EFFECT OF PSYCHOSTIMULANTS ON RATS RELEARNING THE DIRECTION OF AVOIDANCE IN A U-SHAPED MAZE

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The ability of rats to relearn the direction of the avoidance response was studied in a U-shaped maze. Four training series of experiments were carried out, each with a different direction (to right or left) of running. In small and average doses (0.5 and 2 mg/kg) amphetamine shortened the latent periods of the responses and had no effect on the animals ability to relearn. A large dose of amphetamine (5 mg/kg) shortened the latent period of response but, at the same time, impaired relearning of the direction of the avoidance response, and this correlated with the strengthening of spatial preference. Caffeine, in doses of 25 and 50 mg/kg, did not affect the rats' ability to relearn.

KEY WORDS: avoidance; avoidance response; relearning; psychostimulants; amphetamine; caffeine.

According to the results of the writer's previous investigations partial destruction of the striatum in rats disturbs relearning the direction of the avoidance response in a U-shaped maze.

It accordingly seemed useful to study the action of various doses of amphetamine, which affects striatal function [1], on relearning by animals and also to compare the effect of amphetamine, with the aid of this model, and of another psychostimulant – caffeine, which has no such properties.

EXPERIMENTAL METHOD

Experiments were carried out on 144 noninbred albino rats of both sexes weighing 180-280 g in a U-shaped maze with electrified floor. Altogether four consecutive training sessions were given (10 tests in each). In response to a conditioned acoustic stimulus, in order to avoid an electric shock, the animal had to run ten times into the right-hand passage of the maze, after which the direction of the avoidance response was changed to the left (the back walls of the passages were of different colors), after which another two consecutive retrainings were given. The procedure of training and retraining occupied about 3 h.

To assess the ability of the animals to undergo retraining, the mean difference (irrespective of sign) between the number of mistakes in each series (one to two, two to three, three to four) was calculated, i.e., the degree of fluctuations in the number of mistakes was determined. The latent periods of avoidance and the time taken by the animals to correct mistakes they had made also were recorded. The number of times the animal emerged from the correctly chosen passage in the course of 45 sec from the time that the rat was placed in the maze also was taken into account.

Depending on the dose of the drug given, the animals were subdivided into five groups (0.5, 2, or 5 mg/kg amphetamine; 25 and 50 mg/kg caffeine). The animals of the control group received physiological saline in corresponding doses. The drugs were injected intraperitoneally 30 min before the beginning of the experiments.

EXPERIMENTAL RESULTS

The rats of the control group were trained to run into the right-hand passage of the maze without any particular difficulty. The number of incorrect responses was small and did not exceed on average two mistakes

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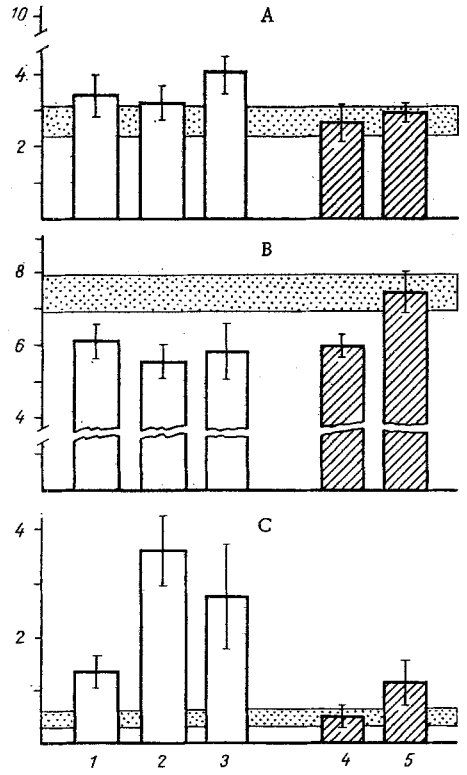

Fig. 1. Effect of amphetamine and caffeine on some indices of the avoidance response in rats: A) variations in number of mistakes; B) latent periods (in sec); C) number of departures from previously occupied passage. Dotted zone represents region of scatter for rats of control group; 1, 2, 3) effect of 0.5, 2.0, and 5.0 mg/kg amphetamine respectively; 4 and 5) 25 and 50 mg/kg caffeine.

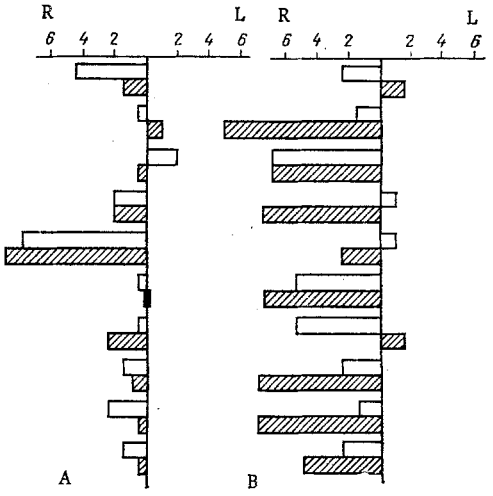

Fig. 2. Character of spatial preference in control animals (A) and rats receiving a large dose of amphetamine (B). Columns show degree of spatial preference, allowing for direction of runs (R – to the right, L – to the left) for each animal in conventional units of the index of preference (P; plotted along horizontal scale); unshaded columns, results of first determination; shaded columns, results of second determination.

in ten runs. Relearning the direction of avoidance also was fairly easy. Whereas the first incorrect responses were abolished with some difficulty, gradually the time taken to correct the mistakes shortened. This tendency was observed with each relearning.

Amphetamine, in the doses given above, had no appreciable effect on the formation of the primary conditioned reflex. A small dose of the psychostimulant (0.5 mg/kg) caused virtually no change in the rats' behavior. Meanwhile the latent periods of the avoidance response were shortened and the rats required less time to correct their mistakes. In this dose amphetamine did not disturb relearning, although a tendency was observed for the variations in the number of mistakes to increase. There was also an increase in the number of times the animal came out of the safe situation passage, and this was interpreted as worsening of passive avoidance (Fig. 1).

After injection of amphetamine in the average dose (2 mg/kg) the behavior of the animals was unchanged, but the shortening of the latent period of the responses and of the time required to correct the mistakes was greater. Considering that these indices characterize active avoidance, the results are in agreement with data

in the literature [3, 4, 6]. Amphetamine, in a dose of 2 mg/kg, did not significantly disturb relearning but greatly increased the number of times the rats emerged from the safe situation passage.

After injection of a large amphetamine dose (5 mg/kg), a stereotyped behavior in the rats was observed throughout the entire experiment. Learning by running through the right-hand branch of the maze did not deteriorate. However, during relearning the overwhelming majority of the animals made considerably more errors than in learning from the first series of runs. The second and third relearning proceeded analogously. In this connection, the fluctuations of the number of errors underwent a significant statistical increase.

Caffeine had a different effect on the avoidance response (Fig. 1). The latent periods were shortened after injection of this drug only in a dose of 25 mg/kg and the time required to correct the mistakes was not changed at all. The number of departures from the maze increased a little only after injection of caffeine in a dose of 50 mg/kg. Relearning by the rats after injection of caffeine was not materially disturbed (the variations in the number of mistakes did not differ from the control). These results are in agreement with those obtained by Belozertsev [2], who found, although admittedly under different experimental conditions, disturbances in relearning after administration of amphetamine but no effect from caffeine.

The sharp worsening of relearning by the animals after injection of the large dose (5 mg/kg) of amphetamine was of the greatest interest. To some extent this can be considered to be connected with a change in spatial preference, more especially because, according to Glick [5], this psychostimulant (under different experimental conditions) revealed an enhanced preference for the direction to the right during the performance of an instrumental response. In the present experiments disturbances of relearning also correlated with the evident preference for a certain direction of the avoidance response. To detect a tendency toward preference by the rats, the conventional preference (P) index was calculated. Allowing for sign, the difference between the number of mistakes in series with running in opposite directions (1 and 2, 3 and 4) was determined. The mean value of this difference was taken as the desired index for each rat.

Control rats and animals receiving the psychostimulant in the great majority of experiments preferred to run into the right-hand passage of the maze. However, the value of the P index varied greatly, making analysis of the changes in spatial preference more difficult. Additional experiments were therefore carried out on 20 rats whose behavior was assessed twice at an interval of 1 week. At the first test physiological saline was injected, at the second test amphetamine was given in a dose of 5 mg/kg. Animals receiving two injections of physiological saline acted as the control. In this group low values of P were mainly recorded. It was shown that the differences between its values at the first and second tests were not significant. Amphetamine, however, enhanced the original right-hand preference in five rats, and this change was fairly considerable. Two other rats which received amphetamine preferred the right-hand passage of the maze (Fig. 2). Parallel with this, the variations in the number of mistakes made by these animals increased.

On the basis of these results it can be postulated that the worsening of relearning by the rats after injection of the large dose of amphetamine is to some extent connected with a change in spatial preference. Amphetamine, in large doses, is known to cause functional blocking of the caudate nucleus through the strengthening of nigro-striatal dopaminergic transmission [1]. On the other hand, Potegal [7] observed that electrolytic injury to the striatum disturbs the solution of problems involving spatial orientation.

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