PHARMACOLOGY AND TOXICOLOGY

Effect of L-Tryptophan on Active Avoidance Response in Male Rats with Increased Testosterone Level

N. S. Sapronov and Yu. O. Fedotova

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The effects of L-tryptophan on acquisition and extinction of active avoidance response and open field behavior were studied in male rates with elevated testosterone content. L-tryptophan improved learning in rats with elevated androgen content without affecting their behavior.

Key Words: *testosterone; L-tryptophan; learning; behavior*

Changes in the level of androgens affect higher nervous activity. Increased level of testosterone modifies neuronal excitability in the substantia nigra and hippocampus [7], while castration reduces functional activity of the reticular formation and disturbs inhibition in the cerebral cortex [4]. There is evidence on mutual regulation of the serotoninergic neurotransmission and the pituitary-gonadal system: serotonin modulates gonadotropin content in the pituitary and affects sensitivity of the gonads to all stimuli, including gonadotropin [1]. In addition, serotonin is involved in the realization of brain cognitive functions [2].

In this study we investigated the effect of serotonin precursor L-tryptophan on learning and behavior in male rats with high blood testosterone content.

MATERIALS AND METHODS

The study was carried out on 70 male albino rats (189-200 g) obtained from the Rappolovo breeding center. The animals were maintained under natural illumination and standard temperature conditions with free access to water and food. The experiments were performed at 10.00-13.00 in the morning. The animals were divided into 3 groups (10-12 animals each): group 1 included intact males, group 2 rats (controls) received testosterone propionate (Rostov Chemical Plant), and group 3 rats received testosterone and L-tryptophan. Testosterone was injected intramuscularly in a daily dose of 5 mg/kg for 4 days before and during the experiment. L-tryptophan (Ferak) in a daily dose of 250 mg/kg was injected intraperitoneally 30 min before behavioral tests.

Active avoidance response (AAR) was used as a model of learning [3]. Animal behavior was assessed using the open field test [5].

The data were analyzed statistically by Student's t test using Statgraphics software.

RESULTS

The rats receiving testosterone exhibited aggression and inappropriate behavior during the first 3 days of active avoidance training. The first avoidance responses were recorded only on day 4 (Fig. 1). The number of avoidance reactions remained practically unchanged and on days 5-7 the number of correct responses was significantly lower than in intact rats ($p<0.001$). On day 8 of the experiment after termination of training session (without electroshock) the rats treated with testosterone reproduced no correct responses.

In the experimental group, the first avoidance response to the conditioned stimulus was recorded on day 2 of training (Fig. 1) and then the number of cor-

Department of Neuropharmacology, S. V. Anichkov Department of Neuropharmacology, Institute of Experimental Medicine, Russian Academy of Medical Sciences, St. Petersburg

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rect responses practically did not differ from that in intact rats.

Twenty-four hours after the last training session without electrical stimulation the number of correct responses gradually decreased.

Testosterone considerably reduced the emotional component of animal behavior in the open filed test (1.0±0.1 defecations, $p<0.001$) without affecting other behavioral indices (Table 1). L-tryptophan reduced grooming and suppressed emotional reactions in rats with high level of testosterone.

Thus, high plasma level of testosterone in male rats dramatically reduced their ability to acquire AAR. This can be due to impairment of differentiation and consolidation processes and an imbalance between the excitation and inhibition processes in the central nervous system. At the same time, this impairment of learning in rats with high androgen content cannot be explained by behavioral changes, since testosterone did not significantly affect behavioral indices. Serotonin precursor L-tryptophan administered to males with high testosterone level normalized both acquisition and retention of AAR, which attests to restoration of both consolidation and retrieval of memory traces. However, it exerted no considerable effects on their behavioral characteristics. It can be suggested that the effects of L-tryptophan on learning and behavior are mediated by different mechanisms. The excess of hormones (in particular, androgens) reduces secretion of tropins (in particular, gonadotropin) by the pituitary via a negative feedback mechanism, which results in an imbalance between the content of tropins and hormones of peripheral endocrine glands [4]. It was reported that L-tryptophan considerably reduces the content of testosterone in male rats [1, 6]. It can be assumed that L-tryptophan-induced decrease in peripheral androgen content is accompanied by elevated secretion of gonadotropins, which restores the balance between the levels of gonadotropin and androgens in the body.

Thus, in male rats with elevated testosterone L-tryptophan improved learning by modulating positively the acquisition and retention of AAR and suppressing the grooming and emotional components of animal behavior.

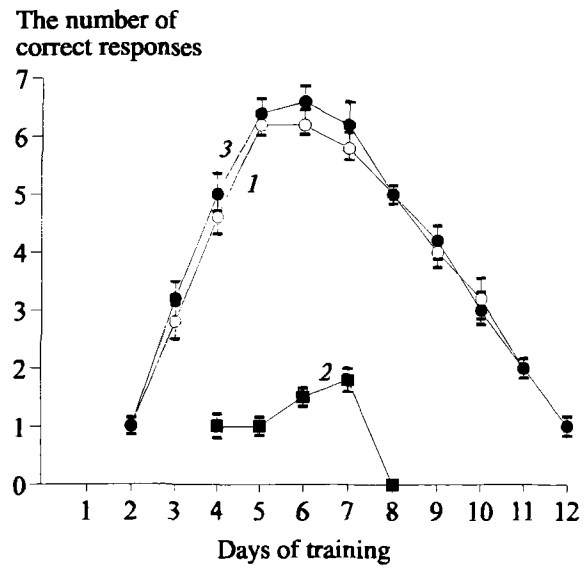

Fig. 1. Effect of L-tryptophan on acquisition and extinction of active avoidance response in rats with high plasma androgen level. *1*) intact rats, 2) control (testosterone), 3) testosterone+L-tryptophan.

TABLE 1. Effect of L-Tryptophan on Open Field Behavior of Male Rats with High Plasma Androgen Level ($M\pm m$, n=10, Observation Time 180 sec)

Index		Intact	Control (testosterone)	Testosterone+ L-tryptophan
Motor activity	runs	52.7±6.9	59.6±6.7	45.0±4.6
	rearings	14.2±3.2	12.8±2.8	13.4±1.9
Exploratory activity		3.0±0.5	2.8±0.4	3.0±0.4
Emotional reactions	grooming	3.2±0.4	4.6±1.2	—
	defecation	2.4±0.2	1.0±0.1*	—

Note. *$p<0.001$ compared to intact controls.

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