PHARMACOLOGY AND TOXICOLOGY

Effect of Thymoptin on the Behavior of Experimental Animals

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A study is made of the effect of thymoptin, a preparation containing a complex of acid peptides from the thymus, on the behavior of experimental animals. It is found that in a dose of 400 μg/kg the preparation enhances motor activity, raises the body temperature, augments pain sensitivity, stimulates behavior in the open field test, and facilitates learning and memory processes.

Key Words: *thymoptin; thymic hormones; passive avoidance response; behavior*

Recent years have seen a steady increase in our knowledge about the functional role of the thymus in the organism. Some thymic factors have been found to participate in the regulation of neuroendocrine processes [7,8] and to modulate the functions of the central nervous system [1,4]. However, the effect of the thymus and thymic hormones on behavior remains poorly understood.

Our aim was to investigate the effect of thymoptin, a preparation containing a complex of acid peptides from the thymus including the hormone thymosin-α_1, on behavioral reactions of experimental animals.

MATERIALS AND METHODS

The experiments were carried out on outbred male mice weighing 20-22 g and male rats weighing 200-250 g. The animals were maintained in cages of standard size (2145 cm^2) at 21-22°C and the standard 12-h illumination regime with food and water *ad libitum*. The thymoptin used in the experiments represented a complex of acid peptides (1000-15,000 D) with an isoelectric point ranging from 3.5 to 4.5 and containing up to 2% thymosin-α_1 (Moscow Endocrine Plant). The control and experimental groups each comprised 10-20 animals. The preparation was injected intraperito-

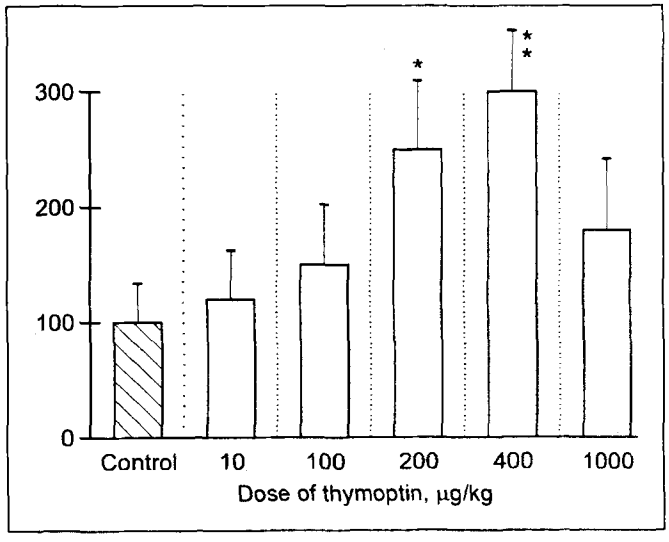

Fig. 1. Effect of thymoptin on motor activity in mice. Ordinate: number of movements, % of control, Here and in Figs. 2 and 3: *$p<0.05$, **$p<0.01$ in comparison with the control.

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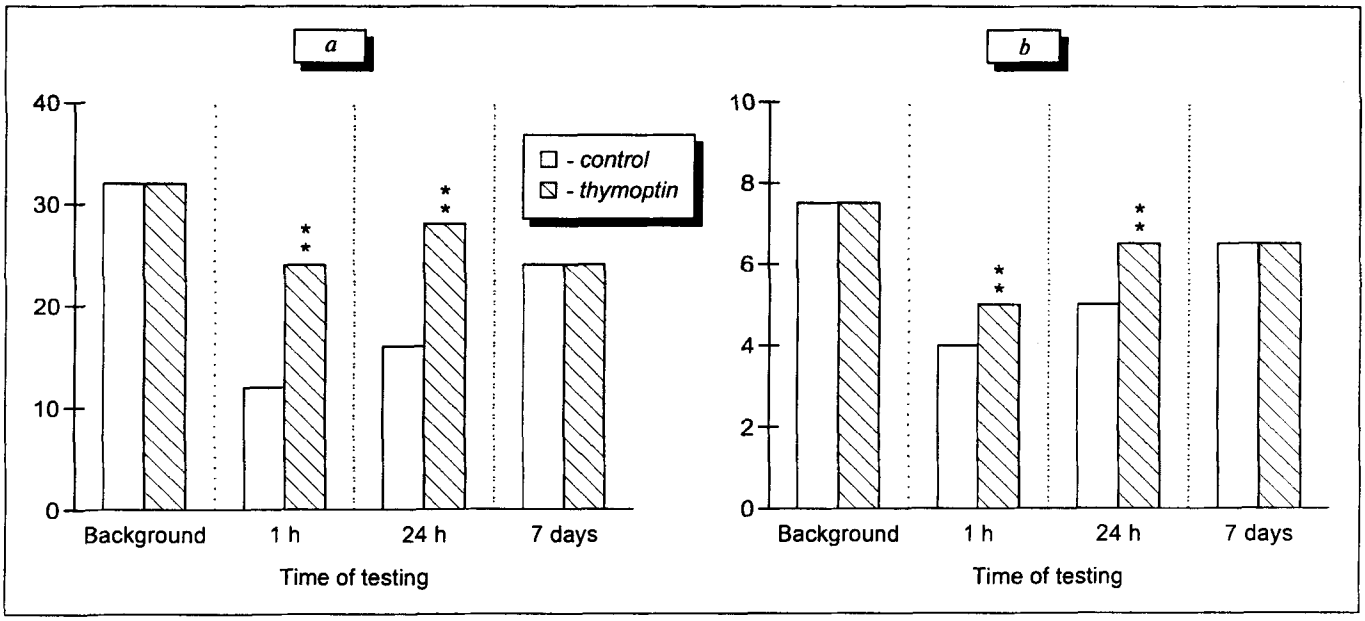

Fig. 2. Effect of thymoptin (400 μg/kg) on rat behavior in the open field test: changes in motor (*a*) and exploratory (*b*) activity. *a*) ambulation; *b*) rearing.

neally in 0.5 ml physiological saline 1 hour prior to the experiment.

In mice we assessed the effects of thymoptin on motor activity, body temperature, and pain sensitivity, and the effects of Nembutal. The possible antidepressant activity of the preparation was studied in the "behavioral despair" test. In rats the effect of thymoptin on orienting and motor responses (OMR) and on the passive avoidance response (PAR) was evaluated.

The effect of thymoptin in doses of 10, 100, 200, 400, and 1000 μg/kg on motor activity was assessed on a DAER-20 recorder (Russia) by counting the number of movements during a 10-min test. These data were used for choosing the doses of preparation for further experiments. The body temperature was measured rectally. The threshold of pain sensitivity was determined on the hot plate test [11] before and 15, 60, and 120 min after injection of 200 and 400 μg/kg thymoptin. A mouse was placed on a plate heated to 55±0.5°C and the time which elapsed until the characteristic sign of discomfort (intense licking of the paws) appeared served as the measure of the pain threshold. After this the animal was removed from the plate. The effect of thymoptin (400 μg/kg) on the narcotic effect of Nembutal (20 and 40 mg/kg, subcutaneously) was judged from the duration of lying on the side and the number of animals in which this posture was observed. The antidepressant activity was evaluated in the behavioral desperair test [9] by measuring the time of "standstills." Thymoptin was injected in doses which either enhanced (400 μg/kg) or did not affect (100 and 1000 μg/kg) motor activity.

OMR was studied in the open field test [6]. The rats were preliminarily tested 24 hours before the experiment and divided into groups which did not differ statistically. Motor (ambulation) and exploratory (rearing) activities and the emotional state (number of fecal pellets) of each animal were assessed during a 2-min test 1 and 24 hours and 7 days after injection of 200 or 400 μg/kg thymoptin.

The effect of thymoptin on conditioned-response activity was assessed by PAR under conditions of 50% learning in the control group [2]. The latency of passage from the illuminated to the dark compart-

TABLE 1. Effect of Thymoptin on the Pain Threshold in Mice, sec

Group	Background	Time of testing, min			
		15	45	60	120
Control (*n*=22)	5.8±0.3	7.9±0.6	9.5±1.2	8.5±0.6	8.3±0.6
Thymoptin, 200 μg/kg (*n*=22)	5.8±0.3	7.8±0.8	8.6±1.6	8.2±0.7	8.2±0.9
Control (*n*=29)	6.9±0.5	9.4±0.8	9.6±0.6	8.9±0.7	10.6±0.9
Thymoptin, 400 μg/kg (*n*=29)	6.9±0.5	7.1±0.6*	9.0±0.9	7.5±0.8	10.8±0.9

Note. *$p<0.05$ in comparison with the control.

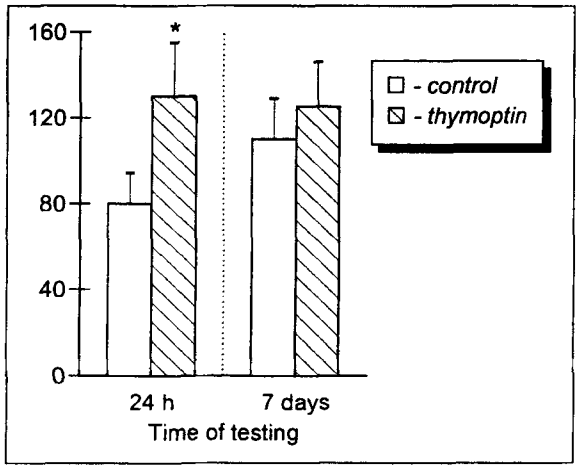

Fig. 3. Effect of thymoptin (400 μg/kg) on PAR conditioning in rats. Ordinate: latency of passage to dark compartment, sec.

ment was recorded. The rats were trained 1 hour after the injection of 400 μg/kg thymoptin and tested 1 and 24 hours and 7 days after training.

RESULTS

In doses of 10 and 100 μg/kg thymoptin did not affect the motor activity of mice, whereas in doses of 200 ($p<0.05$) and 400 ($p<0.01$) μg/kg it increased motor activity. This effect disappeared when the dose was increased to 1000 μg/kg (Fig. 1). For this reason we used doses of 200 and 400 μg/kg in our further experiments. The dose of 400 μg/kg was found to raise the body temperature by 1°C ($p<0.05$) but did not affect the narcotic effect of Nembutal. Thymoptin reliably lowered the pain threshold (by 36%) 15 min postinjection (Table 1). The open field test on rats revealed (Fig. 2) that the dose of 400 μg/kg enhanced horizontal motor activity and the exploratory component of OMR 1 and 24 hours postinjection without affecting the emotional state throughout the observation period. The same dose of thymoptin reliably improved PAR conditioning 24 hours postinjection (Fig. 3). These findings suggest that thymoptin possesses an antidepressant effect. On the other hand, the preparation did not alter standstill time in the behavioral despair test.

Thus, we have demonstrated that thymoptin has an effect on the central nervous system which manifests itself in increased motor activity, heightened pain sensitivity, and elevated body temperature in mice, and in more active behavior in the open field test and improved conditioning in rats. Bearing in mind that the administration of thymic hormones results in the appearance of a number of humoral factors in the serum (adrenocorticotropin, β-endorphin, cortisol, luteinizing hormone, interleukin-2, and interferon) modulating the state of the central nervous system [3,5,7,8,10], we can attribute the observed effect of thymoptin on the behavior of experimental animals to both the direct action of the thymic hormones and the above-mentioned factors.

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