Effect of Thymoptin on Passive Avoidance Reaction Conditioning in 18-Month-Old and Castrated Rats

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The effect of the immunomodulator thymoptin containing thymic peptide hormones on the conditioned passive avoidance reaction is studied in aging and postcastration. The preparation, which inhibits atrophy of the thymus, is found to improve conditioning in aging rats and has no effect on learning or memory in castrated rats.

Key Words: *thymoptin; passive avoidance reaction; aging; thymus; castrated rats*

Aging processes in the organism are accompanied by a broad spectrum of changes in the central nervous system (CNS) and in the hormonal and immunological status [4,8,10]. In particular, the thymus, one of the central organs of the immune system, undergoes age-associated involution, which impairs the immunoreactiviy of the organism [4]. This state may be successfully corrected with thymus-derived immunomodulating factors [5,6]. The preparation thymoptin represents a complex of peptide hormones of the thymus and differs from analogous preparations in an elevated concentration (up to 2%) of thymosin α_1, a thymic hormone helping to regulate immune and neuroendocrine functions of the organism [9].

Earlier we showed that the immunomodulator thymoptin, similarly to the nootropic pyracetam [2], enhances elaboration of the conditioned passive avoidance reaction (PAR) in intact rats [1].

The aim of the present study was to investigate the effects of thymoptin on PAR conditioning in rats during physiological aging and postcastration.

MATERIALS AND METHODS

The experiments were carried out on 3- and 18-month-old nonpedigree male rats (150-180 g and 500-600 g, respectively). The animals were maintained in cages of the usual size (2145 cm^2) at 21-22°C under a standard 12-hour illumination regime with free access to food and water. Rats weighing less than 200 g were caged in groups of 10 and those over 400 g in groups of 5 animals per cage.

The thymoptin preparation used in the study represents a complex of acid peptides (1000-15,000 D) with the 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 comprised 20 animals each. The preparation was injected intraperitoneally in a previously studied dose of 400 μg/kg [2] in 0.5 ml physiological saline. The control animals received an injection of the same volume of physiological saline.

The aging 18-month-old animals received a single injection of thymoptin 1 hour before PAR conditioning. Castration was performed as described earlier [3]. The castrated animals received the preparation starting from the 10th day postoperation according to the following two schemes: a single injection 1 hour before conditioning or injections during 5 days (the last one given 1 hour before conditioning).

Conditioned-response activity was assessed by PAR as described previously [3]. The animals were tested 24 hours after conditioning.

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Statistical processing of the results was performed using the Student t test.

RESULTS

A single injection of 400 μg/kg thymoptin reliably improved PAR conditioning in 18-month-old rats (Fig. 1). However, neither the single nor the repeated injections of the preparation to castrated animals were effective.

Thus, it has been shown for the first time in the present study that the immunomodulator thymoptin improves PAR conditioning in aging rats but has no effect on learning and memory in castrated animals.

It is possible that under conditions of physiological aging the thymoptin-produced normalization of the level of thymic hormones ameliorates the impaired function of the CNS. The fact that thymoptin had no effect on PAR in castrated rats may mean that the disturbances in endocrine regulation of learning and memory in the case of castration differ from those in physiological aging. Taking into account the data on age-dependent atrophy of the thymus [4], it may be assumed that the age-related disfunction of the CNS (learning and memory) and immunity (immunoreactivity) arises from disturbances of common adaptive mechanisms, some of which are functionally associated with the thymus. This assumption is confirmed by our previous data on improved PAR conditioning in rats treated with the immunomodulator cyclophosphane affecting the mass and cellularity of the thymus [2].

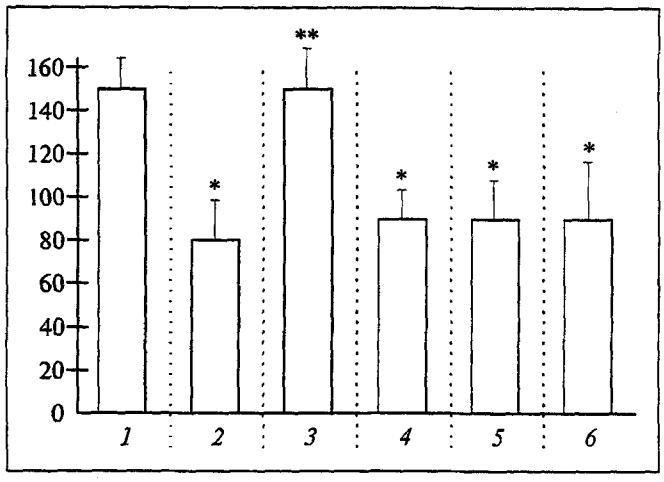

Fig. 1. Effect of thymoptin on PAR conditioning in rats. Ordinate: latency of transition from illuminated to dark compartment of the chamber, sec. *1*) 3-month-old rats; *2*) 18-month-old rats; *3*) 18-month-old rats + thymoptin, single injection; *4*) castrated rats; *5*) castrated rats + thymoptin, single injection; *6*) castrated rats + thymoptin during 5 days. $^{*}p<0.05$ in comparison with intact control, $^{**}p<0.05$ in comparison with 18-month-old rats.

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