Effect of Chronic Inhalation of Toluene on Behavior of Rats of Various Age Groups in Multi-Branched Maze

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The effect of a 40-day toluene inhalation on learning of young and adult rats was examined in a multi-branched maze. Experimental rats of both age groups needed more time to pass the maze and made more errors than controls. This impairment was observed in young rats immediately after termination of toluene inhalation and in adult rats immediately and 90 days after toluene.

Key Words: *toluene chronic inhalation; maze; learning; rat*

Xenobiotic toluene belongs to the most widely spread inhalants [5,8,12]. Even a short-term inhalation of toluene stimulates mesoaccumbens transmission by activation of dopaminergic neurons in ventral tegument, which relates toluene to addictive substances [11]. Chronic inhalation of toluene provokes disorders in emotional, motor, cognitive, and perceptual spheres. Cell sites and mechanisms mediating these disturbances are still unknown, but the influence of toluene on dopamine-, GABA-, serotonin-, and cholinergic neurons is thought to play a role [9,10]. There are data that chronic inhalation of toluene produces a negative effect on memory and learning [3,4] and this effect depends, among other factors, on age [2,4].

Our aim was to examine the effect of toluene on young and adult rats in a multi-branched maze.

MATERIALS AND METHODS

The experiments have been carried out on laboratory mature albino male rats; animal age at the start of the tests was 25 (group 1) and 90 days (group 2). The rats were daily (for 40 days) placed into a closed exsiccator filled with toluene vapor for 3-5 min until they fell on the side, which was assumed to be close to drug intoxication. The control group comprised age-matched rats maintained under standard vivarium conditions. Maze testing was started immediately or on day 90 after the end of inhalation period; 7 rats from each group were tested.

The multi-branched maze consisted of a nest box with adjacent start platform, open arms, and closed arms mounted 30 cm above the floor. Each rat was placed into the nest box for several minutes of the adaptation period; thereafter it was transferred to the start platform. The animals needed some time (from few seconds to several minutes) to find the optimal trajectory by the trial and error method. The total session time was 10 days; each rat passed the maze 5 times per day. The task was considered as completed when the rat returned to the nest box. The learning process was assessed by the number of errors (visits to blind arms) made by a rat searching for the way to the nest box and by the time spent to passing the maze [1].

The data were analyzed statistically by ANOVA. Significance of differences between the groups was assessed by Student's t test at $p<0.05$.

RESULTS

Group 1 rats spent longer time (88.5 sec) for passing the maze than the controls (69.1 sec, $p<0.05$, Fig. 1,

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a) and made more errors (2.4 and 1.1, respectively, $p<0.001$, Fig. 1, *b*). However, if maze testing was started 90 days after termination of toluene exposure, the time of passing the maze was similar in experimental and control rats (76.3 and 69.1 sec, respectively, Fig. 1, *a*); the mean number of errors also differed insignificantly (Fig. 1, *b*).

Group 2 rats spent the same time for passing the maze (84.5 sec) as the control rats (76.9 sec, Fig. 2, *a*), but the number of errors in the experimental group (1.03) was significantly higher than that in the control group ($p<0.01$, Fig. 2, *b*).

Adult rats tested in 90 days after termination of toluene inhalation needed significantly more time to pass the maze (105.4 sec) than control rats (76.9 sec, $p<0.05$) or experimental rats of the same age tested immediately after toluene exposure (84.5 sec, $p<0.05$, Fig. 2, *a*). Additionally, they made more errors than the control rats of the same age ($p<0.005$) and experimental rats of the same age tested in the maze immediately after toluene inhalation ($p<0.05$, Fig. 2, *b*).

Toluene exposure specifically affected the number of errors made by young and adult rats in the multi-branched maze. In young group, pronounced behavioral disturbances (longer time of passing the maze and greater number of errors) were revealed only immediately after toluene inhalation, while after 90 days they completed the task virtually like the age-matched control rats. This probably suggests that

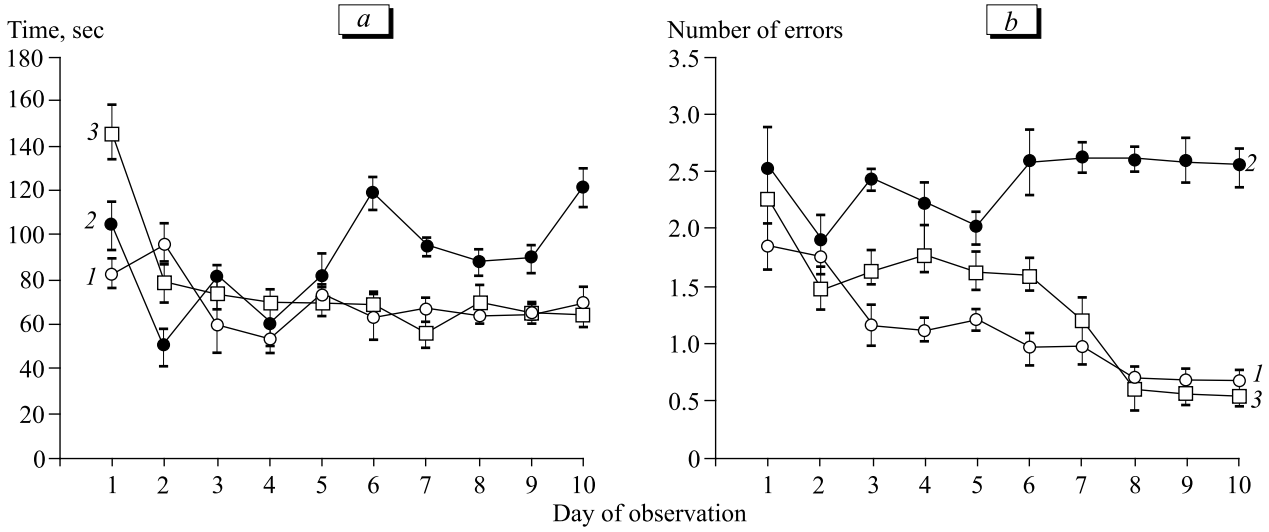

Fig. 1. Time of passing the maze (*a*) and number of errors (entrances into blind arms, *b*) in experimental and controls rats exposed to toluene starting from the age of 25 days. Here and in Fig. 2: *1*) control rats; *2*) experimental rats tested immediately after termination of inhalations; *3*) experimental rats tested in 90 days after the end of toluene inhalations.

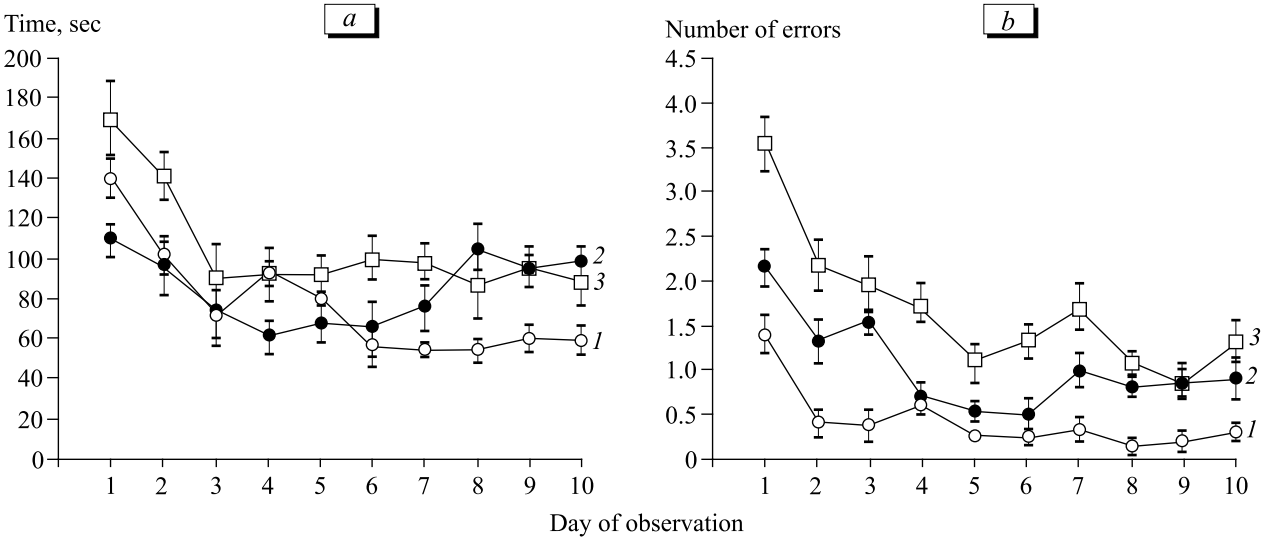

Fig. 2. Time of passing the maze (*a*) and number of errors (entrances into blind arms, *b*) in experimental and controls rats exposed to toluene starting from the age of 90 days.

chronic toluene exposure did not induce hypersensitivity to this toxicant in brain systems of young rats. In adult rats, the negative effects of toluene (longer time of passing the maze and greater number of errors) were observed both immediately and 90 days after termination of toxic exposure. This fact probably reflects the development of sensitivity to the toxicant in adult rats.

The effect of chronic toluene inhalation largely depends on toxicant dose and animal sex [2,4]. In this study, we demonstrated that the toluene effect also depended on animal age. The age-dependence of the toxic effects was also demonstrated in our previous studies [6,7] and in some other reports [2]. We previously showed more rapid motor learning in young rats after chronic toluene inhalation in comparison with adult animals [6]. Toluene inhalation decreased the number of pyramidal cells and interneurons in the hippocampus; in young animals, this effect was observed immediately after toxic inhalation [7], while in adult animals it was also found after 90 days (unpublished data). Moreover, young rats demonstrated lower sensitivity and motor activity after chronic exposure to toluene than adult rats [2]. Sensitization is a specific type of neuron adaptation within the dopamine reward system [13], and hypothetically, the observed age-related specificity of toluene effects originates from different development of the dopamine system in various age groups; it is known that the development of this system is not completed at the pubertal age [2,13]. Moreover, higher plasticity of the nervous system in young animals is worthy of note.

Logically, the next study should address the cellular, molecular, and structural alterations accompanying the above toluene-induced disturbances with due attention to their age-dependence. These enigmas should be solved to clarify the peculiarities of chronic effects of toluene in the young and adult organisms.

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