immunological parameters, but also exhibited a pronounced effect on the higher integrative functions of the brain and produced an antistress effect.

Key Words: *tactivin; avoidance reaction; dysfunction; stress*

Numerous data accumulated by today indicate a close relationship between the immune and nervous systems. The effect of the CNS on activity of the immune system through the hypothalamic-pituitary-adrenal structures and the autonomic nervous system work are no longer doubted [1,2,6,9]. Recent data suggest that the immune system can modulate the function of CNS, *e.g.* modulation of the orientation and exploratory behavior of animals by immunocompetent cells [8]. The relationship between these systems is the most demonstrative during stress. According to the theory of the adaptation syndrome, the main shifts in the hemostasis-regulating systems appear mainly in the pituitary, adrenals, and thymus. Despite the data indicating that the thymus does react to stress, the effects of thymic hormones and polypeptides on the development of this condition are virtually not studied.

Importantly, mental stress in humans develops not so much as a result of physical exposure, but mainly because of the information (signal) significance of this exposure, essential for the vital needs, which was validated by many authors from different viewpoints [5,11]. The model of sudden violation of the relationships between the stimuli, reaction and its results established in animal individual experience and reflecting the regularities objectively existing in the experimental environment, is interesting in this respect. The importance of this model is explained by the fact that sudden modification of the habitation conditions is stressogenic and causes mobilization of energy resources for adaptation to the changing environment. A reversible dysfunction of the active avoidance conditioned reaction (CAAR) in rats, induced by modification of unambiguous cause-and-effect relationships ("violation of avoidance reaction") [7], can serve as the exposure of this kind. The model causes an experimental mental stress and reversible disorders in the previously developed habit.

We studied the effect of tactivin, a thymus preparation well studied in immunology [4], on the development of mental stress in rats, caused by sudden violation of the experiment conditions.

MATERIALS AND METHODS

A series of experiments was carried out on 12 outbred male rats (140-240 g; 6 experimental and 6

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0007-4888/09/1471-0070

control ones). The animals were kept in a vivarium under conditions of 12:12 h light:darkness regimen with free access to water and food. Three days before the start of avoidance conditioning, the experimental animals were intraperitoneally injected with tactivin (100 μg dissolved in 0.5 ml saline); controls were injected with an equivalent volume of saline. The injections were continued (saline every 48 h) after training began. Conditioned active avoidance reaction (CAAR) was developed in a "shuttle" box for 5-7 days (20 presentations daily) [7]. The sound served as the conditioned stimulus, electric current switched on 10 sec later was the unconditioned stimulus. When a rat passed into the other half of the cage, both stimuli were switched off. On days 5-7 (depending on the day when 80% avoidance reaction was attained), CAAR violation was carried out [7]: animal reaction to the stimuli did not lead to their discontinuation, and the animals received electric stimulation after 5 passages to the other half of the cage. This was followed by testing of CAAR level (20 presentations) under previous conditions. The results were processed using Mann—Whitney test.

RESULTS

The results indicate a positive effect of tactivin on CAAR formation: experimental animals reached 80% performance by day 5 *vs.* days 6-7 in the control group. Our results are in line with the previous data indicating that tactivin stimulated CAAR formation in the shuttle box [3].

Violation caused failure of the habit during the first 5 presentations in all control animals: the number of avoidance reactions decreased 1.5 times, while the number of intersignal reactions (IR) increased 4.6 times, this indicating augmenting emotional tension and development of mental stress in the animals (Fig. 1) [7,10]. In the tactivin group, only 1 animal exhibited failure of avoidance reaction during the first 5 presentations of the conditioned signal, while in 5 rats the functional disturbance of the habit was prevented. The number of avoidance reactions was significantly higher in experimental animals compared to controls. It is noteworthy that the level of CAAR was not only restored after violation, but surpassed the level of initial training in all animals (Fig. 1). Hence, tactivin prevented the aftereffects of violation by inhibiting the drop in the level of the avoidance reaction reproduction.

The number of IR also increased, but to a lesser extent than in the control (only 1.8 times). It is known that stress inhibits problem solution, and its

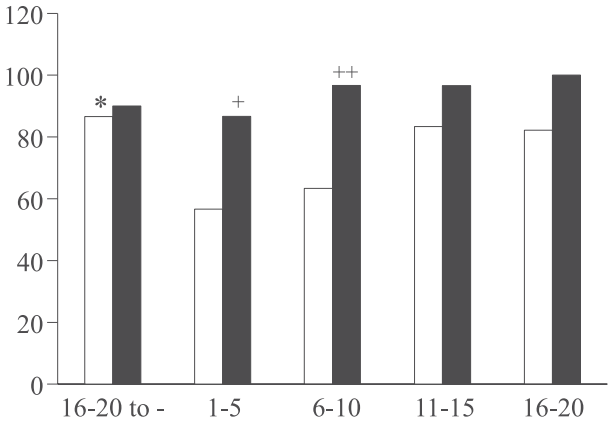

Fig. 1. Effect of tactivin on CAAR failure. Abscissa: blocks of 5 presentations before (block 16-20) and after violation. Arrow shows the moment of violation. Ordinate: number of CAAR, % of presentations. Light bars: control; dark bars: tactivin. $^{*}p<0.05$ compare to the parameter in block 1-5 after violation in the control group; $^{+}p<0.05$, $^{++}p<0.01$ compare to the control.

attenuation cancels this effect. On the other hand, problem solution is also essential for emotional tension and leads to alleviation of stress. Since emotion is the function of requirement and difference between the levels of information which is available and that essential for problem solution [11], emotional strain can be relieved by improving the information on the probable problem solution (meeting the requirement) by activation of the integrative functions of CNS. In addition, emotions and motor activation, manifesting by an increase in the RBS number, reflect the adaptive processes, associated with mobilization of physical potential in situations threatening for the integrity of the organism and with search for a new solution under new conditions, when the previous knowledge is no longer effective [11]. Without inhibiting the above adaptive processes, tactivin prevents their excessive manifestation.

Hence, the results indicate a pronounced effect of tactivin on the higher integrative functions of the brain. The drug attenuates emotional strain and improves adaptation under stressogenic conditions in the rats, which reflects the antistress effect of the drug.

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