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MESCALINE ACTION ON "MEMORY DECAY" AND "PROBLEM SOLVING" BEHAVIOR IN THE RAT

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Abstract

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1. The modifications of behavior caused in the rat by a chronic oral administration of mescaline have been studied in three experimental situations.
2. In the staircase maze mescaline accelerated the spontaneous decay on the conditioned reflex (memory decay) during the period without daily training.Only the results observed at 30 mg/kg/day of mescaline were statistically significant.
3. In a T maze two lateral alleys closed by two swinging doors, 30 mg/kg/day of mescaline increased the time spent in opening the first door. When the two doors of the lateral alleys were closed with a latch, mescaline 30 mg/kg/day, caused an increase in the time spent by the rat in opening the doors.
4. Mescaline caused an increase in food consumption. The increase at 30 mg/kg/day is statistically significant.

Keywords: Food-consumption, memory decay, mescaline, problem-solving behavior, staircase-maze, T-maze.

Introduction

The excitatory effect of mescaline on rat behavior (Fundarò et al. 1986, Bridger et al. 1972, 1973) makes it often difficult to offer evidence of an action of this drug on learning and mnemonic processes. For example, the finding of Bridger and Mandel (1971) that mescaline facilitated the acquisition of shuttle-box avoidance behavior may be attributed to the drug induced increase in motor activity. Similarly the improvement of behavior observed (Fundarò et al. 1986) in a test in which the rat has to "realize" that the responses must be transferred from one lever to the other, was observed at doses of mescaline which increased motor activity, while at lower doses of mescaline a disruption of rat behavior was observed.

To try to overcome these difficulties caused by modification of motor activity,we utilized in present researches the "staircase maze" test, which we used (Cassone and Molinengo 1981, Cassone et al. 1983) in the study of memory decay, and an obstruction box test analogous to that used by Watson (Watson 1930,Farris and Griffith 1971) to study the problem-solving behavior in the rat. It may be accepted that the increase of "errors" in the staircase maze or the increase in time to solve the problem are independent enough from modifications of excitability to allow us to evaluate the modifications caused by mescaline on learning or

memory processes.

Methods

Animals. Forty-three male albino rats (Wistar derived strain) were used. The animals weighing 200-250 g at the beginning of the experiments were kept in groups of 4 or 5 in cages (temperature around 20°C) with food and water ad libitum. Sixteen rats were trained in the staircase maze and the other twentyseven were trained in a T maze. The experiments were performed daily in the morning.

Drug Administration. Mescaline sulfate was dissolved in water. The animals of the control group drank water. The rats of the two experimental groups tested in the staircase maze drank for 16 days a solution of 50 mg/liter and a solution of 100 mg/liter of mescaline.The average dose, calculated from the daily fluid intake and from the weight of the rats, was 4 mg/kg/day and 8.75 mg/kg/day for the two groups of rats drinking respectively 50 or 100 mg/liter of mescaline.

The two groups of rats tested first in the obstruction box test and then in the food consumption test drank for 20 days a solution of 100 mg/liter and a solution of 300 mg/liter of mescaline. The average dose calculated was 9 mg/kg/day (rats drinking 100 mg/liter of mescaline) and 30 mg/kg/day (rats drinking 300 mg/liter of mescaline)

Experimental Procedures. The staircase maze test used in previous researches (Cassone and Molinengo 1981, Cassone et al. 1983) to study drug action on memory decay was employed. The apparatus was a wood staircase of 13 steps which had a corridor 17 cm long in the vertical wall. The rats were trained to find pellets (45 mg, Campden Instruments LTD) in the corridor corresponding to the 3^{rd}, 6^{th}, 9^{th}, 12^{th} steps. The rats were kept without food from 6p.m. to 12 in the morning. Each rat was tested 4-5 times each day in the staircase. After three months of this training, all the rats stopped only on the four reinforced steps. At this point the rats were divided in three groups (controls, 5 rats; mescaline 8 mg/kg/day,6 rats; mescaline 4 mg/kg/day, 5 rats) and a trial without reinforcement was performed in the staircase. In this trial the search for food in the corridor corresponding to the 3^{rd}, 6^{th}, 9^{th}, 12^{th} steps was considered a "correct response" and the search for food on any other step was considered an "error". The daily training was then interrupted and after 20 days, a new trial with no reinforcement was performed: correct responses and errors were again counted. Mescaline was administered only in the first 16 days of the period (20 days) without daily training.

In the obstruction box test the general lines of the procedure given by Watson (1930) were followed. The rats were trained in a wood T maze. The central (35 cm long) and the two lateral alleys (25 cm long) were 15 cm wide. The incentive was a piece of purina chops(0.2g) at the end of the two lateral alleys. After one month's training the rat behavior was stable in successive trials. As this point the two lateral alleys were closed with two doors suspended so they could be opened by pushing them. The time spent by the rats opening one door and reaching the food in one of the lateral alleys and the time spent opening the two doors and reaching the food in the other lateral alley was measured. On the successive day the same experiment was performed but the two swinging doors were closed with a latch, which had to be taken away by the animal to open the doors. In this experiment the time spent reaching the food in one and then in other lateral alleys was measured.

Twenty-seven rats were used; they were divided in three groups of 9 animals; controls (drinking water); 9 mg/kg/day (drinking 100 mg/liter of mescaline) and 30 mg/kg/day (drinking 300 mg/liter of mescaline).

Food Consumption. It was estimated in the same three groups of 9 rats used in the obstruc-

tion box test. Rats were kept without food for 12 hours before the trial. Then in the morning a weighed quantity of food was introduced in the cages of the three experimental groups (controls, mescaline 9 mg/kg/day, mescaline 30 mg/kg/day). After 20 minutes the remaining food in the three cages was weighed and, by difference, the quantity of food consumed in 20 minutes by the 9 rats was evaluated. These measures were repeated 4 times on different days.

Statistical Analysis. As the staircase was composed of 13 steps, the rat had the possibility, in each trial, of making 4 correct responses and 9 errors. In order to evaluate the performance of the animals in the various trials, the ratios (correct responses/total responses) x 100 were calculated, obtaining indexes varying from 100, when the responses given were all correct, to 0, when no correct responses were given. These ratios were evaluated in the trials performed immediately before the interruption of daily training and in the trials performed at the end of the period with no training. The per cent differences between the two indexes were calculated for each rat in order to evaluate the modifications of behavior caused by the training interruption in the various experimental situation. The Student's t test for the differences between means was used to estimate the significance of the differences between the results obtained in control rats and in rats which received the pharmacological treatment during the period of no training.

In the obstruction box test the averages of the time (in seconds) spent by the nine rats to open the swinging doors were calculated separately for the two lateral alleys of the T maze and for the three experimental groups. The Student's t test for the differences between the means was applied firstly to evaluate the differences between the values found in the controls and in the two mescaline groups and secondly to evaluate the significance of the differences between the time spent to reach the food in the first and in the second lateral alley.

In the experiments with the two swinging doors blocked with a latch, rats scored an infinite time when they did not open the door in less than 15 minutes. The reciprocal of the time (1/T) was calculated to transform the infinite time in 0 and the statistical procedures utilized in the experiments with the two swinging doors not blocked was applied.

To evaluate the statistical significance of the differences in food consumption between the controls and the rats treated with 9 or 30 mg/kg/day, the Student's t test for the differences between the means was applied.

Results

Staircase Maze. In Table 1 the means and the standard error of the per cent differences between the indexes (correct responses/ total responses) x 100 found immediately before and at the end of the interruption of the daily training are given for the control group and for the rats treated with mescaline 4 mg/kg/day or 8.75 mg/kg/day.

In the control group a 19.6 % worsening of the rat behavior was observed after the interruption of the daily training. In the rat treated with 4 mg/kg/day of mescaline the worsening of the rat behavior increased to 36.6 % and after 8.75 mg/kg/day it increased to 57.16 %. The probability of a casual result indicate that only the modification of behavior caused by 8.75 mg/kg/day of mescaline is statistically significant.

Obstruction Box. In Table 2 the means and the standard error of the time (in seconds) spent by the rats to open the swinging doors and to reach the food in the two lateral alleys are given separately for the first and the second alley. It may be noted that the time spent to reach the food in the second alley is always shorter than the time spent in the first alley. These differences are statistically significant in the control group and in the rats treated with 9 or 30 mg/kg/day of mescaline.

The comparison of the results obtained in the control group and in the mescaline treated rats indicates that only the increase in the time spent opening the first door by the rats treated with the higher dose of mescaline is statistically significant.

Table 1

Per Cent Differences Between the Performances Before and at the End of the Period with no Daily Training in the Staircase-Maze

	Controls	Mescaline 4 mg/kg/day	Mescaline 8.75 mg/kg/day
$\bar{X}$ ± S.E.	19.60 ± 9.93	36.60 ± 4.12	57.16 ± 7.15
n	5	5	6
Differences between controls and treated rats		17.00	37.56
Probability of a casual result		10-20%	1%

Table 2

Time in Seconds Spent by the Rat to Open the Swinging Doors and to Reach the Food in the First (I) and in the Second (II) Lateral Alley of a T Maze

	Controls		Mescaline 9 mg/kg/day		Mescaline 30 mg/kg/day	
	I alley	II alley	I alley	II alley	I alley	II alley
$\bar{X}$	118.86	47.71	182.57	69.66	202.14	36.43
S.E.	14.00	5.68	37.68	17.20	24.06	6.76
n	9	9	9	9	9	9
Differences between the I and the II alley		71.15		112.91		165.71
Probability of a casual result		0.1%		1-0.1%		0.1%
Differences between controls and treated rats			- 63.71	- 21.95	- 83.28	+ 11.28
Probability of a casual result			10-20%	10-20%	1%	20-30%

The results obtained in the obstruction box when the swinging doors were closed with a latch are reported in Table 3. In this case the reciprocal of the time spent opening the

doors and reaching the food were calculated, in order to transform in 0 the infinite values recorded when the rat spent more than 15 minutes opening the door. Owing to this transformation, smaller values are obtained when the time spent reaching the food increases. The means and the standard error of the transformed values reported in Table 3 have been multiplied by 1000.

In this experimental situation there is no statistically significant difference between the time spent reaching the food in the first and in the second lateral alley. The comparison of the values found in the controls and after mescaline administration indicate that 30 mg/kg/day of mescaline caused a statistically significant increase of the time spent by the rat reaching the food.

Table 3

Reciprocal (Multiplied by 1000) of the Time Spent to Open the Doors Closed with a Latch and to Reach the Food in the First (I) and in the Second (II) Lateral Alley of a T Maze

	Controls		Mescaline 9 mg/kg/day		Mescaline 30 mg/kg/day	
	I alley	II alley	I alley	II alley	I alley	II alley
$\bar{X}$	3.30	0.90	2.98	1.56	0.76	0
S.E.	1.10	0.30	0.90	0.71	0.45	-
n	9	9	9	9	9	9
Differences between the I and the II alley	2.4		1.42		0.76	
Probability of a casual result	5-10%		30-40%		10-20%	
Differences between controls and treated rats			+ 0.32	- 0.66	+ 2.54	+ 0.90
Probability of a casual result			80%	40-50%	5%	2%

Table 4

Quantity of Food (g/rat) Consumed in 20 Minutes

	Controls	Mescaline 9 mg/kg/day	Mescaline 30 mg/kg/day
$\bar{X}$ S.E.	6.48 ± 0.29	8.40 ± 0.82	8.42 ± 0.35
n	4	4	4
Differences between controls and treated rats		- 1.92	- 1.94
Probability of a casual result		5-10%	1-0.1%

Food Consumption. In Table 4 the means and the standard error of the quantity of food (in g) consumed in four successive trials are reported separately for the control group and for the rats treated with 9 or 30 mg/kg/day of mescaline. The two doses of mescaline caused an increase of the food consumption practically of the same size, but owing to the rather high dispersion of the measures obtained at 9 mg/kg/day of mescaline, only the increase in food consumption observed at the higher dose of mescaline is statistically significant.

Discussion

A chronic administration of mescaline caused damage to the capacity of the rat to make use of the negative experiences of preceeding trials (Fundarò et al.1986). This may indicate that mescaline treatment damaged memory processing. But in the same test higher doses of mescaline (Fundarò et al. 1986) caused an improvement of rat behavior which might be determined by the mescaline excitatory effect.

In the staircase maze test we used in this present research, there is no reason to suppose that modifications of the speed with which the rat runs in the maze may interfere with the number of errors or of correct responses given by the rat. The result obtained (Table 1) indicate that the chronic administration of mescaline damaged rat performance in the staircase maze, indicating that mescaline increased the rate with which the conditioned reflex decay when the daily training is interrupted. These observations strongly suggest that a chronic administration of mescaline causes an increase in the rate of memory decay.

It may be accepted that the mescaline excitatory effect has small consequences on rat behavior in the obstruction box test. The rat runs through a short alley (25 cm) and most of the time spent to reach the food is taken up in opening the doors.

The results obtained in this test when the swinging doors were not blocked with a latch indicate that the time spent by the rat in opening the doors and in reaching the food in the second lateral alley is always shorter than the time spent in reaching the food in the first alley. This may indicate that the experience acquired in opening the first door improves rat behavior in opening the door to go out of the first alley and in opening the second door to go into the second alley. The chronic administration of mescaline (Table 2) caused no damage to this rat behavior suggesting that mescaline does not interfere with the ability of the rat to make use of information gathered shortly before. An increase of the time spent in opening the doors may indicate a damage to problem solving behavior. This was observed (Table 2) only with the higher dose of mescaline (30 mg/kg/day) in the time spent opening the door of the first alley.

The results obtained in the obstruction box with the doors closed with a latch (Table 3) indicate that there is no improvement of rat performance in opening the doors and reaching the food in the second alley. This indicates that taking away the latch of the first door does not help the rat to open the door of the other alley. Therefore it may be suggested that the rat did not realize that to open the doors it is necessary to take away the latch and this operation was accomplished by chance.

Accepting this interpretation the worsening of the rat behavior at 30 mg/kg/day of mescaline may not be the consequence of a damage to the problem solving ability of the rat. It may be supposed that 30 mg/kg/day of mescaline caused such a high excitatory effect as to make the rat unable to carry out a coordinated operation.

Mescaline causes nausea and vomiting in man (Goodman Gilman et al. 1985). A similar action in the rat may be responsible for a motivational decrement which might interfere with the behavioral effects when, as in the tests we used, food is the incentive. The results of

Table 4 indicate that the chronic administration of mescaline eventually increases food consumption in the rat. Thus the results we obtained cannot be the consequence of a motivational decrement.

Conclusions

Our results indicate that mescaline causes an acceleration of the spontaneous decay of memory. The capacity to make use of experiences acquired shortly before (short term memory) is not damaged by mescaline and problem-solving behavior is impaired only at rather high doses of mescaline. The dexterity of the rat to execute a complex operation is damaged and the food consumption (hunger drive) is increased by mescaline. It must be stressed that this complex behavioral action of mescaline is further complicated by the excitatory effect of mescaline for which there is ample evidence (Bridger and Mandel 1971, Bridger et al.1972, Bridger et al. 1973, Fundarò et al. 1986).

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