

PHARMACOLOGY AND TOXICOLOGY

Effect of Amiridin on the Conditioning of Rats in a Radial Maze

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The effect of amiridin and of the reference preparations tacrine, picamilon, and piracetam on conditioning in a radial maze is studied in intact rats. Long-term memory was significantly improved by amiridin, tacrine, and picamilon. Short-term memory was enhanced only by picamilon.

Key Words: *amiridin; short- and long-term memory, radial maze*

Amiridin, developed at the All-Russian Center for the Safety of Biologically Active Compounds, has proved to be a promising drug for the treatment of neurodegenerative diseases, including Alzheimer's disease [1,7]. The antiamnestic activity of the preparation was examined in tests of the conditioned reaction of passive and active avoidance [2-5,12,13]. It was shown that amiridin improves rat short-term memory in amnesia [14]. However, the effect of amiridin on different kinds of spatial memory in intact animals remained unclear.

The present investigation was undertaken to examine the effect of amiridin on the short- and long-term memory of intact rats during conditioning in a radial maze. Picamilon, which possesses cerebrovascular and nootropic effects [6], tacrine used to treat Alzheimer's disease [9], and the nootropic piracetam were used as reference drugs.

MATERIALS AND METHODS

Experiments were carried out on 145 outbred male white rats weighing 200-300 g. The animals were kept at 20-22°C, under the standard 12-h light reg-

imen, with water *ad libitum*. The rats were trained in the maze every other day during 40 days (20 training sessions), and were fed immediately after training, i.e., they underwent a 48-h food deprivation before the test [6]. Experiments were carried out in a sound-insulated room in artificial light. The eight-arm radial maze used in the study consisted of a central area 50 cm in diameter with walls of plexiglass 50 cm high. Through openings in the wall the central area was connected to the arms (10 cm in diameter, 50 cm in length). The experiment began with pre-testing, performed as follows: the animal was placed in the maze without any reinforcement in the arms. Locomotor activity, sniffing, standstill, number of upright postures, and visits of arms were recorded for 3 min. Rats which visited less than 3 arms during this period were excluded from the experiment. According to the results of the pretest in the maze the animals were divided into groups which did not differ in horizontal and vertical motor activity and in the number of arm visits. Training was started the day after the pretest. The rat was placed in the central area opposite the first arm. Reinforcement (pieces of bread weighing 100-200 g) was found in the 2nd, 4th, 6th, and 8th arms. When an animal had visited 4 reinforced or any 8 arms, it was removed from the maze. The substances

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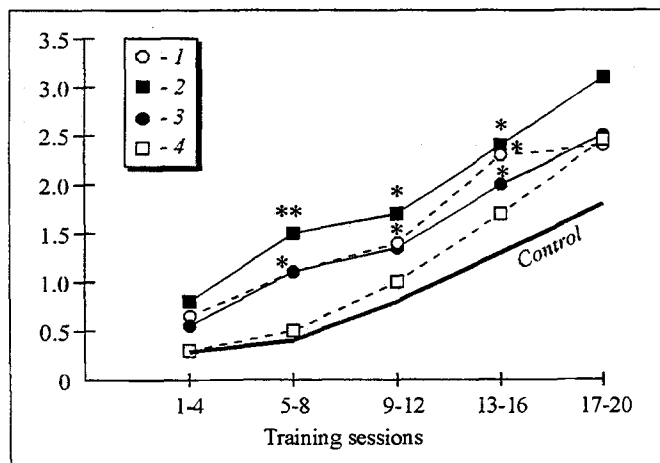


Fig. 1. Effect of amiridin (0.1 mg/kg, 1), tacrine (0.1 mg/kg, 2), picamilon (10 mg/kg, 3), and piracetam (250 mg/kg, 4) on long-term memory of intact rats. Ordinate: number of times three consecutive visits were made to reinforced arms. * $p < 0.05$, ** $p < 0.001$ as compared to the control.

of interest were administered intraperitoneally an hour before placement in the maze. Amiridin was injected at 0.1 mg/kg, tacrine at 0.1 mg/kg, picamilon at 10 mg/kg, and piracetam at 250 mg/kg. The piracetam and picamilon doses were based on a published study [6], while the tacrine and amiridin doses were chosen according to our previous data [3]. The effect of the preparations was assessed by the following indexes of learning and memory: the number of repeated visits to reinforced arms (errors of short-term memory) and consecutive visits of three reinforced arms (long-term memory) [6]. The data were processed statistically using the Student t test.

RESULTS

A significant improvement of long-term memory was noted during the conditioning in the radial maze under the effect of amiridin (5th-16th sessions), tacrine (5th-20th sessions), and picamilon (5th-16th sessions, Fig. 1). Only picamilon improved short-term memory (during the 13th-20th sessions).

The improved learning of rats in the radial maze caused by picamilon and the absence of an effect of piracetam agree with the data of other authors [6]. There are reports that tacrine has no effect on learning and memory in intact rats but does manifest activity on different models of amnesia [3-5,8-10]. We are the first to find an active participation of tacrine in the formation of long-term memory in intact rats. Amiridin was found to improve only long-term memory in this investigation. Considering that amiridin improves short-term memory in amnesia [14] but produces no effect in intact rats, we assume that the drug is active only under pathological conditions.

Thus, the improvement of spatial long-term memory of intact rats under the influence of amiridin and tacrine is documented for the first time here.

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