Pergamon

Pharmacology Biochemistry and Behavior, Vol. 48, No. 1, pp. 23-29, 1994

0091-3057/94 $6.00 + .00

Drug Effects in a Radial Maze Designed for Dissociation of Cues Used by Mice

A. BEUZEN,[1] C. BELZUNG AND P. ROULLET

Laboratoire d'Ethologie et de Psychophysiologie, UFR Sciences et Techniques, Parc de Grandmont, 37200 Tours, France

Received 10 November 1992

BEUZEN, A., C. BELZUNG AND P. ROULLET. *Drug effects in a radial maze designed for dissociation of cues used by mice.* PHARMACOL BIOCHEM BEHAV 48(1) 23-29, 1994.—Scopolamine and amphetamine effects were investigated in a new radial maze. Three distinct procedures were designed to dissociate the use, by C57BL/6 mice, of the different cues available: a procedure where only spatial information was available, a procedure in which both spatial cues and olfactory trails were present, and a nonconfinement procedure where mice could use spatial cues, olfactory trails, and/or algorithmic strategies. We found that while scopolamine impaired performance on the maze in all three procedures, amphetamine tended to improve solving of the maze problem, but only in the procedure where spatial cues alone were available. The results are discussed in relation to hypotheses concerning these drug effects.

Radial maze Scopolamine Amphetamine Spatial working memory Attention Mouse

THE radial maze, first described by Olton and Samuelson (15), has been widely used as a tool for the investigation of the neural basis of learning and memory (5,16,19) and of the effects of pharmacological compounds on spatial orientation in rodents (1,4,7,10,11,22). This apparatus has generally been used to study spatial memory. Olton and Samuelson (15) showed that rats are able to perform the task even if the already-visited arms were interchanged during the session, that is, without using olfactory trails. They concluded that rats use extramaze cues. However, other studies have shown that learning in a radial maze is based not only on spatial information but also on algorithmic strategies—for example, choice of successive adjacent arms (5), and olfactory trails (20). Consequently, the interpretation of lesion or drug effects raises problems in some cases. When rats are confronted with the test situation they may rely primarily on an algorithmic strategy. However, Dale (6) showed that while basically using an algorithmic strategy, animals also use other cues as demonstrated by a "task completion pause," indicating that subjects recognize that they have obtained all the rewards from the arms of the maze. Some authors prevented animals from developing an algorithmic strategy by confining them to the central platform between choices (4,13,16). In this case, animals may still use olfactory trails to orient on the maze (20).

It has been shown that several neurotransmitter systems are implicated in accomplishment of the task and that pharmacological effects vary with procedure used, strategy employed, and training levels (14,22-24). For example, when injected before the session into previously well trained rats, the cholinergic antagonist scopolamine impaired performance only if animals did not employ an algorithmic strategy, while in poorly trained animals it impaired performance whatever the strategy used, suggesting that scopolamine impairs spatial memory (22,24). On the other hand, the nonspecific catecholaminergic agonist amphetamine has been found by some investigators to impair radial maze performance but only when a delay is imposed midway through the session (2-4,7). However, the testing procedures used do not permit us to conclude, for example, whether these compounds act by interfering with the utilization of spatial information stored in working memory during the session or by disturbing algorithmic strategy use or the perception of olfactory trails. Moreover, very little spatial information could be used by rodents in the confinement procedure used in these tests, which generally consisted of bringing down a cylinder around them (5,13,17) so that animals could not use extramaze cues to orient during confinement.

The purpose of the present study was to clarify the action of scopolamine and amphetamine using an eight arm radial maze modified by one of us (P.R.) (20). With this apparatus, three procedures were used to dissociate the different strategies or cues used by mice to perform efficiently on the maze:

[1] To whom requests for reprints should be addressed.

a first procedure in which only spatial cues were available; a second where mice could use both spatial information and intramaze olfactory trails, and a third in which animals could develop algorithmic strategies in addition to using extra and intramaze cues.

METHOD

Subjects

Twenty-four male mice C57BL/6 JIco were used. This strain was used because these mice are able to perform well, using either algorithmic or spatial strategies (21). All mice were 7 weeks old on their arrival at the laboratory. They were individually housed in 24 × 11 × 18 cm disposable cages placed in a rearing room at constant temperature (23 1°C) with a reverse 12 L : 12 D cycle, the onset of the dark phase being at 1330 h. Sessions were run at the beginning of the scotophase, between 1400 and 1800 h. They started 10 days after the arrival of the mice at the laboratory.

Apparatus

The experimental apparatus (Fig. 1) consisted of an elevated maze with eight arms, each 32 cm long and 5 cm wide, radiating from a circular central platform 44 cm in diameter (formed by two concentric sections, a 20-cm center surrounded by a 12-cm ring). Each arm formed a corridor leading to an 8-cm square platform. A cup, 1-cm in diameter, embedded in each platform could contain a hidden 10-mg noodle reward.

The maze had been designed to allow a nondisturbing confinement procedure. The mice were placed on the 20-cm central platform at the beginning of the session for a 30-s period (Fig. 1A), after which the external ring was raised to the level of the platform, thus allowing unlimited access to all eight arms (Fig. 1B). In the confinement procedure, as soon as the mouse had entered one arm, it was confined by mechanically lowering the external ring of the platform (Fig. 1C). The ring supported the proximal parts of the arms which were, thus, lowered except for the arm in which the mouse was engaged. This arm was kept in position by an electromagnet until the mouse had returned to the central platform, then the arm dropped down. The mouse had, therefore, to stand at the very center of the maze on the now reduced platform (20 cm in diameter) for a 10-s period, during which it had unrestricted visual access to extramaze cues. At the end of the confinement period, the external ring and the arms were raised up again, allowing the mouse to enter the arms from a reenlarged platform; this operation was designed to prevent the mouse from using fixed angle turning strategies.

When an arms rotation procedure was used during the central confinement, a small motor located under the apparatus rotated the medial part of the arms between the central platform and the fixed distal platforms containing food (Fig. 1D). The degree of rotation could vary between 45° to 360°, with 45° intervals. This operation prevents the use of intramaze cues in the learning process.

The maze was placed in an air-conditioned room, surrounded by a 3.5-m high curtain, stained dark green on two adjacent sides and white on the other two, thus delimiting a 4 × 3 meter space which also contained the experimenter and the computer used for data recording. Four large black, white, or black and white striped patterns were hung, one on each of the four walls, to provide particularly salient visual spatial cues. Mice were progressively food deprived so that weight loss reached 15 to 20% of initial body weight by the start of testing.

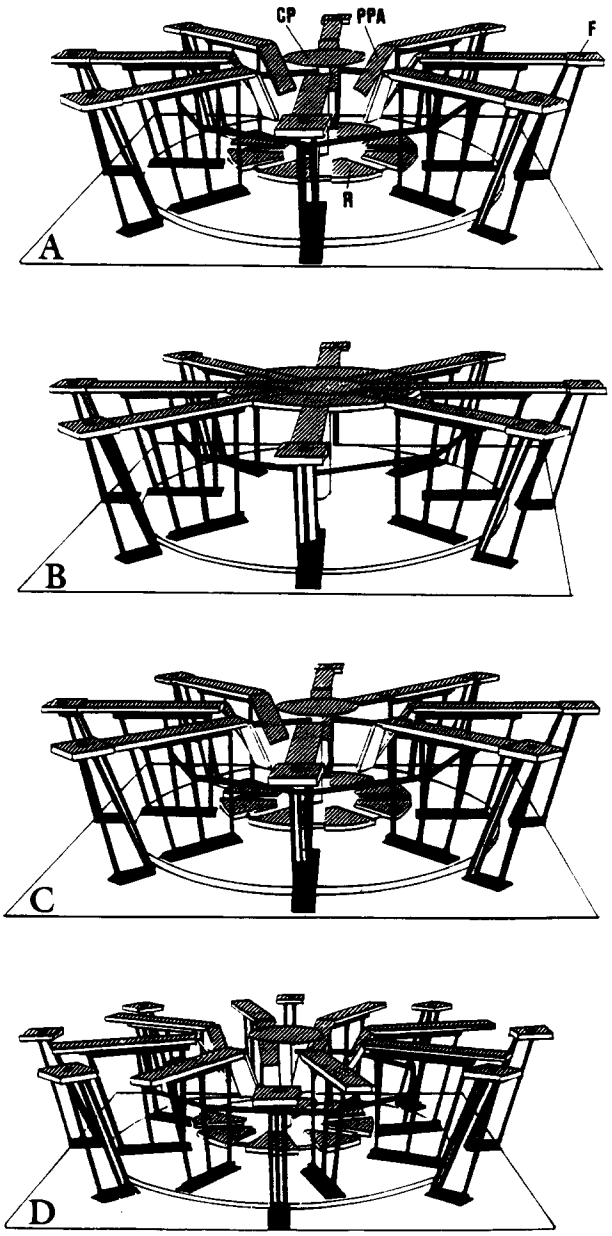

FIG. 1. Radial maze. (A) Confinement. (B) End of the confinement. (C) Visit of an arm and return to the central platform. (D) Rotation. F: Food, R: ring, CP: central platform, PPA: proximal part of the arms.

Protocol

Pretraining procedure. Mice were first given two pretraining sessions at 24-h intervals. They were placed in groups of four on the maze for 20 min per session and could freely explore the eight arms, which were provided with abundant food. Depending on the procedure that would subsequently

be used, mice were familiarized with the confinement procedure and with the rotation of the arms.

Training procedure. Following pretraining, mice were then given 10 training sessions, at 24-h intervals, to reach a good level of performance, i.e., three errors or less over 3 consecutive days (the probability that random performing will result in three errors or less over 3 consecutive days is less than 5%). At the beginning of each training session, a group of male mice were run on the maze to saturate it with mouse odor. After baiting the eight arms with a 10-mg noodle (the noodles were slightly boiled to overcome any swallowing difficulty in the animals treated with scopolamine), a mouse was placed on the central platform for 30 s before the ring was raised. The session ended when all eight arms had been explored, or when 16 choices had been made, with a maximum time of 20 min. The following parameters were recorded: the total number of errors (ERR1 to ERR10) and the rank of the first error (RFE1 to RFE10). If an animal made no error, it was ascribed a score of 9 as the rank of the first error. A radial index was computed as being the mean of the angles formed by successively chosen arms (RAD1 to RAD10). This parameter reflects the algorithm chosen by the mouse. For example, when the radial index is 45°, it means that the mouse always chose the adjacent arm. In addition, the mean time spent on each arm, computed as the total time spent on the maze divided by the number of entered arms, was recorded on drug days.

When each mouse had completed testing, the maze was quickly cleaned with tissue to remove fecal deposits and urine.

Three types of procedure were used in this experiment.

The nonconfinement procedure allowed the mouse to move freely about the maze during the training session (NC procedure, Fig. 1A, B). It was the least restrictive and permitted the use of odor trails as well as spatial cues or algorithmic strategies in performance of the task.

The confinement procedure with full (360°) rotation of the arms imposed on the mouse a 10-s period of confinement to the center after each choice (CFR procedure, Fig. 1A, B, C), thus disrupting the use of any algorithmic strategy. During confinement, the arms were rotated through 360° to control for any disturbing effect on performance caused by rotating the arms in partial rotation conditions.

The confinement procedure with partial rotation of the arms also imposed a confinement to the center for 10 s after each choice, but during confinement, the arms were partially rotated at random through 45°, 90°, or 135° (CPR procedure, Fig. 1A, B, C, D). Random rotation of the arms between trials prevented completion of the task via the use of odor trails.

Mice were randomly assigned to procedures, with eight mice in each.

Drug Treatment

On drug days (11th, 15th, 19th), 30 min prior to testing, the mice received intraperitoneal injections of saline for control, 1.5 mg/kg of scopolamine hydrobromide, or 1 mg/kg of *d*-amphetamine. Each mouse received each of the three treatments in a random order with 3 nondrug testing days occurring between each drug administration. Normal saline was used to dilute scopolamine and amphetamine, so that every drug was administered in 10 ml/kg body weight.

Data Analysis

Learning curves for the ERR, RFE, and RAD indices for training sessions 1 to 10 [ERR(1-10); RFE(1-10); RAD(1-10)] were analysed using a mixed ANOVA, with sessions as the repeated measures.

Scores on drug days were analysed using a two-way analysis of variance with repeated measures on the treatment factor. Additional post hoc analyses were carried out using a Newman-Keuls test. First the Newman-Keuls test was used to compare, in each procedure, scopolamine- and amphetamine-treated mice with controls. Second, it was used to compare, for each treatment, the three procedures (26).

Animals' scores on days prior to drug days (days 10, 14, and 17) were also analyzed using a two-way ANOVA with day as a repeated measures, to see if groups performances had changed in those periods.

RESULTS

Learning (Fig. 2)

Number of errors. Variance analysis demonstrated that the performance of the mice improved significantly on the radial maze over the ten training sessions [Err(1-10): $F(9, 189) = 16.05, p < 0.001$] and equally in all procedures, because there was no significant procedure × session interaction, $F(18, 189) = 1.53$, NS. The number of errors committed during the first session was near 6 while it was near 0 by the tenth session, but the type of experimental procedure affected mean performance, $F(2, 21) = 5.54, p < 0.012$, mice in the NC procedure making fewer errors than mice in the other procedures throughout training.

Rank of the first error. Variance analysis on the rank of the first error further confirmed that the mice had learned the task during the ten training sessions, whatever the experimental procedure employed. Rank of the first error significantly increased over sessions [RFE(1-10), $F(9, 189) = 14.79, p < 0.001$)], and there was no significant interaction between procedure and sessions, $F(18, 189) = 1.4$, NS. This index was also significantly affected by the type of experimental procedure, $F(2, 21) = 9.28, p < 0.012$, in the same way as number of errors.

Radial index. The experimental procedure also affected the mean value of the radial index, $F(2, 21) = 23.56, p < 0.001$, and the analysis revealed an interaction between procedure and sessions, $F(18, 189) = 2.182, p < 0.005$. Figure 2 shows that this index decreased only for the mice in the NC procedure. By the tenth session, the radial index for those mice was near 45°, indicating systematic use of the adjacent arm algorithm in this procedure. This was the only algorithm seen in mice in this study. By the 10th day, six out of eight mice tested with this procedure used the adjacent algorithm systematically.

Drug Days (Fig. 3)

Number of errors. Two-way analysis of variance demonstrated a significant treatment effect, $F(2, 42) = 24.39, p < 0.001$, but neither an experimental procedure effect, $F(2, 21) = 2.57$, NS, nor a procedure × treatment interaction, $F(4, 42) = 1.19$, NS.

Scopolamine effect: the Newman-Keuls tests showed that scopolamine increased the number of errors in the NC ($p < 0.01$) and CPR procedures ($p < 0.05$). In the CFR procedure this impairment was not significant.

Amphetamine effect: the Newman-Keuls test revealed no significant amphetamine effect whatever the experimental procedure employed.

Procedure effect: when we compared the three procedures

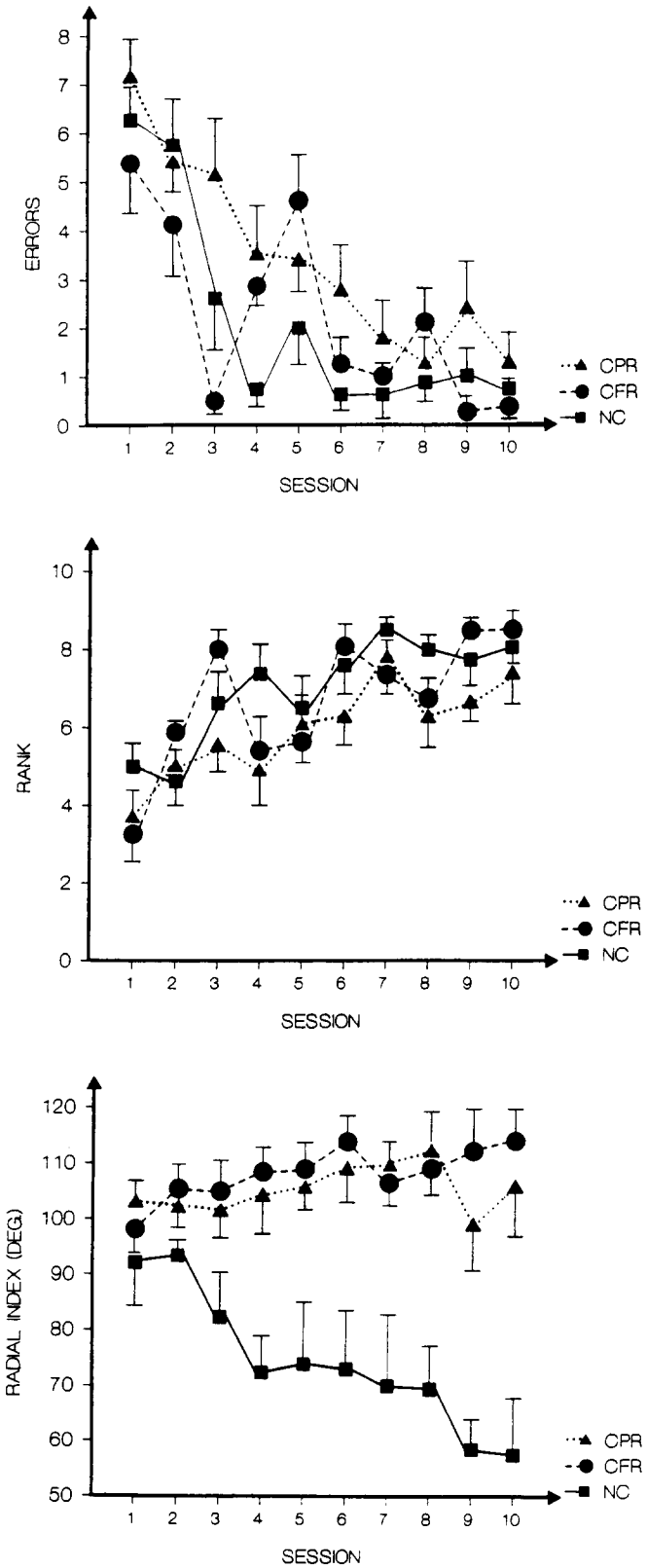

FIG. 2. Number of errors, rank of the first error, and radial index in each procedure during the training. Mean ± SEM. CPR: confinement with partial rotation, CFR: confinement with full rotation, NC: non confinement.

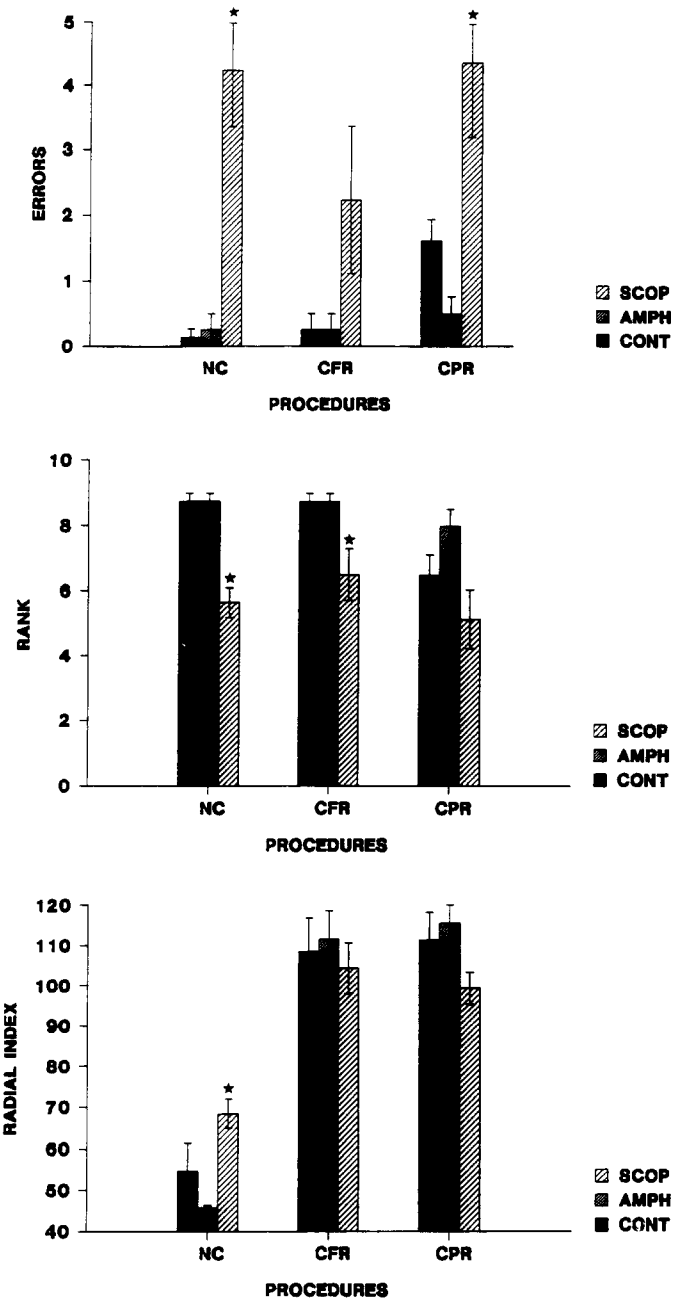

FIG. 3. Number of errors, rank of the first error and radial index according to treatment in each procedure. Mean ± SEM. CPR: confinement with partial rotation, CFR: confinement with full rotation, NC: nonconfinement, CONT: control, SCOP: scopolamine, AMPH: amphetamine. *Significant difference at $p = 0.05$ in a Newman-Keuls test.

within each treatment, the Newman-Keuls test showed that in controls, the CPR procedure significantly differed from the two others ($p < 0.01$), the number of errors in this procedure being greater than in the others. Within the scopolamine group, there were no differences between the three procedures, as scopolamine impaired performance in the same way whatever the procedure employed.

In the amphetamine group, too, the differences between procedures seen in control mice were absent. Indeed, amphetamine-treated mice perform well, regardless of the degree of difficulty inherent in the procedure.

Rank of the first error. A significant treatment effect, $F(2, 42) = 23.19, p < 0.001$, as well as an experimental procedure effect, $F(2, 21) = 5.60, p < 0.025$, were demonstrated by the two-way analysis of variance.

Scopolamine effect: the scopolamine effect was significant in the NC and CFR procedures (respectively, $p < 0.01$ and $p < 0.05$, Newman-Keuls test), the drug increasing the rank of the first error.

Amphetamine effect: the Newman-Keuls test revealed no significant effects within each experimental procedure.

Procedure effect: in the control group, the Newman-Keuls test showed that the CPR procedure significantly differed from the two others ($p < 0.01$). Mice in this procedure made their errors sooner than mice in the other procedures, further suggesting that the CPR procedure was more difficult than the other two. However, in the amphetamine and scopolamine groups there were no significant differences among these three procedures.

Radial index. Statistical analysis demonstrated a significant procedure effect, $F(2, 21) = 67.5, p < 0.001$, and a significant procedure × treatment interaction, $F(4, 42) = 3.5, p < 0.05$.

Scopolamine effect: the Newman-Keuls test revealed a significant scopolamine effect only in the NC procedure ($p < 0.05$). Scopolamine disrupted the algorithmic strategy used by mice in the NC procedure, in which mice had a radial index near to 45° after 10 sessions. The choice sequences were composed of adjacent algorithmics choices (three to five visits) interspersed with random visits. This effect has no parallel in the procedure with confinement because in this case, the radial index was not steady (near 110° for controls).

Amphetamine effect: no significant effects were revealed by the comparison between control and amphetamine groups in each procedure (see Fig. 1).

Procedure effect: within each treatment the Newman-Keuls test showed that the NC procedure differs from the other two ($p < 0.01$). In this procedure, mice adopted an algorithmic strategy. Although scopolamine impaired this index in the NC procedure the differences between this procedure and the two others were found again.

Mean time passed on each arms. Significant procedure, $F(2, 21) = 15.78, p < 0.001$, and treatment effects, $F(2, 42) = 16.17, p < 0.01$, were revealed by the analysis. In each procedure, the mean values in seconds for control, amphetamine, and scopolamine groups were respectively: 3.37, 5.40, 15.32 for the NC procedure; 28.61, 17.7, 33.6, for the CFR; 32.28, 16.49, 28.24 for the CPR.

Scopolamine effect: in the NC procedure, scopolamine significantly increased the mean time passed on each arm ($p < 0.01$, Newman-Keuls).

Amphetamine effect: there was a significant decrease in time passed on each arm in the CFR procedure ($p < 0.05$, Newman-Keuls). These results are not surprising because amphetamine is known to increase locomotion.

Procedure effect: within each treatment, the Newman-Keuls test showed a significant difference between the NC procedure and the two others (respectively, $p < 0.05$ for the CPR procedure in the scopolamine group and $p < 0.01$ for the other cases). Concerning performance on days prior to drug days (Table 1), the last analysis showed that there was no days effects, $F(2, 42) = 0.825$, NS, nor procedures effects, $F(2, 21) = 0.987$, NS, nor days × procedures interaction, $F(4, 42) = 0.987$, NS, on the number of errors. The analysis showed a procedure effect only for the radial index. So during the testing days between drug injections, the mice maintained the same level of performance as before drug treatments began.

DISCUSSION

The present results reinforced those of other authors (1,17,21), showing that C57BL/6 mice are able to solve a radial maze task. Animals quickly reach a good level of performance. In the NC procedure, by the 6th day, the mice were committing very few errors, though this was due largely to their adopting an algorithmic strategy. In the CFR procedure

TABLE 1

PERFORMANCES ON DAYS 10, 14, 18 (BEFORE THE DRUG DAYS) IN EACH PROCEDURE AND RESULTS OF THE ANALYSIS OF VARIANCE

	ERR			RFE			RAD		
	J10	J14	J18	J10	J14	J18	J10	J14	J18
NC	1.93	0.50	0.62	8.12	8.75	8.75	58.22	51.41	47.31
	1.39	1.41	1.77	1.25	0.71	0.71	29.22	12.41	6.52
CFR	0.37	0.25	0.37	8.50	8.50	8.37	114.36	107.77	105.19
	0.74	0.46	0.74	0.93	0.93	1.19	19.22	10.63	23.64
CPR	1.25	1.37	0.12	7.00	7.62	8.25	107.27	117.00	113.06
	1.83	1.68	0.35	2.45	1.19	2.12	24.61	12.30	23.12
Days effect	$F(2, 42) = 0.825$			$F(2, 42) = 1.462$			$F(2, 42) = 0.369$		
	$p = 0.445$			$p = 0.243$			$p = 0.694$		
Proc effect	$F(2, 21) = 0.987$			$F(2, 21) = 2.127$			$F(2, 21) = 82.674$		
	$p = 0.389$			$p = 0.144$			$p = 0.000$		
Days × proc effect	$F(4, 42) = 0.987$			$F(4, 42) = 0.689$			$F(4, 42) = 0.586$		
	$p = 0.425$			$p = 0.604$			$p = 0.674$		

Lower values: mean. Upper values: standard error.

also, where mice could use both spatial information and olfactory intramaze trails but not an algorithmic strategy, a good level of performance was quickly reached. On the other hand, the CPR procedure seems to be the most difficult because mice needed more sessions to reach the same level of performance as in the other procedures. One may note that in this procedure learning is most likely to be primarily based on the utilization of spatial cues stored in working memory. However, in NC and CFR procedures, mice are likely to partially use spatial information to the extent that a modification of extramaze cue position in well-trained C57BL/6 mice induces an impairment of performance (20).

Effects of Scopolamine

Our results show that scopolamine impairs mouse performance in all of the three procedures used. This is not due to an anorexic effect because the dose used here has been found previously not to affect the quantity of food eaten (Beuzen and Belzung, unpublished results).

Our results agree with those obtained by Eckermann (7) in the rat but disagree with other results that show a scopolamine effect only when animals have adopted a spatial strategy and not when they employ algorithmic patterns (1,22,24). This discrepancy might be explained by differences in testing paradigm used, some apparatus not enabling the use of extramaze cues during confinement while our apparatus does. For example, Amassari-Teule and Caprioli (1) who used C57BL/6 as we did, utilized an apparatus in which the extramaze cues available to animals were minimized so that they could not use distal information for orientation. In this case, no scopolamine effect was found. Moreover, it is to be noticed that during the elaboration of an algorithmic strategy animals first employ extramaze cues (8), perhaps explaining why scopolamine impairs performance in poorly trained animals. This may apply to the present animals. Consequently, after scopolamine injection, our mouse performances may have been impaired because spatial cues continued to be available to them in all procedures. This would support Poucet and Buhot's (18) view that scopolamine specifically impairs distal cue processing (22,24).

Many different interpretations exist concerning scopolamine's effects in a radial maze. Our results are consistent with some, but disagree with others such as the hypothesis of an effect on attention and/or arousal (9,14) or a specific alteration in the accomplishment of complex tasks calling for a high level of attention (21), or the hypothesis concerning an impairment of information processing in working memory (11,22,24,27). Indeed, working memory (that is, a system of flexible stimulus response associations which changes from trial) and attention are not involved equally in each of the three procedures used here. Performing in the CPR procedure requires the memorization of arms already visited, thus placing a heavier load on working memory and involving attentional processes to a greater degree than in the other two procedures. So, our results suggest that scopolamine may have a more global effect than previously assumed.

Finally, our results agree with the hypothesis holding that anticholinergic drugs exert their major effects on the rodent's capacity to access information related to situations already experienced or strategies already learned (25). Scopolamine-induced perturbation of the radial index supports this hypothesis.

It is premature to speculate which of these various interpretations, if any, is primary because these different views are not mutually exclusive. Moreover, it is also possible that no single interpretation can be proposed for scopolamine's effects in the three procedures or that the compound's action is due to nonspecific processes. This is not surprising because, as acethylcholine is an excitatory transmitter found in cerebral cortex, thalamus, olfactory bulbs, septum and hippocampus, it can act on different processes including for example, the utilization of olfactory trails and place learning.

Effects of Amphetamine

Our results show that in NC and CFR procedures amphetamine injections did not modify the performance of the mice. Our lack of an effect in a confinement procedure is not consistent with results obtained by others (2,4,7) who found an impairment in performance after amphetamine injection. This discrepancy may be explained by differences in the experimental apparatus used. Previous authors used procedures in which animals were confined to their home cage between two series of arm choices, for time intervals ranging from 5 min to several hours. Animals treated with amphetamine generally had a higher level of arousal and, therefore, became sensitive to interference (2). Consequently, they may have missed pertinent information from the maze and, therefore, shown an impaired performance. In our procedure, mice remained on the maze during a short confinement period and with no other stimuli interfering with the information necessary to complete the task. Amphetamine injections did not cause impairment in performance in our confinement procedure.

On the other hand, animals of the control group made more errors in the CPR procedure compared with the other procedures (CFR and NC) while in the amphetamine-treated mice the number of error is equal whatever the procedure. We suggest that this drug may assist performance when the experimental procedure poses greater difficulties.

This improvement after amphetamine injection cannot be due to an increase in food motivation because in a preliminary experiment we found an anorexic effect of the compound at the dose used here (unpublished data).

Paradoxically, an increase in attention to spatial room cues after amphetamine injection may explain the improvement of mouse performance seen here. The CPR procedure seems to be more difficult than the two others, because to perform efficiently, mice need to remember which arms have already been visited without using kinesthetic or olfactory cues. So, unlike the confinement procedure classically used in psychopharmacology, where mice might pay attention to nonpertinent stimuli during the interval period in the home cage, it might be supposed that, in our maze, animals treated with amphetamine took greater advantage of the confinement period to deal with information from the environment.

GENERAL CONCLUSION

The utilization of this new radial maze designed to dissociate different cues and strategies available to mice (spatial information, odor trails, or elaboration of an algorithmic strategy) allowed us to investigate drug effects on spatial working memory. Scopolamine did not appear to act specifically, and appears to have a global effect on various aspects of radial maze performance. That amphetamine can sustain performance when animals are forced to use spatial cues suggests that it may sometimes enhance radial maze performance via the enhancement of attention.

REFERENCES

1. Amassari-Teule, M.; Caprioli, A. Spatial learning and memory, maze running strategies and cholinergic mechanisms in two inbred strains of mice. Behav. Brain Res. 17:9–16; 1985.
2. Beatty, W.; Bierley, R. A.; Boyd, J. Amphetamine disrupts both working and reference memories of rats trained in a radial maze. Behav. Neural Biol. 42:169–176; 1984.
3. Beatty, W.; Bierley, R. A. Scopolamine degrades spatial working memory but spares spatial reference memory: Dissimilarity of anticholinergic effect and restriction of visual cues. Pharmacol. Biochem. Behav. 23:1–6; 1985.
4. Buresova, O.; Bures, J. Radial arm maze as a tool for assessing the effects of drugs on working memory of rats. Psychopharmacology (Berlin) 77:268–271; 1982.
5. Crusio, W.; Schwegler, H.; Lipp, H. P. Radial maze performance and structural variation of the hippocampus in mice: A correlation with mossy fibre distribution. Brain Res. 425:182–185; 1987.
6. Dale, R. H. I. Spatial and temporal response patterns on the eight-arm radial maze. Physiol. Behav. 36:787–790; 1986.
7. Eckerman, D. A.; Gordon, W. A.; Edwards, J. D.; Mac Phail, R. C.; Gage, M. I. Effect of scopolamine, pentobarbital and amphetamine on radial arm maze performance in the rat. Pharmacol. Biochem. Behav. 12:595–602; 1980.
8. Foreman, N. Algorithmic responding on the radial maze in rats does not always imply absence of spatial encoding. Q. J. Exp. Psychol. 37B:333–358; 1985.
9. Godding, P. R.; Rush, J. R.; Beatty, W. Scopolamine does not disrupt spatial working memory in rats. Pharmacol. Biochem. Behav. 16:919–923; 1981.
10. Jarrard, L. E.; Kant, G. J.; Meyerhoff, J. L.; Levy, A. Behavioral and neurochemical effects of intraventricular AF64A administration in rats. Pharmacol. Biochem. Behav. 21:273–280; 1984.
11. Levy, A.; Kluge, P. B.; Elsemore, T. F. Radial arm maze performance of mice: Acquisition and atropine effects. Behav. Neural Biol. 39:229–240; 1983.
12. Magnami, M.; Pozzi, O.; Biagetti, R.; Banfi, S.; Dorigotti, L. Oxiracetam antagonizes the disruptive effects of scopolamine on memory in the radial maze. Psychopharmacology (Berlin) 106: 175–178; 1992.
13. Mizumori, S. J. Y.; Rosenzweig, M. R.; Kermisch, M. G. Failure of mice to demonstrate spatial working memory in the radial maze. Behav. Neural Biol. 35:33–45; 1982.
14. Okaichi, H.; Jarrard, L. E. Scopolamine impairs performance of a place and a cue task in rats. Behav. Neural Biol. 35:319–325; 1982.
15. Olton, D. S.; Samuelson, R. J. Remembrance of places passed: Spatial memory in rats. J. Exp. Psychol. 2:97–116; 1976.
16. Olton, D. S.; Papas, B. C. Spatial memory and hippocampal function. Neuropsychologia 17:669–682; 1979.
17. Pico, R. M.; Davis, J. L. The radial maze performance of mice: Assessing the dimensional requirements for serial order memory in animals. Behav. Neural Biol. 40:5–26; 1984.
18. Poucet, B.; Buhot, C. Scopolamine impairs response-to-change based on distal cues in the rat. Physiol. Behav. 46:335–359; 1989.
19. Roullet, P.; Lassalle, J. M. Behavioural strategies, sensorial processes and hippocampal mossy fibre distribution in radial maze performance in mice. Behav. Brain Res. 48:77–85; 1992.
20. Roullet, P.; Lassalle, J. M.; Jegat, R. A study of behavioral and sensorial bases of radial maze learning in mice. Behav. Neural Biol. 59:173–179; 1993.
21. Soffié, M.; Lamberty, Y. Scopolamine disrupts visual reversal without affecting the first discrimination. Physiol. Behav. 40: 263–265; 1987.
22. Stevens, R. Scopolamine impairs spatial maze performance in rats. Physiol. Behav. 27:385–386; 1981.
23. Walsh, T. J.; Tilson, H. A.; DeHaven, D. L.; Mailman, R. B.; Fisher, A.; Hanin, I. AF64A, a cholinergic neurotoxine, selectively depletes acethylcholine in the hippocampus and cortex and produces long-term passive avoidance and radial arm maze deficit. Brain Res. 321:91–102; 1984.
24. Watts, J.; Stevens, R.; Robinson, C. Effects of scopolamine on radial maze performance in rat. Physiol. Behav. 26:845–851; 1981.
25. Whishaw, I. Q. Dissociating performance and learning deficits on spatial navigation tasks in rats subjected to cholinergic muscarinic blockade. Brain Res. Bull. 23:347–358; 1989.
26. Winer, B. J. Statistical principles in experimental design, 2nd ed. New York: McGraw-Hill Book Company; 1971.
27. Wirsching, B. A.; Beninger, R. J.; Jhamandas, K.; Boegman, R. J.; El-Defrawy, S. R. Differential effects of scopolamine on working and reference memory of rats in the radial maze. Pharmacol. Biochem. Behav. 20:659–662; 1984.